Published in final edited form as:

Nurs Res. 2013 ; 62(2): 122–129. doi:10.1097/NNR.0b013e318283da67.

Using Temporal Mining to Examine the Development of Lymphedema in Breast Cancer Survivors

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Abstract

Background—Secondary lymphedema is a lifetime risk for breast cancer survivors and can severely affect quality of life. Early detection and treatment are crucial for successful lymphedema management. Limb volume measurements can be utilized not only to diagnose lymphedema but also to track progression of limb volume changes before lymphedema, which has the potential to provide insight into the development of this condition.

Objectives—To identify commonly occurring patterns in limb volumes changes in breast cancer survivors before the development of lymphedema, and to determine if there were differences in these patterns between certain patient subgroups. Furthermore, pattern differences were studied between patients who developed lymphedema quickly and those whose onset was delayed.

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Method—A temporal data mining technique was used to identify and compare common patterns in limb volume measurements in patient subgroups of study participants (n = 232). Patterns were filtered initially by support and confidence values; then t-tests were used to determine statistical significance of the remaining patterns.

Results—Higher body mass index and the presence of postoperative swelling are supported as risk factors for lymphedema. In addition, a difference in trajectory to the lymphedema state was observed.

Discussion—The results have potential to guide clinical guidelines for assessment of latent and early-onset lymphedema.

Keywords

secondary lymphedema; breast cancer; temporal analysis; data mining

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Secondary lymphedema (LE) is a chronic condition commonly observed in breast cancer survivors. It results in protein-rich fluid retention in the arms and other affected body parts, causes functional limitations and impairs limb motion, and can affect quality of life severely (Armer, 2005; Armer, Stewart, & Shook, 2009; Petrek & Heelan, 1998). There are an estimated 2.5 million breast cancer survivors in the United States (American Cancer Society, 2010), and lymphedema is a lifetime risk for this patient group (Ferlay, Bray, Pisani, & Parkin, 2004). The incidence rate for LE in breast cancer survivors is estimated at around 40% (Armer & Stewart, 2010), meaning up to 1 million women in the US have or will develop LE at some point in their lives. Moreover, with the high survival rate of breast cancer and the more than 200,000 new diagnoses estimated each year in the US (American Cancer Society, 2010), the number of survivors, and therefore those at risk for LE, is rapidly increasing. In response to this growing problem, the *Best Practices for the Management of Lymphoedema* document (Lymphoedema Framework, 2006) was developed to provide useful treatment guidelines for LE management. Many of the guidelines, however, require further support from evidence-based research, and to date there has been limited rigorous research documenting factors associated with risk assessment (Cormier, Xing, Zaniletti, Askew, & Armer, 2009; Muscari, 2004; Ridner, 2002).

Early detection and intervention are critical for successful LE management. If not diagnosed and managed in its early stages, LE may become chronic and irreversible in nature (Lawenda, Mondry, & Johnstone, 2009). Both higher body mass index (BMI; Clark, Sitzia, & Harlow, 2005; Helyer, Varnic, Le, Leong, & McCready, 2010; Nesvold, Dahl, Lokkevik, Marit Mengshoel, & Fossa, 2008) and postoperative swelling (Mahamaneerat, Shyu, Stewart, & Armer, 2008) have been documented in the literature. (The data used by Mahamaneerat et al. was a subset of the data set used in this study with different analytic techniques applied.) Awareness of the condition and risk factors, and careful attention to the at-risk limb are important in preventing LE from reaching a more advanced stage.

Anthropometrics of limb volume (LV) changes are the primary quantitative diagnostic tool for LE, with volume and volume changes most commonly assessed by means of water displacement, infrared perometry, and volume estimation via a series of circumferential arm

measurements. While there is no consensus on LE diagnostic criteria, several criteria involving volume or circumference increases have been proposed (Armer & Stewart, 2005; International Society of Lymphology, 2009; Mahamaneerat et al., 2008). These measurements provide a means to track the progression of LE development, progression, and, in the case of successful treatment, limb volume reduction and maintenance.

The state of secondary LE following cancer treatment may vary or fluctuate in occurrence and severity (Armer & Stewart, 2011). No longer is it conceptualized simply as a dichotomous variable (*yes*/*no* for occurrence), but as a condition that may emerge soon after treatment begins or many years later; that may emerge and continue to progress or may come and go; that may improve with or without specialized LE treatment; and that may be latent, mild, moderate, or severe in stage and intensity (Foldi, Foldi, & Kubik, 2006; International Society of Lymphology [ISL], 2009). Indeed, these presentations and patterns of progression or remission may represent various phenotypes of secondary LE with differing underlying molecular mechanisms yet to be understood (Armer & Stewart, 2010).

Foldi et al. (2006) and Stout Gergich et al. (2008) extended the ISL 2009 staging classification for LE by applying the term *latent LE* or *subclinical LE* to describe the pre-emergent state of LE after injury to the lymphatic system has occurred and risk for LE development has been created, but when objective measures do not yet identify the presence of LE. In this latent stage, underlying tissue changes may be occurring and subcutaneous protein-rich fluid accumulation may be in progress. Indeed, the individual may be experiencing subtle tissue changes, such as a sensation of heaviness and observation of transient swelling due to increasing interstitial pressure (Armer, Fu, Wainstock, Zagar, & Jacobs, 2004; Armer, Radina, Porock, & Culbertson, 2003; Armer & Whitman, 2002). Stout Gergich et al. (2008) specify a 3% LV change as subclinical LE in their studies, a threshold less than the generally accepted criteria of 5% or 10% limb volume change for LE occurrence.

There has been little research to investigate the temporal component of LE onset in terms of patterns of limb volumes; this research is needed to better understand patient measurement patterns leading to LE emergence and progression. Such patterns provide the potential to improve the accuracy of LE risk calculations and to predict LE occurrence months before onset. This can be accomplished by matching latent conditions to already observed patterns in other breast cancer survivor patients, both those who have experienced the emergence of LE and those who have not, which may provide an enhanced window of opportunity for early intervention.

Method

A temporal mining approach was applied in this study, analogous to those in previous works (Han, Kamber, & Pei, 2005; Mannila, Toivonen, & Inkeri Verkamo, 1997; Srikant & Agrawal, 1996). The purpose was (a) to identify commonly occurring patterns in LV change in breast cancer survivors before the development of LE, and (b) to determine if there were differences in these patterns between patient subgroups. Furthermore, the study investigated pattern differences between patients who developed LE quickly and those whose onset was

delayed. Institutional review board approval for conducting research with human subjects was obtained from University of Missouri Health Sciences prior to the study.

Data Set

Trained staff collected data according to the schedule in Figure 1 from 232 Midwestern U.S. women who had been diagnosed with breast cancer and scheduled for surgery (*n* = 232). Criteria for patient inclusion consisted of being over 18 years of age with no prior history of LE or breast cancer. Data were obtained at a Midwestern U.S. university-affiliated state cancer center and included limb volume measurements by circumferences and perometry, as well as demographic and historical characteristics such as BMI, age at diagnosis, dominant side, and cancer-affected side.

The average participant age at enrollment was 57 years old (range = 30 to 89). Treatment characteristics of study participants varied greatly. In terms of surgery, 48% had a mastectomy, 39% had a lumpectomy, and 11% had both surgical treatments. Chemotherapy was received by 60% of the sample, while 51% underwent radiation treatment. Forty-three percent of participants had sentinel lymph node biopsy treatment and 30% underwent axillary lymph node dissection, with 11% undergoing both treatments and 16% having neither treatment.

The LE-related measurement used in this study was LV of the cancer-affected side, measured each visit using perometry and circumference. Perometric LV was the primary data source in this study due to high accuracy in volume estimation (Armer & Stewart, 2005; Mayrovitz, Sims, & Macdonald, 2000; Ridner, Montgomery, Hepworth, Stewart, & Armer, 2007; Tierney, Aslam, Rennie, & Grace, 1996). This method utilizes a series of infrared light beams emitted perpendicular to the axis of the limb to accurately measure a transection. Transections are measured every 3 mm along the limb from wrist to axilla, and integrated to form a volume measurement (Petlund, 1991). For patients whose perometric measurements were unavailable (*n* = 31) due to equipment not being in operation or being serviced at the time of the patient visit, circumferential LV was used instead, in which case a nonstretch, flexible tape measure was used to measure circumference (in cm) at the hand, wrist, and every 4 cm thereafter to the axilla (Armer & Stewart, 2005). A trained research nurse took measurements three times at each point, with the mean girth measure being used in the volume calculation. The use of circumferential LV in these situations is justified by the significant correlation (*r* = 0.89) between the perometric and circumferential LVs and the equally high correspondence with the gold standard of water displacement (Armer & Stewart, 2005).

Dynamic patient information, such as LV and weight for BMI calculations, were measured and collected at each visit. Other demographic and historical data such as age, cancer-affected side, and dominant side were self-reported by patients at the initial visit and confirmed at follow-up visits.

Lymphedema Diagnostic Criterion

The 5% BMI-adjusted LV change criterion (Mahamaneerat et al., 2008) was chosen as the proxy for the development of LE because there is built-in consideration for commonly experienced weight fluctuations following breast cancer treatment. Using this method, a patient is said to meet the LE criterion if the change in LV (from baseline LV at the preoperative visit) is 5% or greater than the change in BMI (from the baseline BMI at the preoperative visit).

Patient Partitioning

To facilitate the comparison of patterns to LE in different patient groups, patients were grouped based on BMI and the occurrence of postoperative swelling. The BMI partitions (Table 1) were based on the 2011 guidelines from Centers for Disease Control and Prevention (CDC), and the criteria for having postoperative swelling was limb swelling of at least 3% at the postoperative visit (equivalent to the subclinical LE criteria; Stout Gergich et al., 2008).

Each of these patient groups was split further into two subgroups based on the amount of time needed to reach a LE diagnosis. Those who met the LE criterion in the first 6 months postsurgery were categorized into one subgroup, and those who met the criterion after 6 months into the other subgroup. The sixth postoperative month criterion was used, because it was the closest visit to the average time for onset of LE (6.9 months postoperative) identified by Stout Gergich et al. (2008). This second division facilitates a comparison of the path to LE between patients who develop LE soon after surgery and those who have a more delayed onset.

Data Preprocessing

Before temporal analysis, sequences of LV change were formed by computing the absolute volume change between the current visit and the previous one, for each visit up to and including the LE diagnosis visit. Each LV change between consecutive visits was discretized into one of the three categories: a rise in LV ($\nearrow$), defined as a 3% or greater increase in volume compared to the LV at the previous visit; a drop in LV ($\searrow$), defined as a 3% or greater decrease in LV; or stable LV ($\rightarrow$), defined as a LV change of less than 3%. Because slight fluctuations in weight and fluid retention are natural, the 3% threshold was selected for discretization based on the study by Stout Gergich et al. (2008). If LV was unavailable at either of the visits due to the corresponding patient missing the visit, it was denoted by an *x*. These missing values were not considered in the temporal analysis (see Figure, Supplemental Digital Content 1 for an illustration of converting LVs to temporal sequences).

Temporal Mining

The temporal analysis was conducted by first identifying all LV change patterns of at least length 2 that occurred immediately before the LE criterion was met (i.e., each pattern must end at the visit in which the LE criterion was met). To gain some insight into the importance and significance of each pattern, support and confidence values (Han et al., 2005) were computed. The confidence of an LV change pattern (Equation 1) describes how often a

particular pattern's appearance ends with meeting the LE criterion. A confidence value of 75% for a pattern would mean that when that pattern is seen in a patient, 75% of the time it is accompanied by meeting the LE criterion; in other words, the confidence relates to the overall significance of a pattern to meeting the LE criterion. The support of a LV change pattern (Equation 2), on the other hand, is defined as the percentage of times the data meet the LE criterion due to this pattern.

$$confidence_{LE}(\alpha)=\frac{\#\ of\ times\ the\ pattern\ \alpha\ ends\ with\ LE}{\#\ of\ times\ pattern\ \alpha\ occurs} \quad (1)$$

$$support_{LE}(\alpha)=\frac{\#\ times\ pattern\ \alpha\ ends\ with\ LE}{\#\ times\ any\ pattern\ of\ same\ length\ ends\ with\ LE} \quad (2)$$

To illustrate, a support value of 90% would mean that 90% of the time, this pattern occurs just before meeting the LE criterion; it does not, however, specify anything about how often that pattern occurs without meeting the LE criterion. Only patterns whose support and confidence values were both at least 15% were denoted as commonly occurring. T-tests were used to determine significance of common patterns.

Results

The results of the temporal analysis are presented in two subsections, one for the results of partitioning the patients by BMI and the other for the postoperative swelling partitions.

Body Mass Index Groups

The percentage of women in the study per BMI group and the percentage of women in each BMI group affected by LE (using the 5% BMI-adjusted LV change criterion) are shown in Table 1. The underweight group was not studied due a small sample size (*n* = 2). The LV change patterns leading to LE with support and confidence thresholds of at least 15% in at least one of the BMI patient groups were identified, and the most significant results obtained are shown in Table 2.

The main overarching result from the BMI partitioning is that overweight and obese patients are at a greater risk of meeting the LE criterion. It was first observed that higher percentages of overweight and obese patients met the LE criterion when compared to normal weight patients (51.28% vs. 33.96% [*p* = .051] and 55.1% vs. 33.96% [*p* = .013], respectively; Table 1). In overweight and obese patients, there are a greater number of LV change patterns that lead to LE with high confidence values (Table 2). For example, the LV change pattern $\rightarrow\nearrow\nearrow$ leads to LE with confidence values of 54.54% and 41.67% in overweight and obese patients, respectively. This evidence supports that obesity is an important risk factor for LE and further strengthens the recommendation in the Best Practice document that patients with higher BMI may require closer monitoring for LV changes associated with LE.

An important theme identified was that patients with consecutive LV increases have a greater probability of meeting the LE criterion. The LV change patterns in which LV

increased in at least two consecutive visits (e.g., → ↗ ↗) were observed to have higher confidences of resulting in LE when compared to the patterns with a single increase in LV (e.g. → → ↗) (54.54% vs. 21.73% [p = .058] in overweight patients; Table 2).

Patients in each BMI category were divided into two groups to analyze the frequent LV change patterns associated with LE within and after the first 6 months postsurgery (Table 3). Two main themes were identified. First, stable LV does not rule out the chances of meeting the LE criterion in overweight and obese patients, particularly in the first 6 months after surgery. From Table 3, it was observed that there was a possibility of developing LE in the first 6 months after surgery, even when LV remained stable (→ → → in overweight and obese patients with confidences 25% and 11.11%, respectively), whereas such incidents did not occur often after the first 6 months postsurgery (Table 3). However, a pattern of consecutively stable LVs using the criterion of 3% LV change may reflect slow gradual increases in LV.

Second, a single LV increase has high confidence of leading to LE within the first 6 months postsurgery. After the first 6 months postsurgery, consecutive increases in LV have a greater confidence of meeting the LE criterion when compared to a single LV increase. In general, a single increase in LV resulted in LE with high confidence within the first 6 months after surgery (→ → ↗ with confidences 50% and 40% in overweight and obese patients, respectively). After the first 6 months postsurgery, LV change patterns with consecutive increases were observed to have higher confidences of leading to LE when compared to a single LV increase (44.44% for → ↗ ↗ vs. 8.69% for → → ↗ [p = .019] in overweight patients in Table 3).

Postoperative Swelling Groups

The percentage of patients with and without swelling criteria in the postoperative visit (t_2), and the percentage of LE-affected patients in each group are shown in Table 4. The confidence and support values of frequent LV change patterns leading to LE in patients with and without postoperative swelling are shown in Table 5.

There is evidence for postoperative swelling being an important risk factor for LE development in this dataset, though that factor is not currently in the Best Practice document. Patients experiencing postoperative swelling were more likely to meet the LE criterion at a later point than those without postoperative swelling (Table 4; 64.86% vs. 45.41% [p = .030]). Examining LV change patterns in the postoperative swelling groups further supports this finding. First, LV change patterns typically have a greater probability of leading to LE in patients with postoperative swelling when compared to those without. Patients with postoperative swelling who experience consecutive increases in LV (↗ ↗) had a higher probability of meeting the LE criterion when compared to the patients without postoperative swelling (Table 5; 50% vs. 28.94% [p = .039]). Second, there is an increase in the variety and number of mined patterns that have high confidence values in patients with postoperative swelling. For example, a single instance of LV increase in patients with post-operative swelling was found to lead to LE with high confidence (42.85%, 36.36%, and 50% for LV patterns ↘ ↗, → ↗, and ↗ ↗, respectively), irrespective of whether the volume decreased, remained stable, or increased in the previous visit.

The frequent LV change patterns associated with LE within and after the first 6 months postsurgery in each of the patient groups based on postoperative swelling are shown in Table 6. These results show that, in general, a given LV change pattern has a greater confidence of meeting the LE criterion within the first 6 months after surgery when compared to more than 6 months after surgery. For example, consider the situation when LV remains stable between two visits and then increases at the next visit (→ ↗). When patients without postoperative swelling met the LE criteria within the first 6 months, the occurrence of this pattern was associated with meeting the LE criteria 36% of the time, whereas the association was less likely (only 9.68% [$p < .0001$]) when patients without postoperative swelling met the LE criteria more than 6 months postsurgery (Table 6). In this dataset, the appearance of the same pattern (→ ↗) in patients with postoperative swelling always corresponded to meeting the LE criteria (note the small $n = 2$), whereas the association of the appearance of the pattern to meeting the LE criteria dropped to only 15.38% for patients who did not meet the LE criteria until more than 6 months postoperative. Such evidence-based findings indicate a need for patient vigilance and careful monitoring for LE symptoms in patients both with and without postoperative swelling, especially in the first several months after surgery.

Discussion

The use of such a temporal mining technique was appropriate in this study due to the rigor of the experimental design, particularly the inclusion of preoperative baseline limb measurements, the regularly scheduled measurement of LV using multiple modalities with built-in accuracy checks and long-term patient follow-up, each of which is lacking in many other studies. The patterns extracted from this technique, while useful for better understanding LE development, also can be combined to suggest higher-level findings, and both types of findings are described.

As overarching themes, the results suggest that both higher BMI and the presence of postoperative swelling are associated with higher risk of developing LE, similar to that reported previously. In addition to identifying increased risk of BMI and postoperative swelling, the results of this study also suggest some key points regarding the development of LE.

First, the majority of LV change patterns, across all BMI groups, consisted of stable LV (for 0, 1, or multiple visits) before a single or consecutive increase to the LE state. This finding may be due to the occurrence of an initiating event in the patient's life that triggered the onset of fluid retention, but triggering events were not recorded. Regardless, the fact that LE onset can happen shortly after surgery or can be delayed reinforces the need for close monitoring so that, once the swelling begins, it can be identified and managed properly.

Second, a single increase leading to LE in the first 6 months after surgery was most common, but later (after the first 6 months) consecutive increases were more common to reach the LE state. These data suggest that the trajectory to the LE state may change over time, specifically that the trajectory is steeper when LE occurs (relatively) quickly after surgery than when the onset is more delayed. This change in trajectory is supported further

in this data set by the fact that the later diagnoses have 6 months separating each increase, meaning the consecutive increase corresponds to an entire year, whereas consecutive increases in the earlier diagnoses represent shorter intervals of only 6 months. This finding needs to be confirmed in future studies, but, if true, it again reinforces the need for lifelong monitoring of LVs, as repeated subtle volume increases over time may go unnoticed by patients, especially if bilateral limb volume change occurs.

Implications for Nurses

Nurses working with breast cancer survivors in the outpatient setting should measure limbs for LE with established protocols using circumferences, water displacement, or perometry at regular intervals as part of a survivorship LE surveillance program. Serial measures of both limbs should be carried out over time, with comparisons to baseline preoperative measures and contralateral limbs when possible. Nurses can emphasize the importance of limb self-monitoring as a key self-management action. They can instruct interested patients (and caregivers) in how to measure themselves with tape measures at selected locations such as freckles or other anatomical landmarks. Patients can be empowered in self-monitoring by being given copies of their measurement records from each clinic visit. Patients should be instructed in how to follow-up in case of increased LV change patterns; they may come for follow-up clinic visits or send limb volume diaries electronically in the form of an Excel file or through a website. Since data show that patients with increased BMI are at greater risk for LE, advanced practice and clinical nurses should counsel patients to address weight reduction measures when appropriate. Vigilance among patients with postoperative swelling is imperative to reduce the risk of developing LE and detect early onset of LE for prompt referral for treatment in order to obtain optimal outcomes.

Study Limitations

Due to the nature of the study--an epidemiological community-based study over 30 months--missing data creates some limitations. When missing data corresponded to patients missing entire visits, the support of mined LV change patterns could be affected, particularly if the missed visit occurred prior, yet relatively close, to the LE diagnosis. Other missing data were secondary to missing perometry data, due to equipment maintenance or malfunction; however, circumferential data were used for volume calculation in these cases and were supported by demonstrated intermethod reliability. In addition, though the LE data set used in this study had the advantages of having baseline measurements, preoperative measurements, and several timestamps, the sample was relatively small, especially considering that the data set was further partitioned so patterns can be mined in individual groups, and power could be increased with larger numbers of participants. A final limitation of the study is that only LV values at the time of the lab visits are known; any changes in LV that occur between visits are not captured.

Conclusion

The temporal analysis of the LE dataset shows that, in general, identified LV change patterns have a higher probability of being associated with LE in obese and overweight patients than do the same patterns in normal-weight patients. The same trend holds for patients with postoperative swelling, as compared to patients without postoperative swelling.

Furthermore, the data revealed that a given LV change pattern has a greater chance of resulting in LE within the first 6 months after surgery when compared to the same pattern occurring after 6 months. Such evidence-based findings of interest can be added to expand the practice guidelines in the updated version of the Best Practices document (revision now underway) or used as evidence to strengthen existing recommendations.

The results, especially the slower trajectory to disease state when diagnoses occur more than 6 months postoperatively, reinforce the need for regular close monitoring of LVs in breast cancer survivors, particularly in those patients at higher risks for developing LE, such as those with higher BMIs and those who experienced postoperative swelling.

The findings from this study demonstrate the potential of the temporal mining approach for LE risk detection and for providing opportunities for early intervention, which are particularly important in LE management. Additional data from other clinicians, researchers, and hospitals need to be accumulated and analyzed to verify these results. Once done, a patient's present and future risk of LE could be computed through profile matching; a patient's recent LV history could be matched against existing patterns in the computerized database to determine a probability of LE in future months (e.g., in 3, 6, 12, months). These types of personalized risk estimates could take the LE community one step closer to achieving the goal of designing a decision support system for LE risk reduction and targeted treatment decisions. A similar technique could be utilized to evaluate progression of LE after diagnosis, particularly in response to various treatment modalities or compliance to daily self-care recommendations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The informatics research of this project was supported by the National Library of Medicine (NLM) Grant number 1 G08 LM 010711–01. Jason M. Green, PhD was supported by the NLM Bioinformatics and Health Informatics Training (BHIRT) grant 2T15LM007089-17 and the Shumaker Endowment in Biomedical Informatics. Data were obtained from research studies at the University of Missouri supported by Grant Numbers 1 R01 NR05342-01 and 1 R01 NR010293-01 (Armer, PI) from the National Institute for Nursing Research, National Institutes of Health; MU PRIME fund # PRM-01-007, University of Missouri; and Ellis Fischel Cancer Center research gift funds.

Thank you to Dr. Richard Madsen and Isabella Zaniletti for data management assistance. Thank you also to Ellis Fischel Cancer Center clinical collaborators, the lymphedema research project team at MUSSON and EFCC, and the breast cancer survivors who participated in the study, without whom this work could not have been completed.

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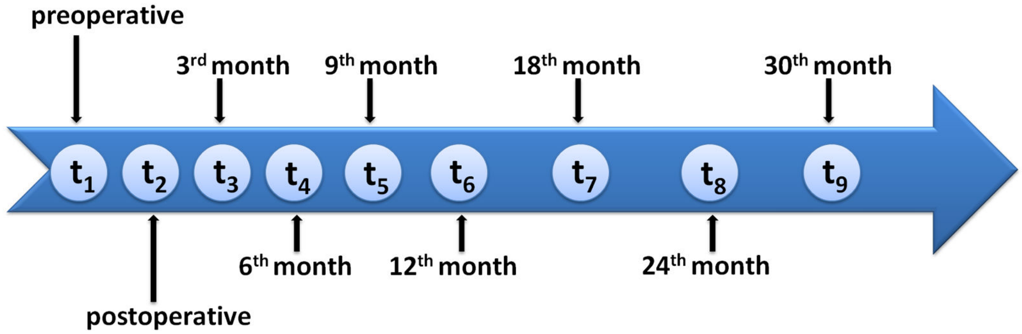

Figure 1. Data Collection Timeline

Notes. Limb volume by perometry, circumferences, and symptoms were collected every visit by trained research nurses.

Table 1

Statistics for Body Mass Index Groups

BMI	Weight Status	*n*	%	% affected by LE
Below 18.5	Underweight	2	0.86%	-
18.5 – 24.9	Normal	53	22.74%	33.96%
25.0 – 29.9	Overweight	78	33.47%	51.28%
30 and above	Obese	98	42.06%	55.1%

Notes. BMI = Body Mass Index; LE = Lymphedema

Table 2

Frequent Limb Volume Change Patterns Associated with Lymphedema by Body Mass Index Groups (N = 229)

LV change Pattern (α)	***confidence***$_{LE}$(α) (in %)			***support***$_{LE}$(α) (in %)		
	Normal	**Overweight**	**Obese**	**Normal**	**Overweight**	**Obese**
→ ↗	14.28 (35)	27.27 (55)	33.33 (57)	35.71 (14)	39.47 (38)	37.25 (51)
↗ ↗	18.18 (11)	35.29 (17)	40.91 (35)	14.28 (14)	15.78 (38)	17.64 (51)
→ → ↗	23.52 (17)	21.73 (23)	29.41 (17)	30.76 (13)	18.51 (27)	17.85 (28)
→ ↗ ↗	-	54.54 (11)	41.67 (12)	-	22.22 (27)	17.85 (28)
→ → → ↗	28.50 (7)	10.00 (10)	37.50 (8)	22.22 (9)	7.14 (14)	17.64 (17)
→ → ↗ ↗	-	100.00 (4)	50.00 (2)	-	28.57 (14)	5.88 (17)

Notes. LV change is computed as the difference in limb volume between consecutive patient visits. These changes are then discretized into one of three categories: a rise in LV (↗), a drop in LV (↘), or stable LV (→). Common sequences of LV changes are denoted as LV change patterns. A dash indicates that the corresponding pattern did not occur in the patient group. The numbers in parentheses represent (for confidence) the number of times the pattern occurred and (for support) the number of times a pattern of this length ended in lymphedema (i.e. the denominator for the respective calculations). For example, the pattern "→ ↗" occurred 35 times among the patients with normal BMI; however, in only 14.28% of those instances (5 times) did the pattern end with the patient meeting the LE diagnosis criteria. Within this same patient group, of all the patterns of length 2 that ended with a patient meeting the LE diagnosis criteria, the pattern "→ ↗" represented 35.71% (or 5/14) of those patterns.

LV = limb volume

Table 3

Limb Volume Change Patterns Associated with Lymphedema Within and After 6 Months Following Surgery by Body Mass Index Groups (N =229)

LV change Pattern (α)	$confidence_{LE}$(α) (in %)				$support_{LE}$(α) (in %)			
	Overweight		Obese		Overweight		Obese	
	LE <= 6 months	LE > 6 months	LE <= 6 months	LE > 6 months	LE <= 6 months	LE > 6 months	LE <= 6 months	LE > 6 months
↘ ↗	25.00 (8)	8.33 (12)	12.50 (8)	16.00 (25)	8.33 (24)	7.14 (14)	3.12 (32)	21.05 (19)
→ ↗	40.00 (30)	7.50 (40)	40.63 (31)	13.95 (43)	50.00 (24)	21.43 (14)	40.63 (32)	31.58 (19)
↗ ↗	18.18 (10)	30.77 (13)	46.15 (13)	13.64 (22)	8.33 (24)	28.57 (14)	18.75 (32)	15.79 (19)
→ → →	25.00 (12)	1.75 (34)	11.11 (18)	4.54 (66)	23.08 (13)	7.14 (14)	20.00 (10)	16.67 (18)
→ → ↗	50.00 (6)	8.69 (18)	40.00 (5)	16.67 (18)	23.08 (13)	14.2 (14)	20.00 (10)	16.67 (18)
→ ↗ ↗	28.5 (7)	44.44 (6)	33.33 (6)	37.5 (8)	15.38 (13)	28.57 (14)	20.00 (10)	16.67 (18)

Notes. LV change is computed as the difference in limb volume between consecutive patient visits. These changes are then discretized into one of three categories: a rise in LV (↗), a drop in LV (↘), or stable LV (→). Common sequences of LV changes are denoted as LV change patterns. The numbers in parentheses represent (for confidence) the number of times the pattern occurred and (for support) the number of times a pattern of this length ended in lymphedema (i.e. the denominator for the respective calculations). For example, the pattern "↘ ↗" occurred 8 times among overweight patients who met the LE diagnosis within 6 months; however, in only 25% of those instances (2 times) did the pattern end with the patient meeting the LE diagnosis criteria. Within this same patient group, of all the patterns of length 2 that ended with a patient meeting the LE diagnosis criteria, the pattern "↘ ↗" only represented 8.33% (or 2/24) of those patterns.

LE = lymphedema

LV = limb volume

Table 4

Basic Statistics for Postoperative Swelling Groups

Postoperative swelling	*n*	%	% affected by LE
No	196	84.12	45.41
Yes	37	15.88	64.86

Notes. LE = lymphedema

Table 5

Frequent Limb Volume Change Patterns Associated with Lymphedema by Postoperative Swelling Groups (N = 233)

LV change Pattern (α)	$confidence_{LE}$(α) (in %)		$support_{LE}$(α) (in %)	
	Without postoperative swelling	With postoperative swelling	Without postoperative swelling	With postoperative swelling
↘ ↗	17.50 (40)	42.85 (7)	8.33 (84)	15.00 (20)
→ ↗	26.27 (137)	36.36 (11)	42.85 (84)	20.00 (20)
↗ ↗	28.94 (38)	50.00 (12)	13.09 (84)	30.00 (20)
→ → ↗	24.49 (49)	25.00 (8)	21.05 (57)	18.18 (11)
→ ↗ ↗	40.00 (25)	50.00 (2)	17.54 (57)	9.09 (11)
↗ ↘ ↗	50.00 (8)	40.00 (5)	7.02 (57)	18.18 (11)
↗ → ↗	23.08 (13)	66.67 (3)	5.26 (57)	18.18 (11)

Notes. LV change is computed as the difference in limb volume between consecutive patient visits. These changes are then discretized into one of three categories: a rise in LV (↗), a drop in LV (↘), or stable LV (→). Common sequences of LV changes are denoted as LV change patterns. The numbers in parentheses represent (for confidence) the number of times the pattern occurred and (for support) the number of times a pattern of this length ended in lymphedema (i.e. the denominator for the respective calculations).

LV = limb volume

Table 6

Limb Volume Change Patterns Associated with Lymphedema Within and After the First 6 Months Following Surgery by Postoperative Swelling Groups (N =233)

LV change Pattern (α)	*confidence*$_{LE}$(α) (in %)				*support*$_{LE}$(α) (in %)			
	Without postoperative swelling		With postoperative swelling		Without postoperative swelling		With postoperative swelling	
	LE <= 6 months	LE > 6 months	LE <= 6 months	LE > 6 months	LE <= 6 months	LE > 6 months	LE <= 6 months	LE > 6 months
→ ↗	36.00 (75)	9.68 (93)	100.00 (2)	15.38 (26)	56.25 (48)	25.00 (36)	14.28 (14)	33.33 (6)
↗ ↗	20.00 (20)	17.94 (39)	50.00 (8)	22.22 (18)	8.33 (48)	19.44 (36)	28.57 (14)	33.33 (6)
→ → ↗	38.89 (18)	11.90 (42)	-	20.00 (10)	33.33 (21)	13.89 (36)	-	40.00 (5)
→ ↗ ↗	26.67 (15)	33.33 (18)	-	33.33 (12)	19.04 (21)	16.67 (36)	-	20.00 (5)

Notes. LV change is computed as the difference in limb volume between consecutive patient visits. These changes are then discretized into one of three categories: a rise in LV (↗), a drop in LV (↘), or stable LV (→). Common sequences of LV changes are denoted as LV change patterns. A dash indicates that the corresponding pattern did not occur in the patient group. The numbers in parentheses represent (for confidence) the number of times the pattern occurred and (for support) the number of times a pattern of this length ended in lymphedema (i.e. the denominator for the respective calculations).

LE = lymphedema

LV = limb volume