A Comparison of Four Diagnostic Criteria for Lymphedema in a Post-Breast Cancer Population

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ABSTRACT

Background: Breast cancer survivors are at life-time risk of developing lymphedema (LE). The goal of this research was to describe LE incidence over time among women treated for breast cancer.

Methods and Results: Limb volume changes (LVC) were evaluated by two measurement methods, circumferences and perometry, among 118 participants followed preoperative to 12 months postdiagnosis. Four diagnostic criteria were used: 200 mL perometry LVC; 10% perometry LVC; 2 cm circumferential increase; and report of heaviness or swelling, either 'now' or 'in the past year.' Using 200 mL, the estimated LE rate was 24% (95% CI = 17%–32%) at 6 months, and 42% (31%–53%) at 1 year. Using 10% LVC, the estimated LE rate was 8% (2%–13%) at 6 months, and 21% (12%–30%) at 1 year. Using 2 cm, the estimated LE rate was 46% (36%–56%) at 6 months, and 70% (60%–79%) at 1 year. Based on reported symptoms of heaviness or swelling, the estimated LE rate was 19% (11%–26%) at 6 months, and 40% (30–59%) at 1 year.

Conclusions: In the absence of a gold standard, we can only say that the different LE definitions are not equivalent, but cannot say which is 'best'. From this data, it appears that 10% LVC corresponds to a more conservative definition, whereas the 2 cm difference corresponds to a more liberal definition. These preliminary findings also document the importance of baseline (preoperative) anthropometric and symptom data and monitoring of changes over time. Further investigation of LE occurrence over an extended time period is warranted.

INTRODUCTION

The overall goal of the reported research was, using four LE diagnostic criteria, to describe the incidence (at 6 and 12 months postdiagnosis) of lymphedema (LE) among persons treated for breast cancer. Limb volume (LV) changes were evaluated by two measurement methods: (a) traditional circumferential measurement and (b) infrared perometry, at se- lected postoperative follow-up points. At the time of this longitudinal analysis, 118 participants had been followed from preoperative to 12 months postdiagnosis.[1]

Extent of the problem of LE among women treated for breast cancer

The American Cancer Society[2] reports that over 200,000 women in the United States de-

velop breast cancer annually. Although typically less than half of the two million breast cancer survivors develop LE, all survivors are at risk. LE occurs as both an acute and chronic condition in which significant and persistent swelling is associated with an abnormal accumulation of protein-rich fluid in the affected area.[3,4] This swelling often causes discomfort and disability; later cellulitis and lymphangitis often occur, predisposing the patient to systemic infection. The physical and psychological impact of LE is significant on women's daily lives.[5,6]

Quantification of LE has been problematic, despite the fact that various methods have been used to measure the lymphedematous arm.[7] Although 200 mL LV difference and 10% LV difference are documented criteria for LE diagnosis, perhaps the most common clinical criterion for diagnosis has been a finding of 2 centimeters or more difference in arm circumference between affected and nonaffected limbs.[8] In addition to objective anthropometric measurements, self-reported signs and symptoms are also identified as predictive of LE.[9]

In part because of difficulties in measurement and diagnosis, the reported incidence of LE varies greatly among women treated with surgery and radiation for breast cancer. The most recent reviews of the literature have estimated the incidence of LE from 6 to 30%[10] and from 6 to 62.5%.[11] Petrek and Heelan[10] noted that the study with the shortest follow-up (12 months) reported the lowest incidence (6%); likewise, one of the studies with the longest follow-up (11 years) reported the highest incidence. This broad statistical range of findings probably reflects major breakthroughs in breast cancer treatment, including progress in breast conservation and therapeutic combinations leading to increased survivorship;[8,12] inconsistent criteria for defining LE;[11] and small samples, retrospective analyses, and the psychometric difficulties (e.g., reliability) in assessing LE.[10,12]

Although common medical assumptions imply LE is not a significant problem of the present or future due to modern procedures such as sentinel lymph node biopsy (SLNB) and breast conservation surgical approaches, the latest data reported in 2003 reveal LE occurrence at a significant level of concern (7%–38%) in spite of these improved techniques.[6,13–16] Clinicians and researchers report modest estimates of LE following breast cancer surgery even for SLNB-only patients.[6,14–19] This group with node-negative disease (SLNB-only) represents the group at lesser risk for LE and this LE occurrence is commonly reported by clinical observation rather than objective limb measurement, posing a high probability of underrepresentation of the condition. Current protocols require further nodal dissection for node-positive disease. The incidence of LE among breast cancer patients, even using the lowest estimates for this country alone, affects hundreds of thousands of women and represents a major societal problem.

Early detection and intervention hold the greatest promise of reducing this widespread condition.[12,19] Identification of epidemiological and clinical factors associated with risk and incidence will provide the necessary foundation for preventive intervention. Before the outcomes of available treatments for the management of LE and its complications can be examined scientifically, three steps are necessary: 1) the establishment of accurate and reliable methods of measuring LV both at the point of diagnosis and for the purpose of evaluating response to treatment alternatives; 2) the determination of the incidence and prevalence across time of LE among women treated for breast cancer with current modalities; and 3) the examination across time of the frequency and impact on daily living of symptoms associated with LE. Investigations with increased precision in measurement of LE to establish its current incidence and prevalence among breast cancer survivors are crucial to the development of a program of intervention research directed at risk reduction, early detection, treatment, and management of signs and symptoms of LE.

The NIH-funded parent study for the reported findings addresses the first step (above), in the establishment of accurate and reliable measurement methods for LE at diagnosis and over time (pre- and postoperative, and quarterly and semiannual measurements through 30 months postdiagnosis). Further, the study examines the incidence and prevalence of LE (step 2), over 30 months postdiagnosis. This re-

port addresses LE findings from preoperative to 12 months postdiagnosis through comparison of four diagnostic criteria for LE. Examination over time of the anthropometric LVC measurements, LE occurrence, and reported symptoms will inform future work aimed at possible risk-reduction interventions.

Measurement issues in LE

The ideal volumetric measurement for LE would be easy to use, accessible, quick, noninvasive, hygienic, inexpensive, reliable, quantifiable, suitable for any portion of the limb, and able to provide information on shape.[7,20] Existing measures that are easy to use and inexpensive have limited reliability and do not address the functional impact of LE.[20] Limb volume measurements need to be done routinely, preoperatively as well as at follow-up. Currently, there is no standard clinical protocol (a clinical "gold standard") that is easy to use, noninvasive, and reliable for the measurement of the affected limb in the clinical setting.[21]

Although *water displacement* has been regarded as the sensitive and accurate "gold standard" for volume measurement in the laboratory setting, it is seldom used clinically because it is cumbersome and messy. Water displacement is usually applied to a certain part of the limb and does not provide data about localization of the edema or the shape of the extremity.[7,21] Moreover, a standard deviation of 25 mL for repeated measures of the arm is reported by Swedberg.[7,23] Finally, water displacement is contraindicated in patients with open skin lesions.

Circumferences at various points of a body part are used most frequently to quantify LE,[23] but several problems exist.[20] Limits for acceptable difference between repeated circumferential measurements of the normal adult arm, forearm, and wrist are 0.2 cm,[24] a standard rarely met clinically. Although circumferences may appear to be simple measures, control of intra- and inter-rater reliability is difficult. Volume calculations assume a circular circumference, which is seldom the case. Studies report correlations with water displacement ranging from 0.70 to 0.98 mL.[7,21] Because of its irregular shape, circumference of the hand is an in-

accurate way of determining volume. There are also severe limitations with this method when skin damage exists. Handling of the extremity and contact with equipment raise hygienic concerns.[7] The circumferential method is time-consuming and requires considerable experience.

The Perometer 400T/350S (Juzo, Cuyahoga Falls, OH) is an optoelectronic volumetry (OEV) device developed to meet the need for a quick, hygienic, and accurate method of LV calculation. It works similarly to computer-assisted tomography but uses infrared light instead of X-rays.[7] Dimensions along the x- and y-axes are measured to an accuracy of 10^{-4} m.[7] Transections are measured every 3 mm and summed to the volume by a computer.[7] The Perometer 400T/350S has a standard deviation with repeated measures of 8.9 mL, less than 0.5% of the arm volume.[7,21] In addition, the volume and transection of any part of the limb can be measured, the shape of the limb or limb segment can be displayed, and accurate calculations of change in volume can be made in seconds. Given the expected precision of the perometer, LE has been conceptualized as a continuous (rather than dichotomous) variable, supporting a more robust test of the link between severity of LE (measured in percent of LV difference between affected and nonaffected limbs).

Self-reported symptoms of heaviness and swelling are reported to correspond with 2 cm or greater changes in limb girth among women treated for breast cancer.[9] It has been reported that patients with LE may experience subjective symptom changes at less than 150 mL LV change.[7] Interviews using a structured symptom assessment tool to guide elicitation of symptoms have proven useful in validating LE occurrence.[9]

MATERIALS AND METHODS

This prospective, longitudinal study examined incidence, prevalence, and effects of LE among persons treated for breast cancer. In the larger NIH-funded study, researchers collected laboratory data at pre-treatment baseline and at selected post-treatment intervals with psychometrically well-developed self-report as-

sessments, face-to-face interviews, and anthropometric measures.

Sample

The nonprobability sample was made up of persons diagnosed with breast cancer (Stages I–IV) in the Midwest. Those persons (1) over age 18; (2) who had been diagnosed with and scheduled for treatment for breast cancer; and (3) with no prior history of LE or breast cancer were invited to participate prior to treatment. Participants were scheduled to be followed over 30 months. At the time of this analysis, attrition was 9 of 221 enrollees (4.1% attrition), due to withdrawal ($n = 5$), death ($n = 3$), and relocation ($n = 1$). Treatment characteristics of the sample include: 48% ($n = 106$) underwent mastectomy, 39% ($n = 86$) lumpectomy, 11% ($n = 25$) both, 1% ($n = 3$) no surgery; 60% ($n = 133$) underwent chemotherapy; 51% ($n = 113$) underwent radiation; 43% ($n = 5$) underwent SLNB, 30% ($n = 66$) axillary lymph node dissection (ALND), 11% ($n = 24$) both, 16% ($n = 35$) none. These treatment characteristics illustrate the diverse yet representative treatment in the sample.

Objective and subjective measures of LV

Background data on age, diagnosis, treatment (including node status), and co-morbidity (such as diabetes) were collected and verified through an interview using a researcher-developed instrument (LBCQ, Lymphedema Breast Cancer Questionnaire) with structured and open-ended questions, and through an examination of patients' treatment records by an oncology nurse clinician.

Circumferential measurement of LV. A specially-designed nonstretch, flexible tape measure was used for circumferences to assure consistent tension over soft tissue, muscle, and bony prominences. The tape measure was calibrated in metric units (0.1 cm divisions). Measures were made on both affected and nonaffected limbs by research nurses trained and supervised by the first author. Measurements were taken at the hand proximal to the metacarpals, at the wrist, and then every 4 cm from the wrist to axilla. Arm length (in cm) from acromion to the tip of the extended longest finger was recorded.[24(pp. 39–40)]

The effect of possible differences in size between dominant and nondominant arms, rarely addressed in the literature, and possible body mass changes over time were controlled for in this study by the use of the preoperative measurement as a baseline and serial measures of each limb. The quality of measurements made by research nurses was monitored on a regular basis. Each nurse made repeat circumferential measurements on the same volunteer subject so that intra- and inter-rater variability could be estimated. The estimated standard deviation of intra- and inter-rater measurements was consistently in the 0.10 cm–0.35 cm range.

Infrared laser perometer measurement of LV. Perometry was performed on each arm in a horizontal position. The Perometer 350S mapped a three-dimensional graph of the affected and nonaffected extremities using numerous rectilinear light beams. The perometer was interfaced with a computer for data analysis and storage. A three-dimensional image of the limb was generated from the data, and LV was calculated using a modification of the disc method.[21,26] The data were used to calculate the LV, and limb shape was displayed in seconds. This optoelectronic method was reported to have a standard deviation of 8.9 mL (arm), less than 0.5% of LV with repeated measuring. Procedures for perometry documented by the European research teams of Tierney et al.[21] and Stanton et al.[27] and modified in the preliminary work were followed. Test-retest with perometry, water displacement, and circumferences are complete, demonstrating perometry to be equally or more reliable than circumferences, as compared to water displacement.

LE and Breast Cancer Questionnaire (LBCQ-Part I). The LBCQ-Part I is a structured interview tool developed, piloted, and revised by Armer et al.[18] to assess signs and symptoms of LVC. The LBCQ was reviewed and revised by expert patient educators for clarity, simplicity of format, and complete coverage of the symptom domain. Part I consisted of 19 symptoms (e.g., "Have you had a change in how your sleeve fits?") to which patients responded to the interviewer with "yes/no" answers regarding whether the symptom was currently present

(today or within the past month) or had been present at any point in the past year.[18] Scores were calculated for the frequency of the total number of current symptoms and the total number of symptoms in the past year. LBCQ reliability was evaluated using Kuder–Richardson-20 and the test–retest method. Kuder–Richardson-20 revealed an acceptable internal consistency (r = 0.785) for all 19 items. Test–retest reliability was evaluated using a sample of healthy women without breast cancer or LE (n = 35) with a 2-hour test–retest interval using principles applied by Porock et al.[28] Findings revealed a high degree of reliability (r = 0.98).[9] Validity was confirmed through application of the self-report symptom tool in two samples to (1) differentiate healthy women and women with known breast cancer LE; and (2) predict limb swelling in a sample of breast cancer survivors with yet undetermined LE.[9] Self-report of swelling and heaviness were associated with 2 cm or greater circumferential differences between limbs among those treated for breast cancer (c = .952).[9] Frequencies of self-report of swelling and heaviness were analyzed for this report.

Procedure

Training of data collectors. Project director, research nurses, and graduate research assistants were recruited, trained, and supervised by the first author. Training in circumferential measurements was carried out by the first author and a physical therapist research team member. On-site training in perometry was carried out for the team by the certified representative of the Juzo Company, the sole distributor for the perometry equipment in this country. The first author supervised data collection.

Recruitment and retention of participants. Patients meeting the inclusion criteria were referred by surgical and medical oncologists in central Missouri. These breast cancer survivors were informed of the study through flyers and invited personally to participate by telephone or at the time of clinic visits. Written consent was obtained from those willing to participate. At the time of the analysis, the project had a retention rate of 95.9%, attributed to patient-centered recruitment and retention practices:[1] the

measuring procedure was noninvasive; there were no toxic side effects to participation; the scheduled data collection points were coordinated with the patients' routine follow-up visits; and participants earned modest financial incentives for participation, with a final bonus for completion of all data collection points. Successful strategies to maintain enrollment included newsletters, follow-up cards, and telephone contacts.

Baseline data collection. For those consenting to participate in the study, background, symptom inventory (LBCQ) and LV data were collected at the time of the preoperative (T0) and early postoperative (T1–T4) visits and verified in each subsequent visit. An easily accessible clinic room at the cancer center was used for data collection. Participants were instructed to wear or bring a loosely fitting garment with no sleeves and also given the option of changing into a patient gown. The clinic room was kept quiet during the assessment, with no bright penetrating outside light. Relative humidity was maintained at 40%–60%. Ambient temperature in the clinic room was maintained at a comfortable 26.0 ± 1.0°C during any one data collection episode. The goal was for the participant to be warm, comfortable, and relaxed, but not sleeping during the data collection.

At each lab visit, limb volume measurements were conducted successively: with perometry, circumferences, followed by the symptom inventory. Three trained research staff members collected data from each patient, under the supervision of the first author. Anthropometric and symptom data collection required approximately 45 minutes at each data point.

Data recording. Perometry data were recorded directly into computer software, which accompanied the equipment. Additionally, data on circumferences, time of day, room temperature, relative humidity, and data collectors were recorded manually on the data collection form. Self-reported data on symptoms (by interview) were manually recorded and later entered into the Excel database.

Follow-up data collection. Each participant was scheduled for future appointments to coincide with regularly scheduled quarterly visits to

their oncologists, when possible. In this way, data collection for this study was integrated into the normal appointment schedule of the patients whenever possible, which enhanced continued participation in this study. Regular quarterly newsletter mailings, holiday and birthday mailings, and appointment reminder phone calls served to maintain contact with the research team, and prompt participants regarding their scheduled appointments. Exactly the same data collection procedure used at the initial visit was used at each follow-up. LV measurements were repeated three times for each limb as described above. Whenever possible, the same data collectors carried out the follow-up measurements.

Data management and analysis. Data were entered and checked for accuracy using double entry techniques, as measurement or instrument errors may result in errors in determining who has LE. Quantitative data were analyzed with SAS[29] using the Lifetest procedure for survival analysis. Perometer estimates of LV and LVC were used. Since it is believed that there could be postoperative swelling that is not LE, only measurements for baseline (preoperative), 6-month postoperative, and 12-month postoperative visits were used in determining the onset of LE for this analysis. That is, immediate postoperative and 3-month postoperative data were not included in this analysis.

The analysis of LE incidence was not simple for a variety of reasons. One primary reason was that there was a different follow-up time for different women. Some were in the study for a short period of time and hence may not have been followed long enough to observe the development of LE. Others may have been followed for a relatively long period of time. Consequently, the data must be analyzed as a survival study. Kaplan–Meier estimates of the survival curves were obtained separately for each of the four definitions of LE. Survival analysis allows one to estimate the probability distribution of time to a specified event. Specifically the survival curve, denoted by S(t), gives the probability that the event of interest will occur later than a given time t. At time 0, the probability is 1.00 (or 100%).

The primary focus of this study was on estimating the incidence of LE. The sample size allowed for reasonable estimates of incidence rates. The incidence rate is a proportion. The estimated proportion is given both as a point estimate and as a confidence interval estimate, which reflects the 'margin of error' in the estimate. Using the standard large sample approximation for a confidence interval for a proportion and using a 95% confidence level, the confidence interval estimate is given by $\hat{p} \pm 1.96 \sqrt{\hat{p}(1 - \hat{p})/n}$, where $\hat{p}$ represents the sample proportion and n represents the sample size.

Assumptions for this analysis

Defining LE as a volume difference of 200 mL (or 10% volume difference or 2 cm girth difference) or more between sides at a given point in time or a difference within a side from the baseline value of 200 mL (or 10% volume difference or 2 cm girth difference) or more requires the baseline values be available for comparison. Similarly, symptom report relies on absence of the symptoms of interest prior to surgery (at baseline).

For 26 individuals, information on the affected side could not be used for the definition of LE due to inconsistencies in the record, such as which arm was the affected one, or due to both breasts being affected. Some participants had bilateral mastectomies or lumpectomies due to cancer or for prophylaxis, at some point in the study. Data from those with both breasts affected at some point during the study were not used for this analysis.

There were 14 participants who had a difference of 200 mL between arms at baseline (i.e., before surgery). Data from these individuals were not included in the analysis since inclusion criteria specified that no one had LE on entry in the study. These participants may have had a 200 mL difference between limbs prior to surgery for reasons other than lymphedema, but they were excluded from this analysis because they met one of the four definitional criteria before treatment began.

RESULTS

Results are reported as a series of four analyses using the four common definitions of lymphedema: 200 mL volume change; 10%

limb volume change; 2 cm limb girth change; and self-reported signs and symptoms (SS) of heaviness and swelling.

In Figure 1, a value of 1.0 means no lymphedema. The estimated probability decreases over time as more events are observed. Ideally, when an event corresponds to an undesirable outcome, one would like to see the survival curve remain high for a long time as this is indicative of fewer cases of the event occurring. The event of interest here would be meeting the definition of LE. The time until one of the four definitions was met was measured. If it was never observed, the time in the study was used in the analysis as a censored observation. Therefore, it is known that the time until LE was at least as long as was observed, but it is not known what the actual time to LE was.

Analysis 1: estimates of LE rates using 200 mL limb volume difference

As indicated above, a participant was defined to have LE at a visit if there was a volume difference between limbs of 200 mL or more or a difference (from baseline) within a limb of 200 mL or more. For this initial analysis, three criteria were examined: difference between limbs

was 200 mL or more; at least one limb had increased by 200 mL over baseline; and both limbs had increased by 200 mL over baseline.

After excluding participants who had a 200 mL difference at baseline or missing data, there were 110 for whom there was usable data. Of these, 44 developed LE (by the above definition of 200 mL difference) at some point in the study. The remaining 66 would be considered censored observations. The proportion of participants that do not have LE could be estimated by a given number of days postoperative. Key numbers in this analysis were 180 days (6 months) and 365 days (12 months). Based on these definitions and a 95% confidence interval for the estimated proportion, the estimated rate of LE at 6 mos. was 24% (17%, 32% at 95% CI), while the LE rate at 12 months was 42% (31%, 53% at 95% CI). The estimated survival curve is shown in Figure 1. Note that some of the flat spots in the graph are artifacts of the fact that the participants were only measured at 3- to 6-month intervals. This was a limitation of this analysis: the results here must be considered only approximations, since the time of the first onset of LE symptoms was not really known in the absence of daily observations.
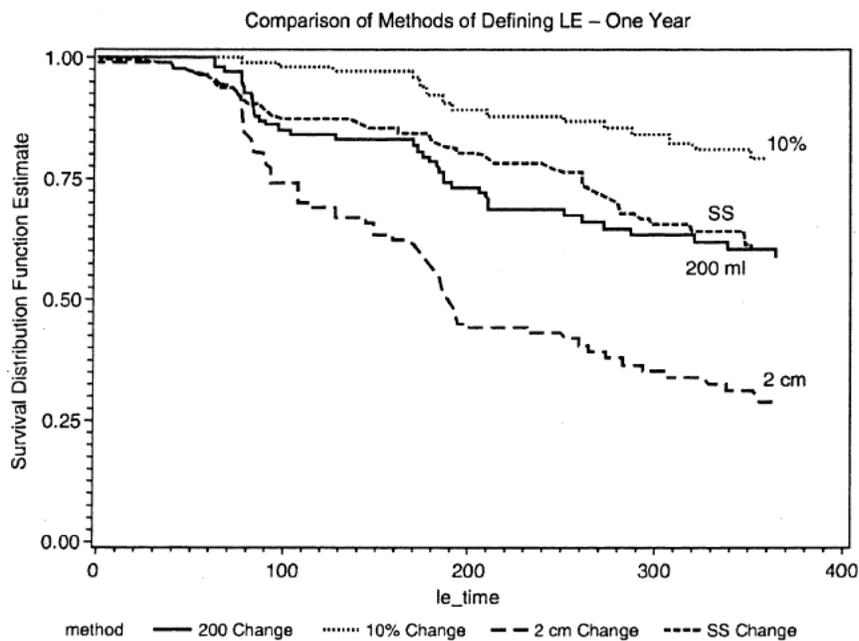

FIG. 1. Survival graph of lymphedema incidence over 12 months using four definitions.

*Analysis 2: estimates of LE rates using
10% change in limb volume*

In a continuation of the first analysis, percent volume change was used to define LE. In particular, if there was more than a 10% difference in estimated volume between arms [(larger arm-smaller arm)/smaller arm], or if there was more than a 10% increase in either arm relative to baseline [(arm now − arm at baseline)/arm at baseline], then the participant was defined to have LE. Two indicator variables were defined so the criteria that were being satisfied could be seen: the percentage difference between limbs was 10% or more; and at least one limb had increased by 10% over the preoperative baseline limb volume.

After excluding women who had a 200 mL difference at baseline or missing data, there were 110 for whom there was usable data. Of these, 23 developed LE (by the above definition) at some point in the study. The remaining 87 would be considered censored observations. Based on these definitions and a 95% confidence interval for the estimated proportion, the estimated rate of LE at 6 months was 8% (2%, 13% at 95% CI) while the LE rate at 12 months was 21% (12%, 30% at the 95% CI). The estimated survival curve is shown in Figure 1.

*Analysis 3: estimates of LE rates using
2 cm limb change*

In the third analysis, a 2 cm difference at any matched anatomical location along the arm was the observed criterion. This difference could be either between sides within a visit or could be between the same location (including side) at a particular visit and the baseline. The participants were then monitored for the first time that they met the 2 cm difference criterion for LE.

After excluding data from participants who had a 2 cm difference at baseline or missing data, there were 106 for whom there was usable data. Of these, 66 developed LE (by the above definition) at some point in the study. The remaining 40 would be considered censored observations. Based on these definitions and a 95% confidence interval for the estimated proportion, the estimated rate of LE at 6 months was 46% (36%, 56% at 95% CI), while the value for 12 months was 70% (60%, 79% at 95% CI). The estimated survival curve is shown in Figure 1.

*Analysis 4: survival analysis results for signs
and symptoms (SS) definition*

In the fourth analysis, SS were used to define LE. Following a definition based on earlier work,[9] reported symptoms of heaviness or swelling, either 'now' or 'in the past year,' were observed. Specifically, the responses to questions on the experience of swelling and/or heaviness on the Lymphedema and Breast Cancer Questionnaire (LBCQ) were reviewed.[9] If swelling and heaviness were reported "now" and/or "in the past year," then LE was defined to be present. The participants were monitored for the first time that they met the SS criteria for LE.

After excluding women who met the SS definition at baseline or missing data, there were 122 for whom we had usable data. Of these, 39 developed LE (by the above definition) at some point in the study. The remaining 83 were considered censored observations. Based on these definitions and a 95% confidence interval for the estimated proportion, the estimated rate of LE at 6 months was 19% (11%, 26%, 95% CI), while the LE rate at 12 months was 40% (30%, 59% at 95% CI). The estimated survival curve is shown in Figure 1.

CONCLUSIONS

As can be seen from the graphs showing estimated survival curves based on various definitions of LE (Fig. 1), the estimated curves are quite different. If there were a 'gold standard' for determining the occurrence of LE, then we would estimate the 'true' survival curve based on that standard. In deciding which of the four definitions of LE was 'best', we would choose the one that gave results closest to the 'gold standard'. In the absence of a gold standard, we can only say that the different definitions of LE are not equivalent but cannot say which is 'best'. From this study, it appears that definition of 10% LV change results in the curve which remains highest the longest. This would correspond to a more conservative definition of LE as fewer apparent cases of LE are detected. On the other extreme, it appears that definition of 2 cm difference results in a curve that drops the most and is lower than the others. This would correspond to a more liberal definition

of LE as more apparent cases of LE are detected. Again we emphasize that in the absence of a gold standard the terms 'conservative' and 'liberal' are used only in a relative sense.

It is impossible to state from these data alone which of these is closest to the truth, but it can be stated that these different criteria are not equivalent.

These data suggest the 2 cm criterion provides the most liberal estimate of LE occurrence, whereas the 10% LV change criterion was a more conservative LE estimate. It is also interesting to note that although the survival curve estimates based on the four different definitions differ considerably, there appears to be a general pattern in the graph that is replicated among three of the four measurements' approaches across time, with increasing observations of lymphedema as time passes (as is suggested in the current literature). Here the focus was on 6- and 12-month postoperative in comparison to preoperative baseline measurements. There is seen a convergence of observations in two of the four measurements (200 mL change and symptom report) at later time points.

Since LE is characterized by swelling that comes and goes, LE may not be detected at a given visit if the swelling is not currently being experienced. Even if swelling is detected, it likely is not the first day that the swelling has appeared. Consequently, if the time until onset of LE (as defined by any given criterion) is being measured, it is likely that the measured time is longer than the actual onset time. Because of this, estimates of the proportion of women who will experience LE at some specific point in time following surgery may be low.

Past research suggests subjective symptom report may be an early indicator of LE,[9] prior to the limb meeting objective criteria of 200 mL (or 10% volume or 2 cm) change. These data appear to support the validation of symptom report as compared to anthropometric measurements of volume change (such as the 200 mL, 10% volume, or 2 cm criteria). This criterion is validated in that it takes into account the subjective change in size of the limb.

Analysis was first carried out for the indicators of LE using the 200 mL criterion, examining visits, and not just individuals. The key finding with the 200 mL criterion was that there were 47 cases where LE was defined based on comparison to baseline values but not defined based on comparison between sides. Using the definition of a 10% change, there were 33 cases where LE was defined based on comparison to baseline values but not defined based on between side values. The 2 cm baseline-comparison definition of LE allowed 105 cases that were not defined based on bilateral comparison. These figures give some indication of the importance of having baseline values. If comparison between sides was depended on, these cases would be missed. In fact, well over half of the cases for 200 mL change (47 out of 93), 10% change (33 out of 48), and 2 cm change (105 out of 179) were diagnosed due to baseline comparison.

Of the 35 visits that had differences from baseline of 200 mL in both arms, 10 also had a difference of 200 mL between arms. Next it was found that among all cases where participants were measured (after the postoperative visit) about 20% of the time the LE criterion of 200 mL change was met. Among all cases where participants were measured (after the postoperative visit), about 10% of the time the LE criterion of a 10% change in volume was met. However, there were more early visits included in these numbers than later visits. It may be that LE was more likely to show up at later visits. It is seen from this data that the 10% LV change criterion is harder to meet than the 200 mL change and hence results in considerably lower estimates of the prevalence of LE.

In summary, these preliminary findings document the importance of baseline anthropometric and symptom data and monitoring of changes over time. These findings also reveal differences and similarities among the four diagnostic criteria applied to assess LE occurrence. Further investigation of LE occurrence over an extended period of time is warranted.

ACKNOWLEDGMENTS

Columbia, our clinical collaborators at Ellis Fischel Cancer Center, and the participants in this study who have taught us so much.

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