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Lymphedema In Ovarian Cancer Survivors: Assessing Diagnostic Methods And Risk Factors

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By

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Abstract

Purpose: Lymphedema is a poorly understood but significant side effect of treatment for gynecologic cancer. We sought to determine the prevalence of lower limb lymphedema (LLL) in a sample of ovarian cancer survivors via three different diagnostic methods while also evaluating the agreement between each method and assessing potential risk factors for LLL. ***Methods:*** LLL was measured via self-report questionnaire, optoelectric perometry, and evaluation by a certified lymphedema specialist in women (n = 48) who had completed treatment for their ovarian cancer and were physically inactive. ***Results:*** LLL prevalence ranged from 19-42% depending on the diagnostic method, with the self-report questionnaire and the lymphedema specialist evaluation having the highest agreement ($\kappa = 0.646$). No risk factors were significantly associated with LLL, although there was a trend towards higher total body fat and BMI among those with LLL versus lower body fat and BMI among those without LLL. ***Conclusion:*** There is a strong need for further research, given that the prevalence of LLL could be as high as 42 percent among women treated for ovarian cancer.

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Introduction

Ovarian cancer represents a significant number of gynecological cancers in the United States, accounting for more than 20,000 cases per year.[1] It is the fourth most frequent cause of cancer death in women, after lung, breast, and colorectal cancer.[2] It is difficult to treat, as patients frequently present late in the course of the disease, which may be asymptomatic until advanced stages. The five year survival for stage I ovarian cancer is over 90 percent, but is only 25 percent for women with stage IV ovarian cancer.[1] Unfortunately more than 60 percent of ovarian cancers are diagnosed at stage IV, which portends a poor prognosis and represents the majority of the estimated 15,000 deaths in 2007.[1,2]

The current standard treatment of ovarian cancer is to optimally remove the tumor surgically and follow with adjuvant chemotherapy. Standard initial therapy most often is five to six courses of systematic chemotherapy with a platinum and taxane regimen. This treatment approach results in a complete clinical response to therapy in 70-80 percent of patients with advanced stage disease.[3] Despite the often seen dramatic clinical response to treatment, the disease will recur in 60-85 percent of patients diagnosed with advanced disease.[1] Unfortunately, no proven curative therapy exists for this group of patients, and the optimal treatment approach for those who relapse after initial treatment remains unknown. However, a growing number of new chemotherapeutic agents for recurrent advanced ovarian cancer have been successful at stabilization of disease and thus are increasing length of survival of women with recurrent ovarian cancer. In turn, the goals of treatment for women with ovarian cancer are to maximize survival and disease-free intervals and to improve quality of life.

Each year, thousands of ovarian cancer patients and survivors will develop and endure the side effects of their cancer, which negatively affect their quality of life. One such side effect, lymphedema, is a debilitating, chronic condition that causes localized swelling when lymph vessels

become blocked, occurring after surgery and treatment for various cancers.[4] Given that the surgical treatment of ovarian cancer often involves removal of the lymph beds in the pelvic sidewalls and para-aortic area, the risk of lower limb lymphedema (LLL) is high.[7] However, few women diagnosed with ovarian cancer know that they are at risk for LLL, and few gynecological oncologists discuss this potential side effect with their patients when discussing treatment for their cancer.[12] Therefore, currently, most women are only referred to a lymphedema specialist when they complain of swelling and pain, signs that LLL may already be occurring.

To date, the majority of research on lymphedema has occurred primarily in patients treated for breast cancer.[5] Existing research on LLL in ovarian cancer patients is extremely limited, with only three published studies. Of the three studies that have examined LLL in women diagnosed with ovarian cancer, all have been retrospective chart reviews examining prevalence of LLL based on a singular diagnostic method.[8-12] These retrospective chart reviews have reported LLL prevalence rates ranging from 7-38 percent. The variation in these reported prevalence rates are the result of different measurement techniques used in each of the studies. Beyond these retrospective chart reviews, no current estimate exists on the prevalence of LLL based on a prospective method, using objective and valid measures that clinicians can use to help guide them to identify those most at risk for developing LLL. The current gold standard for measuring lymphedema is evaluation by a trained lymphedema specialist, although most recently diagnosis via optoelectric perometry has become increasingly common.[13] Previously, a self-report questionnaire has been developed to assess lymphedema in breast cancer patients,[14] providing a quick, low cost method to collect information on a large sample of patients. However, the validity of this questionnaire has not been assessed in ovarian cancer patients.

Due to the limited number of studies, data on the prevalence of LLL in ovarian cancer patients is inadequate as is data on effective treatment of LLL in this population. Improving our

knowledge would help guide clinicians in diagnosing and treating LLL. The purpose of this study was to determine the prevalence of LLL via perometry, self-report questionnaire and an evaluation by a certified lymphedema specialist in a sample of ovarian cancer survivors and to determine risk factors for LLL. A second purpose of our study was to determine the validity of a LLL self-report questionnaire and optoelectric perometry against the lymphedema specialist evaluation.

Methods

Study Participants

Women diagnosed with ovarian cancer (stage I-IV) were recruited as part of an NCI-funded (CA R01 138556) study entitled, "The Women's Activity and Lifestyle Study in Connecticut (WALC)." The WALC study is a randomized controlled trial in physically inactive ovarian cancer survivors examining the impact of a moderate-intensity aerobic exercise intervention (vs. attention control) on overall quality of life, body composition, and serum hormones possibly associated with physical activity and ovarian cancer prognosis.

Women diagnosed with ovarian cancer between the years of 2007 and 2013, were identified from the Rapid Case Ascertainment (RCA) Shared Resource of the Yale Cancer Center, a field arm of the Connecticut Tumor Registry. After Connecticut Department of Public Health and hospital IRB approvals, RCA identified women diagnosed with ovarian cancer at 23 Connecticut hospitals. After study staff initially contacted the women's physician for consent to contact the patient, potential participants were contacted individually and invited to participate in the WALC study, once eligibility was established (see Table 1). Women who contacted study staff without having received a letter of invitation were invited to participate once eligibility had been verified and upon written approval by their physician allowing them to participate in a moderate-intensity exercise program. All women were under the age of 75, had completed adjuvant treatment at least one month prior to

randomization, and were diagnosed within the past four years. They each exhibited a sedentary physical activity pattern (< 90 min/week of moderate-intensity exercise).

Baseline Measures

Baseline visits were scheduled with all new participants, either at their home or in the WALC research center, at which point baseline characteristics, including treatment characteristics were collected via interview-administered questionnaires by WALC research staff. Within one week of completing the initial baseline visit, study participants visited the Smilow Cancer Hospital at Yale-New Haven to receive a physical exam to collect physical characteristics (height, weight, BMI), receive a full-body dual-energy X-ray absorptiometry (DEXA) scan to measure total and percent body fat, and where the initial lymphedema evaluation was completed.

Lower limb lymphedema was assessed using the Norman Lymphedema Survey, a self-administered questionnaire. The Norman Lymphedema Survey is a multi-section survey created to evaluate lymphedema that has been validated in breast cancer survivors.[14] The sections focused on lower limb lymphedema, asked women if they had observed differences in their feet, lower (ankle to knee) legs, upper (knee to hip) legs, and abdomen following treatment for ovarian cancer. The questionnaire also asked about the frequency of these differences, and whether medical evaluation and treatment had been sought when differences were seen. Importantly, the questionnaire also asked women if they had ever been informed about lymphedema previously.

During the baseline visit, an optoelectric perometer test measuring leg volume conducted by a trained lymphedema specialist was also used to assess LLL. The perometer (1000M Perometer: Juzo, Cuyahoga Falls, OH) measures circumference transections every 3mm and sums these to a volume using a computer. It has been evaluated extensively for validity and reliability, with one recent study finding both high intra-rater reliability (ICC = 0.989, 95% CI: 0.98-0.99) and inter-rater

reliability (ICC = 0.993, 95% CI: 0.99-1.01) when compared to other volumetric assessments for lymphedema.[13,15] With the participant standing, leg volume was measured once for each leg. Prior to the assessment, women removed all clothing and jewelry from the area.

Following the perometer measurement, the specialist conducted his own lymphedema assessment. Women were asked if they had any history of swelling in their legs prior to surgery, and any perceived changes in leg swelling following surgery. They were also asked if swelling occurred with physical activity and if any changes in leg appearance were seen in the morning compared to later in the day. Palpations assessing for pitting or induration were performed on both legs and compared. The specialist also conducted a visual assessment of both legs, notably looking for differences at the dorsum of the foot, toes, and ankles.

Defining Lymphedema

Using the results of the self-report questionnaire, lymphedema was defined as seeing any regular difference in limb/abdomen appearance, compared to the other leg/side of abdomen and/or to appearance prior to treatment for ovarian cancer. This was based on the four main questions in the survey asking about differences in the women's feet, lower and upper legs, and abdomen.

Using the optoelectric perometer assessment, lymphedema was defined as having five percent or more inter-limb volume discrepancy. This was based on standard definitions set forth by the International Society of Lymphology, defining mild lymphedema as five percent or more limb volume difference, moderate lymphedema as 10-30 percent discrepancy, and severe lymphedema as more than 30 percent discrepancy.[16]

The lymphedema specialist categorized lymphedema as either lymphedema occurrence or no lymphedema occurrence. Using his visual inspection and palpations, the specialist defined no lymphedema as: no pitting, no palpable induration, no patient-reported history of swelling (with and

without physical activity), no patient-reported appearance change between pre- and post-treatment, and no visual differences in appearance at assessment.

Statistical Analysis

We performed descriptive statistics to describe the characteristics of our study population. To assess agreement between the three diagnostic methods simple kappa (κ) statistics were calculated. A simple kappa statistic was used to measure the level of agreement, and the degree of disagreement, with a maximum value of 1 (perfect agreement) and values great than 0.75 suggest strong agreement.[14] Optoelectric perometer and self-report questionnaire results were compared to results of the lymphedema specialist evaluation, as the gold-standard diagnosis method. Because of the small sample size, logistic regression models could not be used to identify risk factors for LLL. Instead we conducted an analysis of the means of all continuous variables, using a Student's t-test to compare those diagnosed with lymphedema to those without lymphedema, for the various diagnostic methods. A continuous variable, "total number of surgical procedures" was created, to account for the various surgical procedures that the women could have received as part of their ovarian cancer treatments. These surgical procedures included total abdominal hysterectomy, bilateral salpingo oophorectomy, omenectomy, lymph node removal, tumor debulking, bowel resection, and colon resection, as well as any other surgery that they might have undergone as part of their treatment. Fisher's exact tests were run to evaluate differences among the categorical variables. P-values were two-sided and $p < 0.05$ was used as the threshold for statistical significance. All statistical analyses were conducted using SAS 9.3 (Cary, North Carolina).

Results

Participant Characteristics

A total of 83 women completed the baseline evaluations as part of the WALC study. Forty-eight women (57.8%) received *all* three of the lymphedema diagnostic evaluations (self-report questionnaire, optoelectric perometer, lymphedema specialist evaluation), limiting our analyses to these women. Demographic and clinical characteristics of the study participants are depicted in Table 2. The age of participants ranged from 41-71 years, with a mean of 56.1 years (SD: 7.2). The majority of participants were non-Hispanic white (95.8%) and had at least a high school diploma (95.8%). The body mass index (BMI) of study participants ranged from 19-52 kg/m^2, with an average of 30 kg/m^2 (SD: 7.9). Fifty percent of study participants reported having heard of the condition of lymphedema before participating in the study.

The time since diagnosis ranged from 7 months to 48 months, with an average of 17.6 months since diagnosis. The majority of women had been diagnosed with stage III (41.7%) ovarian cancer or later. Forty-six percent of women in the study were diagnosed with localized (stage I or II) ovarian cancer, much higher than the national average of 15 percent.[1] Nearly all of the women had received chemotherapy as part of their cancer treatment (91.7%), and a small minority of the women (16.7%) had experienced recurrence of their ovarian cancer.

In terms of surgical treatments for their ovarian cancer treatment, nearly every woman had a total-abdominal hysterectomy (95.8%), a bilateral salpingo oophorectomy (95.8%), an omenectomy (95.8%), and a local lymph node dissection (91.7%). Of the 33 percent of women who reported having 'other' surgery (n=15) related to their ovarian cancer treatment, 60 percent of surgeries were appendectomies.

Prevalence of Lower Limb Lymphedema

Lower limb lymphedema diagnosis ranged from 19 percent to 23 percent across the various diagnostic methods individually. Twenty-three percent of women (n=11) in our study were diagnosed with LLL via the trained lymphedema specialist evaluation. Among the 23 percent of women (n=11) who were diagnosed via the self-report questionnaire, six women saw lymphedema-like symptoms in their feet, seven saw symptoms in their lower legs, one saw symptoms in her upper leg, and four saw symptoms in their abdomen area. Four women reported lymphedema-like symptoms in multiple regions of their lower limbs. Nineteen percent of women (n=9) were diagnosed via the optoelectric perometer. Of these women, the inter-limb difference ranged from five to nine percent, with an average inter-limb difference of 6.1 percent, indicating that all women would be classified as having mild lymphedema. Forty-two percent of women (n=20) had LLL diagnosis by at least one of the three diagnostic methods, while *zero* study participants had diagnosis by *all* three methods. Prevalence results are summarized in Table 3.

Diagnostic Method Agreement

The self-report questionnaire showed stronger agreement ($\kappa = 0.646$) with the lymphedema specialist evaluation diagnosis compared to the agreement of the optoelectric perometer with the lymphedema specialist evaluation ($\kappa = 0.011$). Hence, neither method met the kappa statistic threshold for strong agreement with the gold standard, the lymphedema specialist evaluation. The comparison of the self-report questionnaire and the optoelectric perometer produced a negative kappa statistics ($\kappa = -0.121$), indicating no agreement between the two methods. Eight of the 11 women (72.7%) diagnosed by the lymphedema specialist were *also* diagnosed by the self-report questionnaire. Comparatively only two of the 11 women diagnosed by the lymphedema specialist (18.2%) were *also* diagnosed by the optoelectric perometer. Only one woman was diagnosed with

LLL by both the self-report questionnaire *and* the optoelectric perometer (out of the 19 women who were diagnosed by either method).

Analysis of Potential Risk Factors

Tables 5-10 summarize the differences in age, BMI, total body fat, percent body fat, time since diagnosis, and number of surgical procedures between those diagnosed with LLL and those not diagnosed with LLL, based on the various diagnostic methods. No statistically significant differences were observed between the two groups among any of the potential risk factors independent of diagnostic method. However, those without LLL were consistently found to have a longer time since diagnosis in every comparison, across all diagnostic methods. Total body fat was found to be higher among those with LLL in five of the six comparisons. Similarly, age, BMI, and percent body fat were found to be higher among those with LLL in four of the six comparisons. No statistically significant differences in stage at diagnosis, chemotherapy as part of treatment, and ovarian cancer recurrence were detected between the two groups.

Discussion

We found that the prevalence of lower limb lymphedema in ovarian cancer survivors ranged from 19 to 42 percent depending on the diagnostic method used. Individually, the three diagnostic methods evaluated, self-report questionnaire, optoelectric perometer, and lymphedema specialist evaluation, each found a prevalence of LLL of about 20 percent, but when used collectively found a prevalence of 42 percent. The self-report questionnaire had a much higher agreement with the gold standard evaluation by a trained lymphedema specialist than the agreement between the optoelectric perometer and the evaluation by a trained lymphedema specialist, although neither achieved strong agreement (defined as a kappa statistic of 0.75 or higher). Those with LLL were consistently found

to have a shorter time since diagnosis across all diagnostic measures compared to women without LLL, although this trend was not statistically significant. Also of interest was the fact that only 50 percent of our study population had heard about lymphedema, and only 60 percent of those diagnosed with lymphedema via any diagnostic method had previous knowledge about the condition prior to study participation.

The prevalence differences observed from using the different diagnostic methods indicate the limitations of each method, even the gold standard method, evaluation by a lymphedema specialist. While the self-report questionnaire is easy and quick to administer, it remains a subjective evaluation of LLL that has not been validated before for LLL or in gynecologic cancer survivors. Our findings represent initial validation for the questionnaire in this population, and indicate that it may be a preferable diagnostic method when compared to the perometer. Unlike the questionnaire, the perometer does provide an objective measurement of limb volume on which to base LLL diagnosis. Furthermore, it can detect even very small differences in limb volume that are symptomatic of lymphedema, which may be overlooked by even the lymphedema specialist. However, it is severely limited by the fact that it is unable to diagnose lymphedema in women who are experiencing LLL in both legs. For these women who would be experiencing swelling in both legs, the perometer would fail to identify a meaningful inter-limb volume difference needed to diagnose LLL. Additionally, the perometer would fail to identify LLL that may be occurring in a woman's abdomen because it is limited to the measurement of limb volume. This may be why the optoelectric perometer had such a low agreement with both of the other diagnostic methods. The lymphedema specialist evaluation remains the likely gold standard because it takes both subjective factors, like patient-reported history of swelling, and objective factors, like induration and pitting, into consideration in diagnosing LLL, but the evaluation is a time-intensive process. The reasonably

high agreement of the self-report questionnaire with the lymphedema specialist indicates that with further validation the self-report questionnaire could be a useful tool in diagnosing LLL.

Previous literature on LLL has found a prevalence of LLL of 7-38 percent in women following treatment for ovarian cancer. All of these studies evaluated LLL through retrospective chart reviews of clinically diagnosed lymphedema via different singular diagnostic methods, a limitation of their findings. These previous results are similar to those seen in the study reported here, a LLL prevalence ranging from 19-42 percent. One previous study found that elevated BMI, at levels consistent with being overweight (BMI of 25-30) or obese (BMI greater than 30), was a strong risk factor for LLL among gynecologic cancer survivors.[12] While our results were not statistically significant, the trend towards higher BMI, percent body fat and total body fat among those with LLL in our study supports this finding. These findings are consistent with literature published about upper limb lymphedema following treatment for breast cancer which has been shown to be strongly associated with greater body weight and higher BMI.[17,18] Previous research has also shown an association between lymph node dissection and LLL, as well as post-operative radiation and LLL.[10] Unfortunately because more than 90 percent of the women in our study received a lymph node dissection as part of their treatment, we had very limited power to detect an association between lymph node removal and LLL in our study. Interestingly, previous research has also shown a general lack of knowledge among patients about lymphedema related to gynecologic cancer treatment,[12] supporting our finding that only 50 percent of our study population had been informed about the condition previously. This represents a deficiency in the current standard of care, particularly if LLL prevalence could be as high as 40 percent.

The finding of an association between lymph node dissection as part of cancer treatment and LLL in previous literature provides insight into the mechanism behind lymphedema occurrence. While no specific literature has been published on the mechanism for LLL related to gynecologic

cancer, previous research has illustrated the mechanism for lymphedema following treatment for breast cancer. When lymph node dissection is performed it can disrupt the flow of lymph through the lymphatic system. This can cause lymph vessels to become congested and dilated, resulting in lymph accumulation in the limbs.[19] Steady accumulation of the lymph fluid, and the failure of reparative and compensatory mechanisms in the body, like lymphatic regeneration, is consistent with lymphedema.[19] Because similar lymph node dissections in the pelvic area are required for treatment of ovarian and other gynecologic cancers, it is probable that LLL follows a similar mechanism. Furthermore, whereas most breast cancers are diagnosed at stage I, before they have metastasized to local lymph nodes, most ovarian cancers are diagnosed at stage III and IV, once the cancer has already spread to local lymph nodes.[1] Thus lymph node dissection is more likely to be required as part of treatment for ovarian cancer, illustrated by the fact that more than 90 percent of the women in our study received lymph node dissection, increasing the risk for lymphedema occurrence.

Our study was the first study to look at LLL prevalence in ovarian cancer survivors utilizing multiple diagnostic methods. While previous studies calculated LLL prevalence via retrospective chart reviews, which was diagnosed by various singular methods, ours used the latest diagnostic standards to assess LLL in ovarian cancer survivors, as they were experiencing symptoms, likely a better measure of LLL prevalence. Furthermore, because each participant was evaluated using all three diagnostic measures, our prevalence findings may be more accurate, because they overcome many of the limitations associated with each diagnostic method individually, such as the failure of the optoelectric perometer to diagnose LLL when it is occurring in both legs. These findings indicate that diagnosis via multiple methods may be the most accurate way of diagnosing LLL, as this may be the best way to detect lymphedema symptoms in the entire leg from abdomen to feet and even in the mildest forms.

However, limitations of our study need to be considered when interpreting our results. While the cross-sectional design was sufficient to assess LLL prevalence, causality between our hypothesized risk factors and LLL was not possible to infer. This was furthered by our small sample size, which limited our ability to detect significant differences between those with and without LLL. Future studies should focus on looking at lymphedema incidence, to better quantify the risk of LLL among ovarian cancer survivors. Furthermore, a prospective cohort design, rather than a cross-sectional design, should be utilized comparing limb appearance and volume pre-and post-treatment for ovarian cancer in order to more accurately measure LLL occurrence, and allow for a better evaluation of potential risk factors.

Conclusion

Among ovarian cancer survivors the prevalence of LLL ranged from 19-42 percent. The fairly high diagnostic agreement between the self-report questionnaire and the lymphedema specialist evaluation indicates the usefulness of the self-report questionnaire in diagnosing LLL. Similarly the low agreement of both of those methods with the optoelectric perometer, illustrates the major limitation of the perometer, that it cannot diagnose LLL when it is occurring in both legs simultaneously or in the abdomen. While our study did not identify any significant risk factors associated with LLL, the trends towards higher BMI and body fat in those with LLL are consistent with previous literature and warrant further study. Despite the fairly high prevalence of LLL that we found, only about half of the women in our study had heard of lymphedema prior to participation indicating a large information gap. The lack of significant literature on the subject on LLL in ovarian cancer survivors, and related to gynecologic cancers in general, indicates a strong need for further research, particularly if the prevalence of LLL could be as high as 42 percent among women treated for these cancers.

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Table 1. WALC Study Eligibility Criteria

- Ages 18-75 at the time of initial contact
- AJCC Stage I-IV invasive epithelial ovarian cancer
- Completed adjuvant therapy (i.e. chemotherapy and/or radiation therapy) at least one month prior to enrollment
- Diagnosed within the past four years
- Physically able to exercise and physician consent given to start an exercise program
- Sedentary activity pattern (< 90 min/week of moderate-to-vigorous recreational physical activity)
- Agreed to be randomly assigned to either the exercise or health education groups
- Able to travel to New Haven for a baseline and a six-month visit
- Accessible by phone
- English speaking
- No recent (within the past 6 months) history of stroke or myocardial infarction

Table 2. Baseline Characteristics of Study Participants[a]

Characteristic	Total Patient Population (n=48)[b]
Age (years)	56.1±7.2
BMI (kg/m^2)	30.0±7.9
Total Body Fat (kg)	31.2±12.1
Percent Body Fat (%)	39.9±5.1
Race/ethnicity	
Non-Hispanic White	46 (95.8)
Black	0
Hispanic	2 (4.2)
Time since diagnosis (months)	17.6±9.8
Stage at diagnosis	
Stage I	10 (20.8)
Stage II	12 (25.0)
Stage III	20 (41.7)
Stage IV	6 (12.5)
Education	
Some high school	2 (4.2)
High school graduate	6 (12.5)
Some college	12 (25.0)
College graduate	13 (27.1)
Graduate school	15 (31.3)
Surgical procedure	
Total abdominal hysterectomy	46 (95.8)
Bilateral salpingo-oophorectomy	46 (95.8)
Omenectomy	46 (95.8)
Lymph node removal	44 (91.7)
Tumor debulking	20 (41.7)
Bowel resection	6 (12.8)
Colon resection	4 (8.3)
Other surgical procedure	15 (32.6)
Total number of surgical procedures[c]	4.7±1.2
Chemotherapy	44 (91.7)
Ovarian cancer recurrence	8 (16.7)

[a] Table values are mean ± SD for continuous variables and n (column %) for categorical variables. For surgical procedure, values are the number of subjects who received that procedure (% of subjects).

[b] Numbers may not sum to total due to missing data, and percentages may not sum to 100% due to rounding

[c] Total number of surgical procedures is defined as total number of surgical procedures received related to ovarian cancer diagnosis

Table 3. Prevalence of Lower Limb Lymphedema[a] (n=48)

Optoelectric Perometer	Lymphedema Specialist	Self-report Questionnaire
9 (18.8)	**11 (22.9)**	**11 (22.9)**
Diagnosis via perometer -or- lymphedema specialist: 18 (37.5)		
	Diagnosis via self-report questionnaire -or- lymphedema specialist: 14 (29.2)	
Any diagnosis of lymphedema: 20 (41.7)		

[a] Table values are the number of subjects diagnosed with lymphedema by that method (% of subjects)

Table 4. Agreement of the Self-Report Questionnaire and Optoelectric Perometer with the Lymphedema Specialist Evaluation

Self-Report Questionnaire	Optoelectric Perometer
κ = 0.646 [0.387,0.905]	**κ = 0.011 [-0.278, 0.300]**
Self-report questionnaire vs. optoelectric perometer	
κ = -0.121 [-0.354,0.113]	

Table 5. Comparison of Means (Diagnosis via Any Method)[a]

Characteristic	LLL (n=20)	Non-LLL (n=28)	p[b]
Age (years)	**56.7±7.1**	55.7±7.4	0.66
BMI (kg/m^2)	**31.4±7.6**	29.1±8.2	0.34
Total body fat	**33.8±10.0**	29.7±13.1	0.32
Percent body fat	**40.5± 4.1**	39.6±5.8	0.62
Time since diagnosis (months)	15.6± 8.1	**19.0±10.8**	0.24
Number of surgical procedures	4.6±1.4	**4.8±1.2**	0.55

[a] Table values are mean ± SD

[b] p-value is for t-test comparing statistical difference between the two groups

Table 6. Comparison of Means (Diagnosis via Lymphedema Specialist Evaluation)[a]

Characteristic	LLL (n=11)	Non-LLL (n=37)	p[b]
Age (years)	**57.5±7.0**	55.7±7.3	0.49
BMI (kg/m^2)	**30.1±7.5**	29.9±8.2	0.95
Total body fat (kg)	**32.7±9.5**	30.9±12.7	0.72
Percent body fat	**40.0±4.2**	39.9±5.4	0.97
Time since diagnosis (months)	15.3±8.8	**18.3±10.2**	0.39
Number of surgical procedures	**4.8±1.2**	4.7±1.3	0.79

[a] Table values are mean ± SD

[b] p-value is for t-test comparing statistical difference between the two groups

Table 7. Comparison of Means (Diagnosis via Self-Report Questionnaire)[a]

Characteristic	LLL (n=11)	Non-LLL (n=37)	p[b]
Age (years)	**58.6±8.5**	55.4±6.8	0.19
BMI (kg/m^2)	28.5±7.1	**30.4±8.2**	0.49
Total body fat (kg)	30.8±9.3	**31.3±12.9**	0.92
Percent body fat (%)	38.9±3.8	**40.2±5.5**	0.52
Time since diagnosis (months)	14.9±8.6	**18.3±10.1**	0.34
Number of surgical procedures	**4.8±1.2**	4.7±1.3	0.79

[a] Table values are mean ± SD

[b] p-value is for t-test comparing statistical difference between the two groups

Table 8. Comparison of Means (Diagnosis via Optoelectric Perometer)[a]

Characteristic	LLL (n=9)	Non-LLL (n=39)	p[b]
Age (years)	53.2±5.0	**56.8±7.6**	0.19
BMI (kg/m^2)	**34.5±7.3**	29.1±7.8	0.08
Total body fat (kg)	**35.5±11.1**	30.4±12.2	0.35
Percent body fat (%)	**41.4±4.1**	39.6±5.3	0.43
Time since diagnosis (months)	16.5±7.7	**17.8±10.3**	0.71
Number of surgical procedures	4.4±1.5	**4.8±1.2**	0.45

[a] Table values are mean ± SD

[b] p-value is for t-test comparing statistical difference between the two groups

Table 9. Comparison of Means (Diagnosis via Lymphedema Specialist Evaluation -or- Self-Report Questionnaire)[a]

Characteristic	LLL (n=14)	Non-LLL (n=34)	p[b]
Age (years)	**57.4±7.9**	55.6±7.0	0.45
BMI (kg/m^2)	29.9±7.0	**30.0±8.4**	0.96
Total body fat (kg)	**31.9±8.7**	31.0±13.2	0.85
Percent body fat	39.6±3.8	**40.0±5.6**	0.81
Time since diagnosis (months)	14.4±8.1	**18.9±10.2**	0.16
Number of surgical procedures	4.7±1.2	4.7±1.3	0.96

[a] Table values are mean ± SD

[b] p-value is for t-test comparing statistical difference between the two groups

Table 10. Comparison of Means (Diagnosis via Lymphedema Specialist Evaluation -or- Optoelectric Perometer)[a]

Characteristic	LLL (n=18)	Non-LLL (n=30)	p[b]
Age (years)	56.0±6.6	**56.2±7.7**	0.94
BMI (kg/m^2)	**31.5±7.8**	29.1±8.0	0.33
Total body fat (kg)	**34.2±10.3**	29.8±12.8	0.31
Percent body fat	**40.7±4.2**	39.5±5.6	0.53
Time since diagnosis (months)	15.9±8.2	**18.7±10.7**	0.36
Number of surgical procedures	4.6±1.3	**4.8±1.2**	0.61

[a] Table values are mean ± SD

[b] p-value is for t-test comparing statistical difference between the two groups