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Original article

Comparison of mastectomy with breast-conserving surgery in invasive lobular carcinoma: 15-Year results

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ABSTRACT

Background: Invasive lobular cancer (ILC) is biologically distinct from invasive ductal cancer and there is disagreement regarding appropriate local management of this disease.
Aim: The current study reports long term results comparing mastectomy with breast-conserving surgery (BCS) in the treatment of ILC.
Material and methods: Study includes 235 women with ILC treated between 1983 and 1987. All of them underwent axillary dissection and either mastectomy ($n = 163$) or BCS ($n = 72$). 50 Gy adjuvant radiotherapy (RT) was given for 53 BCS and 81 mastectomy patients. The BCS group was compared with the mastectomy group.
Results: Patients treated with mastectomy or BCS had a similar outcome at 15 years with regard to distant metastasis-free (62% vs. 70%; p, 0.2017) and breast cancer-specific (62% vs. 70%; p, 0.1728) survival. In the BCS group the actuarial rate of ipsilateral in breast recurrences was 10% with and 53% without RT at 15 years (relative risk [RR], 0.10; $p < 0.0001$). In the mastectomy group the actuarial rate of chest wall recurrences was 16% with and 13% without RT at 15 years (RR, 1.45; p, 0.3965). Isolated ipsilateral in breast recurrence did not (RR, 1.73; p, 0.2767) but isolated chest-wall recurrence did (RR, 2.65; p, 0.0089) adversely affect cause-specific survival.
Conclusion: Breast cancer specific survival is not affected by the type of surgical treatment. BCS and RT is a safe option to control local disease in patients with ILC.

1. Background

Results of several studies indicate that breast-conserving surgery (BCS) followed by radiation therapy (RT) is a suitable alternative to mastectomy for the management of early-stage invasive lobular cancer (ILC). Most of these studies report 5–7-year[1–11] and only few of them report 10-year[12–15] results. Therefore, the outcome of patients after more than 10 years of treatment has not been well described, and some doubts have been expressed about the choice of treatment.

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Table 1 – Baseline characteristics of the two surgical groups.

Characteristic	Mastectomy ($N = 163$)	BCS ($N = 72$)	p-Value
Mean age (years)	58	58	0.9652
Mean tumor size (mm)	21	17	0.0112
Median no. of nodes	12	13	0.4046
Characteristic	**MastectomyNo. of pts (%)**	**BCSNo. of pts (%)**	**p-Value**
Menopause			0.2127
Pre-	54 (33)	18 (25)	
Post-	109 (67)	54 (75)	
Pathologic T			0.0110
T1	99 (61)	56 (78)	
T2	64 (39)	16 (22)	
Pathologic N			0.3228
N0	86 (53)	43 (60)	
N1	77 (47)	29 (40)	
Estrogen receptor			0.0112
Negative	36 (22)	6 (8)	
Positive	127 (78)	66 (92)	
Hormonal therapy for N1[a]			0.1040
No	48 (62)	13 (45)	
Yes	29 (38)	16 (55)	
Chemotherapy for N1[b]			0.6665
No	58 (75)	23 (79)	
Yes	19 (25)	6 (21)	
Local irradiation			0.0006
No	82 (50)	19 (26)	
Yes	81 (50)	53 (74)	
Regional irradiation			0.3051
No	82 (50)	31 (43)	
Yes	81 (50)	41 (57)	

BCS, breast-conserving surgery.
[a] 20 mg Tamoxifen daily for 3 years for node positive pts (patients).
[b] 6 cycles of standard CMF (cyclophosphamide, methotrexate, 5-fluorouracil) for node positive patients.

2. Aim

This report presents the 15-year treatment results of 235 consecutively treated patients with ILC subjected to either mastectomy or BCS.

3. Material and methods

Two hundred and thirty-five consecutive treated women with unilateral Stage I or II invasive lobular breast carcinoma were treated with axillary dissection and either mastectomy ($n = 163$) or BCS ($n = 72$) at the National Institute of Oncology, Budapest between January 1983 and December 1987. Operative decisions regarding breast conservation or mastectomy were based on patient request, but in the eighties mastectomy was often recommended as the surgical treatment of choice. In BCS patients, routine attempts were made to obtain clear surgical margins. Surgery consisted of total resection of the primary tumor with a 1 cm rim of normal tissue. Resection edges were subjected to frozen section and, when the margin was positive wider excision was done. At final pathologic examination, 8 patients had a positive margin. Five of them underwent re-excision and in 3 cases conversion to mastectomy was done. Pathological classification (microscopic tumor size, pT and pN) was done according to the UICC-AJCC TNM System.

Details of adjuvant treatment policy and technique have been described previously.[16] The clinical-pathological and treatment characteristics of the patient population are summarized in Table 1. Mastectomy patients had generally larger primary. Twenty-two percent of the mastectomy and eight percent of the BCS patients had ER negative tumor. The median RT dose of conserved breast, chest wall or supraclavicular fossa/apex of axilla was 50 Gy (ranges, 44–54 Gy, 42–50 Gy and 44–52 Gy, respectively).

Patients were seen in follow-up at 3- to 6-month intervals until the end of the 5th year, and annually thereafter. Chest X-rays, mammograms, bone scans, abdominal ultrasound examinations and blood tests were performed at least yearly. The local-regional recurrences were scored on all patients, including those who also relapsed at distant sites. Malignancy of local-regional recurrence and new primary tumor was proved by histologic or cytologic examination in every case. Distant metastases were defined as a recurrence outside the target volume. Thus, a supraclavicular recurrence was recorded as a regional – not distant – treatment failure. The median follow-up time for surviving patients was 181 months (range, 151–210 months).

Survival times were calculated as the time from surgery to the date of the event or the end of the follow-up period. Patients lost to follow-up were inserted in the analysis as censored data. The following end points were studied: any death for overall survival; death from breast cancer for breast cancer-

Table 2 – Survival outcomes by surgical treatment groups.

	Mastectomy ($N = 163$)		Breast-conserving surgery ($N = 72$)		p-Value	RR	95% CI
	Percent surviving	No. of events	Percent surviving	No. of events			
Local recurrence-free survival		15		14	0.05	2.03	1.07–3.85
5 years	92		84				
10 years	89		82				
15 years	89		77				
Locoregional recurrence[a]*-free survival*		22		14	0.0644	0.21	0.03–1.62
5 years	89		84				
10 years	85		82				
15 years	84		77				
Distant metastasis-free survival		60		21	0.2017	0.73	0.44–1.2
5 years	73		80				
10 years	66		73				
15 years	62		70				
Breast cancer-specific survival		60		21	0.1728	0.71	0.43–1.17
5 years	80		86				
10 years	66		73				
15 years	62		70				
Overall survival		87		28	0.0122	0.58	0.38–0.91
5 years	77		85				
10 years	62		72				
15 years	49		63				

No. (number) of events, p-values, RR (relative risk), and 95% CI (confidence interval) shown are for the entire duration of the follow-up; the group of reference is the mastectomy group.
[a] This category includes locoregional recurrence came before systemic failure.

specific survival; chest wall or ipsilateral in-breast recurrence for local recurrence-free survival; local or regional recurrence, whichever came first, for locoregional recurrence-free survival; distant metastasis for distant disease-free survival. The actuarial rate of survival was estimated by the Kaplan–Meier method.[17] Differences in survival between study groups were compared using the log-rank test. In univariate and multivariate analysis the Cox's regression model was used.[18] Relative risk (RR) and associated confidence intervals (CI) were calculated from the proportional regression coefficients. Statistical differences in proportions and means were assessed by 2-sample t-test. All tests were performed at the 0.05 level of significance.

4. Results

4.1. *All patients*

Three (1.3%) patients were lost to follow-up between 72 and 120 months. During the follow-up period 114 (48.5%) patients died, and 121 of them (51.5%) were still alive. The cause of death was breast cancer in 81 (34.5%), intercurrent disease in 30 (12.7%), and other malignancy in 3 (1.3%) cases. The results of univariate analysis showed that pathological T (T1 vs. T2, $p = 0.0001$) and pathological N (N0 vs. N1, $p < 0.0001$) were but menopausal status (pre vs. post, $p = 0.8706$), ER status (negative vs. positive, $p = 0.2185$) and surgery (mastectomy vs. BCS, $p = 0.1728$) were not significantly related to the length of breast cancer-specific survival. In multivariate analysis both pathological T (RR: 1.6; 95% CI: 1–2.5) and N (RR: 7.2; 95% CI. 4.1–12.8) remained independent predictor of breast cancer specific survival. 15-Year survival with T1 or T2 was 73% and 48%, and with N0 or N1 was 88% and 35%.

4.2. *Surgical treatment groups*

The survival outcomes after 5, 10, and 15 years are shown in Table 2. The 15-year local recurrence-free survival for mastectomy or BCS patients was 89 and 77%, respectively (RR: 2.03; $p = 0.05$). There were no significant differences between the two groups with regard to locoregional recurrence-free, distant recurrence-free or breast cancer-specific survival. However, a significant trend was seen toward a better overall survival in the BCS group ($p = 0.0122$). It is to be noted that the incidence of intercurrent death was 15% in the mastectomy and 12% in the BCS group, and three deaths caused by other malignancy occurred in the mastectomy group.

4.3. *Subgroups by radiotherapy*

Table 3 shows the actuarial local recurrence rate after 5, 10 and 15 years in the two surgical groups by radiotherapy. The 15-year local recurrence rate for BCS patients without or with irradiation was 53% and 10%, respectively (RR: 0.10; $p < 0.0001$). The median time to local failure for irradiated breasts was 87.5 months (2 of 4 relapses occurred after 10 years), as compared to 38.5 months for nonirradiated breasts ($p = 0.0238$). The 15-year chest wall recurrence rate for mastectomy patients without or with irradiation was 13% and 16%, respectively (RR: 1.45; $p = 0.3965$).

4.4. *Survival after isolated local recurrence*

There were 14 isolated in-breast and 15 chest wall recurrence.

The median time to an in-breast recurrence was 47.5 months (mean, 59.9; range, 11–164 months). Thirteen of the fourteen patients with breast recurrence had invasive lobu-

Table 3 – Actuarial local recurrence[a] rate after 5, 10, and 15 years in the surgical treatment groups by radiotherapy.

Site of recurrence	Nonirradiated		Irradiated		*p*-Value	RR	95% CI
	Percent	No.	Percent	No			
Chest wall		9 of 82		12 of 81	0.3965	1.45	0.61–3.45
5 years	8		13				
10 years	13		16				
15 years	13		16				
Ipsilateral breast		10 of 19		4 of 53	<0.0001	0.10	0.03–0.33
5 years	47		2				
10 years	53		3				
15 years	53		10				

The group of reference is the nonirradiated group; *p*-Values, RR (relative risk), CI (confidence interval), and No. (number) of recurrences shown are for the entire duration of the follow-up.

[a] This category includes all local recurrence.

lar carcinoma as the histologic type of recurrence, and one had mucinous carcinoma. Breast recurrences were treated with mastectomy ($n=6$) or tumor excision ($n=8$). For five patients breast irradiation was given after tumor excision. Seven patients died of breast cancer ($n=6$) or intercurrent disease ($n=1$), and seven of them are alive with no evidence of disease. The breast cancer specific survival at 15 years was 74% without and 53% with ipsilateral breast tumor recurrence (RR, 1.73; 95% CI, 0.67–4.46; *p*, 0.2767).

The median time to a chest-wall recurrence was 30.0 months (mean, 36.1; range, 7–97 months). Surgery consisted of excision in 12 and incisional biopsy in 3 cases (multiple-diffuse recurrence). 11 patients died of breast cancer and 4 are alive with no evidence of disease. The breast cancer-specific survival at 15 years was 66% without and 22% with local recurrence (RR, 2.65; 95% CI, 1.39–5.06; *p*, 0.0089).

5. Discussion

Nowadays mastectomy and breast conservation are offered as equally effective treatments for women with early-stage ILC. However, some doubts have been expressed about the choice of treatment because of poorer results published earlier and of the insidious nature of this disease.[1,19–21] In this report, we documented our experience with ILC in a group of 235 women treated with either mastectomy or BCS who were monitored for a median of 181 months. The results of our study indicate that patients treated with mastectomy or BCS have a similar outcome at 15 years after initial surgery with regard to distant metastasis-free and breast cancer-specific survival. After irradiation, the actuarially estimated 15-year local recurrence rate in the breast or in the chest wall was 10% and 16%, respectively. There are at least four studies comparing the mastectomy with BCS for the treatment of ILC.[7–9,20] Of these, only Anwar et al.[20] found that local recurrence rate was significantly higher in patients treated with tumor excision and RT. At a median follow-up time of 168 months, the crude rate of local recurrence for mastectomy or BCS patients was 13.4% and 34%, respectively. In the other three studies the crude rate of local recurrence ranged from 2.8% to 5.4% for BCS and RT, which was similar to the local recurrence rate (3–12%) for mastectomy, at a median follow-up time of 48–60 months. There are only three studies in which ILC patients treated with BCS and RT were followed up for more than 120 months after surgery.[13–15] In these series the crude rate of local recurrence ranged from 8% to 15%. In our series the crude rate of local recurrence for irradiated BCS patients was 12%.

19 of our patients were treated with BCS alone and 10 of them (53%) developed local recurrence. In three other series, some patients were also not subjected to RT after BCS. In the study of Sastre-Garau et al.[12] the local recurrence rate was not reported for these patients. In the study of Nemoto et al.[21] the crude rate of local recurrence was 29% (4 of 14) at 48 months and in Holland et al. study[7] this rate was 13% (2 of 15), at a median follow-up time of 55 months. Information regarding local relapse rate after longer follow-up of ILC patients treated with BCS alone is not available. The NSABP B-06 randomized trial showed that after lumpectomy alone the cumulative incidence of breast recurrence was 53% at 10 years for all nonirradiated patients.[22]

Our practice was that the patients with microscopically positive surgical margin undergo re-excision. At the first surgery, 11% of our cases had positive surgical margin, and after re-excision three of them underwent mastectomy. To obtain clear surgical margins, re-excision is also recommended by others.[23,24] However, in the eighties the margins were evaluated without ink. The high numbers of in-breast failure in our nonirradiated patients indicate that tumor deposits may be left behind by primary surgery. One of the factors which increased the risk of residual disease after BCS is the insidious nature of ILC, characterized by small invasive "satellites" which appear in the 1–2 cm of otherwise uninvolved breast tissue beyond the margin of the principal tumor.[25] This phenomenon also underlines the mandatory use of RT to control microscopic residual disease and to achieve appropriate local control. In the study of van den Broek et al.[26] the risk of margin involvement was 29% after the first operation and 17% after re-excision, but there was no influence of the positive surgical margins on the risk of local recurrence after RT.

To our knowledge none of the studies compared the survival of patients with and without local recurrence in ILC. In our series, an isolated chest wall recurrence predicted significantly increased mortality (RR, 2.65; *p*, 0.0089) but in-breast recurrence did not (RR, 1.73; *p*, 0.2767). The prognosis following in-breast recurrence after BCS is much better than following chest-wall recurrence after mastectomy.[27]

Patients treated with BCS and RT may be at persistent risk of breast failure even 10 years after initial surgery.[20,28,29] In our patients treated with BCS and RT, 2 of 4 in-breast recurrences occurred more than 10 years after treatment.

6. Conclusions

The results of this study indicate that patients with early-stage ILC subjected to mastectomy or BCS have a similar outcome after long-term follow-up with regard to distant metastasis-free and breast cancer-specific survival. BCS can provide a low local recurrence rate when RT is administered. The majority of ipsilateral in breast recurrences are but those of chest-wall recurrences are not curable.

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