Research article

Infiltrating lobular carcinoma of the breast: tumor characteristics and clinical outcome

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Abstract

Introduction: Invasive lobular carcinoma (ILC) comprises approximately 10% of breast cancers and appears to have a distinct biology. Because it is less common than infiltrating ductal carcinoma (IDC), few data have been reported that address the biologic features of ILC in the context of their clinical outcome. In the present study we undertook an extensive comparison of ILC and IDC using a large database to provide a more complete and reliable assessment of their biologic phenotypes and clinical behaviors.

Methods: The clinical and biological features of 4140 patients with ILC were compared with those of 45,169 patients with IDC (not otherwise specified). The median follow-up period was 87 months.

Results: In comparison with IDC, ILC was significantly more likely to occur in older patients, to be larger in size, to be estrogen and progesterone receptor positive, to have lower S-phase fraction, to be diploid, and to be HER-2, p53, and epidermal growth factor receptor negative. It was more common for ILC than for IDC to metastasize to the gastrointestinal tract and ovary. The incidence of contralateral breast cancer was higher for ILC patients than for IDC patients (20.9% versus 11.2%; $P < 0.0001$). Breast preservation was modestly less frequent in ILC patients than in IDC patients. The 5-year disease-free survival was 85.7% for ILC and 83.5% for IDC ($P = 0.13$). The 5-year overall survival was 85.6% for ILC and 84.1% for IDC ($P = 0.64$).

Conclusion: Despite the fact that the biologic phenotype of ILC is quite favorable, these patients do not have better clinical outcomes than do patients with IDC. At present, management decisions should be based on individual patient and tumor biologic characteristics, and not on lobular histology.

Keywords: breast cancer, breast carcinoma, infiltrating ductal carcinoma, infiltrating lobular carcinoma, invasive ductal carcinoma of the breast, invasive lobular carcinoma of the breast, special type of breast cancer

Introduction

Carcinoma of the breast is a histologically heterogeneous disease. Invasive lobular carcinoma (ILC) accounts for 8–14% of all breast cancers [1,2]. Data from a recent epidemiologic study [3] indicate that for unknown causes the incidence of this type of breast cancer is increasing, especially among postmenopausal women.

The morphologic features of lobular carcinoma differ from those of ductal carcinoma. ILC is characterized by small, round cells that are bland in appearance and have scant cytoplasm, which infiltrate the stroma in single file and sur-

round benign breast tissues in a targeted manner [1,4]. Infiltration typically does not destroy anatomic structures or incite a substantial connective tissue response. By virtue of their distinctive growth pattern and biology, lobular carcinomas often fail to form distinct masses that can easily be diagnosed by palpation or mammography. This can make early diagnosis challenging [5,6] and breast conservation approaches more difficult. Lobular carcinomas may have a substantially increased propensity for multifocal and multicentric distribution and for bilaterality [5,7–11]. Metastatic spread with an uncommon pattern of involvement has been reported [12,13].

CNS = central nervous system; DFS = disease-free survival; EGFR = epidermal growth factor receptor; ER = estrogen receptor; IDC = infiltrating ductal carcinoma; ILC = infiltrating lobular carcinoma; OS = overall survival; PgR = progesterone receptor.

Because it is substantially less common than infiltrating ductal carcinoma (IDC), knowledge about the clinical outcome of lobular carcinoma has been based on studies including relatively small numbers of patients. Reported prognosis varies and has been reported to be worse [14,15], no different [16–19], or better [20] than that with IDC. This reported variability might be due to relatively small numbers of cases in each analysis. In addition, few data have been reported on the biologic features of lobular carcinomas within the context of their clinical outcome. We therefore undertook an extensive comparison of ILC and IDC using a large database to provide a more complete and reliable assessment of their biologic phenotypes and clinical behaviors, which might yield information useful for clinical decision making or for further exploring the biologic nature of this disease.

Methods
Study population
The Breast Center at Baylor College of Medicine maintains databases of breast cancer patients whose biopsy or mastectomy specimens were sent to central laboratories for steroid receptor assays. These patients were diagnosed and treated at more than 370 academic and community institutions throughout the USA. The central laboratories were located at the University of Texas Health Science Center at San Antonio and at Nichols Institute in San Juan Capistrano, California. Histologic diagnoses were made by pathologists at community hospitals and were not reviewed centrally. ILC was not further subtyped in these databases, and patients with mixed ILC and IDC were excluded. Follow-up information was obtained from tumor registries, by direct review of medical records conducted by data managers, or by data collection forms completed at the office of the referring physicians. These databases contain information on 50,399 patients with early breast cancer who were diagnosed between 1970 and 1998. Among them, 4140 (8.2%) were diagnosed as having ILC and 45,169 (89.6%) as having IDC. Patients with special histologic types (tubular, mucinous, and medullary) were excluded, as were those with gross distant metastases at diagnosis. Histologic grade was not analyzed in the present study because in most cases this information was not available.

The patient information contained in this report was obtained from two data repositories maintained by the Breast Center at Baylor College of Medicine. Each repository has been reviewed by Institutional Review Boards at the University of Texas Health Science Center at San Antonio and at Baylor College of Medicine.

Prognostic factors
Estrogen receptor (ER) levels were measured using the dextran-coated charcoal method as previously described [21]. From 1970 to 1984, [3H]estradiol was used as a labeled ligand. During the same period, progesterone receptor (PgR) levels were measured by sucrose density gradient [22]. In 1985, the standard multipoint dextran-coated charcoal assay was modified to incorporate [125I]estradiol and [3H]R5020 in a single assay, allowing simultaneous determination of levels of both ER and PgR [23]. Levels of 3 fmol/mg protein or greater were considered positive for ER, and levels of 5 fmol/mg protein or greater were considered positive for PgR. DNA ploidy and S-phase fraction were evaluated using flow cytometry, as previously described [24–26]. S-phase fractions below 6% were considered low, those in the range 6–10% were considered intermediate, and those in excess of 10% were considered high. HER-2 status was determined using Western blotting [27]. The cutoff value between low and high HER-2 expression was 1 U/µg protein. Epidermal growth factor receptor (EGFR) levels were measured by radiobinding assay, using fixed concentrations of radiolabeled EGF and varying concentrations of unlabeled EGF. Levels of 10 fmol/mg or greater were considered positive. This cutoff has been in use at the Nichols Institute since 1992 and its use is in accordance with published studies [28,29]. p53 status was determined by immunohistochemistry, and negative nuclear staining was a surrogate marker for normal p53 [30].

Statistical methods
Descriptive statistics are reported as frequencies or medians. The clinical and biologic characteristics of lobular and ductal carcinoma were compared using contingency tables, χ^2 tests and Fisher's exact tests.

Overall survival (OS) was defined as the interval between the diagnostic biopsy and death from any cause, death being scored as an event, and patients who were still alive were censored at the time of last follow-up. OS after first recurrence was calculated from the date of first recurrence, death being scored as an event, and patients who were still alive were censored at the time of last follow-up. Disease-free survival (DFS) was also calculated from the date of first diagnostic biopsy, with first recurrences, local or distant, being scored as an event, and with censoring of other patients at the time of last follow-up or death. Local recurrence was defined as tumor arising in the treated breast, chest wall or axilla. OS and DFS curves were drawn using Kaplan–Meier estimates, and were compared using log rank tests. Survival rates are presented with their 95% confidence intervals.

Multivariate analyses of DFS and OS, with stepwise variables selection, were conducted using Cox proportional hazard regression models. Analyses were performed using SAS Version 8.00 (SAS Institute Inc., Cary, NC, USA).

Results
Patient and tumor characteristics
From a total of 50,399 patients with early breast cancer in the Baylor College of Medicine Breast Cancer data-

bases, we identified 4140 patients (8.2%) with ILC and 45,169 (89.6%) patients with IDC (not otherwise specified). The median follow-up time was 87 months (range 0–254 months).

Table 1 summarizes the clinical and biologic tumor characteristics according to histologic type. The median ages of patients with ILC and IDC were 64.6 and 60.6 years, respectively. ILCs were slightly larger on average (53.8% larger than 2 cm) than IDCs (48.6% larger than 2 cm; $P < 0.0001$). More revealing, however, was a 50% greater chance of ILC presenting as a large tumor, with 14.0% of ILCs exceeding 5 cm as compared with 9.1% of IDCs. Despite this difference in tumor size, there was no difference in the frequency of axillary node involvement.

Despite the larger tumor size, ILCs had more favorable biologic characteristics (Table 1). The proportion of ER-positive tumors was 92.7% for ILC and 81.2% for IDC ($P < 0.0001$). PgR was expressed in 67.4% of ILCs and in 60.2% of IDCs ($P < 0.0001$). Compared with IDCs, ILCs were much more likely to be diploid (69.8% of ILCs versus 43.6% of IDCs; $P < 0.0001$), have a low or intermediate S-phase fraction (87.8% of ILCs versus 68.6% of IDCs; $P < 0.0001$), have normal p53 status (74.4% of ILCs versus 46.5% of IDCs; $P < 0.0001$), and be negative for EGFR (94.1% of ILCs versus 80.7% of IDCs; $P < 0.0001$) and HER-2 (89.34% of ILCs versus 75.6% of IDCs; $P < 0.0001$). Thus, in comparison with IDC, ILC was more likely to occur in older patients, to be larger in size, to be ER and PgR positive, to have a lower S-phase fraction, to be diploid, and to be negative for HER-2, p53 and EGFR.

The pattern of metastatic dissemination in ILC and IDC was also different (Table 2). Lung and pleura involvement was more frequently observed with IDCs ($P = 0.0019$), as was involvement of distant nodes ($P = 0.018$) and of the central nervous system (CNS; $P = 0.0032$). The detail of coding in the database was not sufficient to permit further distinction between brain, spinal cord, and meningeal metastases, and therefore the incidence of leptomeningeal disease could not be determined. ILC was three times more likely to metastasize to the peritoneum, gastrointestinal tract, and ovaries (6.7% versus 1.8%). Information on contralateral breast tumors was also available on the subset of 2855 patients in whom sites of breast cancer distant from the primary could be assessed. Contralateral breast cancers in this group were more frequent among those with ILC (20.9%) than among those with IDC (11.2%; $P < 0.0001$; data not shown).

Both local and systemic therapy for breast cancer differed according to histologic type (Table 3). Patients with ILC were slightly less likely to undergo lumpectomy (9.5% of patients with ILC versus 12.7% of patients with IDC;

Table 1

Patients and tumor biological characteristics by histologic group

	ILC	IDC	*P*
Patients (*n*)	4140	45169	
Tumor size			
Number with data	3962	43827	
≤2 cm (%)	46.1	51.3	
>2 and ≤5 cm (%)	39.8	39.5	<0.0001
>5 cm (%)	14.0	9.1	
Age			
Number with data	3501	38436	
≤50 years	19.4	27.8	<0.0001
>50 years	80.6	72.2	
Positive lymph nodes			
Number with data	3891	43066	
0	57.3	58.0	NS
≥1	42.7	42.0	
Estrogen receptor			
Number tested	4140	45169	
Positive (%)	92.7	81.2	<0.0001
Progesterone receptor			
Number tested	4075	44307	
Positive (%)	67.4	60.2	<0.0001
Ploidy			
Number tested	3763	40123	
Diploid (%)	69.8	43.6	<0.0001
S-phase fraction			
Number tested	3339	34620	
Low	68.6	46.7	
Intermediate	19.2	21.9	<0.0001
High	12.2	31.4	
p53			
Number tested	86	1009	
Negative (normal; %)	74.4	46.5	<0.0001
HER-2			
Number tested	263	2909	
Negative (%)	89.3	75.6	<0.0001
Epidermal growth factor receptor			
Number tested	203	2366	
Negative (%)	94.1	80.7	<0.0001

IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma.

$P < 0.0001$). Probably because of the higher hormone receptor content, adjuvant endocrine therapy was more frequently given to patients with ILC (28.8%) than to those with IDC (22.9%; $P < 0.0001$). On the other hand, the number of patients with ILC who received adjuvant chemotherapy was significantly lower (16.2% in ILC patients versus 23.7% in IDC patients; $P < 0.0001$).

Disease-free and overall survival

A trend toward better DFS was observed for ILC patients. The 5-year DFS was 85.7% for patients with ILC and 83.5% for those with IDC ($P = 0.13$). This modest difference is not clinically or biologically significant. However,

Table 2

Distant sites of first recurrence

Sites	ILC (n = 179; %)	IDC (n = 2576; %)	P
Lungs/pleura	9.0	17.6	0.0019
CNS	1.7	5.3	0.032
Ovary	2.2	0.7	0.0003
Gastrointestinal tract[a]	4.5	1.1	0.009
Nodes	15.5	22.0	0.018
Bone	34.6	35.5	NS
Skin[b]	31.8	27.3	NS
Liver	7.3	10.9	NS
Pituitary	0.5	0.1	NS

Percentages do not add up to 100% because of multiple metastatic sites in the same patient and infrequent or unknown sites not shown. [a]Stomach, small bowel, colon, appendix, duodenum, and peritoneum. [b]Soft tissue and skin.
CNS, central nervous system; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; NS, not significant.

although ILC patients experienced recurrence less frequently than did IDC patients during the first few years after diagnosis, the two DFS curves converged after longer follow-up (Fig. 1a). Despite having more favorable biologic characteristics, the 5-year OS was not better for ILC (85.6%) than for IDC (84.1%; *P* = 0.64; Fig. 1b). For node-negative patients, DFS and OS were very similar for the two histologic types.

The median survival after the first recurrence was slightly longer for ILC patients (22 months, range 0–115 months)

Table 3

Local and systemic adjuvant therapy by histologic type

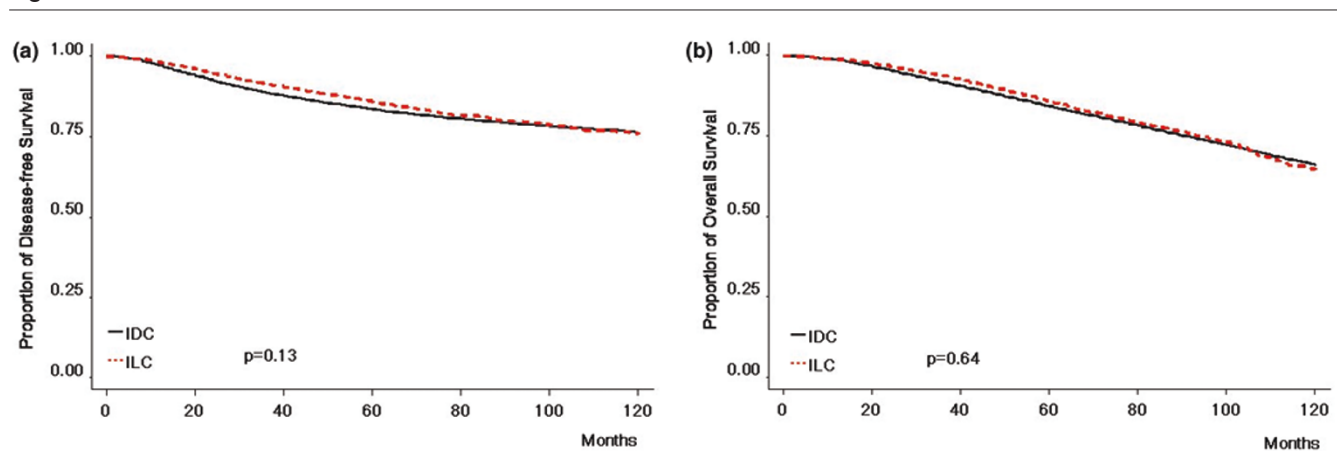| Therapy | Histologic type | | |
	ILC	IDC	P
Surgery			
Number of patients	4197	45995	
None (%)	1.1	0.8	
Modified radical mastectomy (%)	89.4	86.5	<0.0001
Lumpectomy (%)	9.5	12.7	
Adjuvant therapy			
Number of patients	2817	31043	
None (%)	42.4	42.3	
Chemotherapy (%)	16.2	23.7	
Endocrine therapy (%)	28.8	22.9	<0.0001
Chemotherapy and endocrine therapy (%)	12.6	11.1	

IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma.

than for IDC patients (19 months, range 0–119 months; *P* = 0.002), and the 5-year survival after the first recurrence was 32.8% for patients with ILC as compared with 26.7% for patients with IDC (Fig. 2).

Multivariate analyses
Multivariate analyses were performed using Cox regression models to determine whether ILC was an independent prognostic factor for recurrence and death (Table 4). Factors included in these analyses were tumor size, number of involved nodes, age, ER status, PgR status, DNA ploidy, S-phase, and histologic type. Data were available for all of these variables in 33,860 patients. From these variables, the factors that remained independently associated with recurrence, as well as with survival, were

Figure 1

(a) The 5-year disease-free survival (DFS) was 85.7% (95% confidence interval [CI] 84.4–87.1%) for invasive lobular carcinoma (ILC) versus 83.5% (95% CI 83.1–84.0%) for invasive ductal carcinoma (IDC; *P* = 0.13). (b) The 5-year overall survival (OS) was 85.6% (95% CI 84.2–87.0%) for ILC and 84.1% (95% CI 83.7–84.6%) for IDC (*P* = 0.64).

Table 4

Multivariate Cox regression models for disease-free survival and overall survival in patients with invasive ductal carcinoma and patients with invasive lobular carcinoma

	DFS		OS	
Parameter	RR (95% CI)	P	RR (95% CI)	P
Nodes				
0	1	<0.0001	1	<0.0001
1–3	1.8 (1.6–1.9)		1.4 (1.3–1.5)	
>3	3.4 (3.1–3.6)		2.4 (2.2–2.5)	
Tumor size (cm)				
≤2	1	<0.0001	1	<0.0001
2–5	1.5 (1.4–1.6)		1.4 (1.3–1.5)	
>5	1.9 (1.7–2.1)		2.0 (1.8–2.1)	
Age (years)				
≤50	1	0.0005	1	<0.0001
>50	1.1 (1.0–1.2)		1.9 (1.7–2.0)	
S-phase				
Low	1	<0.0001	1	<0.0001
Intermediate	1.4 (1.3–1.5)		1.3 (1.2–1.3)	
High	1.5 (1.4–1.7)		1.4 (1.3–1.5)	
PgR				
Positive	1	<0.0001	1	0.0014
Negative	1.3 (1.2–1.4)		1.3 (1.2–1.4)	
ER				
Positive	1	0.0017	1	0.048
Negative	1.1 (1.0–1.2)		1.1 (1.0–1.2)	

CI, confidence interval; DFS, disease-free survival; ER, estrogen receptor; OS, overall survival; PgR, progesterone receptor; RR, relative risk.

Table 5

Multivariate Cox regression models for disease-free survival and overall survival in invasive lobular carcinoma patients

	DFS		OS	
Parameter	RR (95% CI)	P	RR (95% CI)	P
Nodes				
0	1	<0.0001	1	<0.0001
1–3	2.2 (1.6–3.2)		1.4 (1.1–1.9)	
>3	4.1 (2.9–5.7)		2.2 (1.7–2.9)	
Tumor size (cm)				
≤2	1	<0.0001	1	<0.0001
>2	1.9 (1.4–2.6)		1.6 (1.3–2.1)	
Age (years)				
≤50	–	NS	1	<0.0001
>50	–		2.3 (1.7–3.1)	
S-phase				
Low	1	0.002	1	<0.0293
Intermediate –high	1.7 (1.3–2.2)		1.3 (1.0–1.6)	
PgR				
Positive	1	0.003	–	NS
Negative	1.5 (1.1–1.9)		–	
ER				
Positive	–	NS	1	0.0006
Negative	–		1.9 (1.3–2.8)	
Ploidy				
Diploid	1	0.03	–	NS
Aneuploid	1.7 (1.3–2.2)		–	

CI, confidence interval; DFS, disease-free survival; ER, estrogen receptor; NS, not significant; OS, overall survival; PgR, progesterone receptor; RR, relative risk.

as follows: lymph node status, tumor size, age, S-phase, PgR status, and ER status. Once adjustment based on these six parameters was made, histologic type did not emerge as an important prognostic factor. Thus, the lack of prognostic significance related to ILC versus IDC in univariate analyses is confirmed by the results of the multivariate analyses.

In addition, to determine whether traditional prognostic factors for IDC would be of value in patients with ILC, a second set of multivariate analyses of DFS and OS were performed only in patients with ILC (Table 5). For DFS, lymph node status, tumor size, S-phase, PgR status, and DNA ploidy retained their independent prognostic value. For OS, nodal status, age, tumor size, ER status, and S-phase were independent prognostic factors.

Discussion

The present study demonstrates that ILC has distinctive clinical and biologic characteristics compared with IDC. Lobular carcinomas were more likely to occur in older patients; to be larger in size, ER and PgR positive, and diploid with a low S-phase fraction; and to have normal p53 status and low to absent EGFR and HER-2. The dis-
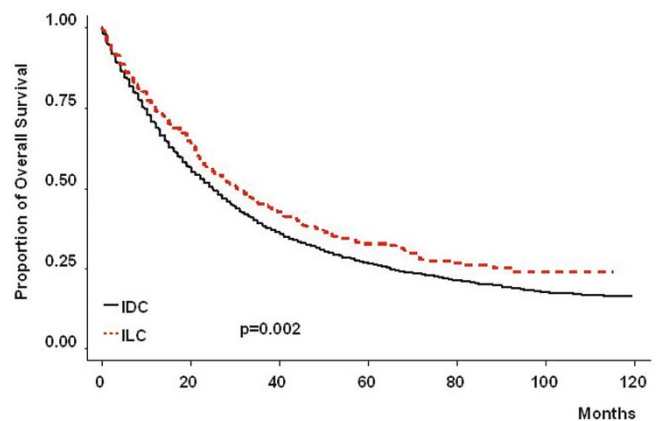
Figure 2

The 5-year overall survival (OS) after the first recurrence was 32.8% (95% confidence interval [CI] 28.0–37.6%) for invasive lobular carcinoma (ILC) and 26.7% (95% CI 25.3–28.0) for invasive ductal carcinoma (IDC). The median survival after first recurrence was 22 months (range 0–115 months) for ILC versus 19 months (range 0–119 months) for IDC (P = 0.002).

tributions of metastases were also different. Despite a substantially less aggressive biologic phenotype, recurrence and survival were very similar between ILC and IDC patients.

To our knowledge this is the largest published report on ILC that comprehensively evaluates biologic characteristics and clinical outcomes. The incidence of ILC observed in the present study (8.2%) is in accordance with the incidence range of 8–14% reported in the literature [1,14,31–33]. In addition, the large number of patients, the multi-institutional nature of the study population, and the median follow-up period of more than 7 years strengthen the reliability of the results and permit extrapolation of the findings to routine clinical practice.

Clinical characteristics at diagnosis are different for ILC than for IDC. Several studies showed that patients with ILC are on average older at presentation than are IDC patients [18,19,34]. Consistent with these data, in the present study the median ages at diagnosis were 64.6 years for patients with ILC and 60.6 years for patients with IDC. This older age at diagnosis in those with ILC could be due to a low proliferative rate or greater difficulties in detecting ILC. In terms of tumor size, 14% of ILCs were found to exceed 5 cm as compared with only 9.1% of IDCs. The lack of a desmoplastic reaction may make the lesion impalpable and invisible, both clinically and mammographically, deferring the identification and probably explaining why lobular carcinomas were larger at diagnosis than IDCs. However, despite the slightly larger size of ILCs, the rate of lymph node involvement was the same in each group. The uniform appearance of bland tumor cells that lack cellular atypia and often have a low mitotic rate make the lobular carcinoma cells more difficult to detect in metastatic lymph nodes. Thus, particular attention should be given to histologic examination of axillary nodes in resection specimens of lobular carcinomas because nodal metastases are more often missed with ILCs, and false-negative results are more frequently reported compared with ductal carcinomas [35].

From this report it is evident that the metastatic pattern for ILC differs from that of IDC. ILC was less likely to affect the lungs, pleura, and CNS than was IDC. By contrast, the peritoneum, ovary, and gastrointestinal system were much more likely to be involved in advanced ILC. Entries for gastrointestinal involvement in the database represent peritoneal and parenchymal involvement. CNS metastases were more common with IDC. This database could not clearly distinguish between brain, spinal cord, or leptomeningeal metastases in its classification of CNS involvement. It has been reported that ILC more often involves the meninges and spinal fluid [13,36–38] but we were unable to address this issue directly because of limitations in the database. The factors that account for this

distinct metastatic pattern are unclear. The difference could be due to a cell size or shape with physical properties that favor certain areas with microanatomy that is more conducive to stopping or trapping these types of cells. Alternatively, the microenvironment of the ovary or peritoneum may provide growth and survival factors that favor ILC cells over IDC cells. Additional molecular or biologic differences might account for this peculiar pattern of metastasis. It has been demonstrated that loss of expression of the cell–cell adhesion molecule E-cadherin in ILC may decrease adhesiveness of cells and facilitate this type of infiltration [19,39,40]. Indeed, the findings of this study support a different molecular biology of ILC.

Bilateral involvement is reported to be 20–29% in lobular carcinoma [10,12,16,41,42]. In our dataset the incidence of contralateral breast cancer in women with ILC was nearly double that in women with IDC. This finding could make a compelling case for the use of tamoxifen to prevent contralateral breast cancer in women with lobular primaries.

Because only a few small and scattered studies have addressed the biologic features of ILC, one of the main objectives of the present study was to characterize more comprehensively its biologic phenotype. This report definitively confirms and extends the findings of some previous studies [11,12,17,43–45] indicating that lobular carcinomas are significantly more likely to be steroid receptor positive than are IDCs. These results also demonstrate that lobular carcinomas are more likely to have low S-phase fractions and to be diploid. The evaluation of S-phase fractions in ILC in other published series confirms our findings [18,20,46]. Few reports have evaluated the well studied growth factor receptors HER-2 and EGFR, or the tumor suppressor gene p53 in ILC. In the present analysis, no more than 5–10% of tumors classified by a broad range of pathologists as ILC over-expressed EGFR and/or HER-2. Positivity for p53 was found half as often in ILC as in IDC. Only two small studies have analyzed these molecules in ILC [47–49] and their results are similar to those reported here. The 5–10% of patients who were positive for HER-2 or EGFR, or who were p53 positive, may not have been of the classic ILC subtype but possibly a variant, such as those found in the pleomorphic or mixed ILC–IDC categories. ILC subtypes have been reported to have different biologic characteristics and clinical behavior as compared with the classic subtype [50–52], but the difference has not found to be statistically significant, although the number of patients included in the various studies is small. Unfortunately, we were unable to subtype further those tumors with lobular histology. More study is needed on these specific subtypes. However, together these findings suggest that ILC is biologically different from IDC.

In general, the management of patients in this study with ILC was somewhat different from the management of

patients with IDC. In practice, the histologic type appears to play a role in the choice of surgical procedure selected [11,44,53,54]. This analysis suggested that ILC was treated by mastectomy slightly more frequently than was IDC. Although this tendency to favor mastectomy may be related to factors specific to the patient and/or surgeon, the choice for these procedures is also influenced by pathologic findings. Indeed, the diminished fibrotic reaction present in ILC makes it difficult for pathologists and surgeons to determine the gross extent of the disease during surgery, and to achieve tumor-free margins after a limited excision. With respect to systemic therapy, because lobular carcinomas are more frequently steroid receptor positive tumors, as expected a greater proportion of ILC patients than of IDC patients received adjuvant endocrine therapy.

From previous studies the prognosis for ILC compared to IDC is unclear. An important finding of the present large study is that the 5-year OS of patients with ILC is not different from that of patients with IDC. Therefore, the fact that ILC has more favorable prognostic factors does not translate into a survival advantage for patients with ILC. Although ILC is associated with a less aggressive phenotype, this is offset by lobular carcinoma being more difficult to detect early, either by clinical examination or mammography. Furthermore, the reported higher rate of false-negative lymph nodes by histologic examination in lobular carcinomas could cause a general under-staging of this histologic type at the time of surgery.

Multivariate analyses did not identify any prognostic differences associated with ILC or IDC. In these analyses, considering all ILC and IDC patients together, lymph nodes status, tumor size, age, S-phase, PgR status, and ER status were found to be associated with both recurrence and survival, but histology was not an important independent predictor of recurrence or survival. Furthermore, the same standard prognostic factors (tumor size, axillary nodal status, hormone receptors, S-phase, and age) used in ductal carcinoma are applicable in lobular carcinoma as well [55].

Conclusion

Results from this large dataset show clearly that ILC and IDC are different entities with different clinical courses and different biologic phenotypes, but no clinically meaningful differences in survival are evident. At present, both types of breast cancer should be managed similarly and histologic subtype (lobular or ductal) should not be a factor in the therapeutic decision-making process, and should not be considered an important prognostic or predictive factor at diagnosis. Emerging technologies such as high throughput genome mapping and microchip cDNA expression arrays may further elucidate molecular differences in these different types of breast cancer.

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