Factors Associated with Early and Late Mortality in Invasive Lobular Carcinoma

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Introduction

Invasive lobular carcinoma (ILC) is the second most common histological type of breast cancer after invasive ductal carcinoma (IDC). ILC accounts for 10-15% of all breast cancer cases. Prior studies have suggested different patterns of short-term (<5 years) and long-term (>5 years) mortality between ILC and IDC. Extended ET is currently used to improve long-term OS. We aimed to identify the factors associated with early and late mortality in patients with ILC.

Methods and Materials

We conducted a retrospective analysis using the National Cancer Database (NCDB) from 2006-2020. Inclusion criteria were female gender, age ≥ 18 years, lobular histology, breast cancer stage I-III and removal of breast cancer tumor and axillary lymph nodes. Our primary endpoint was overall survival (OS). The short-term OS analysis evaluated survival from diagnosis until 5 years from diagnosis. The long-term OS analysis evaluated those patients who were alive after 5 years from diagnosis. Cox hazard regression models were used to identify factors associated with short-term OS and long-term OS

Results

The analysis of short-term OS included 115,159 patients, most of them were Non-Hispanic White (81%) with a median age of 63 years. Most tumors were T1 (57%), N0 (71%), Hormone Receptor positive (ER+ 100%, PR+ 87%), HER2 negative (81%). The 5-year OS rate was 93%. Old age, large tumor size, axillary node involvement, high grade, and LVI, were associated with worse short-term OS; whereas mastectomy, chemotherapy, radiation, PR positivity, and endocrine therapy were associated with improved short-term OS.

Table 1. Baseline characteristics

	Short Term (n= 115,159)	Long Term (n= 67,927)
Median Age (IQR)	63 (54-71)	62 (53-70)
Age Group		
<50 years old	16,539 (14%)	10,635 (16%)
50-70 years old	67,338 (58%)	40,647 (60%)
>70 years old	31,282 (27%)	16,645 (25%)
Race/Ethnicity		
NHWhite	92,965 (81%)	55,377 (82%)
NHBlack	9,392 (9%)	5,198 (8%)
Hispanic	5,366 (5%)	2,764 (4%)
NHOther	7,436 (6%)	4,588 (7%)
Cancer Stage		
I	68,794 (60%)	34,212 (50%)
II	33,989 (30%)	25,466 (37%)
III	12,376 (11%)	8,249 (12%)
Grade		
Well differentiated	31,805 (28%)	19,981 (29%)
Moderately differentiated	75,643 (66%)	43,399 (64%)
Poorly differentiated	7,711 (7%)	4,547 (7%)
LVI		
No	77,022 (67%)	41,005 (60%)
Yes	8,888 (8%)	4,543 (7%)
Unknown	29,249 (25%)	22,379 (33%)
ER		
Negative	144 (0%)	90 (0%)
Positive	114,955 (100%)	67,828 (100%)
Unknown	20 (0%)	9 (0%)
PR		
Negative	14,806 (13%)	8,466 (12%)
Positive	100,050 (87%)	59,258 (87%)
Unknown	303 (0%)	203 (0%)
HER2		
Negative	92,989 (81%)	49,340 (73%)
Positive	1,939 (2%)	1,166 (2%)
Unknown	20,231 (18%)	17,421 (26%)
Oncotype DX (n = 38,000)		
Low	7,709 (20%)	3,688 (20%)
Intermediate	27,557 (73%)	13,366 (73%)
High	2,734 (7%)	1,285 (7%)
Radiation		
No	42,374 (37%)	24,976 (37%)
Yes	72,785 (63%)	42,951 (63%)
Chemotherapy		
No	86,245 (75%)	47,662 (70%)
Yes	28,914 (25%)	20,265 (30%)
Endocrine Therapy		
No	11,458 (10%)	6,527 (10%)
Yes	103,701 (90%)	61,440 (90%)
Surgery Type		
BCS	62,656 (54%)	35,856 (53%)
Mastectomy	52,503 (46%)	32,071 (47%)

Figure 1. Short-term OS in ILC by Oncotype DX

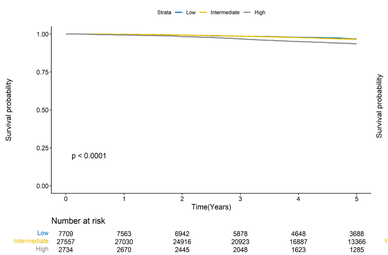


Figure 3. Long-Term OS in ILC by Oncotype DX

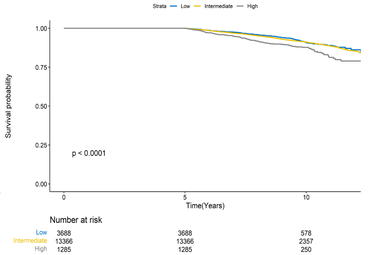


Figure 2. Short-term OS in ILC by T and N stage

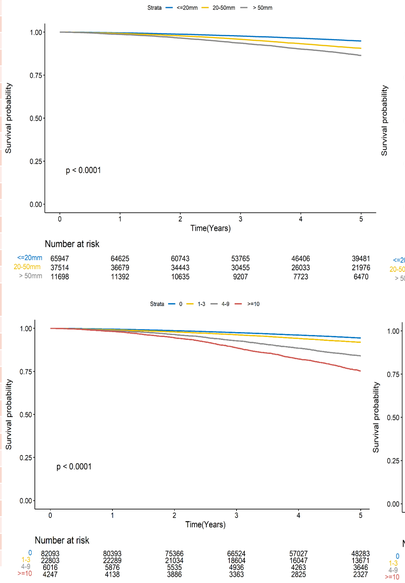


Figure 4. Long-Term OS in ILC by T and N stage

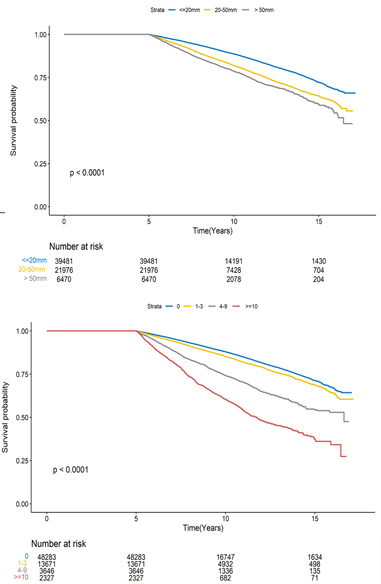


Table 2. Multivariate Analysis for Short- and Long-Term Mortality

Subgroup	Multivariate Short-Term			Multivariate Long-Term		
Overall	HR	95% CI	p	HR	95% CI	p
Age						
50-70	Reference			Reference		
<50	0.58	0.51-0.65	<0.001	0.6	0.55-0.66	<0.001
>70	2.16	2.04-2.29	<0.001	2.84	2.69-2.99	<0.001
Race						
NHWhite	Reference			Reference		
NHBlack	1.10	1.01-1.19	0.03	0.10	0.92-1.08	0.93
Hispanic	0.73	0.63-0.84	<0.001	0.77	0.68-0.87	<0.001
NHOther	1.01	0.91-1.11	0.86	0.92	0.85-1.00	0.06
T Stage						
IS/T1	Reference			Reference		
T2	1.48	1.39-1.56	<0.001	1.35	1.28-1.41	<0.001
T3	1.97	1.82-2.14	<0.001	1.58	1.47-1.71	<0.001
N Stage						
N0	Reference			Reference		
N1	1.64	1.53-1.75	<0.001	1.39	1.31-1.47	<0.001
N2	3.47	3.17-3.80	<0.001	2.54	2.33-2.76	<0.001
N3	5.15	4.70-5.65	<0.001	4.38	4.00-4.80	<0.001
Grade						
Well Diff	Reference			Reference		
Mod Diff	1.09	1.03-1.16	<0.01	1.11	1.05-1.16	0.002
Poorly Diff	1.56	1.43-1.70	<0.001	1.37	1.27-1.48	<0.001
ER						
Negative	Reference			Reference		
Positive	0.74	0.45-1.23	0.25	0.91	0.58-1.45	0.71
Unknown	0.66	0.09-5.04	0.69	3.11	1.05-9.20	0.04
PR						
Negative	Reference			Reference		
Positive	0.75	0.71-0.80	<0.001	0.87	0.83-0.92	<0.001
Unknown	1.01	0.72-1.43	0.94	1.12	0.84-1.48	0.44
HER2						
Negative	Reference			Reference		
Positive	1.17	1.00-36	0.05	1.01	0.86-1.19	0.87
Unknown	0.96	0.89-1.04	0.36	0.89	0.82-0.95	<0.01
Radiation						
No	Reference			Reference		
Yes	0.60	0.57-0.64	<0.001	0.84	0.80-0.90	<0.001
Chemotherapy						
No	Reference			Reference		
Yes	0.77	0.72-0.82	<0.001	0.81	0.77-0.86	<0.001
ET						
No	Reference			Reference		
Yes	0.50	0.46-0.53	<0.001	0.78	0.73-0.83	<0.001
Surgery Type						
BCS	Reference			Reference		
Mastectomy	0.84	0.79-0.89	<0.001	0.94	0.88-0.99	0.04
Oncotype Risk						
Low	Reference			Reference		
Intermediate	1.06	0.90-1.25	0.46	1.17	0.98-1.38	0.08
High	1.68	1.30-2.16	<0.001	1.80	1.37-2.36	<0.001

Abbreviations: CTS5, Clinical Treatment Score Post-5 Years.; NH, non-Hispanic; diff, differentiated; BCS, breast conserving surgery; ET, endocrine therapy; HER2, human epidermoid receptor factor.

Results

Among patients who had Oncotype DX testing (N= 3,800), those with high recurrence score had worse short-term OS when compared to those with low scores but similar for those with intermediate score. The analysis of long-term OS included 67,927 patients. The 10-year OS rate was 86%.

Older age, large tumor size, axillary nodal involvement, high tumor grade, and LVI were associated with worse long-term OS; whereas mastectomy, chemotherapy, radiation, PR positivity and ET were associated with improved long-term OS.

Among patients who had Oncotype DX testing (N= 18,339), those with high Oncotype DX recurrence score had worse long-term OS compared to those with low recurrence score; whereas the long-term OS was similar for those with intermediate recurrence score.

Conclusions

Age, tumor size and lymph nodal status are the strongest predictors of early and late OS in ILC. The effects of adjuvant radiation and ET are larger on late OS than in early OS, whereas adjuvant chemotherapy has a similar effect in early and late OS.

High Oncotype DX score can identify patients who are at high for worse late OS, however, it may underestimate long-term risk for patients with low or intermediate scores.

Tools that incorporate clinico-pathological features and molecular profiling are required to identify patients with worse long-term OS who may be candidates for extended ET

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