

Results of Three-Dimensional Conformal Radiation Therapy for the Treatment of a Solitary Sternal Relapse of Breast Cancer

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Purpose: To evaluate the response and survival rate after three-dimensional conformal radiation therapy (3D-CRT) of patients with a solitary sternal relapse of breast cancer.

Materials and Methods: Seventeen patients between May 1996 and June 2005 were evaluated with the salvage 3D-CRT treatment of a solitary sternal relapse of breast cancer. The treatment fields included the gross tumor volume with 2 cm margins. The total radiation dose was 35.0~61.5 Gy (biologic effective dose of 43.7 ~ 76.9 Gy₁₀ using an α/β ratio of 10 Gy), with a daily dose of 1.8~3.0 Gy. The tumor response was evaluated by the change in maximum tumor size via follow up CT scans 1~3 months after the completion of treatment.

Results: An objective tumor response was achieved in all patients, with a complete response in 5 patients and a partial response in 12 patients. The 5-year overall survival rate was 51.9% (median survival time: 27 months), and the most important factor affecting overall survival was the disease-free interval (interval from primary surgery of breast cancer to the development of sternal metastasis): The 5-year overall survival rate was 61.8% for patients with a disease-free interval ≥ 12 months and 0.0% for patients with disease-free interval < 12 months ($p=0.03$).

Conclusion: The response to 3D-CRT was good in patients with solitary sternal relapse of breast cancer. Particularly, patients with long disease-free interval from primary surgery survived significantly longer than patients with short disease-free interval from primary surgery.

Key Words: Solitary sternal relapse, Three-dimensional conformal radiotherapy, Breast cancer

Introduction

Bone is a frequent site of initial relapse after curative surgery in patients with breast cancer.¹⁾ About 20~40% of bone metastases from breast cancer are presented as solitary lesions initially^{2,3)} and the sternum accounts for 5~34% of solitary skeletal metastases.²⁾ Although the sternum is a frequent site for solitary relapse in patients with breast cancer,

the optimal treatment for these patients is still unknown. The current study is to report the results of the 3D-CRT in patients with solitary sternal relapse of breast cancer.

Materials and Methods

1. Patients

Seventeen patients with solitary sternal relapse of breast cancer treated with 3D-CRT from May 1996 to June 2005 were evaluated. The clinical characteristics of these 17 patients are listed in Table 1. The median time from primary surgery of breast cancer to the development of sternal relapse was 37 months (range, 10~117 months). Six patients had chest wall irradiation before the salvage radiation treatment to the sternum after primary breast surgery: three had chest wall

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Table 1. Patients and Tumor Characteristics

Characteristics	Number of patients (%)
Age	
Range (median)	32~57 (43) years
≥40 years	11 (64.7)
<40 years	6 (35.3)
Initial tumor stage*	
Stage I/II	13 (76.5)
Stage III	4 (23.5)
Pathology of the tumor at primary breast surgery	
IDC [†]	17 (100.0)
Interval from primary surgery to sternal relapse	
Range (median)	10~117 (37) months
≥12 months	14 (82.4)
<12 months	3 (17.6)
Symptoms at relapse	
Pain	11 (64.7)
Mass	2 (11.7)
Vocal cord palsy	1 (6.0)
No symptom	3 (17.6)

*Initial tumor stage: AJCC Cancer staging system 6th edition,
[†]IDC: invasive ductal carcinoma

irradiation using tangential field, 3 had chest wall and supraclavicular fossa irradiation and no patient had internal mammary lymph node irradiation. The previous irradiation dose was 50.4~64.8 Gy with a daily dose of 1.8 Gy. Measuring from the skin surface, 2 to 4 cm-wide area was overlapped with previously irradiated field.

All patients took the chest computer tomography (CT) scan. Among them, 8 patients were histopathologically diagnosed by biopsy of the metastatic lesion and another 9 patients were diagnosed by bone scintigraphy and positron emission tomography (PET). After the radiation therapy, 2 patients received further chemotherapy, 6 patients received hormone therapy and 9 patients were followed without further treatment.

2. Radiation therapy

The radiation therapy was designed with a three-dimensional CT-based computer treatment planning using 4-MV X-rays or 9 MeV electrons from a linear accelerator. The treatment fields included the gross tumor volume with 2 cm margin. Fifteen patients were treated using a 3-field arrangement with a 4 MV photon and 2 patients were treated using a single-field arrangement with a 9 MeV electron. The

radiation field arrangement was decided according to the depth of lesions and the physician's preference. A fraction size ranged from 1.8 to 3 Gy with 5 fractions per week. The total radiation dose was 35~61.5 Gy which was equivalent to a biologically effective dose of 43.7~76.9 Gy₁₀ with an α/β ratio of 10.

3. Follow-up

The radiation response was determined using CT scans one to three months after completion of treatment. The response was evaluated with RECIST (Response Evaluation Criteria in Solid Tumors) criteria: Complete disappearance of lesion was defined as a complete response (CR), more than 30% reduction of the longest diameter of lesion was defined as a partial response (PR), more than 20% increasing the longest diameter of lesion or the appearance of new lesion was defined as a progressive disease (PD) and others defined as a stable disease (SD).

The treatment related morbidity was determined by RTOG (Radiation Therapy Oncology Group) toxicity criteria.⁴⁾

4. Statistical analysis

The statistical analyses was performed with SAS programs (version 8.01, SAS Institute Inc., Cary, NC., USA). Survival time was measured in months, beginning from the start of radiation therapy using the Kaplan-Meier method, and survival was compared using the log-rank test for some variables.

Results

1. Response to radiation therapy

An objective tumor response was achieved in all patients with complete response in 5 patients (29.4%) and partial response in 12 patients (70.6%). Among the 11 patients who complained of pain in the peristernal area at initial presentation, 5 patients experienced a complete relief of the pain and 6 patients experienced a partial relief one to three months after completion of the radiation therapy. One patient who suffered from hoarseness due to vocal cord palsy showed normal vocal cord movement after the radiation therapy.

2. Survival

The median follow-up time was 25 months. The median

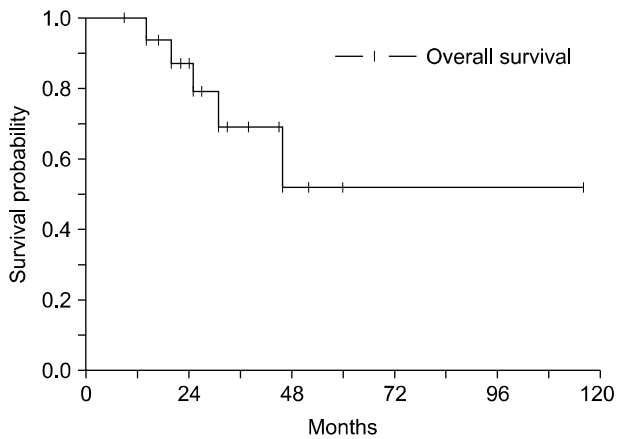


Fig. 1. Overall survival of all 17 patients.

overall survival time, 3-year and 5-year overall survival rate was 27 months, 67.5% and 51.9%, respectively (Fig. 1). The overall survival rate was significantly affected by disease-free interval (interval from primary surgery of breast cancer to the development of sternal relapse): The 3-year and 5-year overall survival rate for patients with disease-free interval ≥ 12 months was 82.5% and 61.8%, respectively. No patients with disease-free interval < 12 months survived 3 years ($p=0.03$) (Table 2). The 5-year local control rate was 64.5% (median survival, 24 months). During follow-up, 3 patients had local disease progression, 10 patients developed distant metastasis other than the sternum and 2 patients had both local disease progression and distant metastasis.

3. Toxicity

Fourteen patients had grade 1 dermatitis, which was recovered several months after completion of radiotherapy. Although six patients had chest wall irradiation before the salvage radiation treatment to the sternum, no patients had osteoradionecrosis or skin necrosis. There were no patients who experienced radiation pneumonitis.

Discussion and Conclusion

Patients with solitary sternal relapse of breast cancer achieved a long-term survival after radiation therapy in the current study. Patients with metastases confirmed to the sternum have longer survival⁵ because the sternum lacks communication to the paravertebral venous plexus, which

Table 2. Univariate Analysis for Overall Survival

Factor	Number of patients (%)	3-year survival rate (%)	p-value*
Age			
≥ 40 years	11 (64.7)	75.0	0.10
< 40 years	6 (35.3)	53.3	
Initial tumor stage [†]			
I/II	13 (76.5)	65.2	0.80
III	4 (23.5)	100.0	
Systemic therapy after sternal radiotherapy			
Yes	9 (52.9)	71.4	0.75
No	8 (47.1)	70.0	
Disease-free interval [‡]			
≥ 12 months	14 (82.4)	82.5	0.03
< 12 months	3 (17.6)	0.0	
Radiation dose (BED [§] Gy ₁₀)			
≥ 65	7 (41.2)	68.5	0.78
< 65	10 (58.8)	76.9	

*p-value corresponding to log-rank analysis, [†]Initial tumor stage: AJCC Cancer staging system 6th edition, [‡]Disease-free interval: interval from primary surgery of breast cancer to development of the sternal metastasis, [§]BED: biological effective dose

carries tumor cells to the pulmonary circulation.⁶ Many of sternal relapse were caused by local tumor invasion from either the primary site or adjacent lymph nodes,⁷ so they are frequently presented as solitary lesion unlike other bone metastasis.² These features make effective local control desired. However, there is a paucity of literature examining the results of local treatment of solitary sternal metastase.

Noguchi et al.⁸ performed sternectomy in nine patients with solitary sternal relapse of breast cancer and reported that the median survival time was 30 months after the sternectomy, which was longer than the survival time in patients with other bone metastases. In this current study, the median survival time was 27 months and the 5-year overall survival rate was 51.9%. These results were comparable to Noguchi's surgical result. Sternectomy is an option for patients with solitary sternal relapse of breast cancer, but the morbidity and mortality associated with sternectomy^{9~12} should be considered. The 3D-CRT enables delivering high radiation dose to the target without excessively irradiating surrounding normal tissues, thereby decreasing treatment-related morbidity.^{13,14} In this study, there was no severe complication

except mild radiation dermatitis. Although it is difficult to decide whether surgery or radiation therapy offers a better treatment result for solitary sternal relapse, radiation therapy should be considered as a reasonable option due to its comparable survival results and little morbidity.

Our study results showed that the objective tumor response and subjective pain relief was excellent. All patients showed decrease of the tumor size more than 30% and all patients with sternal pain experienced pain relief. This good response following radiation therapy is consistent with previous reports. Chung et al.¹⁵⁾ reported that 90.5% (19 patients/21 patients) of patients with a sternal or parasternal recurrence could achieve a complete response following radiation therapy. Because they included 14 patients who were followed without CT scan, it is unclear whether their result was superior to our outcome. Anyway, based on previous and current studies, radiation therapy in patients with sternal relapse showed favorable results with respect to decrease in the size of the mass and relief from pain.

Time interval between the primary surgery of breast cancer and the sternal relapse significantly affected overall survival rate by univariate analysis in the current study. The 5-year overall survival rate was 61.8% for patients with disease-free interval ≥ 12 months and 0.0% for patients with disease-free interval < 12 months. Patients with long disease-free interval from primary surgery survived longer after radiation therapy for solitary sternal relapse. The extended survival of these patients could be attributed to the indolent nature of some patients' disease, however the radiation therapy might have played crucial role in cure of some patients. Although systemic treatment, such as hormone therapy or chemotherapy after local radiation therapy did not affect overall survival rate in this study (Table 2), effective systemic treatment may be necessary because of frequent systemic metastases after radiation therapy of sternal relapse.

We cannot make conclusions which treatment modality is optimal in patients with solitary sternal relapse of breast cancer from this study, because this study was performed retrospectively in small number of patients. There are several treatment options for solitary sternal relapse of breast cancer: concurrent radiochemotherapy, as reported in other study,¹⁶⁾ surgery with or without chemotherapy and particle radiotherapy which increases the biologically effective dose in the

tumor without raising the dose to the adjacent normal tissue.^{17,18)} A further trial of multimodality therapy is necessary to establish whether aggressive local therapy can help to achieve long-term survival and to select optimal treatment in metastatic breast cancer limited to the sternum.

3D-CRT provides patients with pain relief and decrease of the tumor mass with minimal treatment related morbidity in patients with solitary sternal relapse of breast cancer. Patients with long disease free interval from primary surgery could achieve long-term survival after radiation therapy for solitary sternal relapse of breast cancer.

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국문초록

흉골에 단독 전이된 유방암의 삼차원 입체조형 방사선 치료 성적

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목적: 본 연구는 흉골에 단독 전이된 유방암 환자들에 대하여 삼차원 입체조형 방사선요법을 적용한 치료 성적에 대해 알아보고자 하였다.

대상 및 방법: 1996년 5월부터 2005년 6월까지 유방암의 흉골 단독 전이 병변에 대해 구제적 방사선 치료를 받은 17명의 환자를 분석하였다. 방사선 치료 범위는 종양으로부터 2 cm 여유를 두었으며 치료 선량은 하루 1.8~3 Gy로 총 35.0~61.5 Gy이었다. 종양 반응은 방사선 치료 종료 후 1~3개월에 시행한 컴퓨터 전산화 단층촬영영상으로 평가하였다.

결과: 전체 환자 중, 5명이 완전반응을, 12명이 부분반응을 보여, 모든 환자들이 방사선 치료에 객관적 반응을 보였다. 환자들의 5년 생존율은 51.9%, 중앙 생존기간은 27개월이었다. 환자들의 생존율은 유방암의 초기 수술일로부터 흉골 전이가 발견되기까지의 무병 생존기간에 영향을 받았는데, 무병 생존기간이 12개월 이상인 환자들의 5년 생존율은 61.8%이었던 반면, 무병 생존기간이 12개월 미만인 환자들의 5년 생존율은 0.0%였다($p=0.03$).

결론: 흉골에 단독 전이된 유방암 환자들의 방사선 치료에 대한 반응은 우수하였다. 유방암의 초기 수술로부터 흉골 재발이 발생하기까지의 무병 생존기간이 긴 환자에서 방사선 치료 후 생존율이 양호한 것으로 나타났다.

핵심용어: 흉골전이, 삼차원 입체조형방사선치료, 유방암