Published in final edited form as:

Int J Gynecol Cancer. 2014 October ; 24(8): 1507–1512. doi:10.1097/IGC.0000000000000226.

Swelling among women who need education about leg lymphedema (SWELL): A descriptive study of lymphedema in women undergoing surgery for endometrial cancer

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Abstract

Objectives—In addition to hysterectomy and bilateral salpingo-oophorectomy, comprehensive surgical staging for endometrial cancer includes pelvic and para-aortic lymphadenectomy. Clarifying and addressing the morbidity from these surgical procedures is imperative. The goal of this study was to assess the prevalence of lower extremity swelling following surgery for endometrial cancer.

Methods/materials—We performed a descriptive, cross-sectional survey study of women who underwent surgery for endometrial cancer at our institution from 2006–2008. Survey information included symptoms, management, and education regarding lymphedema. Demographic information such as race and education was collected in addition to clinical data such as body mass index (BMI) and age.

Results—Of the 482 patients identified, 440 were determined eligible and 305 (69.3%) responded to the survey with information on lower limb swelling (LLS). Of the 108 (35%) responders who reported swelling, only 68 (22%) participants reported a diagnosis of lower limb lymphedema (LLL). The most commonly experienced symptoms among those who reported LLS were tightness, pain/tenderness and heaviness. Among those with a diagnosis of LLL, a majority (60%) stated it affected their daily activities and noted exacerbating factors such as prolonged standing, heat, and walking. The most common therapies utilized to reduce symptoms included leg elevation (96%), compression stockings (65%), diuretics (46%), massage therapy (35%), and bandaging (25%). There was no association between LLS or LLL diagnosis and BMI, age, race, tobacco use. Only 8% of responders reported receiving preoperative education regarding risks for LLS and a desire for more comprehensive education was frequently noted.

Conclusions—The patient-reported incidence of LLS occurred in approximately 35% of survey participants who underwent surgery for endometrial cancer. However, only 22% reported a diagnosis of LLL. Efforts to obtain the true incidence of LLL and to develop effective educational materials and programs to improve the management of lymphedema are warranted.

Keywords

lower limb lymphedema; endometrial cancer; lower limb swelling

Introduction

Endometrial cancer is the most commonly diagnosed gynecologic cancer in the United States (U.S.) with an estimated 52,000 new cases in 2014 [1]. Due to the presence of symptoms, a majority of patients are diagnosed in early stages of disease, resulting in 5-year survival rates exceeding 80% [2]. As a result, the American Cancer Society reports that there are over 600,000 endometrial cancer survivors currently living in the U.S. [3]. Though co-morbid conditions commonly contribute to mortality, causes of long-term morbidity from surgery and treatment interventions in endometrial cancer patients have been less thoroughly studied [4–5].

One cause of morbidity in women with endometrial cancer is lower limb lymphedema (LLL) or lower limb swelling (LLS) due to the use of surgical staging, including lymphadenectomy, as the primary management [6]. Though lymphedema has been shown to be a physically and emotionally debilitating result of surgical intervention after treatment for breast cancer, the impact of LLL in endometrial cancer survivors has not been well studied [7–8]. The reported rate of LLL varies substantially due to several reasons [9–12]. First, there is a lack of a standardized clinical definition of LLL. Secondly, patients may have confounding medical problems such as congestive heart failure, renal disease, or venous thromboembolism resulting in lower extremity symptoms that may mimic lymphedema. Lastly, despite clinical examination, limb measurements, and the use of instruments such as bioelectrical impedance, there is no evidence regarding the best method for assessment of LLL in this population. For example, Todo et al reviewed medical charts to identify endometrial cancer patients with lower extremity symptoms but then employed serial measurements and imaging to diagnosis LLL and found a 38% rate [9]. However, Abu-Rustum and colleagues reviewed medical records of endometrial cancer patients and accounted for self-reported symptoms, physician documentation, and referrals to a lymphedema specialist and found only a 1.2% incidence of LLL [11]. Therefore, the objective of this study was to obtain a subjective assessment for the presence of LLS and LLL and its impact on women who underwent surgical treatment for endometrial cancer.

Materials and methods

Participants

Women who underwent surgical treatment for endometrial cancer from January 2006 to December 2008 at our institution were identified from an institutional tumor registry database. Eligible patients were contacted and asked to complete and return a self-

administered survey. Eligibility criteria included: primary surgical treatment for endometrial cancer at The Ohio State University (OSU) Wexner Medical Center consisting of at least a hysterectomy; 18 years of age; English literacy; and a current mailing address. Patients were ineligible if they: were incarcerated; did not undergo primary surgery; or were diagnosed with synchronous cancers. Approval to conduct this study was obtained from the OSU Institutional Review Board.

Survey

The self-administered survey was developed from previously validated questionnaires [12–13] and input from locally conducted patient and provider focus groups. The survey included items specific to the participants' treatment for endometrial cancer, symptoms since their surgical procedure, and specific questions about LLL and LLS symptoms (location of swelling, when swelling occurred, severity of swelling, causes of swelling). Participants were also asked if they had ever been told by a health care provider that they had lymphedema, how their diagnosis was made (e.g. used a tape measure to measure legs), and the treatments used to reduce swelling (e.g. compression stockings) and the effectiveness of the treatments. Participants were asked to rate a series of concerns about the effect of their LLL and LLS on their Quality of Life (Likert scale from *not at all* to *very much*), lifestyle changes made because of their LLL or LLS, and about the information they received about LLL/LLS. In addition, participants reported self-rated health, health behaviors (e.g. smoking, changes in diet), use of complementary and alternative medicine, and demographic information.

Procedures

A mailed survey study was conducted in April 2011 to May 2011 and data collection procedures were guided by the survey design method described by Dillman [14]. First, eligible patients were sent an introductory letter informing them of the study and that a survey would be mailed to them in one week. One week later, potential participants were mailed the survey with a return self-addressed stamped envelope. Two weeks after the initial mailing, non-responders were sent a second mailing of the survey. All participants were mailed/mailed a \$10 gift card in appreciation of their time. The response rate was calculated as the number of surveys returned divided by the number of surveys that were sent out and not returned as deceased, wrong address, or ineligible.

Completed electronic surveys were scanned into a database system. Optical character recognition interpreted each data item and exported the data to a Microsoft SQL Server database maintained by the OSU Center for Clinical and Translational Science.

Statistical methods

Patient demographic, LLS/LLL and clinical characteristics are described by basic descriptive statistics including means and standard deviations for continuous covariates and counts for categorical covariates. These characteristics are compared between patients with and without leg swelling, by either the two sample t-test, assuming unequal variances for continuous covariates or Fisher's exact test for categorical covariates. Odds ratios were estimated by logistic regression, along with the associated 95% confidence intervals. All p-

values presented are two-sided and are un-adjusted for multiple comparisons. Analyses conducted in Stata software (StataCorp 2013, College Station, TX).

Results

A total of 482 patients were identified as potentially eligible and were mailed a survey. Surveys were returned as deceased (n=18), wrong address/no forwarding address (n=20), and 4 women were determined to be ineligible from their responses (did not have a surgical procedure, diagnosis was not endometrial cancer). Of the 440 eligible patients, 305 participants (69.3%) responded, 234 participants after the first request and 71 after the second request. All participants provided information about lower extremity symptoms; this group, hereinafter, will be referred to as “responders” and will be the focus of this paper.

The average age of the responders was 62.9 years (range 27–93 years) and the average body mass index was 36.6 (range 19–71). All responders were at least 3 years out from their diagnosis, which occurred in 2006 in 81 responders, 2007 in 121 responders, and in 2008 in 104 responders. When asked specifically about symptoms affecting the lower extremities, swelling was most commonly reported (35%, 108). As reported in Table 1, there was no significant association between any collected demographics and the presence of LLS.

In addition to swelling, a variety of other symptoms were reported. Among all responders, the most commonly reported lower extremity complaints included pain/tenderness (23%), numbness (21%), tightness (16%), heaviness (15%), tingling sensation (15%), and warmth/redness (13%). Responders that reported swelling were statistically more likely to report additional lower extremity symptoms (Table 2). Furthermore, the most commonly reported general symptoms included vaginal dryness (33%), loss of sexual desire (31%), back pain (27%), and constipation (26%). The presence of symptoms associated with sexual dysfunction such as vaginal dryness, loss of sexual desire, and painful intercourse, was similar between those that reported swelling and those that did not. However, responders who reported swelling were significantly more likely to report concurrent pain symptoms, such as back pain, abdominal pain, constipation, and pelvic cramping. Table 3 further details general symptoms among responders who reported swelling.

Despite 35% of all responders reporting lower leg swelling, only 22% (68) stated they had received a clinical diagnosis of LLL. In this subgroup, 88% stated diagnosis was made by a physician, while the remaining diagnoses were made by a nurse, physical therapist, or non-specified professional. Regardless of who made the diagnosis, 33 responders (49%) reported the diagnosis was based on physical examination alone; 27 responders (40%) reported positive diagnosis based on lower extremity measurements, 6 responders (9%) stated that no method was used, and 2 responders (3%) underwent evaluation with bioimpedance measurements.

Of the 68 responders that reported a diagnosis of LLL, 32% (22/68) reported symptoms within 4 weeks of surgery and an additional 31% (21/68) within 1 year of surgery. After a minimum of 3 years from the initial surgical intervention, 84% of responders reported that they still experienced some degree of LLL symptoms. Furthermore, 65 (96%) of responders

with LLL experienced swelling in their calves, ankles, and/or feet, while 22 (32%) had swelling through their thighs and groin. The LLL was reported as mild (12%), moderate (50%), severe (15%), and variable across sites (24%). Symptoms were reported to be most commonly precipitated and/or exacerbated by prolonged standing or walking (66%), driving (31%), and heat (31%). Approximately 60% of LLL responders reported an impact on their ability to perform activities of daily living and 23% noted an impact on their employment. Furthermore, the appearance of their legs resulted in substantial self-consciousness in 38% and required a change in type of clothing worn in 46%.

The most commonly reported treatment modalities used in responders diagnosed with LLL were: leg elevation (93%), compression stockings (64%), diuretics (46%), massage therapy (36%), anti-inflammatory medications (36%), exercise (35%), and bandaging (26%). In general, patient reported efficacy of these therapies was rated as ‘moderately’ effective; however, lower extremity bandaging was reported to be “very” effective.

Regarding lymphedema education, only 8% of all responders reported that they received pre-operative information regarding the risk for the development of LLL. Another 5% reported that they were provided information post-operatively. When information was received, 24% of responders stated it was provided by a physician and 12% received information for ancillary healthcare providers. Additionally, responders reported that they received information from the following other sources: internet (9%), brochures/books (6%), and family/friends (7%). Furthermore, one-third of responders desired information, but were unable to obtain it and 11% of responders felt this information was hard to understand.

Discussion

The prevalence of LLL in women with endometrial cancer varies significantly in the prior studies, with reports documenting prevalence rates ranging from 1% to 40% [9–12]. Though this variation is, in part, due to inconsistent objective methods of diagnosis, the American Cancer Society acknowledges a diagnosis of lymphedema based on patient symptoms, even in the absence of objective measures [15]. Our study, which predominantly focused on subjective assessments of lower extremity symptoms, documented that lower extremity problems affect over one third (35%) of women who undergo surgical intervention for endometrial cancer. This finding is consistent with the results of the Australian National Endometrial Cancer Study Group finding that 39% of women with endometrial cancer experienced LLS or LLL [16].

The morbidity related to lymphedema can be significant. We report that 60% of responders diagnosed with LLL noted an impact on daily activities and most described their symptoms as moderate or severe. Similar to other studies, precipitating and exacerbating factors such as prolonged standing and heat were commonly reported [9,12–13,17]. Additionally, due to associated symptoms, Rowlands and colleagues noted that women with LLL reported a decreased physical quality of life [16]. Preparing patients for the possible effects of cancer treatment may reduce long term psychological and physical ramifications of LLL that significantly impair the patient’s ability to return to a functional baseline. Our study showed that a majority of women did not report any pre-operative information regarding the

development or symptoms of LLL, which is consistent with other studies [12,13]. Furthermore, information that is currently available may not be of the appropriate quality, leaving areas for continued improvement in LLL management.

The participants included in this study had LLL diagnosed at varying lengths of time after their staging surgery. Studies in upper extremity lymphedema have shown that early intervention reduces long-term sequelae with early diagnosis and intervention [12,17]. Whether this benefit translates to LLL is not yet known. As the onset of lymphedema occurred within the first year after surgery in the majority of patients, evaluation for LLL immediately after treatment should be advised [9–11]. However, once diagnosed, identifying effective therapies for LLL remains a challenge. Treatment methods utilized by responders were consistent with other reports; however, identifying interventions with proven benefit should remain a priority in this patient population [12,18].

When evaluating this data, several limitations must be acknowledged. First, this was a patient-reported cross-sectional survey study and the response rate was ~70%. We tried to minimize the lack of response by sending out a second copy of the survey to all eligible participants who did not respond to the first request. Still, about 30% of the women did not return the surveys and therefore, this may contribute to a reporting bias that could artificially increase the rate of LLL. Second, the generalizability of the results is limited by surveying patients from one health center. It is possible that patients from other health centers could experience different post-operative symptoms. Third, all information was by self-report from the participants. Therefore, in the absence of objective measurements and the lack of assessment for other causes of lower extremity swelling, such as thromboembolic disease, congestive heart failure, medications, etc., may overestimate the incidence of lymphedema. However, as 40% of responders reported the onset of symptoms within four weeks of surgery and other reports have shown that confounding health conditions were present in only 5% of patients, this factor is unlikely a large contributor [11]. In addition, patient interpretation of symptom descriptions and their impact were not standardized, therefore, results may be an over or under-representation. Lastly, though long term follow-up care is provided to participants, our study was a subjective assessment of women who were at least three years post-surgical procedure and recall bias may have affected the responses. Despite these limitations, we present a large study of endometrial cancer patients with comprehensive information regarding symptoms, provider counseling about lymphedema, treatment modalities and the effectiveness of the different modalities, adding to our understanding of LLL and LLS among this specific group of women.

In summary, 35% of responders who underwent surgical intervention for endometrial cancer reported LLS, an additional 38% of responders reported at least one symptom associated with LLS/LLL. These findings highlight the likelihood that the prevalence of LLL is much higher than the 22% of participants in our study who reported a diagnosis. Furthermore, gaining insight into which patients with endometrial cancer may be appropriate candidates for sentinel lymph node assessment or even, omission of the lymphadenectomy, may help reduce the incidence of LLS/LLL. Of note, 76% of responders in this study underwent a lymph node dissection and there were no statistically significant differences between responders with LLS and those without (data not shown). Given this finding, every patient

with endometrial cancer should be educated on and assessed for the development of LLS/LLL. Currently, the Gynecologic Oncology Group is conducting a prospective trial using objective measurements, long term assessments, and evaluating quality of life to assess for the development of lymphedema. Understanding the incidence and impact of lymphedema in this population will allow for improved counseling and interventions. Until these data are available, the present study reiterates the impact of LLS/LLL in this population and highlights the need for increased awareness, improved education and effective therapeutic interventions.

Acknowledgments

Funding: The Ohio State University Comprehensive Cancer Center Pilot Project and the National Center for Advancing Translational Sciences (UL1TR001070)

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Table 1

Demographic characteristics of study population by self-report of leg swelling.

	Leg swelling (n=108)	No leg swelling (n=197)	OR (95% CI)	p-value ³
Age mean (sd) ¹	63.7 (10.2)	62.5 (11.1)	1.01 (0.99–1.03)	0.36
BMI mean (sd) ²	37.3 (10.9)	36.4 (10.9)	1.01 (0.98–1.04)	0.61
Race				
Black/Other race	3 (4%)	7 (5%)	1.0	1.00
White	67 (96%)	137 (95%)	1.14 (0.29–4.55)	
Marital status				
Widowed/Divorced/Single	43 (41%)	69 (36%)	1.0	0.41
Married	63 (59%)	124 (64%)	0.82 (0.50–1.33)	
Education				
Less than college education	43 (41%)	66 (34%)	1.0	0.27
At least some college education	63 (59%)	127 (66%)	0.76 (0.47–1.24)	
Work Status				
Retired	42 (40%)	91 (48%)	1.0	0.16
Employed	35 (34%)	68 (36%)	1.12 (0.64–1.93)	
Other	27 (26%)	32 (17%)	1.83 (0.97–3.43)	
Insurance status				
Uninsured	7 (7%)	16 (8%)	1.0	0.62
Insured	98 (93%)	177 (92%)	1.27 (0.50–3.18)	
Tobacco use				
No	103 (95%)	185 (94%)	1.0	0.60
Yes	5 (5%)	12 (6%)	0.75 (0.26–2.18)	

¹ Age available for 300 responders; 195 with leg swelling and 106 without.² BMI available for 170 responders; 45 with leg swelling and 125 without.³ P-values based on logistic regression model. OR for 1 unit increase.

Table 2

Lower extremity symptoms reported by patients following surgery based on LLS

Symptom	All responders (n=305)	Leg swelling (n=108)	No Leg swelling (n=197)
Swelling	108 (35%)	108 (100%)	0 (0%)
Tenderness/Pain	70 (23%)	47 (44%)	23 (12%) ##
Numbness	63 (21%)	31 (29%)	32 (16%) #
Warmth/Redness	40 (13%)	30 (28%)	10 (5%) ##
Tightness	49 (16%)	43 (40%)	6 (3%) ##
Tingling sensation	47 (15%)	25 (23%)	22 (11%) #
Heaviness	47 (15%)	37 (34%)	10 (5%) ##
Stiffness	37 (12%)	27 (25%)	10 (5%) ##
Restricted movement	33 (11%)	23 (21%)	10 (5%) ##
Skin thickening	21 (7%)	17 (16%)	4 (2%) ##
Throbbing sensation	19 (6%)	15 (14%)	4 (2%) ##
Lumps	9 (3%)	7 (6%)	2 (1%)
No symptoms	122 (40%)	0 (0%)	122 (62%) ##

Comparisons between symptoms in LLS groups made by Fisher's exact test.

p-value <0.05##
p-value <0.001

Table 3

General symptoms reported by patients following surgery based on Leg swelling

Symptom	All responders (n=305)	Leg swelling (n=108)	No leg swelling (n=197)
Vaginal dryness	100 (33%)	43 (40%)	57 (29%)
Loss of sexual desire	93 (31%)	40 (37%)	53 (27%)
Back pain	82 (27%)	48 (44%)	34 (17%) ##
Constipation	80 (26%)	43 (40%)	37 (19%) ##
Abdominal pain	44 (14%)	26 (24%)	18 (9%) #
Painful intercourse	31 (10%)	15 (14%)	16 (8%)
Pelvic cramping	27 (9%)	22 (20%)	5 (3%) ##
Vaginal discharge	16 (5%)	8 (7%)	8 (4%)
Vaginal bleeding	5 (2%)	5 (5%)	0 (0%)
No symptoms	83 (27%)	10 (9%)	73 (37%) ##

Comparisons between symptoms in LLS groups made by Fisher's exact test.

p-value <0.05##
p-value <0.001