Case-Control Study to Evaluate Predictors of Lymphedema After Breast Cancer Surgery

Karen K. Swenson, RN, PhD, AOCN®, Mary Jo Nissen, PhD, MPH, Joseph W. Leach, MD, and Janice Post-White, RN, PhD, FAAN

Purpose/Objectives: To identify risk factors for lymphedema after breast cancer surgery.

Design: Multisite case-control study.

Setting: Lymphedema clinics in the upper midwestern region of the United States.

Sample: 94 patients with lymphedema and 94 controls without lymphedema, matched on type of axillary surgery and surgery date.

Methods: The Measure of Arm Symptom Survey, a patient-completed tool, assessed potential risk factors for lymphedema. Severity of lymphedema was measured by arm circumference, and disease and treatment factors were collected via chart review.

Main Research Variables: Risk factors for lymphedema after breast cancer surgery.

Findings: On univariate analysis, patients with lymphedema were more likely than controls to be overweight (body mass index ≥ 25) ($p = 0.009$). They also were more likely to have had axillary radiation ($p = 0.011$), mastectomy ($p = 0.008$), chemotherapy ($p = 0.033$), more positive nodes ($p = 0.009$), fluid aspirations after surgery ($p = 0.005$), and active cancer status ($p = 0.008$). Strength training ($p = 0.014$) and air travel ($p = 0.0005$) were associated with less lymphedema occurrence. On multivariate analysis, the only factor significantly associated with lymphedema was being overweight ($p = 0.022$).

Conclusions: Being overweight is an important modifiable risk factor for lymphedema. Axillary radiation, more extensive surgery, chemotherapy, and active cancer status also were predictive of lymphedema.

Implications for Nursing: This study provides evidence that excess weight contributes to lymphedema; strength training and airline travel did not contribute to lymphedema.

In 2008, more than 182,000 women were diagnosed with breast cancer, and 88% of those women will survive at least five years (Jemal et al., 2008). Lymphedema is a common problem for patients diagnosed with breast cancer, with an estimated 6%–35% developing it sometime after breast cancer treatment (Goffman, Laronga, Wilson, & Elkins, 2004; Hinrichs et al., 2004; Kwan et al., 2002; Lee, Kilbreath, Refshauge, Herbert, & Beith, 2007; Paskett, Naughton, McCoy, Case, & Abbott, 2007; Schrenk, Rieger, Shamiyeh, & Wayand, 2000; Thomas-MacLean et al., 2008).

The reported prevalence of lymphedema varies with the length of follow-up, measurement techniques, and other patient- and treatment-related factors (Armer & Stewart, 2005; Brown, 2004; Hayes, Cornish, & Newman, 2005). Lymphedema can range from mild to severe and can be a chronic condition that affects patients' quality of life for years after cancer surgery (Carter, 1997; Maunsell, Brisson, & Deschênes, 1993; Passik & McDonald, 1998; Thomas-MacLean, Miedema, & Tatemichi, 2005; Tobin, Lacey, Meyer, & Mortimer, 1993; Velanovich & Szymanski, 1999). Patients are concerned about how to prevent lymphedema because it is a common side effect associated with breast cancer treatment (Muscari, 2004).

Axillary lymph node dissection (ALND) for breast cancer causes disruption in the lymphatic vessels in the axilla. Radiation therapy to the axillary bed can cause further edema and fibrosis. The treatments may lead to accumulation of protein-rich fluid in the soft tissues of the hand, arm, breast tissue, and chest wall on the affected side. Oncotic pressure increases, causing progression of lymphedema (Petrek, Pressman, & Smith, 2000).

Sentinel lymph node biopsy (SLNB), a less invasive procedure than ALND, has been associated with lower rates of lymphedema and other arm symptoms (Baron et al., 2002; Burak et al., 2002; Golshan, Martin, & Dowlatshahi, 2003; Lucci et al., 2007; Mansel et al., 2006;

Purushotham et al., 2005; Sener et al., 2001; Wilke et al., 2006). In a study conducted at Park Nicollet Institute, 5% of patients who underwent SLNB reported arm swelling at six months after surgery versus 20% of patients who had full ALND ($p < 0.001$) (Swenson et al., 2002). However, patients are not eligible for SLNB if they have clinically positive nodes or a pathologically positive sentinel node, or if the surgeon is unable to locate the sentinel lymph node.

Several treatment-related factors have been associated with lymphedema, including the extent of axillary dissection, axillary radiation therapy after surgery, type of breast surgery, and the presence of infection in the ipsilateral arm (Gerber et al., 1992; Hoe, Iven, Royle, & Taylor, 1992; Højris, Andersen, Overgaard, & Overgaard, 2000; Kakuda, Stuntz, Trivedi, Klein, & Vargas, 1999; Keramopoulos, Tsionou, Minaretzis, Michalas, & Aravantinos, 1993; Kiel & Rademacker, 1996; Liljegren & Holmberg, 1997; Segerström, Bjerle, Graffman, & Nyström, 1992; Senofsky et al., 1991).

Several patient-related factors also have been evaluated for their association with lymphedema in patients with breast cancer, including increased body mass index (BMI), weight and resistance training exercise, degree of hand use, airline travel, hypertension, weight gain, diabetes, smoking, and older age at diagnosis. Association of those risk factors with lymphedema has been inconsistent in prior studies (Ahmed, Thomas, Yee, & Schmitz, 2006; Casley-Smith & Casley-Smith, 1996; Cheema, Gaul, Lane, & Fitarone Singh, 2008; Edwards, 2000; Johansson, Ohlsson, Ingvar, Albertsson, & Ekdahl, 2002; Ridner & Dietrich, 2008; Segerström et al., 1992; Shaw, Mortimer, & Judd, 2007; Soran et al., 2006; Tengrup, Tennvall-Nittby, Christiansson, & Laurin, 2000; Vignes, Porcher, Champagne, & Dupuy, 2006; Warmuth et al., 1998; Werner et al., 1991).

Previous studies have had several limitations. Most of the studies had a small sample size without a comparison group, making it difficult to determine which factors are significantly associated with lymphedema. Surgery and treatments for breast cancer have changed, with a higher proportion of patients now receiving lumpectomy, SLNB, and adjuvant treatment.

Women are advised to avoid lifting weights, constrictive pressure, and activities that could lead to arm injury or infection, but most of the advice is based on very limited data. Therefore, additional studies should identify factors that contribute to the development of lymphedema in patients with breast cancer.

The primary aim of the current study was to identify risk factors for lymphedema among women who have had axillary surgery for breast cancer. Secondary aims were to assess lymphedema's interference with daily life and to compare arm circumference measurements to patient-reported lymphedema.

Methods

Study Design

The study used a matched case-control design, which permitted identification of risk factors that were present more often in patients with lymphedema than in controls, who had breast cancer surgery but did not develop lymphedema. Cases and controls were matched on time since surgery because some of the potential risk factors (e.g., occurrence of arm infection, air travel since surgery) are expected to vary with time at risk. Cases and controls also were matched on type of axillary dissection (SLNB versus ALND). Clear evidence exists that lymphedema is much more common after ALND than SLNB (Langer et al., 2007; Lucci et al., 2007; Swenson et al., 2002; Wilke et al., 2006). Matching on type of dissection allowed more sensitive examination of other risk factors. Controls were not matched on age or other factors because matching on a variable precludes the possibility of assessing it as a potential risk factor.

The protocol and consent form for the study were reviewed and approved by the participating institutional review boards and the Department of Defense Human Subjects Research Review Board.

Setting

Women with lymphedema after breast cancer treatment were recruited from five clinics in Minneapolis and St. Paul, MN. The clinics and the number of cases from each were as follows: Park Nicollet Health Services (PNHS) (n = 73), a large multispecialty clinic with approximately 400 breast cancer cases diagnosed annually; Fairview-University Medical Center (n = 7), a National Cancer Institute–designated Comprehensive Cancer Center with approximately 150 breast cancer cases diagnosed annually; Fairview Southdale Medical Center (n = 5), a regional hospital with approximately 300 breast cancer cases diagnosed annually; Humphrey Cancer Institute (n = 5), which is affiliated with North Memorial Medical Center, a regional hospital with approximately 320 breast cancer cases diagnosed annually; and HealthEast Care System (n = 4), which includes St. John's Hospital and St. Joseph's Hospital in St. Paul, with approximately 280 breast cancer cases diagnosed annually.

Research Subjects

Women with lymphedema (prevalent and incident cases) were identified at the time they presented to the physical therapy department or cancer center at the five participating institutions. The study enrollment period began in January 2004 and extended through August 2007. All participants signed informed consent forms prior to completing questionnaires and conducting study procedures such as arm measurements.

Eligibility criteria were a clinical diagnosis of lymphedema (referred for lymphedema management), unilateral axillary surgery for invasive breast cancer, no known recurrent disease present in the axilla, and ability and willingness to give consent. Control participants were identified through the PNHS oncology registry, which includes all patients diagnosed or treated for cancer at PNHS. Eligibility criteria for controls were no upper-extremity lymphedema, unilateral axillary surgery for invasive breast cancer, no known recurrent disease in the axilla, and ability and willingness to give consent. The final sample size was 94 women with lymphedema and 94 matched controls.

Study Instruments

All participants completed the **Measure of Arm Symptom Survey (MASS)** (Swenson et al., 2002) as a subjective measurement of lymphedema and risk factors. Patients with lymphedema completed a questionnaire that was identical regarding risk factors, except a clause was added to each question (e.g., "Since your breast surgery, but before you had arm swelling, how often did you travel on an airplane?"). The MASS assessed potential lymphedema risk factors, including age, diabetes, hypertension, smoking, past shoulder injury, flexibility exercises, strength training exercises, medical procedures, arm and hand injury, local infections after surgery, aspirations after surgery (excess fluid removed from the surgery site), airline travel, and occupation. The questionnaires addressed the severity of symptoms by having patients rate them on a five-point Likert scale from 1 (no swelling) to 5 (very severe swelling). The degree of interference with life activities was assessed with a similar five-point scale of 1 (not at all) to 5 (very much). The instrument included 38 total questions (11 questions on symptom severity and interference with daily life, 18 questions on risk factors, and 9 demographic questions). The questionnaire took participants 15–20 minutes to complete. Each risk item was scored separately, so no summary score was calculated.

To establish content validity, the MASS was administered to and critiqued by the lymphedema support group and reviewed and critiqued by surgeons and oncology nurses. Revisions were made accordingly. The MASS was used in a previous study to compare arm symptoms between patients after SLNB versus ALND (Swenson et al., 2002). To assess test-retest reliability, the researchers mailed a second MASS questionnaire to the first 24 subjects in the study within two weeks after the initial questionnaires were completed. Test-retest reliability on the MASS was assessed with Pearson correlations for continuous variables and Spearman correlations for ordinal variables. Test-retest correlations ranged from 0.43–1.0. All correlations were statistically significant. Items with a test-retest correlation less than 0.60 were excluded from further analyses. They included questions related to (a) number of breast, chest, or arm infections; (b) wearing constrictive clothing, jewelry, or underwire bra; (c) performing flexibility exercises; (d) performing aerobic exercises; and (e) vigorous repeated arm motion activities.

BMI was calculated from self-report of weight and height at study entry.

Researchers took arm measurements of patients with lymphedema using a tape measure, starting at the hand and wrist, and measuring every 4 cm along the arm to the shoulder. The circumferences were added, and the percentage difference between the treated and untreated sides was calculated for each case. Circumferential limb measurements have high intra- and inter-rater reliability (Chen, Tsai, Hung, & Tsauo, 2008) and correlate strongly ($r = 0.98$) with limb volume measured by water displacement (Taylor, Jayasinghe, Koelmeyer, Ung, & Boyages, 2006) as well as with self-reported arm swelling and arm firmness (Ridner, Montgomery, Hepworth, Stewart, & Armer, 2007). Circumferential measurements are used commonly in clinical practice.

A patient intake form was completed for each participant enrolled in the study. Type of breast cancer surgery (lumpectomy or mastectomy), tumor size (cm), type and date of axillary surgery (SLNB or ALND), side of surgery (right or left), location of surgery (quadrant), breast reconstruction (yes or no), radiation therapy (yes or no), radiation field (breast, chest wall, axillary, or supraclavicular regions), chemotherapy (yes or no), and hormone therapy (yes or no) were collected from medical records. Lymphedema onset date was recorded for each participant with lymphedema.

Data Analysis

Univariate analysis was conducted to describe the characteristics of women with lymphedema and the matched controls. The relationship between amount of swelling and amount of interference with daily life was assessed with Spearman correlation. The comparison of arm measurements in patients with mild, moderate, or severe swelling was made with analysis of variance (ANOVA). Matched case-control analyses with conditional logistic regression compared women with lymphedema and matched controls on potential risk factors for lymphedema in univariate and multivariate analyses. Age, tumor size, number of nodes removed, number of positive nodes, and number of aspirations were treated as continuous variables. BMI was categorized as overweight (BMI higher than 25) or not overweight (BMI lower than 25). Variables that were significant ($p < 0.05$) in univariate analysis were included in a multivariate analysis. SAS (version 6) was used for all analyses. Statistical tests and corresponding p values were two sided.

Results

Matching Variables

Eight matched pairs involved SLNB and 86 involved ALND. Although participating institutions perform SLNB more frequently than ALND, most lymphedema cases in the current study involved ALND surgery because lymphedema is diagnosed more frequently after ALND. The difference in date of surgery for each woman with lymphedema and her matched control averaged less than one month. Median time from surgery to onset of lymphedema was 11.2 months.

Disease and Treatment Factors

Women with lymphedema and their matched controls did not differ significantly in tumor size, number of axillary nodes removed, side of surgery (dominant versus nondominant side), receipt of reconstructive surgery (either type included), reconstruction with breast implants, reconstruction with the transverse rectus abdominis myocutaneous (TRAM) flap procedure, radiation therapy (any location included), radiation to the breast, radiation to the supraclavicular area, or hormone therapy (see Table 1). They did not differ in having had drainage tubes left in place after surgery. However, several disease and treatment factors distinguished cases from controls. Women with lymphedema were significantly more likely to have undergone mastectomy than lumpectomy ($p = 0.008$), radiation to the axilla ($p = 0.011$), and chemotherapy ($p = 0.033$). Although cases and controls did not differ significantly in positive versus negative nodal status, the number of positive nodes was significantly higher in women with lymphedema than in controls ($p = 0.009$). Women with lymphedema reported significantly more aspirations of fluid from the axilla following breast surgery than did matched controls ($p = 0.005$).

Demographic and Clinical Factors

Baseline characteristics: Women with lymphedema and controls did not differ significantly in current age, age at time of surgery, personal history of diabetes or hypertension, smoking history (ever or never), or a prior medical condition limiting hand or shoulder movement (see Table 2). Women with lymphedema were significantly more likely to be overweight than controls ($p = 0.009$).

Post-treatment factors: The MASS included questions about the occurrence of several events or activities after breast surgery. Women with lymphedema and controls did not differ on injury of the arm or hand on the side of surgery or medical procedures (e.g., blood drawn, IV administration, blood pressure taken) on the side of surgery. They did not differ on whether they wore a breast prosthesis or whether they wore a compression sleeve to prevent arm swelling; whether they used a whirlpool, hot tub, or sauna; or whether they typically lifted more than 10 pounds during daily activities. Those with lymphedema were more likely than controls to report that they participated in routine activities that caused aching of the arm on the side of surgery (such as carrying a purse or typing on a computer) before developing lymphedema ($p = 0.019$). Two additional factors demonstrated protective effects: Women with lymphedema were less likely than controls to report performing strength training exercises using the upper body (such as weight lifting and curl-ups) ($p = 0.014$), and they were less likely than controls to report air travel before developing lymphedema ($p = 0.0005$).

Although no participants had metastatic disease at diagnosis, a query of the oncology registry showed that several participants had experienced recurrent disease. Those with lymphedema were significantly more likely than controls to have evidence of cancer at the time of last contact ($p = 0.008$). Most patients who had cancer at the time of last contact had distant recurrences.

Multivariate analyses: Based on the univariate analyses showing that mastectomy, number of positive nodes, radiation to the axilla, chemotherapy, overweight, number of aspirations of the axilla, routine activities causing arm aching, less frequent strength training, lower rates of air travel, and evidence of cancer at the time of last contact were significant predictors of lymphedema, all of those factors were entered in a multivariate analysis. In the resulting model (see Table 3), only being overweight was significantly associated with lymphedema (odds ratio = 5.58, $p = 0.022$).

Lymphedema Interference With Daily Life

Among women with lymphedema, 45 patients (49%) reported mild arm or hand swelling, 29 (32%) reported moderate arm or hand swelling, and 16 (17%) reported severe or very severe arm or hand swelling. The severity of arm or hand swelling was significantly related to how much it interfered with patients' daily activities (see Figure 1).

Arm Measurements

The mean percentage difference in the sum of arm circumference of the affected and unaffected arms of women with lymphedema was 9 (SD = 8, median = 7.4). The mean percentage differences were 6.5, 9.6, and 16.9 for women who indicated they had mild, moderate, or severe swelling, respectively. ANOVA indicated that arm measurements differed significantly for those who reported mild versus severe swelling ($p < 0.0001$) and moderate versus severe swelling

Table 1. Disease and Treatment Characteristics of the Sample: Univariate Analysis

Characteristic	Women With Lymphedema (N = 94)				Control Group (N = 94)				Odds Ratio	p
	Median	$\bar{X}$	SD	Range	Median	$\bar{X}$	SD	Range		
Years since surgery[a]	3.8	6.1	5.1	0.5–29.3	3.9	6.1	4.8	0.7–25.9	1.58	0.264
Tumor size (cm)	2.5	3	2.1	0–10	2	2.3	1.5	0–9	1.18	0.102
Number of nodes removed	16	15.2	8	1–38	15.5	15	7.6	1–46	1.01	0.657
Number of positive nodes	2	3.9	5.6	0–38	1	1.9	2.5	0–11	1.14	0.009
Characteristic	**n**		**%**		**n**		**%**		**Odds Ratio**	**p**
Type of axillary dissection[a]									1	1
Sentinel lymph node biopsy	8		9		8		9			
Axillary lymph node dissection	86		91		86		91			
Type of surgery									2.18	0.008
Mastectomy	71		75		51		54			
Lumpectomy	23		25		43		46			
Nodal status									1.64	0.198
Positive	65		76		61		65			
Negative	21		24		33		35			
Side of surgery									0.64	0.144
Dominant	41		44		51		54			
Nondominant	53		56		43		46			
Reconstructive surgery									0.81	0.517
Yes	22		24		26		28			
No	71		76		68		72			
Implant surgery									0.76	0.466
Yes	16		17		20		21			
No	77		83		74		79			
TRAM flap surgery									1	1
Yes	6		7		6		6			
No	87		93		88		94			
Radiation therapy									1.05	0.876
Yes	64		69		64		68			
No	29		31		30		32			
Radiation to breast									0.83	0.547
Yes	59		63		64		68			
No	34		37		30		32			
Radiation to axilla									3.6	0.011
Yes	21		23		8		9			
No	72		77		86		91			
Radiation to supraclavicular area									1.21	0.591
Yes	26		28		23		24			
No	67		72		71		76			
Chemotherapy									2.33	0.033
Yes	77		84		65		69			
No	15		16		29		31			
Hormone therapy									0.54	0.075
Yes	58		62		70		75			
No	35		38		24		25			
Drainage tubes									1.44	0.396
Yes	80		87		77		83			
No	12		13		16		17			
Number of aspirations									1.88	0.005
0	66		73		81		87			
1	6		7		7		8			
2	8		9		2		2			
3	3		3		3		3			
More than 3	8		9		–		–			

[a] Controls were matched to women with lymphedema on type of axillary dissection and years since surgery.

TRAM—transverse rectus abdominis myocutaneous

Note. Because of missing data, numbers may not total N values. Because of rounding, percentages may not total 100.

Table 2. Demographic and Clinical Characteristics of the Sample: Univariate Analysis

Characteristic	Women With Lymphedema (N = 94)				Control Group (N = 94)				Odds Ratio	p
	Median	$\bar{X}$	SD	Range	Median	$\bar{X}$	SD	Range		
Current age (years)	57.5	58.4	12	31–92	60	59.5	11.9	34–86	0.99	0.833
Age at time of surgery	53.6	54.5	11	29–85	54.1	54.9	11.2	28–81	0.99	0.794
Characteristic	**n**		**%**		**n**		**%**		**Odds Ratio**	**p**
Diabetes									1.09	0.835
Yes	14		15		13		14			
No	80		85		81		86			
Hypertension									0.9	0.752
Yes	30		32		32		34			
No	64		68		62		66			
Smoking									1.21	0.493
Ever	40		43		35		37			
Never	54		57		59		63			
Prior medical condition limiting hand or shoulder movement									1.8	0.292
Yes	9		10		5		5			
No	83		90		87		95			
Overweight (body mass index of 25 or higher)									2.29	0.0099
Yes	65		69		47		50			
No	29		31		47		50			
Injury on arm or hand on side of surgery									0.61	0.28
Yes	10		11		15		16			
No	82		89		77		84			
Medical procedure on arm or hand on side of surgery									0.94	0.862
Yes	24		26		25		27			
No	67		74		68		73			
Wear breast prosthesis									1.38	0.371
Yes	34		36		29		31			
No	60		64		65		69			
Ever wear compression sleeve									0.8	0.638
Yes	12		13		14		15			
No	82		87		80		85			
Whirlpool, hot tub, or sauna use									0.5	0.258
Frequently or very frequently	4		4		8		9			
Never or occasionally	89		96		84		91			
Usually lift more than 10 pounds									0.64	0.144
Yes	37		41		47		52			
No	53		59		43		48			
Routine activities cause arm to ache									2.25	0.019
Frequently or very frequently	33		35		17		19			
Never or occasionally	61		65		73		81			
Strength training exercises									0.36	0.014
Frequently or very frequently	11		12		26		28			
Never or occasionally	82		88		66		72			
Air travel since breast surgery									0.23	0.0005
Yes	46		49		69		74			
No	47		51		24		26			
Evidence of cancer at last contact									5.33	0.008
Local recurrence	2		–		1		–			
Regional recurrence	3		–		–		–			
Distant recurrence	10		–		3		–			
Unknown site	2		–		2		–			
No	53		76		88		94			

Note. Because of missing data, numbers may not total N values.

Table 3. Comparison of Women With Lymphedema and Control Group: Multivariate Model

Covariate	Odds Ratio (95% Confidence Interval)	p
Mastectomy (versus lumpectomy)	2.45 (0.77–7.81)	0.13
Number of positive nodes	1.04 (0.9–1.19)	0.609
Radiation to axilla (versus no radiation to axilla)	1.44 (0.16–12.89)	0.743
Chemotherapy (versus no chemotherapy)	2.58 (0.43–15.35)	0.298
Number of aspirations	1.49 (0.73–3.02)	0.273
Overweight (versus not overweight)	5.58 (1.29–24.23)	0.022
Routine activities causing arm to ache (frequently or very frequently versus never or occasionally)	1.4 (0.39–5.06)	0.608
Strength training exercises (frequently or very frequently versus never or occasionally)	0.31 (0.07–1.32)	0.114
Any air travel since breast surgery (versus no air travel since breast surgery)	0.31 (0.08–1.22)	0.093
Evidence of cancer at time of last contact (versus no evidence of cancer at time of last contact)	5.75 (0.82–40.04)	0.078

(p = 0.007) but not mild versus moderate swelling (p = 0.10). All of the women in the control group indicated that they had no swelling. Arm measurements were not conducted for women in the control group because the logistics and cost prohibited in-person appointments.

Discussion

This case-control study found that being overweight was a significant predictor of lymphedema. Other prospective and case-control studies have found that BMI was a significant predictor of lymphedema (Passik & McDonald, 1998; Soran et al., 2006; Werner et al., 1991), and a recent clinical trial found that weight loss may significantly reduce lymphedema (Shaw et al., 2007).

Several factors associated with more extensive disease, including mastectomy, chemotherapy, axillary radiation, more positive lymph nodes, and active cancer at the most recent follow-up, were predictors of lymphedema. More frequent fluid aspiration from the axilla also was associated with increased risk for lymphedema. Although patients were excluded from the study if they had a known recurrence to the axilla, patients with lymphedema may have been more likely to have active disease in the breast, chest wall, and regional lymph nodes that contributed to lymphedema. Other studies have found an association among tumor size (Goffman et al., 2004; Kissin, Querci della Rovere, Easton, & Westbury, 1986), positive lymph nodes (Hinrichs et al., 2004; Kiel & Rademacker, 1996; Kissen et al.; Suneson, Lindholm, & Hamrin, 1996), receipt of chemotherapy (Paskett et al., 2007), and lymphedema risk.

The higher prevalence of active cancer status among the women with lymphedema than among those in the control group raises the possibility of case-ascertainment bias. However, analyses restricted to the 50 case-control pairs in which neither the woman with lymphedema nor her matched control had active cancer at the most recent follow-up showed a pattern of results similar to that for the entire sample.

This study provides evidence that age at breast cancer diagnosis and activities of daily living such as lifting, minor arm and hand injuries, strength training, and air

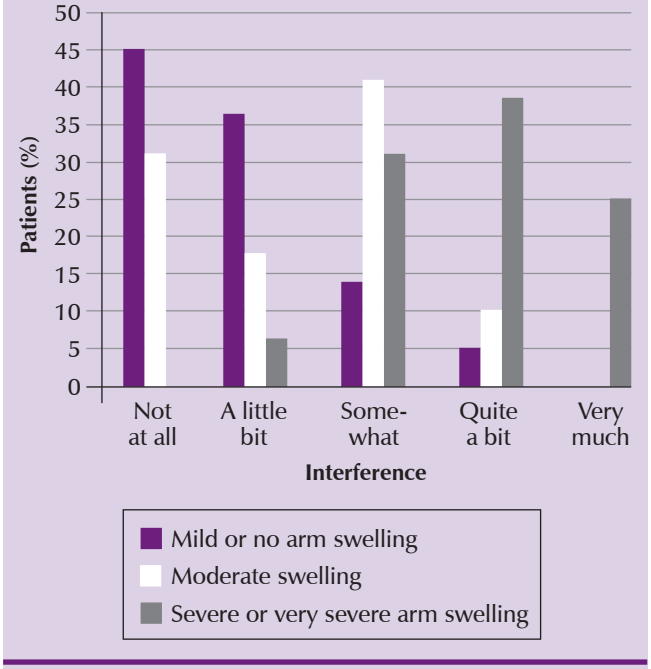

Figure 1. Proportion of Patients Reporting Interference With Daily Activity From Arm or Hand Swelling by Amount of Swelling

travel do not increase lymphedema risk. In fact, women with lymphedema were less likely to report strength training and air travel than those in the control group, and both effects persisted when adjusted for evidence of cancer at the last contact. As Ahmed et al. (2006) pointed out, plausible biologic reasons explain why strength training might help to prevent lymphedema. With regard to air travel, evidence was suggestive of that effect even when analysis was restricted to 35 incident cases (those enrolled within three months of the onset of lymphedema) and their controls, although the effect was no longer significant ($p = 0.097$). No biologically plausible explanation exists for the finding that air travel is "protective." Air travel may be a proxy for socioeconomic status or other factors that were not measured in the study.

A limitation to the study is the inclusion of prevalent as well as incident cases of lymphedema. Although the approach allowed the researchers to reach the projected sample size, it may have been more difficult for women with lymphedema to isolate factors that occurred prior to the development of their lymphedema. Including prevalent cases also may have contributed to decreased reliability of the MASS instrument. The sample frame for cases and controls differed in that all controls but not all cases were from PNHS. Restricting analyses to the 73 case-control pairs from PNHS produced the same pattern shown in Table 1, although the effects of radiation to the axilla and strength training exercises did not reach statistical significance.

Lymphedema is a debilitating consequence associated with breast cancer treatment. Despite decreased incidence because of the widespread use of SLNB for eligible women, lymphedema remains an important problem that interferes with activities of daily living. This study provides evidence that active cancer status and treatment factors such as axillary radiation, type of surgical procedure (mastectomy versus lumpectomy), and receipt of chemotherapy do influence lymphedema, but activities such as strength training and air travel do not increase lymphedema occurrence. Higher BMI is an important and modifiable risk factor for lymphedema occurrence.

Karen K. Swenson, RN, PhD, AOCN®, and Mary Jo Nissen, PhD, MPH, are research scientists, and Joseph W. Leach, MD, is the director, all at the Park Nicollet Institute; and Janice Post-White, RN, PhD, FAAN, is a member of the School of Nursing faculty at the University of Minnesota, all in Minneapolis. This research was supported by the U.S. Army Medical Research and Materiel Command Grant #DAMD17-03-1-0738. Swenson can be reached at karen.swenson@parknicollet.com, with copy to editor at ONFEditor@ons.org. (Submitted April 2008. Accepted for publication July 22, 2008.)

Digital Object Identifier: 10.1188/09.ONF.185-193

References

Ahmed, R.L., Thomas, W., Yee, D., & Schmitz, K.H. (2006). Randomized controlled trial of weight training and lymphedema in breast cancer survivors. *Journal of Clinical Oncology, 24*(18), 2765–2772.

Armer, J.M., & Stewart, B.R. (2005). A comparison of four diagnostic criteria for lymphedema in a post-breast cancer population. *Lymphatic Research and Biology, 3*(4), 208–217.

Baron, R.H., Fey, J.V., Raboy, S., Thaler, H.T., Borgen, P.I., Temple, L.K., et al. (2002). Eighteen sensations after breast cancer surgery: A comparison of sentinel lymph node biopsy and axillary lymph node dissection. *Oncology Nursing Forum, 29*(4), 651–659.

Brown, J. (2004). A clinically useful method for evaluating lymphedema. *Clinical Journal of Oncology Nursing, 8*(1), 35–38.

Burak, W.E., Hollenbeck, S.T., Zervos, E.E., Hock, K.L., Kemp, L.C., & Young, D.C. (2002). Sentinel lymph node biopsy results in less postoperative morbidity compared with axillary lymph node dissection for breast cancer. *American Journal of Surgery, 183*(1), 23–27.

Carter, B.J. (1997). Women's experiences of lymphedema. *Oncology Nursing Forum, 24*(5), 875–882.

Casley-Smith, J.R., & Casley-Smith, J.R. (1996). Lymphedema initiated by aircraft flights. *Aviation, Space, and Environmental Medicine, 67*(1), 52–56.

Cheema, B., Gaul, C.A., Lane, K., & Fiatarone Singh, M.A. (2008). Progressive resistance training in breast cancer: A systematic review of clinical trials. *Breast Cancer Research and Treatment, 109*(1), 9–26.

Chen, Y.W., Tsai, H.J., Hung, H.C., & Tsauo, J.Y. (2008). Reliability study of measurements for lymphedema in breast cancer patients. *American Journal of Physical Medicine and Rehabilitation, 87*(1), 33–38.

Edwards, T.L. (2000). Prevalence and aetiology of lymphoedema after breast cancer treatment in southern Tasmania. *Australian and New Zealand Journal of Surgery, 70*(6), 412–418.

Gerber, L., Lampert, M., Wood, C., Duncan, M., D'Angelo, T., Schain, W., et al. (1992). Comparison of pain, motion, and edema after modified radical mastectomy versus local excision with axillary dissection and radiation. *Breast Cancer Research and Treatment, 21*(2), 139–145.

Goffman, T.E., Laronga, C., Wilson, L., & Elkins, D. (2004). Lymphedema of the arm and breast in irradiated breast cancer patients: Risks in an era of dramatically changing axillary surgery. *Breast Journal, 10*(5), 405–411.

Golshan, M., Martin, W.J., & Dowlatshahi, K. (2003). Sentinel lymph node biopsy lowers the rate of lymphedema when compared with standard axillary lymph node dissection. *American Surgeon, 69*(3), 209–212.

Hayes, S., Cornish, B., & Newman, B. (2005). Comparison of methods to diagnose lymphoedema among breast cancer survivors: Six-month follow-up. *Breast Cancer Research and Treatment, 89*(3), 221–226.

Hinrichs, C.S., Watroba, N.L., Rezaishiraz, H., Giese, W., Hurd, T., Fassl, K.A., et al. (2004). Lymphedema secondary to postmastectomy radiation: Incidence and risk factors. *Annals of Surgical Oncology, 11*(6), 573–580.

Hoe, A.L., Iven, D., Royle, G.T., & Taylor, I. (1992). Incidence of arm swelling following axillary clearance for breast cancer. *British Journal of Surgery, 79*(3), 261–262.

Højris, I., Andersen, J., Overgaard, M., & Overgaard, J. (2000). Late treatment-related morbidity in breast cancer patients randomized to postmastectomy radiotherapy and systemic treatment versus systemic treatment alone. *Acta Oncologica, 39*(3), 355–372.

Jemal, A., Siegel, R., Ward, E., Hao, Y., Xu, J., Murray, T., et al. (2008). Cancer statistics, 2008. *CA: A Cancer Journal for Clinicians, 58*(2), 71–96.

Johansson, K., Ohlsson, K., Ingvar, C., Albertsson, M., & Ekdahl, C. (2002). Factors associated with the development of arm lymphedema following breast cancer treatment: A match pair case-control study. *Lymphology, 35*(2), 59–71.

Kakuda, J.T., Stuntz, M., Trivedi, V., Klein, S.R., & Vargas, H.I. (1999). Objective assessment of axillary morbidity in breast cancer treatment. *American Surgeon, 65*(10), 995–998.

Keramopoulos, A., Tsionou, C., Minaretzis, D., Michalas, S., & Aravantinos, D. (1993). Arm morbidity following treatment of breast cancer with total axillary dissection: A multivariated approach. *Oncology, 50*(6), 445–449.

Kiel, K.D., & Rademacker, A.W. (1996). Early-stage breast cancer: Arm edema after wide excision and breast irradiation. *Radiology, 198*(1), 279–283.

Kissin, M.W., Querci della Rovere, G., Easton, D., & Westbury, G. (1986). Risk of lymphoedema following the treatment of breast cancer. *British Journal of Surgery, 73*(7), 580–584.

Kwan, W., Jackson, J., Weir, L.M., Dingee, C., McGregor, G., & Olivotto, I.A. (2002). Chronic arm morbidity after curative breast cancer treatment: Prevalence and impact on quality of life. *Journal of Clinical Oncology, 20*(20), 4242–4248.

Langer, I., Guller, U., Berclaz, G., Koechli, O.R., Schaer, G., & Fehr, M.K. (2007). Morbidity of sentinel lymph node biopsy (SLN) alone versus SLN and completion axillary lymph node dissection after breast cancer surgery: A prospective Swiss multicenter study on 659 patients. *Annals of Surgery, 245*(3), 452–461.

Lee, T.S., Kilbreath, S.L., Refshauge, K.M., Herbert, R.D., & Beith, J.M. (2007). Prognosis of the upper limb following surgery and radiation for breast cancer. *Breast Cancer Research and Treatment, 110*(1), 19–37.

Liljegren, G., & Holmberg, L. (1997). Arm morbidity after sector resection and axillary dissection with or without postoperative radiotherapy in breast cancer stage I. Results from a randomised trial. *European Journal of Cancer, 33*(2), 193–199.

Lucci, A., McCall, L.M., Beitsch, P.D., Whitworth, P.W., Reintgen, D.S., Blumencranz, P.W., et al. (2007). 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. *Journal of Clinical Oncology, 25*(24), 3657–3663.

Mansel, R.E., Fallowfield, L., Kissin, M., Goyal, A., Newcombe, R.G., Dixon, J.M., et al. (2006). Randomized multicenter trial of sentinel node biopsy versus standard axillary treatment in operable breast cancer: The ALMANAC Trial. *Journal of the National Cancer Institute, 98*(9), 599–609.

Maunsell, E., Brisson, J., & Deschênes, L. (1993). Arm problems and psychological distress after surgery for breast cancer. *Canadian Journal of Surgery, 36*(4), 315–320.

Muscari, E. (2004). Lymphedema: Responding to our patients' needs. *Oncology Nursing Forum, 31*(5), 905–912.

Paskett, E.D., Naughton, M.J., McCoy, T.P., Case, L.D., & Abbott, J.M. (2007). The epidemiology of arm and hand swelling in premenopausal breast cancer survivors. *Cancer Epidemiology, Biomarkers and Prevention, 16*(4), 775–782.

Passik, S.D., & McDonald, M.V. (1998). Psychosocial aspects of upper extremity lymphedema in women treated for breast carcinoma. *Cancer, 83*(12, Suppl.), 2817–2820.

Petrek, J.A., Pressman, P.I., & Smith, R.A. (2000). Lymphedema: Current issues in research and management. *CA: A Cancer Journal for Clinicians, 50*(5), 292–307.

Purushotham, A.D., Upponi, S., Klevesath, M.B., Bobrow, L., Miller, K., Myles, J.P., et al. (2005). Morbidity after sentinel lymph node biopsy in primary breast cancer: Results from a randomized controlled trial. *Journal of Clinical Oncology, 23*(19), 4312–4321.

Ridner, S.H., & Dietrich, M.S. (2008). Self-reported comorbid conditions and medication usage in breast cancer survivors with and without lymphedema. *Oncology Nursing Forum, 35*(1), 57–63.

Ridner, S.H., Montgomery, L.D., Hepworth, J.T., Stewart, B.R., & Armer, J.M. (2007). Comparison of upper limb volume measurement techniques and arm symptoms between healthy volunteers and individuals with known lymphedema. *Lymphology, 40*(1), 35–46.

Schrenk, P., Rieger, R., Shamiyeh, A., & Wayand, W. (2000). Morbidity following sentinel lymph node biopsy versus axillary lymph node dissection for patients with breast carcinoma. *Cancer, 88*(3), 608–614.

Segerström, K., Bjerle, P., Graffman, S., & Nyström, A. (1992). Factors that influence the incidence of brachial oedema after treatment of breast cancer. *Scandinavian Journal of Plastic and Reconstructive Surgery and Hand Surgery, 26*(2), 223–227.

Sener, S.F., Winchester, D.J., Martz, C.H., Feldman, J.L., Cavanaugh, J.A., Winchester, D.P., et al. (2001). Lymphedema after sentinel lymphadenectomy for breast carcinoma. *Cancer, 92*(4), 748–752.

Senofsky, G.M., Moffat, F.L., Jr., Davis, K., Masri, M.M., Clark, K.C., Robinson, D.S., et al. (1991). Total axillary lymphadenectomy in the management of breast cancer. *Archives of Surgery, 126*(11), 1336–1341.

Shaw, C., Mortimer, P., & Judd, P.A. (2007). A randomized controlled trial of weight reduction as a treatment for breast cancer-related lymphedema. *Cancer, 110*(8), 1868–1874.

Soran, A., D'Angelo, G., Begovic, M., Ardic, F., Harlak, A., Samuel Wieand, H., et al. (2006). Breast cancer-related lymphedema—What are the significant predictors and how do they affect the severity of lymphedema? *Breast Journal, 12*(6), 536–543.

Suneson, B.L., Lindholm, C., & Hamrin, E. (1996). Clinical incidence of lymphoedema in breast cancer patients in Jönköping County, Sweden. *European Journal of Cancer Care, 5*(1), 7–12.

Swenson, K.K., Nissen, M.J., Ceronsky, C., Swenson, L., Lee, M.W., & Tuttle, T.M. (2002). Comparison of side effects between sentinel lymph node and axillary lymph node dissection for breast cancer. *Annals of Surgical Oncology, 9*(8), 745–753.

Taylor, R., Jayasinghe, U.W., Koelmeyer, L., Ung, O., & Boyages, J. (2006). Reliability and validity of arm volume measurements for assessment of lymphedema. *Physical Therapy, 86*(2), 205–214.

Tengrup, I., Tennvall-Nittby, L., Christiansson, I., & Laurin, M. (2000). Arm morbidity after breast-conserving therapy for breast cancer. *Acta Oncologica, 39*(3), 393–397.

Thomas-MacLean, R., Hack, T., Kwan, W., Towers, A., Miedema, B., & Tilley, A. (2008). Arm morbidity and disability after breast cancer: New directions for care. *Oncology Nursing Forum, 35*(1), 65–71.

Thomas-MacLean, R., Miedema, B., & Tatemichi, S.R. (2005). Breast cancer-related lymphedema: Women's experiences with an underestimated condition. *Canadian Family Physician, 51*(2), 246–247.

Tobin, M.B., Lacey, H.J., Meyer, L., & Mortimer, P.S. (1993). The psychosocial morbidity of breast cancer-related arm swelling. Psychological morbidity of lymphoedema. *Cancer, 72*(11), 3248–3252.

Velanovich, V., & Szymanski, W. (1999). Quality of life of breast cancer patients with lymphedema. *American Journal of Surgery, 177*(3), 184–187.

Vignes, S., Porcher, R., Champagne, A., & Dupuy, A. (2006). Predictive factors of response to intensive decongestive physiotherapy in upper limb lymphedema after breast cancer treatment: A cohort study. *Breast Cancer Research and Treatment, 98*(1), 1–6.

Warmuth, M.A., Bowen, G., Prosnitz, L.R., Chu, L., Broadwater, G., Peterson, B., et al. (1998). Complications of axillary lymph node dissection for carcinoma of the breast: A report based on a patient survey. *Cancer, 83*(7), 1362–1368.

Werner, R.S., McCormick, B., Petrek, J., Cox, L., Cirrincione, C., Gray, J.R., et al. (1991). Arm edema in conservatively managed breast cancer: Obesity is a major predictive factor. *Radiology, 180*(1), 177–184.

Wilke, L.G., McCall, L.M., Posther, K.E., Whitworth, P.W., Reintgen, D.S., Leitch, A.M., et al. (2006). Surgical complications associated with sentinel lymph node biopsy: Results from a prospective international cooperative group trial. *Annals of Surgical Oncology, 13*(4), 491–500.