Prognostic effect of Clinical Treatment Score Post-5 years (CTS5) in patients with Invasive Lobular Carcinoma and its relationship with Oncotype DX

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Introduction

While patients with early-stage invasive lobular carcinoma (ILC) of the breast often present better survival rates initially, the risk of recurrence and mortality increases later in the disease course.

CTS5 is a validated tool used to estimate the risk of late distant recurrence in patients with HR positive breast cancer after 5 years of adjuvant treatment; however, its application in patients with ILC has not been fully analyzed.

We aimed to assess whether CTS5 can predict long-term OS for patients with ILC, and to evaluate its prognostic effect beyond Oncotype DX recurrence score.

Methods and Materials

We conducted a retrospective analysis using the NCDB from 2006-2020. Inclusion criteria were female gender, ≥18 years of age, diagnosis of ILC, stage I-III, removal of breast tumor and axillary LN, and alive status at least 5 years after diagnosis. Patients were classified into CTS5 low, intermediate and high-risk categories. Our primary endpoint, long-term OS, included survival analysis after 5 years from diagnosis. We used the Pearson X^2 test to evaluate the relationship between categorical variables and the t test for continuous variables

Results

Our study included 67,927 patients with a median age of 63 years. Most of them were NHWhite. Most tumors were stage I , hormone positive, and low grade. While most patients received ET (90%), the use of adjuvant chemotherapy was infrequent (10%).

Patients were divided into 3 groups based on their CTS5 risk: low (n = 32,625), intermediate (n = 21,007) and high (n = 14,295).

Table 1. Baseline characteristics for the long-term cohort

		CTS5			
	Total (n= 67,927)	**Low** (n = 32,625)	**Intermediate** (n = 21,007)	**High** (n = 14,295)	p value
Age Group					<0.001
<50 years old	10,635 (16%)	5,684 (17%)	2,881 (14%)	2,070 (14%)	
50-70 years old	40,647 (60%)	20,602 (63%)	12,031 (57%)	8,014 (56%)	
>70 years old	16,645 (25%)	6,339 (19%)	6,095 (29%)	4,211 (29%)	
Race/Ethnicity					<0.001
NHWhite	55,377 (82%)	26,697 (82%)	17,103 (81%)	11,577 (81%)	
NHBlack	5,198 (8%)	2,425 (7%)	1,582 (8%)	1,191 (8%)	
Hispanic	2,764 (4%)	1,209 (4%)	909 (4%)	646 (5%)	
NHOther	4,588 (7%)	2,294 (7%	1,413 (7%)	881 (6%)	
Cancer Stage					<0.001
I	34,212 (50%)	29,077 (89%)	5,022 (24%)	113 (1%)	
II	25,466 (37%)	3,528 (11%)	15,322 (73%)	6,616 (46%)	
III	8,249 (12%)	20 (0%)	663 (3%)	7,566 (53%)	
Grade					<0.001
Well diff	19,981 (29%)	13,693 (42%)	4,259 (20%)	2,029 (14%)	
Mod diff	43,399 (64%)	18,258 (56%)	15,183 (72%)	9.958 (70%)	
Poorly diff	4,547 (7%)	674 (2%)	1,565 (7%)	2,308 (16%)	
Radiation					<0.001
No	24,976 (37%)	11,907 (36%)	9,272 (44%)	3,797 (27%)	
Yes	42,951 (63%)	20,718 (64%)	11,735 (56%)	10,498 (73%)	
Chemotherapy					<0.001
No	47,662 (70%)	28,571 (88%)	14,386 (68%)	4,705 (33%)	
Yes	20,265 (30%)	4,054 (12%)	6,621 (32%)	9,590 (67%)	
ET					<0.001
No	6,527 (10%)	3,910 (12%)	1,615 (8%)	1,002 (7%)	
Yes	61,400 (90%)	28,715 (88%)	19,392 (92%)	13,293 (93%)	
Surgery Type					<0.001
BCS	35,856 (53%)	22,284 (68%)	10,072 (48%)	3,500 (24%)	
Mastectomy	32,071 (47%)	10,341 (32%)	10,935 (52%)	10,795 (76%)	
Oncotype	**(n=17,882)**				<0.001
Low	3,622 (20%)	1,843 (20%)	1,398 (21%)	381 (22%)	
Intermediate	13,050 (73%)	6,942 (74%)	4,874 (72%)	1,234 (70%)	
High	1,210 (7%)	572 (6%)	500 (7%)	138 (8%)	

Figure 1 Long-Term OS by CTS5 and Oncotype DX

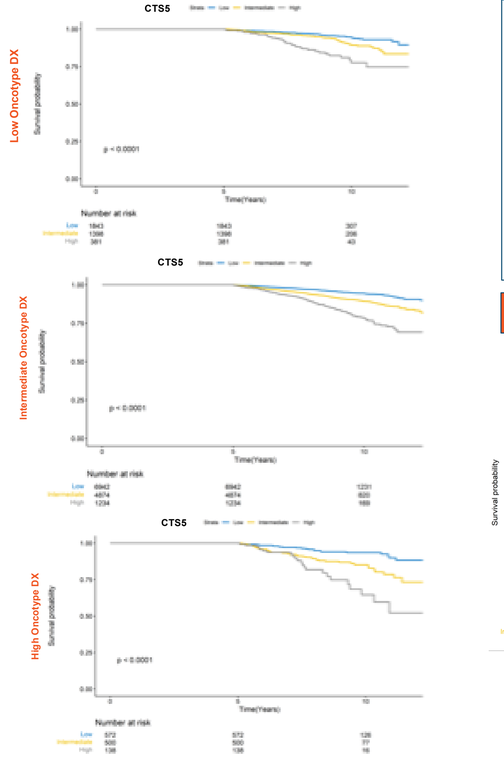


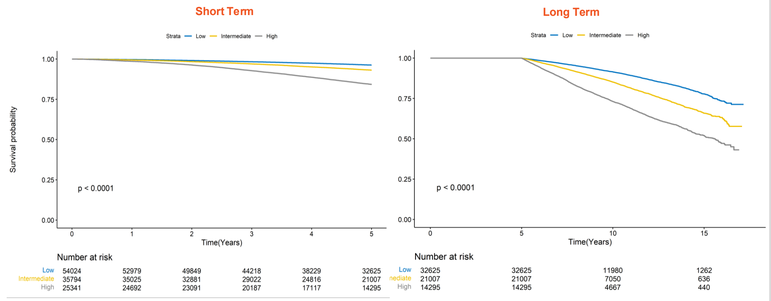
Table 2. Correlation between CTS5 and OncotypeDX

CTS5	Oncotype					
	Low		Medium		High	
	HR	p	HR	p	HR	p
Low	Reference		Reference		Reference	
Intermediate	1.74	<0.01	2.05	<0.001	2.48	<0.01
High	4.60	<0.001	4.33	<0.001	3.99	<0.001

Results

15-year OS differed significantly among these groups with rates of 78%, 66% and 52%, respectively (figure). Advanced stage, poorly differentiated tumors, and high OncotypeDx were more frequent in the high CTS5 group as compared to the low CTS5 group. In a multivariate model, CTS5 remained an independent predictor of long-term mortality (HR 3.63, 95% CI 3.42-3.86; p <0.001). Next, we analyzed 17,882 patients with available Oncotype DX results. CTS5 risk groups were distributed across all OncotypeDX risk groups. Patients with high CTS5 had higher risk of mortality when compared to those with low CTS5 in patients with low, intermediate, and high Oncotype Dx.

Figure 2 Kaplan Meier Curve for OS in ILC divided by CTS5



Conclusions

CTS5 is an independent predictor of long-term OS in patients with ILC and it can identify patients with substantially higher risk of late death beyond 5 years.

CTS5 provides prognostic information that is complementary to OncotypeDX in ILC. Combining CTS5 and OncotypeDx can help to select patients with high risk of late mortality who may benefit from extending ET or intensified surveillance.

Abbreviations: CTS5, Clinical Treatment Score Post-5 Years.; NH, non-Hispanic; diff, differentiated; BCS, breast conserving surgery.

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