Analysis of sentinel lymph node biopsy and non-sentinel lymph node metastasis in invasive ductal and invasive lobular breast cancer: a nationwide cross-sectional study (CSBrS-001)

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Background: Information regarding the implementation of sentinel lymph node biopsy (SLNB) in invasive lobular carcinoma (ILC) is scarce, and whether ILC patients with 1–2 positive sentinel lymph nodes (SLNs) can be omitted from axillary lymph node dissection (ALND) remains controversial. This study aimed to compare involvement of SLNs and non-SLNs between patients with invasive ductal carcinoma (IDC) and ILC.

Methods: We retrospectively collected the clinical and pathological data of invasive breast cancer patients from 37 medical centers in China from January 2018 to December 2018. The number of resected SLNs, positive rate of SLNs, and non-SLNs metastasis were compared between patients with IDC and ILC.

Results: A total of 6,922 patients were included, comprising 6,650 with IDC (96.1%) and 272 with ILC (3.9%). No difference was observed in the number of resected SLNs between patients with IDC and ILC (IDC: 4.0±1.9 *vs.* ILC: 3.9±1.6, P=0.352). The positive rate of SLNs was significantly higher in patients with IDC than that in patients with ILC (19.3% in IDC *vs.* 12.9% in ILC, P=0.008). The difference in positive rate of SLNs between IDC and ILC was mainly attributed to macro-metastasis. For patients with positive SLNs who received ALND, and those with 1–2 positive SLNs, the metastatic rate of non-SLNs in the ILC group was higher than that in the IDC group (for patients with positive SLNs: 50.0% in ILC *vs.* 39.9% in IDC, P=0.317; for patients with 1–2 positive SLNs: 45.4% in ILC *vs.* 34.8% in IDC, P=0.366), but the differences were not statistically significant.

Conclusions: Patients with ILC had similar number of resected SLNs and lower positive rate of SLNs compared to those with IDC. In participants with 1–2 positive SLNs, the ILC group had an increased tendency for non-SLNs metastasis compared with the IDC group. Surgeons may need to be more cautious about omitting ALND for ILC patients with 1–2 positive SLNs.

Keywords: Breast cancer; invasive lobular carcinoma (ILC); sentinel lymph node biopsy (SLNB); non-sentinel lymph node metastasis

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Introduction

Axillary lymph node status is a major prognostic factor in early-stage breast cancer (1). Axillary lymph node dissection (ALND) has been regarded the most accurate method for assessing metastatic spread of lymph nodes. However, ALND may result in lymphedema, motor deficit, and dysesthesia of the operated arm (2). Sentinel lymph node biopsy (SLNB) has spared the morbidity of ALND without compromising diagnostic accuracy and prognostic information (3). Sentinel lymph node metastasis >2 mm, the number of examined sentinel lymph nodes (SLNs) and proportion of involved SLNs have been identified correlated with axillary lymph node metastasis (4). In addition, the multifocality of primary tumor, tumor size, and lymph vascular invasion have been shown to be independent predictors of axillary lymph node metastasis (5). Progesterone receptor status correlated with axillary lymph node involvement, but in other studies the estrogen, progesterone or HER-2 receptor status has not been found to be consistently related to lymph node status (6).

In primary breast cancer, SLNB has supplanted ALND and been established as the standard surgical procedure for staging clinically negative nodes (7,8). The American College of Surgical Oncology Group Z0011 (ACOSOG Z0011) study demonstrated that the omission of ALND among cT1-2N0M0 patients with 1–2 positive SLNs did not result in an inferior outcome compared with patients who underwent ALND (9). After the ACOSOG Z0011 clinical trial was revealed, the use of SLNB increased (10). However, most cases included in previous studies on SLNB were invasive ductal carcinoma (IDC). Information regarding the implementation of SLNB in patients with invasive lobular carcinoma (ILC) is sparse. Whether ILC patients with 1–2 positive SLNs can be exempted from ALND remains controversial (11-13).

Although ILC only accounts for approximately 5–10% of all breast cancer cases, the clinical course of ILC has unique aspects and merits special attention (14). The typical pathological characteristics of ILC are hormone receptor expression and absence of immunohistochemical (IHC) staining for E-cadherin (15). The peculiar growth pattern of ILC makes it difficult to diagnose clinically, as it usually lacks well-defined margins and does not form a palpable lesion (16); however, it tends to be hormone receptor positive and human epidermal growth factor receptor 2 (HER2) negative (14). Compared to IDC, the response of ILC to chemotherapy is significantly lower (17). It remains controversial whether IDC or ILC has a higher risk of non-SLNs involvement, and there is little information regarding the implementation of SLNB in patients with ILC. In our previous study, we described implementation status of SLNB and subsequent processing of positive SLNs among breast cancer patients in China (18). To explore the aforementioned issues, this nationwide cross-sectional study compared the involvement of SLNs and non-SLNs between patients with IDC and ILC. We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi.org/10.21037/atm-21-5169).

Methods

Patients

In this nationwide cross-sectional study, we retrospectively collected clinical and pathological data of breast cancer patients from 37 medical centers in China based on the assistance of Chinese Society of Breast Surgery (CSBrS) (*Table 1*). A total of 12,233 breast cancer patients were admitted to these medical centers and received SLNB surgery from January 2018 to December 2018. The number of cases in the area during the study period determined the sample size. The inclusion criteria were as follows: (I) invasive ductal or invasive lobular breast cancer confirmed by postoperative pathology, (II) underwent SLNB. The exclusion criteria were as follows: (I) male, (II) carcinoma *in situ* without invasive disease, or histologic subtypes other than IDC or ILC, including mixed-type lobular cancer, (III) with metastatic disease at diagnosis, (IV) without complete medical record. Finally, 6,650 patients with IDC and 272 patients with ILC were enrolled in this study. The study flow chart is shown in *Figure 1*. We retrospectively collected detailed SLNB and clinicopathologic data from patient records. This study conformed to the provisions of the Declaration of Helsinki (as revised in 2013) and was approved by the Ethical Committee of Xijing Hospital, The Fourth Military Medical University (KY20192114-C-1). Individual consent for this retrospective analysis was waived.

SLN evaluation

The SLNB technique and classification of molecular subtype were performed as described in our previous study (18). The CSBrS issued a unified data collection form to 37 medical centers in China and defined the classification criteria in the collection form. Uniform data collection methods and classification standards reduced the information bias of this study. The SLNs

Table 1 Distribution of enrolled invasive breast cancer patients in China

District	Proportion of participants	Name of medical center
Northern China	15.6%	Beijing Chaoyang Hospital
		Peking University First Hospital
		Peking University People's Hospital
		Xuanwu Hospital of Capital Medical University
		Beijing Friendship Hospital
		The General Hospital of the People's Liberation Army
		The Fourth Hospital of Hebei Medical University
		Inner Mongolia Autonomous Region People's Hospital
Eastern China	22.0%	The Obstetrics & Gynecology Hospital of Fudan University
		Huashan Hospital of Fudan University
		Zhongshan Hospital of Fudan University
		Second Hospital of Shandong University
		Shandong Provincial Western Hospital
		The First Affiliated Hospital of Zhejiang University
		The Second Affiliated Hospital of Zhejiang University
		Jiangsu Province Hospital
Northeastern China	21.3%	The First Hospital of China Medical University
		The second hospital of Dalian medical university
		Shengjing Hospital of China Medical University
		The Second Affiliated Hospital of Harbin Medical University
		The First Affiliated Hospital of Jilin University
		Jilin Cancer Hospital
Central China	16.0%	Henan Cancer Hospital
		The second affiliated Hospital of Nanchang University
		Xiangya Hospital Central South University
Southern China	11.4%	Sun Yat-sen Memorial Hospital of Sun Yat-sen University
		Fujian Medical University Union Hospital
Southwestern China	7.8%	Southwest Hospital of Third Military Medical University
		Sichuan Provincial People's Hospital
		Yunnan Cancer Hospital
		Affiliated Wudang Hospital of Guizhou Medical University
Northwestern China	5.9%	Xijing Hospital of Fourth Military Medical University
		The First Hospital of Lanzhou University
		The Second Hospital of Lanzhou University
		Gansu Provincial Hospital
		Gansu Provincial Cancer Hospital
		Affiliated Cancer Hospital of Xinjiang Medical University

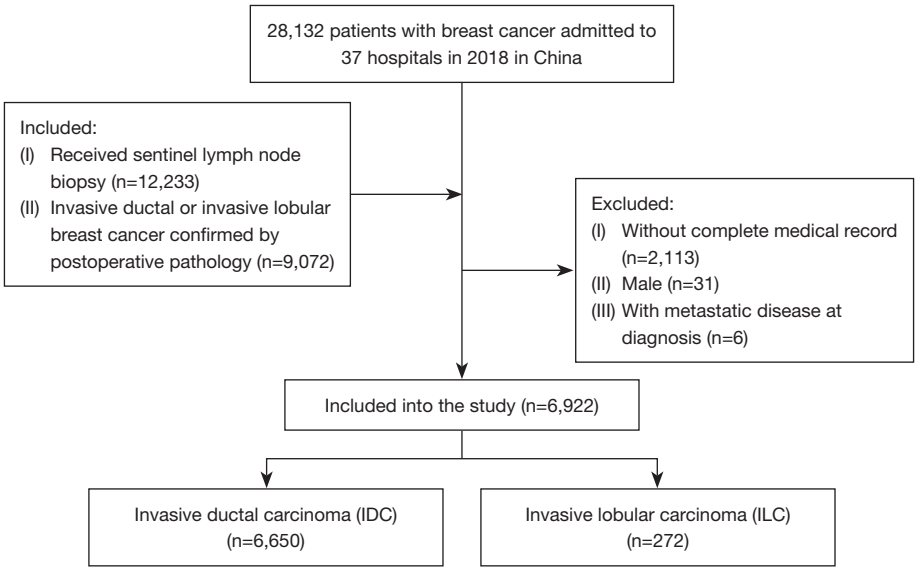

Figure 1 Study flow chart.

were considered positive for metastasis if they contained a macro-metastasis (deposit >2 mm) or a micro-metastasis (deposit ≥0.2 to 2 mm). The positive rate comprised the number of participants with metastatic SLNs/the number of participants who underwent SLNB ×100%. Sentinel lymph node ratio (SLNR) was the number of positive SLNs/the total number of removed SLNs.

Statistical analysis

All statistical analyses were performed using the software SPSS version 23.0 (IBM Corp., Armonk, NY, USA). Normally distributed data were represented by mean ± standard deviation. Cases with missing data were excluded. Student's *t*-test and univariate analysis of variance (ANOVA) were used to compare the difference of continuous variables. Categorical data was compared using χ^2 test. For the multivariable analyses, binary logistic regression was used. Odds ratios (ORs) with their corresponding 95% confidence intervals (95% CIs) were calculated in multivariable analyses. All P values were 2-tailed, and P<0.05 was considered statistically significant.

Results

Participants and tumor characteristics

Participant characteristics and pathological tumor characteristics are shown in *Table 2*. The study group consisted of 6,650 patients with IDC (96.1%) and 272 patients with ILC (3.9%). The main reason for excluding patients with metastatic disease at diagnosis and male patients is that these patients account for a very small proportion, and this group of people may show different SLNs and non-SLNs involvement. Several significant differences between the IDC participant group and ILC participants group were observed, including age at diagnosis, molecular subtype, and pathologic tumor size. Participants with ILC were older at diagnosis than those with IDC (9.2% ≤40 years old in ILC *vs.* 14.8% ≤40 years old in IDC, 29.0% >60 years old in ILC *vs.* 22.3% >60 years old in IDC, P=0.004). The participants with ILC were more associated with luminal A and less associated with HER2 enriched or triple-negative (TN) than those with IDC (41.9% with luminal A in ILC *vs.* 29.6% with luminal A in IDC, 4.0% with HER2 enriched in ILC *vs.* 13.0% with HER2 enriched in IDC, 5.9% with TN in ILC *vs.* 12.0% with TN in IDC, P<0.001). Participants with ILC had smaller tumors than did those with IDC (69.5% with T1 in ILC *vs.* 60.9% with T1 in IDC, P=0.004). No difference was observed in the type of surgery between participants with IDC and ILC (P=0.836).

Factors influencing the number of resected SLNs

The mean number of resected SLNs was 4.0±1.9. No difference was observed in the number of resected SLNs

Table 2 General participant characteristics

Characteristic	IDC (n=6,650)		ILC (n=272)		P value
	N	%	N	%	
Age at diagnosis*					0.004
≤40	984	14.8	25	9.2	
40–60	4,180	62.9	168	61.8	
>60	1,486	22.3	79	29.0	
Molecular subtype					<0.001
Luminal A	1,970	29.6	114	41.9	
Luminal B	3,018	45.4	131	48.2	
HER2 enriched	867	13.0	11	4.0	
TNBC	795	12.0	16	5.9	
Pathologic tumor size					0.004
T1	4,052	60.9	189	69.5	
T2	2,473	37.2	75	27.6	
T3–T4	125	1.9	8	2.9	
Surgical treatment					0.836
Breast-conserving surgery	2,044	30.7	82	30.1	
Mastectomy	4,606	69.3	190	69.9	

*, the patients were divided into three groups according to age: ≤40 (the young group), 40–60 (the middle age group) and >60 (the old group). IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; HER2, human epidermal growth factor receptor 2; TNBC, triple-negative breast cancer.

Table 3 Association between clinicopathological factors and number of resected SLNs among invasive breast cancer patients

Factors	Number of resected SLNs ($\bar{x}$±s)		P value
	IDC	ILC	
Age at diagnosis			
≤40	4.1±1.9	4.0±1.5	0.935
40–60	4.1±1.9	3.8±1.6	0.063
>60	3.8±1.9	4.0±1.8	0.335
P value	<0.001	0.621	
Molecular subtype			
Luminal A	4.0±1.9	3.8±1.6	0.299
Luminal B	4.0±1.9	4.0±1.7	0.785
HER2 enriched	4.0±1.9	3.6±1.2	0.523
TNBC	4.1±1.9	3.5±1.8	0.229
P value	0.803	0.480	
Pathologic tumor size			
T1	3.9±1.9	3.9±1.6	0.619
T2	4.1±1.9	4.0±1.8	0.675
T3–T4	4.5±1.9	3.6±1.7	0.219
P value	<0.001	0.654	
Tracer method			
A single mapping agent	4.1±1.9	4.0±1.6	0.659
Dual-tracer agent	3.6±1.9	3.3±1.8	0.429
P value	<0.001	0.034	

SLNs, sentinel lymph nodes; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; HER2, human epidermal growth factor receptor 2; TNBC, triple-negative breast cancer.

between patients with IDC and ILC (IDC: 4.0±1.9 *vs.* ILC: 3.9±1.6, P=0.352). As shown in *Table 3*, age at diagnosis, tumor size, and tracer method were influencing factors of the number of resected SLNs in patients with IDC. For participants with ILC, tracer method was the only influencing factor of the number of resected SLNs. When a single mapping agent was used, the number of resected SLNs was more than that when mapping was performed with dual-tracer in both participant groups (IDC: 4.1±1.9 *vs.* 3.6±1.9, P<0.001, ILC: 4.0±1.6 *vs.* 3.3±1.8, P=0.034). In the subgroup analysis, there was no statistical difference in the number of resected SLNs between participants with IDC and ILC.

SLNs and non-SLNs involvement in IDC and ILC

In this study, SLNs or non-SLNs were considered positive for metastasis if they contained a macro- or micro-metastasis. As shown in *Table 4*, the positive rate of SLNs was higher in participants with IDC than that in those with ILC (19.3% in IDC *vs.* 12.9% in ILC, P=0.008). The difference in positive rate of SLNs between IDC and ILC was mainly contributed by macro-metastasis (macro-metastasis rate: 17.1% in IDC *vs.* 11.8% in ILC, P=0.022; micro-metastasis rate: 2.6% in IDC *vs.* 1.1% in ILC, P=0.118). No difference was observed in rate of isolated tumor cells, SLNR, and rate of positive SLNs ≥3 between participants with IDC and ILC. For patients with positive SLNs who underwent ALND, the metastatic rate of non-SLNs in group ILC was higher than that in group IDC, but the difference was not statistically significant (50.0%

Table 4 SLNs and non-SLNs involvement in IDC and ILC cases

Variables	IDC (n=6,650), %	ILC (n=272), %	P value
SLNs involvement			
Positive rate of SLNs	19.3	12.9	0.008
Macro-positive rate	17.1	11.8	0.022
Micro-positive rate	2.6	1.1	0.118
Rate of isolated tumor cells	0.5	0.4	1.000
SLNR ≥50%	39.0	31.4	0.387
Positive SLNs ≥3	12.8	14.3	0.796
Non-SLNs involvement*			
Metastatic rate of non-SLNs	39.9	50.0	0.317
Metastatic rate of non-SLNs in 1–2 positive SLNs	34.8	45.4	0.366

*, non-SLNs metastases were calculated in patients with positive SLNs and received ALND. SLNs, sentinel lymph nodes; SLNR, sentinel lymph node ratio; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma.

in ILC *vs.* 39.9% in IDC, P=0.317). For patients with 1–2 positive SLNs, metastatic rate of non-SLNs in the ILC group was also higher than that in the IDC group, but the difference was not statistically significant (45.4% in ILC *vs.* 34.8% in IDC, P=0.366). As shown in *Table 5*, for patients with positive SLNs who underwent ALND, no difference was observed between metastatic rate of non-SLNs and clinicopathological factors (P>0.05), including age at diagnosis, molecular subtype, pathologic tumor size, and tracer method.

Table 5 Association between clinicopathological factors and metastatic rate of non-SLNs among invasive breast cancer patients*

Factors	Metastatic rate of non-SLNs	
	IDC	ILC
Age at diagnosis		
≤40	46.4%	–
40–60	39.4%	52.4%
>60	35.9%	40.0%
P value	0.132	1.000
Molecular subtype		
Luminal A	40.2%	46.2%
Luminal B	41.0%	50.0%
HER2 enriched	43.6%	100.0%
TNBC	33.7%	–
P value	0.504	1.000
Pathologic tumor size		
T1	35.9%	41.7%
T2	43.5%	53.8%
T3–T4	42.9%	100.0%
P value	0.057	0.695
Tracer method		
A single mapping agent	40.8%	56.5%
Dual-tracer agent	34.4%	0.0%
P value	0.203	0.458

*, non-SLNs metastases were calculated in patients with positive SLNs and received ALND; –, no ILC cases were younger than 40 years old or were TN subtype. IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; SLNs, sentinel lymph nodes; ALND, axillary lymph node dissection; TN, triple-negative.

Influencing factors affecting positive rate of SLNs in IDC and ILC

As shown in *Table 6*, in the subgroup analysis, the difference in positive rate of SLNs between IDC and ILC came from participants with luminal B and T1 (luminal B: 21.6% in IDC *vs.* 11.5% in ILC, P=0.005; T1: 15.4% in IDC *vs.* 9.5% in ILC, P=0.028). Age at diagnosis, molecular subtype, and tumor size were factors influencing the positive rate of SLNs in patients with IDC. For patients with ILC, tumor size was the only factor influencing the positive rate of SLNs. To further confirm the factors affecting the positive rate of SLNs in patients with IDC, multivariable analyses were performed. As shown in *Table 7*, older age (age >60, OR =0.78, 95% CI: 0.62 to 0.97 P=0.023) was an independent negative factor for positive rate of SLNs. Taking T1 as contrast, T2 (OR =1.98, 95% CI: 1.73 to 2.26, P<0.001) was a positive independent factor for the positive rate of SLNs. Compared to luminal A, luminal B (OR =1.22, 95% CI: 1.05 to 1.42, P=0.012) was a positive independent factor for the positive rate of SLNs, while HER2 (OR =0.74, 95% CI: 0.59 to 0.94, P=0.013) and TN (OR =0.78, 95% CI: 0.62 to 0.99, P=0.043) were negative independent factors.

Table 6 Association between clinicopathological factors and positive rate of SLNs in IDC and ILC cases

Variables	Positive rate of SLNs, %		P value
	IDC	ILC	
Age at diagnosis			
≤40	21.3	8.0	0.106
40–60	19.6	15.5	0.186
>60	17.3	8.9	0.051
P value	0.035	0.309	
Molecular subtype			
Luminal A	18.2	14.9	0.378
Luminal B	21.6	11.5	0.005
HER2 enriched	13.5	9.1	1.000
TNBC	16.2	6.3	0.491
P value	<0.001	0.976	
Pathologic tumor size			
T1	15.4	9.5	0.028
T2	25.8	21.3	0.387
T3–T4	20.0	12.5	1.000
P value	<0.001	0.038	
Tracer method			
A single mapping agent	18.6	13.3	0.049
Dual-tracer agent	21.0	6.3	0.043
P value	0.091	0.390	

SLNs, sentinel lymph nodes; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; HER2, human epidermal growth factor receptor 2; TNBC, triple-negative breast cancer.

Table 7 Multivariate analyses for positive rate of SLNs among IDC patients

Variables	OR (95% CI)	P value
Age at diagnosis		
≤40	1.00	
40–60	0.92 (0.76–1.10)	0.350
>60	0.78 (0.62–0.97)	0.023
Molecular subtype		
Luminal A	1.00	
Luminal B	1.22 (1.05–1.42)	0.012
HER2 enriched	0.74 (0.59–0.94)	0.013
TNBC	0.78 (0.62–0.99)	0.043
Pathologic tumor size		
T1	1.00	
T2	1.98 (1.73–2.26)	<0.001
T3–T4	1.45 (0.91–2.31)	0.118
Tracer method		
A single mapping agent	1.00	
Dual-tracer agent	1.18 (0.99–1.41)	0.065

SLNs, sentinel lymph nodes; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; HER2, human epidermal growth factor receptor 2; TNBC, triple-negative breast cancer; OR, odds ratio; CI, confidence interval.

Discussion

In the present nationwide cross-sectional study, we compared patients with ILC to those with IDC with respect to the implementation of SLNB and involvement of SLNs and non-SLNs. In this study, the characteristics of patients with ILC included older age at diagnosis, hormone receptor positivity and HER2 negativity, and smaller tumors; these observations were consistent with previous reports of ILC features (14). Moreover, no difference was observed in the number of resected SLNs between patients with IDC and ILC.

In the past, several studies have focused on the comparison of the risk of non-SLNs involvement between patients with IDC and those with ILC. However, information regarding the implementation of SLNB in patients with ILC is sparse. Our study showed that the positive rate of SLNs was higher in participants with IDC than that in those with ILC (19.3% in IDC *vs.* 12.9% in ILC, P=0.008). The difference in positive rate of SLNs between IDC and ILC was mainly attributed to macro-metastasis. This finding is similar to previous studies that reported that 18% ILC and 21% IDC cases were SLN micro-metastasis and macro-metastasis in 171 ILC and 2,168 IDC cases (11). There was no significant difference in the positive rate of SLNs between the ILC and IDC groups in the previous research (P=0.36), which may be due to the race/ethnicity difference of patients and the number of cases. In addition, several studies have found that ILC tended to have higher numbers of positive nodes when it metastasized to ALNs (19,20); however, few studies have explored the difference in the number of positive SLNs between ILC cases and IDC cases. In our study, no

difference was observed in SLNR and rate of positive SLNs ≥3 between patients with IDC and ILC, which indicates that the number of positive SLNs seems to be no different between patients with ILC and IDC.

Several studies have shown that different histological types of breast cancer incur different ALN metastasis burdens. Local removal of SLNs in early breast cancer will change the treatment and surgical strategies of breast cancer. Based on existing clinical trial evidence, if radiotherapy and adequate adjuvant systemic treatments are planned, the omission of ALND and SLNB with 1–2 positive SLNs following breast conserving surgery is not harmful (8). In addition, ALND is not justified for patients with micro-positive sentinel node involvement and that this does not impact on survival. However, for patients with micro-positive sentinel lymph nodes after neoadjuvant chemotherapy, ALND is still recommended for these patients (21). Whether ILC patients with 1–2 positive SLNs can avoid ALND remains controversial.

Many studies have shown that ILC was associated with a high risk of non-SLN involvement or ILC had more non-SLN metastasis than IDC. For example, Majid *et al.* found that ILC was associated with a high risk of non-SLN involvement (OR =1.73, 95% CI: 1.01 to 2.97) (22). Adachi *et al.* discovered that ILC cases had more non-SLN metastasis than IDC cases among SLN macro-metastasis patients (68% in ILC *vs.* 46% in IDC, P=0.03) (11). Fernández *et al.* found that ILC was associated with a higher ratio of positive lymph nodes (0.46±0.30 in ILC and 0.33±0.23 in IDC, P<0.01) (19). In our study, for participants with positive SLNs who received ALND, the positive rate of non-SLNs in the ILC group was higher than that in the IDC group (50.0% in ILC *vs.* 39.9% in IDC), but the difference was not statistically significant. However, a few studies have shown inconsistent conclusions. Corona *et al.* discovered that ILC histology is not associated with the risk of further metastasis at ALND (OR =1.62, 95% CI: 0.77 to 3.41, P=0.20) (13). Gao *et al.* found that ILC had similar rates of non-SLN metastasis compared with IDC among patients with 1–2 positive SLNs (31.2% in ILC *vs.* 28.6% in IDC, P=0.481) (12); however, in their study, there were only 182 IDC and 5 ILC patients with 1–2 positive SLNs (12). In our study, the metastatic rate of non-SLNs in group ILC was 10.4% higher than that in group IDC among patients with 1–2 positive SLNs, although the difference was not statistically significant (45.4% in ILC, n=30 *vs.* 34.8% in IDC, n=1,122, P=0.366). Therefore, surgeons should be more cautious about omitting ALND for ILC patients with 1–2 positive SLNs.

The predictors for the involvement of lymph nodes have been widely studied, while the risk factors for positive SLNs have rarely been explored. We found that tumor size was the only influencing factor affecting positive rate of SLNs in participants with ILC, which was in line with a previous study (23). For patients with IDC, age at diagnosis, molecular subtype, and pathologic tumor size were independent factors for the positive rate of SLNs. Falco *et al.* found that large primary tumor diameter (P=0.0132), molecular type (P=0.0492) and amount of positive SLNs (P=0.0408) were risk factors for positive ALNs based on a total of 391 patients with positive SLNs (24). Chakraborty *et al.* analyzed 426 patients with breast cancer, and they found that age, tumor grade, and tumor size were likely to be associated with number of lymph node metastasis (25). Among 814 patients with T1 and T2 primary breast cancer, Si *et al.* found that luminal HER2– and luminal HER2+ type showed a significantly higher probability of lymph nodes involvement when using triple negative breast cancer (TNBC) as a reference (26). The relationship between SLNs metastasis and age at diagnosis and T stage seems to be similar to that of theirs and lymph nodes, but further study is needed about relationship between molecular subtype and SLNs metastasis.

Our database included patients from 37 medical centers in China, who were treated in different settings. The range of participants was broad: teenagers to elderly people were included. Therefore, our results could be applicable to other IDC and ILC patients. The present study had some potential limitations. First, the number of participants with ILC was relatively low compared to those with IDC, which might be due to the low prevalence of ILC. Second, there was no patient follow-up conducted in this study, so the prognosis of patients with IDC and ILC could not be compared. Therefore, further studies with a larger cohort and follow-up are needed in patients with IDC and ILC.

Conclusions

This study, including a nationwide multi-center cohort of patients with IDC and ILC, demonstrated that patients with ILC had a similar number of resected SLNs, lower positive rate of SLNs, and increased tendency for non-SLNs metastasis compared to those with IDC. In patients with 1–2 positive SLNs, the ILC group also had an increased tendency for non-SLNs metastasis compared with the IDC group. Therefore, different histological types of invasive breast

cancer lead to different SLNs and non-SLNs metastasis burdens. Surgeons may need to be more cautious about omitting ALND for ILC patients with 1–2 positive SLNs.

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