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**RESEARCH ARTICLE**

Cheng et al.: Prognostic models for invasive lobular breast carcinoma

# Analysis of prognostic factors and construction of prognostic models for breast invasive lobular carcinoma

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**ABSTRACT**

Invasive lobular carcinoma (ILC) and invasive ductal carcinoma (IDC) account for most cases of breast cancer. However, there is ongoing debate about any potential variations in overall survival (OS) between ILC and IDC. This study aimed to compare survival between IDC and ILC, identify prognostic factors for ILC patients, and construct a nomogram for predicting OS rates. This retrospective cohort analysis utilized data from the Surveillance, Epidemiology, and End Results (SEER) Cancer Database. Patients diagnosed with ILC and IDC between 2000 and 2019 were enrolled. To minimize baseline differences in clinicopathological characteristics and survival outcomes, a propensity score matching (PSM) method was used. Data from the multivariate Cox regression analyses were used to construct a predictive nomogram for OS at 1, 3, and 5 years, incorporating all independent prognostic factors. Following the PSM procedure, patients with ILC exhibited a better prognosis compared to those with IDC. TNM stage, age >70, radiotherapy, surgery, estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HR-/HER2+) subtype were identified as independent factors for OS in ILC patients. Surgery and radiotherapy effectively reduced the risk of death, while chemotherapy did not demonstrate the same benefit. This model could support clinicians in evaluating the prognosis of ILC for decision-making and patient counseling.



**KEYWORDS**: Invasive lobular carcinoma, SEER, nomogram, prognosis, independent risk factors

## INTRODUCTION

As the second most frequently observed histological subclass of invasive breast carcinoma, invasive lobular carcinoma (ILC) accounts for approximately 5%–15% of all cases [1-4]. In contrast to patients with invasive ductal carcinoma (IDC), the foremost subclass of breast carcinoma, women suffering from ILC tend to have a higher likelihood of lymph node positivity, advanced histologic stage, and larger tumor sizes. Additionally, ILC patients are more prone to be positive for hormone receptor [5-7]. Accurate prognosis evaluations are crucial in making therapy decisions for breast cancer. Incorrect predictions can result in unwanted management for patients with a better prognosis and inadequate management for high-risk ones. Currently, most decisions on ILC treatment are based on clinical trials emphasizing IDC. This probably explains why guidelines from the National Comprehensive Cancer Network (NCCN) and the St Gallen International Expert Consensus remain advocating the ILC management with identical paradigms to IDC. Nonetheless, ILC has distinct characteristics, which is now widely recognized as a unique disease event. As suggested by growing clinical evidence, 'one-size-fits-all' approach to the entire invasive breast carcinomas is undesirable for particular subclasses like ILC. There are controversial results concerning the prognosis of ILC compared to IDC, with the prognosis of ILC reported as worse [8], no different [9, 10], and even better [11] than for IDC. The question of whether there are differences in overall survival (OS) and disease-free survival (DFS) between these two carcinoma subtypes remains disputable. The difference might be related to the number of patients, clinicopathological characteristics, and different databases. Therefore, it is necessary to conduct further comparisons of survival between IDC and ILC using large databases and identify prognostic indicators specifically for patients suffering from ILC. The American Joint Committee on Cancer (AJCC) staging paradigm is traditionally adopted for evaluating the

cancer patient prognosis, where the local (T), regional (N), and distant (M) extents of cancer are considered [12]. Nevertheless, patients with identical AJCC stage have still been observed to have greatly varying prognoses. That is because apart from the T, N, and M stage, a few clinicopathological can also impact the carcinoma patients' prognosis [13]. Breast cancer prognosis may be influenced by factors such as age, race, size of tumor, as well as statuses of human epidermal growth factor receptor-2(HER2), ER and PR. There has been extensive application of reliable tools called nomograms in oncological practice, which help quantitatively predict outcome probabilities in individual patients. Numerous studies have found that nomograms offer higher predictive accuracy than the AJCC staging system [14]. However, no nomogram has been published for the OS estimation in patients with ILC. One of the difficulties in validating prognostic and forecast diagnostics of ILC lies in extended period of time from diagnosis to recurrence/recrudesce, making it challenging to obtain funding for and track prospective studies. This is further supported by occasionally conflicting data concerning if ILC or IDC leads to a worse prognosis with the progression of time. We eagerly anticipate progress in the field, as it is expected to benefit patients greatly. Our current work attempted to make survival comparison of ILC against IDC, identify prognostic factors for ILC patients and to formulate a nomogram for the OS rate forecasting.

## MATERIALS AND METHODS

### National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Database

In our current work, data from the SEER (May 2022 updated version) were adopted, which consist of information on demographic statistics, tumor traits, nodal stage, surgical details, vital status, as well as follow-up documents from 18 different geographic locations. With a patient

count of over 3 million, this database covers approximately 28% of the U.S. population. The database prioritizes quality control and enforces an error rate of less than five percent [15].

For this study, patients diagnosed IDC were defined using the International Classification of Diseases (ICD) 8500/3 histological code, while patients with ILC were defined using the 8520/3 code. We were authorized to obtain the SEER cancer statistics, as well as additional treatment details including surgery, chemotherapy, and radiation therapy. Explicit consent was not necessary since there was no personal patient information involved.

**Case Selection**

Between 2000 and 2019, we initially identified 200,192 IDC women and 23,862 ILC women who met the criteria as described follows: women suffering from breast carcinomas aged 18–90 years, with only primary cancer, unilateral and identified laterality, who were diagnosed with either ductal or lobular carcinoma. Furthermore, we collected detailed information on tumor grade, TNM stages, hormone receptor (ER and PR) status, as well as comprehensive treatment and survival data. These parameters are well recognized indicators that may affect breast cancer prognosis [16]. Relatively old patients (≥ 70 years) could be meaningful among women with breast cancer [7, 8].To ensure comparability between the two groups, propensity score matching (PSM) was employed, resulting in a final cohort of 47,724 patients, with 23,862 IDC patients and 23,862 ILC patients. To account for potential treatment differences and ensure consistent follow-up, we focused on the research period from 2000 to 2019, with the cutoff date being December 31 of 2019. Tumor and nodal staging classification followed the AJCC staging paradigm for breast cancer, where the 6th edition guidelines were adopted for women diagnosed before 2009, and the 7th edition guidelines were adopted for women

diagnosed between 2010 and 2019. Additionally, cases with poorly differentiated, undifferentiated and anaplastic grades were classified as grade III. Focus of our current analysis was on tumors that had either pure lobular or pure ductal histology. We did not include tumors with mixed ductal and lobular histology to have more homogeneous groups.

**Data and Statistical Analysis**

Disparities in characteristic variables between ILC and IDC were compared by the $X^2$ test. The multivariate correlation of tumor characteristic variables with survival outcomes was explored by the Cox regression model. A significance level of 0.05 was set for statistical significance. The survival endpoint in this study was OS, which was assessed by the Kaplan-Meier approach. OS referred to the period from the breast carcinoma confirmation to the mortality due to any cause. Hazard ratio (HR) of OS, along with 95% confidence interval (CI), were determined through the log-rank test. The propensity score matching (PSM) technique was employed for lowering the baseline disparities in clinicopathological traits and survival prognoses. ILC and IDC patients were matched 1:1 based on age, race, laterality, primary site, surgery, TNM phase, subtype, radiation, chemotherapy, as well as statuses of HER2, ER and PR. The propensity score matching method was calculated through the "MatchIt" package in R software (version 3.6.2, Synergy Software, Inc., Essex Junction, VT, USA).

We divided our eligible patients into training and validation sets randomly at a 7:3 ratio, with the former being utilized for creating nomogram, and the latter being employed to make internal validation. The outcomes of the multivariate analysis were utilized in establishing a nomogram that predict the 1-,3- and 5-year OS rates. To assess the nomogram's effectiveness, we employed C-index along with receiver operating characteristic (ROC) graph for assessing

how well it differentiates between outcomes. The degree of forecasted probability consistency with actual outcomes was gauged based on the calibration graphs. Calibration and discrimination were both evaluated by bootstrapping using 1000 resamples. The decision curve analysis (DCA) plots were used to estimate the practicality and advantages of the nomogram. We conducted statistical analysis by utilizing the SPSS software (version 22, SPSS Inc., Chicago, USA). A p-value of less than 0.05 was deemed as statistically significant [17].

## RESULTS

### Patient Characteristics Between ILC and IDC

Differences in patient characteristics observed between ILC and IDC. We utilized the SEER tumor registry database to locate a total of 879,718 patients who were diagnosed with ILC or IDC. By applying specific criteria for inclusion and exclusion, we narrowed down the patients to 224,054 for our study. Ultimately, we divided the patients into two groups, 23,862 patients (10.7%) were categorized as part of the ILC group, while 200,192 patients (89.3%) were classified as the IDC group.

The clinical characteristics of the ILC and IDC groups were summarized in Table 1. The ILC patients, in comparison to IDC patients, were found to be older, have more advanced tumor stage, larger tumor size, higher incidence of axillary lymph node metastasis, greater positivity of ER and PR receptors, lower incidence of HER2 positivity, and were less likely to receive chemotherapy ($p < 0.001$ for all variables). When comparing the surgical procedures, it was found that ILC cases had a higher percentage of mastectomy in comparison to IDC cases (48.0% compared to 36.7%, respectively). Additionally, the ILC group had a higher rate of receiving radiation therapy and a lower rate of receiving chemotherapy (51.5% compared to

47.8% and 31.4% compared to 57.6%, respectively). This difference was statistically significant ($p<0.001$).

**Survival Outcomes Between ILC and IDC Group**

Given the significant inter-group disparities in clinical traits, the PSM technique was adopted based on race, age, laterality, primary site, surgery, TNM phase, subtype, radiation, chemotherapy, as well as statuses of HER2, ER and PR, for lowering the inter-group disparities in survival outcomes. We matched every ILC patient to one IDC patient. According to Table 2, the two groups were constituted by patients in a 1:1 ratio with resembling baseline clinicopathological traits for subsequent analysis. Figure 1a displayed the OS in patients with ILC compared to those with IDC in the unmatched population. The prognosis for ILC was seemed to be better than that for IDC in the first 5 years after diagnosis, but after 5-10 years, ILC patients seemed to have worse prognoses. However, based on comparison of the PSM population database, ILC patients exhibited better OS ($P<0.001$) compared to IDC patients (Figure 1b), Furthermore, as shown in Figure 1b, the survival curves were not divided clearly after a long-time follow-up.

**Independent prognostic factors in ILC**

Based on the univariate Cox regression for OS in the training cohort, age, primary site, laterality, surgery, extents of T, N and M, TNM phase, ER, PR, breast subtype and radiotherapy constituted significant prognostic indicators, which were generally considered to be statistically significant for p-values less than 0.05 and reasonable Hazard ratio （HR） values (Figure 2). The multivariate correlation of tumor characteristic variables with survival outcomes was explored by the Cox regression model. These indicators above were

subsequently subjected to multivariate Cox regression, finding that T stage, N stage, M stage, TNM stage, age>70, radiotherapy, surgery, PR, ER, and HR-/HER2+ constituted independent predictors of OS for ILC group (Figure 3).

**Prognostic nomogram for survival**

By utilizing the multivariate Cox results in the training cohort, we formulated predictive nomograms for 1-, 3- and 5-year OS, where the entire independent prognostic indicators were incorporated (Figure 4). Based on the model, old age was most influential to the prognosis, followed by metastases and surgery. Other factors, including stage, T and N extents, PR and ER statuses, radiotherapy, and HER-2 status, impacted OS moderately. Given the correspondence of every parameter in the nomogram to a score by the multivariate Cox regression-derived weight, our formulated nomogram was interpretable. An overall risk score was yielded for every patient by summing up the entire parameter scores, thereby enabling OS inference. The particular procedure of nomogram interpretation has been described before [18].

During the nomogram computation, for instance, a 45 years-old woman with HR/HER2+ breast cancer categorized under T2N1M0, who has undergone breast-conserving surgery combined with radiotherapy, the scores on various risk predictors are 45 years-old (100), HR-/HER2+ breast cancer (50), T2N1M0 (170), breast-conserving surgery (40), and radiotherapy (50), hence, the overall score is 410. The OS forecasting probabilities of our model are 85% and 75% separately at 3 and 5 years.

## Performance and Validation of the Nomogram

The nomogram's calibration curves displayed excellent consistency between the predicted and actual probabilities of OS in both the training set (Figure 5a) and the internal validation set (Figure 5b). The nomogram achieved a C-index of 0.776 for predicting OS in the training cohort. Additionally, the area under the receiver operating characteristic (ROC) curve (AUC) at 1 year was 0.787, at 3 years was 0.788, and at 5 years was 0.794. In the validation cohort, the predicted OS C-index was 0.785. The AUC values at 1 year, 3 years, and 5 years were 0.794, 0.795, and 0.799, respectively. The calibration curves (Figure 6) demonstrated that the data points were closely aligned with the 45-degree diagonal line, Indicating highly accurate predictive capabilities of the nomogram. To compare the clinical usefulness of the nomogram with the traditional AJCC staging system, decision curve analysis (DCA) was conducted. The DCA curves (Figure 7) revealed that the nomogram had superior predictive abilities for 1-, 3-, and 5-year OS, potentially resulting in greater clinical benefits.

## DISCUSSION

Firstly, we collected information about 200,192 patients diagnosed with IDC and 23,862 patients diagnosed with ILC from the SEER database. We observed that individuals with ILC tended to have a higher age at diagnosis, larger tumor size, positive expression of ER/PR, and were less likely to receive radiation therapy and chemotherapy. Furthermore, during the initial 5-year period after diagnosis, the prognosis for patients with ILC was better compared to those with IDC. However, during 5-10 years, ILC patients seemingly experienced worse prognoses. These findings were consistent with previous research [19].

Secondly, to ensure that the disparities in survival outcomes are not influenced by variations in baseline clinical characteristics, we employed the propensity score matching method to conduct a case-control analysis, matching ILC and IDC patients in a 1:1 ratio. Interestingly, the matched results indicated that patients with ILC had a more favorable prognosis than those with IDC. The existing literature on the prognoses of ILC versus IDC presents conflicting views. Some studies suggest that ILC has a better prognosis [20], whereas others reported similar prognoses [10, 21-23]. Other studies demonstrated that the prognosis for ILC is worse than IDC [8, 24-26]. This discrepancy in the literature may arise from the fact that ILC represents a diverse group of tumors with outcomes closely related to the specific histological variant [27], consequently, aggregating all ILC cases together leads to varying results depending on the prevalence of each variant.

Thirdly, the findings from the current study indicate that age is a significant independent factor in predicting OS. Consistent with previous research, older patients have a higher risk of poor outcomes [21]. One possible explanation for this is that older individuals are more susceptible to multiple health conditions, which increases their risk. This suggests that providing treatment solely for ILC may not be sufficient for

older patients, and their co-existing conditions should also be addressed. In addition, the results confirm that tumor stage (T, N, and M) is an important prognostic factor for breast cancer patients [28]. Furthermore, the study revealed that HR and HER2 status were also significant independent predictors of OS. Classic ILC typically exhibits a luminal A molecular subtype, with a high proportion of cases showing strong ER positivity and PR expression (which is significantly higher compared to IDC) [7, 29], and they are usually negative for HER2 [29]. A recent study conducted on Mexican breast cancer patients comparing the disease-free survival

(DFS) and overall survival(OS) rates between ILC and IDC. The study revealed that the OS rates for both triple-negative ILC and HER2-positive ILC were significantly worse compared to IDC [26, 30]. The study also compared HER2-positive ILC and HER2-positive IDC patients, providing further evidence that HER2-positive ILC exhibits distinct clinical and biological characteristics relative to HER2-positive IDC [31]. Specifically, HER2-positive ILCs were more likely to be multicentric or multifocal, had a lower histological grade and proliferative index, and showed a higher frequency of nodal metastases [31]. Despite these differences, both HER2-positive ILC and IDC patients appeared to benefit similarly from adjuvant treatment with trastuzumab, resulting in similar recurrence rates. This suggests that HER2-positive ILC patients do derive benefits from anti-HER2 therapy [32, 33].

Fourthly, this study found that surgery and radiotherapy were effective in reducing the risk of death, which aligns with previous findings [5, 34, 35]. Similar benefits have been observed in smaller studies conducted at single institutions and in larger population-based analyses, indicating a reduction in local regional recurrence and improved survival rates [35]. However, the incidence of death was not affected by receiving chemotherapy. It is known that ILC generally shows a poorer response to adjuvant chemotherapy compared to IDC [36, 37]. This may reflect the fact that around 90% of ILCs are Luminal A tumors, exhibiting low histologic grades and low mitotic indices, thus limiting their responses to chemotherapy, while the high mastectomy rate of can be attributed to relatively larger tumor size [38].

Finally, our nomogram encompassed a comprehensive range of clinical risk factors that can easily be obtained from historical records. These factors include age, race, laterality, primary site, surgery, TNM phase, subtype, radiation, chemotherapy, as well as statuses of HER2, ER and PR. As indicated by the preferable fitting of calibration graphs and comparatively high C-

indexes, our nomogram performs strongly. Furthermore, this nomogram is user-friendly, since a point score is assigned to every trait at its top, and the overall score can be derived through simple summation of the entire individual item scores. A vertical line plotted from the overall score at the nomogram bottom intersects with three lines, indicating the cumulative incidence risks of death at 1,3, and 5 years for the patients.

Our research has a few shortcomings. At first, it was impossible to differentiate "pure" ILC from "hybrid" ILC across various geographic locations in the SEER database. Prognoses vary by the histological subclass of ILC, with pleomorphic ILC exhibiting more aggressive clinical traits and an inferior outcome compared to common ILC [39]. Given the retrospective cohort nature of our research based on the SEER registries, there exist inherent selection biases, as well as data deficiency. Second, this study only had internal validation and lacked external validation. We are collecting follow-up data from patients with breast lobular carcinoma in our hospital for external validation, but the number of patients is currently insufficient. We will continue to collect and analyze the follow-up data of ILC patients. There is a scarcity of extensive and up-to-date data sets allowing for a thorough contrast of clinicopathologic traits between ILC and IDC. In our research, we conducted a comprehensive analysis of ILC patients using the SEER database and developed a nomogram to predict the rates of OS at 1,3, and 5 years after diagnosis. The model could support clinicians to evaluate the prognosis of ILC in decision-making and patient counseling.



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## TABLES AND FIGURES WITH LEGENDS

**Table 1.** Comparison of clinical characteristics between invasive lobular carcinoma (ILC) and invasive ductal carcinoma (IDC) group in unmatched population.

| | IDC (%) 200192 | ILC (%) 23862 | P |
|---|---|---|---|
| Age | | | |
| ≤35 | 4135 ( 2.1) | 62 ( 0.3) | <0.001 |
| >35, ≤70 | 142470 (71.2) | 15466 ( 64.8) | |
| >70 | 53587 ( 26.8) | 8334 ( 34.9) | |
| Race | | | |
| White | 41206 ( 20.6) | 3388 ( 14.2) | <0.001 |
| Non-white | 158986 ( 79.4) | 20474 ( 85.8) | |
| Laterality | | | |
| Bilateral | 4 (0.0) | 1 (0.0) | 1 |
| Left/Right | 200188 (100.0) | 23861 (100.0) | |
| Primary Site | | | |
| Center | 62513 ( 31.2) | 8032 ( 33.7) | <0.001 |
| Upper | 107384 ( 53.6) | 12771 ( 53.5) | |
| Lower | 30295 ( 15.1) | 3059 ( 12.8) | |
| Surgery | | | |
| No | 11376 ( 5.7) | 1102 ( 4.6) | <0.001 |
| Breast conserving | 115955 ( 57.9) | 11618 ( 48.7) | |
| Mastectomy | 72861 ( 36.4) | 11142 ( 46.7) | |
| AJCC_Stage | | | |
| I | 109090 ( 54.5) | 10698 (44.8) | <0.001 |
| II | 65855 ( 32.9) | 8817 ( 36.9) | |
| III | 18619 ( 9.3) | 3503 ( 14.7) | |
| IV | 6628 ( 3.3) | 844 ( 3.5) | |
| AJCC_T | | | |
| 1 | 126092 ( 63.0) | 12249 ( 51.3) | <0.001 |

| | | | |
|---|---|---|---|
| 2 | 59085 ( 29.5) | 8066 ( 33.8) | |
| 3 | 9258 ( 4.6) | 3048 ( 12.8) | |
| 4 | 5757 ( 2.9) | 499 ( 2.1) | |
| AJCC_N | | | |
| 0 | 136482 ( 68.2) | 15377 ( 64.4) | <0.001 |
| 1 | 49319 ( 24.6) | 5946 ( 24.9) | |
| 2 | 9286 ( 4.6) | 1360 ( 5.7) | |
| 3 | 5105 ( 2.6) | 1179 ( 4.9) | |
| AJCC_M | | | |
| 0 | 193539 ( 96.7) | 23015 ( 96.5) | 0.069 |
| 1 | 6653 ( 3.3) | 847 ( 3.5) | |
| Subtype | | | |
| HR-/HER2- | 25875 ( 12.9) | 343 ( 1.4) | <0.001 |
| HR-/HER2+ | 10098 ( 5.0) | 109 ( 0.5) | |
| HR+/HER2- | 141151 ( 70.5) | 22361 ( 93.7) | |
| HR+/HER2+ | 23068 ( 11.5) | 1049 ( 4.4) | |
| ER_Status | | | |
| Negative | 38352 ( 19.2) | 488 ( 2.0) | <0.001 |
| Positive | 161840 ( 80.8) | 23374 ( 98.0) | |
| PR_Status | | | |
| Negative | 58891 ( 29.4) | 3972 ( 16.6) | <0.001 |
| Positive | 141301 ( 70.6) | 19890 ( 83.4) | |
| HER2_Status | | | |
| Negative | 167026 ( 83.4) | 22704 ( 95.1) | <0.001 |
| Positive | 33166 ( 16.6) | 1158 ( 4.9) | |
| Radiation | | | |
| No | 95117 ( 47.5) | 11734 ( 49.2) | <0.001 |
| Yes | 105075 ( 52.5) | 12128 ( 50.8) | |
| Chemotherapy | | | |
| No | 115238 ( 57.6) | 16558 ( 69.4) | <0.001 |
| Yes | 84954 ( 42.4) | 7304 ( 30.6) | |

**Table 2.** Comparison of clinical characteristics between invasive lobular carcinoma (ILC) and invasive ductal carcinoma (IDC) group in matched population.

| | IDC (%) 23862 | ILC (%) 23862 | P |
|---|---|---|---|
| Age | | | |
| ≤35 | 96 ( 0.4) | 62 ( 0.3) | 0.024 |
| >35, ≤70 | 15480 ( 64.9) | 15466 ( 64.8) | |
| >70 | 8286 ( 34.7) | 8334 ( 34.9) | |
| Race | | | |
| White | 3415 ( 14.3) | 3388 ( 14.2) | 0.734 |
| Non-white | 20447 ( 85.7) | 20474 ( 85.8) | |
| Laterality | | | |
| Bilateral | 1 ( 0.0) | 1 ( 0.0) | 1 |
| Left/Right | 23861 (100.0) | 23861 (100.0) | |
| Primary Site | | | |
| Center | 8011 ( 33.6) | 8032 ( 33.7) | 0.828 |
| Upper | 12747 ( 53.4) | 12771 ( 53.5) | |
| Lower | 3104 ( 13.0) | 3059 ( 12.8) | |
| Surgery | | | |
| No | 1126 ( 4.7) | 1102 ( 4.6) | 0.871 |
| Breast conserving | 11614 ( 48.7) | 11618 ( 48.7) | |
| Mastectomy | 11122 ( 46.6) | 11142 ( 46.7) | |
| AJCC_Stage | | | |
| I | 10718 ( 44.9) | 10698 ( 44.8) | 0.123 |
| II | 8622 ( 36.1) | 8817 ( 36.9) | |
| III | 3631 ( 15.2) | 3503 ( 14.7) | |
| IV | 891 ( 3.7) | 844 ( 3.5) | |
| AJCC_T | | | |

| | | | |
|---|---|---|---|
| 1 | 12259 ( 51.4) | 12249 ( 51.3) | <0.001 |
| 2 | 8214 ( 34.4) | 8066 ( 33.8) | |
| 3 | 2568 ( 10.8) | 3048 ( 12.8) | |
| 4 | 821 ( 3.4) | 499 ( 2.1) | |
| AJCC_N | | | |
| 0 | 15296 ( 64.1) | 15377 ( 64.4) | 0.133 |
| 1 | 5995 ( 25.1) | 5946 ( 24.9) | |
| 2 | 1457 ( 6.1) | 1360 ( 5.7) | |
| 3 | 1114 ( 4.7) | 1179 ( 4.9) | |
| AJCC_M | | | |
| 0 | 22968 ( 96.3) | 23015 ( 96.5) | 0.261 |
| 1 | 894 ( 3.7) | 847 ( 3.5) | |
| Subtype | | | |
| HR-/HER2- | 342 ( 1.4) | 343 ( 1.4) | 0.977 |
| HR-/HER2+ | 108 ( 0.5) | 109 ( 0.5) | |
| HR+/HER2- | 22343 ( 93.6) | 22361 ( 93.7) | |
| HR+/HER2+ | 1069 ( 4.5) | 1049 ( 4.4) | |
| ER_Status | | | |
| Negative | 480 ( 2.0) | 488 ( 2.0) | 0.82 |
| Positive | 23382 ( 98.0) | 23374 ( 98.0) | |
| PR_Status | | | |
| Negative | 3983 ( 16.7) | 3972 ( 16.6) | 0.902 |
| Positive | 19879 ( 83.3) | 19890 ( 83.4) | |
| HER2_Status | | | |
| Negative | 22685 ( 95.1) | 22704 ( 95.1) | 0.702 |
| Positive | 1177 ( 4.9) | 1158 ( 4.9) | |
| Radiation | | | |
| Yes | 11859 ( 49.7) | 11734 ( 49.2) | 0.256 |
| No | 12003 ( 50.3) | 12128 ( 50.8) | |
| Chemotherapy | | | |
| Yes | 16517 ( 69.2) | 16558 ( 69.4) | 0.691 |
| No | 7345 ( 30.8) | 7304 ( 30.6) | |

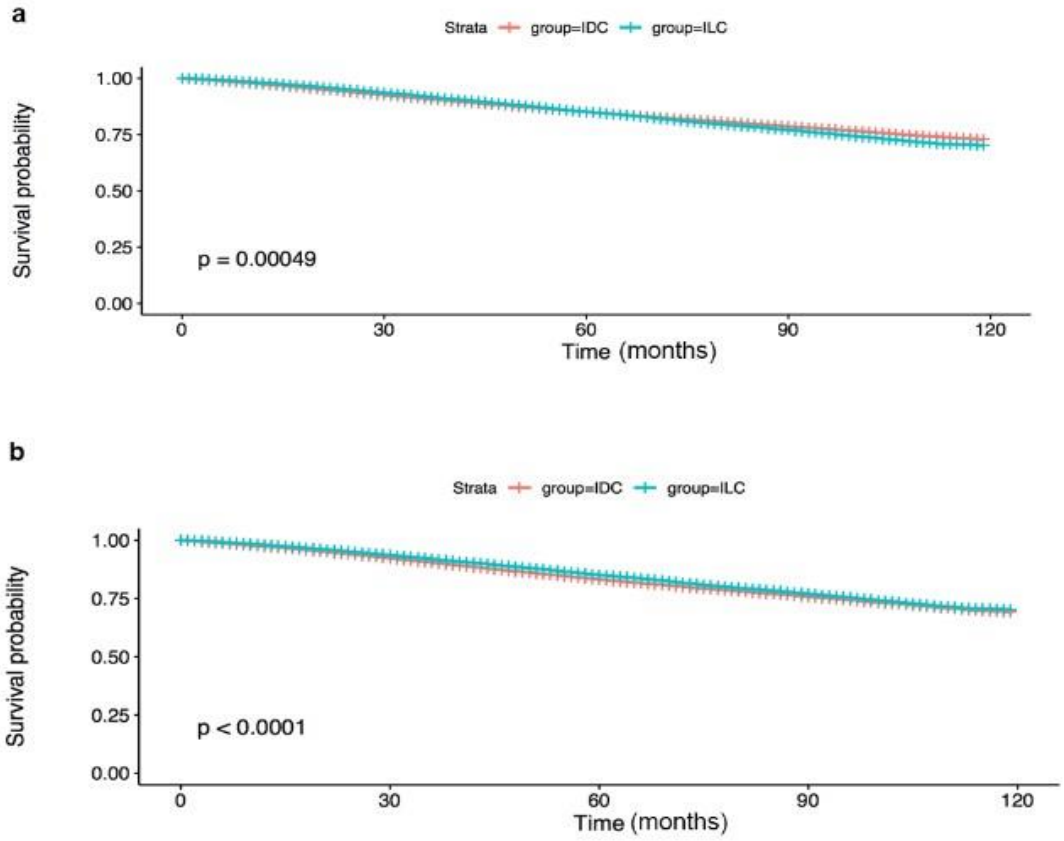


**Figure 1**. **Overall survival curves of all unmatched IDC and ILC patients** (A). Overall survival curves of all matched IDC and ILC patients (B).

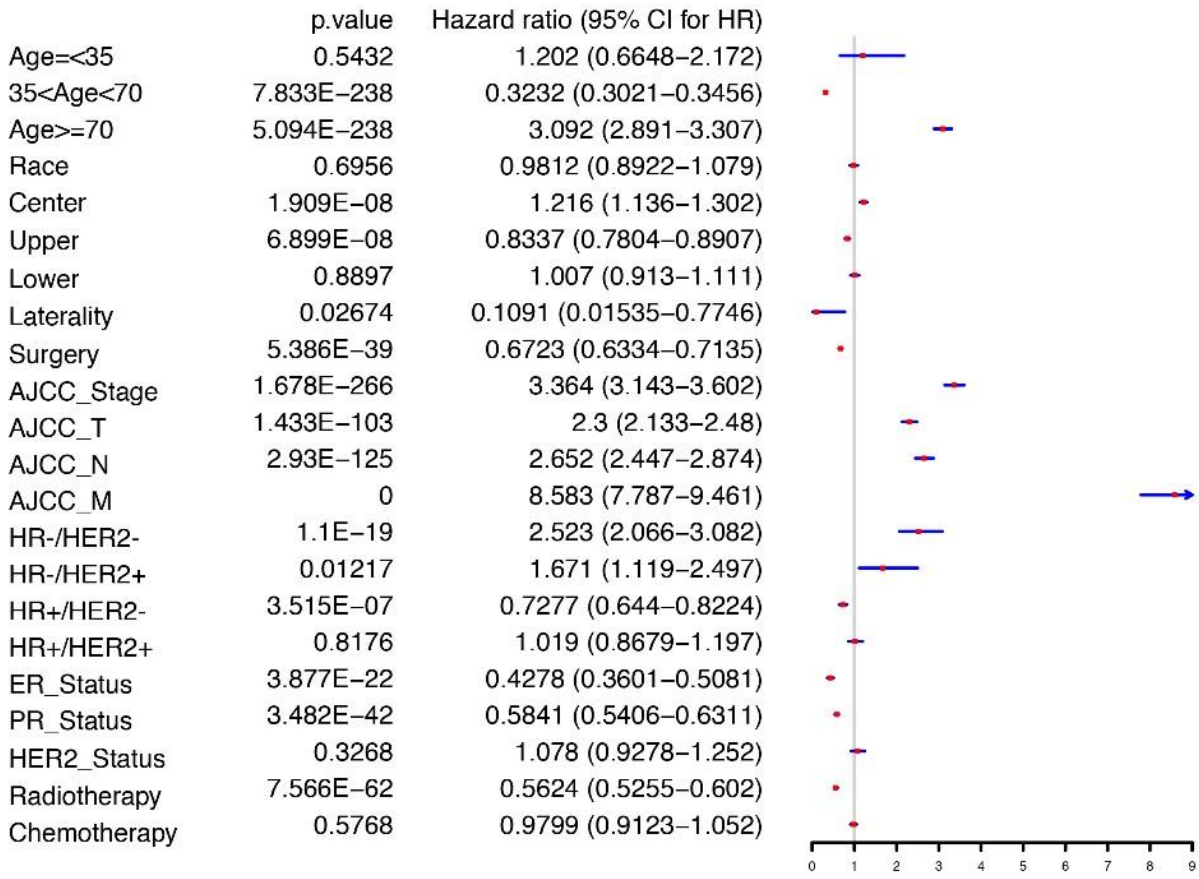


**Figure 2. Univariate Cox analysis for Overall survival of ILC patients.**

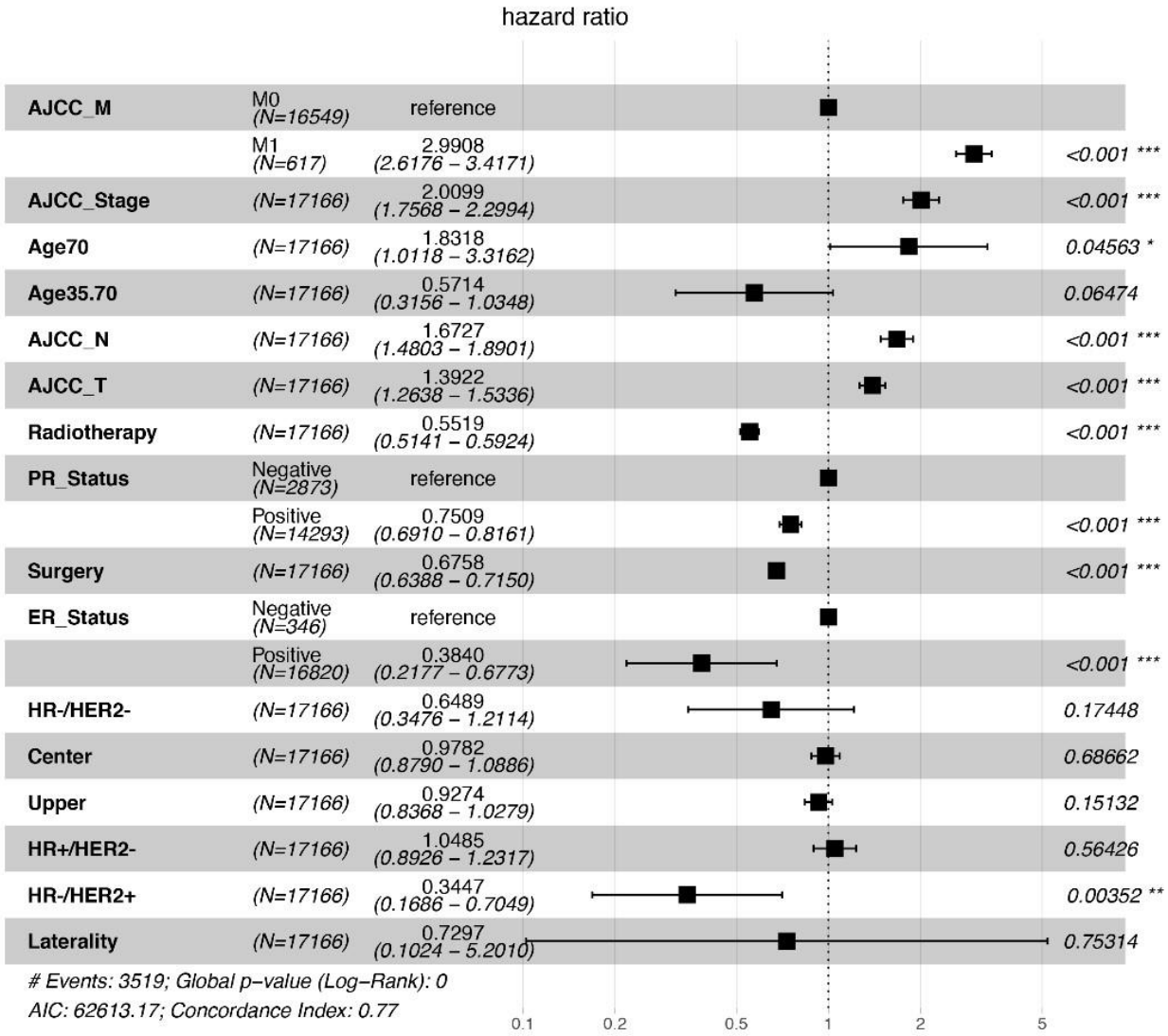


**Figure 3. Forest plot of overall survival for ILC patients.**

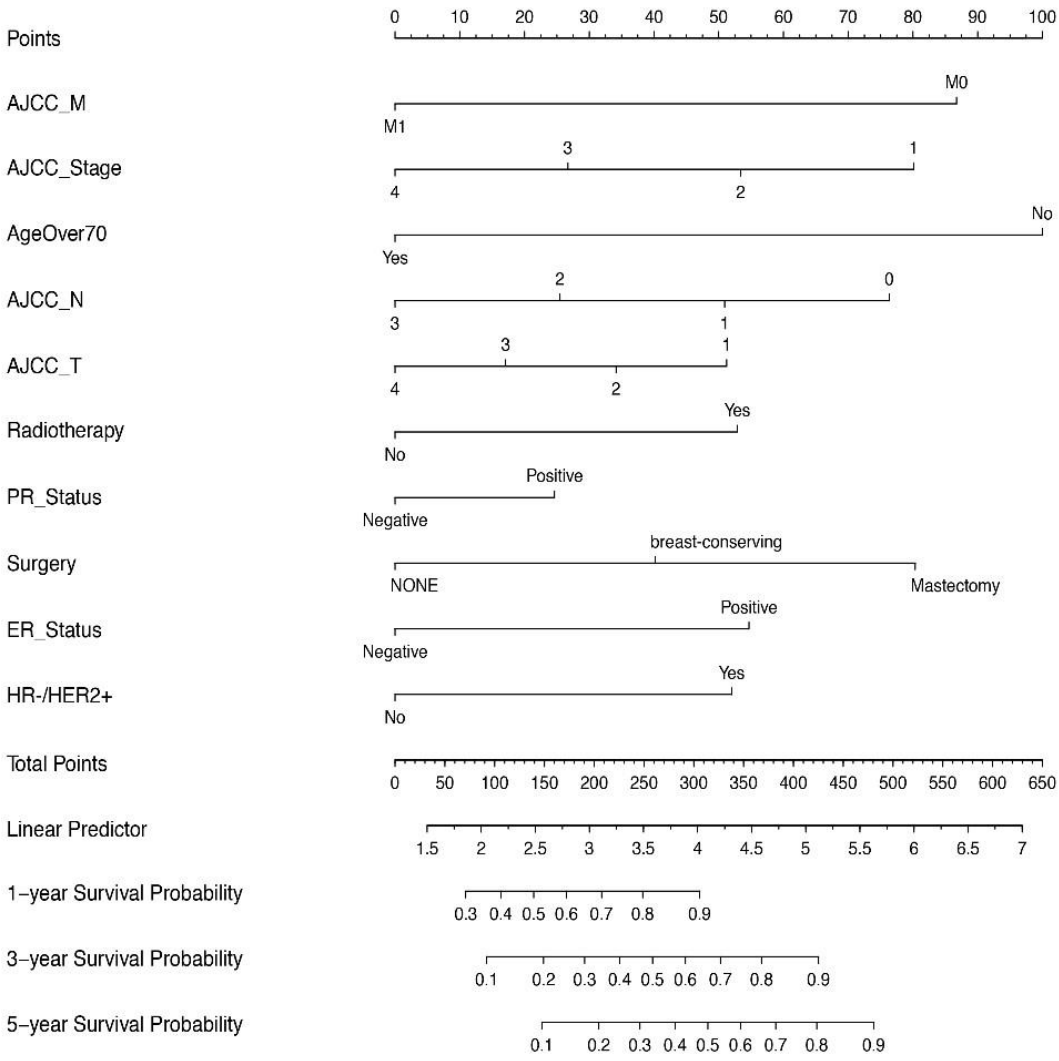


**Figure 4. Nomogram to predict 1-, 3-, and 5-year OS of ILC patients**. Notes: Vertical line between each variable and points scale can be drawn to acquire points of each variable. Predicted survival rate was calculated according to the total points by drawing a vertical line from Total Points scale to overall survival scale.

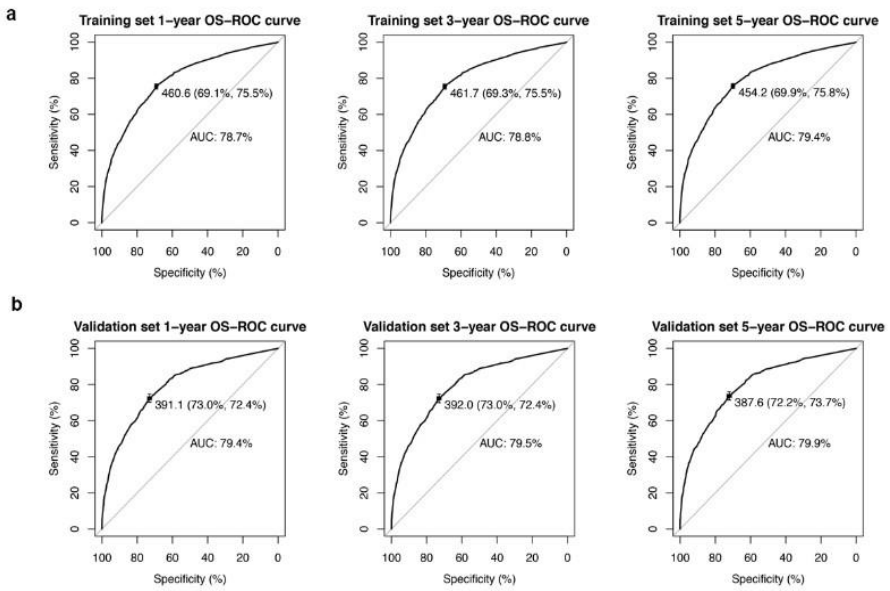


**Figure 5. The receiver operating characteristics (ROC) curve and area under the ROC curve (AUC).** Predicting 1-, 3-, and 5-year OS in the training cohort (a). Predicting 1-, 3-, and 5-year OS in the validation cohort (b).

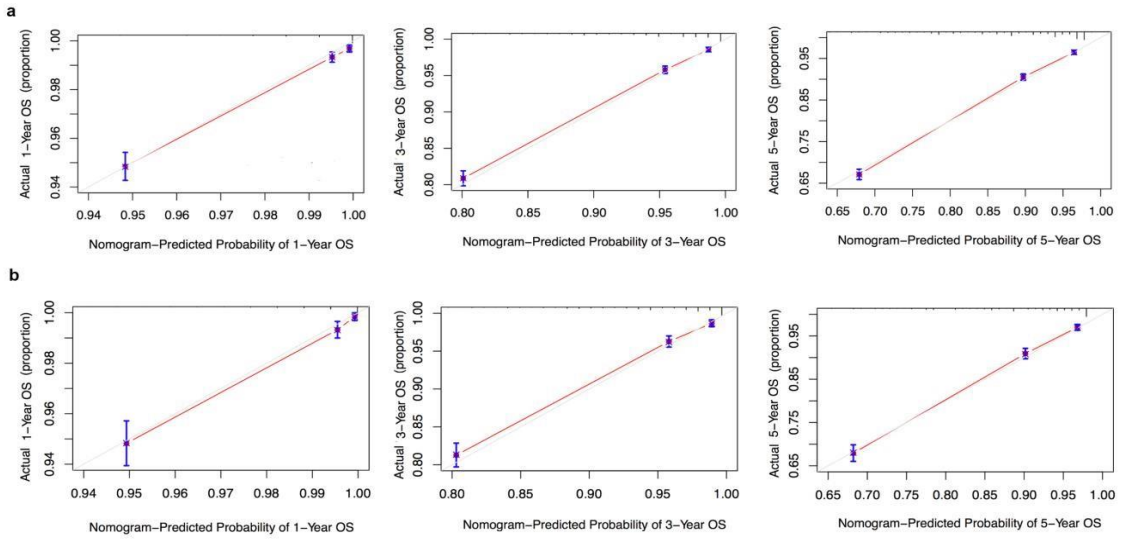


**Figure 6. The calibration curves to predict 1-, 3-, and 5-year OS in the training set (a) and the internal validation set (b).**

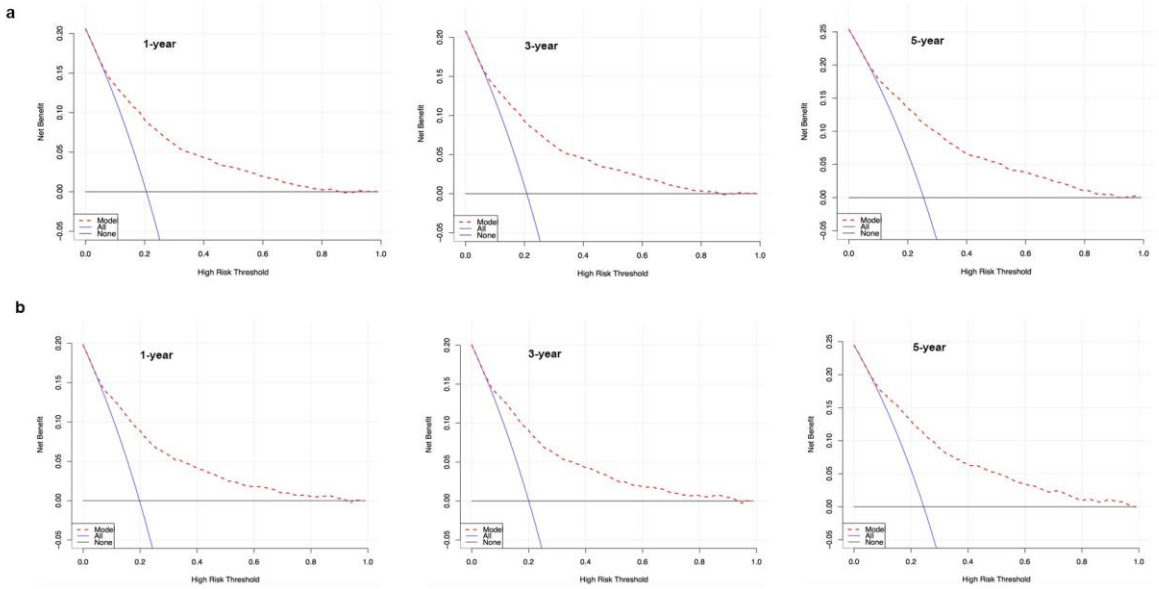


**Figure 7. DCA curves of the nomogram for predicting 3- and 5-year OS in the training set (a) and the internal validation set (b).**