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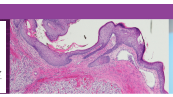

Cleveland Clinic Taussig Cancer Institute | Case Western Reserve University | Case Comprehensive Cancer Center

NCI Designated Comprehensive Cancer Center

BCRF Breast Cancer Research Foundation

Comprehensive comparative analysis of invasive ductal and lobular breast cancer cases in the Great Lakes Breast Cancer Consortium (GLBCS)

HILLMAN FELLOWS For Innovative Cancer Research Program

INSTITUTE FOR PRECISION MEDICINE A partnership of the University of Pittsburgh and UPMC

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Background

Invasive lobular breast cancer (ILC) is the second most common histologic subtype of breast cancer following invasive ductal cancer (IDC). ILC accounts for ~10-15% of all breast cancers (~26-40,000 cases annually in the US) and ranks as the 6th most common cancer in women in the US. While there is increasing recognition that ILC has distinct clinical, histologic, molecular, and biological characteristics compared to IDC, it remains understudied. There are very few large retrospective cohort analyses comparing clinicopathological features of ILC.

Methods

Investigators from UPMC Hillman Cancer Center, James Cancer Hospital/OSU, and Cleveland Clinic Taussig Cancer Institute/CWRU formed the Great Lakes Breast Cancer consortium and worked with their respective cancer registries to collect comprehensive data on patients with IDC and ILC seen at their institutions between 1990 and 2017.

Descriptive statistics were performed to compare clinicopathological features, treatments, metastases sites, and co-morbidities. Survival rates were analyzed using the Kaplan–Meier (KM) method and compared using the log-rank test. Oncotype Dx® data were provided by Genomic Health, Inc. The studies were approved by local IRBs and transferred between institutions after DUA approvals.

Cohort

Invasive Breast Carcinoma 1990-2017 — **44,341 Records (42,801 patients)**

- UPMC HCC/Magee — 17,996 Records (16,993 patients)
- CCF — 16,336 Records (15811 patients)
- OSUCCC — 10,009 Records (9,997 patients)

- 273 records (273 patients) excluded with Tis and Stage 0
- 4,457 records (3,302 patients) with multiple records removed

5,893 records (5,818 patients) excluded with ICD histology codes not consistent with either IDC or ILC

Patients included in GLBC consortium: **N=33,718**

- **UPMC (n = 14,089)** — IDC = 12,746; ILC = 1,343
- **CCF (n = 12,194)** — IDC = 10,687; ILC = 1,507
- **OSUCCC (n = 7,435)** — IDC = 6,667; ILC = 768

Results

Table 1: Demographics, clinicopathological characteristics and treatment by histological subtype

Variable	Total sample, N (%) 33,718	IDC, N (%) 30,100	ILC, N (%) 3,618	p-value
Median Age at diagnosis (years)	57	57	61	<0.001
Race/Ethnicity				0.012
White	29,961 (89%)	26,685 (89%)	3,276 (91%)	
Black	3,025 (9.0%)	2,749 (9.2%)	276 (7.6%)	
Asian	223 (0.7%)	204 (0.7%)	19 (0.5%)	
Other	396 (1.2%)	357 (1.2%)	39 (1.1%)	
Missing	113	105	8	
Menopausal status				<0.001
PreM	4,637 (32%)	4,252 (33%)	385 (27%)	
PostM	9,646 (68%)	8,621 (67%)	1,025 (73%)	
Missing	19,435	17,227	2,208	
Tumor Size				<0.001
T0	942 (3.1%)	929 (3.3%)	13 (0.6%)	
T1	18,657 (62%)	17,550 (63%)	1,107 (49%)	
T2	7,254 (24%)	6,558 (23%)	696 (31%)	
T3	1,083 (3.6%)	776 (2.8%)	307 (14%)	
T4	351 (1.2%)	336 (1.2%)	15 (0.7%)	
TX	1,863 (6.2%)	1,763 (6.3%)	100 (4.5%)	
Missing	3,568	2,188	1,380	
Nodal involvement				<0.001
N0	19,293 (62%)	17,400 (63%)	1,893 (57%)	
N1	7,241 (23%)	6,436 (23%)	805 (24%)	
N2	1,289 (4.1%)	1,116 (4.0%)	173 (5.3%)	
N3	569 (1.8%)	419 (1.5%)	150 (4.6%)	
Nx	2,690 (8.7%)	2,417 (8.7%)	273 (8.3%)	
Missing	2,636	2,312	324	
Stage				<0.001
I	14,801 (54%)	13,395 (54%)	1,406 (46%)	
II	9,647 (35%)	8,638 (35%)	1,009 (33%)	
II	2,478 (9.0%)	1,976 (8.0%)	502 (17%)	
IV	705 (2.6%)	593 (2.4%)	112 (3.7%)	
Missing	6,087	5,498	589	

Table 1: Continued

Grade				<0.001
G1	4,685 (17%)	4,054 (16%)	631 (24%)	
G2	12,670 (46%)	11,014 (44%)	1,656 (64%)	
G3	10,460 (38%)	10,165 (40%)	295 (11%)	
Missing	5,903	4,867	1,036	
ER status				<0.001
Positive	19,843 (79%)	17,278 (77%)	2,565 (96%)	
Negative	5,371 (21%)	5,267 (23%)	104 (3.9%)	
Missing	8,504	7,555	949	
PR status				<0.001
Positive	17,125 (68%)	14,980 (67%)	2,145 (81%)	
Negative	7,950 (32%)	7,442 (33%)	508 (19%)	
Missing	8,643	7,678	965	
HER2				<0.001
Positive	2,316 (17%)	2,147 (18%)	169 (9.4%)	
Equivocal	271 (2.0%)	251 (2.1%)	20 (1.1%)	
Negative	11,046 (81%)	9,439 (80%)	1,607 (89%)	
Missing	20,085	18,263	1,822	
Oncotype Dx				<0.001
Low	2,057 (60%)	1,824 (59%)	233 (66%)	
Medium	1,046 (30%)	933 (30%)	113 (32%)	
High	334 (9.7%)	328 (11%)	6 (1.7%)	
Missing	30,281	27,015	3,266	

Figure 1: Survival analyses comparing patients with ER+ IDC (N=17,278) and ER+ ILC (N=2,565).

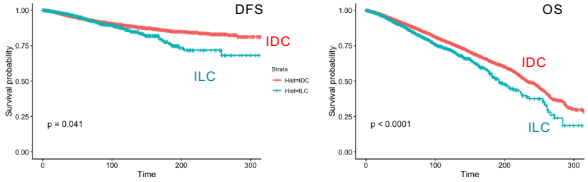

Table 2: Treatments performed for primary tumor by histological subtype

Variable	Total sample, N (%) 33,718	IDC, N (%) 30,100	ILC, N (%) 3,618	p-value
Chemotherapy				0.004
Yes	15,060 (47%)	14,088 (47%)	972 (44%)	
No	16,973 (53%)	15,736 (53%)	1,237 (56%)	
Missing	1,685	276	1,409	
Hormonal therapy				<0.001
yes	20,862 (63%)	18,090 (61%)	2,772 (78%)	
no	12,367 (37%)	11,576 (39%)	791 (22%)	
Missing	489	434	55	
Radiation				<0.001
yes	18,777 (56%)	16,901 (57%)	1,876 (52%)	
no	14,481 (44%)	12,780 (43%)	1,701 (48%)	
Missing	460	419	41	
Surgery				<0.001
Lumpectomy	13,325 (40%)	12,241 (41%)	1,084 (31%)	
Mastectomy	17,068 (52%)	14,951 (51%)	2,117 (60%)	
None	2,713 (8.2%)	2,380 (8.0%)	333 (9.4%)	
Missing	612	528	84	

Summary

In the largest cohort of patients with ILC made possible by a multi-center collaboration, we show that lobular histology carries distinct prognostic implications and that outcomes are significantly worse. This highlights the need for more ILC research and clinical trials for patients with ILC. We are currently extending the analyses to answer additional clinical questions for patients with ILC such as sites of metastasis.

Acknowledgements

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LBCA Lobular Breast Cancer Alliance