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Psychological Stress and Its Correlations to Patients with Acute Lymphedema After Breast Cancer Surgery

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Background: Lymphedema and psychological distress, including anxiety and depression, are common in breast cancer patients post-surgery. This study aimed to assess the incidence and determinants of anxiety and depression in patients with acute lymphedema (ALE) following breast cancer surgery.

Methods: A retrospective study was conducted on 1613 breast cancer patients who underwent surgery at Fudan University Shanghai Cancer Center in 2018. ALE was defined as lymphatic fluid accumulation causing limb swelling and was classified by the difference in arm circumference. Anxiety and depression were evaluated using the Hospital Anxiety and Depression Scale (HADS) at discharge. Descriptive statistics and logistic regression were used to identify psychological distress-related factors.

Results: Among the 1613 patients, 363 (22.5%) had ALE. Anxiety was observed in 31% and depression in 21% of patients. ALE significantly impacted anxiety in the multivariate analysis (OR = 1.57, 95% CI: [1.04–2.38], P = 0.033). Multivariate analysis of ALE patients showed that longer hospital stays (OR = 0.51, 95% CI: [0.30–0.88], P = 0.017) and invasive disease (OR = 0.39, 95% CI: [0.19–0.78], P = 0.008) were associated with reduced anxiety; while lymph-vessel invasive disease was associated with increased anxiety (OR = 5.97, 95% CI: [1.15–30.97], P = 0.034). ALE had no significant impact on depression in the multivariate analysis. However, menopause (OR = 0.72, 95% CI: [0.56–0.94], P = 0.014) and longer hospitalization (OR = 1.30, 95% CI: [1.00–1.68], P = 0.047) influenced depression in all patients. In the ALE group, lymph node surgery was the only significant factor for depression (OR = 8.67, 95% CI: [1.56–48.23], P = 0.014) in the multivariate analysis.

Conclusion: Psychological stress, influenced by both surgical factors and emotional states, is associated with ALE development. Addressing both psychological and surgical factors is crucial for improving outcomes and quality of life in post-surgery breast cancer patients.

Keywords: breast cancer, psychological stress, anxiety, depression, acute lymphedema, invasive breast cancer, lymphatic invasive cancer

Introduction

Over the past 20 years, breast cancer incidence and mortality rates have risen rapidly, making it the most commonly diagnosed cancer among females worldwide. Recent estimates indicate that both the number of new cases and deaths continue to increase globally each year.[1] Although early detection and improved treatments have led to better prognoses,[2] breast cancer survivors face significant challenges beyond survival, including physical complications like lymphedema,[3] and psychological issues

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such as anxiety and depression.[4] These complications not only impact quality of life but also affect work ability and productivity, highlighting the need for comprehensive care addressing both physical and mental health.

Lymphedema, characterized by regional swelling due to fluid accumulation after lymphatic disruption,[5] affects a significant portion of breast cancer patients, with incidence rates ranging from 2% to 65%,[6–8] depending on diagnostic criteria, timing, surgical techniques, and patient characteristics. Beyond its physical effects, lymphedema greatly impacts body image, which in turn influences emotional well-being. Addressing body image concerns is crucial for psychological health during completion of treatment.[9,10] Symptoms such as pain, reduced sensation, and mobility in the affected limb contribute to emotional distress, anxiety, and depression.[11,12] Acute lymphedema (ALE) refers to the onset of lymphedema shortly after surgery, typically within the first few weeks.[13,14] Understanding ALE is essential for developing targeted interventions that address both the physiological and emotional challenges faced by patients post-surgery, ultimately enhancing their overall quality of life and promoting better treatment outcomes.

Psychological distress in breast cancer patients is influenced by both the extent of the disease and the surgical treatment required. Patients who are well informed about their cancer stage and surgical options, such as mastectomy or breast-conserving surgery, tend to experience lower levels of anxiety and depression. Effective communication from healthcare providers about treatment outcomes can significantly reduce psychological distress. Psychiatric symptoms, including anxiety and depression, affect 13% to 46% of breast cancer patients, often arising during diagnosis, treatment, or recurrence phases.[15,16] The highest levels of distress typically occur between initial diagnosis and post-surgery, driven by concerns over treatment outcomes and body image changes, which can impact treatment adherence.[17,18] Psychological interventions focusing on these issues have shown promise in improving emotional resilience and body image among breast cancer patients.[10]

This study aims to evaluate the incidence and determinants of anxiety and depression in breast cancer patients with ALE, focusing on the relationship between psychological distress and both physical (eg, lymphedema and surgery) and emotional (eg, body image) factors. Using the Hospital Anxiety and Depression Scale (HADS), we seek to understand how these factors contribute to anxiety and depression, with the goal of informing tailored psychological interventions to improve patient well-being and treatment adherence.

Materials and Methods

Patients Database

A total of 1830 patients who underwent breast cancer surgery between January 1 and March 30, 2018, were initially enrolled in the study, with informed consent obtained before surgery. Eligible patients were at least 18 years old, newly diagnosed with breast cancer, and scheduled for breast surgery. Exclusion criteria included bilateral breast cancer, absence of pre-surgery or discharge arm circumference measurements, inability to complete the HADS assessment, or withdrawal of consent.

The recruitment process involved identifying eligible participants through medical records and contacting them during follow-up visits. A dedicated team of research nurses was responsible for managing patient communication, explaining the study details, and obtaining informed consent from those who agreed to participate. Data collected included age at diagnosis, menopausal status, weight status, marital status, professional status, education level, stage, type of breast surgery, type of axillary lymph node dissection, length of hospital stay, clinical-pathological features, arm circumference at discharge, and HADS assessment results at discharge.

Ultimately, 1613 patients met the inclusion criteria and were included in the final analysis. This study protocol was approved by the independent ethics committee/institutional review board of Fudan University Shanghai Cancer Center.

Anxiety and Depression Assessment

Anxiety and depression were measured using the 14-item HADS, which includes two subscales: anxiety and depression.[19] The HADS is well accepted in oncology,[20] with excellent psychometric properties.[21] Each subscale score ranges from 0 to 21, with higher scores indicating greater levels of anxiety or depression.[22] While we acknowledge the ongoing debate regarding the optimal scoring method and cut-off point for the HADS,[23] we used the established

subscale cut-off score of ≥8 to identify cases of anxiety and depression in our study. A score of 14 or higher was used to identify severe cases.[22,24] The HADS demonstrated good reliability in our study, with Cronbach's Alpha values of 0.83 for the anxiety subscale and 0.82 for the depression subscale, indicating satisfactory internal consistency.

Lymphedema Measurement

Arm circumference (AC) was measured at ten sites on both limbs using a tape measure. The locations measured were the mid-metacarpal, the wrist and 20, 15, 10 and 5 cm below and above the elbow fold. The sum of these circumferences was calculated for each limb. We defined ALE as mild (Ipsilateral AC difference [IACD] < 3 cm or sum of bilateral AC difference [SBACD] < 10 cm), moderate (IACD 3 to 5 cm or SBACD 10 to 15 cm), and severe (IACD > 5 cm or SBACD > 15 cm) level, using the difference in the AC between the affected and unaffected limbs.[16,25]

Data Analysis

Patient and clinical characteristics were described using descriptive statistics. Continuous variables were evaluated for normal distribution and expressed by providing the median and range. χ^2 was used to test the relationship between categorical variables. To identify potential factors associated with anxiety and depression, we used univariate and multivariate logistic regression models. A P value < 0.05 was considered statistically significant. Analysis was conducted using SPSS version 26 (SPSS Inc., Chicago, Illinois).

Results

Patient Characteristics

We enrolled 1613 patients who underwent breast cancer surgery in 2018 in our center. According to the HADS scale, 500 (31%) patients were in a state of anxiety and 341 (21%) patients were in a state of depression. Among all the patients, 363 (22.5%) cases were identified as ALE, and 1250 (77.5%) were non-acute lymphedema (non-ALE). The characteristics of the two populations are summarized in Table 1.

Table 1 Characteristics of All Patients in This Study

Characteristic	All Patients (n=1613, 100%)		ALE Patients (n=363, 22.5%)		Non-ALE Patients (n=1250, 77.5%)		P
	n	%	n	%	n	%	
Age at diagnosis, y							0.900
Mean (SD)	51.1 (11.2)		51.5 (11.4)		50.9 (11.2)		
<50	773	48	173	48	600	48	
≥50	840	52	190	52	650	52	
Menopause							0.700
Yes	902	56	206	57	696	56	
No	711	44	157	43	554	44	
Weight status							**0.001**
BMI, <25 kg/m^2	1237	77	252	69	985	79	
BMI, 25–29.9 kg/m^2	331	20	95	26	236	19	
BMI, ≥30 kg/m^2	45	3	16	4	29	2	
Marital status							0.400
Married or cohabitant	1573	98	352	97	1221	98	
Widow/single/divorced	40	2	11	3	29	2	

(*Continued*)

Table 1 (Continued).

Characteristic	All Patients		ALE Patients		Non-ALE Patients		P
	(n=1613, 100%)		(n=363, 22.5%)		(n=1250, 77.5%)		
	n	%	n	%	n	%	
Professional status							0.700
Employed	418	26	100	28	318	25	
Retired	1175	73	259	71	916	73	
Unemployed	20	1	4	1	16	1	
Education level							0.164
Primary or below	83	5	26	7	57	4	
Secondary education	462	29	110	30	352	28	
College/University	869	43	185	51	684	55	
Postgraduate or above	199	23	42	12	157	13	
Stage							0.702
I	552	34	131	36	421	34	
II	535	33	120	33	415	33	
III	526	33	112	31	414	33	
Type of surgery							0.800
Breast-conserving	398	25	86	24	312	25	
Mastectomy	964	60	215	59	749	60	
Reconstruction	241	15	59	16	182	15	
Neither	10	1	3	1	7	1	
Type of axillary lymph node dissection							**0.014**
ALND	643	40	167	46	476	38	
SLNB	890	55	176	48	714	57	
Neither	80	5	20	6	60	5	
Hospital stays, days							**<0.001**
3–8	844	52	91	25	753	60	
≥9	769	48	272	75	497	40	
Anxiety status							**0.002**
No	1113	69	227	63	886	71	
Yes	500	31	136	37	364	29	
Depression status							0.400
No	1272	79	280	77	992	79	
Yes	341	21	83	23	258	21	

Note: Bold numbers indicate statistically significant findings ($p < 0.05$).
Abbreviations: ALE, Acute lymphedema; SD, Standard deviation; BMI, Body mass index; ALND, Axillary lymph node dissection; SLNB, Sentinel lymph node biopsy.

Anxiety and Depression Evaluation by HADS

Anxiety was identified in 500 (31%) breast cancer patients after surgery, with a significantly higher percentage in ALE patients than in non-ALE patients (37% vs 29%, P = 0.002). The median of HADS-Anxiety Score was 5.7 in the overall cohort, 5.5 for the non-ALE subgroup and 6.1 for the ALE subgroup (P = 0.008). The distribution of HADS-Anxiety score in the overall cohort is shown in Figure 1a, while the score distribution in ALE and non-ALE subgroups are shown in Figure 1b and c.

Depression was detected in 21% of patients in the overall cohort, but no statistical difference was observed between ALE patients and non-ALE patients (23% vs 21%, P = 0.40). The median score of HADS-Depression was 4.3 for the

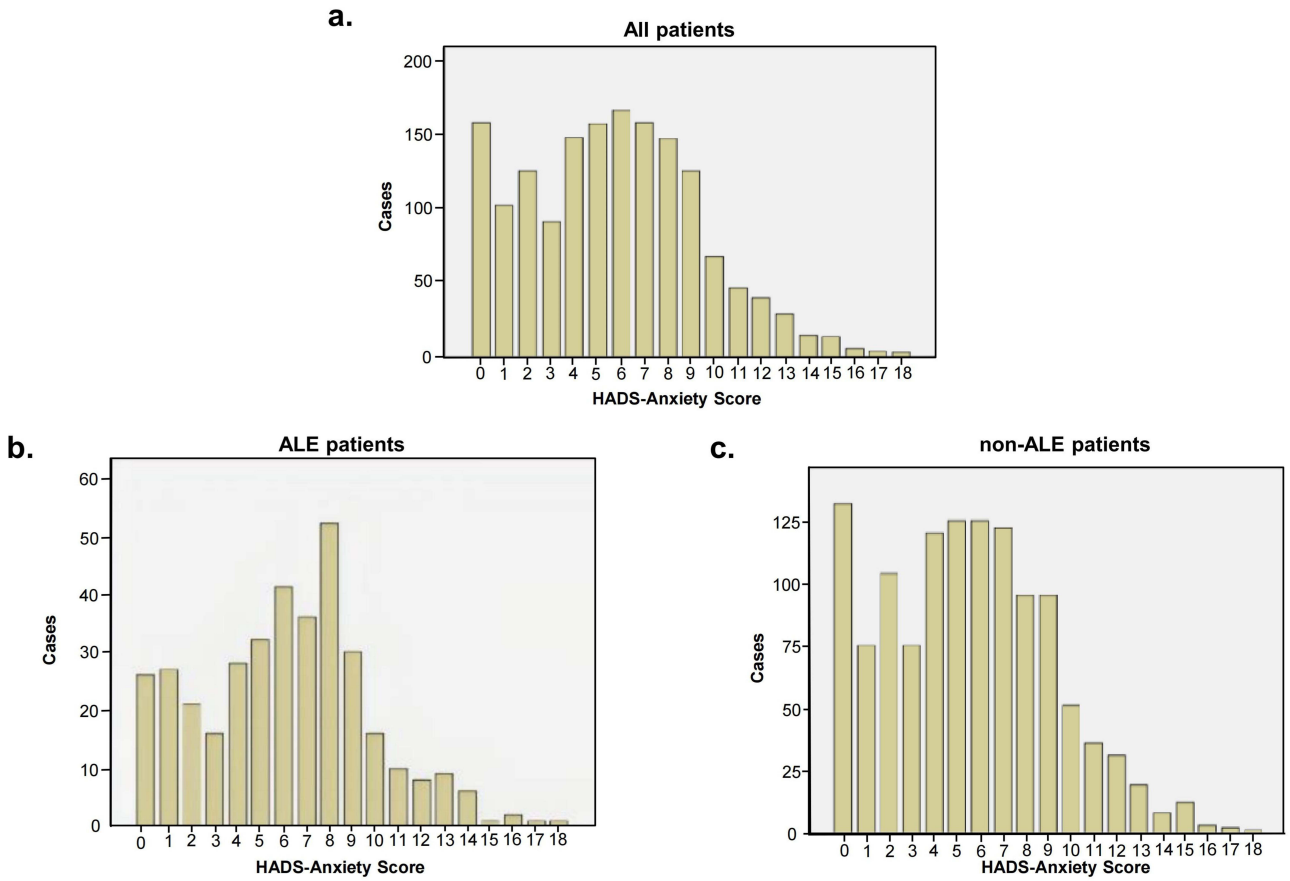

Figure 1 The distribution of HADS-Anxiety Score in all patients (**a**), ALE patients (**b**), and non-ALE patients (**c**).

non-ALE subgroup and 4.6 for the ALE subgroup (P = 0.16). The overall distribution of HADS-Depression score is shown in Figure 2a, and we observed a similar distribution in ALE and non-ALE subgroups in Figure 2b and c.

Furthermore, anxiety and depression disorders for different degrees of ALE were evaluated. The proportion of patients with HADS-anxiety and HADS-depression were significantly higher in the severe ALE group than in the mild ALE and moderate ALE groups (P < 0.001 for HADS-anxiety; P = 0.011 for HADS-depression; Table 2).

Factors Associated with Anxiety and Depression

In the univariate analysis, the only factor significantly associated with anxiety was ALE (OR = 1.46, 95% CI: [1.14–-1.86], P = 0.003). The statistical significance of ALE remained in the multivariate analysis (OR = 1.57, 95% CI: [1.04–2.38], P = 0.033). During subgroup analysis, we observed that in the ALE group, a longer period of hospital stay (OR = 0.51, 95% CI: [0.30–0.88], P = 0.017) and invasive disease (OR = 0.39, 95% CI: [0.19–0.78], P = 0.008) were related to less anxiety; lymph-vessel invasive disease was related to increased anxiety (OR = 5.97, 95% CI: [1.15–30.97], P = 0.034). In the non-ALE group, no factors were significantly associated with a patient's anxious status in the multivariate analysis (Table 3).

On the other hand, there was no statistically significant correlation between depression and ALE in the univariate analysis (OR = 1.14, 95% CI: [0.86–1.51], P = 0.36), whereas menopause (OR = 0.74, 95% CI: [0.58–0.95], P = 0.018) and the length of hospitalization (OR = 1.28, 95% CI: [1.01–1.62], P = 0.045) were the impact factors of depression. Multivariate analysis showed that menopause (OR = 0.72, 95% CI: [0.56–0.94], P = 0.014), and the length of hospitalization (OR = 1.30, 95% CI: [1.00–1.68], P = 0.047) were the factors influencing depression in all breast cancer patients. Among ALE group, only lymph node surgery (OR = 8.67, 95% CI: [1.56–48.23], P = 0.014), whether axillary lymph node dissection or sentinel lymph node biopsy, was the impact factor to depression. Meanwhile, in the non-ALE

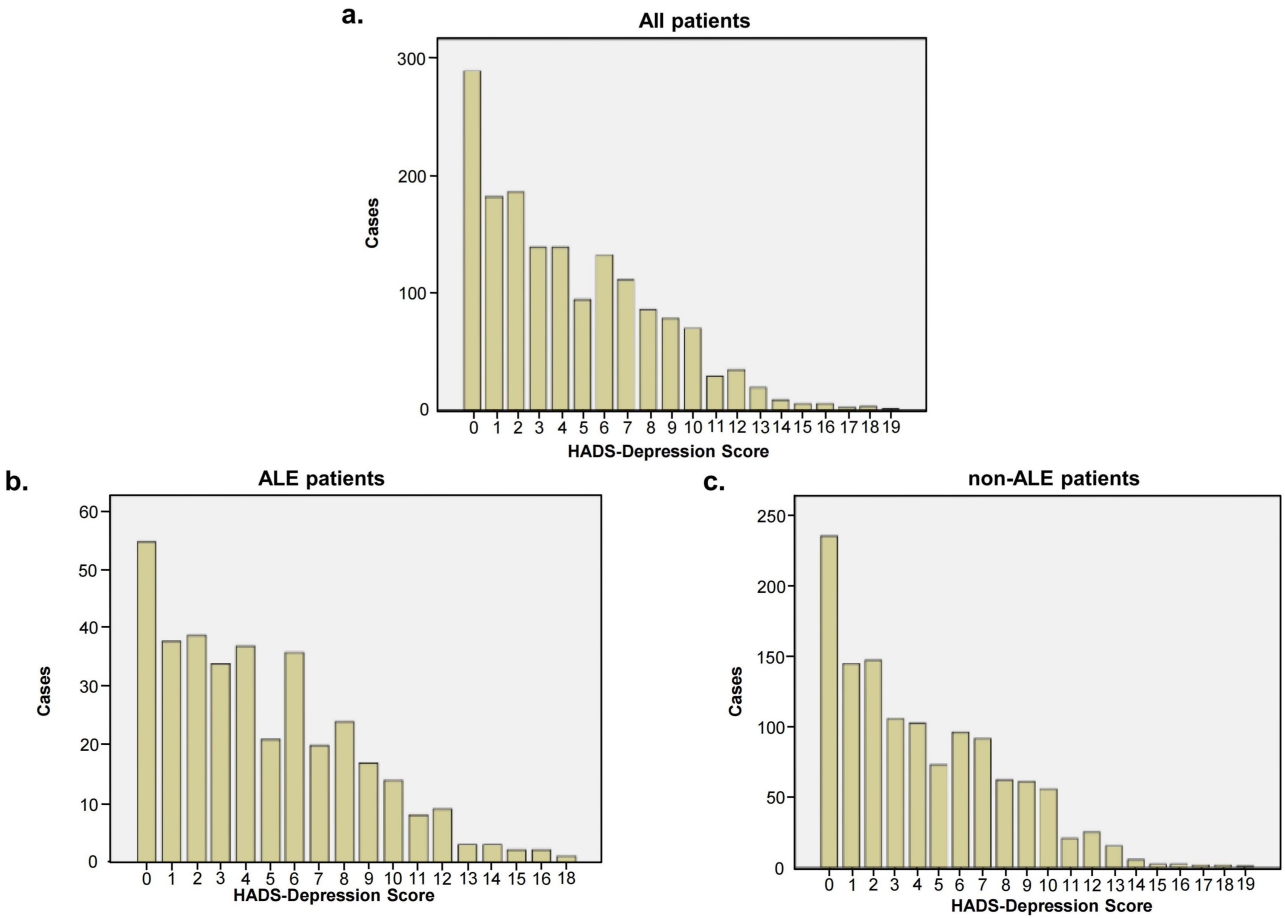

Figure 2 The distribution of HADS-Depression Score in all patients (**a**), ALE patients (**b**), and non-ALE patients (**c**).

group, depression was impacted only by the length of stay in hospital (OR = 1.45, 95% CI: [1.07–1.95], P = 0.015) (Table 4).

Discussion

The purpose of this study was to evaluate the incidence and determinants of anxiety and depression in breast cancer patients with ALE, focusing on the correlation between psychological distress and both physical and emotional challenges. Our findings highlight the importance of addressing both clinical and emotional factors in order to improve patient outcomes in the immediate postoperative period. To date, this is the largest study to address these issues among breast cancer patients with ALE. In this study, ALE after breast cancer surgery was found to be related to anxiety, but was not significantly related to patient depression.

Table 2 Prevalence of HADS-Anxiety and Depression After Breast Surgery in ALE Patients

Comorbidity	Mild ALE			Moderate ALE			Severe ALE			P
	n	%	95% CI	n	%	95% CI	n	%	95% CI	
HADS-anxiety	78	32.4	26.4–38.3	44	42.3	32.7–52.0	14	77.8	56.5–99.1	**<0.001**
HADS-depression	48	19.9	14.8–25.0	26	25.0	16.5–33.5	9	50.0	24.4–75.6	**0.011**

Note: Bold numbers indicate statistically significant findings (p < 0.05).
Abbreviations: ALE, Acute lymphedema; HADS, Hospital Anxiety and Depression Scale.

Table 3 Multivariate Analysis of Anxiety and Its Correlations in All Patients, ALE Patients and Non-ALE Patients

	All patients		ALE Patients		Non-ALE Patients	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
ALE	1.57 (1.04–2.38)	**0.033**				
Age	0.99 (0.78–1.24)	0.910	1.29 (0.78–2.14)	0.320	0.84 (0.62–2.14)	0.250
Hospital length of stay	1.08 (0.86–1.36)	0.510	0.51 (0.30–0.88)	**0.017**	1.13 (0.83–1.53)	0.450
Lymph node surgery	1.82 (0.85–2.40)	0.680	4.32 (0.78–23.72)	0.093	0.50 (0.16–1.52)	0.220
Invasive disease	0.85 (0.62–1.17)	0.320	0.39 (0.19–0.78)	**0.008**	2.91 (1.00–8.49)	0.050
Lymph node number >4	1.07 (0.73–1.59)	0.720	1.79 (0.84–3.81)	0.130	1.50 (0.62–1.64)	0.970
Lymph-vessel invasion	1.40 (0.72–2.70)	0.330	5.97 (1.15–30.97)	**0.034**	1.50 (0.62–3.60)	0.370

Note: Bold numbers indicate statistically significant findings ($p < 0.05$).
Abbreviations: ALE, Acute lymphedema; OR, Odds ratio; CI, Confidence interval.

Table 4 Multivariate Analysis of Depression and Its Correlations in All Patients, ALE Patients and Non-ALE Patients

	All Patients		ALE Patients		Non-ALE Patients	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Menopause	0.72 (0.56–0.94)	**0.014**	0.57 (0.33–1.01)	0.054	0.78 (0.58–1.05)	0.100
Hospital length of stay	1.30 (1.00–1.68)	**0.047**	0.73 (0.39–1.36)	0.320	1.45 (1.07–1.95)	**0.015**
Lymph node surgery	1.28 (0.58–2.82)	0.550	8.67 (1.56–48.23)	**0.014**	0.49 (0.14–1.69)	0.260
Invasive disease	1.07 (0.73–1.55)	0.740	0.60 (0.28–1.29)	0.190	1.30 (0.83–2.03)	0.250
Lymph node number >4	1.06 (0.75–1.50)	0.730	1.78 (0.90–3.52)	0.096	0.93 (0.62–1.40)	0.720
Lymph-vessel invasion	0.78 (0.34–1.81)	0.560	1.27 (0.24–6.72)	0.770	0.72 (0.27–1.93)	0.510

Note: Bold numbers indicate statistically significant findings ($p < 0.05$).
Abbreviations: ALE, Acute lymphedema; OR, Odds ratio; CI, Confidence interval.

Lymphedema may occur at any point following axillary lymph node surgery or radiation therapy and can begin immediately after treatment or be delayed by several years.[26] Our findings revealed that among the 1613 women who underwent breast surgery in our center, 22.5% patients were diagnosed with ALE on discharge. This result suggests that the incidence of acute swelling during hospitalization following breast cancer surgery is considerable. Our findings align with global data, including the study by Abbasi et al[27] which highlights the role of the primary hospitalization and treatment phase in the development of lymphedema. Reported lymphedema incidence rates globally range from 2% to 65%, and our results fall within this range, emphasizing the importance of early postoperative interventions to manage this complication. Early assessment and diagnosis of ALE are necessary for breast cancer patients to maintain upper extremity functioning and quality of life because of the reversible nature of ALE and its relation to anxiety.[28]

Many studies have focused on reporting the swelling rate of long-term breast cancer survivors and the quality of life in the rehabilitation period,[29] yet few studies have assessed the incidence rate of ALE and its impact on anxiety and depression. In our study, postoperative anxiety was a key factor in psychological distress, consistent with Cai et al's findings[30] on the impact of fatigue and sleep quality. However, we acknowledge that using only a single HADS assessment may not fully capture the relationship between these factors. Future studies should use additional tools and multiple assessments, pre- and post-operatively, to better understand the interplay between anxiety, fatigue, and sleep quality, especially in large-scale studies.

From our study, anxiety level was also significant after breast surgery and was higher in patients who suffered from ALE in comparison to those without ALE.

Previous research has shown that lymphedema negatively impacts an individual by causing side effects such as psychological distress.[4] However, few studies have specifically examined the prevalence of mental disorders and their association with the development of ALE. Our study found that about one-third of patients had anxiety after surgery and over one-fifth of ALE patients had depression after surgery. Compared with non-ALE patients, the prevalence of anxiety was significantly higher among ALE patients after surgery, while the prevalence of depression showed no significant difference between the two groups. Among the severe-ALE population, the rate of anxiety and depression were both higher than those among the mild- or moderate-ALE patients. These findings revealed that psychosocial problems may have negative impact on the development of ALE. Univariate and multivariate analyses further confirmed that only the ALE status was related to anxiety at discharge. These results suggest a strong interaction between ALE status and patient anxiety. As previously mentioned, using additional tools and multiple assessments would provide a more detailed understanding of this relationship. Study from Taghian et al[31] confirmed that lymphedema led to patient anxiety after surgery, while anxiety itself may inhibit the parasympathetic system which results in the dysfunction of lymphatic system and aggravates the ALE.[31] One study from Abbasi et al[27] revealed that relaxation techniques reduced the anxiety and depression scores and the volume of edema in the patients with lymphedema. Our research highlights the importance of screening for anxiety and depression in breast cancer patients to reduce ALE risk. Therefore, breast cancer patients, surgeons, therapists, and psychologists should collaborate to reduce anxiety and ALE levels simultaneously, improving patients' quality of life.[32,33] However, comparing at least two HADS assessment scores, both pre- and postoperatively, would provide a clearer measure of the medical staff's success in reducing anxiety and ALE development during hospitalization.

Additionally, among ALE patients, anxiety was associated with the length of hospitalization, invasive disease diagnosis, and lymph-vessel invasion, while depression was related to lymph node surgery. In contrast, for non-ALE patients, only hospital stay was linked to depression. This highlights the importance of postoperative care, particularly during hospitalization, as the prognosis and uncertainty of adjuvant treatment can significantly affect the mental state of patients.[34,35] While this is a strength of our study, comparing at least two HADS assessments would further validate the findings and enhance the study's robustness, especially given the large patient sample and detailed statistical analysis. Specialists should pay special attention to the patient's anxiety status and arrange to discuss and conduct their adjuvant treatment as soon as possible to reduce the patients' anxiety. Some study showed that regular nursing and follow-up after discharge and routine intervention through a novel multi-perspective physical activity methodology could have a positive effect on breast cancer patients' quality of life including lymphedema and anxiety.[34–36]

The limitations of this study were as follows: First, there is a lack of social epidemic information in the database, which may cause a bias when analyzing the causes and factors affecting anxiety and depression. Second, brief scales such as the HADS are limited in their ability to accurately predict a clinical diagnosis, high scores identify those who may warrant referral for clinical evaluation. Finally, follow-up for ALE and psychological stress was not conducted regularly after the patients' discharge from the hospital. It is necessary to extend the regularity of follow-up time to 1 month, 3 months, and 6 months after surgery to deepen our understanding of ALE and psychological stress.

Conclusion

This study underscores the strong association between ALE and anxiety in breast cancer patients following surgery, with ALE contributing to higher anxiety levels, while depression is less impacted. Early detection and management of ALE are critical to alleviating both physical and psychological burdens. A multidisciplinary approach that incorporates both medical and psychological care is essential for enhancing patients' quality of life. Integrating psychological and physical care in follow-up is crucial for improving outcomes in patients at risk of ALE, providing more comprehensive support for breast cancer patients.

Ethics Approval

This observational study was reviewed and approved by the Medical Ethics Committee, Fudan University Shanghai Cancer Center (NO.1612167-18), in accordance with applicable regulations. As formal patient consent to review medical

records was not required by the Committee, the waiver was granted based on the retrospective nature of the study and the use of anonymized data. All patient data were handled with strict confidentiality in compliance with relevant privacy regulations. The study was conducted in accordance with the Helsinki Declaration.

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Disclosure

The authors have no relevant financial or non-financial interests to disclose.

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