Evaluating Clinical and Molecular Correlates of Inflammatory Breast Cancer Using a Scoring System-Based Chart Review from the Dallas Metastatic Cancer Study

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Chloe Atallah[1,2], A Varner[1,2], C Kang[1,2,3], L Conklin[1,2], P Gowda[1,2], K Anderson[1,2], D Tovar[1,2], R Morey[1,2], E Oyefeso[1,2], C Hauer[2,3], R Sridharan[2,3], S Huang[1,2,3], K Lei[1,2,3], S M Reddy[2,3], H L McArthur[2,3], J Maues[4], C Hodgdon[4], B Zhang[5], M Dang[6,7], V Merrill[6,7], X Zhang[8], B Lim[9], I S Chan[1,2,3,6]

1. University of Texas Southwestern Medical School, Dallas, TX, USA; 2. Department of Internal Medicine, Division of Hematology and Oncology, University of Texas Southwestern Medical Center, Dallas, TX, USA; 3. Harold C. Simmons Comprehensive Cancer Center, University of Texas Southwestern Medical Center, Dallas, TX, USA; 4. GRASP Cancer, Baltimore, MD, USA; 5. Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, TX, USA; 6. Division of General Internal Medicine, Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, Texas; 7. Biostatistics, Epidemiology, and Research Design (BERD), UT Southwestern Medical Center, Dallas, TX; 8. Molecular and Cellular Biology, Baylor College of Medicine, Houston, TX, USA; 9. University of Texas MD Anderson Cancer Center, Houston, TX, USA

Introduction

Inflammatory breast cancer (IBC) is a rare and aggressive form of breast cancer characterized by a distinct clinical presentation and poor prognosis. Because of its rare occurrence, diagnostic accuracy remains a significant clinical challenge. Jagsi et al. (2022) proposed a scoring system aimed at improving the accuracy of clinical IBC diagnosis. In this study, we apply that scoring system to 180 patients treated for IBC at UT Southwestern Medical Center to validate its utility. We further analyze trends across the five IBC score groups to identify patterns that distinguish patients with higher versus lower IBC scores against those not clinically diagnosed with IBC. Our goal is to enhance diagnostic accuracy and strengthen clinical and molecular characterization of IBC.

Methods

This study was a retrospective chart review conducted through the Dallas Metastatic Cancer Study (DMCS) at UT Southwestern Medical Center. Electronic medical records were reviewed to identify patients evaluated for IBC between 2000-2025. Charts were reviewed for breast cancer characteristics described in Jagsi et al. (2022) as well as patient demographics, disease progression, and clinical characteristics.

Patients were scored by characteristics of their IBC disease course according to the Jagsi et al. scoring system (Table 1). They were then categorized into five IBC score groups (Table 2). An additional comparison group was composed of 612 patients who were clinically determined not to have IBC. These groups were used to evaluate trends and associations across increasing likelihood categories of IBC.

Statistical Analysis

Descriptive statistics were used to summarize demographic and clinical characteristics. Continuous outcomes were analyzed using linear regression; binary variables with binary logistic regression; ordered categorical variables with proportional ordinal logistic regression; and unordered categorical variables with multinomial logistic regression.

Table 1: Scoring system for classifying IBC patients

Characteristic	Score			Priority Factor
	3	2	1	
Skin changes	Any peau d'orange	Skin edema/thickening over ≥ 1/3 of the breast	Focal skin edema/thickening	×3
Swelling/engorgement of the breast	Clinically apparent enlargement/ new asymmetry in breast size	*Not an option*	Breast edema identified on imaging	×3
Erythema or other skin discoloration	Complete or near complete involvement of the breast	Greater than minimal involvement of the breast	Minimal involvement or ambiguous color change	×2
Nipple abnormalities	New nipple inversion	New nipple flattening/asymmetry	Crusting of the nipple/areola	×2
Lymphatic tumor cell emboli	Dermal lymphatic emboli present	Non-dermal lymphatic emboli present	*Not an option*	×2
Breast imaging	Diffuse involvement of breast parenchyma	*Not an option*	Enlargement of non-axillary nodes	×1

Table 2: Classification of IBC patients based on Total Score

Classification	Definitely IBC	Strong Possibility of IBC	Weak Possibility of IBC	Probably Not IBC	Not Diagnosed as IBC
Total Score	Total score ≥ 42	Total score 25–41	Total score 14–24	Total score < 14	(not scored)

Results

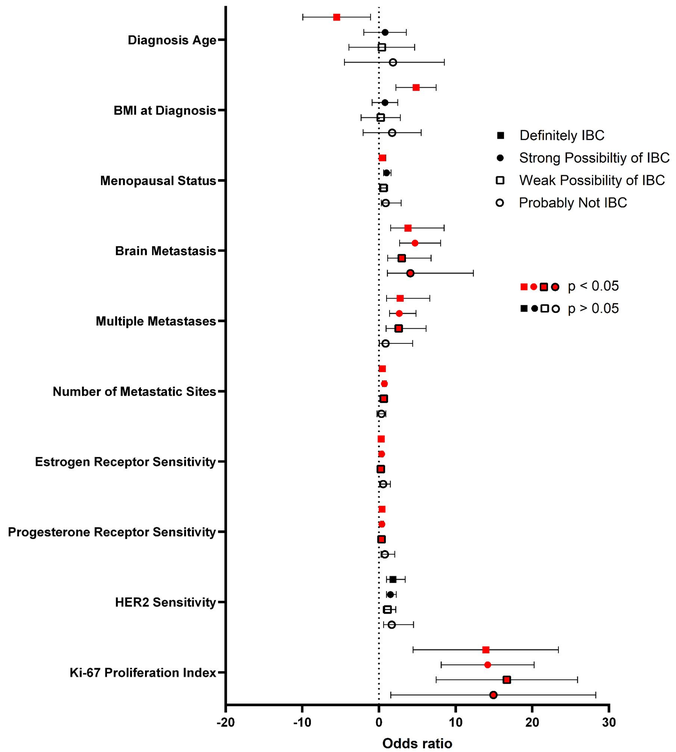


Figure 1: Association between Score-Based IBC Classification and Clinical Characteristics

Forest plot showing adjusted estimates for differences in several clinical characteristics across score-based IBC classification categories relative to reference group (patients diagnosed with non-IBC breast cancer). Points represent model estimates; horizontal bars show 95% confidence intervals. Points denoted in red are statistically significant.

Factors with statistically significant variation in odds ratio were:

- Younger age at diagnosis
- Higher BMI at diagnosis
- Menopausal status at diagnosis
- Higher likelihood of brain metastasis
- High likelihood of multiple metastatic sites
- Higher number of metastatic sites
- Decreased Estrogen Receptor Sensitivity
- Decreased Progesterone Receptor Sensitivity
- Increased HER-2 Receptor Sensitivity
- Higher Ki-67 Proliferation Index

Discussion

- Consistent with known literature, key characteristics were associated with IBC: younger age and higher BMI at diagnosis, higher metastatic rate, more aggressive tumor biology (ER-, PR-, HER2+), and higher KI-67 proliferation index. These findings support that our dataset is consistent with prior studies.
- Several characteristics varied significantly (relative to non-IBC patients) in higher-likelihood IBC groups, but not in lower-likelihood IBC groups. This suggests that the scoring system may successfully distinguish IBC-like from non-IBC-like presentation with greater precision than clinicians, supporting the scoring system's potential as a diagnostic tool for IBC.
- We identified a novel finding of higher brain-metastasis rates across all IBC scored groups compared to non-IBC breast cancer controls, suggesting a potential metastatic tropism of IBC for the brain.

Future Directions

As we expand upon this study, we aim to further validate the IBC scoring system as a diagnostic tool by investigating its specificity and sensitivity. We also aim to perform further statistical analysis of our data to include matching techniques, and to determine which factors within the scoring system are most significant.

Future work will integrate analysis of pathology samples to detect characterize the molecular and histopathologic biomarkers that relate to higher IBC likelihood. Comprehensive tissue analyses will identify distinct histological patterns correlating with higher IBC likelihood to improve diagnostic precision and distinguish IBC from mimics.

Given the increased brain metastases observed across all IBC groups, future studies may investigate the underlying biological mechanisms driving this metastatic tropism, including profiling metastatic lesions and assessing blood–brain barrier interactions.

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