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Lack of prognostic significance of “classic” lobular breast carcinoma: a matched, single institution series

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Abstract Whether invasive lobular carcinoma of the breast per se constitutes a prognostically favorable type has been debated. The present series comprises 301 consecutive “classic” lobular breast carcinomas seen at one institution between 1994 and 2001, compared to an equal number of invasive ductal carcinomas at the same institution during the same period, matched for year of surgery, age, menopausal status, primary tumor size, nodal involvement, hormone receptor status and where possible histological grade. Despite matching, the lobular carcinomas were more frequently multifocal, had more involved nodes, lower grade

and lower proliferative fraction. There was no significant difference in disease-free or overall survival, locoregional relapse or time to distant metastasis between the lobular and ductal groups overall or within any examined subset, though the lobular group showed a trend to earlier appearance of contralateral breast cancer. Classical lobular histology is not an independent factor in the prognosis of early breast cancer.

Keywords Breast cancer · Lobular carcinoma · Prognosis · Matched study

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Introduction

Carcinoma of the breast may be classified according to their presumed origin from epithelial cells of the secretory lobules or those lining the draining ducts. Pathologists have long recognized specific patterns among breast cancers, but the majority lack these features and are classified as infiltrating ductal carcinomas (IDC) not otherwise specified. Invasive lobular cancers (ILC) are the second most common type, constituting 5–16% of all breast cancer [1–3]. Based on a variety of study designs, some previous authors have concluded that ILC carries a favorable prognosis compared to IDC [4–8], while others have found the outcome of the two groups to be similar [9–19]. In two recent studies with prolonged follow-up, it was noted that the disease-free and overall survival curves crossed, with an initial favorable and later unfavorable impact of ILC type [20, 21].

Several previous series have used a matched design to allow for imbalances of prognostic factors other than ILC type [4, 9, 10, 17, 22]. Among series which compared unmatched groups of ILC and IDC, ILC has been associated with larger primary tumor size [5, 8, 13, 15, 16, 18, 20]; most [5, 13, 15, 16] but not all [12] have reported higher expression of hormone receptors, while the degree of nodal involvement has variously been noted as less [16, 21], similar [12] or greater [5]. There is uniform agreement that the organ distribution of metastatic disease tends to be different, with ILC displaying a tendency to metastasize to the gastrointestinal tract, pelvic organs and retroperitoneum [9, 10, 13, 23].

The experience at the European Institute of Oncology (IEO)

The present series is based on an earlier report of 530 cases of ILC [24] from this institution, describing the more favorable outcome of the classic subtype of ILC as distinct from alveolar, solid, pleomorphic, signet ring histiocytoid or apocrine variants. The 301 cases of classic ILC identified in that study were matched 1:1 with cases of IDC treated at the institution during the same period based on year of surgery, age, menopausal status, primary tumor size, lymph node involvement, hormone receptor status and when possible tumor grade. Matching between the groups was close for most variables with the exceptions that the ILC group had more frequent multifocality ($P < 0.001$); more involved lymph nodes ($P = 0.001$); a lower proliferative fraction as measured by ki67 labeling index [25, 26] ($P = 0.005$); and a higher proportion of histological grade I tumors ($P = 0.022$).

As has been described by others [9, 10, 13, 23], we observed a different pattern of distribution of metastases between the groups, in that ILC was associated with more

metastases to the gastrointestinal tract and pelvic organs. Median follow up was 7.3 years (7.8 years for IDC, 7.0 years for ILC). Disease-free and overall survival curves as well as time to locoregional relapse, distant metastasis, contralateral breast cancer and the appearance of other (non-breast) cancer were prepared for each group by the Kaplan-Meier method and compared by the log rank test. For none of these endpoints was there any significant difference between the ILC and IDC groups. Effects within subgroups defined by age, menopausal status, primary tumor size, multifocality, nodal status, histological grade, hormone receptor status, ki67 labeling index, type of surgery and adjuvant systemic therapy were compared using Cox proportional hazard models. No subgroup showed effects on disease-free or overall survival significantly different from the overall result (Fig. 1).

We conclude that, once allowance is made for routinely collected prognostic factors, the outcome of classic ILC does not differ significantly from IDC (Table 1).

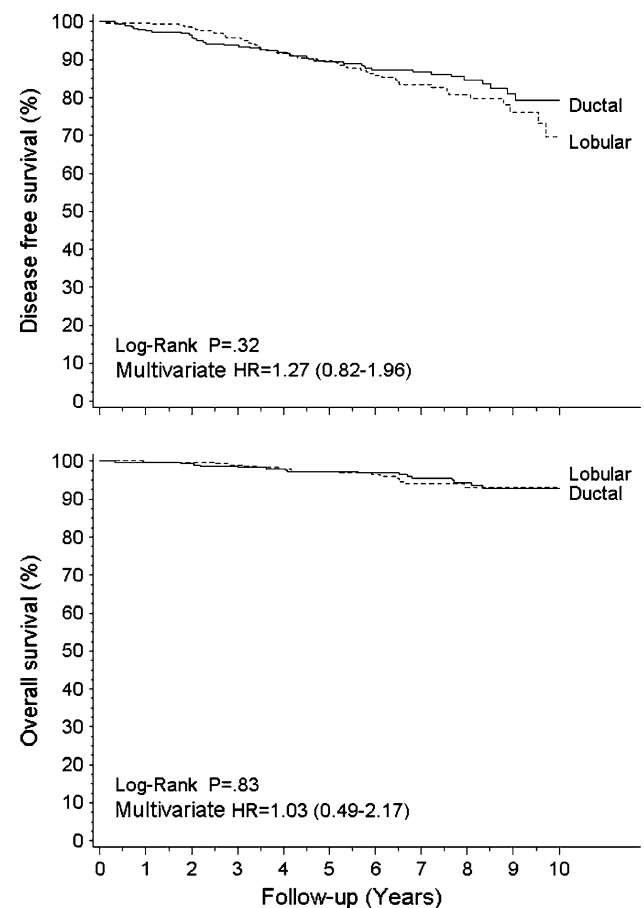


Fig. 1 Disease-free survival (top) and overall survival (below) curves comparing classic infiltrating lobular carcinoma with infiltrating ductal carcinoma. Hazards Ratios (HR) and 95% confidence intervals obtained from multivariate Cox proportional hazards regression model adjusted for age, pT, pN, multifocality, grade, hormonal receptor status, ki67 and type of surgery

Table 1 Patient and tumor characteristics

	All patients	Classical		P-value
		Ductal	Lobular	
All patients	602	301	301	
Age group				
<40	32 (5.3%)	16	16	
40–49	147 (24.4%)	70	77	
50–59	217 (36.0%)	114	103	
60–69	140 (23.3%)	70	70	
70+	66 (11.0%)	31	35	0.97 ^a
Menopausal status				
Pre/peri-menopausal	218 (36.2%)	109	109	
Post-menopausal	184 (63.8%)	192	192	1.00
pT				
pT1	390 (64.8%)	195	195	
pT2	168 (27.9%)	86	82	
pT3–pT4	44 (7.3%)	20	24	0.79 ^a
Multifocality				
Monofocal	465 (77.2%)	256	209	
Multifocal	137 (22.8%)	45	92	<0.0001
pN				
pN0 (AD)	177 (29.4%)	92	85	
Sentinel node negative	189 (31.4%)	101	88	
pN+	212 (35.2%)	106	106	0.79
pNx	24 (4.0%)	2	22	
Number of positive nodes				
None	366 (60.8%)	193	173	
1–3	141 (23.4%)	78	63	
4–10	43 (7.1%)	23	20	
>10	28 (4.7%)	5	23	0.001 ^a
pNx	24 (4.0%)	2	22	
Tumor grade				
Grade 1	319 (53.0%)	145	174	
Grade 2	283 (47.0%)	156	127	0.022
Hormone receptors status				
Estrogen & progesterone receptor negative	31 (5.1%)	15	16	
Estrogen or progesterone receptor positive	571 (94.9%)	286	285	0.85
Proliferative fraction				
ki67 labeling index <20%	471 (78.2%)	222	249	
ki67 labeling index ≥20%	129 (21.4%)	79	50	0.005
Unknown	2 (0.3%)	0	2	
Type of surgery				
Breast conserving surgery	467 (77.6%)	243	224	
Total mastectomy	135 (22.4%)	58	77	0.078
Type of adjuvant systemic therapy				
None	39 (6.5%)	26	13	
Endocrine alone	320 (53.2%)	150	170	
Non-anthracycline	143 (23.8%)	74	69	
Anthracycline	87 (14.5%)	41	46	0.11
Unknown	13 (2.2%)	10	3	

^a Trend

Bold values indicate statistically significant values

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