Impact of allostatic load on breast cancer risk prediction among racially / ethnically diverse women

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Introduction

- Current validated risk calculators for invasive breast cancer (IBC) underestimate risk among Black and Hispanic women[1]
- Many risk prediction models—such as the Breast Cancer Surveillance Consortium (BCSC) Risk Calculator—rely on risk factors not readily available or under-reported in electronic health record (EHR), such as family history
- Allostatic load (AL) is a measure of accumulated physiologic stress across major regulatory systems, including standard laboratory results and vital signs[2]
  - Associated with: ↑ risk of IBC[3], ↑ mortality in patients with IBC[4], ↑ odds of poorly differentiated tumor[5]
- **Hypothesis:** Routinely-collected laboratory & vitals data can improve IBC risk prediction among racially / ethnically diverse women

Methods and Materials

- **Study design:** Retrospective analysis of EHR data
- **Population:** Women undergoing screening mammogram at CUIMC (11/1/14-4/7/25), excluded those with ductal carcinoma *in situ* (DCIS) or missing mammographic density (MD)
- **Outcome:** "IBC" vs "No IBC" defined by breast pathology report with diagnosis of IBC *after* index mammogram
- **Predictors:** Age at index mammogram, race / ethnicity, MD (BIRADS classification), prior breast biopsy, first-degree family history of breast cancer (FHx)
  - Albumin (alb), alkaline phosphatase (AP), glucose (glc), blood urea nitrogen (BUN), creatinine (Cr), white blood cell count (WBC), heart rate (HR), systolic (SBP) & diastolic blood pressure (DBP), body mass index (BMI)
  - Imputed with multiple imputation by chained equations
  - Composite AL score = # of abnormal values out of ten
- **Analysis:** Models evaluated with area under the curve (AUC) and DeLong's test

Key Findings

1. Routinely-collected lab & vital data may improve IBC risk prediction—particularly for Hispanic & Black women
2. Composite AL score does not improve IBC risk prediction

Figure 1. Cohort Selection Diagram

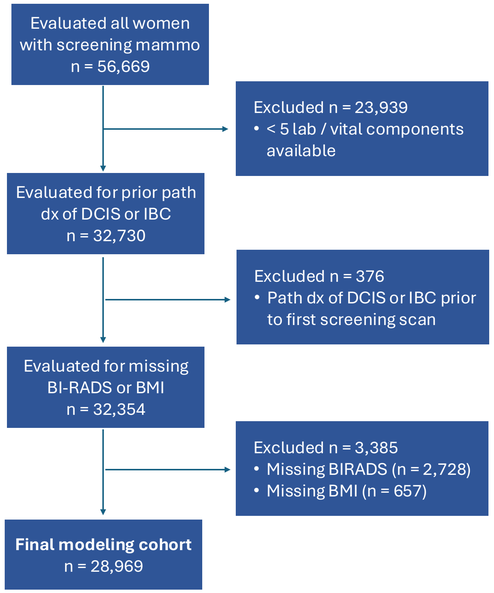


Table 1. Cohort Characteristics

Characteristic	No IBC N = 28,702	IBC N = 267	Overall N = 28,969	p-value
Mean Age, years (SD)	59 (12)	65 (12)	59 (12)	<0.001
Race / ethnicity, n (%)				0.014
Hispanic	11,278 (39%)	98 (37%)	11,376 (39%)	
Non-Hispanic White	8,466 (29%)	103 (39%)	8,569 (30%)	
Non-Hispanic Black	4,164 (15%)	39 (15%)	4,203 (15%)	
Other or Multiracial	3,831 (13%)	22 (8.2%)	3,853 (13%)	
Non-Hispanic Asian	921 (3.2%)	5 (1.9%)	926 (3.2%)	
BI-RADS MD, n (%)				0.013
A	1,037 (3.6%)	4 (1.5%)	1,041 (3.6%)	
B	12,601 (44%)	115 (43%)	12,716 (44%)	
C	14,068 (49%)	146 (55%)	14,214 (49%)	
D	996 (3.5%)	2 (0.7%)	998 (3.4%)	
Mean BMI, kg/m^2 (SD)	28 (6)	29 (6)	28 (6)	0.200
1st degree FHx, n (%)	222 (0.8%)	4 (1.5%)	226 (0.8%)	0.500
Prior breast biopsy, n (%)				0.003
NP	493 (1.7%)	4 (1.5%)	497 (1.7%)	
PDWA	350 (1.2%)	2 (0.7%)	352 (1.2%)	
AH	93 (0.3%)	2 (0.7%)	95 (0.3%)	
LCIS	58 (0.2%)	0 (0%)	58 (0.2%)	

NP=non-proliferative, PDWA=Proliferative disease without atypia, AH=atypical hyperplasia, LCIS=lobular carcinoma in situ

Results

- Pathology dx extraction algorithm agreed with manual review in 97% of 250 reviewed reports
  - For IBC, sensitivity & specificity were ~99%
- 1% of 28,969 patients had IBC after index scan (**Table 1**)
- Lab & vitals data improved risk prediction primarily for Hispanic & Black women (**Table 2**)

Table 2. Model Performance

Patient group	Model	AUC (95% CI)	p-value[1]
Full cohort	Baseline (age + MD + race / eth + FHx + prior path) = BCSCv2	0.667 (0.635, 0.700)	--
	Baseline + composite AL score	0.672 (0.640, 0.704)	0.326
	Baseline + BMI + alb + AP + glc + BUN + Cr + WBC + HR + SBP + DBP	0.679 (0.646, 0.711)	**0.049**
	Age + MD + race / eth + BMI + alb + AP + glc + BUN + Cr + WBC + HR + SBP + DBP	0.670 (0.638, 0.703)	0.680
Hispanic	Baseline (age + MD + race / eth + FHx + prior path) = BCSCv2	0.655 (0.600, 0.709)	--
	Baseline + composite AL score	0.662 (0.606, 0.718)	0.496
	Baseline + BMI + alb + AP + glc + BUN + Cr + WBC + HR + SBP + DBP	0.686 (0.631, 0.742)	**0.011**
	Age + MD + race / eth + BMI + alb + AP + glc + BUN + Cr + WBC + HR + SBP + DBP	0.681 (0.626, 0.736)	0.067
Non-Hispanic White	Baseline (age + MD + race / eth + FHx + prior path) = BCSCv2	0.663 (0.613, 0.712)	--
	Baseline + composite AL score	0.665 (0.615, 0.714)	0.797
	Baseline + BMI + alb + AP + glc + BUN + Cr + WBC + HR + SBP + DBP	0.680 (0.631, 0.729)	0.196
	Age + MD + race / eth + BMI + alb + AP + glc + BUN + Cr + WBC + HR + SBP + DBP	0.666 (0.616, 0.715)	0.840
Non-Hispanic Black	Baseline (age + MD + race / eth + FHx + prior path) = BCSCv2	0.655 (0.574, 0.737)	--
	Baseline + composite AL score	0.681 (0.592, 0.771)	0.254
	Baseline + BMI + alb + AP + glc + BUN + Cr + WBC + HR + SBP + DBP	0.697 (0.612, 0.782)	**0.042**
	Age + MD + race / eth + BMI + alb + AP + glc + BUN + Cr + WBC + HR + SBP + DBP	0.677 (0.590, 0.765)	0.348

AUC = area under receiver operating characteristic curve; [1]DeLong's test

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