

A Comparison Between Radiotherapy on Breast Tissue and The Complications Associated with Modified Radical Operation Procedures

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Abstract

Breast cancer is a female malignant tumor. With improved diagnosis rate, surgery is the preferred alternative. We aim to compare the complications of breast-conserving surgery plus radiotherapy with the complications of modified radical mastectomy in 186 patients with stage I breast cancer. 186 patients were equally assigned into two groups, 98 patients with breast-conserving surgery received 5-6 periods of radical radiation therapy after six periods of CMF (cyclophosphamidu, methotrexate, and fluorouracil) and 86 patients received chemoradiotherapy after modified radical mastectomy. Our results revealed that the complications of breast-conserving surgery were significantly less than that of the modified radical mastectomy, such as upper limb lymphedema, intercostobrachial nerve syndrome, shoulder movement limitation, axillary vein and thrombus injury. However, there were no statistical differences between the overall survival rate and the local recurrence rate of both. In conclusion, breast conserving surgery combined with axillary radiotherapy displays fewer complications compared to modified radical mastectomy with axillary lymph node dissection (ALND).

Key words: breast cancer, radiotherapy, modified radical operation, efficacy

Introduction

In recent years, breast cancer incidence is increased significantly and surgery remains main treatment approach for breast cancer. In addition, the traditional radical breast resection surgery and modified radical surgery brought great harm to the patient's healthy such as upper limb lymphedema, rib, shoulder and arm nerve comprehensive syndrome, limited shoulder function and other complications. Therefore, it is of great clinical significance to explore a way to treat the patients' quality of life, and to explore a kind of minimally invasive, safe and reliable treatment, and can effectively improve the quality of life of patients. Compared with ALND, sentinel lymph node biopsy or axillary radiotherapy has similar efficacy with ALND, and has a low complication rate. It may be possible to replace ALND.

This research intends to compare the complications of breast-conserving surgery plus radiotherapy with modified radical mastectomy in breast cancer patients. From June 1993 to December 2008, 186 stage I breast cancer patients

of Enshi State Central hospital were recruited in our research, including 98 cases receiving breast-conserving surgery and 86 cases receiving modified radical mastectomy.

Methods

186 female patients with negative lymph node and breast tumor less than 2cm were included in this research. According to UICC (1988) standard, it is the phase I. The inclusion criteria were: early breast cancer; Stage I; no treatment; Aged 18-75. The exclusion criteria were: pregnancy; Metastasis or stage IV; Male breast cancer. Abiding by the voluntary principal, the 186 patients were allocated into two groups in a non-randomized manner. 98 patients aged from 23 to 69 (median age is 45) received breast-conserving surgery. 88 patients aged from 24 to 73 (median age is 48) received modified radical mastectomy. All of those tumors were single lump. In breast-conserving surgery group, the lump glands were in superior lateral quadrant from 70 patients in lower outer quadrant from 16 patients, in upper inner quadrant from 6 patients and in lower inner quadrant from 6 patients. In modified radical mastectomy group, 52 patients' lumps were in superior lateral quadrant, while 16 in lower outer, 10 in upper inner and 10 in lower inner quadrant.

Breast-conserving surgery group: Excision of

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primary tumor and the breast tissue 2cm around, no ALND. The resected specimens were frozen immediately, and all the resection margin was negative. 6 weeks of CMF chemotherapy (500mg/m² cyclophosphamidu +40mg/m² methotrexate +600mg/m² fluorouracil) was given to 107 patients from the first day after surgery. 9 patients failed to complete the 6 cycles of chemotherapy due to its side effects. Radiotherapy was performed in the third week after surgery. The routine radiotherapy dose is 40-50Gy in the whole breast tangential field and breast primary tumors, here we added another 20-26Gy dose to the primary breast lesions. The radiotherapy dose was 40-44Gy in the internal mammary lymph node fields, 60-66Gy in the axillary lymph nodes anterior posterior field and 44-50Gy in the supraclavicular and subclavian lymph nodes fields and.

Modified radical mastectomy group: Patients received ALND except for primary lesion dissection. After surgery, 95 patients received the same chemotherapy therapy as that of the Patients in breast-conserving surgery group. 7 patients gave up the treatment due to the side effect of chemotherapy. Among these 88 patients, the pathological results of postoperative lymph nodes were negative in 50 patients, 1-3 positive lymph nodes in 23 patients who didn't accept chemotherapy of upper limb and armpit, more than 4 positive lymph nodes in 15 patients who received about 40-50Gy chemotherapy in upper limb and armpit.

Follow-up: once every three months within two years after operation, once every six months for more than 2 years, once a year for more than 5 years. The complications, local recurrence, tumor free survival rate (DFS) and survival time of 186 patients were recorded. The follow-up time varied from 13 to 222 months and with a median of 148 months until December 2011. Of the 186 patients, 8 were lost in the follow-up including 3 in surgery group and 5 in modified group. The overall follow-up rate was 95.7%.

Statistical analysis

Chi-square test analyzed the difference between 2 groups. Survival rates were analyzed using survival analysis and iron test. $P < 0.05$ indicates a statistical significance.

Result

Breast-conserving surgery group: Of 98 patients, 3 were lost in follow-up, 4 died (4.2%) of bone metastases, pleural metastasis or multiple metastases, 4 relapsed (4.2%), 5 (5.1%) suffered from different degrees of upper limb lymphedema,

3 (3.1%) developed inter-costobrachial nerve syndrome, 4 (4.2%) suffered from different degrees of shoulder movement limitation, 1 (1.1%) developed axillary vein injury or thrombosis, 3 (3.1%) developed axillary fibrosis. Both sides of the breast were in normal form and there is a better quality of life. The form of breast was normal.

Modified radical mastectomy group: Of the 88 patients, 5 were lost in follow-up, 4 (4.8%) died of bone metastasis, pulmonary metastasis, hepatic metastasis or multiple metastasis, 5 (5.6%) relapsed, 22 (25.0%) suffered from different degrees of upper limb lymphedema, 48 (54.5%) developed intercostobrachial nerve syndrome, 25 (28.4%) suffered from different degrees of shoulder movement limitation, 28 (31.8%) developed injury of axillary vein or thrombus, 5 (5.6%) developed fossa axillaris fibrosis. Owing to excising one breast, the morphological changes in the chest wall and 68 (81.9%) patients lost their female feature that their psychological health and life quality was severely influenced (sheet2 and sheet 3).

The comparison between breast-conserving surgery and modified radical operation: The 5-year survival was 96.4% and 95.9% ($P > 0.05$). The five-year local recurrence rate was 3.6% and 3.5% ($P > 0.05$). The 10-year local recurrence rate was 4.2% and 4.0% ($P > 0.05$) without differences between these 2 groups (sheet 4). The occurrence rate of upper limb lymphedema was 5.1% and 26.5% respectively ($P > 0.05$). The occurrence rate of intercostobrachial nerve syndrome was 3.1% and 54.5% ($P > 0.05$) while that of shoulder movement disorder was 4.2% and 30.1% ($P > 0.05$). The occurrence rate of axillary vein and thrombus injury was 1% and 31.8% ($P > 0.05$) while that of fossa axillaris fibrosis was 3.1% and 5.1% ($P > 0.05$). Our data illustrates that the occurrence rate of upper limb lymphedema, intercostobrachial nerve syndrome, shoulder movement limitation and axillary vein or thrombus injury in patients with modified radical operation was higher than patients with surgery. However, no statistical significance was found in fossa axillaris fibrosis rate between 2 groups. By analyzing the data, we speculated that only 15 patients receiving the modified radical mastectomy might be the reason. Therefore, more patients receiving modified radical mastectomy should be collected to verify the findings in the future.

Discussion

If the ALND were not performed, the earliest recurrence rate of axillary lymph nodes will be 20%. For patients with invasive breast cancer, following ALND has a 5.4% survival advantage over that

without doing this. For patients with axillary node negative, if ALND was not performed in the whole or partial breast dissection surgery, the 10 years axillary recurrence rate will be around 21-41%^[1] in a follow-up research. Therefore, ALND can significantly reduce the axillary occurrence rate and improve overall survival and disease-free survival.

Nevertheless, it also brings a series of potential sequelae such as upper limb lymphedema, neurodynia and the limb movement limitation which would cause great harm to the patients and seriously affect the quality of life. It is reported that for patients with level I and II ALND, lymphedema incidence was around 13.9% while the lymphedema incidence was 27.98% and 37% for patients with level III and whole ALND. In the ALND surgery, patients with intercostobrachial nerve mutilation, almost all (100%) suffered from axillary numbness and lateral hypoesthesia of upper arm, while patients with intercostobrachial nerve preservation suffered much less in degree and duration with syndromes above. Moreover, 10-15% patients with ALND suffered from limb movement limitation including decrease of grip strength, arm activity and shoulder activity [3]. Therefore, under the premise of ensuring the curative effect, to reduce unnecessary invasive operation and subsequently adverse effects and complications, improve the quality of life has great clinical significance in the diagnosis. Recently, ALND is not necessary at present. The possible reasons we speculated might be the followings: one reason is that ALND can lead to serious complications such as upper limb edema, rib, and shoulder and arm nerve syndrome, limb movement disorder which brought great harm to patients in physical and psychological. A study of AMAROS demonstrated that the recurrence rate of patients with biopsy positive sentinel lymph node was below 2% whether they received axillary irradiation or axillary axillary while the five-year incidences of lymphedema were 23% and 11% respectively^[4]. Thus, the incidence of upper limb lymphedema with axillary irradiation was significantly lower than that of the axillary dissection. Xie et al^[5] showed that that the rate of lymphedema with ALND was 2.72 times higher than that without dissection. The other reason is that throughout the long-term efficacy, axillary lymph node radiotherapy and ALND resulted in a similar treatment efficacy. Et al Chua [6] conducted a clinical randomized controlled trials on stage I breast cancer patients with negative lymph node consisting of 782 cases treated with ALND and 229 cases treated with axillary only radiotherapy and found no difference of local recurrence in both groups. Louis-Sylvertre C [7] et allocated 658

patients with regional lymph node negative and tumors less than 3cm in diameter randomly into ALND group and axillary radiotherapy group, the 10 years and 15 years survival rate was basically the same in both groups. NSABP b-04 revealed that the recurrence rate of axillary lymph node negative patients with simple mastectomy was up to 19% and <2% with lymph node dissection. However, the axillary lymph node irradiation instead of ALND could also obtain similar local recurrence rate^[8]. Vacek^[9] reported that with the widespread of annual breast examination, the detection rate of breast tumors less than 2cm in diameter raised from 2% in 1974-1984 to 36% in 1995-1999. The proportion of axillary lymph node metastasis in breast tumors with small size decreased as well as the early detection rate increased.

In the present study, the five years survival rate of 58 patients undergoing breast conserving operation and axillary lymph node radiotherapy is 94.3% and there was no statistical significance in both survival and recurrence incidence compared with modified radical mastectomy group. But the incidence of upper limb lymphaden, the intercostobrachial nerve syndrome, the shoulder movement limitation, injury of axillary vein and thrombus of breast conserving group was significantly lower than that of modified radical mastectomy group.

In conclusion, ALND of patients in stage I causes long-term side effects and the radiotherapy afterwards will increase the side effects. However, the axillary radiotherapy only leads to low rate of complications while the overall survival rate and local recurrence rate were not statistically significant. Therefore, the breast conserving surgery combined with axillary radiotherapy might be a better treatment approach for breast cancer patients in stage I with negative axillary lymph node. However, with small number of patients, which is a main limitation, large patient studies are needed to confirm the findings.

Disclosure of conflict of interest

None.

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Table and Figure legends

Table 1. The comparison between upper lymphedema and shoulder movement disorder (n, %)

Item	Modified Radical Mastectomy				Breast-Conserving Surgery			
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 0	Grade 1	Grade 2	Grade 3
Upper extremity lymphedema	66(75)	10(11.4)	7(8.0)	5(5.6)	93(94.9)	2(2.0)	2(2.0)	1(1.1)
Shoulder movement disorder	63(71.6)	9(10.2)	10(11.4)	6(6.8)	94(95.8)	2(2.0)	1(1.1)	1(1.1)

Table 2. The comparison of other complications (n, %)

Item	Modified Radical Mastectomy	Breast-Conserving Surgery
Intercostobrachial nerve syndrome	48(54.5)	3(3.1)
Axillary vein thrombosis or injury	28(31.8)	1(1.1)
Axillary fibrosis	5(5.6)	3(3.1)

Characteristic	Patients, n	
	Breast-Conserving Surgery	Modified Radical Mastectomy
Total Cases	98	88
Age, Years		
>60	1	16
40-60	61	58
<40	36	14
Pathologic Tumor Size, cm		
1.5-2.0	52	46
1.0-1.5	41	40
<1.0	5	2
Histological Type		
Invasive ductal carcinoma	67	60
Invasive lobular carcinoma	21	12
Tubular carcinoma	7	4
Invasive cribriform carcinoma	3	2
Chemotherapy	98	88
Radiotherapy	98	88
Hormonal Therapy	56	48

Figure 1. the comparison of two groups' data

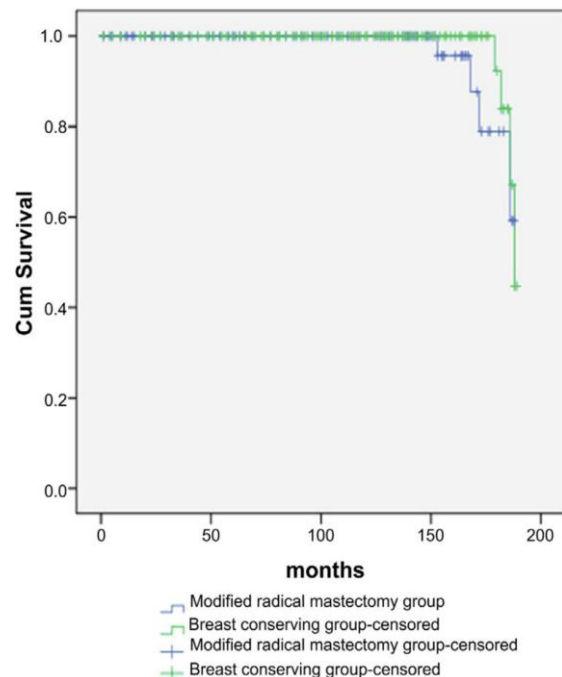


Figure 2. The survival rate of two groups (month, %)