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Follow-Up of Breast Cancer Stages I and II. An Analysis of Some Common Methods

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Abstract—*A retrospective analysis of the follow-up methodology was done in 343 cases of breast cancer Stages I and II, in order to ascertain the effectiveness of the explorations performed and the usefulness of the follow-up program. The actuarial probability of relapse at 6 years was 35% for the 237 patients with negative axillary nodes and 46% for the 106 patients with nodal involvement. Fifty-eight per cent of the relapses were detected by the patients themselves, 24% of relapses were found by physical examination and 9% of relapses were discovered in chest radiographs, leading to 91% of relapses diagnosed by combination of these explorations. The authors conclude that follow-up methodology for these patients could be limited to the above-mentioned methods, without significant reduction of curability or survival possibilities after relapse.*

INTRODUCTION

THE FOLLOW-UP of patients with breast cancer in order to achieve the early detection of recurrence is a topic scarcely dealt with in the literature; nonetheless, its importance—as reflected in the frequency of this neoplasm, as well as in the social and sanitary costs involved—ought not to be minimized. However, the value of follow-up to the patient is unclear, as there is no recurrence in nearly 50% of breast cancer patients, and we don't know if early detection in the asymptomatic patient would significantly prolong the survival.

The present study retrospectively analyzes 343 patients who underwent radical mastectomy, in an effort to evaluate the utility of the clinical tests and explorations routinely performed in the follow-up of patients with Stage I or Stage II disease.

MATERIALS AND METHODS

Three hundred and forty-three patients who had undergone radical mastectomy for Stage I or Stage II carcinoma of the breast were included in the study. This population consisted of the addition of 2 different series, each of them having been the object of previous studies at our center: one consisted of 237 consecutive patients with negative axillary nodes (N−), seen between December 1977 and December 1980; and the other was made up of 106 consecutive patients with axillary nodal involvement (N+), treated between December 1977 and December 1979. The average follow-up time in both groups was similar, 40 and 47 months respectively.

None of the N− patients received postoperative therapy, whereas all N+ patients received 12 courses of CMF polychemotherapy as well as 40 mg/day of tamoxifen for 12 months following surgery. Fifty-three patients from the N+ group also received postoperative radiation therapy with cobalt-60.

Follow-up visits (FUV) for N− patients were performed every 4 months during the first 2 years and subsequently every 6 months. For the N+ group FUV took place every 3 months during the first year and subsequently every 6 months. After the fifth year, FUV were done annually in both groups. Post-intervention surveillance consisted of medical history together with physical examination, chest, pelvic and skull radiographs, as well as complete blood counts and liver function tests.

The probability of disease-free survival was estimated using Kaplan and Meier's actuarial method. An analysis of the location and the clinical signs of recurrence was done. Besides, the effectiveness of the tests performed was evaluated.

RESULTS

Locoregional recurrence (LR) and/or metastases

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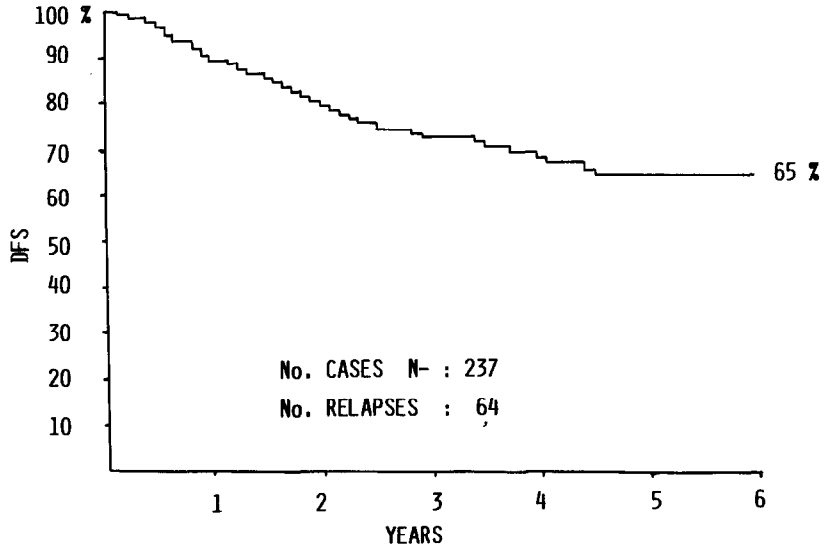

Fig. 1. Disease-free actuarial survival (DFS) of N− patients with breast cancer Stages I and II.

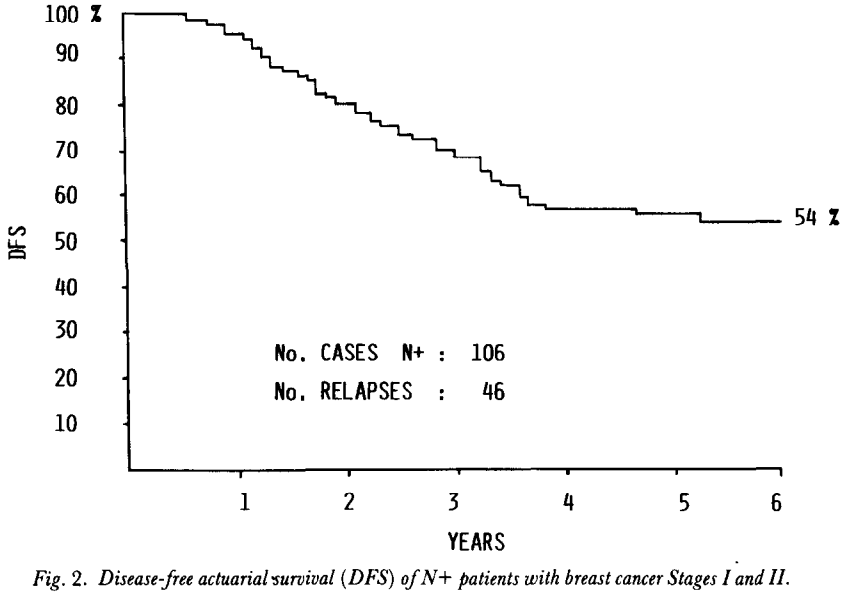

Fig. 2. Disease-free actuarial survival (DFS) of N+ patients with breast cancer Stages I and II.

were observed in 110 of the 343 patients studied. The actuarial probability of relapse in N− patients at 6 years after mastectomy was 35%. Relapse had already been detected in 64 N− patients at the time the study was done. The actuarial probability of recurrence was stable during the first 3 years but it subsequently decreased (Fig. 1). The actuarial probability of relapse in N+ patients was 46% at 6 years after surgery. LR or metastases were detected in 46 N− cases at regular intervals during the first 4 years, and a progressive decrease in frequency was observed thereafter (Fig. 2). No significant differences were observed in the site of the recurrence, between the 2 (N+ and N−) groups (Table 1). LR and/or skin or nodal metastases (SNM) were the most frequent initial sites of relapse, (31%); followed by bone (30%), and lung (17%) metastases. Initial recurrences in the liver and other sites (contralateral breast, brain, etc.) did not exceed 5% and initial multiple site recurrences were observed in only 12% of cases. The pelvis was the most frequent among the initial locations of bone metastases (38%), followed by the vertebral bodies (31%). The skull was involved in only 3 cases (7%), and in one patient it was the only location of recurrence. Pleuropulmonary involvement as the first location occurred most frequently in the form of nodular metastases (43%) and pleural effusion (36%).

Recurrences heralded by symptoms prior to FUV, in relation to the type of dissemination, are shown in Table 2. Twenty-five (54%) of 46 cases of LR and/or SNM were detected by the patients themselves. Bone dissemination was symptomatic in 30 of 39 cases (77%). Pleuropulmonary involvement produced symptoms in 16 of 28 cases (57%).

Table 1. Distribution of initial sites of relapse in N+ and N− groups

Site of relapse	Negative nodes (64 cases) No.	(%)	Positive nodes (46 cases) No.	(%)	Total (110 cases) No.	(%)
LR	16	(25)	8	(17)	24	(22)
SNM	5	(7)	5	(11)	10	(9)
Bone	19	(30)	14	(30)	33	(30)
Lung	12	(19)	7	(15)	19	(17)
Liver	2	(3)	2	(4)	4	(4)
Opposite breast	1	(2)	2	(4)	3	(3)
Other	2	(3)	2	(4)	4	(4)
Multiple site	7	(11)	6	(13)	13	(12)

Table 2. Frequency of symptoms according to the site of relapse

Site of relapse	Negative nodes S/T	(%)	Positive nodes S/T	(%)	Total S/T	(%)
LR and/or SNM	15/28	(54)	10/18	(56)	25/46	(54)
Pleura and lung	9/17	(53)	7/11	(64)	16/28	(57)
Bone	18/22	(82)	12/17	(71)	30/39	(77)
Liver	1/2	—	0/2	—	1/4	—

Table 3. Presence or absence of symptoms at the time of relapse

Symptoms	Negative nodes (64 cases) No.	(%)	Positive nodes (46 cases) No.	(%)	Total (110 cases) No.	(%)
Present	37	(58)	27	(59)	64	(58)
Absent	23	(36)	16	(35)	39	(35)
Not specified*	4	(6)	3	(6)	7	(8)

*All cases had LR and/or SNM.

Sixty-four (58%) of the 110 patients with recurrence sought medical attention between scheduled FUV (Table 3). In 36 of the cases the relapse was detected simply by means of physical examination was diagnosed during FUV in 39 patients (35%), who were free of symptoms: 19 of them presented LR and/or SNM, 9 had nodular lung metastases, 9 had bone involvement, one had liver metastases and one presented mediastinal nodal involvement. We can't state if in the remaining 7 cases the relapse had been discovered by the patients themselves, but all of them had LR and/or SNM at the time of the FUV, (Table 3). In 36 of the cases the relapse was detected simply by means of physical examination and/or chest radiographs. Thus in 100 cases (91%) the relapse was diagnosed merely by means of history, physical examination and chest radiographs (Table 4).

The total number of FUV which took place until relapse was detected, or until the study finished in patients that had no recurrence, was 2944. The low relative effectiveness of FUV in diagnosis of undetected relapses (39 cases or 1.3%, Table 5) is probably related to the large number of visits performed. The effectiveness of each method used in the follow-up surveillance is detailed in Table 6.

DISCUSSION

The follow-up of patients with breast cancer usually comprises the performance of complementary radiologic and laboratory tests in order to achieve the early detection of recurrences. Given the frequency of this neoplasm and the prolonged survival of the patients, the social and economic

Table 4. Method of detection of recurrence

Method	Negative nodes (64 cases) No.	(%)	Positive nodes (46 cases) No.	(%)	Total (110 cases) No.	(%)
Symptoms (before the FUV)	37	(58)	27	(59)	64	(58)
Physical examination (FUV)	15	(23)	11	(24)	26	(24)
Chest radiograph (FUV)	7	(11)	3	(6)	10	(9)
Pelvic and skull radiographs Blood analysis (FUV)	5	(8)	5	(11)	10	(9)

Table 5. Effectiveness of FUV on the detection of relapse

	Total patients included No.	FUV performed No.	FUV in which relapse was detected No.	(%)
Negative nodes	237	1832	23	(1.2)
Positive nodes	106	1112	16	(1.4)
Total	343	2944	39	(1.3)

Table 6. Effectiveness of the methods in diagnosis of undetected relapse during the FUV

Method	Relapses detected: Negative nodes (1832 FUV) No.	(%)	Positive nodes (1112 FUV) No.	(%)	Total (2944 FUV) No.	(%)
Physical examination	11	(0.6)	8	(0.7)	19	(0.6)
Chest X-rays	7	(0.4)	3	(0.3)	10	(0.3)
Pelvic X-rays	3	(0.1)	3	(0.3)	6	(0.2)
Skull X-rays	1	(0.05)	2	(0.1)	3	(0.1)
Blood analysis	1	(0.05)	0	(0)	1	(0.03)
Total	23	(1.2)	16	(1.4)	39	(1.3)

costs of thorough long-term follow-up are great. However, there are only a few reports in which the effectiveness of the more common methods is analyzed.

In the present series, 82% of the relapses were detected by means of history and physical examination. In 58% of cases, patients developed symptoms or discovered the recurrence themselves prior to the FUV. Symptoms of bone involvement appeared before the FUV in 77% of patients, and in the remaining 23% of cases symptoms developed shortly after diagnosis. Lung involvement—although asymptomatic when only nodular metastases were present (43%)—was always visible in the chest radiographs. Physical examination during the FUV led to the discovery of 24% of relapses undetected by the patients, corresponding in all cases to LR or SNM. Only 9% of recurrences were detected by chest radiographs and another 9% were diagnosed using other tests (pelvic and skull radiographs and blood analyses). These results coincide with those reported by Pandya *et al.* [1] and Valagussa *et al.* [2]. The actuarial probability of recurrence was highest during the first 3 years for N− patients and during the first 4 years for N+ patients.

There was a high actuarial probability of relapse in the N− patients (35% at 6 years) and a great percentage of LR and SNM in the whole series

(22% and 9% respectively). The treatments applied to the patient had been standard, and we found no explanation for these results.

Our results, as well as those reported elsewhere [3, 4], have important implications for the follow-up methodology after radical treatment for curable breast cancer. Current evidence shows that at least 59% of Stage I and II patients will not relapse at 6 years. Moreover, it is generally agreed that LR, in addition to being one of the most frequent, is the only potentially curable form of relapse. Other types of recurrence can be treated but not cured; and we don't know if their early detection would significantly increase survival. It should be stressed that all the complementary studies performed during follow-up focused on the diagnosis of incurable metastatic disease.

The fact that 91% of all recurrences from this series were diagnosed by the combination of history, physical examination and chest radiographs questions the usefulness of other tests employed, for clinical practice purposes. Besides, given their elevated cost, their continued application ought to be critically evaluated. Although we have no direct experience on serial bone scans, our opinion seems to be supported by Winchester [3] and Khandekar [5], who found a low effectiveness of bone scans in detection of asymptomatic metastases.

In conclusion, the available evidence suggests that adequate follow-up care in clinical practice should consist of history, physical examination and chest radiographs, whereas other complementary studies might be reserved for clinical research programs. Providing the patient with information about possible signs and symptoms of relapse would clearly improve the effectiveness of follow-up surveillance. Follow-up visits ought to be more frequent during the known high-risk periods, and scheduled at longer intervals thereafter. Attention should be paid to the screening of second primary cancers of the remaining breast, as well as ovary, endometrium and colorectal neoplasms, which have a higher than normal incidence in breast cancer patients [6, 7].

We think that an advisable follow-up program for clinical practice purposes should consist of history, physical examination and chest radiographs to be made every 6 months for 5 years, and every 12 months thereafter. Additionally, annual mammograms of the remaining breast and gynecological examination should be performed for screening of second neoplasms.

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