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EPIDEMIOLOGY

Early arm swelling after breast surgery: changes on both sides

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Abstract
Introduction Lymphedema is a common complication of treatment for breast cancer. However, little information is available describing changes in upper limb volumes in the early stages following surgery.
Method Study design: Retrospective audit. Participants: Women who underwent unilateral mastectomy or axillary node removal for breast cancer at the Princess Alexandra Hospital, Brisbane, Australia. Measurements: Circumferential measurements taken at 10 cm intervals from the ulnar styloid on each arm were converted to segmental volumes using the frustum approach. Procedure: Pre-surgery baseline measures were taken by a physiotherapist at Preadmission Clinic at the Princess Alexandra Hospital. Follow-up measures were taken 6 weeks after surgery by Domiciliary Allied Health Acute Care and Rehabilitation Service physiotherapists in patients' homes.
Results Limb segment volumes increased in the proximal upper limb segments at follow-up. The proportion of patients with a 10% or greater increase in volume in one or more segments of their upper limb were similar for ipsilateral (35%) and contralateral (32%) sides (to side of surgery), respectively. No significant interaction between time and arm (ipsilateral versus contralateral) was identified.
Discussion These findings demonstrate that limb segment volume changes affect a greater proportion of patients during the first 6 weeks following surgery than previously recorded. They also indicate that flow of lymph from the side of surgery to the contralateral side may disperse lymph between sides during this early post-operative period. This has implications for how swelling is measured during this period and strategies to prevent onset of lymphedema.

Keywords Lymphedema · Breast cancer · Incidence · Risk factors

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Introduction

Breast cancer is a frequently occurring disease amongst Australians with an annual age standardised incidence of between 63 and 65 cases per 100,000 population [1]. As with many developed countries, the incidence of, morbidity, and mortality caused by breast cancer in Australia is a considerable public health concern. One element of the morbidity associated with breast cancer and its treatment is secondary lymphedema. Upper limb lymphedema is a worrying complication for many breast cancer survivors that has been associated with lower self-reported quality-of-life scores [2], sleeping disturbance, difficulty carrying objects and completing daily function activities [3], and physical discomfort [4].

Lymphedema is the accumulation of lymph fluid in the interstitial space [5]. A characteristic progression of lymphedema has been described from swelling where pitting occurs upon application of pressure and edema reverses with limb elevation, to swelling that becomes larger and harder and no longer pits under pressure, to swelling that worsens such that skin changes occur [6]. The aetiology of lymphedema is multifactorial, though a ''traditional'' view predominates whereby damage to the axillary lymphatic system caused by surgery and/or radiotherapy impairs lymph drainage from the arm. However, far more tissue damage is necessary to produce experimental lymphedema than is ever created from breast cancer treatments [7], indicating that other factors are required to generate lymphedema secondary to breast cancer. Such factors might include an increase in lymph production brought about by surgery, inflammation or infection, capillary angiogenesis increasing the surface area for increased net filtration rate, thus increasing filtration load [7] and further blockage of lymph nodes and vessels by metastatic disease.

Reported incidence rates of lymphedema secondary to breast cancer have varied greatly. Even within the same patient sample, incidence rates varied between 0.6% and 27.8% depending on the method used to measure lymphedema [8]. A trend has also been identified across studies that those with longer follow-up also report higher incidence rates [9]. Factors associated with development of lymphedema secondary to breast cancer have included removal of axillary nodes [10] or surgery to the axilla [11], axillary radiotherapy [11, 12], treatment on the dominant side [8], having blood pressure taken on the dominant side [8], previous radiation therapy [13], skin puncture, mastectomy, body mass index ≥26 [12, 14] and many more.

A majority of these and similar studies have employed follow-up periods of greater than 12 months duration [9]. In contrast, relatively little has been presented of changes in limb volumes in the period immediately following surgery, and following from this relatively little is known of the characteristics, swelling pattern and factors associated with changes during early stages. Echoing the need to address this deficit has been recent calls for greater investigation of lymphedema secondary to breast cancer in its early stages [7]. One study reported that approximately 3% of women could be classified as having secondary lymphedema within the first 2 months following surgery while undertaking a study of longer follow-up duration [14], though the pattern of changes at this time and factors associated with these were not described.

This study aims to address the relative paucity of information available describing early changes in upper limb volumes that may be attributable to lymphedema shortly following surgery for breast cancer. Specifically this study aims (i) to investigate the changes in upper limb volumes that occur during the first 6 weeks in both ipsilateral (to the side of surgery) and contralateral upper limbs, (ii) to compare changes in volume between different segments of each upper limb, (iii) to document the incidence of lymphedema amongst women with breast cancer in the first 6 weeks following diagnosis/surgery, and (iv) to identify factors associated with development of lymphedema at this time.

Methods

Study design

Retrospective audit.

Subjects and setting

Consecutive women undergoing unilateral surgery for breast cancer (mastectomy and/or axillary lymph node removal) at the Princess Alexandra Hospital between 2002 and 2005 who had pre-surgical and 6 week post-surgical measurements taken. This hospital provides health services primarily to people residing in the southern areas of Brisbane, Australia. Records missing measurements for the contralateral limb or for one segment of either limb were included. Women who initially had lumpectomy only, and subsequently had mastectomy and/or axillary lymph node removal were also included (the baseline and follow-up measures in this case were relative to the mastectomy/axillary lymph node dissection). The records of 193 women met the inclusion criteria and were included in the analysis.

Measurements

Circumferential upper limb measurements were taken with the arm abducted at 30° from the level of the ulnar styloid, then 10, 20, 30, and 40 cm proximal to this point along both the affected (side of surgery/treatment) and unaffected side. Calculation of limb segment volumes was undertaken using a ''frustum'' (truncated cone) approach [15]. Use of circumferential measures to estimate upper limb segment volumes in this manner has previously been employed [16]. Frustum calculations of limb segment volumes using circumferential measurement of segments 3, 6, and 9 cm apart have all been reported to have an intra- and inter-rater reliability of ICC = 0.99, while the standard error of measurement for this approach was lower than for cylindrical calculation and volumetry measurement approaches [15]. Measurements of the hand were not converted to volumes and included in this analysis due to the irregular shape of the hand making calculation of volumes from circumferential measurements invalid.

Surgical (type of surgery performed, number of lymph nodes removed, side of surgery, post-operative development of seroma, or infection) and demographic factors (age, previous mastectomy) were gleaned from patient medical records.

Criteria for defining lymphedema

Direct measurement of the presence and severity of lymphedema is difficult, and many variations in classifying the presence of lymphedema have been described, including comparisons between pre- and post-surgery measurements within the ipsilateral arm, and comparing measurements between ipsilateral and contralateral arms [8, 14, 16, 17]. Intuitively, comparisons within the affected arm over time may overstate the incidence of lymphedema if concomitant intracellular fluid volume increases have occurred (e.g. due to an increase in adipose tissue). However, comparisons between affected and unaffected arms may be confounded by pre-existing asymmetries between arms that are not related to lymphedema. These comparisons will also be insensitive to increases in extracellular lymph fluid that are distributed across both upper limbs due to anatomical anastomoses in the superficial lymphatic system allowing communication of lymph between ‘‘quadrants’’ of the body [18]. Although lymph only occasionally drains from the breast region to the contralateral axilla, its incidence may be increased if there is blockage of ipsilateral lymphatics [19]. Therefore, examining changes in volume of both ipsilateral and contralateral sides was considered important in this investigation and a criterion of 10% increase from pre-surgical volumes within arm was used to address study aims (iii) and (iv) [20].

Procedure

Baseline measures were taken by the radiation-oncology physiotherapist at preadmission clinic appointments at the Princess Alexandra Hospital prior to surgery. Follow-up measures were taken 6 weeks following surgery by the Domiciliary Allied Health Acute Care and Rehabilitation Service (DAART) physiotherapists visiting patients at this time. Baseline, follow-up and demographic data were entered onto a database by an investigator (PS) following their collection. When undertaking circumferential measurements, patients rested with their shoulder in 30° of abduction and elbow resting in 20° of flexion.

During the follow-up period, patients were provided with a list of self-management strategies designed to reduce their risk of developing secondary lymphedema. This primarily consisted of advice regarding completion of circulatory exercises in the upper limb, advice to reduce swelling, protecting the skin from cuts, burns and other potential sources of infection, avoidance of having injections on the operated side, and avoidance of having blood pressure taken on the operated side.

Analysis

Upper limb segments were labelled from one to four in a distal to proximal direction. Changes in volumes were compared between arms, over time, and between the four upper limb segments measured using a three-way, repeated measures analysis of variance (ANOVA) with the variables arm (ipsilateral versus contralateral), segment (four levels) and time (baseline and 6 week follow-up) as factors in the analysis. Post-hoc two-way repeated measures ANOVA tests were used to further investigate interaction effects identified. The correlation in volume changes between limb segment volumes was analysed using product–moment correlation coefficients. The incidence of lymphedema (10% volume increase from baseline) was identified by examining both the sum of segments, and any one segment within the ipsilateral and contralateral arms, and bilaterally. Factors associated with a 10% increase from pre-surgical volumes for each of these were identified using univariate logistic regression. Analyses were conducted using STATA SE version 8.0.

Ethics

Approval for this study was gained from the Princess Alexandra Hospital Human Research Ethics Committee.

Results

Baseline characteristics of the 193 women who had their histories reviewed are presented (Table 1). The predominant surgical procedure undertaken was that of lymph node removal.

Output from the three-way, repeated measures analysis of variance incorporating time (baseline versus 6 week follow-up), arm (affected versus unaffected), and limb segment predictor variables and volume (the outcome variable) is presented (Table 2). This analysis demonstrated significant main effects of time and

Table 1 Participant baseline characteristics

n	193
Age (years)	58.7 (12.5)
Previous mastectomy	18 (9%)
Mastectomy	73 (37.8%)
Lumpectomy	127 (65.8%)
≥1 Lymph nodes removed (yes or no)	172 (89.1%)
Lymph nodes removed (count)	14.1 (9.3)
Dominant side right	163 (84.5%)
Surgery on dominant side	103 (53.4%)
Infection during 6-week-period	14 (7.3%)
Seroma during 6-week-period	5 (2.6%)

Data presented are mean (standard deviation) or frequency (percentage)

segment, and a significant interaction effect of time*segment. These effects are presented graphically (Fig. 1). The interaction effects of arm*segment and arm*segment*time approached but did not reach statistical significance ($P = 0.07$ and $P = 0.12$, respectively). Post-hoc analyses were conducted to further investigate the time*segment interaction. Four two-way repeated measures ANOVA analyses (time and arm variables in model) were conducted, each employing data from only one limb segment. Results from these analyses identified no main effect of time within the first and second limb segments, but a significant main effect of time was identified for the third ($P < 0.001$) and fourth ($P = 0.002$) limb segments. All ANOVA results were consistent across standard and Box's conservative correction factor calculations. These results indicate that limb segment volumes increased over the first 6 weeks post surgery, particularly so in the more proximal segments.

The correlation between changes (follow-up minus baseline) in limb segment volumes in ipsilateral and contralateral arms is presented (Table 3). Correlations between adjacent segments on the same arm were greater than those between non-adjacent segments and between the same segment on opposing arms.

The number (proportion) of patients demonstrating a 10% increase in volume for individual limb segments, for the sum of all four segments, and for any one segment is presented (Table 4). Also presented are the number (proportion) of participants who demonstrated a 10% increase in limb volumes bilaterally. The fourth (most proximal) limb segment recorded the greatest number of patients with a 10% increase in segment volume on the affected arm, unaffected arm, and bilaterally.

Associations between baseline variables and a 10% increase in the sum of all four segments and for any one segment for the ipsilateral and contralateral arms, and bilaterally are presented (Table 5). Previous mas-

Table 2 Output of three-way, repeated measures analysis of variance incorporating time, arm and limb segment as predictor variables and volume as the outcome variable

Source	Partial SS	df	MS	*F*	Prob > *F*
Model	152548789	2886	52858.2083		
id	47960935.6	192	249796.54	24.91	0.0000
Time	63420.5217	1	63420.5217	6.32	0.0127
Time*id	1925381.17	192	10028.0269		
Arm	1801.11336	1	1801.11336	0.32	0.5719
Arm*id	1061884.61	189	5618.43711		
Segment	82473124.2	3	27491041.4	1211.98	0.0000
Segment*id	13042555.1	575	22682.7046		
Time*arm	684.081006	1	684.081006	0.22	0.6361
Time*arm*id	453455.8	149	3043.32752		
Time*segment	67962.3128	3	22654.1043	15.96	0.0000
Time*segment*id	813225.948	573	1419.24249		
Arm*segment	5601.5021	3	1867.16737	2.40	0.0668
Arm*segment*id	438407.288	564	777.317887		
Arm*segment*time	2192.68262	3	730.894207	1.96	0.1194
Arm*segment*time*id	163052.236	437	373.117244		
Residual	0	0			
Total	152548789	2886	52858.2083		

Error terms for each main effect and interaction effect were the interactions between patient id and the main effect or interaction effect

Between-subjects error term: id

Levels: 193 (192 df)

Lowest b.s.e. variable: id

Number of obs = 2887; Root MSE = 0

R-squared = 1.0000

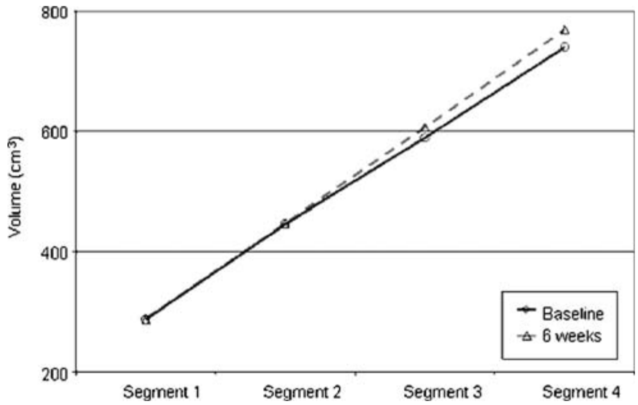

Fig. 1 Graph demonstrating main effects of segment and time, and time*segment interaction effect

tectomy was significantly associated with increased volume on the ipsilateral side (both sum and any one segment), the total number of lymph nodes removed was significantly associated with increased volume bilaterally (sum only), and infection during the 6-week-period was significantly associated with increased volume on the unaffected limb (any one segment).

Discussion

This study has made several findings, which may impact upon our understanding of early lymphedema and the mechanisms of lymphedema development. It is apparent that a moderate proportion of patients have 10% changes or more in their limb segment volumes over the first 6 weeks following surgery. A previous lymphedema incidence estimate of 3% in the first 2 months post surgery [14] provides a stark contrast to the 35% of patients who had a 10% volume change in one or more of their upper limb segment volumes on their ipsilateral side identified in the present study.

Table 4 Proportion of patients demonstrating a 10% increase in volume for individual limb segments and for the sum of all four segments, by individual arms and for both limbs at the same time

	n	Frequency (proportion) with 10% volume increase
Ipsilateral arm		
Segment 1 (US to 10 cm)	192	27 (14%)
Segment 2 (10–20 cm)	193	19 (9%)
Segment 3 (20–30 cm)	193	33 (17%)
Segment 4 (30–40 cm)	188	47 (25%)
Sum all 4 segments	187	29 (16%)
Any one segment	193	68 (35%)
Contralateral arm		
Segment 1 (US to 10 cm)	150	24 (16%)
Segment 2 (10–20 cm)	150	16 (11%)
Segment 3 (20–30 cm)	150	23 (15%)
Segment 4 (30–40 cm)	142	31 (22%)
Sum all 4 segments	142	14 (10%)
Any one segment	150	48 (32%)
Bilateral		
Segment 1 (US to 10 cm)	149	11 (7%)
Segment 2 (10–20 cm)	150	6 (4%)
Segment 3 (20–30 cm)	150	14 (9%)
Segment 4 (30–40 cm)	141	22 (16%)
Sum all 4 segments	140	10 (7%)
Any one segment	150	31 (21%)

Although patient characteristics between these studies were similar, the criteria for defining lymphedema were not consistent with the earlier study adopting an adjusted volume difference approach (between ipsilateral and contralateral arms) or clinical diagnosis by health professional as their criterion for classifying patients as having lymphedema [14]. Arguably, the criterion used in the present study may have had a lower threshold than that in the earlier study. However, previous research has also indicated that approximately 25% of patients who do not have a >10% increase in volume still experience subjective

Table 3 Pairwise product–moment correlations in volume change (from baseline) between limb segments both within and between arms

	Ipsilateral				Contralateral			
	Seg 1	Seg 2	Seg 3	Seg 4	Seg 1	Seg 2	Seg 3	Seg 4
Ipsilateral								
Seg 1	1.000							
Seg 2	0.887	1.000						
Seg 3	0.494	0.743	1.000					
Seg 4	0.490	0.613	0.785	1.000				
Contralateral								
Seg 1	0.440	0.409	0.369	0.530	1.000			
Seg 2	0.382	0.418	0.438	0.521	0.888	1.000		
Seg 3	0.216	0.355	0.548	0.564	0.668	0.841	1.000	
Seg 4	0.260	0.409	0.639	0.641	0.480	0.637	0.870	1.000

Table 5 Association [odds ratio (95% confidence interval)] between baseline variables and change in volume across all four segments, or in any one segment in the affected arm, the unaffected arm, and bilaterally

	Affected		Unaffected		Bilateral	
	All four segments	Any one segment	All four segments	Any one segment	All four segments	Any one segment
Age (years)	0.99 (0.96, 1.03)	0.99 (0.97, 1.02)	0.98 (0.94, 1.02)	1.01 (0.98, 1.03)	0.97 (0.93, 1.03)	1.00 (0.97, 1.03)
Previous mastectomy	3.48 (1.18, 10.34)[a]	3.25 (1.20, 8.83)[a]	2.63 (0.64, 10.78)	1.76 (0.61, 5.06)	4.21 (0.96, 18.46)	2.62 (0.87, 7.87)
Mastectomy	1.75 (0.79, 3.88)	1.24 (0.68, 2.28)	1.46 (0.48, 4.41)	1.26 (0.63, 2.52)	1.50 (0.41, 5.44)	1.63 (0.74, 3.62)
Lumpectomy	1.19 (0.51, 2.78)	0.84 (0.45, 1.56)	0.52 (0.17, 1.59)	0.76 (0.38, 1.55)	0.82 (0.22, 3.06)	0.59 (0.26, 1.32)
≥1 Lymph nodes removed (yes or no)	1.85 (0.41, 8.39)	1.85 (0.65, 5.29)	1.60 (0.19, 13.14)	2.39 (0.65, 8.74)	$Chi^2_{(1)} = 1.29$, $P = 0.25$[b]	2.09 (0.45, 9.67)
Lymph nodes removed (count)	1.02 (0.98, 1.07)	1.01 (0.98, 1.05)	1.05 (0.99, 1.12)	1.02 (0.98, 1.06)	1.10 (1.01, 1.18)[a]	1.04 (1.00, 1.09)
Surgery on dominant side	0.56 (0.25, 1.25)	0.81 (0.45, 1.47)	0.58 (0.19, 1.78)	0.57 (0.28, 1.13)	0.32 (0.08, 1.31)	0.56 (0.25, 1.25)
Infection during 6-week-period	0.90 (0.19, 4.25)	1.41 (0.47, 4.26)	2.50 (0.48, 13.14)	10 (2.03, 49.15)[a]	1.49 (0.17, 13.14)	2.79 (0.74, 10.58)
Seroma during 6-week-period	1.38 (0.15, 12.76)	2.84 (0.46, 17.42)	2.38 (0.25, 22.96)	0.52 (0.06, 4.790)	3.5 (0.35, 34.68)	0.96 (0.10, 8.89)

[a] Odds ratios significant where 95% confidence interval does not include the value 1.00

[b] Unable to calculate odds ratio due to all patients with 10% increase in sum of all four segments bilaterally having ≥1 lymph node removed. Chi square was therefore employed with *P* value indicating no significant difference between groups which was consistent with results when Yates correction [22] was employed

sensations of arm swelling indicating that a higher threshold criterion should not be set [21].

The potential for flow of lymph from the ipsilateral side to the contralateral side has been established through surgical findings [19], however, definitions of lymphedema that involve comparison of volumes between arms imply that increased lymph within the contralateral arm is either absent, not important, or that only volumes in the ipsilateral limb in excess of those in the contralateral limb are important. Four findings from this study provide argument for greater focus to be placed on the role of contralateral lymph flow. First, the higher than expected incidence of increases in limb segment volumes both contralaterally and bilaterally. Second, the significant association between previous mastectomy with increased limb segment volumes ipsilaterally. Arguably, if contralateral lymph flow was important for minimising lymphedema on the ipsilateral side, then disruption to channels for contralateral flow which could potentially have been brought about by previous mastectomy surgery would increase the risk of ipsilateral volume increases. Third, the presence of a significant time effect but not a significant arm*time interaction effect on limb segment volumes. Fourth, the significant association between number of lymphnodes removed and bilateral increase in sum of all four upper limb segments examined.

These findings paint a picture that during the first 6 weeks following surgery, the removal of a greater number of lymph nodes increases the risk of increasing upper limb segment volumes, and that increases in upper limb segment volumes are distributed between sides of the body unless there are impediments to lymph flow possibly brought about by previous surgery (mastectomy) in the area. One could hypothesise from this that the typically unilateral presentation of later stage lymphedema could be contributed to by blockage of contralateral channels of lymph flow arising from surgery or edema-related fibrosis of these vessels or the tissue that they run through. This finding also indicates that estimates of lymphedema incidence made during the early post-operative period that employ a comparison between arms criterion for defining lymphedema may underestimate the true incidence of lymphedema.

The pattern of changes in limb segment volumes was not consistent across the length of either affected or unaffected arms, nor symmetrical between arms. Proximal limb segments displayed greater increases in volumes than did distal segments. Segments not adjacent to each other displayed lower levels of correlation in volume change over the follow-up period than adjacent segments. This, however, may have been an artefact of employing the frustum approach to calculating segmental volumes in that adjacent segments held in common one of the circumferential measures involved in their calculation. It may be that some segments (particularly the proximal segments) are more prone to pooling of lymph fluid during early stages than distal segments. Why this may be the case is unclear, as anatomically there is greater muscle tissue to aid movement of lymph through initial lymphatic vessels in these upper-limb segments than in the more distal segments [7]. Possibly, there is an increased volume of lymph produced during this period which is transported towards the axillary nodes, resulting in excess accumulating near the axilla.

The association between infection and a 10% increase in any one limb segment on the contralateral side without evidence of a similar association with the ipsilateral side was a surprising finding. Possibly, knowledge of the presence of the infection may have prompted the patient to undertake self-management strategies such as circulatory exercises to manage anticipated lymphedema on the ipsilateral side only.

There are several limitations of the study design employed. First, the sample was restricted to a group of patients attending only one hospital. Characteristics particular to the sampled population and the treating hospital may limit the external validity of these results, though the authors have no reason to suspect systematic differences between this population and populations from other developed nations, nor the care provided by this hospital and hospitals in other developed countries. Second comparing volumes based on circumferential measures only provides an indirect measure of lymphedema. Changes in circumferential measures could also be attributable to changes in muscle tissue, adipose tissue, and non-lymph fluid volumes. These factors confound how strongly increases observed in limb segment volumes can be directly attributed to lymphedema. Third, hand volumes were not considered in this investigation. Considering the poor correlation between changes in volumes of non-adjacent segments observed in this study, it would be inappropriate to extrapolate findings from this study to the hand.

As this is one of a very small number of trials to investigate early lymphedema following breast cancer surgery and that the results have been generated from only one hospital, future research is required to determine if these results are consistent with those from patients of other hospitals. Research is required to determine whether the changes demonstrated during this early post-operative period resolve with time, and whether they are predictive of developing established lymphedema. Further investigation of contralateral lymph flow during this time should also be investigated, particularly from the perspective of whether this flow pathway can be exploited for the prevention and management of established lymphedema.

Lymphedema continues to be a concerning complication for women following surgery or radiation therapy for breast cancer. Understanding fully the mechanisms for the development of established lymphedema cannot be achieved through this study with only one snap-shot follow-up. However, this study has highlighted a potentially greater role of contralateral flow of lymph during this time which is important when considering how to measure lymphedema and may be important for the development of future strategies to prevent its onset.

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References

1. Wilkinson D, Cameron K (2004) Cancer and cancer risk in South Australia: what evidence for a rural–urban health differential? Aust J Rural Health 12:61–66
2. Beaulac SM, McNair LA, Scott TE et al (2002) Lymphedema and quality of life in survivors of early-stage breast cancer. Arch Surg 137:1253–1257
3. Hull M (1998) Functional and psychosocial aspects of lymphedema in women treated for breast cancer. Innov Breast Cancer Care 3(97–100):117–118
4. Tobin MB, Lacey HJ, Meyer L et al (1993) The psychological morbidity of breast cancer-related arm swelling. Psychological morbidity of lymphoedema. Cancer 72:3248–3252
5. Morrell RM, Halyard MY, Schild SE et al (2005) Breast cancer-related lymphedema. Mayo Clin Proc 80:1480–1484
6. Casley-Smith JR (1992) Modern treatment of lymphoedema. I. Complex physical therapy: the first 200 Australian limbs. Australas J Dermatol 33:61–68
7. Mortimer PS (1998) The pathophysiology of lymphedema. Cancer 83:2798–2802
8. Hayes S, Cornish B, Newman B (2005) Comparison of methods to diagnose lymphoedema among breast cancer survivors: 6-month follow-up. Breast Cancer Res Treat 89:221–226
9. Petrek JA, Heelan MC (1998) Incidence of breast carcinoma-related lymphedema. Cancer 83:2776–2781
10. Larson D, Weinstein M, Goldberg I et al (1986) Edema of the arm as a function of the extent of axillary surgery in patients with stage I–II carcinoma of the breast treated with primary radiotherapy. Int J Radiat Oncol Biol Phys 12:1575–1582
11. Kissin MW, Querci della Rovere G, Easton D et al (1986) Risk of lymphoedema following the treatment of breast cancer. Br J Surg 73:580–584
12. Ozaslan C, Kuru B (2004) Lymphedema after treatment of breast cancer. Am J Surg 187:69–72
13. Hinrichs CS, Watroba NL, Rezaishiraz H et al (2004) Lymphedema secondary to postmastectomy radiation: incidence and risk factors. Ann Surg Oncol 11:573–580

14. Clark B, Sitzia J, Harlow W (2005) Incidence and risk of arm oedema following treatment for breast cancer: a three-year follow-up study. QJM 98:343–348
15. Sander AP, Hajer NM, Hemenway K et al (2002) Upper-extremity volume measurements in women with lymphedema: a comparison of measurements obtained via water displacement with geometrically determined volume. Phys Ther 82:1201–1212
16. Box RC, Reul-Hirche HM, Bullock-Saxton JE et al (2002) Physiotherapy after breast cancer surgery: results of a randomised controlled study to minimise lymphoedema. Breast Cancer Res Treat 75:51–64
17. Ryttov N, Holm NV, Qvist N et al (1988) Influence of adjuvant irradiation on the development of late arm lymphedema and impaired shoulder mobility after mastectomy for carcinoma of the breast. Acta Oncol 27:667–670
18. Bourgeois P, Leduc O, Leduc A (1998) Imaging techniques in the management and prevention of posttherapeutic upper limb edemas. Cancer 83:2805–2813
19. Perre CI, Hoefnagel CA, Kroon BB et al (1996) Altered lymphatic drainage after lymphadenectomy or radiotherapy of the axilla in patients with breast cancer. Br J Surg 83:1258
20. Christensen S, Lundgren G (1989) Sequelae of axillary dissection vs axillary sampling with or without irradiation for breast cancer. Acta Chir Scand 155:515–520
21. Borup Christensen S, Lundgren E (1989) Sequelae of axillary dissection vs. axillary sampling with or without irradiation for breast cancer. A randomized trial. Acta Chir Scand 155:515–519
22. Cochran W (1954) Some methods for strengthening the common Chi2 tests. Biometrics 10:417–451