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PO4-02-12: MDA iLobular Prognostic Tool: A Novel Approach for Risk Stratification in Invasive Lobular Carcinoma

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Background:

- Risk stratification is essential in breast cancer for tailoring treatment plans to the individual patient's needs, maximizing the chances of successful outcomes and minimizing unnecessary interventions.
- Retrospective analysis of existing risk stratification tools for early-stage breast cancer revealed their limited efficacy when applied to patients with ILC
- **Gap in the field**: There is currently not a risk stratification tool that is specific for ILC

Methods:

- Retrospective review of MD Anderson Cancer Center breast cancer database for patients with stage I-III ILC
- The study focused on two primary endpoints: Overall Survival (OS) and Distant Recurrence Free Survival (DRFS).
- We utilized univariate and multivariate Cox Proportional Hazard (PH) regression models to assess the statistical significance of all variables.
- The univariate Cox analysis identified prognostic factors, which were further analyzed using backward and stepwise multivariate Cox proportional hazards regression analysis.
- To evaluate the performance of the fitted multivariate Cox PH regression models for OS and DRFS, we randomly divided two-thirds of the data points (n=2,950) into a training dataset (n=1,266), while the remaining one-third constituted the test dataset.
- We assessed the discrimination capacity of each model using Harrell's C-index

Results:

- We identified 4,216 patients with stage I-III ILC treated at MDACC between 1966 and 2021.
- The median pathological tumor size was 2 cm, and the median number of lymph nodes was one.
- After evaluating various prognostic models, we identified the model with the highest prognostic accuracy for OS and DRFS.
- This selected model demonstrated a Harrell's C-index of 0.704 for OS and 0.718 for DRFS on the training dataset and a Harrell's C-index of 0.702 for OS and 0.671 for DRFS on the test dataset.
- The model incorporated several covariates, including age at the time of diagnosis, number of lymph nodes, pathological tumor size, ER status, tumor grade, ILC histology, and the presence or absence of concomitant LCIS.

The MDA iLobular PT is the first clinic-pathological risk stratification tool that has been developed specifically for ILC patients

Future Direction: Combine the MDA iLobular PT with genomic, molecular and tumor microenvironment factors to create a state-of-the-art prognosticator and treatment predictor for early stage ILC

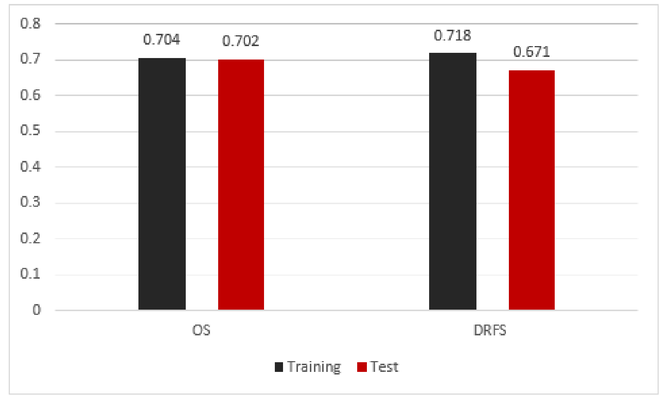

Figure 1. Harrell's C-index for OS and DRFS

	Overall Survival			Distant Recurrence-free Survival		
Parameter	**Hazard Ratio**	**HR 95% Confidence Limits**	**p-value**	**Hazard Ratio**	**HR 95% Confidence Limits**	**p-value**
Age (year)	1.022	(1.013, 1.031)	<0.001	1.007	(0.999, 1.016)	0.075
Number of lymph nodes	1.068	(1.056, 1.080)	<0.001	1.078	(1.068, 1.089)	<0.001
Pathological tumor size	1.048	(1.013, 1.085)	0.008	1.061	(1.031, 1.092)	<0.001
ER status						
<10%	--------			-----		
≥10%	0.548	(0.354, 0.849)	0.007	0.620	(0.412, 0.933)	0.022
Grade						
G1	-----			-----		
G2	1.130	(0.862, 1.482)	0.38	1.067	(0.837, 1.361)	0.60
G3	1.386	(1.017, 1.890)	0.039	1.476	(1.115, 1.953)	0.007
ILC histology						
Non-classical	-----			-----		
Classical	0.632	(0.474, 0.842)	0.002	0.622	(0.480, 0.806)	<0.001
Concomitant LCIS						
Absent	-----			-----		
Present	0.737	(0.608, 0.894)	0.002	0.674	(0.567, 0.801)	<0.001

Table 1. Multivariate Cox proportional hazard model parameter estimates for OS and DRFS

Reference

1. Abel, M.K., Shui, A.M., Melisko, M. et al. The incidence of discordant clinical and genomic risk in patients with invasive lobular or ductal carcinoma of the breast: a National Cancer Database Study. npj Breast Cancer 7, 156 (2021).
2. Abel MK, Shui AM, Chien AJ, Rugo HS, Melisko M, Baehner F, Mukhtar RA. The 21-Gene Recurrence Score in Clinically High-Risk Lobular and Ductal Breast Cancer: A National Cancer Database Study. Ann Surg Oncol. 2022 Nov;29(12):7739-7747