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Risk Factors Associated with Breast Cancer-Related Lymphedema in the WHEL Study

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Abstract

Introduction—Lymphedema is a significant health problem faced by a large percentage of breast cancer survivors. The Women's Healthy Eating and Living (WHEL) Study has a unique data set collected after the completion of breast cancer treatment, which allowed a focused analysis of risk factors for breast cancer-related lymphedema.

Methods—Participant characteristics, treatment modalities, and health behaviors were examined as potential predictors of lymphedema among breast cancer survivors with univariate analyses and multivariate logistic regression.

Results—Lymphedema status was assessed for 83% of the study cohort (2431 of the 2917 WHEL participants). Among these respondents, 692 (28.5%) women reported yes to either a physician's diagnosis of lymphedema or a question on arm/hand swelling. When compared to other participants, women with lymphedema were diagnosed at a younger age, more likely to have a higher body mass index, had a larger tumor size, had more lymph nodes removed, more likely to have a mastectomy with radiation therapy, and more likely to have chemotherapy. In the final multivariate-adjusted model, body mass index greater than 25 kg/m² ($p < 0.01$), the removal of 11 or more lymph nodes ($p < 0.01$), and breast cancer surgery plus radiation therapy ($p < 0.01$) showed a strong independent association with developing breast cancer-related lymphedema.

Conclusions—The results of this study highlight the importance of educating breast cancer survivors about the modifiable risk factors (e.g., body mass index) associated with the development of lymphedema.

Implications for Cancer Survivors—Breast cancer survivors at risk for lymphedema may benefit from interventions aimed at achieving or maintaining a healthy body weight.

Keywords

Breast cancer survivors; Lymphedema; Risk factors; Body mass index; Lymph node removal; Breast cancer treatment

INTRODUCTION

Over 2.6 million women are estimated to be breast cancer survivors in the United States [1]. One difficulty facing breast cancer survivors is the risk of secondary lymphedema of the ipsilateral arm/hand. Breast cancer-related lymphedema can occur months or years after

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CONFLICT OF INTEREST

All authors declare no conflicts of interest.

breast cancer treatment (e.g., surgery, radiation) and is estimated to affect approximately 6 to 30% of women who receive such treatment [2]. Erickson and colleagues' (2001) review reports the overall incidence of arm edema in breast cancer survivors as 26% (with a range of 0 to 56%) [3]. One of the main risk factors for breast cancer-related lymphedema is lymph node removal [3–6]. In the past decade, the incidence of breast cancer-related lymphedema has decreased with the use of sentinel lymph node biopsy (SLNB); however, lymphedema is still a considerable problem [7–9]. McLaughlin and colleagues (2008) reported that the development of lymphedema occurred among 5% of the 600 patients who underwent SLNB alone [8]. Among older breast cancer survivors, Yen and colleagues (2009) found that lymphedema developed in 5.7% of women who had no axillary surgery, 7% who underwent SLNB, and 21% who underwent axillary lymph node dissection (ALND) [7]. These studies indicate that while lymph node removal is a key risk factor, it is not the only risk factor for breast cancer-related lymphedema. Other potential risk factors include tumor stage, radiation therapy, chemotherapy, infections, injury, body weight, age, inflammation, and poor hygiene [6, 8, 10–15]. While breast cancer treatment-related risk factors for lymphedema may be unavoidable, other risk factors may be modifiable.

The main objective of this study was to examine participant baseline characteristics (e.g., age, body mass index, treatment type, and level of physical activity) as potential predictors of lymphedema among early stage breast cancer survivors enrolled in the Women's Healthy Eating and Living (WHEL) Study. The WHEL Study's unique data set was collected after the completion of breast cancer treatment and allows focused analyses of a variety of topics relating to breast cancer survivorship, including lymphedema.

METHODS

Study Population

The WHEL Study tested the effect of a plant-based diet on breast cancer recurrence and mortality among breast cancer survivors. The WHEL Study enrolled 3088 women within 4 years of diagnosis of early stage breast cancer categorized using American Joint Committee on Cancer (edition IV) criteria as stage I (< 1cm), stage II, or stage IIIA [16]. Participants were recruited at seven study sites in California, Arizona, Oregon and Texas through physicians, tumor registries and community breast cancer events between March 1995 and November 2000. Over a median 7.3 years of follow-up, 16.9% of the women in the comparison group and 16.7% of women in the intervention group experienced an additional breast cancer event, and 155 women in the intervention group died compared to 160 women in the comparison group [17].

Procedures

Participants in the WHEL Study were asked to complete a series of questionnaires at 5 study time points [baseline, 1 year, 2 or 3 years (randomly determined), 4 years, and 6 years]. These study assessments were completed by self-administered questionnaires and in-person interviews. Participants were also contacted twice per year by WHEL staff to collect information on health status, hospitalizations, medical procedures and other breast cancer and health related topics (one of which was lymphedema). Additional study protocols have been described elsewhere [16]. Procedures for this study were approved by the institutional review boards of each participating institution.

Baseline Dataset

Upon enrollment into the WHEL Study and prior to randomization, participants completed a series of baseline assessments described in detail below.

Demographics—Demographic data, including age at diagnosis, marital status, ethnicity, and education, were collected at baseline by a telephone screening interview and intake forms. Height and weight were measured during the first clinic visit and used to calculate body mass index (BMI), which was categorized as underweight/normal weight (BMI < 24.9 kg/m²), overweight (BMI = 25 to 29.9 kg/m²), and obese (BMI ≥ 30 kg/m²).

Tumor and Treatment Characteristics—Medical records including pathology reports were reviewed for each participant. Axillary lymph node dissection was an eligibility inclusion criterion for all WHEL participants. Variables that were documented included tumor grade and size, number of lymph nodes removed, type of breast cancer surgery (i.e., lumpectomy or mastectomy), administration of chemotherapy and/or radiation therapy, and use of anti-estrogen therapy. The present analysis uses three categories to describe breast cancer treatment: mastectomy with no radiation therapy, lumpectomy plus radiation therapy, and mastectomy plus radiation therapy.

Health Behaviors—At each of the 5 study time points, participants completed a questionnaire on their personal health habits, including smoking status and a validated 9-item physical activity scale [18]. The present analysis uses only the baseline assessment of the personal health habits questionnaire. Physical activity frequency, duration and intensity were converted into metabolic units (METs) using a standard compendium in accordance with Ainsworth et al. [19]. Following other studies [18, 20, 21], we classified mild physical activity as equivalent to 3 METs, moderate activity to 5 METs, and strenuous activity to 8 METs. Slow, average, fast, and very fast walking were assigned values of 2, 3, 4, or 6 METs, respectively. Total energy expenditure was calculated by weighting time (in minutes) spent per week by METs. As per Hong et al., 2007, we created a physical activity variable based on total MET-hours per week (MHW) values with four categories: inactive (MHW < 3.3), mildly to moderately active (3.3 ≤ MHW < 10.0), active (10.0 ≤ MHW < 20.0) and highly active (MHW ≥ 20.0) [20].

Comorbid medical conditions—Participants completed a health status questionnaire that assessed the prevalence of some diagnosed diseases and conditions. Some of these conditions were combined into general systems (i.e., cardiovascular conditions) to increase the sample sizes in each category and to avoid the potential for overlapping diagnoses. For example, cardiovascular conditions include high blood pressure, angina, any use of cholesterol-related medications, peripheral arterial disease, and other heart-related conditions.

Lymphedema Special Dataset

Starting in March 2003 through August 2006 as part of the semi-annual calls, WHEL staff conducted telephone interviews with participants to assess lymphedema status. The interview questions were adapted from Norman and colleagues' (2001) validated telephone lymphedema questionnaire [22]. Prior to starting the questionnaire, participants were informed that lymphedema is a swelling of the arm or hand due to fluid buildup following surgery. To assess lymphedema status, women were asked two questions: 1) "Since your breast cancer treatment, was there ever a time when your arms or hands were different sizes from each other?", and 2) "Since your breast cancer treatment, has a health care professional ever told you that you have lymphedema?". The responses for both items were "yes", "no", or "not sure/don't know". Women were grouped into two categories based on their responses to the above two questions. The lymphedema group consists of women who answered "yes" to one or both of the above questions. Women who responded "no" or "not sure/don't know" to both questions were categorized as not having lymphedema.

Statistical Methods

Univariate analyses were conducted to examine if participant demographics (e.g., age, ethnicity, BMI), tumor and treatment characteristics (e.g., tumor size, number of lymph nodes removed, treatment modality), health behaviors (e.g., smoking and physical activity) and comorbid medical conditions (e.g., arthritis, osteoporosis) were significantly associated with lymphedema status. Categorical variables were analyzed using χ^2 tests and continuous variables with independent samples T-tests and Wilcoxon Rank Sum test. Lastly, logistic regression modeling was used to examine the association between baseline participant characteristics and self-report of lymphedema. Independent variables that were statistically significant in the univariate analyses were entered into the model using a stepwise entry procedure. In addition, we examined interaction terms between each of the variables included in the logistic regression model. Significance for all analyses was set at $P < 0.05$. All analyses were conducted using SPSS v.16.0 (Chicago, IL).

RESULTS

By March 1, 2003, 2917 WHEL participants were alive and contacted for the lymphedema semi-annual call. Of those contacted, 83% (N=2431) of the study cohort responded and self-reported their lymphedema status. Among these 2431 respondents, 466 (19.2%) reported that a health care professional had told them they had lymphedema, and 676 (27.8%) self-reported swelling of the arm or hand. In total, 692 (28.5%) women reported yes to either a physician's diagnosis of lymphedema or arm/hand swelling; of these women, 450 (18.5%) reported yes to both a physician's diagnosis and self-report of arm/hand swelling. Demographic, medical characteristics, and health behaviors reported at baseline are provided in Table 1. For all respondents, the average age at diagnosis was 51 years. Most women were non-Hispanic White, college graduates, and married. Over half of the women were classified as overweight or obese. In terms of physical activity, the majority reported participating in at least 3.3 MHW. Approximately 4% of the respondents were current smokers, and over half were never smokers. Most women either had a lumpectomy plus radiation therapy or a mastectomy plus radiation therapy, and the majority received chemotherapy. The average number of lymph nodes removed was fifteen. Most women in the sample did not report having a comorbid medical condition at baseline. When compared to other participants, women with lymphedema were diagnosed at a younger age, more likely to have a higher body mass index, had a larger tumor size, had more lymph nodes removed, more likely to have a mastectomy with radiation therapy, and more likely to have chemotherapy.

Based on results of the univariate tests, variables that were significant were added to binary logistic regression models to determine the association between the baseline variables and lymphedema status. Since the association between lymphedema and osteoporosis was close to statistical significance in the univariate tests, we created a regression model that included it with the other variables that were significant. However, after adjusting for the other variables included in this model, osteoporosis was no longer statistically significant ($p=0.214$) and not included in the final model. In the final multivariate-adjusted model (Table 2), BMI, the number of lymph nodes removed, and breast cancer treatment were significantly associated with lymphedema status. There were 2425 participants included in the final model: 3 participants were missing data on tumor size, 2 were missing data on the number of lymph nodes removed, and 1 participant was missing data on breast cancer treatment.

As shown in Table 2, compared to women of normal weight, those who were overweight had 33% higher odds of having lymphedema and those who were obese had twice the odds. Women who underwent a lumpectomy with radiation therapy had 12% higher odds of

having lymphedema than those who only had a mastectomy although this result was not significant at the 5% level. In addition, women who had a mastectomy with radiation therapy had over twice the odds to self-report lymphedema compared to those who only had a mastectomy. The more lymph nodes removed increased the odds of developing lymphedema. Compared to women who had 1 to 10 lymph nodes removed, women who had 16 or more lymph nodes excised had 65% higher odds of lymphedema. In summary, having a BMI greater than 25.0 kg/m², breast cancer surgery with radiation therapy, and more than 11 lymph nodes removed were significantly associated with developing breast cancer-related lymphedema.

Figure 1 illustrates the significant interaction between BMI and the number of lymph nodes removed [χ^2 (4, N=2425) = 20.20, $p < 0.01$]. Regardless of the number of lymph nodes removed, obese women had higher rates of lymphedema than normal weight and overweight women: odds ratios ranged from 2.31 to 3.60 for obese women across lymph node categories compared to odds ratios of 1.00 to 1.69 for normal weight women.

Further, sensitivity analyses were conducted among women who self-reported a physician diagnosis and arm/hand swelling (N=450) compared to women with no report of lymphedema (N=1739) to further examine the association between baseline risk factors and lymphedema. The results of these analyses were similar to those presented in Tables 1 and 2 (data not shown).

DISCUSSION

Breast cancer-related lymphedema is an adverse and chronic health condition that affects a significant number of breast cancer survivors. The purpose of this study was to identify the prevalence of lymphedema in the WHEL cohort of breast cancer survivors and to examine the factors associated with lymphedema among our participants. In our study sample, approximately 29% of the women self-reported lymphedema. Considering the varying definitions used to define lymphedema, our percentage of self-reported lymphedema is comparable to other studies reporting the prevalence of lymphedema among breast cancer survivors [2, 3, 6, 10, 15, 23]. Ahmed and colleagues (2011) stated that 8% of their population reported a lymphedema diagnosis and 37% reported only arm symptoms of lymphedema [6]. Meeske et al., 2009 found that 24% of their population reported lymphedema [15]. Hayes and colleagues (2008) reported that 33% of their study cohort had lymphedema within 6 to 18 months after surgery [23]. Also among a cohort of younger breast cancer survivors, 32% reported persistent arm and/or hand swelling [10].

This cohort analysis identified breast cancer surgery plus radiation therapy, lymph node removal, and body mass index as having a significant association with developing breast cancer-related lymphedema. In terms of breast cancer treatment, having a mastectomy plus receiving radiation therapy showed a twofold increased odds of developing lymphedema in comparison to having a mastectomy alone. In contrast, other studies have not found breast cancer surgery and/or radiation therapy to be associated with lymphedema [4, 7, 10, 14, 15]. Ahmed and colleagues (2011) did not find breast cancer surgery or radiation therapy to be risk factors for those diagnosed with lymphedema; however, they did report that axillary radiation was associated with self-report of arm symptoms among their study population [6]. Hayes and colleagues (2008) did not find radiation treatment to be associated with lymphedema, yet mastectomy was shown to be a risk factor for lymphedema in their study population [23].

The differences in our results from other studies regarding breast cancer treatment as a risk factor for lymphedema may be attributed to differences in demographics of the study

populations or the definition of the breast cancer treatment variable. For example, the age at breast cancer diagnosis varies from study to study; some of the studies have a study population that is younger [4, 10, 15] or older [6, 7] than the WHEL Study population. Further, the percentage of women who received breast cancer surgery or radiation therapy also differs among studies. For example, some studies reported that less than 50% of their population underwent a mastectomy [4, 10, 14, 23] or received radiation therapy [4, 6, 15]. Another key difference is how breast cancer treatment was classified. We chose to combine breast cancer surgery with radiation therapy as our treatment variable; whereas, some of the other studies left these as two separate variables in their analyses. For example, Ahmed and colleagues (2011) classified breast surgery as no surgery or lumpectomy, simple mastectomy, radical mastectomy, or unknown, and they classified radiation therapy into two regions: the axilla and the breast [6]. Our study results confirm findings from other studies that have shown the removal of axillary lymph nodes to be an independent risk factor for lymphedema [4, 6, 7, 10, 13–15]. We found that women with 16 or more lymph nodes removed had 1.65 higher odds of having lymphedema compared to those with 10 or fewer nodes removed. Similar to our findings, Ahmed and colleagues reported that the odds of lymphedema among women with greater than 20 lymph nodes excised was 3.52 times the odds of women with no lymph nodes removed [6]. Meeske et al., 2009 found that those with 10 or more lymph nodes removed had 2.16 higher odds of developing lymphedema compared to those with no lymph nodes removed [15]. Further, studies have shown that even removing only a few lymph nodes can still result in the development of lymphedema [10, 14]. Kwan and colleagues (2010) found that the risk of lymphedema increased by 4.1% for each lymph node removed [14]. These findings in addition to our study results highlight the importance of removing as few lymph nodes as possible when examining the axillary region for tumor metastases.

While lymph node removal is the most common risk factor cited for breast cancer-related lymphedema, our results show that it is not the only risk factor for lymphedema. Our study found that the higher the BMI, the higher the odds of reporting lymphedema. We found that obese participants had twice the odds to self-report lymphedema as normal weight women. These results are consistent with those of previous studies that have found an association between BMI and lymphedema [6, 8, 10, 11, 13–15]. For example, Ahmed et al., 2011 found that among women with a baseline BMI ≥ 30 kg/m² the odds of having lymphedema were increased by a factor of 3.24 times compared to women with a baseline BMI < 24.9 kg/m² [6]. Among younger breast cancer survivors, Paskett and colleagues (2007) found the odds of persistent swelling were 2.24 times higher for those with a BMI > 30 kg/m² compared to those with a BMI < 25 kg/m² [10]. Ridner et al., 2011 reported that women with a BMI ≥ 30 kg/m² at the time of treatment had a 3.6 times higher odds of developing lymphedema than women with a BMI < 30 kg/m² [11]. In contrast to these findings, Hayes and colleagues found no association between body weight and lymphedema [23]. This difference could be due to the method of measuring lymphedema among the studies. Hayes et al., 2008 used bioimpedance spectroscopy to measure lymphedema status [23]; whereas, our study as well as most of the other studies used self-report of lymphedema.

Additionally, we found that when BMI and the number of excised lymph nodes were considered together, the odds of having lymphedema increased compared to when these variables were considered independently. Obese participants had higher odds of developing lymphedema, irrespective of the number of lymph nodes removed, when compared to normal weight and overweight women. To date, there are no published studies that have examined the association of BMI/number of lymph nodes removed with lymphedema status. Our finding of an interaction between BMI and lymph node removal is novel, and if replicated in other studies, has implications for counseling women about the risk of lymphedema prior to and after breast cancer treatment. Lymphedema patient education is of

particular importance for all women who undergo lymph node dissection surgery and have a BMI greater than 30 at the time of cancer diagnosis. In addition, women who have a BMI greater than 30 after cancer treatment should also be educated about the risks factors associated with developing lymphedema.

While the risk factors identified in our study have been reported by others, our analyses did not identify any other participant characteristics (e.g., age, chemotherapy, physical activity, or comorbid medical conditions) associated with lymphedema. Other literature have reported chemotherapy to be associated with lymphedema status [4, 6, 13], yet in our study, chemotherapy was not associated with lymphedema in the multivariate model. Similar to our findings, others have reported no association between chemotherapy and lymphedema status [7, 15, 23]. Additionally, some studies have reported age to be associated with lymphedema [15, 23]; whereas, similar to our study, others have not found this association [6, 10, 14]. In terms of physical activity, our study findings are comparable to other studies that did not find a significant association between level of physical activity and lymphedema [6, 10, 14, 15]. Similar to the Ahmed et al., 2011 study, we found that comorbid medical conditions at baseline were not associated with lymphedema [6]. While osteoporosis was borderline significant in the chi-square tests, its significance disappeared once it was included in the regression model with the other variables. In contrast to our findings, Meeske et al., 2009 reported that a diagnosis of high blood pressure prior to breast cancer diagnosis was associated with lymphedema [15]. Another study found that breast cancer survivors with lymphedema experience more comorbid medical conditions than those without lymphedema [24].

The inconsistency in findings related to the above characteristics may be due to differences in study designs, sample sizes, or the time frame of assessing lymphedema status after cancer treatment. A key difference between the studies presented above is the type of study design. Some studies were prospective cohort studies [6, 10, 14]; whereas, others were retrospective studies examining claims or registry data [4, 7, 15]. In terms of sample size, our study population of 692 women self-reporting lymphedema is much larger than the other studies; most of which had fewer than 200 women with lymphedema [4, 7, 11, 14, 15, 23]. Some of these studies may not have found significant associations between risk factors and lymphedema due to their small sample size. Further, the time frame between the completion of breast cancer treatment and the assessment of lymphedema varies from study to study. For example, some studies assessed lymphedema status within 3 years of breast cancer surgery [4, 10, 13, 14, 23]; whereas, other studies, including the WHEL Study, assessed lymphedema status at least 4 years postoperatively [6, 7, 15].

The primary limitation for this study is its reliance on self-report for assessing lymphedema status rather than a physical measurement. However, our sensitivity analysis, which compared those with a self-report of a physician's diagnosis and swelling (N=450) to those with no lymphedema (N=1739), produced similar results to the analyses shown in Tables 1 and 2 comparing women who self-reported arm/hand swelling and/or a physician diagnosis (N=692) to those with no lymphedema (N=1793). These findings support the use of self-report for breast cancer-related lymphedema status. Also the lymphedema questionnaire used in this study has been validated and shown to accurately identify lymphedema [22]. Additionally, many of the other study variables, such as breast cancer treatment and physical activity, were assessed using self-report measures, which are subject to response bias and may influence the results of the study. Since the baseline information was collected at study entry, which for some participants was up to 4 years after cancer diagnosis, we cannot evaluate the causative relationships between lymphedema and some of the risk factors, such as body mass index, identified in this study. Furthermore, our study baseline BMI variable assessed BMI post-treatment, not pre-treatment or pre-diagnosis. Another study limitation is

that participants in the WHEL Study are not representative of all breast cancer survivors; women in the WHEL Study were primarily White, college educated, and highly motivated to participate in a dietary intervention. Hence, the findings from this study may not be generalizable to other breast cancer populations. In contrast to the study limitations, the primary strengths of the study are a large sample size, a 7.3 year average follow-up period, and substantial data collection on health behaviors, treatment variables, and comorbid medical conditions at baseline.

In conclusion, BMI, lymph node removal, and breast cancer treatment were significantly associated with lymphedema among participants in the WHEL Study. These results are consistent with previous findings on the prevalence of lymphedema among breast cancer survivors and may help educate physicians and patients as to the modifiable risk factors associated with lymphedema. While the number of lymph nodes removed and the type of breast cancer treatment may be unavoidable, maintaining or achieving a healthy weight is a valid target for health behavior interventions aimed at reducing the rates of lymphedema. Future research needs to focus on whether or not modifiable risk factors associated with lymphedema can be effectively targeted in health behavior interventions to prevent the development of breast cancer-related lymphedema.

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Fig. 1. Lymphedema rates according to BMI and the number of lymph nodes removed (N=2425)

Note: N (%) is the number and percentage of women with lymphedema in each category.

The total number of women with lymphedema equals 692.

Odd ratios (OR) adjusted for the following variables: age at diagnosis, tumor size, treatment, and chemotherapy.

Confidence intervals are indicated by the error bars on the graph.

“Ref” on the first bar indicates that this is the reference category.

Table 1

Baseline participant characteristics by lymphedema status in a cohort of breast cancer survivors

Characteristic	Overall (n=2431) N (%)	Women with Lymphedema (n=692) N (%)	Women without Lymphedema (n=1739) N (%)	P value
Demographics				
Age at Diagnosis, mean [SD (range)], years	51.0 [8.7 (26.0 – 70.0)]	50.4 [8.6 (26.0 – 70.0)]	51.2 [8.7 (27.0 – 70.0)]	0.03
Ethnicity				0.40
White, not Hispanic	2089 (85.9)	585 (84.5)	1504 (86.5)	
Hispanic	126 (5.2)	38 (5.5)	88 (5.1)	
Asian American	80 (3.3)	21 (3.0)	59 (3.4)	
Black/ African American	78 (3.2)	29 (4.2)	49 (2.8)	
Other	58 (2.4)	19 (2.8)	39 (2.2)	
Education				0.39
College Graduate	1349 (55.5)	374 (54.0)	975 (56.1)	
Other	1082 (44.5)	318 (46.0)	764 (43.9)	
Marital Status				0.07
Married	1735 (71.4)	475 (68.6)	1260 (72.5)	
Other	696 (28.6)	217 (31.4)	479 (27.5)	
Body Mass Index				<0.01
< 25 kg/m ² (normal/underweight)	1086 (44.7)	249 (36.0)	837 (48.1)	
25 – 29.9 kg/m ² (overweight)	756 (31.1)	216 (31.2)	540 (31.1)	
30 kg/m ² (obese)	589 (24.2)	227 (32.8)	362 (20.8)	
Menopausal Status				0.24
Pre-menopausal	252 (10.4)	73 (10.6)	179 (10.3)	
Post-menopausal	1948 (80.3)	541 (78.5)	1407 (81.0)	
Peri-menopausal	227 (9.3)	75 (10.9)	152 (8.7)	
Tumor and Treatment Characteristics				
Grade				0.14
I	423 (17.4)	119 (17.2)	304 (17.5)	
II	963 (39.6)	254 (36.7)	709 (40.8)	
III	840 (34.6)	263 (38.0)	577 (33.1)	
Not applicable or available	205 (8.4)	56 (8.1)	149 (8.6)	
Tumor Size				<0.01
< 1.5 cm	715 (29.4)	181 (26.2)	534 (30.7)	
1.5 – 1.9 cm	553 (22.8)	142 (20.6)	411 (23.7)	
2.0 – 2.9 cm	649 (26.7)	188 (27.2)	461 (26.5)	
3.0 cm	511 (21.1)	180 (26.0)	331 (19.1)	
No. Nodes Removed, mean [SD (range)]	15.0 [7.0 (1 – 69)]	16.3 [7.0 (2 – 54)]	14.5 [6.6 (1 – 69)]	<0.01
1 to 10 nodes	614 (25.3)	132 (19.1)	482 (27.8)	
11 to 15 nodes	793 (32.6)	216 (31.2)	577 (33.2)	
16 nodes	1022 (42.1)	344 (49.7)	678 (39.0)	

Characteristic	Overall (n=2431) N (%)	Women with Lymphedema (n=692) N (%)	Women without Lymphedema (n=1739) N (%)	P value
Treatment				<0.01
Mastectomy No Radiation	935 (38.5)	239 (34.5)	696 (40.0)	
Lumpectomy plus Radiation	1188 (48.9)	319 (46.1)	869 (50.0)	
Mastectomy plus Radiation	307 (12.6)	134 (19.4)	173 (10.0)	
Chemotherapy	1664 (68.4)	499 (72.1)	1165 (67.0)	0.02
Anti-estrogen Therapy				0.28
Ever Use	1687 (69.5)	468 (67.8)	1219 (70.2)	
No Use	740 (30.5)	222 (32.2)	518 (29.8)	
Health Behaviors				
Smoking status				0.58
Never	1326 (54.9)	380 (55.3)	946 (54.7)	
Former	996 (41.2)	285 (41.5)	711 (41.2)	
Current	93 (3.9)	22 (3.2)	71 (4.1)	
Physical Activity, median	10.96	10.00	12.00	0.09
METs-hour/week (MHW)				
Inactive (MHW < 3.3)	544 (23.1)	172 (25.8)	372 (22.1)	
Mildly-moderately Active (3.3 MHW < 10.0)	540 (22.9)	159 (23.8)	381 (22.6)	
Active (10.0 MHW < 20.0)	583 (24.8)	163 (24.4)	420 (24.9)	
Highly Active (MHW ≥ 20.0)	687 (29.2)	173 (26.0)	514 (30.4)	
Comorbid Medical Conditions				
Arthritis	382 (18.8)	113 (19.0)	269 (18.8)	0.98
Cardiovascular Conditions	457 (22.5)	144 (24.2)	313 (21.9)	0.28
Diabetic Conditions	83 (4.1)	28 (4.7)	55 (3.8)	0.45
Digestive Conditions	189 (9.3)	60 (10.1)	129 (9.0)	0.51
Miscellaneous Conditions	166 (8.2)	55 (9.2)	111 (7.8)	0.31
Osteoporosis	119 (5.9)	25 (4.2)	94 (6.6)	0.05

Note: 2×2 tables were tested with Yates' χ^2 test.

Categorical variables with three or more categories were tested with Pearson's χ^2 test.

Continuous variables were tested with independent-samples T-test and Wilcoxon Rank sum test.

Table 2

Baseline participant characteristics associated with lymphedema status in a cohort of breast cancer survivors (N=2425)

Women with Lymphedema				
Characteristic	N (%)	OR	P value	(95% CI)
<i>Demographics</i>				
Age at diagnosis, mean [SD (range)], years	50.4 [8.6 (26.0 – 70.0)]	0.99	0.08	(0.98 – 1.00)
Body Mass Index			<0.01	
< 25 kg/m ² (normal/underweight)	249 (36.0)	1.00		---
25 – 29.9 kg/m ² (overweight)	216 (31.2)	1.33		(1.07 – 1.66)
30 kg/m ² (obese)	227 (32.8)	2.08		(1.66 – 2.60)
<i>Tumor and Treatment Characteristics</i>				
Tumor Size			0.41	
< 1.5 cm	181 (26.2)	1.00		---
1.5 – 1.9 cm	142 (20.6)	1.02		(0.78 – 1.32)
2.0 – 2.9 cm	188 (27.2)	1.07		(0.83 – 1.38)
3.0 cm	180 (26.0)	1.25		(0.95 – 1.67)
No. Nodes Removed			<0.01	
1 to 10 nodes	132 (19.1)	1.00		---
11 to 15 nodes	216 (31.2)	1.28		(0.99 – 1.65)
16 nodes	344 (49.7)	1.65		(1.30 – 2.09)
Treatment			<0.01	
Mastectomy with no Radiation	239 (34.5)	1.00		---
Lumpectomy plus Radiation	319 (46.1)	1.12		(0.91 – 1.37)
Mastectomy plus Radiation	134 (19.4)	2.02		(1.52 – 2.69)
Chemotherapy	499 (72.1)	1.02	0.90	(0.81 – 1.28)

Note: Odd ratios adjusted for all variables in the table. CI indicates confidence interval.