RESEARCH ARTICLE

Phase II Study on Breast Conservative Surgery Plus Chemo- and Radiotherapy in Treating Chinese Patients with Early Staged Breast Cancer

Yang-Chen Liu[1,2], Shao-Bing Zhou[1], Fei Gao[1], Xiao-Xiang Yin[1], Ying Zhao[1], Xin-En Huang[2]*

Abstract

Purpose: To evaluate the efficacy of conservative surgery plus chemo-, radio-therapy in treating patients with early stage breast cancer. Patients and Methods: Eligible patients were treated by postoperative chemotherapy as well as whole-breast irradiation with tumor bed boost. Postoperative radiotherapy consisted of 6 MV whole breast linear accelerator irradiation with two tangential half fields to a total dose of 45~50 Gy, followed by 10~15MeVβ boost irradiation to tumor bed for 10~20Gy, total dose 56~66Gy. Results: Fifty-two patients were enrolled. Overall 1-, 2- and 3 year survival rates were 98.1%, 92.3%, and 90.4%, respectively, with a local recurrence rate of 5.77%. Cosmetic results were evaluated as good by doctors in 90.4% of patients. Conclusions: Breast conservative surgery combined with chemo- radio-therapy could be a treatment option for Chinese patients with early stage breast cancer.

Keywords: Breast cancer - conservative surgery - radiotherapy - chemotherapy

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Introduction

BC incidence appears to be increasing in Chinese women and Chinese people have experienced rapid socioeconomic changes, especially in large cities (Liu et al., 2000). Based on clinical reports, breast-conserving therapy has become the first choice for patients with early staged breast cancer in developed countries (Neff et al.,1996). A large number of clinical studies have demonstrated that the equivalent survival and local control rates can be achieved in women treated with breast-conserving therapy compared to those treated with mastectomy (Neff et al., 1996; Blair, 2010; Zhang et al., 2012)

In this paper, we describe our experience with postoperative chemo- or radiotherapy for Chinese women with an early staged breast cancer who underwent breast-conserving therapy.

Materials and Methods

Patients eligibility

Patients were required to be pathologically/cytologically diagnosed with breast cancer; to sign an informed consent before treatment; to have a score of karnofsky performance status ≥ 70; to be aged between 25 and 75 years old and to be alived until the end of this study. Other eligibility criteria included: adequate hematological (white blood cell count > 3.0×10^9 and platelet count > 150×10^9), liver (bilirubin and transaminases < 1.5 times the upper normal limit) and renal function (creatinine leval < 1.5 times the upper normal limit); patients were excluded from the study if they were diagnosed with any serious medical or psychiatric condition, or other malignancies. Pregnant or lactating women are also excluded from this study.

Surgical Technique

All patients with general anaesthesia or epidural anesthesia, supine, limb abduction, preoperative tumor boundary marker, underwent lumpectomy and axillary lymph node dissection, Lumpectomy consisted of complete removal of the tumor and an additional 1-2 cm margin of normal surrounding tissue.

Radiation Therapy

All patients after 3 to 16 weeks received postoperative radiotherapy on the whole breast from a 6-MV X ray linear accelerator with two tangential half field to a dose of 45-50 Gy, followed by an additional sequential boost of 10-20 Gy in 5-10 fractions over 2 weeks to tumor bed with 10-15MeVβ ray to a total dose of 56-66 Gy. Radiation therapy

[1]*Department of Radiation Oncology, The People's Hospital of Taixing City, Taixing,* [2]*Department of Chemotherapy, the Affiliated Jiangsu Cancer Hospital of Nanjing Medical University & Jiangsu Institute of Cancer Research, Nanjing, China *For correspondence: huangxinen06@aliyun.com*

to the infraclavicular region and supraclavicular area was given to the patients with positive lymph nodes, using 6-MV X ray and 12 MeVβ-ray to a dose of 50Gy. Eligible patients should receive CAF chemotherapy (CTX600mg/m^2 d1; ADM 50mg/m^2 d1; 5-FU 500mg/m^2 d1, d8) or ET chemotherapy (PTX135 mg/m^2 d1; E-ADM 75mg/m^2 d1) for 1-3 cycles. And endocrine therapy was ordered to patients with ER and/or PR-positive.

Evaluation Criteria

Evaluation of cosmetic effect is divided into excellent, good, general, and poor result, using Harris score standard reference (Cassileth et al., 2012). Patients who got excellent, good and general cosmetic effect were considered to be satisfactory. Adverse reaction caused by radiotherapy was evaluated by RTOG acute and chronic standard reference (Denham et al., 1995). To observe survival or recurrence status, all patients should be followed for more than 3 years.

Research experience

We have enough experience in conducting medical researches, including clinical researches, and have published some results elsewhere (Jiang et al., 2010; Gao et al., 2011; Huang et al., 2011; Li et al., 2011; Li et al., 2011; Li et al., 2011; Xu et al., 2011; Xu et al., 2011; Xu et al., 2011; Yan et al., 2011; Zhang et al., 2011; Gong et al., 2012; Gong et al., 2012; Gu et al., 2012; Li et al., 2012; Yu et al., 2012; Zhan et al., 2012; Zhan et al., 2012; Deng et al., 2013; Huang et al., 2013; Liu et al., 2013; Liu et al., 2013; Lu et al., 2013; Wu et al., 2013; Yin et al., 2013; Yin et al., 2013).

Results

Between February 2005 and March 2008, a total of 52 breast cancer patients were enrolled into this study. All patients were female, and the median age was 42 (range, 31-65) years. Of all 52 patients, 23 had the tumor in the left, and 29 in the right breast. Thirteen patients had a tumor in the inner quadrant, 39 patients had a tumor in the outer quadrant. All patients (distance of the tumor edge and areola > 3 cm, skin and pectoral muscle uninvolved, nipple no outflow, negative lymph nodes) underwent lumpectomy plus axillary lymph node dissection, 30 of them had a single tumor of invasive duct carcinoma ≤2.0 cm in largest diameter, and the rest >2.0 cm, <5.0 cm. Pathologic stage included, stage I in 24, IIA in 19 in and IIB in 9 patients. No patient had distant metastasis. Postoperative pathological diagnosis included invasive duct carcinoma in 36, lobular carcinoma in situ in 3 patients, invasive lobular carcinoma in 8 and invasive tubular carcinoma in 5 patients. All patients received anthracycline- or taxane-based chemotherapy for 2-6 cycles after radiotherapy.

Neutropenia and digestive tract side effects were observed in 40 patients. Twenty-four of these 40 patients experienced grade 1 leucopoenia and others grade 2 (no grade 3 and 4 recorded). Radiation related toxicities were mild dry cough and moist skin reactions occurred in a few patients, and all recovered after corresponding treatment. The incidences of radiation pneumonitis, radiation pericarditis and shoulder dysfunction were 9.6%, 0 %and 0%, respectively.

One-, 2- and 3-year survival rates were 98.1%, 92.3% and 90.4% respectively, while 3-year local recurrence rate was 5.8%. Excellent, good, general, and poor cosmetic results were 63.8%, 21.8%, 11.5% and 9.6% respectively.

Discussion

Breast cancer is one of the most common malignancies in women today (Wang et al., 2013). Treatment depends on whether distance micrometastases were diagnosed. For those with early disease, compared with radical resection, breast conserving resection has no negative impact on survival (Park et al., 2011). Thus breast-conserving therapy is regarded as a standard treatment for patients with staged I or II breast cancer in Europe and the United States (Garcia-Etienne et al., 2012). For patients with invasive breast cancer and treated by breast-conserving therapy, surgical margin, postoperative radiotherapy and adjuvant chemotherapy are considered (Collins et al., 2013). However, sequencing and timing of radio- or chemotherapy after breast conservative surgery should be properly determined. In China, breast-conserving therapy is conducted from 1980s (Du et al., 2000). Chinese women have different breast volume compared with Western women. When breast-conserving therapy is conducted for Chinese women with breast cancer, surgery procedure, radio- or chemotherapy should be arranged individually. Radiotherapy is reported to significantly decrease local recurrence after breast-conserving therapy (Gage et al., 1995). The recurrence rate will be above 60% without, while the rate will decrease to about 9% with postoperative radiotherapy (Rouanet et al., 1993). Thus, in China adjuvant RT is currently recommended for all patients after breast-conserving lumpectomy, regardless of the size of the primary disease, age of patient, and hormonal receptor. In this study, patients without axillary dissection, the target includes the ipsilateral chest wall, whole breast, ipsilateral axilla and supraclavicular area. In patients with axillary dissection, the ipsilateral chest wall and whole breast are included in those of negative axillary lymph node, while the lateral border of the supraclavicular field including the axilla should be treated in lymph node-positive patient. If internal mammary lymph nodes are clinically or pathologically positive, radiation therapy is given to this area; if it is negative, the internal mammary area will not be irradiated. But this practice should be validated by further randomized clinical studies to show if it has preventive effects on local recurrence or distant metastasis, and increases the long-term complications of cardiovascular system. Recent years in China, conformal, intensity-modulated radiotherapy and proton radiation are considered mainstay of therapy for patients underwent breast-conserving surgery. These techniques could be applied without increasing toxicities to heart and lung. Attention should also be paid to the timing of postoperative radiotherapy. It is hypothesized that postoperative radiotherapy followed by chemotherapy will decrease risk of local recurrence, while chemotherapy followed by

radiotherapy will reduce risk of distant metastasis. Thus, patients at higher risk for distant metastasis usually receive chemotherapy first, while those at higher risk for local failure (incomplete local mass resection or close margins) should receive radiation first. To achieve better local control, decrease the possibility of distant metastasis and improve overall survival, some studies were conducted to verify the effectiveness of concurrent chemoradiotherapy (Karasawa et al., 2013). However, the incidence rate of severe side effects and complications was high (Karasawa et al., 2013). Current recommendations are as follows: the interval between surgery and radiotherapy should be less than 8 weeks. It is reported that local recurrence rates of patients who receive postoperative radiation less than 120 days and more than 120 days are 2% and 8% respectively, with marginal statistical significance (Schnitt et al., 1994). This is the reason that we set our start-time of radiotherapy at 3 to 16 weeks after surgery, and the median is 7 weeks.

In summary, for our cohort of patients with early staged breast cancer who received conservative surgery plus chemo-, radiotherapy, 1-, 2- and 3 year survival rate was 98.1%, 92.3%, and 90.4%, respectively, with local recurrence rate of 5.77%. Cosmetic result was evaluated as good in 90.4% of patients. We conclude that breast conservative surgery combined with chemo- radiotherapy could be a treatment option for Chinese patients with early staged breast cancer.

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