Int J Clin Exp Med 2017;10(12):16688-16693
www.ijcem.com /ISSN:1940-5901/IJCEM0066458

Original Article

Clinical efficacy and safety of short-term radiotherapy after breast conserving surgery in the treatment of breast cancer

Jianwen Li[1], Xinbo Wang[2]

Departments of [1]Radiotherapy, [2]Surgical Oncology, Weifang People's Hospital, Weifang City, Shandong Province, China

Received September 29, 2017; Accepted October 29, 2017; Epub December 15, 2017; Published December 30, 2017

Abstract: Objective: To investigate the clinical efficacy and safety of short-term radiotherapy and traditional radiotherapy after breast conserving surgery for breast cancer. Methods: A total of 128 patients with breast cancer, who underwent radiotherapy after breast conserving surgery from January 2013 to June 2015 at our hospital, were enrolled in this study. All of them were randomly divided into the traditional radiotherapy group (conformal intensity-modulated radiotherapy combined with electron beam boost) and the short-term radiotherapy group (conformal intensity-modulated radiotherapy with tumor bed boost). The duration and expense of hospitalization, and the cosmetic effects of breast were evaluated and compared between the two groups. In addition, the survival rate, recurrence rate, and the incidences of distant metastasis and the side effects in both groups were evaluated and compared. Results: The results showed that there were no significant differences between the two groups with respect to the 2-year overall survival rate, recurrence rate, cosmetic effects, the incidence of side effects, and the expenses of hospitalization (all P>0.05). However, the duration of hospitalization in the short-term radiotherapy group was lower than that in the traditional radiotherapy group (28.3±2.5 d vs. 45.5±3.7 d, P=0.021). What's more, the incidence of distant metastasis in the short-term radiotherapy group was lower than that in the traditional radiotherapy group (3.1% vs. 15.8%, P=0.034). The progression-free survival rate, in the short-term radiotherapy group was higher than that of the traditional radiotherapy group (89.1% vs. 70.3%, P=0.008). Conclusion: The short-term radiotherapy can effectively shorten the duration of hospitalization, improve the progression-free survival, and reduce the incidence of distant metastasis, in comparison with the traditional radiotherapy.

Keywords: Breast conserving surgery, short-term radiotherapy, clinical efficacy, side effects

Introduction

Recently, the morbidity of breast cancer in females has been increasing to about 5%, with an upward trend in younger women [1-3]. In some areas, the incidence of breast cancer has become the second highest cancer following lung cancer [4]. With the continuous development of medical technology and in-depth research on breast cancer, most breast cancers can be screened at the early stage, and treated timely. Meanwhile, the treatment of breast cancer has gone through different historical stages, from the traditional radical mastectomy, to modified radical mastectomy, then to breast conserving surgery [5]. Breast preserving surgery can not only remove the lesions, but also abandon the destruction on breast appearance that caused in traditional radical surgery by local tumor removal. Therefore, currently, breast conserving surgery is recommended as a standard surgery for breast cancer, especially for the patients at the early stage. Usually, patients are required to undergo traditional postoperative radiotherapy and chemotherapy after resection of the tumor and axillary lymph node, so as to reduce the risk of tumor recurrence, distant metastasis and mortality [6, 7].

With the development of medical equipment, there are a number of radiotherapy techniques, among which, three-dimensional conformal radiotherapy and intensity-modulated radiotherapy are the most commonly adopted [8]. However, the duration of these two kinds of treatment is relatively longer, however, a long-term radiotherapy will result in delayed chemo-

therapy, which may increase the risk of distant metastasis [9, 10]. Therefore, the radiotherapy duration is vital for the prognosis of patients with breast cancer and the control of radiotherapy duration is necessary.

In order to shorten the radiotherapy duration, conformal intensity-modulated radiotherapy with tumor bed boost has gradually been recognized [11]. To further elucidate the importance of the radiotherapy duration, and optimize the radiotherapy modality in the treatment of breast cancer, a total of 128 patients with breast cancer were enrolled in this study and the patients were given either traditional or short-term radiotherapy after breast conserving surgery to analyze and compare the clinical efficacy and side effects of these two treatments.

Materials and methods

Patients

This study was approved by local Ethics Committee, and the signed consent was obtained from every patient before the experiment started. A total of 128 female patients with breast cancer who underwent radiotherapy after breast conserving surgery from January 2013 to June 2015 at our hospital were enrolled in this study.

The patients all met the following criteria: primary breast cancer; patients underwent breast conserving surgery; single tumor lesions were confirmed pathologically; no calcification lesions in the breast; non-postmenopausal women and without other endocrine or metabolic diseases. The exclusion criteria included: patients accompanied with severe heart, lung, brain, liver and kidney dysfunction; pregnant women; patients with distant metastasis.

The patients were divided randomly into the traditional radiotherapy group (64 cases) and the short-term radiotherapy group (64 cases). Patients in the traditional radiotherapy group received conformal intensity-modulated radiotherapy combined with electron beam boost, and patients in the short-term radiotherapy group were given conformal intensity-modulated radiotherapy with tumor bed boost.

Intervention

The radiotherapy should be taken within 3-20 weeks after breast conserving surgery, using 6 MV-X intensity modulated radiation to the whole breast, interpectoral lymph nodes and axillary lymph node at a prescription dose to 95% isodose line [12].

In traditional radiotherapy, the target radiation dose was 46 GY (2.0 GY/time, 23 times), followed by electron beam boost of 15 GY (2.5 GY/time, 6 times) at a period of 6 weeks. In short-term radiotherapy, the target radiation dose was 48 GY (2.0 GY/time, 24 times), and tumor bed boost was added to gain a total dose of 60 GY at a period of 5 weeks. In addition, a total of 50 GY (2 GY/time, 25 times) radiation was given to the supraclavicular lymph drainage area on the condition that the number of positive axillary lymph node metastasis was over 3.

After radiotherapy, patients received chemotherapy for 3 courses with 21-day as a course, by using CAF modality (cyclophosphamide 600 mg/m^2, intravenously, at d1 and d8; pirarubicin 50 mg/m^2, intravenously, at d2; fluorouracil 600 mg/m^2, intravenously, at d1 and d8) or TE modality (epirubicin 60 mg/m^2, intravenously, at d1; docetaxel 75 mg/m^2, intravenously, at d1). All the patients were followed up for two years by outpatient consultation or phone calling every three months for the first year after discharge, and every six months thereafter.

Outcome measures

Major outcome measures covered 2-year survival rate (overall survival and progression-free survival), 2-year recurrence rate, and 2-year distant metastasis rate.

Secondary outcome measures included the expense of hospitalization, side effect incidences (involving radiation pneumonitis, pericarditis, radioactive esophagitis, acute skin reaction (grade I-II)), and the cosmetic effects of breast which was divided into four grades in accordance with the Joint Center for radiotherapy standard [13]. The content of evaluation consisted of breast symmetry, breast hardness, nipple color, and patients' feelings.

Statistical analysis

All the data were processed by statistical software SPSS16.0. Continuous data were expressed as mean ± sd and analyzed by using independent t test. Besides, categorical data were expressed as percentage and analyzed by using Chi-square test. $P<0.05$ was considered statistically significant.

Table 1. Patients' characteristics

	Short-term radiotherapy group (n=64)	Traditional radiotherapy group (n=64)	t/X^2	P
Age (year)	39.6±5.3	39.1±5.6	0.681	0.269
Tumor size (cm)	1.47±0.2	1.50±0.3	1.210	0.310
TNM staging (n)			0.040	0.980
I	31	30		
IIa	21	22		
IIb	12	12		
BMI (kg/m^2)	26.1±3.6	26.1±3.6	0.991	0.699
Chemotherapy (n)			0.791	0.374
CAF	38	33		
TE	26	31		

Table 2. The overall survival rate, progression-free survival rate, recurrence rate, and the distant metastasis rate

	Short-term radiotherapy group (n=64)	Traditional radiotherapy group (n=64)	X^2	P
Overall survival	98.4%	96.9%	0.000	1.000
Progression-free survival	89.1%	70.3%	6.950	0.008
Recurrence	6.2%	10.9%	0.398	0.528
Distant metastasis	3.1%	15.8%	4.506	0.034

Table 3. Duration and expense of hospitalization

	Short-term radiotherapy group (n=64)	Traditional radiotherapy group (n=64)	t	P
Duration (d)	28.3±2.5	45.5±3.7	3.421	0.021
Expense (ten thousand yuan)	2.5±0.2	2.6±0.5	1.082	0.366

Results

Patient characteristics

As shown in **Table 1**, there were no significant differences between the two groups regarding to age, tumor size, tumor-node-metastasis (TNM) staging and chemotherapy modality (P>0.05).

The overall survival rate, progression-free survival rate, recurrence rate and distant metastasis rate

As shown in **Table 2**, the distant metastasis rate in the short-term radiotherapy group was 3.1%, which was significantly lower than that in the traditional radiotherapy group (P=0.034), The progression-free survival rate, in the short-term radiotherapy group was higher than that of the traditional radiotherapy group (89.1% vs. 70.3%, P=0.008). And there was no difference between the two groups in the overall survival rate and local recurrence rate (both P>0.05).

The duration and expense of hospitalization

The duration to receive radiotherapy and expense of hospitalization in the two groups are provided in **Table 3**. The statistical analysis indicated that the duration of hospitalization in the short-term radiotherapy group (28.3±2.5 d) was shorter than that in the conventional radiotherapy group (45.5± 3.7 d, P=0.021). And there was no significant difference between the two groups with respect to the expense of hospitalization (2.5±0.2 *vs.* 2.6±0.5 ten thousand yuan, P=0.366).

The cosmetic effects in the two groups

Table 4 describes that both radiotherapy modalities achieve satisfactory cosmetic effects. In the short-term radiotherapy group, the number in excellent, good, moderate and poor levels was 29, 24, 10 and 1, respectively. And the number in excellent, good, moderate and poor levels in the traditional radiotherapy group was 28, 25, 9 and 2, respectively. No statistically significant difference was found between the two groups (P=1.000).

Side effects of the two groups

As shown in **Table 5**, the incidence of radiation pneumonitis, radiation esophagitis, pericarditis and acute skin reaction (grade I-II) in the short-term radiotherapy group was 1 (1.5%), 10 (15.6%), 2 (3.1%) and 31 (48.4%), respectively.

Table 4. The comparison of cosmetic effects between the two groups

	Excellent	Good	Moderate	Poor	X^2	P
Short-term radiotherapy group (n=64)	29	24	10	1	0.000	1.000
Traditional radiotherapy group (n=64)	28	25	9	2		

Table 5. Side effect incidences

Side Effects	Short-Term Radiotherapy Group, n (%)	Traditional Radiotherapy Group, n (%)	X^2	P
Radiation Pneumonitis	1 (1.5%)	2 (3.1%)	0.000	1.000
Radiation Esophagitis	10 (15.6%)	12 (18.8%)	0.055	0.815
Pericarditis	2 (3.1%)	4 (6.2%)	0.175	0.676
Acute Skin Reaction (Grade I-II)	31 (48.4%)	32 (50%)	0.000	1.000

And the incidence of radiation pneumonitis, radiation esophagitis, pericarditis and acute skin reaction (grade I-II) in the traditional radiotherapy group was 2 (3.1%), 12 (18.8%), 4 (6.2%) and 32 (50%), respectively. No significant difference was found in the abovementioned measures between the two groups (P=1.00).

Discussion

In this study, a total of 128 breast cancer patients who received breast conserving surgery were enrolled and divided into two groups to receive two different radiotherapy modalities, the short-term radiotherapy and the traditional radiotherapy. The results represented that the duration of hospitalization in the short-term radiotherapy group after breast conserving surgery was shorter than that in the traditional radiotherapy group. The cause of this difference may be that the short-term radiotherapy used a higher target dose in tumor bed in a relatively short period [14, 15]. As the high dose of radiation would not cause serious injury to the organs, the short-term radiotherapy not only guaranteed the safety and efficacy, but also shortened the radiotherapy duration [16, 17].

When it came to the cosmetic effects, this study demonstrated no significant difference between the two groups (P>0.05), which was consistent with the results reported by Whelan et al. [18]. It is noted that the cosmetic effects are mainly associated with the range of surgical trauma, and there is no direct relationship with radiation dose and/or radiation duration. Whelan reported that, the breast cosmetic effects were different in individual surgical resections according to the different types of breast cancer [18, 19]. To be specific, for general breast cancer, 90% of patients can obtain negative margins in normal tissue after the resection of 1 cm normal tissue outer of tumor margins and the cosmetic effect was relative good, while for patients with extensive intraductal component in breast cancer, the cosmetic effect was relative poor. Because the cancer cells invaded the surrounding tissue, so lead to the expanded area of surgical resection. Moreover, it has been reported that tumor location, clinical stage, tumor size and local infection were related to cosmetic effects [20]. Therefore, we believed that cosmetic effects can be improved by modifying surgical techniques.

In addition, this study presented that there was no significant difference regarding to the 2-year overall survival rate and local recurrence rate. However, the progression-free survival rate in the short-term radiotherapy group was higher than that of the traditional radiotherapy group, indicating short-term radiotherapy can improve the clinical prognosis. What's more, our study also found that the incidence of distant metastasis in the short-term radiotherapy group was significantly lower than that in the traditional radiotherapy group. This may because the short-term radiotherapy can shorten the radiotherapy duration, which guaranteed the timely chemotherapy post radiotherapy, and reduced the risk of tumor metastasis [12, 20, 21]. This study also showed that the incidence of side effects in both groups were very similar, including radiation-induced pneumonia, esophagitis, pericarditis and acute skin reaction (grade I-II). Although the radiation duration was shortened in patients received short-term radiotherapy, the total dose of radiation was the same in the two groups, indicating that the two radiotherapy modalities were relatively safe.

There are still some limitations in the current study, such as the small size of patients, and the short term of follow-up, which may cause some statistical bias in this study. So, there is a need to collect more cases with a long-term follow-up to further verify the findings in this paper.

In conclusion, the short-term radiotherapy can effectively shorten the duration of hospitalization, improve the progression-free survival, reduce the incidence of distant metastasis compared with the traditional radiotherapy, which can be popularized in the clinical practice as a new method in the treatment of breast cancer.

Disclosure of conflict of interest

None.

Address correspondence to: Xinbo Wang, Department of Surgical Oncology, Weifang People's Hospital, No.151 Guangwen Street, Weifang 26-1000, Shandong Province, China. Tel: +86-0536-8192170; E-mail: lijianwen0907@163.com

References

[1] Budrukkar AN, Sarin R, Shrivastava SK, Deshpande DD and Dinshaw KA. Cosmesis, late sequelae and local control after breast-conserving therapy: influence of type of tumour bed boost and adjuvant chemotherapy. Clin Oncol (R Coll Radiol) 2007; 19: 596-603.

[2] Touboul E, Belkacemi Y, Lefranc JP, Uzan S, Ozsahin M, Korbas D, Buffat L, Balosso J, Pene F, Blondon J, et al. Early breast cancer: influence of type of boost (electrons vs. iridium-192 implant) on local control and cosmesis after conservative surgery and radiation therapy. Radiother Oncol 1995; 34: 105-113.

[3] Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, Luini A, Aguilar M and Marubini E. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N Engl J Med 2002; 347: 1227-1232.

[4] Lee JU, Jang WS, Lee YO and Cho JY. Long-term follow-up of the half-turned truncal switch operation for transposition of the great arteries with ventricular septal defect and pulmonary stenosis. Korean J Thorac Cardiovasc Surg 2016; 49: 112-114.

[5] Fisher B, Bryant J, Dignam JJ, Wickerham DL, Mamounas EP, Fisher ER, Margolese RG, Nesbitt L, Paik S, Pisansky TM and Wolmark N. Tamoxifen, radiation therapy, or both for prevention of ipsilateral breast tumor recurrence after lumpectomy in women with invasive breast cancers of one centimeter or less. J Clin Oncol 2002; 20: 4141-4149.

[6] Malmstrom P, Holmberg L, Anderson H, Mattsson J, Jonsson PE, Tennvall-Nittby L, Balldin G, Loven L, Svensson JH, Ingvar C, Moller T, Holmberg E and Wallgren A. Breast conservation surgery, with and without radiotherapy, in women with lymph node-negative breast cancer: a randomised clinical trial in a population with access to public mammography screening. Eur J Cancer 2003; 39: 1690-1697.

[7] Bantema-Joppe EJ, van der Laan HP, de Bock GH, Wijsman R, Dolsma WV, Busz DM, Langendijk JA and Maduro JH. Three-dimensional conformal hypofractionated simultaneous integrated boost in breast conserving therapy: results on local control and survival. Radiother Oncol 2011; 100: 215-220.

[8] Goldberg H, Prosnitz RG, Olson JA and Marks LB. Definition of postlumpectomy tumor bed for radiotherapy boost field planning: CT versus surgical clips. Int J Radiat Oncol Biol Phys 2005; 63: 209-213.

[9] Vaz-Luis I, Hughes ME, Cronin A, Rugo HS, Edge SB, Moy B, Theriault RL, Hassett MJ, Winer EP and Lin NU. Trends in the use of mastectomy in women with small node-negative breast cancer treated at US academic centers. Breast Cancer Res Treat 2016; 155: 569-578.

[10] Yu K, Ichikawa H, Sakata J, Sakata E, Tatsuda K, Hasegawa M, Toshikawa C, Manba N, Ikarashi M and Wakai T. The association between sentinel lymph node metastasis and Ki-67 labeling index. Adv Breast Cancer Res 2013; 2: 60-65.

[11] Van Parijs H, Reynders T, Heuninckx K, Verellen D, Storme G and De Ridder M. Breast conserving treatment for breast cancer: dosimetric comparison of different non-invasive techniques for additional boost delivery. Radiat Oncol 2014; 9: 36.

[12] Matthiesen C, Herman Tde L, Singh H, Mascia A, Confer M, Simpson H, Higby C, Arain A, Keole S, Herman T, Bogardus C, Zhao YD and Ahmad S. Dosimetric and radiobiologic comparison of 3D conformal, IMRT, VMAT and proton therapy for the treatment of early-stage glottic cancer. J Med Imaging Radiat Oncol 2015; 59: 221-228.

[13] Eblan MJ, Vanderwalde NA, Zeman EM and Jones E. Hypofractionation for breast cancer: lessons learned from our neighbors to the north and across the pond. Oncology (Williston Park) 2014; 28: 536-546.

[14] Holland R, Veling SH, Mravunac M and Hendriks JH. Histologic multifocality of Tis, T1-2 breast carcinomas. Implications for clinical tri-

als of breast-conserving surgery. Cancer 1985; 56: 979-990.
[15] Aaron J, Balukrishna S, Ebenezer S, Thangakunam B, Antonisamy B. Impact of breathing on post-mastectomy radiotherapy: a dosimetric comparison between intensity-modulated radiotherapy and 3D tangential radiotherapy. Astro Meeting 2014.
[16] Sasidharan B, Judith A, Ebenezer S, Thangakunam B, Antonisamy B and Selvamani B. Impact of breathing motion on IMRT (intensity modulated radiation therapy) of the chest wall in postmastectomy breast cancer patients: a dosimetric comparison with 3D conformal radiation therapy. International Journal of Radiation Oncology Biology Physics 2014; 90: S862-S862.
[17] Benda RK, Yasuda G, Sethi A, Gabram SG, Hinerman RW and Mendenhall NP. Breast boost: are we missing the target? Cancer 2003; 97: 905-909.
[18] Whelan TJ, Lada BM, Laukkanen E, Perera FE, Shelley WE and Levine MN. Breast irradiation in women with early stage invasive breast cancer following breast conservation surgery. Provincial Breast Disease Site Group. Cancer Prev Control 1997; 1: 228-240.
[19] Barry M, Ho A and Morrow M. The evolving role of partial breast irradiation in early-stage breast cancer. Ann Surg Oncol 2013; 20: 2534-2540.
[20] Ling TC, Slater JM, Nookala P, Mifflin R, Grove R, Ly AM, Patyal B, Slater JD and Yang GY. Analysis of intensity-modulated radiation therapy (IMRT), proton and 3D conformal radiotherapy (3D-CRT) for reducing perioperative cardiopulmonary complications in esophageal cancer patients. Cancers (Basel) 2014; 6: 2356-2368.
[21] Sun Z, Adam MA, Kim J, Czito B, Mantyh C and Migaly J. Intensity-modulated radiation therapy is not associated with perioperative or survival benefit over 3D-Conformal radiotherapy for rectal cancer. J Gastrointest Surg 2017; 21: 106-111.