



Noninvasive Breast Carcinoma

Results of a National Survey by the American College of Surgeons

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This study evaluates the data of noninvasive (*in situ*) lobular (ISLC) and ductal (ISDC) carcinoma, collected from 498 hospitals in a National Breast Cancer Survey, carried out by the American College of Surgeons in 1978. ISLC and ISDC were identified in 323 (3.2%) of 10,054 female patients with lobular and ductal carcinoma, of the total of 23,972 patients with histologically proven breast cancer surveyed (1.4%). The frequency of ISLC was significantly higher (18.5%) than ISDC (2.1%) suggesting a less aggressive nature of ISLC, with a slower progression to invasion than ISDC. There was a different age distribution of ISLC and ISDC: about 80% of ISLC and 50% of ISDC were diagnosed in patients who were less than 54 years old, and the incidence showed a marked decrease in the older age groups in ISLC, whereas the incidence remained high in the following decade in ISDC. In this series there was a distinctly better five-year cure rate in the patients with ISLC (83.5%) than in the patients with ISDC (68.8%), in spite of the fact that radical surgery was performed more frequently in ISDC (67.8%) than ISLC (36.3%). The recurrence rate was five times higher (10.5%) in ISDC than in ISLC (2.5%). In

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black patients the recurrence rate (21.3%) was significantly higher in ISDC than in white patients (9.3%). In the present study there were no statistically significant differences in the five-year cure and recurrence rate in patients with noninvasive carcinoma, treated by more conservative procedures (72.9% and 8.5%) and those treated by more extensive surgeries (76.2% and 7.7%). The results of this study suggests that the biologic behavior of ISLC and ISDC may be different with regard to their propensity to invade and their overall prognosis. In contrast, the infiltrative form of lobular and ductal carcinoma, were found to have the same prognosis, regardless of the type of operative procedure performed.

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DURING THE PAST FOUR DECADES, since Foote and Stewart¹⁰ described lobular carcinoma *in situ* and simultaneously Muir²³ defined the same entity as lobular neoplasia, considerable interest has been aroused concerning the diagnosis and therapy of noninvasive carcinomas. The description and definition of the criteria for the histologic diagnosis of noninvasive (*in situ*) carcinoma, both lobular and ductal tumors, has been generally agreed upon with the exception of borderline lesions. However, controversy still exists regarding the clinical management of this breast disease. Various schemes have been proposed concerning the surgical management of patients with noninvasive

lobular and ductal carcinoma, varying from biopsy alone to radical mastectomy. The available information relating the results of therapy may be contradictory and generally based on a limited number of treated patients.^{1,4,5,18,21,22}

A recent survey, carried out in 1978 by the American College of Surgeons Commission on Cancer, collected a large number of pathologically diagnosed lobular and ductal noninvasive and invasive carcinomas from a large number of hospitals and provided current nationwide information on the management and follow-up results.

In this study, we have attempted to evaluate the incidence, race distribution and type of therapy of noninvasive lobular and ductal carcinoma, on the basis of data collected in this national survey. Review of these cases afforded us a comparison of the results of different therapeutic modalities from conservative to radical surgery used in noninvasive carcinomas. We have also attempted in this review, to study the different biologic patterns of *in situ* lobular carcinoma (ISLC) and *in situ* intraductal carcinoma (ISDC). At the same time, we compared the biologic behavior of noninvasive carcinomas with minimal invasive lobular and ductal cancers, defined as those of 1 cm or less in diameter.

It is our purpose in presenting this study to summarize the present knowledge of the disease with emphasis on recent developments that provide the participating hospitals with a possible national average which may offer a more representative picture of the management and results of noninvasive carcinoma.

Methods

In this series the data were collected from the American College of Surgeons, Commission on Cancer, long-term survey 1978. Four hundred ninety-eight hospitals with approved cancer programs from 47 states, Washington, DC and Puerto Rico supplied the actual information. An abstract was requested on each breast cancer patient which provided individual information of the disease, pathology, initial treatment, etc. Each participating hospital was requested to compile abstracts on 50 consecutive eligible patients from December 1972 backward chronologically to allow at least analysis of five-year results.

According to the extent of the disease three groups of breast cancer patients were selected for analysis:

1) *Noninvasive Carcinoma*

In situ lobular carcinoma (ISLC) and in situ intraductal carcinoma (ISDC): A cluster of cancer cells confined to the site of origin, the lobules and/or

the terminal ducts, with no evidence of micro-invasion.

2) *Minimal Invasive Lobular and Ductal Carcinoma*

Tumor of 1 cm or less in diameter, with extension to adjacent tissue.

3) *Invasive Lobular and Ductal Carcinoma*

Infiltrative tumor above 1 cm.

The invasive carcinomas were subdivided according to the absence or presence of axillary nodal metastasis.

Review of these cases allowed us to compare results of different therapeutic modalities (*i.e.*, conservative or radical surgery).

Types of surgical procedures were classified as follows: a) wedge excision or wide local excision (WE), b) total or simple mastectomy (TM), c) radical surgery: total mastectomy with low axillary dissection, modified radical mastectomy, extended radical with internal mammary dissection.

In the analysis of the five-year results, the patient status living with no evidence of disease (5 LNED) was defined as any case known to be alive and clinically free of cancer, five years from the date of initial treatment. Recurrence (R) was defined as confirmed appearance of disease following the surgical treatment, whether the patient was alive or dead within five years. Five-year follow-up information for the whole group was available in 94% of the patients and 91% of those with noninvasive carcinoma. The majority, *i.e.*, 85% of the patients surveyed, were treated in 1972 and 1971 and an additional 7% in 1970. Statistical *p* values were calculated, using Chi square test and Student's *t*-test for proportions. The percentages for the cure rates and recurrence rates were calculated from all patients originally observed.

Results

In the Breast Cancer Survey carried out by the American College of Surgeons in 1978 there were 23,972 female patients with histologically confirmed breast cancer. The present study deals with 10,054 patients with histologically confirmed noninvasive and invasive lobular and ductal carcinoma.

Incidence

Noninvasive carcinomas were identified in 323 patients: 121 lobular (37.4%) and 202 ductal (62.5%) (Table 1). Of the total of 23,972 patients with breast cancer surveyed, 1.4% were classified as noninvasive carcinoma. The incidence of noninvasive carcinomas in the lobular and ductal group was 3.2% (323 of 10,054). However, the frequency of ISLC in the lobular car-

Table 1. Distribution of Lobular and Ductal Carcinoma by Tumor Type and Size

Stage	Lobular			Ductal			Lobular/Ductal Ratio		
	No. Patients (%)	1 cm or less	>1 cm	No. Patients (%)	1 cm or less	>1 cm	Total	1 cm or less	>1 cm
Noninvasive	121 (18.5)	28 (23.1)	93 (76.9)	202 (2.1)	38 (18.8)	164 (81.2)	0.6	0.7	0.6
Invasive									
Axillary lymph node negative	326 (49.8)	56 (17.2)	270 (82.8)	5321 (56.6)	613 (11.5)	4708 (88.5)	0.06	0.09	0.06
Axillary lymph node positive	208 (31.7)	15 (7.2)	193 (92.8)	3876 (41.2)	185 (4.8)	3691 (95.2)	0.05	0.08	0.05
Total invasive	534 (81.5)	71 (13.3)	463 (86.7)	9197 (97.8)	798 (8.7)	8399 (91.3)	0.06	0.09	0.05
Total	655 (100.0)	99 (15.1)	556 (84.9)	9399 (100.0)	836 (8.8)	8563 (91.2)	0.07	0.1	0.06

cinoma group was significantly higher (18.5%) than ISDC (2.1%) in the intraductal carcinoma group ($p < 0.001$): 121 of 655 lobular carcinomas and 202 of 9399 intraductal carcinomas were of the noninvasive type. The ratio of lobular to ductal carcinoma was significantly greater ($p < 0.001$) for noninvasive cases (0.6:1.0) than for infiltrating tumors (0.06:1.0), regardless of the size of the primary tumor.

Size of the Tumor

Twenty-eight of 121 patients (23.1%) with ISLC and 38 of 202 with ISDC (18.8%) presented clinically with a mass measuring less than 1 cm, whereas their invasive counterpart were diagnosed as minimal cancers in 13.3% (71 of 534) and 8.7% (798 of 9197) respectively (Table 1).

The case percentage of ISLC (76.9%) larger than 1 cm (93 out of 121) was lower (86.7%) than that found in invasive lobular carcinomas (463 out of 534) ($p < 0.001$). In the intraductal group the percentage of noninvasive (81.2%) primary cancers more than 1 cm in size (164 out of 202) was also lower than in the invasive type (91.3%); 8399 of 9179 ($p < 0.001$).

The size of noninvasive carcinomas did not detectably influence the survival. At five years the cure rate (LNED) was not statistically different ($p > 0.1$) between the noninvasive carcinomas with tumor below 1 cm or above 1 cm: 53 of 66 were LNED (80.3%) in the group with tumors measuring less than 1 cm whereas 187 of 237 (72.8%) were free of disease at five years in the group having tumors above 1 cm. It must be noted that the size of noninvasive primary carcinomas may be relatively meaningless considering the fact that the initial diagnosis of noninvasive carcinoma, particularly of ISLC, is made mainly by chance, as an

incidental microscopic finding in a benign surgical specimen.

Axillary Node Status

Of 655 lobular carcinomas, 121 (18.5%) were noninvasive. Of 121 patients reported as *in situ* lobular carcinoma, 110 were reported as node negative, and in 11 patients the status of axillary nodes was unknown. However, 326 (49.8%) were an invasive type with negative axillary nodes and 208 (31.7%) were invasive with positive axillary nodes (Table 1).

Of 9399 ductal carcinomas, 202 (2.1%) presented as noninvasive. In the group of 210 patients with noninvasive intraductal carcinoma, eight patients (3.8%) were reported as having positive nodes. These eight patients were excluded from the analysis and all 202 patients included in this study were reported as node negative or nodal status unknown. Five thousand three hundred twenty-one ductal carcinomas (56.6%) were invasive without axillary node metastasis and 3876 (41.2%) were invasive with axillary lymph node metastasis.

Age Distribution

The mean age of patients with noninvasive lobular and ductal carcinomas was 54.3 years, approximately five years younger than minimal invasive cases with negative axillary nodes: these patients had a mean age of 59.9 years ($p < 0.01$). The highest percentage (36.8%) of noninvasive breast carcinoma was in the age group of 45–54 ($p < 0.001$). However, the age distribution of noninvasive lobular and ductal carcinoma was somewhat different in each group (Table 2). More than one-half (51.2%) of ISLC were present in the

TABLE 2. Age Distribution of Noninvasive and Invasive Lobular and Ductal Carcinoma

Age Group		Noninvasive		Invasive Lymph Node (Negative)		Invasive Lymph Node (Positive)	
		#	%	#	%	#	%
1-34	L	5	4.1	11	3.4	8	3.8
	D	8	4.0	183	3.4	132	3.4
35-44	L	29	24.0	51	15.6	38	18.3
	D	38	18.8	657	12.4	569	14.7
45-54	L	62	51.2	97	29.8	70	33.6
	D	57	28.2	1341	25.2	1104	28.5
55-64	L	18	14.9	52	16.0	50	24.0
	D	32	15.8	1254	23.6	1001	25.8
65-74	L	4	3.3	67	20.5	24	11.6
	D	41	20.3	1080	20.3	695	17.9
75+	L	3	2.5	48	14.7	18	8.7
	D	26	12.9	806	15.1	375	9.7
All ages	L	121	100.0	326	100.0	208	100.0
	D	202	100.0	5321	100.0	3876	100.0

L: Lobular
D: Ductal.

patients who were in the decade of 45-54 age, whereas only about one-quarter (28.2%) of the patients with ISDC were in the same age group.

Of the 121 ISLC, 79.3% were diagnosed in patients who were under age 54 years. This incidence showed a sharp decrease in the older groups: 14.9%, 3.3% and 2.5% in the age groups of 55-64, 65-74 and 75 and above. Of the 202 ISDC about one-half (51.0%) were present in patients under 54 years of age, and the frequency remained higher, as opposed to ISLC, in the following decades: 15.8% in the age group 55-64; 20.3% in the 65-74 age group and 12.9% above 75 years of age.

Noninvasive ductal carcinomas occurred more frequently (20.3%) than noninvasive lobular carcinomas at ages 65-74 (3.3%). No significant difference was noticed between invasive lobular and ductal in the same age group.

Location of the Tumor

The location of primary tumor of noninvasive carcinomas did not show any significant differences in regard to the side of the breast or the quadrant comparing lobular or ductal tumor type. In both lobular and ductal tumors the outer upper quadrant was most frequently involved; 56.6% and 46.1%, followed by the outer lower quadrant, 13.3% and 18.5% respectively. The invasive carcinomas showed also a similar location of the primary tumor in both lobular and ductal types with the same predominance in the lateral half of

the breast. In noninvasive carcinomas, the five-year cure rate was not apparently influenced either by the site or the quadrant of the breast involved.

The White-Black Patient Ratio

Race distribution was assessed in 305 patients with noninvasive carcinomas and in 9845 patients with invasive lobular or ductal carcinomas (Table 3). Patients of races other than white or black or in cases where race was not mentioned were excluded from this analysis. In noninvasive carcinomas, the white-black patient ratio was 12:1, a finding close (10:1) to other general hospital admissions.⁶ There were 24 noninvasive carcinomas (7.8%) in black women and 281 (92.1%) in white women.

A similar ratio was observed in infiltrative lobular and ductal carcinomas: 739 (7.5%) and 9106 (92.5%) carcinomas were present in black and white women respectively.

In the Breast Cancer Survey carried out by the American College of Surgeons in 1978, black women accounted for 9.1% of all female breast cancer patients surveyed. Tumors of larger size were more frequent in black than in white patients in both groups, regardless of whether the carcinoma was noninvasive or invasive. The white patients with noninvasive carcinoma presented with minimal sized tumors, smaller than 1 cm in 21.3% (60 out of 281) versus 8.3% in black patients (2 of 24). The same trend was observed in infiltrative lobular and ductal tumors, where 5.8% (43 of 739) of black patients presented with minimal sized tumors

TABLE 3. Distribution of Noninvasive and Invasive Lobular and Ductal Carcinoma by Race, and Size of the Tumor

Type of Tumor	1 cm or less	Above 1 cm	Total
	No. Patients (%)	No. Patients (%)	No. Patients (%)
Noninvasive			
Black	2 (8.3)	22 (91.7)	24 (7.8)
White	60 (21.3)	221 (78.7)	281 (92.2)
Total	62 (20.3)	243 (79.7)	305 (100.0)
Invasive			
Black	43 (5.8)	696 (94.2)	739 (7.5)
White	838 (9.2)	8268 (90.8)	9106 (92.5)
Total	881 (8.9)	8964 (91.1)	9845 (100.0)

TABLE 4. Distribution, Five-year Living No Evidence of Disease and Recurrence Rates, Noninvasive and Invasive Lobular and Ductal Carcinoma by Race

Stage of Disease	Lobular Carcinoma			Ductal Carcinoma		
	No. Patients	5LNED %	R %	No. Patients	5LNED %	R %
Noninvasive						
White	109	84.4	2.7	172	68.6	9.3
Black	10	80.0	20.0	14	64.3	21.3
Invasive						
White	484	55.8	26.6	8285	51.3	31.0
Black	35	42.8	45.7	663	40.4	41.3

5LNED: Five year living, no evidence of disease.
R: Five year recurrence.

smaller than 1 cm, whereas 9.2% (838 of 9106) of the white patients presented with a similar size tumor.

Five-year cure and recurrence rates in white and black patients are tabulated in Table 4. The five-year cure was similar for both races in noninvasive lobular and ductal carcinomas, regardless of the size of the tumor: 84.4% and 80.0% in ISLC and 68.6% and 64.3% ISDC were LNED at five years. However, the recurrence rate was significantly higher in black patients. In ISLC 20.0% of black patients presented with recurrence versus 2.7% of white patients. A similar high rate of recurrence (21.3%) was noticed in black patients

versus white patients (9.3%) with ISDC. In both groups, white and black, five-year cure rates for ISLC were significantly higher (84.4% and 80.0%) versus ISDC (68.6% and 64.3%). When the lobular or ductal carcinomas were invasive there were significant differences in the five-year survival (LNED) between white and black patients in both types of carcinoma: 55.8% and 42.8% in invasive lobular carcinoma and 51.3% and 40.4% in invasive ductal carcinoma, respectively.

The poorer results in black patients may be attributed to later or different clinical presentation. It is apparent that the tumors with larger size were more frequent in blacks than whites, particularly in invasive carcinomas. A definitive cause was not determinable.

Types of Surgical Procedures

Table 5 lists the initial treatment given to each of 323 patients with noninvasive carcinomas included in this study: seven patients (2.2%) had biopsy alone, 46 patients (14.3%) were treated with wedge excision, 89 patients (27.6%) underwent total mastectomy. Another 181 patients (55.9%) had radical surgeries as follows: 26 patients (8.0%) total mastectomy with low axillary dissection, 67 patients (20.7%) modified radical mastectomy, 85 patients (26.3%) radical mastectomy, 85 patients (26.3%) radical mas-

TABLE 5. Distribution, Five-year Living No Evidence of Disease and Recurrence Rates, Noninvasive and Minimal Invasive Carcinomas by Type of Surgery

Type of Surgery	Noninvasive			Minimal Invasive Lymph Node Negative			Minimal Invasive Lymph Node Positive		
	No. Patients (%)	5LNED	R	No. Patients (%)	5LNED	R	No. Patients (%)	5LNED	R
Biopsy alone	7 (2.2)	71.4	14.3	13 (1.2)	38.5	15.4	1 (0.3)	—	100.0
Wedge excision	46 (14.3)	76.1	2.2	33 (2.9)	69.7	15.1	3 (1.0)	66.7	33.3
Total mastectomy	89 (27.6)	69.7	9.0	149 (13.3)	61.7	9.4	5 (1.6)	—	80.0
Radical surgeries									
Total mastectomy with low axillary dissection	26 (8.0)	76.9	7.7	75 (6.7)	62.7	13.3	9 (3.0)	44.4	44.4
Modified radical	67 (20.7)	79.1	7.5	271 (24.2)	71.2	9.6	83 (27.6)	53.0	32.5
Radical mastectomy	85 (26.3)	74.1	8.2	555 (49.5)	73.9	10.8	197 (65.2)	53.8	30.1
Extended radical	3 (0.9)	66.7	—	25 (2.2)	72.0	4.0	4 (1.3)	100.0	—
Total radical surgeries	181 (55.9)	76.2	7.7	926 (82.7)	72.1	10.5	293 (97.1)	53.9	29.8
Total	323 (100.0)	74.3	7.7	1121 (100.0)	70.3	10.5	302 (100.0)	53.0	31.8

5LNED: Five year living, no evidence of disease.

R: Five year recurrence.

TABLE 6. Distribution, Five-year Living No Evidence of Disease and Recurrence Rates, Noninvasive and Invasive Lobular and Ductal Breast Cancer in Females According to Type of Surgery

Type of Surgery		Noninvasive Cases				Invasive Lymph Node Negative Cases				Invasive Lymph Node Positive Cases			
		No. Patients	%	5LNED	R	No. Patients	%	5LNED	R	No. Patients	%	5LNED	R
Biopsy alone	L	2	1.7	100.0	—	2	0.6	—	—	—	—	—	—
	D	5	2.5	60.0	20.0	36	0.7	30.6	30.6	49	1.3	4.1	75.5
Wedge excision	L	31	25.6	80.6	—	19	5.8	47.4	31.6	3	1.4	—	100.0
	D	15	7.4	66.7	6.7	143	2.7	39.9	30.1	24	0.6	16.7	62.5
Total mastectomy	L	44	36.4	77.3	2.3	47	14.5	63.8	8.5	5	2.4	20	80
	D	45	22.3	62.2	15.5	705	13.2	42.8	25.4	136	3.5	16.2	64.7
Total and low ax. dissection	L	8	6.6	100.0	—	19	5.9	63.1	10.5	12	5.8	16.7	58.3
	D	18	8.9	66.7	11.1	314	5.9	63.1	16.2	238	6.2	28.6	50.8
Modified radical	L	20	16.5	85.0	10.0	86	26.5	73.2	7.0	78	37.5	39.7	50.0
	D	47	23.3	76.6	6.4	1287	24.2	64.3	16.3	1028	26.5	34.6	48.0
Radical	L	16	13.2	93.7	—	144	44.3	61.8	16.7	108	51.9	43.5	46.3
	D	69	34.1	69.6	10.1	2744	51.6	66.2	17.5	2335	60.3	38.1	49.2
Radical & internal mammary	L	—	—	—	—	7	2.1	71.4	28.6	1	0.5	100.0	—
	D	3	1.5	66.7	—	78	1.5	64.1	16.7	49	1.3	42.8	38.8
Super radical	L	—	—	—	—	1	0.3	—	100.0	1	0.5	100.0	—
	D	—	—	—	—	12	0.2	83.3	8.3	13	0.3	15.4	69.2
Total	L	121	100.0	83.5	2.5	325	100.0	64.0	13.8	208	100.0	39.9	49.5
	D	202	100.0	63.8	10.4	5319	100.0	61.6	18.6	3872	100.0	35.2	50.0

5LNED: five year living no evidence of disease.
R: five year recurrence.

L: Lobular.
D: Ductal.

tectomy and three patients (0.9%) extended radical mastectomy.

In this survey about one-half (44%) of the patients with noninvasive carcinomas (142 of 323) were treated by conservative procedures and the other half (56%) underwent radical surgery (181 of 323 patients).

In minimal invasive, lobular and ductal carcinomas, with primary tumors smaller than 1 cm, radical surgery was the treatment of choice in both groups with negative and positive axillary nodes: 82.7% and 97.1%, respectively. In comparing this to all operable breast cancer treated by surgery in this national survey, radical surgery was performed in 84.9% versus 10.7% treated by conservative procedures. No one patient, included in this study, with noninvasive carcinoma, treated by radical surgery, presented with proven axillary node metastasis.

The five years LNED of noninvasive carcinomas treated by radical surgery (76.2%) did not differ statistically from those cases treated by wedge excision (76.1%) or total mastectomy (69.7%) ($p < 0.25$). The recurrence rate, at five years, in noninvasive carcinoma was also similar in the patients treated by conservative procedures (7.0%) versus patients who had radical surgery (7.7%) ($p < 0.25$). Only in a small group of seven patients who had biopsy alone did the recurrence rate reach 14.3%.

The five-year cure rates (LNED) in noninvasive, lobular and ductal carcinomas was 74.3%. This was not statistically different than those with minimal invasive, lobular and ductal carcinomas with negative axillary nodes (70.3%).

The five-year cure rate in patients with either noninvasive cancers (74.3%) or minimally invasive cancers with axillary negative nodes (70.3%) were significantly higher ($p < 0.001$) than those of patients with minimally invasive tumors with axillary lymph node metastasis (53.0%). Also, the five-year recurrence rates of noninvasive (7.7%) and of minimally invasive cancers with axillary nodes negative (10.5%) were significantly lower ($p < 0.001$) than in the group of patients with minimally invasive tumors with axillary metastasis (31.8%). Out of 323 patients with noninvasive carcinoma, 294 (91%) were followed for a five-year period and 29 patients (9%) were lost to follow-up during this period.

Five-year cure rates of patients with lobular versus ductal carcinoma are tabulated in Table 6. A statistically significant difference ($p < 0.001$) in five-year survival (LNED), was observed between noninvasive lobular and intraductal carcinoma, regardless of the type of therapy. Lobular carcinoma *in situ* has a better prognosis than *in situ* ductal carcinoma. There was a distinctly better overall five-year survival rate (LNED)

in the patients with ISLC (83.5%) than in patients with ISDC (63.8%). The recurrence rate was five times higher (10.4%) in noninvasive ductal than in noninvasive lobular carcinomas (2.5%) ($p < 0.025$). The cure rate was lower in patients with ISDC in spite of the fact that twice the number of patients (67.8%) underwent radical surgeries compared with the group of patients with LCIS (36.3%) ($p < 0.001$).

The type of surgical procedure did not apparently influence the five-year cure rates in each category of lobular or ductal carcinoma.

No statistically significant differences were observed in the five-year cure rates in patients with noninvasive lobular carcinoma treated by nonradical surgery (78.9%) from those treated by radical operations (92.9%).

Noninvasive ductal carcinomas treated by radical surgery showed no significant differences ($p < 0.25$) in five-year cure rates (71.5%) from those treated either by wedge excision (66.7%) or total mastectomy (62.2%). The recurrence rate was also similar in patients with noninvasive ductal carcinoma treated with conservative surgery (11.1%) and in those who had radical surgery (9.2%).

In this survey, four patients with ISDC of 323 with noninvasive carcinomas died from breast cancer in a period of five-year follow-up; one patient was treated with wedge excision, one had simple mastectomy with low axillary dissection, one underwent modified radical mastectomy and the fourth patient had a radical mastectomy. Out of 323 patients with noninvasive carcinoma, 11 patients died from other causes but without evidence of cancer; another six patients died due to other causes, but recurrent breast cancer was present and 11 patients died of unknown causes.

When the lobular or ductal carcinomas were invasive, no differences in the five-year cure rates were observed. Patients with invasive lobular carcinoma with negative axillary nodes presented five-year cure rates of 64.0% which were similar to those in ductal carcinoma (61.6%). Similar results were noticed at five years in lobular invasive lesions (39.9%) and ductal invasive carcinoma (35.2%) when axillary metastasis were found.

Discussion

The information obtained by the American College of Surgeons National Cancer Survey on 10,054 patients with lobular and ductal carcinomas, provided us an opportunity to gather records on a relatively large number of patients in this area of interest.

In this study, there were 323 patients with noninvasive lobular (121 patients) and ductal (202 patients) carcinomas. The overall incidence of noninvasive cancer of the breast was 1.4% of the 23,972 patients with histologically confirmed breast cancer surveyed.

Of all lobular and ductal carcinomas diagnosed, the incidence of noninvasive types was 3.2%. The frequency of noninvasive carcinoma in previously reported studies varied from 0.6% to 10.2%. We feel that such variations may reflect the limited number of cases studied.^{10,24} In a large analysis of 8,587 cases of breast cancer diagnosed in the year 1975, noninvasive carcinomas accounted for 5.3% of these cases.²⁸ The low frequency of noninvasive carcinoma encountered in this survey may reflect a more likely national figure. However, the actual incidence may not reflect the true incidence of the disease, since many patients with *in situ* lobular or ductal carcinoma might not have had a biopsy unless clinical findings such as a palpable mass or mammography called for this procedure. Also, the diagnosis of ISLC depends in part on the extent of histologic sections taken.

In recent years with increasing use of radiologic examination of the breast (mammography or xeroradiography) and expansion of breast screening programs, more cases of minimal invasive and *in situ* carcinomas, particularly of the intraductal type, are being detected long before a mass is palpated, either by the presence of microcalcifications or appearance of a new density in serial mammographic follow-up.²⁰ In one study which used a yearly mammographic follow-up in 408 women at high risk who previously had unilateral mastectomy, 12 carcinomas were diagnosed before any mass was palpable. Four of 12 asymptomatic carcinomas were noninvasive, suggesting that *in situ* carcinoma might also be detected by mammography.²⁷

In this study lobular and ductal noninvasive carcinoma exhibited a different pattern in incidence, age distribution and prognosis.

The frequency of LCIS in the lobular carcinoma group was significantly higher (18.5%) than ISDC (2.1%) in the intraductal group. Some authors have suggested that the low incidence of noninvasive intraductal cancer may be an indication of the aggressive nature of this lesion which might become more rapidly invasive than *in situ* lobular carcinoma which has a slower progression to invasion.^{12,29}

The highest number of noninvasive breast carcinomas were found in patients in the age group 45–54 (36.8%). However, there was a different age distribution of ISLC and ISDC. About 80% of LCIS were diagnosed in patients who were less than 54 years old, with more than a half in patients who were 45–54. The incidence showed a marked decrease in the following decades from 15% to 3.3% and 2.5%. The noninvasive ductal carcinoma was diagnosed in about a half of the patients under age 54 years, and the incidence remained high in the following decades.

The ratio for lobular to ductal carcinoma was greater

for noninvasive carcinomas (0.6:1.0) than for infiltrating cancers (0.06:1.0). The difference in the ratio of ISLC and ISDC may well be related to their different degree of invasiveness. In this study, the mean age of patients with noninvasive lobular and ductal carcinoma was 54.3, approximately five years younger than patients with minimal invasive carcinoma with negative axillary nodes.

Because of the relatively small number of patients in previous published series, and the complexity of the problem of noninvasive carcinomas, the surgical approach for treatment of both types is still unsettled, and understandably various schemes have been proposed for surgical management. Recommendations regarding the extent of surgery for noninvasive carcinoma have varied from biopsy alone to radical mastectomy.

Simple mastectomy, as first suggested by Foote and Stewart,¹⁰ was supported by many oncologists.^{3,19} The advocates of simple mastectomy base their viewpoints on multicentricity of noninvasive carcinoma, since many foci of ISLC and ISDC have been found in mastectomy specimens.^{2,4,5,7,10,11,21} Another opinion in favor of mastectomy is the risk that another focus of invasive carcinoma may be present at the time of diagnosis with an attendant potential cumulative risk for further development of invasive carcinoma.²¹ In a recent study the risk of occult invasive disease in patients with ISLC was found to be exceptionally low (1.2%).²⁶ An average of 15% of patients with ISLC and 39% of patients with ISDC treated by biopsy alone are reported to have subsequent ipsilateral invasive carcinoma with an average latent period of about ten years.^{1,4,18} Although the proportion of cases eventuating in carcinoma was similar (22%) in the Memorial group²¹ and Columbia¹⁴ series, the recommendation for treatment differs: the Memorial Hospital group favored simple mastectomy and biopsy of the contralateral breast and Haagensen favored a close and prolonged follow-up.^{14,21}

Taking into consideration the risk of opposite contralateral breast cancer, which appears to be no less than 15%, ipsilateral mastectomy may not offer a valid solution.³⁰ A "prophylactic" bilateral mastectomy may constitute a more drastic therapy, particularly in younger women, where this disease is more frequent. Some investigators^{2,5,6,8,18,24} recommended modified or radical mastectomy considering the remote possibility (4–6%) that the breast might harbor an occult invasive carcinoma. There have been reports of metastases in axillary nodes in an exceptional few cases of *in situ* intraductal carcinoma, where no actual infiltration of the stroma of the breast could be demonstrated.^{2,5,9,11,25}

Studies using electron microscopy have indicated that invasion is present in most cases presumed to

be noninfiltrating by light microscopic examination.²⁵ The need for extensive studies of multiple blocks and multiple levels to exclude evidence of small foci of stromal invasion is well recognized and because of the extreme difficulty of diagnosing such presence some surgeons have recommended simple mastectomy with low axillary dissection or radical mastectomy as the curative therapy.^{2,5,6,8,18,24}

In the present survey of 323 patients with noninvasive carcinoma treated by mastectomy with axillary dissection, there were no patients who presented with proven axillary metastasis.

Because of the especially favorable nature of the noninvasive lobular^{1,15,18} or ductal²² lesions, some investigators have been advocating less extensive operations,^{9,16} *i.e.*, local excision followed by a close observation.^{1,13,15,17,31} In the present series, there was no difference in the five-year cure rate (LNED) in patients with noninvasive carcinomas, treated by wedge excision (76.1%) or total mastectomy (69.7%) and those treated by radical surgeries (76.2%), either modified or radical mastectomy.

In the noninvasive lobular carcinoma, conservative surgery, either wedge excision or total mastectomy, offered five-year cure rates of 80.6% and 77.3% respectively; radical surgeries offered 92.9%. The same effect on cure rate was observed in noninvasive ductal carcinomas, treated by wedge excision (66.7%) or total mastectomy (62.2%) and those treated by radical surgeries (71.5%) ($p < 0.25$).

The recurrence rate, at five years, in noninvasive carcinoma was also similar in the patients treated by conservative procedures (7.0%) versus the patients who had radical surgeries (7.7%) ($p < 0.25$). Only in the small group of seven patients who had biopsy alone did the recurrence rate reach 14.3% and this is statistically meaningless.

In this survey about half (44%) of the patients with noninvasive carcinoma were treated by conservative procedures and the other half (56%) underwent radical surgeries. This figure is in sharp contrast with operable invasive carcinoma in the same national survey where radical procedures were the treatment of choice in 85% versus 11% treated by conservative procedures.

This study suggests that *in situ* lobular carcinoma and *in situ* ductal carcinoma are not equivalent lesions, in spite of their noninvasiveness. In this series the five-year cure rate for *in situ* lobular carcinoma was significantly higher (83.5%) than for *in situ* ductal carcinoma (63.8%), in spite of the fact that radical surgery was performed more frequently in noninvasive ductal (67.8%) than in noninvasive lobular carcinoma (36.3%). The recurrence rate was five times higher (10.4%) in noninvasive ductal than in noninvasive lobular carcinoma (2.5%) ($p < 0.025$).

In the present study four patients with noninvasive

ductal carcinoma died from breast cancer in a period of five-year follow-up; in contrast, no patient with noninvasive lobular carcinoma died from breast cancer during the same period of follow-up. The risk of subsequent development of infiltrating cancer in the breast with proven ISLC, thus appears to be substantially less than indicated by other authors.^{14,21} In a follow-up of 17.5 years only 4% of the patients developed subsequent invasive carcinoma.³¹ In spite of the relatively large number of women, reported in the literature, who have had mastectomy for ISLC, we have found only one case of local recurrence to be reported.¹³ In a review of the literature of 228 patients with ISLC followed for approximately ten years, there were nine deaths (4%) caused by invasive carcinoma.¹ Both noninvasive lobular and ductal carcinoma have a favorable prognosis versus invasive type, but in the group of noninvasive carcinomas, there is a significant difference in cure and recurrence rates between lobular and ductal carcinoma.

The results of this study thus suggests that the biologic behavior of noninvasive lobular carcinoma is different from *in situ* ductal carcinoma with regard to their propensity to invade and the ultimate prognosis. In contrast, the infiltrative form of lobular and ductal carcinoma were found to have the same prognosis regardless of the operative procedure performed.

By presenting the actual data obtained in this national survey our purpose is to emphasize the observation that conservative surgery may, in some instances, cure at least as many patients with noninvasive carcinoma as those treated by radical surgery. In spite of the fact that the present data reflects a short-term, and not a randomized study, we believe that the number of patients and data presented provide a rational basis for a surgeon to consider conservative surgery and close, prolonged follow-up in patients with noninvasive lobular carcinoma.

Considering the poorer prognosis of noninvasive ductal carcinoma, due to the more aggressive nature of this lesion, a total mastectomy with low axillary dissection or modified radical mastectomy seems indicated for this type of breast cancer.

However, further prospective studies on long-term follow-up must be conducted to determine which type of surgical therapy is the preferred choice for treatment of noninvasive lobular or ductal carcinoma.

References

- Andersen JA. Lobular carcinoma in situ of the breast. An approach to rational treatment. *Cancer* 1977; 39:2597.
- Ashikari R, Hajdu SI, Robbins GF. Intraductal carcinoma of the breast. *Cancer* 1971; 28:1182.
- Benfield JR, Fingerhut AG, Warner NE. Lobular carcinoma of the breast-1969: A therapeutic proposal. *Arch Surg* 1969; 99:129.
- Betsill WL, Jr, Rosen PP, Lieberman PH, Robbins GF. Intraductal carcinoma. Long-term follow-up after treatment by biopsy alone. *JAMA* 1978; 239:1863.
- Brown PW, Silverman J, Owens E, et al. Intraductal "non-infiltrating" carcinoma of the breast. *Arch Surg* 1976; 111:1063.
- Davis RP, Nora PF, Kooy RG, Hines JR. Experience with lobular carcinoma of the breast. Emphasis on recent aspects of management. *Arch Surg* 1979; 114:485.
- Farrow JH. Clinical considerations and treatment of in situ lobular breast cancer. *Am J Roentgenol Radium Ther Nucl Med* 1968; 102:652.
- Farrow JH. Current concepts in the detection and treatment of the earliest of the early breast cancer. *Cancer* 1970; 25:468.
- Fisher ER, Fisher B. Lobular carcinoma of the breast: An overview. *Ann Surg* 1977; 185:377.
- Foote FW, Jr, Stewart FW. Lobular carcinoma in situ: A rare form of mammary cancer. *Am J Pathol* 1941; 17:491.
- Gallager HS, Martin JE. Early phases in the development of breast cancer. *Cancer* 1969; 21:1170.
- Gillis DA, Dockerty MB, Clagett OT. Pre-invasive intraductal cancer. *Surg Gynecol Obstet* 1960; 110:552.
- Giordano JM, Klopp CT. Lobular carcinoma in situ: incidence and treatment. *Cancer* 1973; 31:105.
- Haagensen CD. Diseases of the Breast. Second edition. Philadelphia, W.B. Saunders, 1971. p. 503.
- Haagensen CD, Lane N, Lattes R. Neoplastic proliferation of the epithelium of the mammary lobules. *Surg Clin North Am* 1972; 52:497.
- Haagensen CD, Lane N, Lattes R. Lobular neoplasia (so called lobular carcinoma in situ) of the breast. *Cancer* 1978; 42:737.
- Herrman JB. Treatment of in situ mammary carcinoma. *Int Surg* 1972; 57:127.
- Hutter RVP, Footo FW. Lobular carcinoma in situ: Long term follow-up. *Cancer* 1969; 24:1081.
- Lewison EF, Finney GG. Lobular carcinoma in situ of the breast. *Surg Gynecol Obstet* 1968; 126:1280.
- Martin JE, Gallager HS. Mammographic diagnosis of minimal breast cancer. *Cancer* 1971; 28:1519.
- McDivitt RW, Hutter RVP, Footo FW, et al. In situ lobular carcinoma. A prospective follow-up study indicating cumulative risks. *JAMA* 1967; 201:82.
- Millis RR, Thynne GS. In situ intraduct carcinoma of the breast: a long term follow-up study. *Br J Surg* 1975; 62:957.
- Muir R. The evolution of carcinoma of the mammae. *J Pathol Bacteriol* 1941; 53:155.
- Newman W. Lobular carcinoma of the female breast. *Ann Surg* 1966; 164:305.
- Ozzello L, Sanpitak P. Epithelial-stromal junction of intraductal carcinoma of the breast. *Cancer* 1970; 26:1186.
- Rosen PP, Senie R, Schottenfeld D, Ashikari R. Non-invasive breast carcinoma. Frequency of unsuspected invasion and implications for treatment. *Ann Surg* 1979; 189:377.
- Rosner D, Nemoto T, Dao TL. Detection of asymptomatic breast cancer in the second breast by mammographic follow-up. A 5-year survey. *In Prevention and Detection of Cancer, part II, Detection, Volume 1, New York, M. Dekker* 1978. p. 1281.
- Smart CR, Myers MH, Gloeckler LA. Implications from SEER data on breast cancer management. *Cancer* 1978; 41:787.
- Somers SC. Histologic changes in incipient carcinoma of the breast. *Cancer* 1969; 23:822.
- Warner NE. Lobular carcinoma of the breast. *Cancer* 1969; 23:840.
- Wheeler JE, Enterline HT, Roseman JM, et al. Lobular carcinoma in situ of the breast. Long-term follow-up. *Cancer* 1974; 34:554.