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Original Article

Effect of modified radical mastectomy combined with neo-adjuvant chemotherapy on postoperative recurrence rate, negative emotion, and life quality of patients with breast cancer

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Abstract: Breast cancer (BC) is mainly treated by surgery combined with chemotherapy, radiotherapy, and drugs comprehensively in clinical practice, and such a combined treatment can improve the survival rate of patients. This study was designed to determine the effect of modified radical mastectomy (MRM) combined with neo-adjuvant chemotherapy on patients with BC. Clinical data of 80 patients with BC were analyzed retrospectively. The patients were assigned to the control group (n=39) treated with MRM or the therapy group (n=41) treated with additional neo-adjuvant chemotherapy based on MRM. In this study, patients treated with MRM combined with neo-adjuvant chemotherapy experienced significantly shorter operation time and hospitalization time, less bleeding volume, and higher effective treatment rate than the control group. Moreover, the therapy group showed a significantly lower incidence of complications and higher life quality than the control group. Cox regression analysis showed that neo-adjuvant chemotherapy was an independent factor affecting the progression-free survival time of patients. This study has revealed the application value of MRM combined with neo-adjuvant chemotherapy in patients with BC.

Keywords: Breast cancer, modified radical mastectomy, neo-adjuvant chemotherapy, life quality

Introduction

Breast cancer (BC) is the second most pervasive cancer among women as a complex heterogeneous disease [1]. The proliferation of mammary epithelial cells is out of control under the action of various carcinogens [2]. Its early symptoms include nipple discharge, breast lump, and axillary lymph node enlargement. It is manifested by multiple organ lesions after the metastasis of cancer cells at the advanced stage, and it is life-threatening if it is not treated timely [3]. According to studies, women with the following high-risk factors are more prone to BC: menarche <12 years old, late menopause age (>55 years), not giving birth or not conducting breastfeeding after delivery, first delivery age >35 years, received estrogen replacement therapy after menopause, and family history of BC [4]. BC shows an annually increasing incidence and gradually affects younger population, seriously compromising the life quality and physical and mental health of women [5]. Thus, choosing an effective treatment plan to improve the survival rate and life quality of patients has always been the focus of medical research.

BC is primarily treated by traditional radical operation in clinical practice [6]. Some scholars have pointed out that most patients with BC have favorable clinical treatment effect, but they will suffer serious psychological and physiological damage during traditional radical operation [7]. Thanks to the continuous development of medical technology, the way to treat BC is not limited to surgery. Modified radical mastectomy (MRM) combined with neo-adju-

vant chemotherapy is also an option [8]. Neo-adjuvant chemotherapy is a systemic treatment before operation, which can reduce BC mass, inhibit tumor proliferation, differentiation, and metastasis, improve the breast-conserving opportunity and reduce preoperative staging [9]. According to the study [10], after neo-adjuvant chemotherapy, the masses of 50-70% of patients can be reduced, and some even disappear completely, so neo-adjuvant chemotherapy can effectively inhibit tumor progression, improve life quality of patients and increase the success rate of surgery.

Over the past few years, neo-adjuvant chemotherapy has been applied increasingly in the treatment of BC, which provides an effective prognosis guarantee for patients with BC and also provides a crucial choice for the treatment of advanced BC [11]. This study analyzed the influence of MRM combined with neo-adjuvant chemotherapy on postoperative recurrence rate, negative emotion, and life quality of patients with BC.

Materials and methods

General materials

This study was approved by the ethics committee of our hospital (LL2018 (review) 081(A)), and all patients signed informed consent forms after being informed of the study. A total of 80 patients who were diagnosed as BC and scheduled to receive surgery in our hospital from January 2018 to January 2020 were enrolled as study objects. The 80 patients were assigned to the control group (n=39) or the therapy group (n=41). The inclusion criteria: Patients meeting the diagnosis criteria of BC [12], patients at TNM stage I-II, patients between 31 and 65 years old, patients whose Karnofsky Performance Scale (KPS) score was not lower than 80 points, patients without distant metastasis according to clinical examination, and patients without abnormality in chest X-ray examination and abnormal liver function. The exclusion criteria: Patients with intestinal diseases, diabetes mellitus, hematological diseases, or hypertension and those with a history of chemotherapy or radiotherapy before operation.

Therapy means

Neo-adjuvant chemotherapy: Patients in the therapy group were treated with 3 cycles of chemotherapy before operation (one cycle consisted of 21 days). The chemotherapeutic drugs mainly included fluorouracil (Fu, Jiangsu Wuzhong Pharmaceutical Group Corporation, Jiangsu, China, State Food and Drug Administration (SFDA) approval number: H120209-59) combined with pirarubicin (THP, Shenzhen Main Luck Pharmaceuticals Inc., Guangzhou, China, SFDA approval number: H10930106) and cyclophosphamide (CTX, Shenzhen Main Luck Pharmaceuticals Inc., Guangzhou, China, SFDA approval number: H20046025). On the first and eighth days of chemotherapy, 500 mg/m^2 Fu and 550 mg/m^2 CTX were given to each patient through intravenous drip, and 40 mg/m^2 THP was given intravenously on the first day. During treatment, the adverse reactions of the patients were evaluated, and measures to ameliorate vomiting and protect stomach were taken as necessary.

Modified radical mastectomy (MRM): The patient was in a supine position, and general anesthesia was given. Before surgery, the operation site was positioned, disinfected and applied with a disinfection towel. A transverse or longitudinal fusiform incision was done on the surgical site, the breast tissues including the lesion was removed, and it was freed in the superficial layer of pectoralis major fascia. During operation, attention should be paid to remove fat and lymphatic tissue. After the lesion was removed, axillary lymph nodes should be cleaned, and axillary blood vessels and nerves should be protected to avoid collateral injury during operation. The lymph nodes in the apical, the central and the subclavian areas should be removed one by one. After operation, the wound was soaked with distilled water to kill the metastatic malignant tumor cells, and the nodules were sutured. The drainage tube was indwelled, and pressure bandaging was conducted. At 3-5 days after operation, the chest strap was bandaged again every day, and attention should be paid to check effusion under the armpit and ensure smooth drainage before pulling out the drainage tube.

Outcome measures

The clinical efficacy in patients was evaluated according to related criteria released by the World Health Organization (WHO) [13]. Progressive disease: there is a newly formed lesion, or the volume of the current lesion increases by 25% or more compared with the

Table 1. Clinical data of patients

Clinical data	The control group (n=39)	The therapy group (n=41)	t/χ^2 value	*P*-value
Age (Y)	51.59±2.69	52.96±3.46	0.488	0.627
Tumor diameter (cm)	3.6±1.3	3.9±1.5	0.954	0.343
TNM stage			0.216	0.642
Stage I	22 (56.41)	21 (51.22)		
Stage II	17 (43.59)	20 (48.78)		
Differentiation			0.747	0.388
High/moderate differentiation	30 (76.92)	28 (68.29)		
Low differentiation	9 (23.08)	13 (31.71)		
Estrogen receptor (ER)			0.834	0.361
Positive	28 (71.79)	33 (80.49)		
Negative	11 (28.21)	8 (19.51)		
HER2			0.021	0.884
Positive	27 (69.23)	29 (70.73)		
Negative	12 (30.77)	12 (29.27)		
Menopause			0.230	0.632
Yes	23 (58.97)	22 (53.66)		
No	16 (41.03)	19 (46.34)		
Tumor site			0.083	0.773
Left breast cancer	14 (35.90)	16 (39.02)		
Right breast cancer	25 (64.10)	25 (60.98)		

Note: Chi-square test was used to analyze the count data.

original lesion; Stable disease: compared with the original lesion, the volume of the existing lesion decreases by less than 50% or increases by less than 25%; Partial remission: compared with the original lesion, the volume of the present lesion decreases by 50% or more, and the duration is shorter than 4 weeks; Complete remission: the lesion disappears completely and the duration is longer than 4 weeks. The total effective rate = partial remission rate + complete remission rate.

The operation conditions of the two groups were analyzed, including operation time, bleeding volume, hospitalization time, and complications after operation. The overall survival (OS) rate and progression-free survival (PFS) rate of the two groups were analyzed. The follow-up methods included outpatient visits, door-to-door follow-up and telephone follow-up.

The life quality of patients was evaluated using the quality of life scale for patients with BC [14]. The scale consists of 40 items (physical function, emotional function, role function, social function, and cognitive function) in total, with 0-5 points for each item. The patients were asked to answer the questions according to their own actual situation, and a higher score indicates better life quality.

Statistical analyses

Statistical analyses were carried out using SPSS 17.0 (software Co., Ltd., Beijing, China). Enumeration data were expressed as n (%) and compared via the χ^2 test. Measurement data were expressed as the mean ± SD, and compared via the t test. In addition, the Kaplan-Meier method was adopted to plot survival curves, and the Log-rank test was used to compare the survival of two groups. Cox regression was used to analyze the prognostic factors of OS and PFS. $P<0.05$ indicated a significant difference.

Results

Clinical data of the two groups

According to analysis on the clinical data of the two groups, there was no significant difference in age and tumor diameter between the two groups (all P>0.05, **Table 1**).

Comparison of intraoperative and postoperative indexes between the two groups

We observed the related indexes of patients during and after operation, including operation time, bleeding volume and hospitalization time. According to the results, the therapy group experienced significantly shorter operation and hospitalization time, as well as significantly less bleeding volume than the control group (all P<0.05, **Figure 1**).

Comparison of efficacy between the two groups after treatment

After treatment, the control group showed a total effective rate of 35.90%, with 12 cases of progressive disease, 13 cases of stable disease, 6 cases of partial remission, and 8 cas-

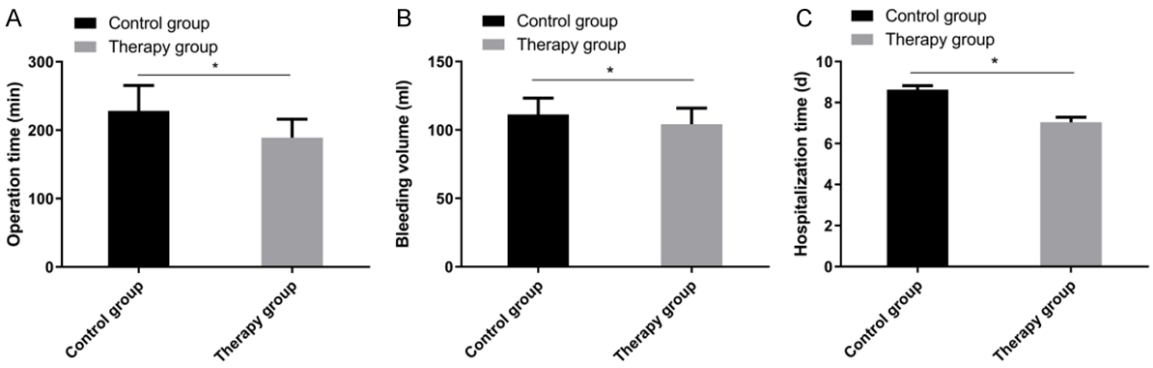

Figure 1. Intraoperative and postoperative indexes of patients. Compared with the control group, the therapy group experienced notably shorter operation time (A), less bleeding volume (B), and shorter hospitalization time (C). Note: *P<0.05, and independent sample t test was used for comparison between groups.

Table 2. Treatment efficacy in patients

Group	n	Progressive disease	Stable disease	Partial remission	Complete remission	The total correction efficiency (%)
The control group	39	12 (30.77)	13 (33.33)	6 (15.38)	8 (20.51)	35.90
The therapy group	41	5 (12.20)	9 (21.95)	11 (26.83)	16 (39.02)	65.85
χ^2 value	-	-	-	-	-	7.179
P-value	-	-	-	-	-	0.007

Note: Chi-square test was used to analyze the count data.

Table 3. Comparison of postoperative complications between the two groups

Group	n	Subcutaneous hemorrhage	Flap necrosis	Subcutaneous effusion	Upper limb lymphedema	Postoperative infection	The total incidence
The control group	39	1 (2.56)	3 (7.69)	2 (5.13)	2 (5.13)	1 (2.56)	23.08
The therapy group	41	1 (2.44)	0 (0.00)	1 (2.44)	0 (0.00)	0 (0.00)	4.88
χ^2 value	-	0.463	1.492	0.002	0.566	0.001	5.582
P-value	-	0.496	0.222	0.965	0.452	0.980	0.018

Note: Chi-square test was used to analyze the count data.

es of complete remission. The therapy group showed a total effective rate of 65.85%, with 5 cases of progressive disease, 9 cases of stable disease, 11 cases of partial remission, and 16 cases of complete remission. Therefore, the effective treatment rate of the therapy group was significantly higher than that of the control group (P<0.05) (**Table 2**).

Comparison of postoperative complications between the two groups

According to statistical analysis of postoperative complications in the two groups, the control group showed a total incidence of complications of 23.08%, with 1 case of subcutaneous hemorrhage, 3 cases of flap necrosis, 2 cases of subcutaneous effusion, 2 cases of upper limb lymphedema, and 1 case of postoperative infection. The therapy group showed a total incidence of complications of 4.88%, with 1 case of subcutaneous hemorrhage and 1 case of subcutaneous effusion. Although there was no significant difference in the individual complications between the two groups (P>0.05), the total incidence of complications in the therapy group was significantly lower than that in the control group (P<0.05, **Table 3**).

Cox regression analysis

In order to evaluate the OS and PFS of the two groups of patients, we followed up the patients to January 2021, with a follow-up rate of

Table 4. Cox univariate analysis of factors influencing OS and PFS of patients with breast cancer

Factors	Univariate Cox analysis of OS			Univariate Cox analysis of PFS		
	P-value	HR	95 CI%	*P*-value	HR	95 CI%
Age (≥50 years *vs.* <50 years)	0.923	1.067	0.288-3.958	0.672	0.815	0.316-2.101
Tumor diameter (≥4 cm *vs.* <4 cm)	0.007	0.212	0.069-0.649	0.491	0.733	0.303-1.773
TNM stage (stage I *vs.* stage II)	0.021	11.131	1.442-85.954	0.022	3.027	1.174-7.805
Differentiation degree (medium/high differentiation *vs.* low differentiation)	0.007	6.065	1.656-22.215	0.018	2.805	1.191-6.608
ER (+/-)	0.563	0.641	0.142-2.895	0.458	1.432	0.555-3.692
HER2 (+/-)	0.125	0.307	0.068-1.390	0.359	0.624	0.228-1.707
Menopause (yes/no)	0.409	1.588	0.529-4.765	0.579	1.275	0.541-3.005
Tumor site (left/right)	0.388	1.768	0.485-6.445	0.171	2.017	0.739-5.506
Treatment plan (combined *vs.* alone)	0.340	1.723	0.563-5.272	0.027	2.914	1.13-7.515

Table 5. Cox multivariate analysis of factors influencing OS and PFS of patients with breast cancer

Factors	Multivariate Cox analysis of OS			Multivariate Cox analysis of PFS		
	P-value	HR	95 CI%	*P*-value	HR	95 CI%
Age (≥50 years *vs.* <50 years)	0.553	0.651	0.158-2.689	0.414	0.669	0.255-1.755
Tumor diameter (≥4 cm *vs.* <4 cm)	0.596	0.686	0.171-2.759	0.828	1.11	0.432-2.856
TNM stage (stage I *vs.* stage II)	0.041	8.565	1.166-71.669	0.050	2.62	1.001-6.863
Differentiation degree (medium/high differentiation *vs.* low differentiation)	0.022	4.562	1.393-19.633	0.027	2.693	1.120-6.477
ER (+/-)	0.788	0.776	0.122-4.923	0.615	1.293	0.475-3.52
HER2 (+/-)	0.270	0.417	0.088-1.973	0.525	0.713	0.251-2.023
Menopause (yes/no)	0.219	2.11	0.641-6.942	0.553	1.311	0.536-3.204
Tumor site (left/right)	0.472	1.703	0.399-7.266	1.525	0.217	0.687-5.233
Treatment plan (combined *vs.* alone)	0.104	2.595	0.822-8.192	0.012	3.391	1.304-8.815

100.00%. We first conducted a univariate Cox regression analysis to investigate the factors affecting OS and PFS. The results showed that tumor diameter, TNM stage and differentiation were risk factors for OS; while TNM stage, differentiation and treatment scheme were risk factors for PFS (all P<0.05) (**Table 4**). Factors affecting OS and PFS that were significant in univariate Cox regression were analyzed using multivariate analysis. The Backward LR method was used for processing. The results showed that TNM stage and differentiation were independent factors of OS, while differentiation degree and treatment scheme were independent factors of PFS (both P<0.05) (**Table 5**).

Comparison of life quality between the two groups in one year after operation

According to observation results of the life quality of the two groups in one year after operation, the therapy group got notably better scores in physical function, emotional function, role function, social function, and cognitive function than the control group (all P<0.05, **Figure 2**).

Discussion

BC is a pervasive malignant condition among women, which is mainly triggered by breast structural changes due to abnormal hyperplasia of mammary gland epithelial cells [15]. For beauty-loving women, BC will not only cause pain, but also give rise to negative psychology, and the patients usually react negatively to treatment because of the particularity of the lesion location, and finally suffer unfavorable therapeutic effect [16].

Clinical treatments for BC include surgery, radiotherapy and chemotherapy, among which surgery is the most common one [17]. MRM is a novel and innovative operation scheme based on the expanded radical operation. It only resects the breast and axillary lymph node lesions, so the operation scope is narrowed and the recovery of patients is accelerated, which enables it to be the standard operation scheme for BC [18, 19]. However, surgery alone is not enough to completely cure BC and solve the problems of distant metastasis of cancer cells and complications after surgery,

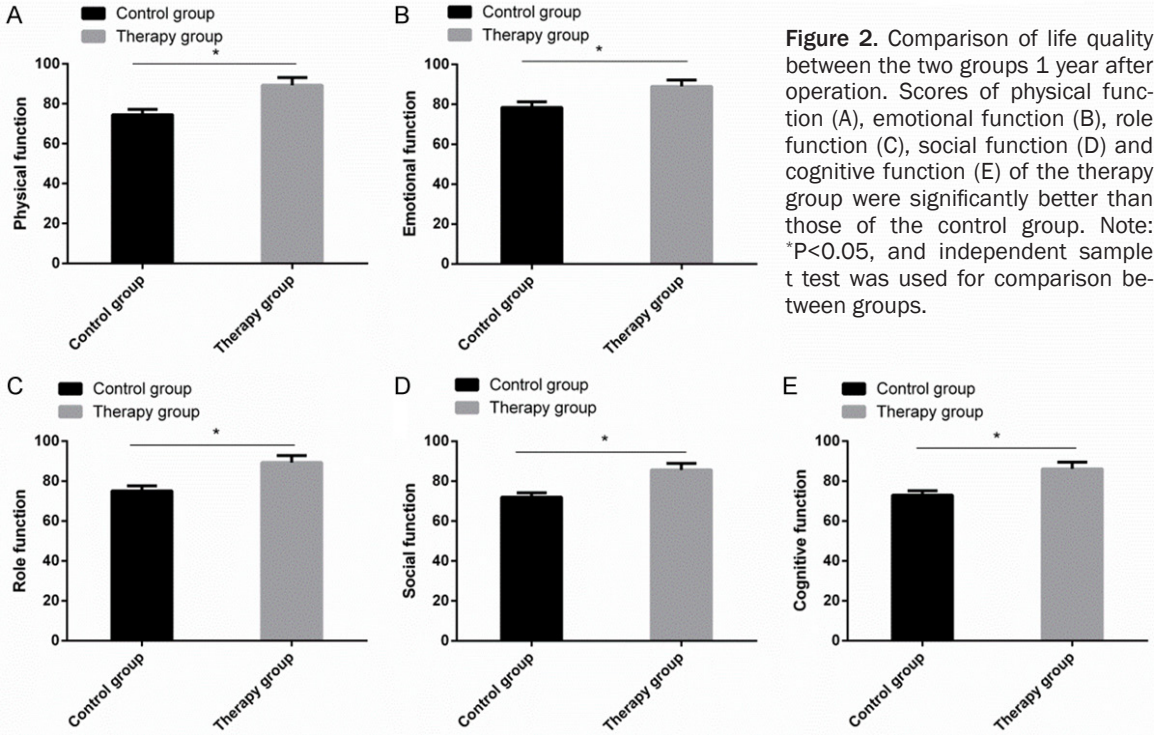

Figure 2. Comparison of life quality between the two groups 1 year after operation. Scores of physical function (A), emotional function (B), role function (C), social function (D) and cognitive function (E) of the therapy group were significantly better than those of the control group. Note: *P<0.05, and independent sample t test was used for comparison between groups.

so other effective treatments should also be additionally adopted in combination with surgery [20, 21].

Neo-adjuvant chemotherapy refers to systemic chemotherapy before breast surgery [22]. In one prior research, addition of bevacizumab to neo-adjuvant chemotherapy significantly increased the pathological complete remission rate of patients with HER2-negative early BC [23]. In our study, patients treated with neo-adjuvant chemotherapy experienced significantly shorter operation time and suffered significantly less bleeding volume, and neo-adjuvant chemotherapy also improved the effective treatment rate, and shortened the hospitalization time for patients. The results demonstrate the efficacy of neo-adjuvant chemotherapy in improving clinical efficacy in patients. Similarly, in one study by Poggio et al., neo-adjuvant chemotherapy with platinum improved the pathological complete remission of triple negative BC from 37.0% to 52.1%. According to the postoperative complications of patients, although there was no remarkable difference in the incidence of individual complications such as subcutaneous hemorrhage and flap necrosis between the two groups, the total incidence of complications in the therapy group decreased greatly after neo-adjuvant chemotherapy [24]. It may be explained by the fact that neo-adjuvant chemotherapy can narrow the scope of BC resection, and the smaller incision is conducive to patients' recovery, so it can reduce the occurrence of complications. Then, we evaluated the postoperative recurrence and survival of patients, and found that after neo-adjuvant chemotherapy, the incidences of axillary lymphadenectasis and local recurrence among patients with BC decreased notably and the survival time of them was longer. Similarly, in one study by Spring et al. [25], patients treated with neo-adjuvant chemotherapy showed better pathological complete remission and overall survival time, especially in patients with triple negative and HER2+ BC. It may be due to the fact that BC metastasis is micrometastasis, and neo-adjuvant chemotherapy can control lymph node metastasis, eliminate micrometastasis lesions, and reduce tumor cell activity, so as to inhibit tumor cell metastasis [26]. Therefore, neo-adjuvant chemotherapy is safer than traditional MRM for patients with early BC after surgery, and can also improve the postoperative survival rate. Similar to the result of previous studies, neoadjuvant chemotherapy was found to be an independent risk factor for PFS in patients with BC

in our study. Finally, we investigated the life quality of patients, and found remarkable improvement in life quality among patients treated with neo-adjuvant chemotherapy. The improvement may be due to the fact that MRM narrowed the scope of operation, accelerated the healing of wounds and alleviated the discomfort of patients. In addition, the modified surgery largely maintained the external chest contour of patients and retained the upper arm movement function, which greatly improved the patients' life quality.

However, our study still has some limitations. For instance, we didn't evaluate the changes of immune function before and after treatment. In addition, we didn't conduct long time follow-up to understand their long-term survival. These limitations need to be addressed in future research.

To sum up, compared with surgery alone, MRM combined with neo-adjuvant chemotherapy can exert positive effects on patients with BC in terms of operation time, hospitalization time, intraoperative bleeding, postoperative complications and life quality, and the combined treatment is safe and reliable.

Disclosure of conflict of interest

None.

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