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Differences in limb volume trajectories after breast cancer treatment

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Abstract

Purpose—~20% of patients develop lymphedema (LE) following breast cancer (BC) surgery. An evaluation of distinct trajectories of volume change may improve our ability to diagnose LE sooner. The purposes of this study were to identify subgroups of women with distinct trajectories of limb volume changes following BC surgery and to evaluate for phenotypic differences among these classes.

Methods—In this prospective longitudinal study, 380 women were enrolled prior to unilateral BC surgery. Upper limb bioimpedance was measured preoperatively and serially for one year postoperatively. Resistance ratios (RR) were calculated. A RR of >1 indicates affected limb volume > unaffected limb volume. Latent class growth analysis (LCGA) was used to identify classes of women with distinct postoperative RR trajectories. Differences among classes were evaluated using analyses of variance and Chi square analyses.

Results—Three distinct classes were identified: RR <0.95 (37.9%), RR ~1.00 (46.8%), RR >1.05 (15.3%). Patients in the RR >1.05 class were more likely to have diabetes (p=0.036); were more likely to have BC on their dominant side (P<0.001); had higher RR ratios at the preoperative and one-month assessments (P<0.001); and were more likely to be diagnosed with LE (p<0.001).

Conclusions—LCGA is a useful analytic technique to identify subgroups of women who may be at higher risk for the development of LE, based on trajectories of limb volume change after BC surgery.

Implications for cancer survivors—Assessment of preoperative and one-month bioimpedance RRs may allow for the earlier identification of patients who are at higher risk for the development of LE.

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Keywords

breast cancer; lymphedema; bioimpedance spectroscopy; resistance ratios; upper extremity; latent class analysis

INTRODUCTION

Breast cancer related lymphedema (LE) is the accumulation of interstitial fluid as a result of damage to lymph nodes and vessels during cancer treatment [1]. Approximately 1 in 5 women develop upper extremity LE after surgical treatment for breast cancer [2]. Untreated, LE can lead to significant disability [3]. Compared to breast cancer patients without LE, women with LE have greater limitations in shoulder function and poorer quality of life [4–7] and incur higher medical costs [8]. Life-long management of LE is time consuming and burdensome for patients [9]. Therefore, it is imperative to identify women at higher risk for the development of LE so that preemptive measures can be undertaken to prevent its development or limit its progression.

Currently, preoperative assessment, to establish baseline values, and postoperative screening are recommended (though not routinely performed) to identify increases in limb volume that warrant treatment [10–12]. The initiation of LE treatment early results in improved outcomes [13,14]. In one study [12], this approach was found to be cost effective during the first year of surveillance. However, a large amount of inter-individual variability exists in patient outcomes associated with LE preventive or treatment strategies [15,16]. Understanding distinct patterns of limb volume change after breast cancer treatment may provide insights into the natural behavior of these changes, and assist with identification of a subset of women at higher risk for the development of LE who can then be targeted for increased surveillance. If phenotypic characteristics associated with the development of LE were identified, then risk-based screening for the development of LE could be tiered so that patients at higher risk would have more frequent assessments following breast cancer surgery.

In a study that evaluated for differences in patterns of limb volume change in patients after breast cancer surgery, women (n=232) were partitioned into four groups based on body mass index (BMI) and two groups based on postoperative swelling [17]. Over the 30 months of the study, higher BMI and the presence of postoperative swelling (defined as limb swelling of at least 3% at the postoperative visit) were associated with the development of LE (defined as a 5% BMI-adjusted limb volume change). Compared to the normal-weight patients, in the obese and overweight patients, their limb volume change patterns had a higher probability of being associated with LE. In another study [18], 266 patients were grouped by stage of LE (i.e., mild, moderate, or severe) and medical records were reviewed to determine time course and risk factors for progression of LE to a more severe stage. One third of the patients with LE progressed to a more severe LE within the 5-year follow-up period. Using multivariate Cox proportional hazards regression, predictors for progression to a more severe stage of LE were being older than 65 years of age and receipt of a posterior axillary radiation boost.

Both of these studies used investigator-identified grouping criteria. In addition, most conventional approaches to modeling longitudinal changes in an outcome assume that all of the members of the study sample come from a single population, that one growth model will represent the entire population, and that covariates affect all of the individuals in the same way. These methods include repeated measures analysis of variance (ANOVA) and multilevel regression. In contrast, an evaluation of between-group (i.e., inter-individual) differences in within-group changes over time (i.e., trajectories) may provide a better understanding of the development of LE in women following breast cancer treatment. We hypothesized that differences in limb volume trajectories likely exist in the population. The use of latent class growth analysis (LCGA) allows for the identification of groups or "latent" classes of individuals based on individual patterns of change in the outcome of interest [19]. Once these classes are identified, differences in phenotypic characteristics among the classes can be evaluated and used to identify patients at higher risk for the development of LE. Therefore the purposes of this study, in a sample of breast cancer patients (n=380), were to identify subgroups of women with distinct trajectories of bioimpedance resistance ratios (RR) from one month to 12 months after breast cancer surgery and to evaluate for differences in demographic and clinical characteristics among the latent classes.

MATERIALS AND METHODS

Patients and Settings

This study is part of a larger, prospective longitudinal study that evaluated for neuropathic pain and LE in a sample of women who underwent breast cancer surgery. The methods for this study are described in detail elsewhere [20,21]. Patients were recruited from Breast Care Centers located in a Comprehensive Cancer Center, two public hospitals, and four community practices. Patients were eligible to participate if they: were adult women (>18 years) who would undergo unilateral breast cancer surgery; were able to read, write, and understand English; and gave written consent. Patients were excluded if they were having bilateral breast cancer surgery or had distant metastases at the time of diagnosis. Of the 516 patients approached, 410 were enrolled (response rate 79.5%), and 396 completed the study. The major reasons for refusal were: too busy, overwhelmed with the cancer diagnosis, or insufficient time available to do the assessment prior to surgery. Written informed consent was obtained from all patients. Data from 380 women are included in this analysis.

Subjective measures

The demographic questionnaire obtained information on age, marital status, education, ethnicity, employment status, living situation, activity level, and financial status. The Self-Administered Comorbidity Questionnaire (SCQ) was used to assess comorbidities [22]. The Karnofsky Performance Status (KPS) scale was used to evaluate functional status using a self-report scale that ranged from 30 (I feel severely disabled and need to be hospitalized) to 100 (I feel normal; I have no complaints or symptoms) [23].

Objective Measures

Bioimpedance analysis of both upper limbs was done using established procedures [24–26]. Patients were instructed to refrain from exercise and sauna for 8 hours and from drinking alcohol for 12 hours prior to the bioimpedance assessment. Patients lay supine with their arms abducted 30 degrees and legs not touching for at least 10 minutes prior to the measurements. Bioimpedance measurements were taken using the Quantum X Bioelectrical Impedance Device (RJL Systems, Clinton Township, MI). Measurement electrodes were placed on the skin at either end of the 40-centimeter (cm) length over which the circumference measurements were made and the ‘drive’ electrodes were placed 8 cm to 10 cm distal to these measurement electrodes. Two readings of resistance from each limb were averaged.

Circumferential measurements of the upper limbs were done using a spring-loaded narrow tape measure at 10 cm intervals from the pisiform prominence of the wrist up to a total distance of 40 cm proximally. Each measure was repeated twice by the same research nurse, for each patient. Volumes of each 10 cm segment of the limb were calculated using the average of 2 circumferential measurements. Segment volumes were summed to obtain total limb volume. Limb volume was calculated from the circumference measurements using the formula for volume of a truncated cone [27]. All of the nurses, who had at least two years of oncology nursing experience, were trained to do the circumferential measures. Every six months, the project director did inter-rater reliability assessments (using inter-class correlation) with all of our research nurses. At every evaluation, inter-rater reliabilities of >0.80 were achieved.

Active shoulder range of motion (ROM) for flexion and abduction were assessed with the patient supine, using a goniometer and standardized procedures reported by Norkin and White [28]. Two measurements were taken for each motion and a mean obtained. Grip strength was assessed using a Jamar hydraulic hand dynamometer (Patterson Medical, Bolingbrook, IL). Patients stood with the arm held down at their side and were instructed to squeeze with maximal effort. Three trials for each extremity were done and a mean grip strength score was calculated. BMI was calculated from height and weight.

Study Procedures

The study was approved by the Committee on Human Research at the University of California, San Francisco and by the Institutional Review Boards at each of the study sites. During the patient’s preoperative visit, a clinician explained the study to the patient, determined the patient’s willingness to participate, and introduced the patient to the research nurse. The research nurse determined patient eligibility. After providing written informed consent, patients completed the study questionnaires. Then, the research nurse performed the objective measurements. Disease and treatment information were abstracted from the patients’ medical records. The research nurse met with the patients either in their home or in the clinical research center at 1, 2, 3, 4, 5, 6, 8, 10, and 12 months after surgery. During each of the study visits, patients completed the study questionnaires and had the objective measures assessed by the research nurse.

Data analysis

Descriptive statistics and frequency distributions were generated for demographic and clinical characteristics using SPSS Statistics for Windows, Version 22.0 (IBM Corporation, Armonk, NY). LCGA was performed using Mplus Version 6.11 [29].

Resistance ratios (RR) were calculated from the bioimpedance resistance measures of the unaffected limb to that of the affected limb. A RR of >1 indicates that the affected limb volume is greater than the unaffected limb volume. For the LCGA, RRs were multiplied by 100 to better analyze inter-individual variability. LE was defined as RR of 1.139 (if the dominant arm was at risk) and 1.066 (if the nondominant arm was at risk) [30], using the data obtained from each woman during her participation in the study.

LCGA with robust maximum likelihood estimation was used to identify latent classes (i.e., subgroups of patients) with distinct limb RR trajectories over the 12 months of the study. A single growth curve that represented the "average" change trajectory was estimated for the total sample. Then, the numbers of latent growth classes that best fit the data were identified using published guidelines [19,31].

Analyses of variance and Chi-square analyses were done to evaluate for differences among the latent classes identified using LCGA. A p-value of < 0.05 was considered statistically significant. Post hoc contrasts were done using the Bonferroni procedure to control the overall family alpha level of the pairwise contrasts for the three RR classes. For any one of the three pairwise contrasts, a p-value of 0, (0.05/3) was considered statistically significant.

RESULTS

Identification of RR latent classes using LCGA

As shown in Table 1, the 3-class solution provided the best model fit. The 3-class model was selected because the Vuong-Lo-Mendell-Rubin (VLMR) likelihood ratio test for the 3-class versus the 2-class solution was significant and each class had a reasonable size and interpretability [19]. Radiation therapy (RT) and number of lymph nodes removed were included as covariates in the model. While RT retained statistical significance in the model, number of lymph nodes removed did not. However, because the model fit was better when number of nodes removed was kept in the final model, it was retained.

Parameter estimates for the three classes are provided in Table 2. Classes were named according to the intercept RR, which corresponds to the one-month postoperative assessment. Of the 380 women evaluated, the largest percentages of patients were classified in RR ~1.00 class (47.5%) and the fewest in the RR >1.05 class (15.8%). While, RRs for all three classes were fairly stable over time, the RR ~1.00 class had a significant linear slope (Figure 1).

Differences in demographic and preoperative clinical characteristics among the RR classes

No significant differences were found in any demographic characteristics among the three classes (Table 3). In terms of preoperative clinical characteristics (Table 4), compared to the other two RR classes, women in the RR >1.05 class had greater interlimb volume differences and RR at the preoperative assessment. In addition, compared to the RR ~1.00 class, a higher percentage of patients in the RR >1.05 class had diabetes.

Differences in intraoperative and postoperative characteristics among the RR classes

In terms of intraoperative characteristics (Table 5), compared to the other two classes, a higher percentage of women in the RR >1.05 class had cancer in their right breast and had cancer diagnosed on their dominant side. In terms of postoperative characteristics (Table 6), compared to the other two RR classes, a higher percentage of patients in the RR ~1.00 class had received RT within the 12 months following surgery. As shown in Figures 2A and 2B, compared to the other two classes, patients in the RR >1.05 class had higher interlimb volume differences one month after surgery and a significantly higher percentage of these women developed LE. Details on receipt of treatment of LE during the first year were not obtained, however, no differences were found among groups with regard to receipt of physical therapy.

DISCUSSION

To our knowledge, this study is the first to use LCGA to identify latent classes of patients after breast cancer treatment with distinct limb volume trajectories using bioimpedance RRs. Subtle differences in RRs were associated with three distinct trajectories that remained relatively stable from 1 to 12 months postoperatively. These three distinct classes were named for their RRs at the one-month postoperative assessment (i.e., RR < 0.95, RR ~1.0, and RR >1.05). A RR of >1 indicates that the volume of the affected limb is greater than the unaffected limb. When comparisons were done among the three classes, patients in the RR >1.05 class were more likely to have breast cancer on their dominant side; had higher RRs at the preoperative and one month assessments; and were more likely to be diagnosed with LE. Taken together, these findings suggest that postoperative RRs are a stable trait that may be useful to identify women at higher risk for the development of LE following breast cancer surgery.

In terms of phenotypic characteristics that distinguished among the latent classes, compared to the other two classes, the interlimb volume differences in the RR >1.05 class increased from the preoperative to the one month postoperative assessment. While this change did not reach statistical significance (mean increase 29.2 ml, 95% CI: −14.7, 73.2), a higher percentage of these women went on to develop LE. These findings are consistent with a longitudinal study that evaluated relative volume change (RVC) in the affected and unaffected arms and the development of LE [32]. In this study, a RVC of > 3% in the first 3 months following surgery was associated with an increased risk for LE. In our study, 29.5% of the women in the RR >1.05 class had a >3% increase in RVC one month postoperatively, compared to only 10.3% and 9.4% of the patients in the RR ~1.00 and RR <0.95 classes, respectively ($p = 0.022$).

A higher percentage of women in the RR >1.05 class had cancer in their right breast (84.5%), which was also the dominant side for 86.2% of these women. This association could account, in part, for the greater volume and higher RRs in the affected compared to the unaffected limb in this group. However, it is important to consider that breast cancer surgery on the dominant side may be an independent predictor for the development of LE because more women in this group developed LE over the course of the study. Previous findings on the association between surgery on the dominant side and the development of LE are equivocal [2,33,34]. One potential explanation for the "right-sided" findings is the asymmetrical lymph drainage territories and terminal lymphatic vessel anatomy in the neck. The variable lymphatic ducts on the right, which receive lymph from the right upper quadrant of the body, are much smaller than thoracic duct on the left [35,36].

More women in the RR >1.05 class reported having diabetes. This finding was unexpected and was not accounted for by differences among the RR classes in BMI or percentages of women who were obese. Because the occurrence of diabetes was low, findings should be interpreted with caution. However, while the impact of diabetes on peripheral lymphatic vessel function is not known, alterations in blood microvascular function are documented in patients with diabetes [37]. It is possible that the lymphatic vessels may be at risk for greater damage in patients with diabetes, which would impair their function. Alternatively, the rate of the lymph formation may be altered in patients with diabete [38], which may overload the transport capacity of the lymphatic system. Our findings are consistent with findings from a descriptive cross-sectional study, in which 11% of women with LE, compared to only 4% without LE, reported diabetes [39]. However, this difference was not statistically significant.

While receipt of RT was significantly different among the RR groups, it was the RR ~1.0 class that had the highest percentage of women who received RT. We expected that the RR >1.05 class would have had the highest percentage of women who received RT, since receipt of RT was associated with development of LE in previous studies [40,41]. We did not account for possible synergistic or interaction effects between RT and other treatments or clinical characteristics among the groups that could contribute to this finding.

Study limitations warrant consideration. While time to onset of lymphedema was not an outcome of this analysis, this is an issue that warrants attention, since at the time of diagnosis a woman may have been referred to treatment of lymphedema. If patients received physical therapy for limb volume changes, this treatment may have influenced the volume trajectories and development of LE. However, only 24% of the women in our study received physical therapy during the first year following breast cancer surgery and the percentages of women who received physical therapy were similar among the RR groups. Additionally, while patients were asked at each assessment if they received physical therapy, details about the type of and purposes for physical therapy were not obtained. Second, most of the women in the study were white and well educated, which limits the generalizability of our findings. Finally, results should be interpreted with caution until these findings are replicated in future studies.

Findings on specific risk factors for the development of LE are inconclusive. Factors linked to the development of LE include axillary lymph node dissection (ALND) compared to sentinel lymph node biopsy (SLNB), higher BMI, more lymph nodes removed, field of radiation, postoperative seroma, infection, early edema, and surgery plus RT [32,42–45]. Our study sought to identify subgroups of women who may be at increased risk for the development of LE, based on trajectories of limb volume change after breast cancer surgery. The predictors of the RR classes need not be the same as those reported for LE. While changes in RRs are used to diagnose LE, RR as used in this study is a unique outcome that may be used to identify women at higher risk for the development of LE. Results of this study support preoperative and one-month assessments of bioimpedance RRs in women who undergo breast cancer surgery. If our findings are replicated in an independent sample, this type of assessment would allow for the identification of patients who are at higher risk for the development of LE following breast cancer surgery. This type of proactive surveillance would allow for the earlier initiation of treatment to decrease the morbidity associated with this condition.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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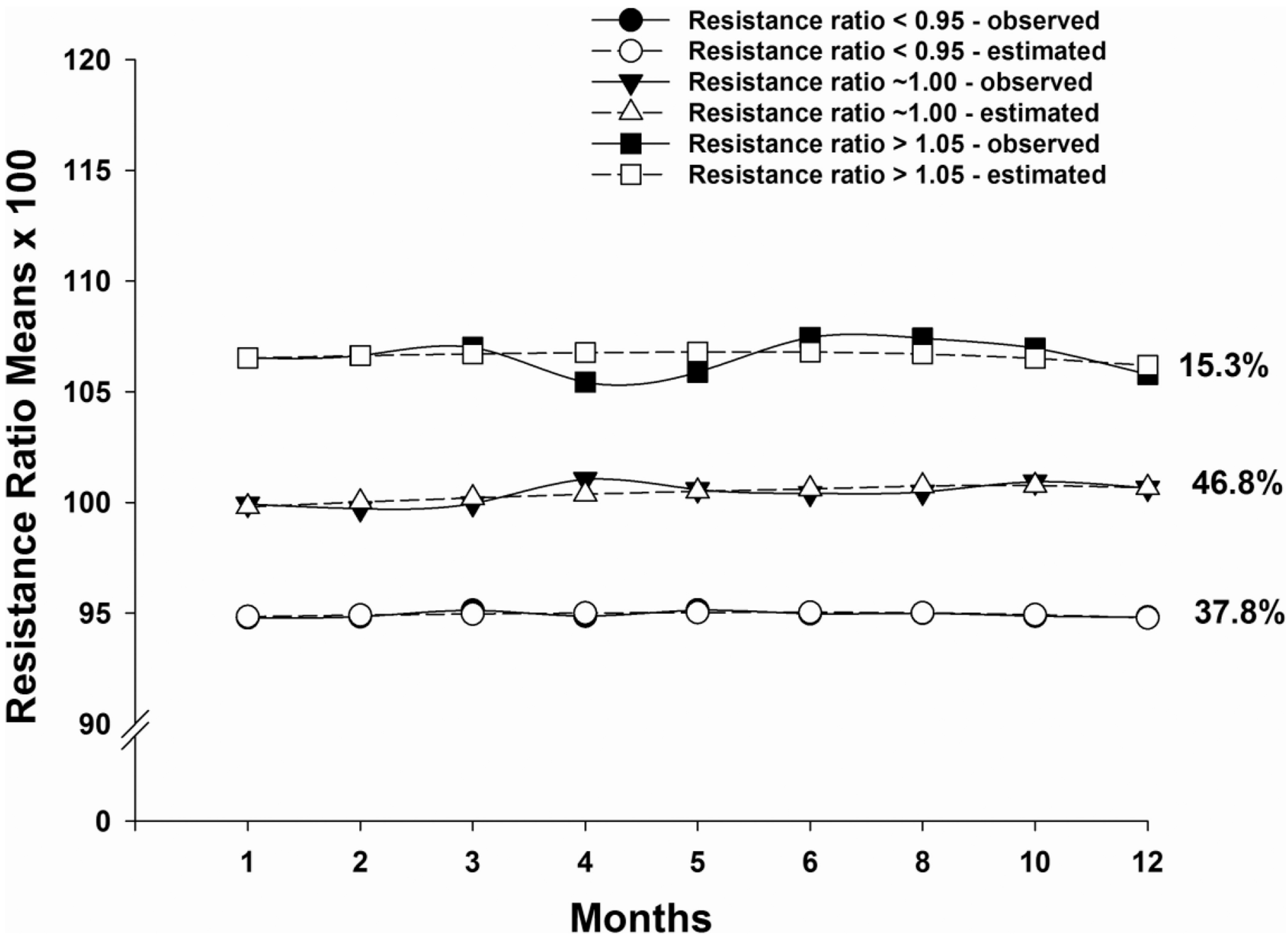

Figure 1.

Observed and estimated resistance ratio (RR) means for patients in each of the latent classes.

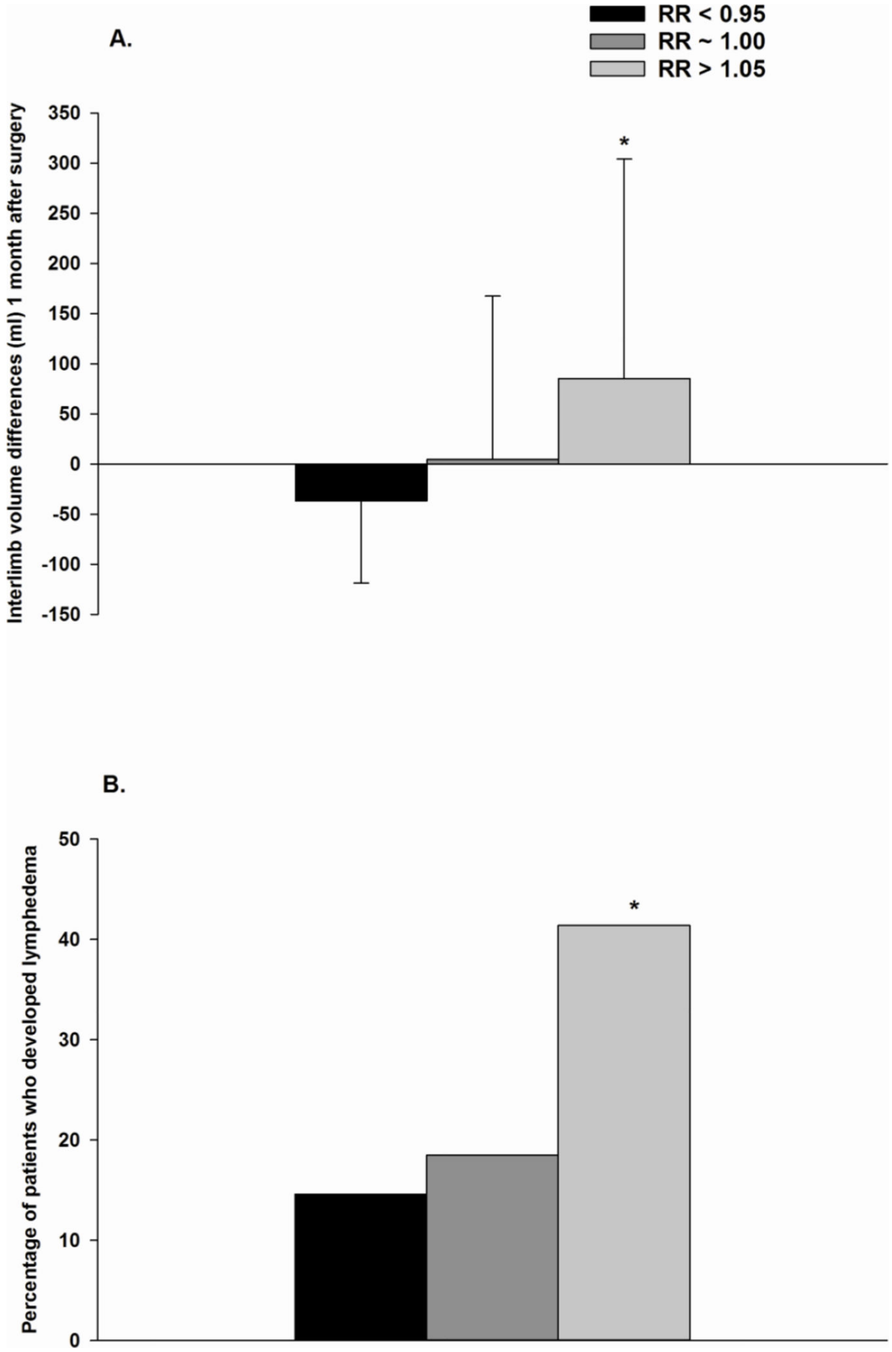

Figure 2.

A – Interlimb differences among the three resistance ratio (RR) classes assessed at 1 month following breast cancer surgery. All values are plotted as means +/− standard deviations in milliliters (ml). Compared to the other two classes, patients in the RR > 1.05 class had higher interlimb volume differences ($p < 0.001$).

B – Differences among the resistance ratio (RR) classes in the percentage of patients who developed lymphedema (LE). A higher percentage of of women in the RR > 1.05 class developed LE compared to the other two classes (X^2 = 10.01, p < 0.001)

Table 1

Fit Indices for the Latent Class Growth Model Solutions for Resistance Ratios

LCGM Solution	LL	AIC	BIC	Entropy	VLMR (df)
1-Class[a]	−9910.06	19844.13	19891.87	n/a	n/a
2-Class	−9061.30	18158.61	18229.53	.84	963.72† (6)
3-Class[b]	−8873.47	17794.95	17889.51	.85	375.66† (6)
4-Class	−8797.93	17655.86	17774.06	.87	151.09[ns] (6)

ns = not significant;

† $p < .05$

[a] Latent growth curve model with linear and quadratic components; Chi^2= 1123.20, 42 df, $p < .00005$

[b] 3-class model was selected based a significant VLMR for 3- vs 2-classes and a non-significant VLMR for 4- vs 3-classes. Further, the 4-class solution included a very small class that is unlikely to replicate to other samples (21 participants, 5.5% of the sample).

Abbreviations: AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion; df = degrees of freedom; LCGM = latent class growth model; LL = loglikelihood; n/a = not applicable; VLMR = Vuong-Lo-Mendell-Rubin likelihood ratio test for K-1 (H0) vs K classes.

Table 2

Parameter Estimates for Predicted Latent Class Growth Analysis Classes from Nine Assessments of Resistance Ratios[a]

Parameter Estimates[b]	RR < 0.95 N = 144 (37.8%)	RR ~ 1.00 N = 178 (46.8%)	RR > 1.05 N = 58 (15.3%)
	Mean (S.E.)	Mean (S.E.)	Mean (S.E.)
Intercept[c]	94.84† (0.409)	99.80† (0.608)	106.53 (0.868)†
Linear slope	0.076ns (0.135)	0.232* (0.110)	0.124ns (0.307)
Quadratic slope	−0.007ns (0.012)	−0.014ns (0.009)	−0.014ns (0.023)
Variances[d]	0	0	0

Abbreviations: ns = not significant; RR = resistance ratio; S.E. = standard error

*p<.05;

†p <.0005

[a]Trajectory group sizes are for classification of individuals based on their most likely latent class probabilities.

[b]Latent class growth analysis estimates were obtained with robust maximum likelihood.

[c]Intercept represents estimates of the resistance ratios at the one month postoperative assessment, × 100.

[d]Latent class growth analyses are fit with within-class intercept and slope variances set to zero.
This strategy was selected because models could not be estimated with growth mixture models that allowed within-class variances.

Table 3

Differences in Demographic Characteristics at Enrollment Among the Resistance Ratio Classes

Characteristic	RR < 0.95 N = 144 (37.8%)	RR ~1.00 N = 178 (46.8%)	RR > 1.05 N = 58 (15.3%)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	
Age (years)	56.0 (12.3)	54.2 (11.8)	55.2 (9.7)	NS
Education (years)	15.7 (2.8)	15.7 (2.6)	15.8 (2.9)	NS
	% (N)	% (N)	% (N)	
Lives alone				
Yes	22.5 (32)	25.4 (45)	26.8 (15)	NS
No	77.5 (110)	74.6 (132)	73.2 (41)	
Marital status				
Married/partnered	37.3 (53)	43.3 (77)	51.8 (29)	NS
Single, separated, widowed, divorced	62.7 (89)	56.7 (101)	48.2 (27)	
Ethnicity				
White	62.9 (90)	66.7 (118)	56.9 (33)	NS
Non-white	37.1 (53)	33.3 (59)	43.1 (25)	
Working for pay				
Yes	45.5 (65)	48.9 (86)	51.7 (30)	NS
No	54.5 (78)	51.1 (90)	48.3 (28)	
Annual household income below poverty level				
Yes	13.9 (16)	16.4 (24)	15.7 (8)	NS
No	86.1 (99)	83.6 (122)	84.3 (43)	

Abbreviations: NS = not significant; RR = resistance ratio; SD = standard deviation

Table 4

Differences in Preoperative Clinical Characteristics Among the Resistance Ratio Classes

Characteristic	RR < 0.95 N = 144 (37.8%)	RR ~1.00 N = 178 (46.8%)	RR > 1.05 N = 58 (15.3%)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	
Body mass index (kg/m^2)	26.8 (5.9)	26.9 (6.5)	26.6 (6.2)	NS
KPS score	93.2 (11.3)	92.7 (10.2)	94.5 (8.4)	NS
SCQ score	4.5 (3.2)	4.1 (2.6)	4.2 (2.6)	NS
Abduction ROM (degrees)				
Affected	148.7 (20.4)	150.0 (19.9)	145.3 (24.5)	NS
Unaffected	150.1 (18.3)	151.2 (18.4)	148.3 (19.5)	NS
Flexion ROM (degrees)				
Affected	166.0 (10.0)	165.5 (9.8)	163.6 (14.2)	NS
Unaffected	166.8 (8.4)	166.5 (8.4)	165.3 (14.6)	NS
Grip strength (kilograms)				
Affected	22.6 (5.5)	23.5 (6.0)	24.4 (5.9)	NS
Unaffected	24.2 (6.0)	23.4 (6.0)	23.0 (5.4)	NS
Resistance ratio	0.957 (0.078)	1.008 (0.037)	1.054 (0.045)	F = 67.46; p < 0.001 3 > 2 > 1, p < 0.001
Interlimb volume difference (ml) (affected limb – unaffected limb)	−37.00 (80.1)	16.7 (107.3)	57.1 (97.1)	F = 23.40; p < 0.001 3 and 2 > 1, p < 0.001 3 > 2, p = 0.017
	% (N)	% (N)	% (N)	
Obesity (BMI ≥30 kg/m^2)	25.5% (36)	22.5% (40)	29.1% (16)	NS
Exercise on a regular basis	68.3 (97)	70.1 (124)	72.4 (42)	NS
Postmenopausal	63.8 (88)	64.2 (113)	69.1 (38)	NS
Occurrence of comorbid conditions (% and number of women who reported each comorbid condition from the SCQ)				
Diabetes	8.3 (12)	5.1 (9)	15.5 (9)	X^2=6.65; p = 0.036; 3 > 2, p = 0.009
Heart disease	4.9 (7)	3.9 (7)	1.7(1)	NS
High blood pressure	28.5 (41)	32.6 (58)	32.8 (19)	NS
Lung disease	3.5 (5)	3.9 (7)	0.0 (0)	NS
Ulcer	2.1 (3)	4.5 (8)	5.2 (3)	NS
Kidney disease	2.1 (3)	0.0 (0)	0.0 (0)	NS
Liver disease	3.5 (5)	1.1 (2)	5.2 (3)	NS
Anemia	11.1 (16)	5.6 (10)	8.6 (5)	NS

Characteristic	RR < 0.95 N = 144 (37.8%)	RR ~1.00 N = 178 (46.8%)	RR > 1.05 N = 58 (15.3%)	Statistics
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	
Depression	22.9 (33)	19.7 (35)	20.7 (12)	NS
Osteoarthritis	21.5 (31)	14.0 (25)	17.2 (10)	NS
Back pain	31.3 (45)	26.4 (47)	20.7 (12)	NS
Rheumatoid arthritis	4.2 (6)	2.8 (5)	3.4 (2)	NS
Stage of disease				
Stage 0	17.4 (25)	14.6 (26)	15.5 (9)	
Stage I	37.5 (54)	39.9 (71)	39.7 (23)	NS
Stage IIA and IIB	38.2 (55)	36.0 (64)	34.5 (20)	
Stage IIIA, IIIB, IIIC, and IV	6.9 (10)	9.6 (17)	10.3 (6)	
Received neoadjuvant chemotherapy	16.8 (24)	23.0 (41)	22.4 (13)	NS

Abbreviations: BMI = body mass index; kg/m^2 = kilogram/meter squared; KPS = Karnofsky Performance Status; ml = milliliter; NS = not significant; ROM = range of motion; RR = resistance ratio; SCQ = Self-Administered Comorbidity Questionnaire; SD = standard deviation

Table 5

Differences in Intraoperative Characteristics Among the Resistance Ratio Classes

Characteristic	RR <0.95 N = 144 (37.8%)	RR ~1.0 0 N = 178 (46.8%)	RR >1.05 N = 58 (15.3%)	Statistics
	Mean (SD) Median (range)	Mean (SD) Median (range)	Mean (SD) Median (range)	
Number of lymph nodes removed	5.7 (7.3) 3 (0–38)	5.7 (6.4) 3 (0–35)	6.5 (6.2) 4 (0–22)	NS
Number of positive lymph nodes	0.7 (1.8) 0 (0–11)	1.0 (2.6) 0 (0–21)	1.0 (2.3) 0 (0–12)	NS
Number of drains placed during surgery	0.5 (0.7) 0 (0–4)	0.5 (0.7) 0 (0–4)	0.7 (0.8) 0.5 (0–3)	NS
	% (N)	% (N)	% (N)	
Type of surgery Mastectomy Breast conserving	21.5 (31) 78.5 (113)	17.4 (31) 82.6 (147)	29.3 (17) 70.7 (41)	NS
Cancer in the right breast	23.6 (34)	56.2 (100)	82.8 (48)	$X^2 = 67.17$, $p < 0.001$ 3 > 2 > 1, $p < 0.001$
Breast cancer surgery on dominant side	20.1 (29)	56.2 (100)	86.2 (50)	$X^2 = 83.5$, p = < 0.001 3 > 2 > 1, $p < 0.001$
Had sentinel lymph node biopsy	87.5 (126)	85.4 (152)	81.0 (47)	NS
Has axillary lymph node dissection	34.3 (49)	41.0 (73)	44.8 (26)	NS
Had reconstruction at the time of surgery	19.4 (28)	20.2 (36)	28.1 (16)	NS
Placement of surgical drain	43.1 (62)	37.9 (66)	52.6 (30)	NS

Abbreviations: NS = not significant; RR = resistance ratio; SD = standard deviation

Table 6

Differences in Postoperative Characteristics Among the Resistance Ratio Classes

Characteristic	RR < 0.95 N = 144 (37.8%)	RR ~1.00 N = 178 (46.8%)	RR > 1.05 N = 58 (15.3%)	Statistics
	% (N)	% N	% (N)	
Had any postoperative complications Yes No	 21.0 (30) 79.0 (113)	 20.9 (37) 79.1 (140)	 21.1 (12) 78.9 (45)	NS
Had a seroma Yes No	 7.0 (10) 93.0 (133)	 13.1 (23) 86.9 (152)	 10.5 (6) 89.5 (51)	NS
Had a hematoma Yes No	 9.1 (13) 90.9 (130)	 3.4 (6) 96.6 (169)	 5.3 (3) 94.7 (54)	NS
Had bleeding Yes No	 0.7 (1) 99.3 (142)	 1.1 (2) 98.9 (173)	 1.8 (1) 98.2 (56)	NS
Had a wound infection Yes No	 4.9 (7) 95.1 (136)	 4.0 (7) 96.0 (168)	 3.5 (2) 96.5 (55)	NS
Received radiation therapy during first year Yes No	 62.7 (89) 37.3 (53)	 80.3 (143) 19.7 (35)	 63.8 (37) 36.2 (21)	$X^2 = 13.82$, $p = 0.001$ (Yes) 2 > 1 and 3
Received adjuvant chemotherapy during first year Yes No	 32.4 (46) 67.6 (96)	 35.4 (63) 64.6 (115)	 43.1 (25) 56.9 (33)	NS
Received hormonal therapy during first year Yes No	 57.7 (82) 42.3 (60)	 62.9 (112) 37.1 (66)	 62.1 (36) 37.9 (22)	NS
Received biologic therapy during first year Yes No	 14.1 (20) 85.9 (122)	 13.5 (24) 86.5 (154)	 8.6 (5) 91.4 (53)	NS
Received complementary therapy during the first year Yes No	 31.7 (45) 68.3 (97)	 32.0 (57) 68.0 (121)	 34.5 (20) 65.5 (38)	NS
Received physical therapy during the first year Yes No	 20.4 (29) 79.6 (113)	 25.3 (45) 74.7 (133)	 31.0 (18) 69.0 (40)	NS
Received breast reconstruction during the first year Yes No	 7.7 (11) 92.3 (131)	 13.5 (24) 86.5 (154)	 17.2 (10) 82.8 (48)	NS
Had re-excision or mastectomy during the first year Yes No	 31.7 (45) 68.3 (97)	 30.3 (54) 69.7 (124)	 20.7 (12) 79.3 (46)	NS
Any other surgery during the first year Yes No	 14.8 (21) 85.2 (121)	 15.2 (27) 84.8 (151)	 24.1 (14) 75.9 (44)	NS
Interlimb volume differences at one month post-op (ml) (Affected limb – Unaffected limb)	−36.9 (81.9)	4.5 (162.8)	85.3 (218.8)	$F = 13.97$, $p < 0.001$ 3 > 1 and 2

Abbreviations: NS = not significant; RR = resistance ratio; SD = standard deviation