Lymphedema and Quality of Life in Survivors of Early-Stage Breast Cancer

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Background: The standard of care for early-stage breast cancer includes surgical removal of the tumor and axillary lymph node dissection (ALND). Despite increased use of breast-conserving surgery, lymphedema rates are similar to those with more radical surgery.

Hypothesis: Women who experience breast cancer–related lymphedema have a measurable reduction in quality of life compared with women without lymphedema.

Design: In a retrospective cohort study, we explored the association between lymphedema and quality of life, controlling for patient demographics, surgical factors, and treatment types.

Settings: An urban academic medical center and a community hospital.

Participants: A total of 151 women surgically treated for early-stage breast cancer (stages 0-II) were assessed at least 1 year after their ALND. The women had been treated with either conservative surgery and radiation or mastectomy without radiation.

Main Outcome Measures: Arm volume was measured by water displacement. Grip strength and range-of-motion measurements assessed arm function. The Functional Assessment of Cancer Therapy–Breast (FACT-B) quality-of-life instrument assessed breast, emotional, functional, physical, and social well-being.

Results: Lymphedema (an arm volume difference ≥200 cm³) was measured in 42 women (27.8%). Mastectomy or conservative surgery patients had similar lymphedema rates. Women with lymphedema in both surgical groups scored significantly lower on 4 of the 5 subsections than women without lymphedema, even after adjusting for other factors influencing quality of life.

Conclusions: Lymphedema occurs at appreciable rates, and its impact on long-term quality of life in survivors of early-stage breast cancer should not be underestimated.

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Eligible women had been treated with either mastectomy or breast-conserving surgery. Breast-conserving surgery was defined as a lumpectomy or segmentectomy followed by whole breast radiation therapy. Woman who had breast-conserving surgery without radiation therapy were excluded, as were women who had a mastectomy and radiation therapy. All patients had also had a standard (level I and II) axillary lymph node dissection. Patients became eligible for the study at least 1 year after their node dissection. Women were excluded from the study if they had bilateral node dissection or axillary, supraclavicular, or mediastinal node recurrence. Women who underwent neoadjuvant chemotherapy were excluded. Patients with a known neurologic or rheumatologic condition that led to self-reported significant upper extremity weakness or impairment of either arm, diagnosed before surgery or known to be unrelated to surgical therapy, were also excluded from the study.

DATA COLLECTION

During the patient’s scheduled appointment, the purpose of the study was explained and informed consent was obtained. The patient completed a quality-of-life questionnaire and then underwent measurements for arm volumes, upper extremity range of motion, and handgrip strength.

The Functional Assessment of Cancer Therapy–Breast (FACT-B) scale was used to assess quality of life. This validated, 36-item, cancer site–specific instrument includes questions regarding breast, emotional, functional, physical, and social well-being. The FACT-B uses the 5-point Likert scale (each item has a possible score of 0–4, corresponding to the phrases not at all, 0; a little bit, 1; somewhat, 2; quite a bit, 3; and very much, 4). Patients choose the number corresponding to how true each statement has been for them during the last 7 days. The scores from the 36 items are given equal weight and then summed to create a total FACT-B score. The total FACT-B score has a range of 0 to 144, with a higher number correlating to a more favorable quality of life. The breast well-being subsection addresses questions associated with adverse effects of breast cancer and therapy, such as hair loss, changes in weight, and body image. This section has 9 items, with a range of points from 0 to 36. The emotional well-being subsection asks questions regarding sadness, health outlook, and mental health (6 items; point range, 0–24). The functional well-being subsection assesses a woman’s ability to perform work and her fulfillment with work and normal hobbies (7 items; point range, 0–28). The physical well-being subsection focuses on energy, nausea, pain, and other physical adverse effects of treatment and recovery (7 items; point range, 0–28). The social well-being subsection assesses relationships with friends and family and includes questions regarding the woman’s satisfaction with her support system and her sex life (7 items; point range, 0–28). Quality-of-life measurements as assessed by the FACT-B survey were scored and interpreted in accordance with the standardized scoring protocol.

Arm volume was measured using a modification of the volume displacement technique described by Kissin et al, which has been found to be more precise than circumference measurements. Each arm was marked circumferentially at a point 15.24 cm proximal to the olecranon. The arm was then immersed slowly into a large cylindrical chamber with a sidewall runoff tube, which directed displaced water to a graduated cylinder for volume measurement. When the water level equilibrated, the arm was removed and the volume of water displaced was recorded. The water was then replaced in the tank and the measurement repeated on the other side. Lymphedema was defined as being present when the volume of the ipsilateral arm was 200 cm$^3$ or greater than that of the contralateral arm. This definition was chosen as the cutoff point for lymphedema because Kissin et al$^4$ determined that this volume difference best described lymphedema both objectively and subjectively, and it allows for comparisons with other studies also based on those original measurements.

Arm function was assessed by measuring range of motion and handgrip strength. Three aspects of shoulder movement (flexion, abduction, and rotation) were examined. Based on recommendations of the Boston University Medical Center Physical Therapy Department, shoulder movement was measured (as opposed to elbow or wrist), because limited shoulder range of motion is more common and more difficult to compensate for than limited elbow or wrist movement in patients with severe lymphedema. Results were recorded based on a scale from 1 to 6, with 1 representing almost no movement and 6 representing full comfortable motion. Handgrip strength was measured using a hydraulic hand dynamometer. The average of 3 grip strength measurements was recorded for each hand.

STATISTICAL ANALYSIS

The focus of the study was to compare women with lymphedema with women without lymphedema with respect to different aspects of quality of life. Differences between these groups were initially explored using t tests and analysis of variance for continuous variables and 2-sided $\chi^2$ or Fisher exact tests for categorical variables. Differences were further explored using stratification and multiple linear regression to adjust for confounding. A forward stepwise regression approach looked at the relationship among lymphedema, quality-of-life scores, and other variables such as age, race, body mass index (BMI) (calculated as weight in kilograms divided by the square of height in meters), menopause status, surgery type, surgery-to-measurement time, reconstruction, stage, tumor location, sidedness, chemotherapy, radiation, range of motion, handgrip strength, volume of axillary specimen removed (where available), total number of nodes dissected, and number of positive nodes. All analyses were performed using SAS statistical software (SAS Institute Inc, Cary, NC) and are presented as mean±SE.

RESULTS

One hundred fifty-one women were measured for lymphedema and completed the FACT-B questionnaire. The age at measurement was 62.4±1.0 years. The time from surgery to measurement was 4.8±0.2 years. All women had a standard level I or II axillary node dissection; the number of nodes resected was 17.1±0.5 (range, 5–36). Mastectomies had been performed in 71 women, and 80 women had been treated with breast-conserving surgery. In the mastectomy group, 26 women (36.6%) had undergone a reconstructive procedure. Lymphedema was present in 42 women (27.8%); 28.2% of women treated with mastectomy and 27.3% of women treated conservatively ($P = .90$).

The total FACT-B score reported for all 151 women was 118.9±17.0 (range, 58–144). Significant differences in total FACT-B score were seen for race, range of motion, menopausal status, BMI, lymphedema, and arm volume difference. No significant relationship was found between total FACT-B score and the type of surgery, pathologic stage, reconstruction, chemotherapy, ipsilateral arm trauma, handgrip strength, age at measurement, time from surgery to measurement, number of nodes removed, or the volume of axillary specimen removed.
EFFECTS OF RACE

For the purpose of this study, race was categorized as white or nonwhite (African American, Hispanic, Asian, and Middle Eastern). The total FACT-B score for white women was 120.3 ± 1.4 compared with 108.9 ± 4.9 for nonwhite women (P = .006). The racial differences in the FACT-B scores were primarily seen for women without lymphedema. The 99 white women without lymphedema scored 123.6 ± 1.4, whereas the 10 nonwhite women scored 113.4 ± 6.4 (P = .03). In contrast, the FACT-B scores were more similar between white and nonwhite women with lymphedema. The 33 white women with lymphedema scored 110.5 ± 3.1 on the FACT-B compared with 104.0 ± 7.7 for 9 nonwhite women with lymphedema (P = .40).

EFFECTS OF RANGE-OF-MOTION LIMITATIONS

Those with full range of motion had a total FACT-B score of 120.2 ± 1.5, whereas those with decreased range of motion had a lower total FACT-B score of 113.0 ± 3.4 (P = .04). Women who had a decreased range of motion recorded lower breast, functional, and physical well-being and total FACT-B scores. Although these relationships remained significant when looking at all 151 women, they were most pronounced among the conservative surgery patients. Two thirds of the women who had a decreased range of motion, in both the lymphedema and nonlymphedema groups, had been treated by conservative surgery.

EFFECTS OF MENOPAUSE

Quality-of-life differences were measured for premenopausal and postmenopausal women who underwent mastectomy. Premenopausal women who underwent mastectomy recorded higher emotional (P < .001) and social well-being (P < .001) and increased range of motion, in both the lymphedema and nonlymphedema groups, had been treated by conservative surgery.

EFFECTS OF BMI

Women with a higher BMI scored lower on the FACT-B questionnaire (r = −0.23, P = .005). The inverse relationship seen between BMI and quality of life was measured in the total FACT-B and the breast, functional, and physical well-being subsections.

EFFECTS OF LYMPHEDEMA

Table 1 provides quality-of-life scores for women with lymphedema and women without lymphedema. Women with lymphedema had a lower total FACT-B score: 109.1 ± 2.9 vs 122.7 ± 1.4 for women without lymphedema (P < .001). Individuals with lymphedema also scored significantly lower in each quality-of-life subsection, with the exception of social well-being. On a continuous scale, arm volume difference was inversely related to total FACT-B score (r = −0.30, P < .001).

Lymphedema was the primary independent variable of interest, but many other factors can influence quality of life in these patients. Therefore, we sought to determine other factors associated with quality of life. Table 2 summarizes differences between women with and without lymphedema. Women with lymphedema were more likely to be nonwhite (P = .04), were more likely to have experienced postsurgical ipsilateral arm trauma (P = .01), and had higher BMIs (P < .001). They also had a higher number of axillary nodes dissected (P = .04) and an increased volume of axillary tissue removed (P = .003). In addition, 38% of the women with lymphedema had a decreased range of motion compared with 13% of patients without lymphedema (P = .001). The lymphedema and nonlymphedema groups did not differ significantly with respect to age, menopausal status, pathologic stage, type of surgery, or frequency of reconstruction, radiation therapy, or chemotherapy. In addition, women with lymphedema did not have a significant reduction in handgrip strength.
Many of the factors associated with quality of life were also significantly associated with lymphedema. To better assess the independent effect of lymphedema on quality of life, we explored these associations further using multivariate analysis to control for confounding. This analysis suggested that lymphedema, nonwhite race, and postmenopausal status were independently associated with decreased quality-of-life scores. Moreover, the standardized coefficients suggested that, among these 3 factors, lymphedema had the greatest impact on quality of life (standardized β = .332 compared with .135 for postmenopausal status and .183 for nonwhite race). After adjusting for lymphedema, race, and menopausal status, neither BMI (P = .40) nor decreased range of motion (P = .40) seemed to be significantly associated with quality of life.

MULTIVARIATE ANALYSIS

The key finding of this study is that the presence of lymphedema following breast cancer surgery with axillary lymph node dissection is associated with a decreased self-reported quality-of-life score. Additionally, nonwhite race, decreased range of motion, premenopausal status, and increased BMI were associated with a decreased quality of life in the univariate analyses. Although these factors were also shown to be associated with lymphedema, multivariate analysis demonstrated that lymphedema had a significant independent effect on quality of life.

This is the first report, to our knowledge, to address the impact of lymphedema on quality of life using the FACT-B questionnaire in a population of long-term breast cancer survivors. An advantage of using this questionnaire is that it is specifically designed to assess quality of life after breast cancer therapy. This instrument is being used in other current investigative studies. Coester et al7 supplemented the FACT-B with a 4-item subscale and found in their validation study of this new questionnaire that women with lymphedema had greater arm problems and scored significantly lower than a matched sample of preoperative trial participants.

In this study, lymphedema rates were comparable in both surgical groups and equally associated with lower quality-of-life scores in both surgical groups (Figure 1).

Previous studies have compared quality-of-life differences in mastectomy patients and conservative surgery patients, using other validated surveys, and found results comparable to our own. Wapnir et al6 using the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36), found that similar quality-of-life scores were reported for women undergoing lumpectomy with axillary lymph node dissection and women undergoing mastectomy. Additionally, Poulsen et al12 found no significant psychosocial differences between women treated with conservative surgery and mastectomy, with the exception of body image being more impaired in the mastectomy group.

Our results add further support to previous reports correlating lymphedema with both physical and psychological impairment. Velanovich and Szymanski8 using the SF-36, found that women with lymphedema had quality-of-life scores that were significantly lower than the national norms in the areas of bodily pain, mental health, and general health. Maunsell et al9 used the Psychiatric Symptom Index10,11 to determine that the adjusted odds ratio for psychological distress was proportional to the number of arm problems (including swelling, weakness, limited range of motion, stiffness, pain, or numbness). Further studies9,12-21 have linked the measured physical and functional impairment to concomitant swelling, pain, weakness, stiffness, and limited range of motion. Previously reported psychological morbidity associated with lymphedema has included anxiety, depression, sexual dysfunction, disturbance of body image, and social avoidance.9,14,15,18-21

Earlier reports show that the number of women who experience lymphedema-related arm problems depends on the extent of surgery and adjuvant treatment and on the definition of lymphedema and the measurement technique. Lymphedema ranges in reported incidence from 0% with sentinel lymph node dissection22 to 56% with axillary lymph node dissection and radiation therapy to the axilla.23 In their literature review, Erickson et al24 estimated the overall incidence of lymphedema at 26%. Werner et al25 studied the elapsed time from surgery to onset of lymphedema in women treated with conservative surgery and radiation and found that 97% of the cases developed within 4 years of treatment. The mean time in our study from axillary dissection to arm measurement was 4.8 years for both surgical groups combined, so we believe that we have captured most lymphedema cases that might be expected to occur.

The frequency of lymphedema and its considerable impact on quality of life underscore the importance of vigilance by health care practitioners, particularly since functionally significant lymphedema may not be identified by cursory examination. Figure 2 shows a patient who has an appreciable arm volume difference of 543 cm³. Just 2 months before this photograph was taken, the patient had an arm volume difference of 380 cm³ (moderate lymphedema). In this short time, her lymphedema became more discernible and disruptive. Although functionally significant, even 343 cm³ of lymphedema may be difficult to detect on casual examination, particularly in a fully clothed patient. Moderate lymphedema frequently goes undetected, even though these patients have
significant reduced quality-of-life scores. These effects are likely to have a clinically significant impact on the quality of life, since a difference of 3 points in any subsection could mean a shift of response for a single question from “not at all” to “quite a bit” or a shift for 3 separate questions from an answer of “somewhat” to “quite a bit.” Taking the statement, “I am able to enjoy life” as an example, a shift from “not at all” to “quite a bit” is clinically significant. Consequently, although lymphedema may be subtle, it has a functionally significant impact on quality of life, yet without proper detection, available treatments will not be instituted. Our results show that an attempt by physicians to educate women on ways to improve their range of motion may lead to improvements in quality of life as well.

This project continues to accrue data and, with an increased sample size, future publications will further explore the risk factors for lymphedema. Learning more about the advances in the treatment of breast cancer, including new surgical techniques (sentinel node dissection) and radiation therapy techniques, may play a role in decreasing the incidence of lymphedema. With a greater understanding of the risk factors for lymphedema, the possible benefit of early detection, and the potential benefits of treatment advances, we hope to decrease rates of lymphedema and thus improve the quality of life for breast cancer survivors.

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