Assessment of Arm Lean Mass, Fat Mass, and Bone Mineral Density in Breast Cancer Survivors Without Lymphedema

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OBJECTIVES: To compare lean mass, fat mass, and bone mineral density (BMD) in the affected arm (the arm on the side where breast cancer was present) and unaffected arm of breast cancer survivors without lymphedema.

SAMPLE & SETTING: 38 breast cancer survivors who had completed primary treatment were included in this analysis at a university in Florida.

METHODS & VARIABLES: Arm lean mass, fat mass, and BMD were obtained using dual-energy x-ray absorptiometry. Paired t tests were used to compare tissue composition and BMD between the affected and unaffected arm. Independent t tests were used to compare interlimb differences between those participants whose affected arm was on the dominant and those whose affected arm was on the nondominant side. Significance was accepted at $p \leq 0.05$.

RESULTS: The affected arm had lower fat mass and BMD as compared to the unaffected arm. Differences in lean mass were not statistically significant ($p = 0.06$). In breast cancer survivors whose nondominant arm was affected, lean mass, fat mass, and BMD were significantly lower in the affected arm.

IMPLICATIONS FOR NURSING: The results show that the affected arm of breast cancer survivors is susceptible to negative tissue and BMD changes. This highlights the importance of educating individuals with breast cancer about these changes and supports the benefits of upper body resistance training.

Breast cancer survivors experience long-term treatment-related side effects, including negative changes in body composition and bone density. Chemotherapy has been associated with losses in lean mass and bone mineral density (BMD) and gains in fat mass in breast cancer survivors (Vance et al., 2011; Vehmanen et al., 2014). Aromatase inhibitors, which are commonly prescribed after completion of treatment with chemotherapy, are also associated with lower BMD and increased fracture risk (Kwan et al., 2018; Tseng et al., 2018). Other treatment-related side effects, such as fatigue, pain, and lymphedema concerns, serve as barriers to exercise (Browall et al., 2018), and physical activity levels have been found to decline in breast cancer survivors following treatment (Sabiston et al., 2014). These lower physical activity levels may further contribute to the negative body composition and BMD changes experienced by breast cancer survivors.

Treatments for breast cancer can also result in functional impairments in the affected arm (i.e., the arm on the side where breast cancer was present). Surgery, lymph node dissection, and/or radiation therapy can lead to arm and shoulder impairments, including limited range of motion, weakness, pain, and lymphedema (Hidding et al., 2014). Despite research supporting the benefits and safety of upper body resistance exercise, many breast cancer survivors avoid strenuous arm activity because of inaccurate arm care advice, fear of lymphedema, and self-efficacy regarding arm exercise (Lee et al., 2009).

The body composition and BMD changes that can occur from breast cancer treatments, combined with functional impairments and decreased arm activity, may increase susceptibility of the affected arm for accelerated gains in fat mass and losses in lean mass and BMD. In contrast, previous studies using dual-energy x-ray absorptiometry (DXA) have

reported higher lean mass and fat mass in the affected arm as compared to the unaffected arm, with mixed evidence regarding bone density in breast cancer survivors with lymphedema (Brorson et al., 2009; Zhang et al., 2017). Brorson et al. (2009) hypothesized that mechanical stress from excess arm weight because of lymphedema may promote increased muscle and bone mass. However, Dylke et al. (2013) suggested that higher lean mass in the affected arm may be evidence of an increase in fibrotic tissue—not muscle mass—as lean mass assessed by DXA comprises all soft tissues, including fibrotic and connective tissues. This finding is supported by Borri et al. (2017), who found no difference in bilateral arm muscle mass assessed via MRI in breast cancer survivors. In addition, these previous studies all focused on breast cancer survivors with lymphedema (Borri et al., 2017; Brorson et al., 2009; Dylke et al., 2013; Zhang et al., 2017).

Because lymphedema can alter arm tissue composition and lead to increased fibrosis (Azhar et al., 2020), more research is needed to examine arm tissue composition and BMD in breast cancer survivors without lymphedema. Therefore, the purpose of this study was to compare lean mass, fat mass, and BMD in the affected and unaffected arms of breast cancer survivors without lymphedema. These measures were also evaluated regarding affected arm dominance to determine whether the affected arm would have lower lean mass and BMD and higher fat mass than the unaffected arm and whether interlimb differences would be higher in breast cancer survivors whose affected arm was on the nondominant side.

Methods

This analysis was conducted using baseline data from an intervention study that examined the effects of functional impact training on body composition in breast cancer survivors (Artese et al., 2021). Three additional breast cancer survivors who participated in a pilot study were also included. Participants were postmenopausal, sedentary (defined as participating in aerobic or yoga training no more than one day per week and not participating in a resistance training program) breast cancer survivors who were two or more months postsurgery or three or more months post-treatment with radiation therapy or chemotherapy. Breast cancer survivors who were currently receiving primary treatment (surgery, chemotherapy, or radiation therapy), exercising regularly, or taking medications affecting muscle or fat metabolism, or those who had uncontrolled hypo- or hyperthyroidism, hypertension, diabetes, or heart disease were

excluded. Women with stage IV breast cancer were excluded because of the cancer affecting other sites beyond the breast, which may have affected body composition and BMD differently than those individuals with nonmetastatic cancer. Participants were also excluded from this analysis if they had cancer in both breasts, had an interlimb arm volume difference of 10% or higher, and/or indicated on a researcher-developed questionnaire that they had previously experienced arm swelling. The Florida State University Institutional Review Board approved the study.

Testing for lean mass, fat mass, and BMD was completed in an exercise physiology research laboratory, and all measurements were assessed by the same researcher. Following informed consent, participants completed a health/cancer history questionnaire that included questions regarding cancer stage, treatment, treatment-related issues, and overall health. After completing the questionnaire, participants' height and weight were measured. Body composition and BMD were assessed using a total body DXA scan (Lunar iDXA) from an anteroposterior view, with the participants in a supine position. Arm measurements for lean mass, fat mass, and BMD were also obtained from this scan. Arm circumference measurements were assessed using a Gulick tape measure. Measurements began at the styloid process of the ulna and were taken in 3 cm increments along the arm for 45 cm. Total arm volume was determined by summing the volumes of each arm segment, which were calculated using the formula for the volume of a truncated cone (Sander et al., 2002).

Statistical Analysis

Descriptive statistics were calculated for all variables and included means, standard deviations, and ranges, as well as frequency values for cancer stage and treatment type. The associations between body weight and arm lean mass, fat mass, and BMD were determined using Pearson's correlations. Partial correlations were used to assess the relationship between arm measures and age, time since diagnosis, and time since treatment completion, while controlling for body weight. Paired t tests were used to determine differences in arm tissue composition and BMD between the affected arm and the unaffected arm in all participants, in breast cancer survivors whose dominant arm was affected, and in breast cancer survivors whose nondominant arm was affected. To examine the effects of arm dominance, independent t tests were used to compare interlimb differences among participants whose affected arm

was on the dominant or nondominant side. Data were analyzed using IBM SPSS Statistics, version 26.0. Significance was accepted at $p \leq 0.05$.

Results

Of the 48 participants who consented to participate, 38 were included in the final analysis. Ten participants were excluded because they reported previous arm swelling (n = 6), had breast cancer on both sides (n = 3), or did not attend testing (n = 1). The mean age of participants was 61.7 years (SD = 7.8), and the mean time since diagnosis was 9.2 years (SD = 7.8). Participant characteristics are presented in Table 1.

There were no associations between age, time since diagnosis, or time since treatment completion and the measures for volume, tissue composition, or BMD in either arm. Body weight and interlimb differences had no relation to age, time since diagnosis, or treatment completion. Participants with higher body weight had higher overall arm volume (r = 0.81), lean mass (r = 0.74), fat mass (r = 0.87), and BMD (r = 0.64). Affected and unaffected arm volumes did not differ. Fat mass and BMD were significantly lower in the affected arm than in the unaffected arm. Differences in lean mass were approaching significance (p = 0.06), with lower values in the affected

TABLE 1. Sample Characteristics (N = 38)			
Characteristic	**X̄**	**SD**	**Range**
Age (years)	61.7	7.8	43–77
Weight (kg)	76.7	13.1	49.2–110.3
Body mass index (kg/m^2)	28.7	4.5	17.8–36.7
Time since diagnosis (years)	9.2	7.8	0.4–30.3
Time since treatment completion (years)	8.1	8	0.2–30.3
Body fat (%)	44	6.8	17.5–51.2
Total lean mass (kg)	40.77	5.58	30.77–57.45
Total fat mass (kg)	32.94	8.7	8.28–51.92
Total bone mineral density (g/cm^2)	1.063	0.108	0.843–1.351
Arm lean mass (kg)	4.33	0.96	2.69–7.45
Arm fat mass (kg)	3.39	1.12	1.13–6.8
Arm bone mineral density (g/cm^2)	0.661	0.085	0.493–0.843
Characteristic			**n**
Cancer stage			
Stage 0			4
Stage I			16
Stage II			11
Stage III			6
Unknown			1
Cancer treatment[a]			**n**
Surgery			38
Chemotherapy			19
Radiation therapy			21
Hormone therapy[b]			21
[a] Participants were able to select more than 1 option. [b] 12 participants were currently receiving hormone therapy.			

TABLE 2. Affected and Unaffected Arm Tissue Composition and Bone Mineral Density

Variable	Unaffected Arm		Affected Arm		Interlimb Difference	
	$\bar{X}$	SD	$\bar{X}$	SD	$\bar{X}$	SD
All participants (N = 38)						
Arm volume (ml)	2,385	479	2,374	494	11	102
Arm lean mass (g)	2,202	511	2,132	476**	70	225
Arm fat mass (g)	1,753	599	1,607	500*	146	276
Arm bone mineral density (g/cm^2)	0.668	0.091	0.654	0.085*	0.014	0.043
Dominant side affected (N = 20)						
Arm lean mass (g)	2,097	441	2,098	442	–1	197***
Arm fat mass (g)	1,662	582	1,625	563	37	175***
Arm bone mineral density (g/cm^2)	0.641	0.084	0.643	0.078	–0.002	0.023***
Nondominant side affected (N = 18)						
Arm lean mass (g)	2,319	569	2,171	522*	148	234
Arm fat mass (g)	1,856	619	1,588	436*	267	319
Arm bone mineral density (g/cm^2)	0.699	0.090	0.667	0.092*	0.032	0.053

*$p \leq 0.05$, significantly different from the unaffected arm
**$p = 0.06$, approaching significance; different from the unaffected arm
***$p \leq 0.05$, significantly different between the dominant side affected and nondominant side affected groups in interlimb difference measures
Note. Interlimb difference was calculated by subtracting affected arm measures from unaffected arm measures.

arm. The dominant arm and the nondominant arm were affected in 20 and 18 participants, respectively. There were no differences in any measures between arms in participants whose dominant arm was affected. In breast cancer survivors whose nondominant arm was affected, lean mass, fat mass, and BMD were significantly lower in the affected arm as compared to the unaffected arm. Results from the independent t tests indicated that calculated interlimb differences (unaffected minus affected) for lean mass, fat mass, and BMD were significantly higher in participants whose affected arm was on the nondominant side as compared to those whose dominant arm was affected (see Table 2).

Discussion

The results of this study support the hypothesis that the affected arm would have lower lean mass and BMD but do not support the hypothesis that fat mass would be higher in the affected arm. These results differ from previous studies, which have reported increased lean mass and fat mass in the affected arm of breast cancer survivors with lymphedema (Brorson et al., 2009; Zhang et al., 2017). Although Zhang et al. (2017) similarly reported lower BMD in the affected arm as compared to the unaffected arm, the interlimb difference was greater in participants in the current study. Therefore, the current study's results suggest that, in the absence of lymphedema, the affected arm is more susceptible to losses in lean mass, fat mass, and BMD. This is further supported by the results of the analysis of affected arm dominance. The dominant arm of healthy women has been found to have higher lean mass and BMD than the nondominant arm (Coin et al., 2012). In the current study, the lack of difference in lean mass and BMD between the arms of participants whose dominant arm was affected may indicate accelerated losses in lean mass and BMD in the affected dominant arm. In addition, the interlimb difference in lean mass in breast cancer survivors whose affected arm was on the nondominant side was slightly higher than what

was reported in healthy women (Coin et al., 2012), suggesting greater losses in lean mass in the non-dominant arm when it is affected by breast cancer. These losses are likely attributed to decreased use of the affected arm, and therefore less overload and mechanical strain, which may ultimately make the affected arm further susceptible to functional limitations and fractures.

Regardless of dominance, fat mass was not higher in the affected arm of participants in the current study. The reasons for this are unknown because disuse of the affected arm would most likely favor increased fat, as Zhang et al. (2017) reported decreased fat mass following arm resistance training in breast cancer survivors with lymphedema. Although lower fat mass is generally a desirable outcome, reduced fat in the affected arm in breast cancer survivors who are not experiencing lymphedema may also be an unfavorable outcome because lower fat mass is associated with increased fracture risk (Moayyeri et al., 2012).

Arm volume, lean mass, fat mass, and BMD were positively correlated with total body weight. This most likely explains why the measurements for arm volume, lean mass, fat mass, and BMD for both the affected and unaffected arm were lower than previously reported measures in breast cancer survivors who had a higher body mass index than the participants in the current study's sample (Zhang et al., 2017). After controlling for body weight, affected and unaffected arm volume, lean mass, fat mass, and BMD were not found to be related to age, time since diagnosis, or time since treatment completion. Interlimb difference was also not associated with age and time since diagnosis or treatment completion. This suggests that treatment-related losses in lean mass, fat mass, and BMD in the affected arm may persist over time and do not improve as breast cancer survivors move further out from treatment.

Strengths of the study include the use of DXA, the consideration of affected arm dominance in the analysis, and this being the first study to assess arm tissue and bone density in breast cancer survivors without lymphedema. Limitations include the inclusion of only postmenopausal breast cancer survivors, the small sample size, and the determination of lymphedema by self-reported arm swelling or arm circumference measurements. Because the study participants were postmenopausal, the results may not be applicable to premenopausal breast cancer survivors. In addition, specific information regarding lymphedema diagnosis was not obtained. Including premenopausal breast cancer survivors, a larger

KNOWLEDGE TRANSLATION

- For breast cancer survivors who are not presenting signs and symptoms of lymphedema, the affected arm is at risk for losses in lean mass, fat mass, and bone mineral density, which could result in further strength and functional impairments and increased fracture risk in the affected arm.
- Nurses should promote the benefits and safety of upper body resistance training in breast cancer survivors to prevent negative changes in arm tissue composition and bone mineral density.
- Future research is needed to determine the optimal resistance training mode, frequency, intensity, and timing needed to prevent losses and improve tissue composition and bone mineral density, particularly in the affected arm.

sample size, and specific criteria for confirming the absence or presence of lymphedema would be beneficial in future studies.

Implications for Nursing

The results of this study highlight the importance of educating individuals with breast cancer about potential negative tissue and BMD changes that can occur in the affected arm, as well as how those changes may affect future function and fracture risk. Although unfavorable arm tissue changes are associated with lymphedema, this study demonstrated that breast cancer survivors without lymphedema may also be at risk for changes associated with losses in lean mass, fat mass, and BMD in the affected arm. Therefore, nurses should promote the benefits of and guidelines for resistance training provided by the National Cancer Comprehensive Network (2020) to help prevent these losses. In addition, nurses can refer individuals to a trained exercise specialist to ensure appropriate quality care and safe upper body exercise guidance.

Conclusion

To the authors' knowledge, this is the first study to investigate arm tissue and BMD in breast cancer survivors without lymphedema. The results of this study indicate that, in breast cancer survivors without lymphedema, the affected arm is susceptible to negative tissue and BMD changes. Therefore, future efforts should be directed toward educating individuals with breast cancer about the benefits and safety of upper body resistance training. In addition, more research is needed to determine optimal upper body exercise programs designed to prevent losses in muscle mass and BMD.

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