Breast Cancer Res Treat (2009) 113:383–391
DOI 10.1007/s10549-008-9940-5

EPIDEMIOLOGY

Risk factors for arm lymphedema following breast cancer diagnosis in Black women and White women

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Received: 6 February 2008 / Accepted: 8 February 2008 / Published online: 24 February 2008

Abstract *Purpose* Lymphedema of the arm is a potential complication of breast cancer therapy. This study examines pre-disposing factors that may operate in conjunction with treatment-related factors in the development of arm lymphedema in a large cohort of White and Black breast cancer survivors. *Methods* 494 women (271 White and 223 Black) with in situ to Stage III-A primary breast cancer completed a baseline interview within 18 months of diagnosis. Information on lymphedema was collected during a follow-up interview, conducted on average 50 months after diagnosis. Self-reported data were used to classify women with or without lymphedema. Multivariable logistic regression models were developed to identify risk factors for arm lymphedema. *Results* Arm lymphedema was associated with younger age at diagnosis (odds ratio, OR per year of age = 0.96; 95% confidence interval, CI = 0.93–0.99), positive history of hypertension (OR = 2.31; 95% CI = 1.38–3.88), obesity (OR for body mass index, BMI≥30 = 2.48; 95% CI = 1.05–5.84) and having had surgery where 10 or more lymph nodes were excised (OR = 2.16; 95% CI = 1.12–4.17). While Black women had higher prevalence of arm lymphedema than White women (28% vs. 21%), race was not associated with lymphedema risk in models adjusted for multiple factors (adjusted OR = 1.01; 95% CI = 0.63–1.63). *Conclusion* Risk of arm lymphedema did not differ significantly for Black and White women. Risk factors identified in this study offer opportunities for interventions (weight loss, control of blood pressure, use of sentinel node biopsy where possible) for reducing incidence of lymphedema or controlling the symptoms associated with this condition.

Keywords Breast cancer survivors · Black breast cancer survivors · Arm lymphedema · Risk factors for arm lymphedema · Hypertension · Body mass index · Race

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Introduction

Lymphedema of the arm is a potential complication of breast cancer therapy that can range in severity from mild to quite severe. This condition is caused by the accumulation of protein-rich fluid in the soft tissues secondary to inadequate lymphatic drainage [1]. Arm lymphedema tends to be a chronic and progressive condition frequently leading to long-term disability [2]. Women with arm lymphedema often experience swelling, pain, numbness, a feeling of heaviness or tightness and a loss of strength in the affected limb [3, 4]. These women are at high risk for

infection and can develop adverse skin changes as tissues become fibrotic [5]. Although extremely rare, lymphangiosarcoma can develop in the presence of longstanding severe lymphedema [6].

In addition to the physical manifestations, lymphedema is associated with substantial psychological and functional morbidities [7, 8]. It can limit range of arm motion, restricting the woman's ability to manage normal activities of daily living [3]. The enlarged arm can prevent the wearing of usual clothing. Psychological consequences include poor body image and poor self-perception leading to an increase in depression and anxiety [9, 10]. Women with arm lymphedema have reported poorer quality of life in areas of emotional, cognitive, sexual and social functioning than those with no edema [11, 12].

Rates of arm lymphedema in breast cancer patients vary according to the group of women studied, treatment methods used, length of patient follow-up and extent of swelling necessary to define the presence of lymphedema; hence, the range of reported rates in the literature is broad (ranging from 3% to 56%) [13–17]. Arm lymphedema can develop immediately after surgery or many years after treatment ends. The cumulative incidence of arm lymphedema increases steadily with time [18, 19].

Treatment is acknowledged as a predisposing factor for arm lymphedema with axillary surgery and axillary radiotherapy considered as the most important factors. The literature is mixed on the relative importance of each treatment mode and with regard to axillary surgery whether the number of lymph nodes excised or the number of positive lymph nodes matters [20–24]. Arm lymphedema also has been reported among patients who received radiation therapy, but who did not have axillary surgery [21].

Other factors also may influence the risk of arm lymphedema among breast cancer patients, including systemic therapies (chemotherapy and tamoxifen) [22] and patient-related factors such as age [25], body mass index (BMI) [26, 27], hypertension [26, 28], history of infection [26] and co-morbidities [18, 29]. While a few studies have reported an increase in arm lymphedema among racial minorities compared to White women [11, 22], study samples have been too small to support any exploration on how lymphedema risk factors may differ among racial groups. In addition, physical activity has often been hypothesized as a risk factor for arm lymphedema. However, two small clinical trials and one observational study indicate that upper body aerobic and strength training exercise do not result in additional risk of lymphedema [30, 31]. These clinical trials found no increase in arm lymphedema among women who participated in upper body weight training/resistance exercise. Whether women who were physically active before their breast cancer diagnosis might have lower risk of lymphedema is not known. Similarly, the impact of other breast cancer risk factors has not been studied.

In this study, we collected substantial information on potential risk factors present before the diagnosis of breast cancer. We use these data to examine pre-disposing factors that may operate in conjunction with treatment-related factors in the development of arm lymphedema in a large cohort of White and Black breast cancer survivors.

Methods

Subjects

Women with in situ to Stage III-A primary breast cancer who participated in the Los Angeles portion of the Women's Contraceptive and Reproductive Experiences (CARE) Study, a case–control study of invasive breast cancer, or who had participated in a parallel (Los Angeles based) case–control study of in situ breast cancer, were considered eligible for this study. Details of the aims, study design and recruitment procedures for these two case–control studies have been published previously [32, 33]. A subset of participants enrolled in these studies also participates in the Health, Eating and Lifestyle (HEAL) Study, a multi-center, prospective cohort study of breast cancer patients [34].

The two parent case–control studies recruited women newly diagnosed with either in situ or invasive breast cancer through the Los Angeles County Cancer Surveillance Program, the population-based Surveillance, Epidemiology and End Results (SEER) cancer registry for Los Angeles County. Eligibility was restricted to Black as well as Latina and non-Latina White women aged 35–64 years at diagnosis who were English speaking, born in the United States with no prior diagnosis of in situ or invasive breast cancer. Based on HEAL eligibility criteria, participants diagnosed between May, 1995 and May, 1998, with in situ through stage III-A breast cancer were considered eligible for this study of post-diagnosis breast cancer experiences.

We identified 733 women enrolled in the two parent studies who were eligible for this study, 367 White women and 366 Black women. Four hundred ninety-four of these women (67%) participated in a follow-up interview an average of four years after diagnosis and are included in the analyses. Reasons for non-participation in the follow-up interview were death (n = 58, 7.5%), too ill (n = 5, 0.6%), refusal (n = 86, 11.7%) and unable to contact or locate (n = 90, 12.3%). We compared distributions of participants and non-participants on a number of factors using a Chi-square test. Non-participants had lower family incomes ($P < 0.01$) and less education ($P < 0.05$); a greater proportion of White patients participated (74%) than did Black patients (61%) ($P < 0.001$). Non-participants were

diagnosed at an earlier age ($P < 0.001$) than participants and were more likely to have been diagnosed with invasive disease ($P < 0.05$). A greater proportion of non-participants than participants was treated with chemotherapy ($P < 0.01$). As a result of their younger age, non-participants had fewer years since their last pregnancy and were more often pre-menopausal. Participants and non-participants did not differ significantly as to family history of breast cancer, body mass index, type of breast cancer surgery, number of lymph nodes excised, treatment with radiation, oral contraceptive use, physical activity, smoking, alcohol intake, use of high blood pressure medication or frequency of pre-existing co-morbidities, including hypertension, diabetes, arthritis, migraine headaches and phlebitis.

Data collection

Breast cancer characteristics and treatment information were obtained from Los Angeles County SEER registry records. Disease stage at diagnosis was classified as in situ, Stage I or Stage II–IIIA breast cancer. Several breast cancer surgery variables were created: type of surgery (lumpectomy or mastectomy); whether axillary surgery was performed (yes/no); number of lymph nodes excised (0, 1–9, 10+) and number positive lymph nodes present (0, 1–9, 10+). Treatment was coded as chemotherapy (yes/no), radiation therapy (yes/no) and tamoxifen (yes/no).

Women in this study participated in a face-to-face interview within 18 months (mean 5.7 months, sd 3.3) of their breast cancer diagnosis. In this baseline interview, we collected information on demographic factors, reproductive history, use of oral contraceptives and hormonal therapy, history of uterine and ovarian surgeries, menopausal status, family history of breast cancer, weight history, height, medication history and lifetime histories of lifestyle factors (physical activity, smoking and alcohol intake).

In addition, participants were asked if before their cancer diagnosis a doctor or health professional had ever told them that they had hypertension, diabetes, arthritis, migraine headaches or phlebitis (yes/no). During this interview, we created a calendar of life events to facilitate recall.

We used self-reported information on height and weight five years prior to diagnosis to estimate BMI at five years prior to diagnosis. Menopausal status was categorized as pre- or peri-menopausal, post-menopausal or unknown. Women were considered post-menopausal if they reported a bilateral oophorectomy or designated themselves as post-menopausal and not having had a menstrual period during the 12 months before their diagnosis. Women whose menstrual periods stopped due to radiation or chemotherapy at least six months before diagnosis and women who had reached the age of 55 years and had not designated their menstrual status as pre-menopausal were also classified as post-menopausal. Women who had a hysterectomy without a bilateral oophorectomy or who began hormone therapy and had not experienced 12 months without any menstrual period were classified as having unknown menopausal status unless they were age 55 years or older. Date of last pregnancy was used to calculate number of years between last pregnancy and breast cancer diagnosis. From the information collected on lifetime exercise activity, we created a physical activity variable representing average activity in the three years prior to diagnosis. Each activity was represented by its metabolic-equivalents-of-energy expenditure (MET) score based on the Compendium of Physical Activities [35]. This score was multiplied by the number of hours per week a woman engaged in a particular activity. These MET-hours per week values were summed across all activities and then averaged over the three-year period. Using this calculated value, we created approximate tertiles of physical activity among women who were active during the time period: 0, <8, 8–18 and 19+ MET-hours per week.

First degree family history was considered positive if the participant's biological mother or full sister had been diagnosed with breast cancer. Oral contraceptive use and smoking status were coded as never, former or current. Average number of alcoholic drinks per week for the five years preceding breast cancer diagnosis was calculated.

Participants also completed a follow-up telephone interview on average 50 months (range, 33–74 months) after their diagnosis. In this interview, women were asked if they had ever experienced arm lymphedema, which was explained as "swelling due to an accumulation of fluid in their arm, not to be confused with swelling that occurs after surgery". Women who responded positively were considered to have lymphedema, and were asked the date when arm swelling first occurred and whether they still had this condition. They also were asked if they had an infection associated with their lymphedema (yes/no).

Informed consent was obtained from each subject at each assessment. Study procedures were approved by the University of Southern California Research Committee, in accordance with assurances filed with and approved by the U.S. Department of Health and Human Services.

Statistical analyses

We fit univariable and multivariable unconditional logistic regression models, calculating odds ratios (OR) and corresponding 95% confidence intervals (CI) to identify factors associated with arm lymphedema. To test for linear trend, we fit age, number of lymph nodes excised, number of positive lymph nodes and BMI as continuous variables in the models. We created interaction terms between race and other factors. The *P*-value for interaction was used to determine whether

risk estimates for Black women and White women were statistically significantly different (P-for-interaction <0.05). Data analyses were conducted using SAS statistical software (Version 9.0) (SAS Institute; Cary, NC).

Results

Overall, 24% of the women interviewed (120/494) reported lymphedema. Of these, 103 continued to experience lymphedema-related symptoms three to five years after diagnosis. Average duration of symptoms was 38 months (standard deviation 16.1, range 4–66 months). While the majority (71%) experienced arm swelling during the first year, some (12%) developed symptoms three or more years after diagnosis (Fig. 1). The lag time between diagnosis and development of arm lymphedema was not related to family history of breast cancer, physical activity, oral contraceptive use, BMI, type of breast cancer surgery, number of lymph nodes excised, chemotherapy, radiation therapy or race. We did find, however, that lag time was longer for younger women (time for women less than 45 years = 17 months (sd 16.5) vs. 10 months (sd 13.4) for older women, t-test $P < 0.02$) and for those treated with chemotherapy (lag time = 14 months (sd 15.9) vs. 8.6 months (sd 11.3) for untreated women, $P = 0.04$). Nine percent of the women reported that the onset of their lymphedema was associated with infection.

A number of factors were associated with risk of arm lymphedema in univariable models. A woman's BMI five years prior to her breast cancer diagnosis was positively associated with her risk of arm lymphedema (per unit of BMI, OR = 1.08, 95% CI = 1.04–1.12) (Table 1). Compared with normal-weight women, those with a BMI of 30 kg/m^2 or higher had a three-fold increased risk of arm lymphedema (95% CI = 1.46–6.38), and women who were overweight had a 2-fold increased risk (BMI 25–27, 95% CI = 1.20–5.06; BMI 28–29, (95% CI = 0.94–5.36). Post-

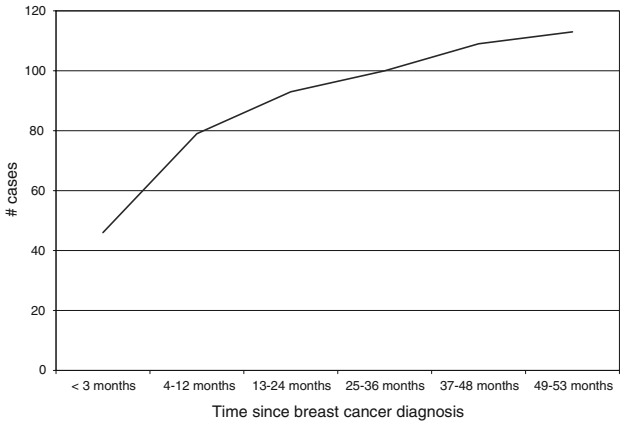

Fig. 1 Cumulative case count of lymphedema over time

menopausal women were less likely to develop arm lymphedema than pre-menopausal women (OR = 0.59; 95% CI = 0.38–0.92). When age was added to this model, menopausal status was no longer a significant risk factor (data not shown). A history of oral contraceptive use was associated with increased risk of lymphedema (OR = 1.73; 95% CI = 1.01–2.94). Women with a history of hypertension were twice as likely to develop arm lymphedema as those with no such history (OR = 2.21; 95% CI = 1.45–3.36).

While not reaching statistical significance, Black women were more likely to develop arm lymphedema than White women (28% vs. 21%, OR = 1.41, 95% CI = 0.94–2.14). In univariable models, arm lymphedema was not associated with family history of breast cancer, alcohol intake during the five years before diagnosis, physical activity during the three years before diagnosis or the following co-morbidities: migraine headaches, diabetes/high blood sugar, phlebitis or arthritis (Table 1). Nor was arm lymphedema associated with education or income level, marital status, smoking status, years since last pregnancy or months of breast feeding (data not shown).

In relation to disease and treatment factors, we found an inverse association between age at diagnosis and lymphedema (OR per year of age = 0.97; 95% CI = 0.95–0.99) in the univariable model. Women diagnosed before the age of 55 were nearly twice as likely to develop lymphedema as those diagnosed at an older age (OR = 1.80; 95% CI = 1.14–2.84). There was more than a two-fold increase in risk of lymphedema associated with axillary surgery (OR = 2.41; 95% CI = 1.33–4.34). Risk was positively associated with the number of lymph nodes excised (trend P-value < 0.0001) but was not related to the number of positive lymph nodes (trend P-value = 0.81). Arm lymphedema risk was significantly increased for women who had 10 or more lymph nodes excised (OR = 2.73; 95% CI = 1.55–4.84). Women who received chemotherapy were twice as likely to develop lymphedema as those who did not receive chemotherapy (OR = 2.17; 95% CI = 1.42–3.32). There was no relationship between lymphedema and type of primary breast cancer surgery, reconstructive surgery, radiation therapy or tamoxifen. Restricting our univariate analyses to women with persistent symptoms (n = 103) produced similar results to those shown in Table 2, which includes all women (n = 120) who developed arm lymphedema.

In our multivariable model (Table 2), arm lymphedema was positively associated with BMI (five years prior to diagnosis) (OR per unit of BMI = 1.07; 95% CI = 1.02–1.12), 10 or more lymph nodes excised (OR = 2.16; 95% CI = 1.12–4.17) and a previous diagnosis of high blood pressure (OR = 2.31; 95% CI = 1.38–3.88). Age at diagnosis remained significant in this model, with younger

Table 1 Subject characteristics and their association with lymphedema

Characteristic	Categories	Lymphedema		OR (95% CI)[a]
		Yes N (%)	No N (%)	
Total		120 (24)	374 (76)	
Race	White	58 (21)	213 (79)	1.00
	African American	62 (28)	161 (72)	1.41 (0.94–2.14)
First degree family history of breast cancer	No	93 (23)	314 (75)	1.0
	Yes	20 (30)	47 (70)	1.44 (0.81–2.55)
	Unknown	7 (35)	13 (65)	1.82 (0.71–4.69)
Body mass index (kg/m^2)[b]	<21	13 (15)	74 (85)	1.00
	21–24	32 (19)	137 (81)	1.33 (0.66–2.69)
	25–27	32 (30)	74 (70)	2.46 (1.20–5.06)
	28–29	13 (28)	33 (72)	2.24 (0.94–5.36)
	30+	30 (35)	56 (65)	3.05 (1.46–6.38)
Per unit of BMI				1.08 (1.04–1.12)
Menopausal status	Pre	69 (28)	152 (72)	1.00
	Post	43 (19)	186 (81)	0.59 (0.38–0.92)
	Unknown	17 (32)	36 (68)	1.20 (0.63–2.29)
Ever used oral contraceptives before breast cancer diagnosis	No	20 (17)	96 (83)	1.00
	Yes	100 (26)	278 (74)	1.73 (1.01–2.94)
Co-morbidities diabetes	No	113 (25)	344 (75)	1.0
	Yes	7 (19)	30 (81)	0.71 (0.30–1.66)
Arthritis	No	97 (25)	294 (75)	1.0
	Yes	23 (23)	79 (77)	0.88 (0.53–1.48)
Migraine headaches	No	102 (24)	328 (76)	1.0
	Yes	18 (29)	45 (71)	1.29 (0.71–2.32)
Phlebitis	No	113 (24)	361 (76)	1.0
	Yes	7 (37)	12 (63)	1.87 (0.72–4.86)
Hypertension	No	61 (19)	260 (81)	1.0
	Yes	59 (34)	114 (66)	2.21 (1.45–3.36)
Alcohol intake in 5 years pre-diagnosis	None	72 (25)	221 (75)	1.00
	<1.5 drinks/wk	14 (23)	47 (77)	0.92 (0.48–1.77)
	1.5–3.9/wk	15 (23)	47 (77)	0.95 (0.50–1.99)
	4+ drinks/wk	19 (26)	55 (74)	1.07 (0.60–1.92)
Physical activity (average MET hours per week)[c]	None	53 (56)	154 (74)	1.0
	<8	22 (24)	71 (76)	0.91 (0.51–1.60)
	8–18	21 (23)	71 (77)	0.87 (0.49–1.54)
	19+	24 (24)	77 (76)	0.91 (0.52–1.59)
Age at breast cancer diagnosis (years)	35–44	39 (28)	101 (72)	1.00
	45–54	50 (28)	179 (72)	1.00 (0.61–1.64)
	55–64	31 (18)	144 (82)	0.56 (0.33–0.95)
Per year of age				0.97 (0.95–0.99)
Breast cancer surgery	Lumpectomy	67 (23)	221 (77)	1.00
	Mastectomy	53 (26)	152 (74)	1.15 (0.76–1.74)
Reconstructive surgery at time of initial surgery	No	111 (25)	326 (75)	1.00
	Yes	9 (16)	48 (84)	0.55 (0.26–1.16)

Table 1 continued

Characteristic	Categories	Lymphedema		OR (95% CI)[a]
		Yes N (%)	No N (%)	
Axillary surgery	No	15 (14)	96 (86)	1.00
	Yes	103 (27)	274 (73)	2.41 (1.33–4.34)
Number of lymph nodes excised[d]	0	15 (14)	96 (86)	1.00
	1–9	11 (13)	76 (87)	0.85 (0.38–1.92)
	10+	92 (32)	198 (68)	2.73 (1.55–4.84)
Per lymph node				1.05 (1.03–1.08)
Number of positive lymph nodes[e]	0	56 (23)	184 (77)	1.00
	1–9	46 (37)	80 (63)	2.28 (1.46–3.57)
	10+	3 (20)	12 (80)	0.99 (0.27–3.61)
Per positive lymph node				0.99 (0.92–1.07)
Radiation therapy	No	64 (23)	210 (77)	1.00
	Yes	56 (25)	164 (75)	1.12 (0.74–1.69)
Chemotherapy	No	52 (19)	226 (81)	1.00
	Yes	65 (33)	130 (67)	2.17 (1.42–3.32)
Tamoxifen therapy	No	54 (24)	172 (76)	1.00
	Yes	66 (25)	202 (75)	1.04 (0.69–1.57)

[a] OR = Odds ratio, CI = Confidence interval

[b] BMI at 5 years pre-diagnosis

[c] Physical activity, average MET hours per week in 3 years pre-diagnosis

[d] Mean number of lymph nodes excised = 15 (sd = 7.3), range 1–44 (limited to women who had lymph nodes excised)

[e] Mean number of positive lymph nodes = 1(sd = 3.0), range 0–23 (limited to women who had lymph nodes excised)

women having higher risk than older women (OR per year of age = 0.96; 95% CI = 0.93–0.99). Race was not associated with lymphedema risk (OR = 1.02; 95% CI = 0.63–1.63). Neither use of oral contraceptives nor chemotherapy was associated with risk of lymphedema in the multivariable model.

When we compared Black and White women on the presence of arm lymphedema risk factors, we found that Black women had higher BMI than White women (27.5 vs. 24.2, t-test P-value < 0.0001). Black women also reported a history of high blood pressure more often than White women (46% vs. 25%, chi-square P-value < 0.0001). Black and White women did not differ on age at diagnosis (t-test P-value = 0.27) or number of lymph nodes excised (t-test P-value = 0.35). In our multivariate analyses we found no significant interaction between race and the individual risk factors for arm lymphedema (interaction P-values: age, $P = 0.65$; number of lymph nodes excised, $P = 0.22$; previous diagnosis of high blood pressure, $P = 0.19$; BMI, $P = 0.84$).

Discussion

Twenty-four percent of the breast cancer survivors in this cohort reported arm lymphedema at an average of four years follow-up. The majority developed arm lymphedema within one year of their treatment. For most, this condition was chronic, i.e., symptoms lasting on average three years. These findings are consistent with other reports in the literature [15, 18, 27].

A major strength of our study is the racial diversity of our study sample. Our cohort of breast cancer survivors includes a large number of Black women. Black breast cancer survivors have been poorly represented in previous studies of lymphedema.

Although the numbers are small for non-White participants, a few recent breast cancer studies suggest that ethnic minorities may have an increased risk of arm lymphedema. In a retrospective cohort study that used arm volume measurements to define lymphedema, 28% of the women had arm lymphedema [11]. Prevalence was higher for non-White woman (Black, Hispanic, Asian/Pacific Islander, n = 19) than White women (n = 132) ($P < 0.04$). A second study, which also compared White (n = 555) and non-White women (n = 67), found an increased risk of self-reported arm swelling among non-White women (non-White, OR = 1.69; 95% CI = 1.03–2.75) [22]. A third study which examined self reported arm swelling provided prevalence estimates for Black (n = 35), Latina (n = 29) and 'other' women (n = 17) separately; each of these

Table 2 Multivariable model for arm lymphedema

		OR (95% CI)[a]
Body mass index (kg/m^2)[b]	<21	1.00
	21–24	1.29 (0.60–2.80)
	25–27	2.11 (0.81–5.71)
	28–29	2.15 (0.69–5.84)
	30+	2.48 (1.05–6.15)
Per unit of BMI		1.07 (1.02–1.12)
Diagnosis of high blood pressure before breast cancer diagnosis	No	1.00
	Yes	2.31 (1.38–3.88)
Age at breast cancer diagnosis	35–44	1.00
	45–54	0.91 (0.52–1.59)
	55–64	0.45 (0.23–0.86)
Per year of age		0.96 (0.93–0.99)
Number of lymph nodes excised	0	1.00
	1–9	0.76 (0.31–1.84)
	10+	2.16 (1.12–4.17)
Per lymph node		1.04 (1.01–1.07)
Race	White	1.00
	Black	1.02 (0.63–1.63)
Chemotherapy	No	1.00
	Yes	1.58 (0.97–2.59)
Oral contraceptive use	Never	1.00
	Ever	1.46 (0.78–2.56)

[a] OR = Odds ratio, CI = Confidence interval

[b] BMI at 5 years pre-diagnosis

groups reported more arm swelling (lymphedema) than did White women (n = 35) [36]. In this study, 77% of the Black women self-reported arm swelling (lymphedema) compared to 39% of the White women ($P < 0.001$). While prevalence of arm lymphedema in our cohort was higher for Black women than White women (28% vs. 21%), other factors accounted for this difference (Black vs. White multivariable adjusted OR = 1.02, 95% CI = 0.63–1.63).

Obesity is one of the more consistently reported risk factors for arm lymphedema following breast cancer treatment [11, 22, 27, 37, 38]. In our study, risk for arm lymphedema increased with increasing BMI, and obese women (i.e., BMI≥30) had a 2.5-fold greater risk of arm lymphedema than lean women. Why overweight/obese women are at higher risk is unknown; some suggest that poor healing may play a role [18]. A randomized controlled study was recently conducted with 64 breast cancer survivors with arm lymphedema [39]. Two dietary interventions were tested, a reduced-energy intake diet and a low-fat diet. After 24 weeks, investigators found a significant connection between weight loss and a reduction in arm volume irrespective of dietary group (r = 0.42). This area of research is very promising because weight reduction has the potential to improve many health outcomes, including hypertension, one of the other lymphedema risk factors identified in this study.

Only recently have investigators begun to recognize and evaluate the potential effect of co-morbidities such as hypertension on the development of arm lymphedema following breast cancer therapy [29, 38]. One study reported increased risk of lymphedema among women with hypertension [26]. Another recent study found decreased risk of arm lymphedema among women who were in treatment for hypertension [18]. The proposed theory linking hypertension to arm lymphedema is that high pressure in the capillaries facilitates leakage of fluid into the tissues. In the general population, obesity increases risk of hypertension [40]. This positive association was also present in our cohort. Sixty-two percent of the women with BMI ≥ 30 had a history of hypertension compared to 29% of the women with BMI < 30 (chi-square P-value < 0.0001). While race was not a significant risk factor for arm lymphedema in this study, it is important to note that obesity and hypertension were more prevalent among

Black women than among White women. These racial differences are also present in the general population [41]. Hypertension and obesity are therefore two key target areas for risk reduction intervention.

Number of lymph nodes excised is one of the most frequently cited disease/treatment risk factors for lymphedema [7, 42]. Engel et al. [43] found that women who had 10 or more lymph nodes removed were 2.6 times more likely to develop swelling than those with no axillary lymph node surgery. These findings are similar to our results. Recently, investigators have found that the incidence of arm lymphedema is reduced in women who have undergone sentinel nodes biopsies, a staging procedure in which a limited number of lymph nodes are excised [20]. While sentinel node biopsies appear to be a preventive measure for arm lymphedema, not all women with breast cancer are eligible. Women with more advanced disease will still require extended lymph node dissection for complete staging. These women who have undergone extensive axillary surgery are likely to be a high-risk group that will require additional prevention interventions.

Although younger age at breast cancer diagnosis previously has been reported as a risk factor for arm lymphedema [18, 44], this has not been a consistent finding across studies. Some studies have reported an increased risk among older women [13, 43] while others have found no relationship between age and arm lymphedema [22, 25]. Why these results vary from study to study is unknown. It has been suggested that younger women may have a higher risk of arm lymphedema because their cancers are more aggressive and they receive more intensive treatment. In this cohort, we found that younger women were more likely to receive chemotherapy than older women (50% (ages 35–54) compared to 25% (ages 55–64), chi-square P-value $<$ 0.0001). We also found that younger women took longer to develop lymphedema than older woman (Pearson correlation r $= -0.23$, $P = 0.01$). This area needs further study.

The major limitation of this study is that lymphedema and other factors were measured by self-report and not validated with objective measures. With respect to case determination, moderate correlation has been found between objective measurements of swelling and self-report of swelling [45]. Baseline data were collected after diagnosis but before the follow-up interview for lymphedema. Thus, differential recall of baseline risk factors among survivors with and without lymphedema is unlikely. However, it is possible that our study under-estimated the prevalence of lymphedema. Similarly, we did not measure blood pressure, and therefore the prevalence of hypertension may be underestimated in our sample.

One of every four breast cancer survivors in this cohort developed arm lymphedema. The physical and psychological morbidities associated with this disease/treatment-related complication are well documented. Risk factors identified in this study offer opportunities for interventions (weight loss, control of blood pressure, use of sentinel node biopsy where possible) for reducing incidence of lymphedema or controlling the symptoms associated with this condition.

Acknowledgements This project has been supported with funds from the National Institutes of Health: National Cancer Institute Contract No. N01-PC-35139 for the Los Angeles HEAL Study, National Cancer Institute grant CA 116848 for the USC Center for Transdisciplinary Research on Energetics and Cancer and National Institute of Child Health and Human Development Contract N01 HD 3-3175 for the Women's CARE Study. A STOP CANCER Career Development Award also supports Dr. Meeske. The collection of California cancer incidence data providing the patient base for this publication was supported by the California Department of Health Services as part of the statewide cancer reporting program mandated by California Health and Safety Code Section 103885. The ideas and opinions expressed herein are those of the authors, and no endorsement by the State of California, Department of Health Services is intended or should be inferred.

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