

The 10-Year Local Recurrence and Partial Breast Radiotherapy for Early Breast Cancer Treated by Conservative Surgery

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OBJECTIVE To study the local recurrence and the role of whole breast radiotherapy for early breast cancer treated by conservative surgery.

METHODS From April 1990 to December 2000, 49 patients with early primary breast cancer were treated by conservative surgery in our hospital. The cases were comprised of Stage 0, 1; Stage I, 31; and Stage IIa, 17. Forty cases underwent quadrantectomy plus axillary lymph node dissection, and the other 9 cases had lumpectomy alone. Irradiation, which was received by 39 patients, was administered by using low tangential half fields with 6 MV X-ray to decrease the pulmonary irradiative volume. The dose to the whole breast was 45 Gy/22~23f/4.5W, then a 15 Gy boost dose was delivered to the tumor bed by an electron beam. The other patients underwent an irradiated regional field according to postoperative pathology.

RESULTS All patients were followed-up for 10 years or more. The 10-year local recurrence rates, distant metastasis rates and survival rates were 6.1%, 4.1% and 98.0% respectively. All of the 3 patients who had a local recurrence had infiltrative carcinomas and negative lymph nodes. The 10-year local recurrence rate was higher (2.6% vs. 20.0%) with non-postoperative whole breast radiotherapy, but the statistical difference was not marked because of the low number of cases. All of the recurrent lesions localized within 3 cm of the primary lesion.

CONCLUSION Original recurrence of the tumor was the main type of local recurrence. Radiotherapy after conservative surgery is very essential. After conservative surgery it is feasible that irradiation can be delivered alone to the neighboring region of the tumor bed. Partial breast radiotherapy can substitute for whole breast radiotherapy.

KEYWORDS: early breast cancer, conservative surgery, partial breast radiotherapy, local recurrence, original recurrence, whole breast radiotherapy.

Conservative surgery for early breast cancer was proposed by Keynes in 1924 and has been one of the main therapeutic measures. It has been confirmed by abundant literature that the efficacy of conservative surgery plus whole breast radiotherapy is the same as Halsted's radical operation or Patey's improved radical operation. Some 50%~70% of the patients with early primary breast cancer annually receive this conservative surgery in America.^[1] In China clinical surgical research initiated in the 1980's but caseloads in the reports were few, as patients worried about a possible local recurrence. In our study, clinical results and local recurrence of the integrated treatment is summarized as a base for the possibility of future changes in treatment for early breast cancer.

MATERIALS AND METHODS

Clinical information

From April 1990 to December 2000, 49 patients with early primary breast cancer were treated with conservative surgery. The patients were staged as follows: Stage 0, 1; Stage I, 31; and Stage IIa, 17, according to the 1997 TNM staging standard by the UICC. Forty cases underwent quadrantectomy plus axillary lymph node dissection and the other 9 cases had lumpectomy alone. All of the patients were 24~63 years old, with a mean age of 40.4 and a median age of 40.5. Twenty-one patients were diagnosed by biopsy before operation.

Applicable standards of conservative surgery

(1) Patients were willing to accept conservative surgery; (2) Stages I and IIa; (3) A small tumor ($T \leq 3$ cm); (4) Clinical mono-focus and non-multi-calcified focus on X-ray; (5) The distance from tumor location to areola was more than 2 cm; (6) The tumor volume was in appropriate proportion to the breast; (7) Elderly patients with severe systemic disease had a local extensive lumpectomy alone.

Pathological data

From the year 1990, specimens from quadrantectomy plus axillary lymph node dissections were serially sectioned up to 8~43 sections every other 5 mm parallel along the direction from the nipple to the tumor center. By this method pathological changes can be serially examined in the cut margin and in every part of the dissected breast tissue. A positive margin was defined when the cancerous tissue was less than 5 mm apart from the cut margin. The positive-margin rate was 10.2% (5/49), including 3 patients with intraductal carcinoma and 2 with infiltrative carcinoma. According to postoperative histological diagnosis the results were as follows: 9 patients with non-infiltrative carcinoma, 1 with early infiltrative carcinoma, 12 with infiltrative specific carcinoma, 24 with infiltrative non-specific carcinoma, and 3 with a rare-type carcinoma. From 5 to 45, axillary lymph nodes in each case were dissected. Eleven of all patients had positive lymph nodes (1~5 positive lymph nodes) resulting in a lymph node metastasis rate of 22.5% (11/49). Estrogen or progesterone receptors were examined by DCC and enzyme-mark immune-histological methods for 24 patients in whom 17 cases had positive estrogen receptors, for a positive rate of 70.8% (17/24).

Treatment process

Prior to their operation, 21 of the patients, who were diagnosed with cancer by biopsy, received 2~3 cycles of chemotherapy (one cycle per week). Chemotherapeutic regimens consisted of cyclophosphamide plus colchicine (CC) before 1992 and later cyclophosphamide and methotrexate plus 5-fluorouracil (CMF). As for the other patients, they were first diagnosed by frozen sections during the operations, and then received conservative surgery. Quadrantectomy plus axillary lymph node dissection was administered to 40 cases and the other 9 had lumpectomy alone. If the tumor bed existed in the outer-superior quadrant, a single incision was utilized. A double incision was used if the tumor bed was located in other quadrants. Quadrantectomy included removal of a quarter of the gland tissue in which the lump was located and the exterior skin of the lump and fascia pectoralis below. Axillary lymph nodes were dissected to level III. Irradiation, which was delivered to 39 patients, was administered by using low tangential half fields with 6 MV X-ray to decrease the pulmonary irradiated volume. The dose to the whole breast was 45 Gy/22~23f/4.5W, and then a 15 Gy boost dose was delivered to the tumor bed by electron beam. Additional patients with more than 3 positive lymph nodes were irradiated with 50 Gy to the sub-clavicular and supra-clavicular regional fields according to postoperative pathology, and those whose tumor lay in the inner quadrant, were irradiated with 50 Gy targeting the inner mammary regional field. The regimen of post-operative chemotherapy, CMF or CAF (cyclophosphamide, Adriamycin plus 5-fluorouracil), was used in 47 patients. Tamoxifen (TAM) was administered 10 mg bid. for 3~5 years if estrogen or progesterone receptors were positive.

Statistical methods for analysis

The recurrent and survival rates were estimated to compare with published data from China and overseas. Data were analyzed that involved postoperative radiotherapy to local recurrence and the range of local recurrent positions. Statistical methods employed cross-tab χ^2 analysis by SPSS 10.0.

RESULTS

Clinical effect of conservative treatment

From April 1990 to December 2000, 49 patients with early primary breast cancer were treated by conservative surgery in TianJin Cancer Hospital. All were followed up for 10~15 years (median 12 years), so the

follow-up rate was 100%. Within 10 years after treatment, 3 patients had a local recurrence including homolateral breast and regional lymph nodes, and 2 patients had metastasized to the lungs, bone and liver and one patient had died. The 10-year local recurrent, distant metastatic and survival rates were 6.1%, 4.0% and 98.0% respectively.

Ten-year local recurrent status after conservative treatment

Three recurrent cases, who were 36~40 years old, were comprised of 2 in Stage I and one in Stage IIa. Among these, 2 patients had been operated by lumpectomy alone; the other one received a quadrantectomy plus axillary lymph node dissection. It was confirmed by postoperative pathology that all had infiltrative carcinoma and regional lymph nodes were negative. Only one patient (33.3%) received postoperative whole breast tangential radiotherapy (WBTR) plus a boost to the tumor bed (BTB) by electron beam.

Impact of postoperative WBTR plus BTB on local recurrence

At 10 years postoperations, among 39 patients who received postoperative WBTR plus BTB, there was one (2.6%) recurrence whereas among 10 without postoperative WBTR plus BTB, there were two (20.0%). Although there was no statistical difference, possibly due to the few cases in both groups ($\chi^2=4.210$, $P=0.040$, Fisher exact probability value $P=0.102$), it suggested that the local recurrent rate may increase without postoperative WBTR plus BTB.

Impact of the mode of operation on local recurrence

Among 40 patients receiving quadrantectomy plus axillary lymph node dissection, plus the 9 aged patients with lumpectomy alone, there was a total of 3 recurrent cases at 10 years postoperation. The local recurrent rates were respectively 2.5% (1/40) and 22.2% (2/9) resulting in marked statistical difference between the two groups ($\chi^2=4.972$, $P=0.026$, Fisher exact probability value $P=0.083$).

Relation of recurrent focus and tumor bed

An original recurrence (OR) was indicated if the recurrent focus was located in the same quadrant as the primary lesion, and was within 3 cm of the tumor bed. The 3 recurrent patients all were OR, and the 10-year OR rate for all patients was 100%. To some degree, these results show that an OR was the main form of lo-

cal recurrence, and postoperative radiotherapy can effectively increase the local control.

DISCUSSION

Therapeutic effect of conservative treatment

Conservative surgery had the same effect as radical surgery. In 1995, the EBCTCG analyzed the results of nine randomized studies, of which six (3,107 cases) were used to observe recurrent rates. In their report, the 10-year local recurrent rate was 6.2% in a radical-surgery group and 5.9% in a conservative surgery group, resulting in no statistical difference between the two groups.^[2] McBain et al.^[3] found a 5-year local recurrent rate of 6.3% from 2,159 patients following conservative surgery. It was reported recently in China that the 5-year local recurrent rate was 4.6%~6.1% for Stages I and II breast cancer with conservative surgery plus postoperative radiotherapy.^[1] The 10-year local recurrent rate in our research (6.1%) was close to the published values cited. Compared with our hospital's historical data (6.3%),^[4] the results are similar.

Influence of the surgical method

The curative results of conservative treatment were determined by the surgical method, especially for infiltrative carcinoma.^[5] All of our recurrent cases were diagnosed as infiltrative carcinoma by postoperative pathology. Our results showed that the 10-year local recurrent rate of the group treated with lumpectomy alone was significantly higher than of the group treated with quadrantectomy plus axillary lymph node dissection. Patients treated with lumpectomy alone were elderly, so the operative intention was principally palliative and operative extension was possibly narrower than with quadrantectomy. Because of the multifoci of the tumor there may have been several isolated and latent foci near the operating field, so the possibility of cancerous remnants in the cut margin increased. We conclude that with enough operative extension during conservative surgery, especially for infiltrative carcinoma, the operations lead to lower local recurrence.

Need for radiotherapy after conservative treatment

Radiotherapy is still an indispensable method of conservative treatment for early breast cancer. Normative radiotherapy has a very clear effect for eradication of most cancerous remnants and decreases the postoperative local recurrence. It has been validated by three randomized clinical studies from NsABP B-13, NS-

ABP B14, and the Stockholm group.^[2] Now WBTR plus BTB is the most common clinical mode of radiotherapy.

Hayman et al.^[6] summarized a prospective study of 87 patients with breast cancer from JCRT in 1995 and suggested that conservative surgery alone for early breast cancer had a high risk of local recurrence, even with a careful operation and strict standards of patient selection. The results were similar with several randomized groups of research, e.g. NSABP B-06,^[7] Ontario et al.^[8] and Uppsala-Orebro Breast Cancer Study Group.^[9] A Germanic Breast Cancer Seminar (GBCS)^[10] showed that the local recurrent rate in a group of patients treated by conservative surgery alone was three times greater than in a group treated by conservative surgery, postoperative radiotherapy and/or endocrinotherapy.

In our study, the local recurrent rates of patients with and without postoperative WBTR plus BTB were respectively 2.6% and 20.0%. Although no statistical difference existed between the two groups ($P=0.102$), which only was comprised of a few cases, it is proposed that the local recurrent rate, without postoperative WBTR plus BTB, will increase. Recent statistical results relating to this difference based on large sample sizes are summarized in Table 1. Results from these

studies provide convincing evidence.

Radiotherapy after conservative surgery can markedly decrease the local recurrent rate. It has been confirmed by multicentre clinical trials that integrated conservative treatment including postoperative radiotherapy decreased the local recurrent rate more than 75%.^[5] The role of radiotherapy in conservative treatment is standard and no other therapy should be substituted.

Characteristics of local recurrence after conservative treatment

After the primary malignant tumor is extensively resected and axillary lymph nodes are dissected, lesions which remerge in the homolateral breast, chest wall or axilla, are defined as local recurrences. Local recurrences arise in 2~7 years after an operation. An OR, which is the main form of local failure, centralizes on the tumor bed and tissues around, and seldom arises in other areas. The same situation can be seen in patients who fail to receive postoperative radiotherapy. The MD Anderson Cancer Center in Houston, TX, USA found 139 recurrent cases in 1,339 patients with conservative surgery, in which the true original local recurrence was 38%.^[17] True original local recurrence is located within 3 cm of the tumor bed and has the same

Table 1. Local recurrent rates with or without postoperative radiotherapy

Author	Case	Follow-up (years)	With radiotherapy (%)	Without radiotherapy (%)	Statistically significant
Freedman ^[11]	912	10	7.2	27.5	Yes
Liljegren ^[12]	381	10	8.5	24.0	Yes
Fisher ^[13]	1851	20	14.3	39.2	Yes
Meng J ^[14]	132	3	1.0	12.1	Yes
Liu YS ^[15]	111	10	7.5	75.0	Yes
He CT ^[16]	415	10	9.1	36.6	Yes
Wang ZZ*	49	10	2.6	20.0	No

* This report

Table 2. Comparison of local recurrent rates with WBTR, WBTR + BTB and PBRT

Author	Case	Follow-up (months)	WBTR (%)	WBTR + BTB (%)	PBRT (%)	Statistically significant
Benitez PR ^[18]	199	60	-	-	1.2	-
Vicini FA ^[20]	199	65	1.0	-	1.0	No
Polgar C ^[21]	125	60	4.7	5.7	4.4	No
Polgar C ^[22]	126	30	5.6	-	1.4	No
Polgar C ^[22]	41	4~36	-	-	2.4	-
Baglan KL ^[23]	37	31	-	-	2.6	-

pathological diagnosis as a primary lesion. Analogous data have been reported from many studies^[2,5,12,18] outside China but not from within. Our conclusion that OR is the main form of local recurrence is similar to others, and was found to be 100% in our study, although cases were few.

Possibility of altering the modality of postoperative radiotherapy

Since OR is the main form of local recurrence, radiotherapy after conservative surgery is very important. Is WBTR essential? It has been considered by most doctors that the local recurrent rate is related to the total dose of radiotherapy. REORTC^[2] studied 5,569 patients with early breast cancer by randomized classification from 1989 to 1996, and confirmed that an increase of radiotherapy dosage to the tumor bed after WBTR reduced the local recurrent rate even for patients with a negative cut margin. Zhang^[19] drew the same conclusion in China. Our results also support this conclusion.

It is often a burden for the patients and hospital when, after conservative surgery, WBRT continues for six weeks, so some patients will finally be compelled to choose radical surgery. For patients receiving chemotherapy, radiotherapy may not begin in time because of the long chemotherapeutic cycle. Partial breast radiotherapy (PBRT) such as interstitial brachytherapy ensures greater doses of irradiation to the tumor bed to enhanced local control, and less normal tissue is irradiated. Does PBRT substitute for WBRT? Many overseas studies present an affirmative answer with positive results as shown in Table 2.

Analysis shows that the local recurrent rate with PBRT is close to that with WBTR and even less than WBRT in some studies. In conclusion, it is feasible after conservative surgery that irradiation with adequate dosage can be delivered alone to the neighboring region of the tumor bed.

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