ORIGINAL ARTICLE

Obesity is a Risk Factor for Developing Postoperative Lymphedema in Breast Cancer Patients

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■ **Abstract:** Lymphedema (LE) is a well-known postoperative complication after axillary node dissection (ALND). Although, sentinel lymph node dissection (SLND) involves more focused surgery and less disruption of the axilla, early reports show up to 13% of patients experience some symptoms of LE. The purpose of this study was to determine predictors of arm LE in our patients under going SLND with or without an ALND. One hundred and thirty-seven breast cancer patients were treated at a comprehensive cancer center. Prospective measurement of arm volume was carried every 6 months from date of diagnosis. This data base was retrospectively reviewed for tumor stage, treatment, and subjective complaints of LE. Objective LE was defined as a change greater than 200 mL compared with the control arm. Univariate and multivariate analyses were performed. Arm volume changes were measured over 24 months (median follow-up 20 months) in 137 women: 82 stage I, 48 stage II, and 5 stage III; median age 56 years. Breast-conserving surgery was performed in 133 patients. All patients underwent SLND for axillary staging and for 52 patients this was the only axillary staging procedure. All node-positive patients (31) and 54 node-negative patients under went an immediate completion ALND, the latter as part of a study protocol. At 24 months, 16 (11.6%) patients were found to have objective LE (>200 mL increase). Patient age, tumor size, number of nodes harvested, or adjuvant chemotherapy was not found to be predictive of LE by univariate analysis. The risk of developing postoperative LE was primarily and significantly related to the patients' BMI ($p = 0.003$). Multivariate analysis revealed patients with a BMI >30 (obese) had an odds ratio of 2.93 (95% CI 1.03–8.31) compared with those with a BMI of <25 of having LE. Symptomatic LE (SLE), as defined by patient complaints was recorded in six of the above 16 patients, no SLE was recorded in patients without objective signs of edema. Univariate subgroup analysis compared the symptomatic to the nonsymptomatic patients and revealed the median number of nodes removed was higher in the symptomatic patients (17 verses 9, $p = 0.045$); however, these patients had a lower BMI ($p = 0.0012$). The mean change in arm volume was not significantly different between the groups. SLE occurs in one third of patients with objective arm swelling and most likely is multi-factorial in etiology. Although patients undergoing SLN were recorded as having objective LE, none reported SLE. The development of LE within 2 years of surgery is associated with the patient's BMI and this should be considered in preoperative counseling. ■

Key Words: lymphedema, obesity, sentinel node biopsy

Lymphedema (LE) is a chronic condition caused by the accumulation of protein rich fluid in the interstial space. It commonly afflicts many patients after treatment of their breast cancer, often affecting both the breast and ipsilateral limb. Although three quarters of patients have symptoms within 1 year of surgery, the onset can be insidious and patients remain at risk for the rest of their lives (1–3). The development of LE is multifactorial and is associated with both patient characteristics, such as age, menopausal status and body mass index (BMI), as well as disease factors such as stage, extent, and treatment including extent of surgery and use of adjuvant treatment (1–12). The risk of developing LE after axillary lymph node dissection (ALND) is considerable (10). Gallagher and Algrid in 1966 demonstrated 66% of ALND patients had some measurable arm swelling; a more recent study with 20 years of follow-up showed 49% of patients with ALND had a sensation of arm swelling (3,13). The physical and psychological consequences of LE range from minor discomfort; swelling, and

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increased susceptibility to infections, to more serious life-threatening secondary malignancies, depression, and body image disorders (1,14). The symptoms attributed to LE are correlated to a decrease in quality of life (2,15,16).

Sentinel lymph node biopsy (SLND) is an established surgical technique using lymphatic mapping and sampling of axillary nodes directly draining the carcinoma. It has the advantage of better pathologic assessment of the nodes at risk of harboring disease and if negative, avoids the risk of requiring an ALND and its associated morbidities (17–19). The development of LE has been strongly correlated with the extent of axillary surgery and the number of lymph nodes removed (10), as a result the development and use of the sentinel node biopsy is believed to diminish this risk to patients. Consequently, it has been proposed that the risk of LE to women with breast cancer undergoing a SLND is much reduced in comparison with ALND (17,20).

The objective of this study was to determine the predictors of arm LE in patients under going SLND with or without a completion ALND.

METHODS

Women were prospectively accrued to the study from December 2000 to March 2004 when diagnosed with an early stage breast cancer. The study was performed at a tertiary care cancer center. One hundred and thiry-seven patients were identified and follow-up is on going, four patients withdrew and results are calculated including them (intention to treat). Median follow-up is currently 20 months. Study approval was obtained from the local research and ethics board.

Sentinel lymph node biopsy technique has been described previously (21). Sentinel lymph nodes were localized by peri-tumoral injection of a radioactive colloid (30–40 MBq of unfiltered Tc99 sulfur colloid in 6–8 mL) and/or isosulphan blue dye (total volume = 5 mL). Lymphoscintigraphy was performed for patients who underwent radioactive colloid injection. Radioactive nodes were considered sentinel nodes if the count per 10 seconds was greater than or equal to 10% of that of the most radioactive node. Intra-operative localization of the sentinel lymph nodes was performed with the help of a handheld gamma probe (Cancer Wise Medical, Morgan Hill, CA) and also by visualizing the blue lymphatic ducts and lymph nodes. At the time of surgery, the sentinel lymph nodes and the axillary dissection specimens were labeled separately.

Pathologic evaluation of each sentinel lymph node was performed following a standard grossing protocol. Each sentinel and nonsentinel lymph node was bisected along its longitudinal axis to yield tissues slices 2–3 mm thick, and the slices were submitted in toto for histologic examination. The sentinel lymph nodes were reported as either positive or negative for metastatic disease and the size of the largest focus of metastatic disease and the primary detection method (either hematoxylin–eosin or immunohistochemistry) was recorded. The number of positive nodes and the total number of nodes removed in the axillary lymphadenectomy were also noted.

Patients with positive sentinel nodes underwent an axillary dissection of levels I and II. Women with negative sentinel nodes (54) also had an axillary dissection; this was performed to detect our false-negative rate on study protocol.

Arm volume has been shown to provide highly reproducible data and is currently the standard manner in which arm volumes are followed (1,22,23). Arm volume measurements were recorded preoperatively and then every 6 months. A dedicated study nurse, always using the same protocol, performed arm volume measurements. The arm was submersed to 10 cm above the olecranon and the volume was recorded. The study arm and control arm were measured each visit. Measurement changes of greater than 200 cc from baseline, after correction for changes in the control arm, were considered evidence of objective LE (OLE).

$$[(\text{Study arm volume at time } X) - (\text{Study arm volume preop})] - [(\text{Control arm volume at time } X) - (\text{Control arm volume preop})] = \text{Volume change at time } X.$$

The clinic charts (surgical oncology, radiation oncology, and medical oncology) were reviewed for demographic, treatment, and pathologic data. Symptomatic LE (SLE) was defined for the study purpose as [1] the physician or nurse in follow-up noting swelling of the ipsilateral arm with included hyperemia, and pitting edema. Or [2] the patient raising concern over persistent to intermittent findings of swelling, heaviness or stiffness in the forearm, hand or fingers.

It is our routine practice to refer patients with subjective findings of LE for assessment by the LE clinic. Here, management and treatment options are offered.

The definition of BMI was derived by the WHO and is calculated using the weight and height of a patient.

$$\text{BMI} = \text{Weight (kg)}/\ \text{Height (m)}^2$$

The BMI ranges are based on the relationship between body weight and disease and death (24). People with a BMI less than 18.5 are considered under weight, 18.5–24.9 normal weight, 25–29.9 over weight and those with a BMI greater than 30 are obese. BMI can be considered an alternative for direct measures of body fat. Additionally, BMI is an inexpensive and easy-to-perform method of screening for weight categories that may lead to health problems.

Statistical evaluation was performed using univariate and multivariate analysis where appropriate. The associations between the potential risk factors and response variable were assessed using *T*-test for continuous variables. For categorical risk factors, Pearson's chi-squared test or Fisher's exact test was carried out for nominal variables, and Cochran-Armitage trend test was performed for ordinal explanatory variables. Multivariate analysis was performed using logistic regression. The variable selection procedure was stepwise selection. For subgroup analysis, only univariate analysis was performed because of few cases in the study. All reported p-values are two-sided. Statistical significance level was set at 0.05.

RESULTS

One hundred and thirty-seven women were accrued to the study from December 19, 2000 to April 3, 2004, median follow-up of 20 months (range 6–36 months). Four patients were accrued but failed to have any arm measurements recorded, they are included in the analysis. The patient population's median age was 56 years (range 36–78), 23% were premenopausal (<50 years) (Table 1).

All tumors were invasive cancers with the majority classified as ductal subtype (87%) with a median size of 1.5 cm (range 0.1–7.7 cm), 43% grade 2. On pathologic review, 75% of patients were diagnosed with a T1 tumor and 60% were classified as having stage I diseases. Node-positive patients were found to have a higher proportion of T2/T3 tumors and as a result had more advanced disease (Table 1).

The majority (97%) of patients were initially treated with breast-conserving therapy. Eleven patients initially treated with breast-conserving surgery had a subsequent mastectomy for positive margins. The total mastectomy rate was 11%. SLND biopsy was performed on all patients (137). Those found to be node positive by SLND had an ALND (n = 31). ALND was also performed for 54 node-negative patients, as per protocol.

Table 1. Characteristics of Patients, their Tumor Pathology, Surgical Procedure and Stage of Disease Included in this Study

	All PT n = 137 (%)	Node-neg pt n = 106 (%)	Node-pos pt n = 31 (%)
Age (years), median (range)	56 (36–78)	56 (36–78)	56 (37–75)
Ductal histology (%)	119 (87)	91 (86)	28 (90)
Size of tumor (cm), median (range)	1.5 (0.1–7.7)	1.4 (0.1–6.9)	1.6 (0.6–7.7)
Grade			
1	48* (35.5)	41† (38.7)	7 (24)
2	58* (43)	45† (42.5)	13 (45)
3	29* (21.5)	20† (18.9)	9 (31)
Lumpectomy	133 (97)	104 (97)	29 (97)
Mastectomy after lumpectomy	11 (8)	8 (7.5)	3 (9.7)
Mastectomy	4 (3)	4(3)	0
No. nodes removed, median (range)	13 (1–28)	8 (1–28)	17.5 (11–24)
No. pt SLN only	54 (39)	54 (100)	0
Average no. SLND, median (range)	3 (1–11)	3 (1–10)	4 (1–11)
Stage I (%)	82* (60)	82† (80)	0
Stage 2 (%)	Iia 39*(28)	Iia 20 (18)	Iia 19 (61)
	Iib 9*(6.5)	Iib 2 (2)	Iib 7 (23)
Stage3 (%)	5*(4)	0	5 (16)

*n = 135 and †n = 104 because of tumors being removed by core biopsy and having no documented size of tumor.

OLE

Objective defined lymphedema measured by a corrected arm volume increase of 200 cc, was observed in 11.7% (n = 16) of patients. Univariate statistical analysis found OLE was associated with BMI (p = 0.003). The relative increase in arm volume (% increase) was correlated to BMI; those with a high BMI showed a trend to have a larger change in their arm volume after surgery (Fig. 1). There was no statistically significant association between OLE and type of axillary surgery performed (ALND- 62.5% versus SLND-37.5%). Patients who had a SLND dissection had an 11% incidence of measurable OLE as compared with a 12% incidence in those who had an ALND, p = ns. The median number of lymph nodes examined in the LE group was 10 versus 13 in the non-OLE group (p = 0.9). However, a trend showing

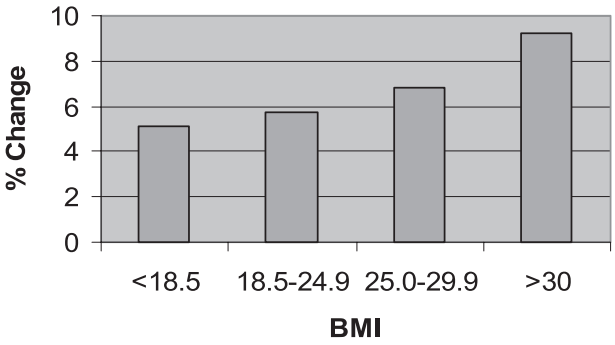

Figure 1. The association of arm volume change and body mass index.

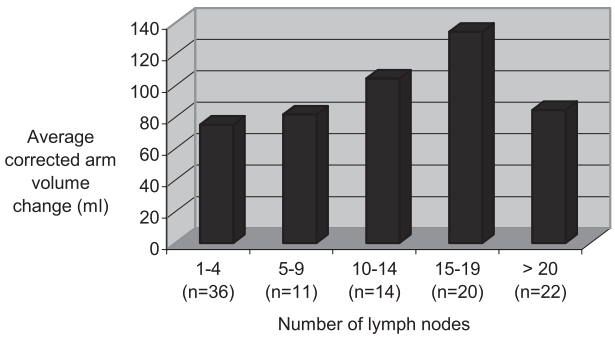

Figure 2. The number of lymph nodes examined compared to the change in the observed corrected arm volume (mL).

that arm volume increased for increasing numbers of axillary nodes examined could be demonstrated in the OLE group, but this was not statistically significant (Fig. 2). Postoperative treatment with chemotherapeutic agents or hormonal agents was not associated with the development of OLE. Similarly radiation therapy was not found to be associated with the development of OLE. The majority of our patients had small tumors (73% T1) and negative nodes (77%). Consequently, most patients received radiation only to the breast (89%) and the majority did not require chemotherapy (69%). Thirteen patients with positive nodes had axillary radiation following the completion ALND and none exhibited objective evidence of LE during follow-up.

Change in arm volume was also expressed as percentage change, and can account for changes in the control arm volume over time. All patients with <200 mLs change were also found to have less than 10% volume change; the mean percentage change for these patients was 0 ± 5.9 (mean ± SEM) range −16 to 10%. The mean percentage change for those with greater than 200 mL difference in corrected arm volume was $13 \pm 8.8\%$ (range 6–24%) $p < 0.0001$. There was no difference in mean percentage change between those with OLE and SLE.

On multivariate analysis, BMI remained the only variable associated with the development of OLE. The estimated odds ratio was 1.082 for every unit increase of BMI (95% CI 1.0004–1.165). The odds of an obese women having LE compared with a woman with a normal BMI were 2.9 times greater.

SLE

Extensive chart review found only six patients to have SLE of the 137 patients; all of these patients had documented OLE. There were no patients with SLE who did not exhibit OLE. Subgroup analysis was performed comparing the symptomatic patients to the remaining 131 patients (Table 2).

There were no differences between the symptomatic and asymptomatic patients on analysis of patient age, tumor size, or stage. Half of the symptomatic patients

Table 2. Comparative Analysis of Lymphedema; Factors Predicting Patients with Symptomatic Versus Objective Findings

	No lymphedema *n* = 121	Objective lymphedema *n* = 11	Symptomatic lymphedema *n* = 6	OLE versus SLE p-value
Age (years)	56	59	55	ns
Size of tumor (cm)	1.45	1.74	1.28	ns
Estrogen receptor positive	93 (77%)	10 (90%)	5 (83%)	ns
Mastectomy	12 (10%)	2 (18%)	1 (16%)	ns
Lumpectomy	109 (90%)	11 (100%)	6 (100%)	ns
SLND only	48 (40%)	6 (54%)	0	0.02
Total no. LN (median)	13	9	17	0.045
Chemotherapy	36 (30%)	1 (9%)	2 (33%)	ns
XRT to breast	108 (89%)	15 (94%)	6 (100%)	ns
BMI	25.8	32	24.8	0.012
Mean change in arm vol. (mL)	30.4	280	386	0.577

had a tumor located in the upper outer quadrant of the breast in comparison with 20% in the nonsymptomatic group. Those patients with symptoms had more lymph nodes dissected from the axilla (17.2 versus 9, p = 0.047). All patients with SLE had an ALND performed after or concurrently with SLND, consequently they may be considered as having had more surgery (p = 0.056). In this group, there was no correlation between BMI and SLE (p = 0.44). Symptomatic patients were found to have a larger arm volume increase (386 mL) than those with OLE but no documented symptoms (280 mL) p = 0.44 (Table 2); however, there was no difference in the percent volume increase between those with SLE compared with those with OLE (p = 0.577).

Chart review revealed one patient sustained an injury to her hand, shortly after her breast surgery, this may have precipitated the LE. All other women presented asymptomatically. All symptomatic patients were referred to a LE clinic where treatment was prescribed. On chart review, no relationship could be identified between LE and comorbid disease. Of those with OLE, seven (43%) had no previous medical history documented: 2/6 with SLE and 5/10 with asymptomatic LE. Essential HTN was documented in three patients (1SLE), hypercholestrolemia in one(1SLE) and two patients were asthmatic (1SLE). Arthritis was documented in one patient in each group. In addition, each group had one patient with diabetes.

DISCUSSION

Sentinel lymph node dissection is a 'smaller', less invasive operation than ALND and was initially described to be associated with fewer complications and consequently less LE (17,25–27). However, as the technique gains wider acceptance and the reported sequella become better understood, SLND complications appears to be similar in incidence and nature to axillary node dissection. Temple et al. in comparing patients undergoing ALND versus SLND found the acute complications and side effects were similar between the two groups, and there was very little difference between the two procedures at 1 year of follow-up (14).

Lymphedema defined as an accumulation of interstitial fluid in the subcutaneous tissues, has many different clinical definitions. As a result, the incidence of reported LE varies between studies based on the method of objective measurement, arm volume versus arm circumference. LE was reported to occur in 6–55% of patients undergoing an ALND, the incidence varying with length of follow-up. Currently, the incidence of LE in the SLND literature ranges from 0 to 13% and our incidence of 11% correlates (25–31). Similarly, the incidence of SLE is variable, depending mostly on the manner in which information is collected, for example through active questioning or via passive nonprompted reporting.

Lymphedema may also be defined as a volume gain expressed as a percentage of the original arm volume corrected for changes in the control arm (32). This method when used did not identify any new patients with OLE and failed to better distinguish between those with SLE and OLE. LE is more than the visible signs of arm/hand/breast swelling or increases in measurable arm volume and consequently symptom measurement instruments should be employed in combination with arm volume measurements to better ascertain the population at risk.

Many groups report associations between LE and the extent of axillary surgery or the total number of examined lymph nodes (7,10,15,29). Our data were unable to support this premise; however, there was a nonsignificant trend to show larger arm volumes were measured in those patients where more lymph nodes were examined. Reasons for this lack of statistical significance may be due to similar numbers of nodes removed in each group (non-LE versus SLE: 13 versus 17). This data was also collected relatively early in our institution's experience with SLND and our early technique may have incurred extensive axillary disruption and consequently harvesting of more than the required number of nodes.

Lymphedema is also reported to occur more frequently in those undergoing adjuvant radiation (2,4,6,7,9,10). The majority of our patients received radiation; however, this was limited to the breast fields only, as most patients were lymph node negative. In those patients who were node positive, only 13 had radiation to the axilla, supraclavicular, and/or chest wall. These patients either had more than four positive nodes or had evidence of extra capsular extension. Consequently, our lack of association between LE and radiation therapy is likely a product of the small sample size and early follow-up.

There are many patient factors associated with the development of LE; age, menopausal status, and BMI. Pezner et al. found 25% of patients greater than 60 years had LE compared with 7% of those less than 60 years and concluded those greater than 60 years

were at an increased risk (11). The majority (77%) of our patients were postmenopausal, median age 56 years (range 36–78 years). We were unable to show LE was associated with advancing patient age or menopausal status. BMI is also well described to be associated with LE (3,4,7,8,12,32–34). Indeed, our patients with a BMI greater than 30 had a twofold risk of developing LE. The etiology of this is poorly understood; is it a product of a heavier limb with more subcutaneous tissue, adipose, and skin, acting as a reservoir for lymphatic fluid (12,35), or is it because of the surgery needing to be more extensive as a result of the presence of adipose tissue and therefore more destructive to the lymphatics (35). Very little is known regarding the determinants of lymphatic flow and more study on lymphatic drainage and impedance should to be performed to accurately determine the pathogenesis of LE in the obese.

The stage of cancer, tumor size, and location of the tumor in the breast has been associated with the development of arm LE; however, the majority of our patients had small (T1) tumors and was node negative and we could not associate LE to stage. The burden of disease in our node-positive patients was small as only 13% had greater than four nodes involved. Although the patients with stage 3 disease ($n = 16$) displayed no evidence of LE, they should be considered too small a sample to be truly representative of this patient population.

Lymphedema in women with breast cancer, even with the use of sentinel lymph node dissection, is not a rare event and for the affected individual greatly impacts their day to day living and quality of life (36). The multi-factorial causation of this problem makes it difficult to avoid and implement preventative strategies. Preoperative counseling of patients undergoing sentinel node biopsy must include LE as a possible sequella, especially in those with a high BMI. However, in this study only women undergoing completion ALND reported SLE. In these patients, further studies should be centered on diminishing their risk of LE and exploring better therapies. Currently, there are several independent groups of researchers investigating microsurgery for lympho-venous anastomosis and the transplantation of lymph nodes from nonaffected areas to improve lymphatic drainage (37–39). Current case reports are promising.

Lymphedema could be demonstrated in patients undergoing SLND for axillary staging; however, only those having a completion ALND recorded symptoms. Obesity was associated with an increase risk of developing LE and is considered in our preoperative patient counseling.

REFERENCES

1. Pain SJ, Purushotham AD. Lymphoedema following surgery for breast cancer. *Br J Surg* 2000;87:1128–41.
2. Hinrichs CS, Watroba NL, Rezaishiraz H, *et al.* Lymphedema secondary to postmastectomy radiation: incidence and risk factors. *Ann Surg Oncol* 2004;11:573–80.
3. Petrek JA, Senie RT, Peters M, Rosen PP. Lymphedema in a cohort of breast carcinoma survivors 20 years after diagnosis. *Cancer* 2001;92:1368–77.
4. Meric F, Buchholz TA, Mirza NQ, *et al.* Long-term complications associated with breast-conservation surgery and radiotherapy. *Ann Surg Oncol* 2002;9:543–9.
5. Zissiadis Y, Langlands AO, Barraclough B, Boyages J. Breast conservation: long term results from Westmead Hospital. *Aust N Z J Surg* 1997;67:313–9.
6. Kissin MW, Querci della Rovere G, Easton D, Westbury G. Risk of lymphoedema following the treatment of breast cancer. *Br J Surg* 1986;73:580–4.
7. Goffman TE, Laronga C, Wilson L, Elkins D. Lymphedema of the arm and breast in irradiated breast cancer patients: risks in and era of dramatically changing axillary surgery. *Breast J* 2004;10:405–11.
8. Johansson K, Ohlsson K, Ingvar C, Albertsson M, Ekdahl C. Factors associated with the development of arm lymphedema following breast cancer treatment: a match pair case-control study. *Lymphology* 2002;35:59–71.
9. Schunemann H, Willich N. Lymphedema of the arm after primary treatment of breast cancer. *Anticancer Res* 1998;18: 2235–6.
10. Herd-Smith A, Russo A, Grazia Muraca M, Rosselli Del Turco M, Cardona G. Prognostic factors for lymphedema after primary treatment of breast carcinoma. *Cancer* 2001;92:1783–7.
11. Pezner RD, Patterson MP, Hill LR, *et al.* Arm lymphedema in patients treated conservatively for breast cancer: relationship to patient age and axillary node dissection technique. *Int J Radiat Oncolo Biol Phys* 1986;12:2079–83.
12. Ozalan C, Kuru B. Lymphedema after treatment of breast cancer. *Am J Surg* 2004;187:69–72.
13. Gallagher PG, Algird JA. Post radical mastectomy edema of the arm: the role of phlebitis. *Angiology* 1966;17:377–88.
14. Temple LKF, Baron R, Cody H, *et al.* Sensory morbidity after sentinel lymph node biopsy and axillary dissection: a prospective study of 233 women. *Ann Surg Oncol* 2002;9:654–62.
15. Ivens D, Hoe AL, Podd TJ, *et al.* Assessment of morbidity from complete axillary dissection. *Br J Cancer* 1992;66:136–8.
16. McWayne J, Heiney S. Psychological and social sequelae of secondary lymphedema. *Cancer* 2005;104:457–66.
17. Burak WE, Hollenbeck ST, Zerros EE, *et al.* Sentinel lymph node biopsy results in less postoperative morbidity compared with axillary lymph node dissection for breast cancer. *Am J Surg* 2002;183:23–7.
18. Shultz T, Mucke J, Markwardt J, Schlag PM, Bembenek A. Long-term morbidity of patients with early breast cancer after sentinel lymph node biopsy compared to axillary lymph node dissection. *J Surg Oncol* 2006;93:109–19.
19. Silberman AW, McVay C, Cohen J, *et al.* Comparative morbidity of axillary lymph node dissection and the sentinel lymph nodes technique. *Ann Surg* 2004;240:1–6.

20. Lucci A, McCall LM, Beitsch PD, *et al.* Surgical complications associated with sentinel lymph node dissection (SLND) plus axillary lymph node dissection compared with SLND alone in the American College of Surgeons Oncology Group Trial Z0011. *J Clin Oncol* 2007;25:3657–63.

21. McCready DR, Yong WS, Ng AK, *et al.* Influence of the new AJCC breast cancer staging system on sentinel lymph node positivity and false-negative rates. *J Natl Cancer Inst* 2004;96:873–5.

22. Engler HS, Sweat RD. Volumetric arm measurements: techniques and results. *Am Surg* 1962;28:465–8.

23. Taylor R, Jayasinghe UW, Koelmeyer L, *et al.* Reliability and validity of arm volume measurements for assessment of lymphedema. *Phys Ther* 2006;86:205–14.

24. World Health Organization. *Physical Status. The Use and Interpretation of Anthropometry*. Geneva, Switzerland: World Health Organization, 1995. WHO Technical Report Series.

25. Haid A, Kuehn T, Konstantiniuk P, *et al.* Shoulder-arm morbidity following axillary dissection and sentinel node only biopsy for breast cancer. *Eur J Surg Oncol* 2002;28:705–10.

26. Swenson KK, Nissen MJ, Ceronsky C, Swenson L, Lee MW, Tuttle TM. Comparison of side effects between sentinel lymph node and axillary lymph node dissection for breast cancer. *Ann Surg Oncol* 2002;9:745–53.

27. Schijven MP, Vingerhoets AJJM, Rutten HJT, *et al.* Comparison of morbidity between axillary lymphnode dissection and sentinel node biopsy. *EJSO* 2003;29:341–50.

28. Ronka R, von Smitten K, Tasmuth T, Leidenius M. One-year morbidity after sentinel node biopsy and breast surgery. *Breast* 2005;14:28–36.

29. Schrenk P, Rieger R, Shamiyeh A, Wayand W. Morbidity following sentinel lymph node biopsy versus axillary lymph node dissection for patients with breast carcinoma. *Cancer* 2000;88:608–14.

30. Blanchard E, Herman L, Larson L, *et al.* Understanding the role of sentinel lymph node biopsy in breast cancer and melanoma. *JAAPA* 2003;16:49–54.

31. Leidenius M, Leivonen M, Vironen J, Von Smitten K. The consequences of long-time arm morbidity in node-negative breast cancer patients with sentinel node biopsy or axillary clearance. *J Surg Oncol* 2005;92:23–31.

32. Wilke LG, McCall LM, Posther KE, *et al.* Surgical complications associated with sentinel lymph nodes biopsy: results from a prospective international cooperative group trial. *Ann Surg Oncol* 2005;13:491–500.

33. Clark B, Sitzia J, Harlow W. Incidence and risk of arm oedema following treatment for breast cancer: a three-year follow-up study. *Q J Med* 2005;98:343–8.

34. Meek AG. Breast radiotherapy and lymphedema. *Cancer* 1998;12:2788–92.

35. Werner RS, McKormick B, Petrek J, *et al.* Arm edema in conservatively managed breast cancer. *Radiology* 1991;180:177–84.

36. Fleissig A, Fallowsield LJ, Langridge CI, *et al.* Post-operative arm morbidity and quality of life. Results of the ALMANAC randomized trial comparing sentinel node biopsy with standard axillary treatment in the management of patients with early breast cancer. *Breast Cancer Res Treat* 2006;95:279–93.

37. Campisi C, Davini D, Bellini C, *et al.* Is there a role for microsurgery in the prevention of arm lymphedema secondarily to breast cancer treatment. *Microsurgery* 2006;26:70–2.

38. Becker C, Assouad J, Riquet M, Hidden G. Postmastectomy lymphedema: long-term results following microsurgical lymph node transplantation. *Ann Surg* 2006;243:313–5.

39. Yamamoto Y, Horiuchi K, Sasaki S, *et al.* Follow-up study of upper limb lymphedema patients treated by microsurgical lymphaticovenous implantation (MLVI) combined with compression therapy. *Microsurgery* 2003;23:21–6.