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# BREAST EDEMA AFTER CONSERVATIVE SURGERY FOR EARLY-STAGE BREAST CANCER: A RETROSPECTIVE SINGLE-CENTER ASSESSMENT OF RISK FACTORS

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## ABSTRACT

Breast-conserving surgery (BCS) is the standard of care for early-stage breast cancer. We retrospectively enrolled 530 patients (mean age: 62.96 ± 12.69 years) undergoing BCS between January 1, 2018, and December 31, 2019. During the COVID-19 pandemic, all patients with at least 1 year of follow-up were telephonically asked after surgery to provide clinical signs and symptoms attributable to postoperative breast cancer-related lymphedema of the breast (BCRL-B). Thirty-one (5.8%) patients reported breast edema and were visited to measure the tissue dielectric constant (TDC) and to assess the induration of the skin. There was a difference seen in treatment with lumpectomy + ALND performed more frequently in patients with (29%) than without (12%) BCRL-B. In the subgroup of patients with BCRL-B (n=31), significantly higher values of local total water were calculated in the nine patients who underwent Lump + ALND procedure (1.86  $\pm$  0.48 vs. 1.48  $\pm$  0.38; p = 0.046). Among patients with BCRL-B (n=31),

in eight patients (25.8%) tissue induration measured with SkinFibroMeter was >0.100 N, thus suggesting tissue fibrosis. Cumulative survival probability at 1-year after surgery was 0.992. No statistical differences in 1-year survival after surgery were found for type of surgery (p = 0.890) or absence/presence of BCRL-B (p = 0.480). In univariate logistic regression, only lumpectomy + ALND surgery (p = 0.009) and any subsequent axillary lymph node removal surgery (p = 0.003) were associated with BCRL-B. Both of these variables were also found to be statistically significant in the multivariate regression model. Further prospective research is warranted to analyze potential predictors of BCRL-B and to reduce/ prevent this complication.

**Keywords:** breast edema, lymphedema, breastconserving surgery, breast cancer

Breast cancer is the most common cancer in women (1). Developments in breast cancer treatment have led to new treatment options, such as breast-conserving therapy in early-stage breast cancer with adjuvant radiotherapy that can yield cancer outcomes comparable to mastectomy. Breast-conserving surgery (BCS) followed by whole-breast irradiation has become the standard of care for early-stage breast cancer. Currently, BCS can also be offered to women with large tumors because of the advent of neoadjuvant systemic therapy and oncoplastic surgical techniques. Because of the evolution in the treatment of breast cancer and despite these advantages, some women develop postoperative breast cancer-related lymphedema (BCRL-B) on the operated and irradiated breast (2). BCRL-B may cause an unsatisfactory cosmetic result, influencing the quality of life in the long term (3). Breast edema also delays the healing process, which may cause negative future health issues (4). In the literature several risk factors are linked to BCRL-B and they could be grouped into five categories related to: 1) surgery, 2) radiotherapy, 3) systemic chemo- or endocrine therapy, 4) tumor characteristics, 5) personal factors.

Arm lymphedema is more commonly mentioned in the literature, whereas lymphedema of the breast has still been under-investigated in the literature. This may be attributed to the lack of standard diagnostic criteria and the absence of a consensus on its definition. Lymphedema is a subcutaneous swelling caused by excess interstitial fluid in the affected tissues. Breast edema after breast conservative surgery is owing to the interruption of lymphatic vessels and lymph nodes and to the radiotherapy. Perbeck et al (5) reported that there seems to be a long-term increase in lymph flow probably as a consequence of an inflammatory reaction in a surgically- treated, irradiated breast that might lower the lymphatic transport reserve of the breast. Breast edema comprises two components. Parenchymal breast edema is characterized by swelling or enlargement of the parenchyma of the breast, and cutaneous breast edema is caused by edematous changes in the epidermis and dermis of the breast (6). Histological changes associated with lymphedema include fibrosis, inflammatory changes, skin thickening, keratinization, expansion and proliferation of

lymph and blood vessels, and increasing permeability of lymphatic vessels according to findings in clinical and animal experimental models (7).

Although the association between breast surgery and lymphedema of the arm is well known, fewer studies about BCRL-B are available. Understanding prevalence and risk factors for BCRL-B could be a starting point to prevent this complication, guide clinical decisions, and develop targeted therapies. The aim of this retrospective study is to describe the incidence of breast edema in female breast cancer patients after BCS and to identify risk factors that influence the development of breast edema.

#### **METHODS**

#### **Participants**

We retrospectively included 578 women with invasive breast cancer who underwent BCS between January 1, 2018, and December 31, 2019, at the Breast Surgery **Clinic of IRCCS - Ospedale Policlinico San** Martino. The aim of this study was to evaluate the prevalence and determinants of breast edema in this large retrospective cohort of women. Patient, tumor, and neoadjuvant/adjuvant treatment characteristics were retrospectively collected and obtained from electronic patient files. Each patient signed the standard Privacy Module and the study was approved by the Regional Ethics Committee (Comitato Etico Regionale della Liguria). All patients with at least 12 months of follow-up were included in our analysis. Fourteen patients who underwent mastectomy after BCS, 7 patients with synchronous bilateral breast tumors, 2 patients with rare breast cancer (carcinosarcoma and basosquamous carcinoma), one patient who previously underwent contralateral breast surgery, and 24 patients with inconsistent follow-up were excluded from the study. Thus, 530 women were finally enrolled.

## Data Collection

The following potential variables were studied: age; body mass index (BMI); hormonal phase: neoadjuvant systemic therapy (chemotherapy and/or endocrine therapy); histological features of the tumor; sentinel lymph node biopsy (SLNB); axillary lymph node dissection (ALND); oncoplastic surgery; number of nodes surgically removed; staging according to TNM (Tumor, Node, Metastasis) staging system; grading; immunophenotype; Ki67 index; tumor side and quadrant; drainage; adjuvant therapy (chemotherapy and/or endocrine therapy), adjuvant radiotherapy; subsequent breast or axillary surgery. The Coronavirus Disease 2019 (COVID-19) pandemic required a significant re-allocation of healthcare resources with a sudden re-organization of all clinical activities, including Breast Units. In order to spare our patients and our healthcare workers any undue risk of exposure to COVID-19, all 530 patients were subjected to a telephonic questionnaire to investigate breast edema after BCS and/or adjuvant treatment between October 1, 2020, and December 31, 2020. The presence at least of two signs among the following (peau d' orange; redness of the skin; positive pitting sign; increased volume of the breast; skin thickening, and hyperpigmented skin pores) and of one symptom among the following (heaviness of the breast; numbness, tingling, stabbing pain, and skin twitching of the breast) were considered suggestive of breast edema. Based on the telephonic interview, 40 patients had a probable diagnosis of breast edema.

# Clinical Examination and Skin Tissue Measurement

Because nine patients refused to or could not be examined in January 2021, only 31 patients underwent examination with measurement of skin tissue dielectric constant (TDC) with MoistureMeterD Compact and assessment of induration of the skin with SkinFibroMeter. The SkinFibroMeter is a medical device with a measuring function constituted of an indenter and two force sensors and can be used to help assessing skin and subcutis induration degree. The indenter touches the skin first, then the base plate shortly. The indenter imposes a constant deformation when the base plate is in full contact with the skin. The force sensors recognize the skin contact and the measurement starts automatically. Five short, successful measurements on the same site need to be done to get the induration reading. The induration reading is the force as a unit N (Newton). If the measured force exceeds 1.25 N, the measured tissue is too hard to be measured with the SkinFibroMeter. In each patient, SkinFibroMeter was first placed on the edematous surface of the operated breast and then was positioned on the specular area of the contralateral breast. Five measurements were repeated for each side. The Moisture-MeterD Compact is a portable device for the localized measurement of water content of biological tissues. The TDC measured noninvasively and within seconds in skin is converted into percentage water content (PWC) scale from 0 to 100%. The MoistureMeterD Compact generates a low power 300 MHz microwave field exposed to tissue. Part of the signal is absorbed, and part is reflected back to permit the calculation of a dielectric constant, which is directly proportional to the water content of the measured tissue. The value increases with increasing water content and edema. The local tissue water (LTW) ratio was obtained dividing the LTW value of edematous breast/LTW value of normal breast.

# Statistical Analysis

The results are expressed as means  $\pm$  standard deviations, medians, counts, and percentages (%). The Shapiro-Wilk test was preliminarily used to assess the normal distribution of the continuous variables. For a p value <0.05, the null hypothesis of the normal distribution is rejected. Based on the results of the Shapiro-Wilk test, the Mann-Whitney U-test was used to compare continuous variables between groups. The Fisher's exact test was used to compare categorical variables. Correlation analysis was performed by using the Spearman rho test, with density plots to show

TABLE 1Main Clinical Characteristics of the Enrolled Patients (n = 530)			
Continuous variable	Mean ± SD (median)		
Age (years)	62.96 ± 12.69 (64)		
BMI (Kg/m <sup>2</sup> )	$25.20 \pm 4.65 \ (24.60)$		
Resected lymph nodes (n)	$3.59 \pm 4.37$ (2)		
ER (%)	$85.16 \pm 29.66$ (98)		
PgR(%)	$57.11 \pm 38.87 (72.50)$		
<u>Ki-67 (%)</u>	23.66 ± 19.09 (18)		
Categorical variables	n (%)		
Tumor side			
Right	248 (46.8%)		
Left	282 (53.2%)		
pT	22(420/)		
0 1a	23 (4.3%)		
1a 1b	40 (7.5%)		
10 1c	159 (30%) 233 (44%)		
2	74 (14%)		
4b 2	1 (0.2%)		
pN	1 (0.270)		
0	377 (71.1%)		
0 (ITC)	13 (2.4%)		
1a	84 (15.8%)		
1mi	31 (5.8%)		
2c	23 (4.3%)		
3c	2 (0.4%)		
Type of surgery			
Lump+ALND	69 (13%)		
Lump+SLNB	461 (87%)		
Drainage	93 (17.6%)		
Oncoplastic	44 (8.3%)		
Neoadjuvant chemotherapy	50 (9.4%)		
Neoadjuvant hormonotherapy	11(2.1%)		
Adjuvant chemotherapy	142 (26.8%)		
Adjuvant hormonotherapy	453 (85.5%)		
Adjuvant radiotherapy	485 (91.5%) 5 (0.9%)		
Subsequent breast surgery	5 (0.9%) 16 (3%)		
Subsequent ALND Breast lymphedema	31 (5.8%)		
Dieuserrymphedema	51 (5.070)		

BMI: body mass index; ER: estrogen receptor expression; PgR: progesterone receptor expression; Ki-67: Ki-67 index; Lump+ ALND: lumpectomy + axillary lymph node dissection; Lump + SLNB: lumpectomy + sentinel lymph node biopsy.

the distribution of the continuous variables. Patient survival was evaluated by using the Kaplan-Meier estimator, with the log-rank test for comparing survival curves. Logistic regression was performed to evaluate potential predictors for the breast edema occurrence after conservative surgery. The Hosmer-Lemeshow test was used for goodness-of-fit evaluation of each significant logistic regression model. Only significant logistic regression models that passed the goodness-of-fit test were presented. Significant variables to univariate logistic regression were entered in a multivariate model. The regression coefficient  $\beta$  and odds ratio (OR) with the 95% confidence interval (95% CI) were the main outputs for each logistic regression model. A receiver operating characteristic (ROC) curve was calculated for estimating the number of resected lymph nodes (RLN) that maximized sensibility and specificity for the breast edema occurrence. Statistical significance was assumed in each test with a two-tailed p value <0.05. Statistical analysis was carried out by using the R software/environment (version 4.0.3, R Foundation for Statistical Computing, Vienna, Austria).

# RESULTS

In our study, we included 530 patients with invasive breast cancer treated with BCS between January 2018 and December 2019. Fifty (9.4%) patients received neoadjuvant chemotherapy (NAC) and 11 (2.1%) neoadjuvant endocrine therapy. Surgically, 461 (87%) patients underwent SLNB and 69 (13%) axillary lymph node dissection (ALND); in 44 (8.3%) patients oncoplastic surgery was done. A total of 485 (91.5%) patients received wholebreast irradiation, 142 (26.8%) adjuvant chemotherapy, and 453 (85.5%) endocrine therapy after surgery. Prevalence of breast edema was 5.8% (Table 1). The patients who underwent lumpectomy + ALND surgery, in comparison with lumpectomy + SLNB surgery, more frequently received NAC [19 (27.5%) vs. 31 (6.7%); p <0.001] and/or adjuvant chemotherapy [45 (65.2%) vs. 97 (21%); p <0.001], as well as a post-operative drainage [65 (94.2%)]vs. 28 (6.1%); p <0.001], respectively. The oncoplastic breast surgery was performed more frequently in patients who underwent lumpectomy + ALND surgery [14 (20.3%) vs. 30 (6.5%); p <0.001]. Among 31 patients with BCRL-B, 22 (71.0%) underwent SLNB and 9

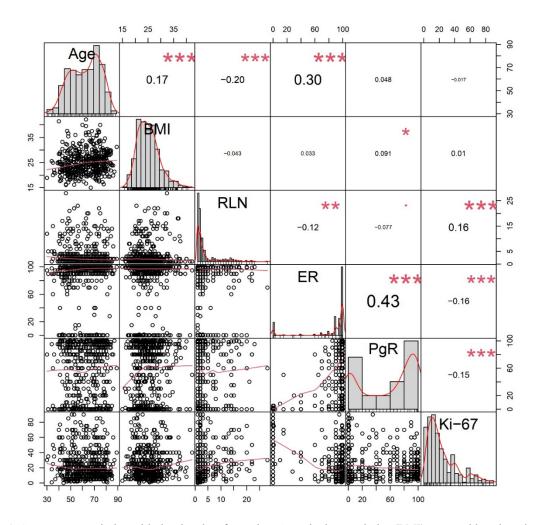


Fig. 1. Spearman correlation with density plots for patients' age, body mass index (BMI), resected lymph nodes (RLN), estrogen receptor (ER) expression, progesterone receptor (PgR) expression, and Ki-67 index (Ki-67). \* p < 0.05; \*\* p < 0.01; \*\*\* p < 0.001.

(29%) ALND and in 9 (29%) patients an axillary drainage was positioned during surgery. All patients with breast edema received adjuvant radiotherapy. Ten (32.3%) patients received adjuvant chemotherapy and hormonal therapy and 3 (9.7%) only adjuvant chemotherapy. Four (13.9%) patients underwent subsequent ALND after BCS.

A significantly positive correlation occurred between age and BMI (rs = 0.17; p <0.001), age and expression of estrogen receptor (ER) (rs = 0.30; p <0.001), expression of progesterone receptor (PgR) (rs = 0.09; p <0.05), ER and PgR expression (rs = 0.43; p <0.001), Ki-67 index and resected lymph nodes (RLN) (rs = 0.16; p <0.001), as well as BMI and PgR expression (rs = 0.09; p <0.05), while a significantly negative correlation occurred between age and RLN (rs = -0.20; p <0.001), ER expression and RLN (rs = -0.12; p <0.01), ER expression and Ki-67 index (rs = -0.16; p <0.001), as well as PgR expression and

	BCRL-B group $(n = 31)$	Non-BCRL-B group	P value
		(n = 499)	
Age (years)	$63.42 \pm 11.20$	$62.93 \pm 12.79$	0.911
BMI (Kg/m <sup>2</sup> )	$26.77 \pm 4.92$	$25.09 \pm 4.62$	0.080
RLN (n)	$4.94 \pm 5.76$	$3.51 \pm 4.27$	0.299
ER (%)	$87.87 \pm 29.51$	$84.99 \pm 29.69$	0.122
PgR (%)	$60.19 \pm 38.40$	$56.92 \pm 38.93$	0.539
Ki-67 (%)	$23.26\pm14.48$	$23.68\pm19.35$	0.470
Sumor side			0.998
Right	14 (45.2%)	234 (46.9%)	
Left	17 (54.8%)	265 (53.1%)	
DT	()	()	0.610
0	0 (0.0%)	23 (4.6%)	
la	2 (6.4%)	38 (7.6%)	
1b	9 (29%)	150 (30.1%)	
1c	13 (41.9%)	220 (44.1%)	
2	7 (22.6%)	67 (13.4%)	
4b	0 (0.0%)	1 (0.2%)	
N			0.008
0	16 (51.6%)	361 (72.3%)	
0 (ITC)	1 (3.2%)	12 (2.4%)	
1a	9 (29%)	75 (15%)	
1mi	0 (0.0%)	31 (6.2%)	
2a	5 (16.1%)	18 (3.6%)	
3a	0 (0.0%)	2 (0.4%)	
ype of surgery		× /	0.010
Lump+ALND	9 (29%)	60 (12%)	
Lump+SLNB	22 (71%)	439 (88%)	
Drainage	9 (29%)	84 (16.8%)	0.089
Dncoplastic	3 (9.7%)	41 (8.2%)	0.740
Neoadjuvant chemotherapy	3 (9.7%)	47 (9.4%)	0.999
Neoadjuvant hormonotherapy	0 (0.0%)	11 (2.2%)	0.998
Adjuvant chemotherapy	13 (41.9%)	129 (25.9%)	0.060
Adjuvant hormonotherapy	27 (87.1%)	426 (85.4%)	0.998
Adjuvant radiotherapy	31 (100%)	454 (91%)	0.102
Subsequent breast surgery	0 (0.0%)	5 (1%)	0.999
Subsequent ALND	4 (12.9%)	12 (2.4%)	0.010

 TABLE 2

 Comparisons Between Patients with and Without Breast Edema after Conservative Surgery

BCRL-B: breast cancer-related lymphedema of the breast; BMI: body mass index; RLN: Resected lymph nodes; ER: estrogen receptor; PgR: progesterone receptor; Ki-67: Ki-67 index; Lump+ ALND: lumpectomy + axillary lymph node dissection; Lump + SLNB: lumpectomy + sentinel lymph node biopsy.

Ki-67 index (rs = -0.15; p < 0.001) (*Fig. 1*).

No significant differences between patients with or without BCRL-B were found for age, BMI, RLN, expression of ER and PgR, Ki-67 index, size of the tumor according to TNM, drainage, oncoplastic and (neo)adjuvant chemo-hormono- and/or radiotherapy (*Table 2*). There was a difference seen in treatment with lumpectomy + ALND performed more frequently in patients with (29%) than without (12%) BCRL-B (*Table 2*). In the subgroup of patients with BCRL-B where LTW ratio was calculated [overall mean value: 1.59  $\pm$  0.44 (95% CI: from 1.44 to 1.75)], significantly higher values were observed in the nine patients who underwent lumpectomy + ALND procedure  $(1.86 \pm 0.48 \text{ vs.} 1.48 \pm 0.38; \text{ p} = 0.046)$ . No significant differences in the LTW ratio were found by stratifying for any other categorical variables (data not shown). Indu-

ration of the skin assessed by SkinFibroMeter was checked in patients with breast edema (n = 31): in eight patients (25.8%) tissue fibrosis measured into the edematous breast was

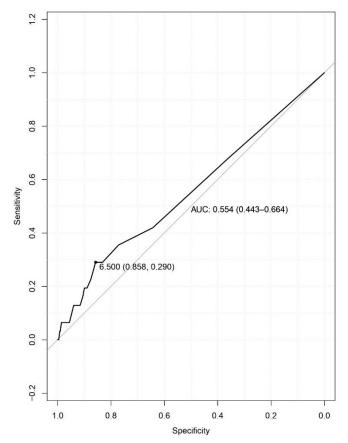


Fig. 2. Optimal cut-point value (6.5) of the resected number of lymph nodes that maximize sensitivity (0.858) and specificity (0.290) for post-operative breast edema occurrence [AUC = area under curve (95% confidence interval)].

>0.100 N, thus suggesting tissue induration.

Survival cumulative probability at 1year after surgery was 0.992. No statistical differences in 1-year survival after surgery were found by grouping for type of surgery (p = 0.890) or absence/presence of BCRL-B (p = 0.480).

In the univariate logistic regression models carried out by entering presence of BCRL-B as the dependent variable, only lumpectomy + ALND surgery [( $\beta$  = 1.096; OR = 2.994 (95% CI: from 1.256 to 6.616; p = 0.009)] and subsequent axillary node removal surgery [( $\beta = 1.796$ ; OR = 6.024 (95% CI: from 1.603 to 18.643; p = 0.003)] reached statistical significance. Also, in the multivariate regression model, both variables resulted statistically significant [Lump + ALND surgery:  $\beta = 0.889$ ; OR = 2.433 (95% CI: from 0.969 to 5.598; p = 0.044. Subsequent axillary node removal surgery:  $\beta = 1.449$ ; OR = 4.257 (95% CI: from 1.067 to 14.039; p = 0.024)].

Finally, the RLN was evaluated for obtaining the optimal cut-point in a ROC curve for BCRL-B occurrence. The ROC curve returned 6.5 RLN as the best value for maximizing sensitivity (0.858) and specificity (0.290) (*Fig. 2*).

## DISCUSSION

The incidence of BCRL-B in the literature ranges from 24.8% to 90.4%, which is an extensive range. According to categories of degree of breast edema assessed with physical examination, Adriaenssens et al (4) reported an incidence of 81.8% for mild breast edema, 16.2% for moderate breast edema and 2.0% for severe breast edema. Although some patients still suffer from breast edema more than 5 years after breast surgery, Clarke et al (8) demonstrated that breast edema occurs in the first 2 months (early onset breast edema) or in about 20 months (late onset breast edema) after breast cancer treatment.

The most common method to assess BCRL-B is physical examination. Although the lack of a diagnostic standardization, edema of the breast is characterized by an increased skin thickness and breast parenchymal density with prominent interstitial markings (9). Common clinical criteria for breast edema are peau d'orange, redness of the skin, pain in the breast, a positive pitting sign, increased breast volume, skin thickening, heaviness of the breast, and hyperpigmented skin pores. Subjective symptoms of breast edema in the operated and irradiated breast are heaviness, swelling, redness, numbness, tingling, stabbing pain, and skin twitching of the breast. Breast ultrasound (US) is considered to be a more reliable and quantitative measure for breast edema on a continuous scale for the repeated measures (10). However, as our assessment was accomplished during the Covid-19 Pandemic, with the inherent difficulties in providing also an ultrasonography evaluation of breast edema, this imaging procedure was not performed in our clinical series.

Different etiologies and imaging appearances can be related to unilateral breast edema: inflammatory breast carcinoma, cutaneous metastasis, breast lymphoma, mastitis, congestive heart failure, post-radiation or post-partial mastectomy state, and granulomatous diseases. All those conditions may be associated with the interruption of lymphatic vessels and associated lymph stasis.

In our study, we identified two risk factors for breast edema after BCS: more than 6.5 lymph nodes removed during surgery, and a second axillary node removal surgery. Our data demonstrate that there is not significant correlation between BCS and occurrence of breast edema.

In our cohort, breast edema was reported in 13% of the 9 patients who underwent ALND and in 4.8% of the 22 patients who underwent SLNB which is consistent with the literature (8.11). Our results demonstrate that breast edema is significantly less common after SLNB than after a more extensive axillary treatment. In particular, greater than 6.5 nodes removed during surgery is correlated with BCRL-B. Because of the removal of axillary lymph nodes, the lymphatic drainage of the arm is affected, and this could result in more accumulation of lymph fluid in the breast area. An operation on the dominant side is not reported as a significant risk factor for breast edema.

Radiotherapy may not cause direct damage to the lymph vessels or lymph nodes on a short-term period, but it does cause sclerosis of the skin which may obstruct lymph flow and slow down regeneration and neoformation of lymph vessels. Some researchers hypothesize that breast irradiation itself does not initiate cutaneous edema, unless other predisposing or aggravating factors are present.

Data concerning the role of chemotherapy are inconsistent. A study demonstrated that patients who received chemotherapy had a significantly higher degree of breast edema (4). Another study demonstrated that chemotherapy decreases the risk of acute breast edema after radiotherapy (12). The addition of taxanes to anthracycline regimens in the adjuvant setting has both improved the prognosis for longer survivorship and increased the incidence of edema. Nakagawa et al (7) reported that patients who had received NAC had more angiogenesis in skin and subcutaneous fat tissues distant from the primary tumor than did those who had not received NAC. They also found that neoadjuvant chemotherapy had no effect on lymphangiogenesis in the skin. These findings can help in identifying patients with persistent edema after chemotherapy and developing effective treatments for these patients. Our study does not demonstrate the role of adjuvant chemotherapy on the onset of breast edema.

According to our results, location of breast tumor is not associated with breast <u>edema</u>. However, all our patients underwent axillary surgery which may cause the interruption of breast lymphatic drainage. To study the real role of location of the tumor, a patient group undergoing breast surgery without any axillary procedure should be investigated.

Finally, in our population, age, menopausal state, and BMI are not associated with breast edema. Two studies investigated the correlation between age and edema, with conflicting conclusions (4,12). While the role of BMI on the onset of lymphedema of the arm has been documented, its association with breast edema is unclear.

TDC measurement, which is sensitive to skin-to-fat tissue water, may be useful for the diagnosis of breast edema. In literature, it is reported that an at-risk arm/contralateral arm TDC ratio of 1.2 and above could be a possible threshold to detect pre-clinical lymphedema (13). In our study, a higher LTW ratio was found in patients who underwent lumpectomy and ALND than lumpectomy and SLNB.

Our study has several limitations. First of all, we used a telephonic interview to identify patients with breast edema, as a measure to prevent the exposure of patients and staff to COVID-19. Thus, baseline data may also include factors that could be labeled by patients as breast swelling (hematoma, seroma) or some patients may not have recognized symptoms or signs of breast edema. Second, among 40 patients with a probable diagnosis of breast edema, nine patients could not or refused to be examined. Furthermore, TDC assessment was only made in patients with clinical lymphedema without a control group.

#### CONCLUSIONS

This study identified two main risk factors for BCRL-B: ALND (with more than 6.5 removed nodes) and second axillary lymph node removal surgery. Conversely, breast edema is significantly less common after SLNB than after a more extensive axillary treatment. Unfortunately, these risk factors could not be modified before surgery in order to apply an adequate prevention. However, the current trend of breast surgery is a progressive reduction of indications for ALND, and this could probably be the key to reduce risk of lymphatic complications.

Further prospective research is warranted to analyze potential predictive factors of breast edema and to reduce risk for its occurrence. Early diagnosis is crucial for earlier treatment and TDC measurement should become part of follow-up in patients with increased skin thickness and breast parenchymal density, redness of the skin, breast pain/heaviness with a positive pitting sign, and hyperpigmented skin pores.

To date, the only intervention for BCRL-B is a conservative management (manual lymphatic drainage, skin care and breast compression), but tailored therapies have potential to reduce the impact of breast edema on the quality of life of breast cancer patients.

First of all, attention should be reserved to the treatment of skin complaints. Skin hygiene, wound care, and trauma prevention can reduce the risk of infection with higher risk of breast edema. Compression methods currently used as part of complete decongestive therapy vary considerably in efficacy. Positive results have increasingly been reported whenever compression garments have been used as part of the treatment (14). A compression vest could be an acceptable and effective treatment option for patients with painful breast/chest wall edema and it should be recommended to all patients who under-went BCS: in compliant patients, swelling and pain was significantly reduced (15).

Another proposed intervention technique is kinesiology taping, wherein medical tape is applied to pull the breast skin off the underlying pectoralis muscle fascia in order to improve lymphatic drainage, decreasing swelling and pain, and enhancing muscle activity, but evidence of efficacy of these treatments is still lacking (16).

The major problem is that evidencebased treatments are not available because no gold standard exists for detecting breast edema. The delayed diagnosis of BCRL enables the disease to progress with symptoms worsening and this may lead to inadequate or palliative treatment and to exacerbate the symptoms experienced by patients (17).

In conclusion, an early recognition of this condition would be the key to improve the quality of life from the physical and psychological standpoint.

# CONFLICT OF INTEREST AND DISCLOSURE

The authors declare no competing financial interests exist.

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