

Results of Postoperative Radiotherapy for Breast Carcinoma

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Between December 1983 and December 1989, twenty-five breast carcinoma patients were treated with surgical resection and postoperative radiotherapy at Inje University Seoul Paik Hospital. Twenty-three of 25 were evaluable and there were 7 patients with stage II, 14 patients with stage III, and 2 patients with stage IV. Twenty-one patients were treated with modified radical mastectomy and the remained 2 patients with simple mastectomy. The follow-up period ranged from 2 to 8 years. The local control rate was 83% for the entire group. The local control rates for each stage were 100% (6/6) for stage II, 73% (11/15) for stage III, and 100% (2/2) for stage IV. The number of metastatic axillary nodes was a good predictor of locoregional control. It was 100% for the patients with 0-3 metastatic nodes and 72% for more than 4 nodes, respectively. The 5-year overall survival rate for the entire group was 59%, and the disease-free survival rate was 32%. The 5-year survival rates for each stage II, III and IV was 83%, 59% and 50%, respectively. The distant metastasis occurred in 10 out of 23 patients and the most common site was bone. The results indicate that postoperative radiotherapy continues to play an important role in the primary management of the high-risk breast cancer patients.

Key Words: Breast cancer, Postoperative radiotherapy

INTRODUCTION

Breast cancer is considered as a systemic disease. The overall incidence of distant metastases reported by the previous studies ranged from 37% to 60%^{1,2)}. However, a proportion of patients tend to have persistent locoregional disease without dissemination. If these proportion of patients had effective postoperative radiotherapy, there is a reduction of locoregional recurrence, and thus, also a significant reduction of distant metastases and a trend toward improved overall survival^{3,4)}. The randomized clinical study by Host et al⁵⁾ suggests that there is a subset of patients who may benefit in survival as well as local control by adding a postoperative radiotherapy. Danoff et al⁶⁾ and other authors report that adjuvant chemotherapy does not show advantage in local-regional control when compared to mastectomy alone.

We analyze 23 patients with primary breast carcinoma treated with mastectomy followed by radiotherapy to find a subset of patients who gets benefit from postoperative radiotherapy.

METHODS AND MATERIALS

Between December 1983 and December 1989,

Twenty-five primary breast carcinoma patients were treated with surgical resection and postoperative radiotherapy at Inje University Seoul Paik Hospital. All patients were proved to have breast carcinoma histologically. Of them, two patients were excluded from this study due to incomplete treatment. Three patients were lost for follow-up at 2, 2 and 6 months, respectively. There were 7 patients with stage II, 14 patients with stage III, and 2 patients with stage IV. The distribution of patients by T and N status is seen in Table 1. Of the 23 patients, 21 underwent a modified radical mastectomy and 2 underwent a simple mastectomy. Table 2 remarks the distribution of patients by stage and surgical procedure.

The indications of chest wall irradiation were the

Table 1. Distribution of Patients by Primary and Nodal Status in 21 Patients with Modified Radical Mastectomy

	N0	N1	N2	N3	Total
T1	-	-	2	-	2
T2	2	3	5	1	11
T3	-	4	3	-	7
T4	-	-	-	1	1
Total	2	7	10	2	21

presence of metastatic tumor in the axillary nodes, the large size (>5 cm) of primary tumor, the medial lesion, and the suspicious or positive resection margin. The chest wall was irradiated using parallel opposed tangential fields and the regional nodes were including the axillary nodes, supraclavicular nodes and internal mammary nodes treated using one anterior-posterior beam by 4 MV Linear accelerator. The majority of the patients received 5000 cGy to 5220 cGy in 5.5 to 6 weeks to the chest wall and the regional nodes, and boost doses of 1000 cGy to the tumor bed, if indicated.

Table 2. Distribution of Patients by Surgical Procedure and Stage

Surgery	Stage			Total
	II	III	IV	
MRM	7	12	2	21
SM	-	2	-	2

MRM; modified radical mastectomy, SM; simple mastectomy

Table 3. Locoregional Relapse Rates by Primary Tumor Size and Number of Pathologic Lymph Nodes

No of nodes	Primary tumor size			Total
	<2 cm	2-5 cm	>5 cm	
0	-	0/2	-	0/2
1-3	-	0/3	-	0/3
>4	1/2	1/6	3/10	5/18
Total	1/2	1/11	3/10	5/23

The fourteen patients received adjuvant systemic chemotherapy consisting of a cytoxan, methotrexate, and 5-fluorouracil (CMF).

The follow-up period ranged from 2 to 8 years. Follow-up was performed at a regular interval, 3-months interval within 1 year after completion of treatment and then interval of 6 months. At each visit, patients have taken careful physical examination, complete blood count, blood chemistries and chest roentgenography. Mammography, whole body bone scintigraphy, computed tomography and other studies are performed, if indicated.

The overall and disease-free survival rates were calculated using the Kaplan-Meier method. The significance of survival differences was measured by the log rank test.

RESULT

All patients were female. The ages of patients ranged from 31 to 70 years (median; 43 years), with 65% of the patients being less than 50 years at the time of diagnosis. All the patients complained of palpable breast mass (23/23), associated with pain in 3 patients, nipple discharge and retraction in one patient. The most common location of mass at presentation was upper outer quadrant of breast, occurring in 57% (13/23) of patients.

The overall locoregional control rate is 83%, and when assessed by stage, is 100% (6/6) for stage II, 73% (11/15) for stage III, and 100% (2/2) for stage IV. Table 3 gives the incidence of locoregional relapse related to primary tumor size and number of pathologic lymph nodes. The higher

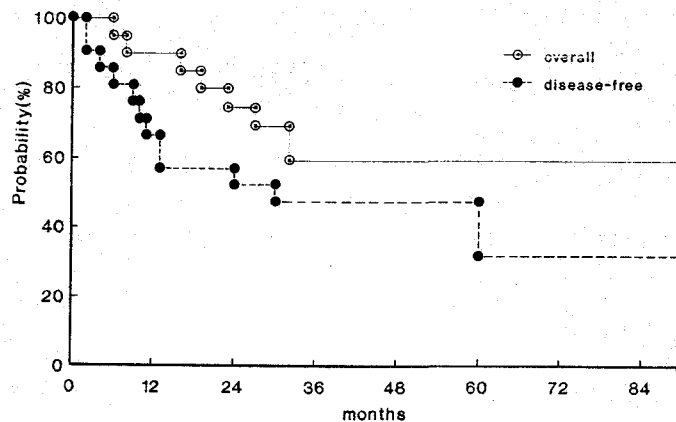


Fig. 1. The overall and disease-free survival rate for the entire patient.

relapse rates are found in the patients with greater than 5 cm of the primary tumor size and more than 4 of the number of metastatic axillary lymph nodes. Eighty percent of relapses are developed within 24 months after radiation therapy.

The overall survival and disease-free survival rates for the entire study group are 59% and 32% at 5 years, respectively (Fig. 1). There is statistically significant difference in survival between stage II, III, and IV revealed 83%, 59% and 50%, respectively (Fig. 2). There is statistically significant difference in survival between stage II and III ($p < 0.1$). But in stage IV, we can't find significant difference due to small number of patients. One out of two patients in stage IV is alive with a persistent disease for 27 months.

The survival rates are analyzed by the primary tumor size (Fig. 3). The patients with less than 2 cm, 2 to 5 cm, and more than 5 cm of tumor size revealed 50%, 60% and 50% 5-year survival rate, respectively. There data did not show significant difference between each tumor stage due to small number of patients.

Fig. 4 shows the survival rates by the number of metastatic axillary lymph nodes. The 5-year survival rates in patients with no metastatic nodes, 1 to 3 metastatic nodes, and 4 or more metastatic nodes are 100%, 67%, and 48%, respectively.

The distant metastasis are noted in 10 out of 23 patients. The most common site is bone (39%), and next common sites follow lung, liver and pleura. Twenty-five percent of metastases are associated

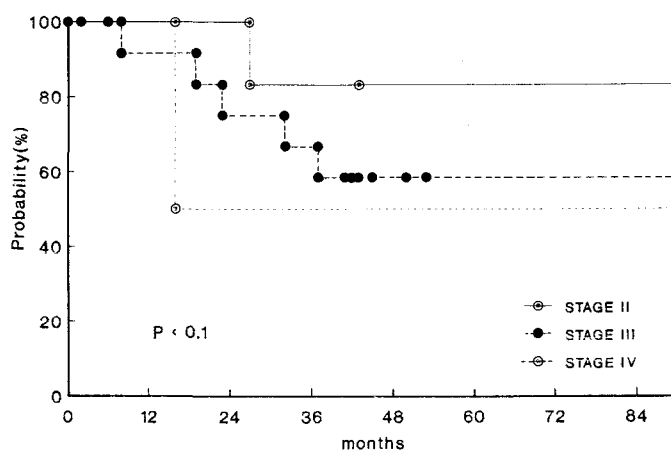


Fig. 2. 5-year survival rate by stage.

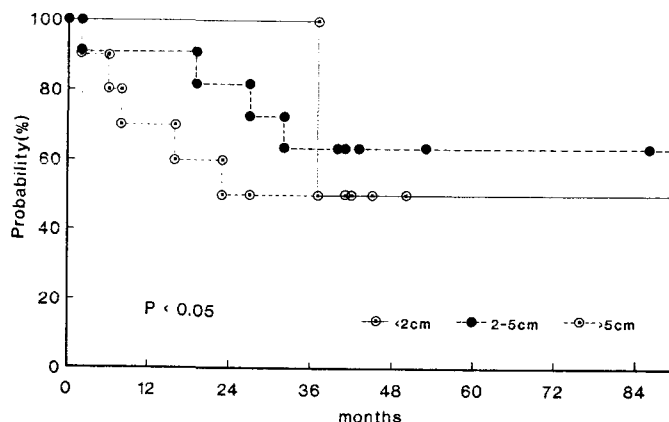


Fig. 3. survival rate by primary tumor size.

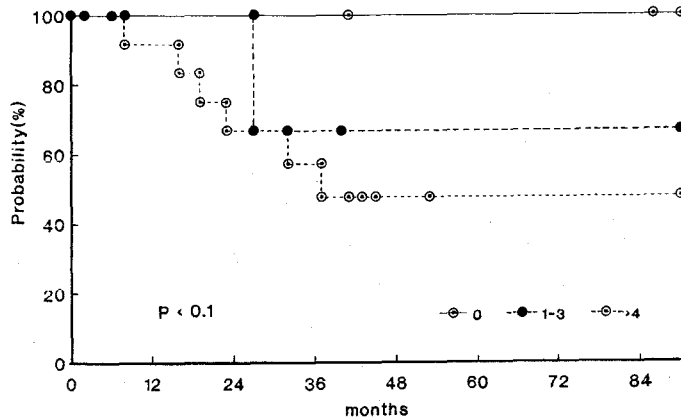


Fig. 4. Survival rate by number of metastatic lymph nodes.

with locoregional relapse.

Acute reactions include mild to moderate degree of esophagitis, trachitis and skin reaction. Lymphedema of arm is noted in one patients, and mild degree of radiation pneumonitis is developed in two patients. There is no treatment-related death.

DISCUSSION

Although breast carcinoma is considered as a disseminate disease few patients failed locoregionally without systemic disease. Adjuvant chemotherapy has been used for operable breast carcinoma to reduce the locoregional recurrence as well as to treat the disseminated disease⁶⁻⁸). Several recent studies⁹⁻¹¹) have identified a subset of patients who remain at high risk for isolated locoregional recurrence despite chemotherapy, and the reported incidence of such a recurrence is 15-36% with chemotherapy alone. A review of the Eastern Cooperative Oncology Group Trials¹²) revealed a 15 and 19% incidence of isolated local-regional recurrence at 3 years for patients with 4 or more positive nodes or T3 primary tumors.

Many studies continue to demonstrate the ability of adjuvant radiotherapy to decrease the incidence of locoregional recurrence following mastectomy in a high risk group of patients^{13,14}). Griem et al³) have documented the decreased locoregional recurrence rate by adding adjuvant radiotherapy to mastectomy in a high risk group of patients (5% vs 12%, $p < 0.01$). Stockholm Trial¹⁵) reported that 7% (46/639) of irradiated patients have experienced a locoregional recurrence, compared to 26% (84/321) of surgery alone group,

showing a highly significant difference ($p < 0.01$). Hortobagyi et al¹⁶) reported that locoregional recurrence rates are 29% for the patients with surgery and 19% with additional radiotherapy. Muss¹⁷) demonstrated that only 1.4% (1/72) of patients who had been administered postoperative radiotherapy after chemotherapy developed local recurrence, as opposed to 14% (14/99) of those treated with chemotherapy alone, and neither relapse-free nor overall locoregional relapse rate, which is comparable to other data. Local control in breast carcinoma correlates with the extent of axillary node involvement and other factors, such as, size of primary tumor, presence of lymphatic invasion, clinical stage, histologic grade, nuclear grade, estrogen receptor, and blood vessel invasion^{18,19}). Grohn et al²⁰) suggest that the axillary nodal status is of great prognostic significance in locoregional control. Irrespective of the type of treatment, the patients with negative nodes have a recurrence rate of 27% as compared with 52% with positive nodes. In Stockholm trials¹⁵), the corresponding cumulative incidence of locoregional recurrence for the patients with metastatic lymph nodes was 13% after postoperative radiotherapy versus 45% by surgery alone ($p < 0.001$). In our series, the incidence of locoregional relapse in patients with more than 4 axillary nodes is 28%. Locoregional recurrence rate in our data is slightly higher than other results with postoperative radiotherapy, but lower locoregional recurrence rate than the usual surgical group.

Several randomized trials¹⁸⁻²⁰) failed to show an

improved survival with an addition of radiation therapy compared with surgery alone. Stockholm trial¹⁵⁾ showed that the survival difference of 5%, between irradiated and non-irradiated patients at eight years, was not statistically significant. However, a few clinical studies with postoperative radiotherapy demonstrated improvement of survival rate, especially in patients with medially located lesion or metastatic lymph nodes. In our data, the overall and disease-free survival rate are comparable to those of other data.

Metastatic spread from carcinoma of the breast can be present in a variety of organs. The most common site of metastases is bone. If persistent residual or recurrent local disease increase the incidence of dissemination, then the addition of radiation therapy would reduce locoregional failure and therefore enhance the likelihood of survival. Group of patients with positive axillary nodes receiving postoperative radiotherapy had a significantly lower rate of distant metastasis and a reduction in breast cancer deaths. Wallgren et al²¹⁾ showed significant lower rate of distant metastases for node positive patients following radiotherapy (47% at 11 years) than in control group (60%, $P=0.01$).

Acute complications of radiotherapy include erythema of the treated skin, occasionally with moist desquamation, mild to moderate degree of arm edema, radiation pneumonitis, and rib fracture which occurred in a small proportion of patients. Significant long-term complications are uncommon.

Based on our results and those of others, we believe that postoperative radiotherapy contributes to significant reduction of locoregional control in the patients with breast carcinoma, and increase the survival in a subset of patients.

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= 국문초록 =

유방종양에서 수술방사선치료의 결과

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1989년부터 1989년까지 인제대학교 의과대학 서울백병원에서 25명의 환자가 수술 및 수술 방사선치료를 받았다. 25명의 환자가 고찰이 가능하였고, 이중 II병기에 7명, III병기에 14명, 그리고 IV병기에 2명이 속해있었다. 21명의 환자가 변성근치유방절제술을, 2명의 환자가 단순유방절제술을 실시하였다. 추적관찰기간은 2년에서 8년이었다. 전체군에서의 국소치유율은 83%이었다. 전이된 액와임파절의 수가 국소치유에 영향을 미치고 있었다. 전이된 임파절이 없거나 3개 이하의 임파절을 갖고 있는 환자의 국소치유율은 100%이고, 4개 이상을 갖고 있는 환자에서는 72%이었다. 전체환자군의 5년 생존율은 59%이고 5년 무병생존율은 32%이었다. 각 병기에 따른 5년 생존율은 II병기에서 83%, III병기에서 59%, IV병기에서 50%이었다. 원격전이는 23명중 10명에서 발생하였고 가장 빈발부위는 골부위였다. 결론적으로 수술방사선치료가 실패율이 높은 유방종양환자의 치료에서 중요한 역할을 하고 있었다.