Radiotherapy in Locoregional Recurrent Breast Carcinoma

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Thirty eight women with recurrent breast carcinoma involving chest wall and/or regional lymph nodes after surgery with or without systemic therapy were treated with radiation between 1979 and 1986. Among them, 5 patients were excluded from analysis because of incomplete treatment. The median follow up of survivors was 30 months (randged 1-79 months). Fifteen (45%) patients had their disease confined to the chest wall and eighteen patients had lymph node involvement as some of their locoregional recurrent disease. Within 36 months after the initial treatment, 87 % of recurrences manifested themselves. All patients had radiotherapy to at least the site of involvement. In 8 patients, recurrent tumors were treated with complete excision followed by radiation. Of the remaining 25 patients, 18 (72%) had complete response (CR) following radiotherapy. The actuarial 3-year survival of all patients following locoregional recurrence was 50%. Three year survival was 24% in those 25 patients who had recurrences within 24 months of the initial treatment. For those 8 patients whose recurrences occurred after more than 24 month disease free interval, the 3-year survival was 100%. For those patients with recurrences confined to chest wall alone, 3-year survival was 57%. The patients who had lymph node involvement as part of their locoregional recurrences had a 43% 3-year survival. The majority of them developed distant metastases. Those patients who had a CR showed 63% 3-year survival. On the other hand, 1 year survival was only 33% for those patients who had a less than CR. Three patients developed carcinoma of the contralateral breast following radiotherapy. Three year survival following locoregional recurrence was 40% for patients whose initial treatment for their primary breast carcinoma was surgery and adjuvant systemic therapy. For those patients whose primary breast carcinoma was treated by surgery alone, the 3-year survival following locoregional recurrence was 71%. In patients who had subsequent recurrence after radiotherapy, the actuarial survival was 25% at 2 years.

Key Words: Radiotherapy, Breast cancer, Recurrent

INTRODUCTION

A significant proportion of breast carcinoma patients treated with mastectomy will ultimately present with recurrent tumor involving the chest wall and/or the regional lymph node areas as the first sign of relapse. Donegan et al[1] reported chest wall recurrence as the first sign of relapse in 80 out of 704 patients undergoing a radical mastectomy. Fisher et al[2] reported loco-regional recurrence as the first evidence of relapse in 10.4% of 654 patients treated with radical mastectomy.

The role of radiotherapy in the treatment of isolated loco-regional recurrence of breast carcinoma after mastectomy is quite important. Aberizk et al[3] have reported 42% of 5 year actuarial probability of local control after treatment. Janjan et al[4] have pronounced 65% of loco-regional contol, Deutch et al[5] have reported 78.5% of complete response rate. Donegan et al[1] and Haagensen et al[6], both recommended radiotherapy as the treatment of loco-regional recurrence.

However, 5 year survival was less than 12% in both series. Bedwinek et al[7,8] and more recently Deutch et al[5] have reported 5 year survival of 36% and 34.6%, each. And they have emphasized the

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importance of agressive radiotherapy in the management of loco-regional recurrent breast carcinoma.

In this report, we review our experiences in treating patients with loco-regional recurrence after mastectomy. The purpose of this study is to assess more fully the results of radiotherapy with respect to local tumor control and overall survival. In addition, we analyze the patterns of failure after radiotherapy in an attempt to understand better the nature of isolated loco-regional recurrence and to identify patients who might benefit from such treatment.

MATERIAL AND METHOD

Thirty eight women with locoreginal (LR) recurrent breast carcinoma were treated with radiotherapy at the Department of Therapeutic Radiology, Seoul National University Hospital between March 1979 and December 1986. Of them, 5 patients were excluded; two patients had incomplete treatment, two patients because of lung metastases during radiotherapy, and remaining one patient had been excluded because of histology of cystosarcoma phylloides. Therefore, 33 patients were analyzed.

Table 1. Patient Characteristics

	No. of pts (%)
Stage	
II	18 (55)
IIIA	9 (27)
IIIB	4 (12)
unknown	2 (6)
No. of axillary node	
0	7 (21)
1–3	7 (21)
≥4	8 (24)
unknowm	11 (34)

Table 2. Site of Recurrence

Single site	No. of pts (%)	Multiple sites	No. of pts (%)
CW	15 (45)	CW, SCL	3 (9)
SCL	3 (9)	CW, AX	4 (12)
AX	3 (9)	CW, SCL, AX	2 (6)
		SCL, AX	3 (9)
Total	21 (64)	Total	12 (36)

All patients had isolated LR recurrences of breast carcinoma after previous mastectomy with or without adjuvant systemic therapy. And none of them had received radiotherapy as a initial treatment. Surgical staging and axillary lymph node status at the time of mastectomy are shown in Table 1.

The site of locoregional recurrencs were classified into three; chest wall (CW), supraclavicular area (SCL), and axilla (AX). Twenty-one patients (64 %) had recurrent disease confined to only one site. The chest wall was the most common site of LR recurrence (Table 2). Twelve patients had recurrences involving two or more sites. The majority of cases of recurrent tumor became evident within 2 years of mastectomy (Table 3). By 3 years, 87% of the patients had recurrent tumor.

Therapy for the initial breast carcinoma was surgery alone in 14 patients (42%), surgery and chemotherapy in 14 patients, and five patients were treated with surgery and hormonal manipulation.

The recurrences were diagnosed by excisional biopsy in 13 patients and by incisional biopsy in 4 patients (Table 4). All the patients were treated with radiation for their locoregional recurrent tumors. In addition, 12 patients also received systemic therapy either right before or after radiotherapy. In the

Table 3. Interval from Operation to Recurrence

Interval (year)	No. of pts. (%)	Cumulative %
≤ 1	16 (48)	48
1 – 2	9 (27)	75
2 – 3	4 (12)	87
3 – 4	1 (3)	90
4 – 5	1 (3)	93
5 – 6	2 (6)	100

Table 4. Present Treatment

	No. of pts (%)
Biopsy	
no	16 (48)
excision	13 (40)
incision	4 (12)
RT alone	12 (36)
RT + chemotherapy	6 (18)
RT + hormone	6 (18)
RT + ?	9 (27)

remaining 9 patients, we have no information about further treatment because they were referred to other hospital soon after radiotherapy.

Of the 15 patients who had chest wall recurrence only, 4 patients received radiotherapy to chest wall alone and 11 patients to chest wall and lymphatic area. Nine patients with recurrences in chest wall and lymphatic area had irradiation of the chest wall and lymphatic area. Of the 9 patients with recurrences in lymph node only, 7 had radiotherapy to chest wall and lymphatic area and two patients received radiotherapy to involved area only. Both of these latter two patients received adjuvant systemic therapy (Table 5).

Radiation was delivered with 6-15 MeV electron and/or Co-60 gamma ray. Patients were typically treated to a dose of about 5,000 cGy in 25-28 fraction over 5 weeks to the chest wall and/or draining lymph node region. Additional irradiation of 1,000-1,500 cGy was given to gross tumor sites.

RESULTS

We have reviewed the radiation response in 25 patients excluding 8 patients who had been biopsied completely by excision of their single recurrent tumor. In 18 patients(72%), there was complete diappearance of all the locoregional recurrent tumors following radiotherapy. Five patients (20%) had a partial response. Of the 18 patients who had a complete response, 12 had subsequent locoregional recurrences (Table 6).

The 3 year survival after treatment for locoregional recurrence was 50%, 3 year NED survival was 29%, and the 3 year locoregional control rate was 50% (Fig. 1).

We reviewed the factors that seemed to affect the survival. Patients whose initial therapy prior to development of recurrence was surgery alone did fairly well with post-recurrence 3 year survival of 71 %. Surprisingly, patients whose initial therapy was surgery and systemic therapy had a poor 3 year survival subsequent to recurrence (40%) (Fig. 2). The interval from initial therapy to recurrence affected survival. Patients whose disease recurred after 2 year survival from mastectomy had a 100% 3-year survival in contrast to 24% for the patients whose LR recurrence occurred within 2 years of initial therapy ($p<0.05$). Survival was especially

Table 5. Radiation Treatment

Site (No. of pts)	Treated volume		
	CW only	CW+LN	LN only
CW only (15)	4 (2)*	11 (1)	—
CW + LN (9)	—	9 (3)	—
LN only (9)	—	7 (4)	2 (2)

* ( ) ; No. of pts received adj. systemic tx.

Table 6. Response

Response	No. of pts (%)
CR	18/25 (72)
continuous control	6/18 (33)
subsequent recurrence	12/18 (67)
PR	5/25 (20)
MR	1/25 (4)
NR	1/25 (4)

Table 7. 3 Year Survival by Interval to Recurrence

Interval (year)	No. of pts	3 YSR (%)
≤ 1	16	20
1 – 2	9	32
2 – 3	4	100
> 3	4	100
Total ≤ 2	25	24
Total > 2	8	100

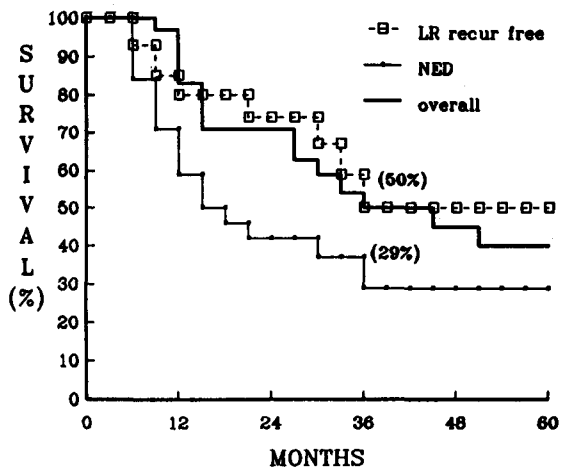

Fig. 1. Survival of recurrent breast carcinoma. The overall 3-year survival after treatment for locoregional recurrence was 50%, 3-year NED survival was 29%, and the 3-year actuarial locoregional control rate was 50%.

poor for patients with a recurrence within 1 year of initial treatment (Table 7).

There was no relationship between survival and the treatment modality after recurrence (Table 8). Patients whose locoregional recurrence was limited just to the chest wall did fairly well with 3-year survival of 57% and 3-year NED survival of 36% (Table 9). Patients with recurrence in the lymph node area did poorly with 43% of 3-year survival, and none of them lived 3 year without evidence of disease (Table 10).

Of the 18 patients with recurrence in lymph nodes, 61% developed ultimately distant metastases compared with 33% in isolated chest wall recurrence group. Patients whose locoregional recurrence was limited to lymph node area had 3-year survival of 31%. Patints with a single site of locoregional recurrence had 50% 3-year survival and this was not different from 3 year survival of patients with multiple site involvement (Table 11).

Patients with a CR had 3 year survival of 63%, and patients who had a less than CR did very poorly with 1 year survival of 33%. And the latter group, most of them died with distant metastases within 2 years (Fig. 3). The 3 year survival was 37% in

Table 8. Survival by Treatment

Treatment	No. of pts	3 YSR (%)
RT alone	12	52
RT + Syst. Tx	12	52

Table 9. Isolated Chest Wall Recurrence (N=15)

Subsequent result	No. of pts (%)
Recurrence	
LR only	2 (13)
LR + DM	1 (7)
DM only	4 (26)
contralateral	1 (7)
3 year NED survival	36%
3 year survival	57%

Table 10. Lymph Node Recurrence N=18

Subsequent result	No. of pts (%)
Recurrence	
LR only	2 (11)
LR + DM	5 (28)
DM only	6 (33)
contralateral	2 (11)
3 year NED survival	0
3 year survival	43%

Table 11. 3 Year Survival by Site of Recurrence

Site	No. of pts	3 YSR (%)
CW only	15	57
SCL only	3	–
AX only	3	–
Total single site	21	50
Multiple sites	12	50
All CW	24	56
All SCL	11	63
All AX	12	43

Table 12. Site of Subsequent LR Recurrence

	No. of pts (%)
Within field	6 (67)
Out of field	1 (11)
Ipsilateral not specified	2 (22)

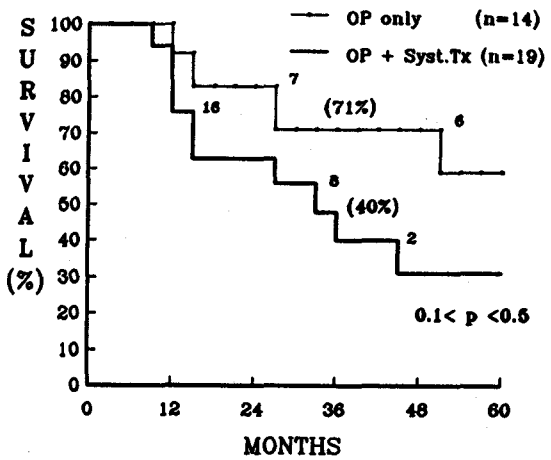

Fig. 2. Survival by initial treatment. Patients whose initial therapy prior to development of recurrence was surgery alone did fairly well with post-recurrence 3-year survival of 71%. Surprisingly patients whose initial therapy was surgery and systemic therapy had a poor 3-year survival subseguent to recurrence (40%). ($0.1 < p < 0.5$).

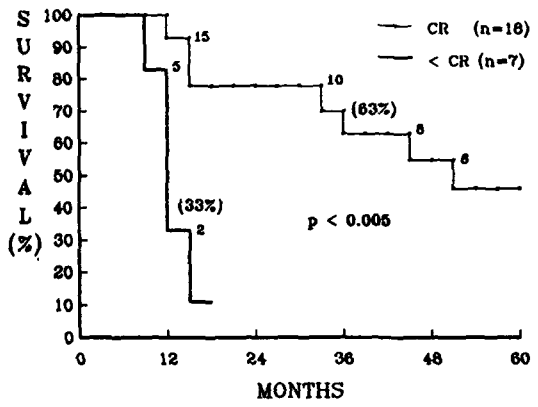

Fig. 3. Survival by response. Patients with a CR had a 3-year survival of 63%, and patinets who had a less than CR did very poorly with a 1-year survival of 33%. And, In the latter group, all died with distant metastases within 2 years of recurrence. ($p < 0.005$).

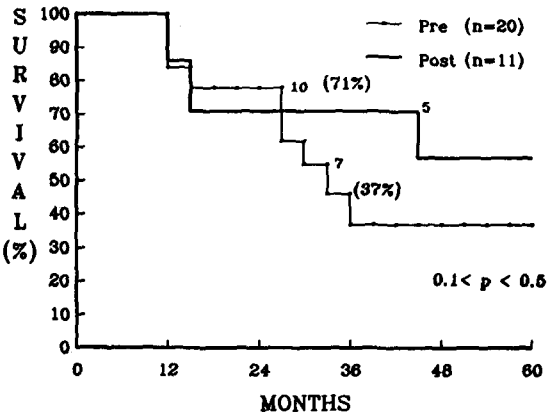

Fig. 4. Survival by menopausal status. Three year survival was 37% in premenopausal women and 71% in postmenopausal women at the time of recurrence. ($0.1 < p < 0.5$)

premenopausal women and 71% in postmenopausal women according to the status at the time of recurrence (Fig. 4).

The pattern of subsequent locoregional recurrence was reviewed. All 9 patients failed in ipsilateral site; 6 patients (67%) within radiation field and 1 patient out of field. The majority of patients came to have distant metastases with bone being the most common site; 3 year actuarial distant metastasis free survival was 30%.

Three patients developed tumor involving opposite breast following locoregional recurrence. It is not possible to state whether the contralateral breast tumors represented metastatic involvemnt or new primaries. However, all of them ultimately developed other evidence of metastases (Table 13). Twenty patients who showed subsequent recurrence had a 2-year survival of 25% (Fig. 5).

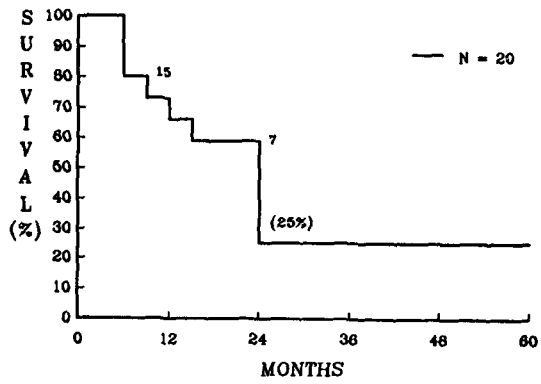

Fig. 5. Survival after subsequent recurrence. Twenty patients who showed subsequent recurrence had a 2-year survival of 25%.

DISCUSSION

The results of this retrospective study confirm the conclusion of others concerning the overall poor prognosis of locoregional recurrent breast carcinoma. The great majority of the patients ultimately develop distant metastases and die of tumor. However, the actuarial 3-year survival in this series is 50%. This is rather similar to the overall 5-year survival of 34.6% reported by Deutch et al for patients with isolated locoregional recurrent breast carcinoma[5]. For patients with isolated chest wall recurrence, the 3 year survival is 57%. These results support the aggressive treatment of locoregional recurrent breat carcinoma in hopes of achieving at least long term locoregional control.

Factors associated with a relatively high likelihood of 3-year survival following locoregional recurrence were recurrence confined to the chest wall and a long disease free interval following initial therapy. Factors that had little, if any, influnce on survival following locoregional recurrence were initial treatment that did not include systemic therapy and menopausal status at the time of recurrence. The poor survival of the patients who were initially treated with surgery and systemic therapy

Table 13. Contralateral Breast Carcinoma

Pt	Stage	Recurred site	Subsequent Tx	Status
1	II	AX + SCL	horm. Tx*	35 Mo dead
2	IIIB	AX + SCL	RT**	9 Mo dead
3	IIIB	AX	RT + horm Tx + chemo Tx***	60 Mo dead

* Hor. Tx = hormonal therapy
** RT = radiotherapy
*** Chemo Tx = chemotherapy

seemed to be related to the earlier onset of distant metastasis.

From this retrospective review, it is not possible to define the role of systemic therapy in the management of locoregional recurrence. Although there was no clear benefit of systemic therapy for recurrence in this study, the systemic therapy administered varied widely and there probably some selection factors involved in determining who received systemic therapy in addition to radiotherapy. Aberizk et al[3] have emphasized that local radiotherapy should not be used routinely as a initial treatment for patient who develop locoregional recurrence soon after mastectomy, since these patients typically manifest systemic metastasis after such treatment. Janjan et al[4] reported that addition of chemotherapy produced a trend toward improved disease free survival and irradiation should be followed by elective aggressive chemotherapy.

The question arises whether the likelihood of freedom from distant metastasis and survival would be improved by an increased level of local tumor control. In a report from Chen et al[9] in which somewhat higher doses of radiotherapy were used, survival was not greatly improved. Aberizk et al[3] pronounced that locoregional recurrence after mastectomy was nearly always associated with systemic involvement and increase in local tumor control would be unlikely to result in improved survival.

Neverthless, in our study, overall response rate is 92% (CR; 72%), and 3-year actuarial locoregional control rate is 50%. And patients with CR has higher survival rate than patient with PR or less than PR.

It must be emphasized that patients who have locoregional recurrent breast carcinomas are at high risk for further locoregional recurrent disease and distant metastasis. Further locoregional recurrence involving the chest wall should be treated aggressively since there have been occasional long term disease free survivors following re-irradiation and/or adjuvant systemic therapy[3].

CONCLUSION

We analyzed 34 patients with loco-regional recurrent breast carcinoma treated at Department of Therapeutic Radiology, Seoul National University Hospital between March, 1979 and December, 1986. Within 3 year after the initial treatment, 87% of recurrences manifested themselves. After radiation to locoregional recurrent tumor, the response rate was 92% (CR; 72%). Overall 3-year survival and 3 year NED survival were 50% and 29%, respectively.

Three year actuarial locoregional control was 50 %, and 3-year actuarial distant metastasis free survival was 30%. Favorable prognostic factors were recurrence confined to chest wall and long disease free interval following initial treatment. Factors that had little, if any, influence on survival were initial treatment (not include systemic therapy) and menopausal status (postmenopausal women).

In conclusion, the importance of controlling locoregional recurrent breast carcinoma by radiation cannot be overemphasized, not only because it improves the quality of life, but also because patients with controlled disease displayed significantly better survival rates. In addition, because most of locoregional recurrent breast carcinoma developed distant metastasis, a combination of aggressive local therapy and intensive multiagent chemotherapy can alter the natural history of patients with isolated locoregional recurrent breast carcinoma.

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= 국문초록 =

국소 재발된 유방암의 방사선치료

서울대학교 의과대학 치료방사선과학교실

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방 영 주 • 김 노 경

외 과 학 교 실

최 국 진

국소적으로 재발된 유방암의 경우, 근래에 와서 치료법의 발달로 관해율도 증가되고, 또한 환자의 수명도 연장시킬 수 있다는 보고가 증가되고 아울러 관심도 높아지고 있는 상태이다. 따라서 이런 국소 재발된 유방암을 가진 환자의 특성과 치료에 대한 실패양상, 그리고 예후에 영향을 미치는 인자들을 분석하여 이들 환자에 대한 치료에 도움이 되고자, 서울대학교 병원에서는 1979년에서 1986년까지 치료받은 총 33예에 대해서 분석을 하여 다음과 같은 결과를 얻었다. 15예(45%)에서 흉벽에 국한되어 재발하였고, 18예가 임파절에 재발을 하였다. 초기 치료후 36개월만에 87%가 재발을 보였다. 완전절제를 받아 방사선치료에 대한 판정을 할 수 없었던 8예를 제외한 25예에서 72%(18예)가 방사선치료 후 완전관해를 보였다. 국소재발 후 3년 동안의 생존율은 50%였다. 초기 치료후 2년 이내 재발한 환자들의 3년 생존율은 24%였고, 2년 이후 재발한 경우는 100%였다. 흉벽에만 재발한 경우, 3년 생존율은 57%였고, 임파절에만 재발한 경우는 43%였다. 후자의 경우 대부분이 원격전이를 보였다. 완전관해를 보인 예와, 그렇지 않은 예에서는 각각 63%의 3년 생존율, 그리고 33%의 1년 생존율을 보였다. 3명의 환자가 대측 유방에 암을 보였다. 원발성 유방암에 대해서 수술과 전신치료를 함께 받은 경우는 3년 생존율이 40%였고, 수술만 시행한 경우는 71%였다. 방사선 치료후 후속적 재발을 보인 경우의 2년 생존율은 25%였다.