Acta Radiologica Oncology 25 (1986) Fasc. 1

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CHEST RADIOGRAPHY IN THE FOLLOW-UP OF BREAST CANCER

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Abstract

The significance of routine chest radiography in the follow-up of breast cancer was evaluated. This evaluation also included correlation of symptoms with site of intrathoracic relapse. Ten per cent of the patients developed intrathoracic recurrence; 54 per cent thereof were asymptomatic. Eighty-six per cent of the intrathoracic relapses appeared within five years. The significance of prognostic factors was obvious: a higher stage or grade gave a higher risk of intrathoracic relapses. The presence of symptoms was dependent on the site of relapse. The disease-free survival and survival after recurrence were not significantly different in symptomatic and asymptomatic patients. The contribution of routine chest radiography to the detection of relapses in asymptomatic patients was poor: one positive finding among 263 chest radiographic examinations. Routine chest radiography should be limited to high risk groups (stage II, III and grade III), preferably within the first five years after the primary treatment.

Key words: Breast neoplasms; carcinoma, follow-up, chest radiography.

In the Western World, breast cancer is the most common malignant tumor in women (6, 14). In 1979 about 1500 new cases were reported in Finland (4.8 million inhabitants), and this figure is predicted to have doubled by the year 2000 (7). In Finland, the incidence of breast cancer is highest in the southern part of the country.

The follow-up system of breast cancer patients in our country has until now been rather uniform, irrespective of individual prognostic factors. In our department signs of metastases have been looked for by physical examination, blood count, liver enzyme tests and routine chest radiography. Due to the steadily increasing number of cancer patients, and limited resources, it is necessary to rationalize the follow-up examinations according to their usefulness.

CANTWELL et coll. (4) analyzed the follow-up methods for breast cancer in a small patient material. They concluded that the value of chest radiography and radionuclide scans was limited in asymptomatic patients, compared with careful history-taking and physical examination. They did not study the survival of asymptomatic and symptomatic patients and their follow-up time was short, only 1 to 5 years.

TESORO TESS et coll. (11) analyzed the value of routine chest radiography and radiographic bone survey in a small breast cancer series. They regarded it as incorrect to delay chest or bone examinations, or both, until the onset of symptoms, because of the theoretical advantage of instituting therapy for metastases as soon as possible and thereby possibly preventing pain (9, 10). They did not compare survival of asymptomatic and symptomatic patients. The significance of routine chest radiography was also analyzed by BRØYN & FRØYEN (2). The survival of asymptomatic and symptomatic patients was not significantly different in their small material. The sizes of the groups varied greatly, and many patients were lost to routine follow-up, which may have influenced the result. The survival of symptomatic and asymptomatic patients was similar in a material reported by CIATTO & HERD-SMITH also (5). The size of their material was the same as in the present work. They concluded that routine chest radiography in the follow-up of breast cancer did not improve survival significantly as a result of early diagnosis of intrathoracic relapse.

The aim of the present investigation was to evaluate the influence of the main prognostic factors on the incidence of intrathoracic relapses and the significance of chest radiography in the follow-up of breast cancer. The evaluation further included correlation of symptoms with the site of the intrathoracic relapse.

Material and Methods

Patients. The material included 1486 female patients with breast cancer and without distant metastases at referral, admitted between 1970 and 1975 to this Department. All tumors were confirmed histologically. Four hundred and forty-eight patients (30%) were premenopausal and

Accepted for publication 21 September 1985.

1038 (70%) postmenopausal. Histopathologic specimens taken in 1970 and 1975 were re-examined by two pathologists. Of the 492 specimens taken, 413 were available. These were considered a representative sample of the whole material. Three hundred and sixty-two of these represented ductal carcinoma, and these were graded according to the WHO classification. Thirteen per cent of the cases were grade I, 56 per cent grade II, and 31 per cent grade III.

The distribution of TNM classes (pure clinical staging) is presented in Table 1. The nodal status was confirmed in 66 per cent of the patients by axillary clearance and histology. In 34 per cent, the axillary status was confirmed only clinically or by excisional biopsy. In 34 cases, information was lacking regarding tumor size, nodal involvement or both. Three of these cases developed intrathoracic recurrence.

At the end of the follow-up on 31 December 1982, 656 patients (44%) were alive and 830 (56%) were dead. Breast cancer was the cause of death in 618 patients (74%).

Staging and follow-up. Staging was based on chest radiography, liver function tests, blood count and physical examination. Radionuclide scans were not primarily performed during 1970–1975. The material was classified into clinical stages according to the TNM classification (12).

The follow-up was uniform, all patients being examined every 3rd month during the first year, every 4th month during the second, every 6th month during the next three years, every 9th month during the next five years, and finally, once a year for the rest of their lives. The patients were also instructed to contact an oncologist in case of emergency symptoms between the routine follow-up visits. The staging examinations, including chest radiography, were repeated at each follow-up visit. Appropriate radiologic, radionuclide and surgical examinations were carried out whenever recurrence was suggested or clinically evident.

Statistics. For the statistical analyses the BMDP-81 computer program (1) was used. Frequencies were calculated directly from the total patient material and cumulative relapse rates by actuarial estimates from life tables. The Mantel–Haenszel test was used to evaluate the difference between actuarial estimates. The number of chest radiograms which would have been taken according to the routine follow-up system was calculated using a program specifically designed for this purpose. Patients with other sites of first recurrence were excluded from the time of this recurrence. Differences between groups were determined on the basis of differences between means, calculating the mean error for the differences and the confidence limits.

Primary treatment. The most common surgical methods were modified radical mastectomy (66%) and simple mastectomy (27%). Breast conserving surgery was done in 7 per cent of the patients, all of whom received postoperative radiation therapy. Stage II and III patients were routinely irradiated postoperatively. Of the entire patient material, 15 per cent (mostly T1N0 patients) were not irradiated postoperatively. Radiation therapy was given with a ^{60}Co unit (83%) and with conventional roentgen rays (17%). Adjuvant chemotherapy or endocrine therapy was not used.

Secondary treatment. Patients with recurrent disease in distant sites were treated in various ways. The majority of premenopausal patients underwent ovariectomy or radiologic castration. In general, hormonal manipulations followed by single agent chemotherapy represented the

Table 1

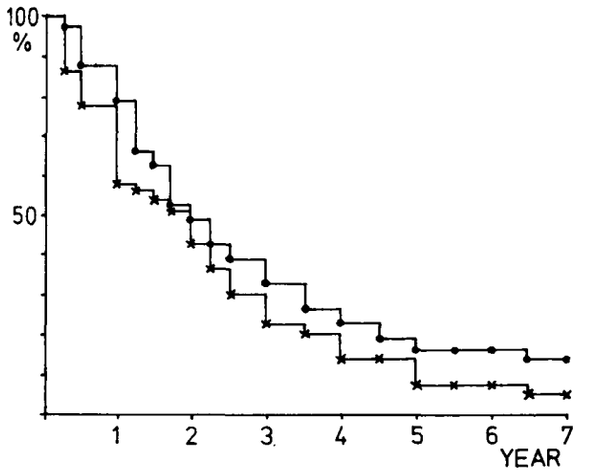
Distribution of patients by tumor size and nodal status. Data on tumor size or axillary involvement was incomplete in 34 cases

TNM class	Number of patients	Per cent
T0N0	1	0
T0N1	5	0
T1N0	284	20
T1N1	64	4
T2N0	422	29
T2N1	328	23
T3N0	106	7
T3N1	135	9
T4N0	9	1
T4N1	24	2
T1–4N2	62	4
T1–4N3	12	1
Total	1 452	100

Table 2

Intrathoracic relapses (ITR) by T and N classes and stages. Actuarial estimate at the end of follow-up. Clinical staging: 34 cases lacked information regarding tumor size, nodal status or both

	No. of cases	Per cent of ITR
T class		
T0	6	0
T1	356	8
T2	781	17
T3	274	20
T4	39	22
N class		
N−	835	12
N+	642	21
Stage		
I	285	8
II	819	17
III	348	19



Survival of asymptomatic (×) (n=82) and symptomatic (●) (n=71) patients after intrathoracic recurrence. The difference between survival curves was not significant (p=0.0552).

Table 3

Distribution of intrathoracic metastases and symptoms

Site of relapse	Asymptomatic	Symptomatic
Lung		
≤5 metastases	28	11
>5 metastases	8	4
Lymphangitis	0	1
Pleura		
Unilateral	14	18
Bilateral	3	7
Hilar adenopathy	2	2
Combined sites	4	4
Total	59	47

treatment of choice in the beginning of the 1970s. Later on, different forms of combination chemotherapy and hormonal therapy were more often applied to patients with progressive disease.

Results

Follow-up. During the follow-up, 809 (54%) out of 1 486 patients relapsed and 153 (10%) developed intrathoracic recurrence as the first recurrence. Intrathoracic recurrence included pleural metastases, parenchymal lung metastases, and mediastinal and hilar lymph node metastases. Eighty-two out of the 153 (54%) patients were asymptomatic. In 48 per cent of the cases where the intrathoracic relapse was the first recurrence it appeared within two years, in 65 per cent within three, and in 86 per cent within five years after the primary treatment. Actuarial estimates of the incidence rate of intrathoracic recurrences appear in Table 2.

It was impossible to count every radiographic examination performed, but according to the routine follow-up system, the number of radiographic chest examinations required for the entire material would have been 21 582. The number of asymptomatic findings in relation to the number of radiographic chest examinations performed would thus have been 82/21 582=1/263.

Significance of prognostic factors on intrathoracic recurrence. The significance of tumor size, axillary lymph node status and stage on the probability of intrathoracic recurrence is shown in Table 2. The relapse rate for the T1 group was significantly lower ($p<0.01$) than for the T2 and T3 groups. The group with axillary metastases at referral developed intrathoracic recurrences significantly more often ($p<0.001$). The relapse rate for stage III was also significantly higher ($p<0.001$) than for stage I.

One of the prognostic factors in breast cancer is the histologic grade. As only the specimens of two years were graded, the number of intrathoracic recurrences was small in the re-examined groups. However, the relapse rate for grade III was significantly higher ($p=0.015$) than for grade I. The relapse rates (actuarial estimates) were 2, 15 and 19 per cent for grade I, II and III, respectively, at the end of the follow-up. There were no significant differences between the age groups or between the menopausal groups concerning the rate of intrathoracic relapses.

Survival after intrathoracic recurrence. Half of the patients in whom intrathoracic metastasis appeared as the first relapse died within two years. The prognosis for asymptomatic and symptomatic patients was not significantly different (Figure).

Site of intrathoracic metastases and symptoms. Chest radiograms of 106 patients were available and reviewed by a radiologist for analysis of the site of relapse in correlation with symptoms. The presence of symptoms (mostly cough or dyspnea, or both) was dependent on the site of relapse (Table 3). Two-thirds of the patients with lung metastases (≤5 metastases) were asymptomatic. Pleural metastases caused more symptoms ($p<0.01$), especially if the pleural effusion was bilateral.

Discussion

The risk of intrathoracic recurrences was in the present investigation shown to be significantly correlated with the size of the primary tumor and the axillary lymph node status. Similar findings were reported by CIATTO & HERD-SMITH (5). Histologically more aggressive tumors also gave a higher risk of intrathoracic relapses than low-grade tumors, a result in agreement with a report by BUNTING et coll. (3).

More than half of patients with breast cancer have been reported to have symptoms at the time of recurrence, irrespective of the site (4, 8). In the present material, more than half of the intrathoracic recurrences were asymptomatic, as was the case in the report by CIATTO & HERD-

SMITH (5). Only one-third of the patients with intrathoracic relapses were symptomatic in the materials of TESORO TESS et coll. and VALAGUSSA et coll. (11, 13).

The presence of symptoms was found to be dependent on the site of the intrathoracic relapse, and pleural metastases caused symptoms more often than lung metastases (≤5 metastases). A similar finding was reported by TESORO TESS et coll. (11). The pleura is sensitive to pain and pleural effusion often causes dyspnea.

The contribution of routine chest radiography to the detection of an asymptomatic relapse is poor. Although the examination is inexpensive, radiographic evaluation is time-consuming and constitutes a substantial part of the radiologic work for an oncology department, where breast cancer patients are frequent.

Small tumors usually respond better to treatment than large tumors (9, 10). In the present analysis, however, the survival rates of symptomatic and asymptomatic patients were not significantly different, and similar findings were reported by BRØYN & FRØYEN (2) and CIATTO & HERD-SMITH (5). The patients were not randomized for secondary treatment in these studies. In the present series there were more pleural metastases among the symptomatic patients, but the prognosis of these metastases did not differ from other intrathoracic metastases. The difference between survival rates of asymptomatic and symptomatic patients which might be caused by diagnostic delay is probably so small that several thousand patients would be required to demonstrate it. The preceding disease-free survival was the same in symptomatic and asymptomatic patients, and BRØYN & FRØYEN (2) and SCANLON et coll. (8) reported a similar observation in their materials. Most metastases will probably cause symptoms soon after their appearance.

If chest radiography is performed routinely, it should, according to the author, be concentrated to the high risk groups (stage II and III and grade III) and after five years from primary treatment radiography of the chest should not be performed in any asymptomatic patient. The few metastases which do appear after this time can be found on the basis of symptoms, and an earlier detection would probably not influence survival essentially.

It is important that patients, during the follow-up, should feel safe and confident. A good doctor–patient relationship with sufficient time for conversation can give a better support than routine chest radiograms of questionable value.

ACKNOWLEDGEMENTS

The investigation was supported by grants from the Finnish Cancer Society. The author would also like to thank Docent P. Virkkunen for reviewing the chest radiograms.

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