

Effect of fluorouracil and plastic breast-conserving surgery in young patients with early breast cancer

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Abstract: To explore the effect of fluorouracil and plastic breast-conserving surgery on the immune level, psychological status and quality of life of young patients with early breast cancer. Seventy-six young patients with early breast cancer admitted to Cangzhou Central Hospital from January 2016 to January 2017 were selected and divided into a control group (n=38, conventional breast-conserving surgery) and an observation group (n=38, Fluorouracil and plastic breast-conserving surgery). The observation group had shorter operation time and hospital stay and less intraoperative blood loss in comparison to the control group ($P<0.05$); the CD4+, CD8+ and IL-8 of the observation group were higher, and the CD4+/CD8+ and IL-10 were lower ($P<0.05$); the HAMD and HAMA scores of the observation group were significantly lower ($P<0.05$); the physiological, emotional, and family, functional, and additional concerns were lower in the observation group ($P<0.05$); the postoperative breast shape satisfaction was higher in the observation group ($P<0.05$). Fluorouracil combined with plastic breast-conserving surgery has a better treatment effect on young patients with early breast cancer, which can promote postoperative recovery, maintain normal breast morphology, reduce the immune function damage caused by the surgery, improve patients' psychological status and quality of life, and reduce the incidence of postoperative complications and deaths.

Keywords: Plastic breast-conserving surgery, early breast cancer, immune level, mental state, quality of life.

INTRODUCTION

Breast cancer is a common malignant tumor in the clinic, and its manifestations include axillary lymphadenopathy, nipple discharge, and breast lumps in early stage. In advanced stages, cells or glandular duct epithelium can become malignant, resulting in metastasis and multiple-organ diseases and seriously threatening the lives of patients (Cameron *et al.*, 2017; Sun *et al.*, 2016). It is reported that the incidence of breast cancer accounts for about 24.2% of female cancers worldwide, ranking first among female cancers (De Lorenzi *et al.*, 2016). Since the most patients are young, the incidence of breast cancer gradually tends to be younger. In recent years, with the improvement of diagnosis and early screening of breast cancer, many patients have received accurate diagnosis and effective treatment at an early stage, thereby improving survival rate. Women always pay much emphasis on morphological aesthetics of their breast. Once the female characteristics are flawed, it will tremendously affect their mental health (El-Sabawi *et al.*, 2015). Most breast cancer patients have abnormal immune function (Cruz *et al.*, 2016). Conventional breast-conserving procedures used in the past is conducted by peeling a wide range of the chest skin with large trauma and heavy bleeding, and it cannot effectively maintain the shape of the breast, which adversely affects the physical and mental health of patients. Studies have shown that plastic breast-conserving surgery has a good therapeutic effect, can maximize the integrity and aesthetic

appearance of the body, relieve the patient's immune function damage, lessen the patient's psychological burden and boost quality of life (Lorenzi *et al.*, 2016). Fluorouracil is a fluorine-containing pyrimidine base C₄H₃FN₂O₂ used as a neoplastic agent to treat some kinds of cancer and treats various cancers by working to slow the growth of the cancerous cells and slowly destroy them (Du *et al.*, 2019; Wu *et al.*, 2019). The reports on the combination of Fluorouracil and plastic breast-conserving surgery on breast cancer patients were rarely seen. This study was designed on 76 young patients with early breast cancer admitted to Cangzhou Central Hospital from January 2018 to January 2020, to explore the clinical effect of fluorouracil and plastic breast-conserving surgery.

MATERIALS AND METHODS

General information

76 young patients with early breast cancer admitted to Cangzhou Central Hospital from January 2018 to January 2020 were selected. Inclusion criteria: (1) patients who met the diagnostic criteria for early breast cancer (Rosenberger *et al.*, 2016); (2) patients with complete clinical data; (3) patients who signed informed consent. Exclusion criteria: (1) patients with malignant tumors in other parts; (2) patients with severe liver, kidney, heart and other organ dysfunction; (3) patients with poor surgical tolerance.

The control group was 25 to 50 years old, with an average of (38.70±4.31) years old; the tumor diameter was 0.72cm to 3.20cm, with an average of (1.42±0.56) cm; there were

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21 patients with clinical stage I and 17 cases with stage II. The observation group was 36-52 years old, with an average of (38.72±4.32) years old; the tumor diameters was 0.70cm to 3.22cm, with an average of (1.45±0.55) cm; there were 23 cases with stage I and 15 cases with stage II. No difference was seen with respect to the general data between the two groups (P>0.05).

Methods

The control group used conventional breast-conserving surgery. The specific procedures were as follows. Determine the appropriate incision position according to the size, location of the tumor, and breast sagging, volume, etc.; perform incisions or parallelogram incisions if the lesion was in the upper half of the breast; perform radial incision or "J" type incision if the lesion was in the lower half of the breast; remove the outer edge and upper and lower parts of the breast after the shape of the incision was determined, or remove 0.5 to 1.5 cm of normal breast tissues around the lesion; clean the surrounding lymph during the resection, and keep the residual cavity open, and then extract the lymph for examination.

The observation group was treated with fluorouracil and plastic breast-conserving surgery. Perform mastectomy in the same way as the control group; suture the glands immediately after the resection; implement lifting, rotating and filling etc.; fill the breast according to the needs of the patient; repeat the fixation and shaping; pay attention to observe if there was any deviation in nipple and areola after the completion of the filling. If any, seek medical advice promptly. Fluorouracil (National Standard 31020593, Shanghai Xudong Haipu Industry Co., Ltd., specification 10mL: 0.25g/bottle) 600mg/(m²·d), continue for 1~5 d, 2 consecutive courses of treatment with 21 d as a course.

Outcome measures and evaluation standards

(1) Operation time, intraoperative blood loss and hospital stay. (2) T lymphocyte subsets and serum IL-8 and IL-10 before and after treatment; 5ml of peripheral venous blood was extracted from patients before and after treatment, flow cytometry produced by American BD was used to detect T lymphocyte subsets CD4+, CD8+, and CD4+/CD8+, and enzyme-linked immunosorbent assay was used to detect serum IL-8 and IL -10 level. (3) Psychological state before and after treatment. Hamilton Anxiety Scale (HAMA) was applied (Sherwell-Cabello *et al.*, 2015), which includes 14 items, with <7 points

indicating normal, 7-20 points mild anxiety, 21-28 points moderate anxiety, ≥29 points severe anxiety. The Hamilton Depression Scale (HAMD) (Kawano *et al.*, 2016) was used, which includes 17 items and is graded using a five-grade scaling (0 to 4 points), with the total score > 35 points representing severe depression, 21-35 points moderate depression, 8-20 mild depression, <8 points normal. The higher the scores of the two scales, the more serious the anxiety and depression. (4) The quality of life before and after treatment. The functional assessment of cancer therapy-breast cancer (FACT-B0) (Naqvi *et al.*, 2016) was used, which includes 5 dimensions and 36 items, covering physiology (7 items), emotion (6 items), family (7 items), physical function (7 items), and additional concerns (9 items), etc., and adopts a five-grade scaling from not a bit to very (0 ~ 5 grades); the higher the score, the worse the quality of life. (5) The satisfaction of postoperative breast shape. (6) The survival rate.

Ethical approval

This study was approved by the ethics committee of our hospital with the No. of 2017-21-03.

STATISTICAL ANALYSIS

SPSS19.0 software was applied for the data process. The qualitative data was described by n (%) and the χ² test was performed. The quantitative data that conformed to the normal distribution were expressed by (x̄ ± s), and the t test was performed. The Kaplan-Meier method was used to draw the survival curves of the two groups. P<0.05 indicated a statistical difference.

RESULTS

Comparison of the operation time, intraoperative blood loss and hospitalization time

The observation group had shorter operation time and hospital stay and less intraoperative blood loss in comparison with the control group (P<0.05, table 1).

Comparison of T-lymphocyte subsets and serum IL-8 and IL-10 levels before and after treatment

Before treatment, the levels of T lymphocytes CD4+, CD8+, CD4+/CD8+ and serum IL-8 and IL-10 in the two groups were similar (P>0.05); the observation group's CD4+, CD8+, IL -8 after treatment was higher, CD4+/CD8+ and IL-10 were lower (P<0.05, table 2).

Table 1: Comparison of operation time, intraoperative blood loss and hospital stay

| Groups | Operation time (min) | Intraoperative blood loss (ml) | Hospital stay(d) |
|--------------------------|----------------------|--------------------------------|------------------|
| Observation group (n=38) | 119.80±12.25 | 86.03±10.04 | 8.40±1.26 |
| Control group (n=38) | 152.12±12.56 | 113.13±10.20 | 14.85±1.30 |
| t | 11.360 | 11.670 | 21.960 |
| P | <0.001 | <0.001 | <0.001 |

Table 2: Comparison of T-lymphocyte subsets and serum IL-8 and IL-10 levels before and after treatment

| Groups | CD4+(%) | | CD8+(%) | | CD4+/CD8+ | | IL-8(pg/ml) | | IL-10(pg/ml) | |
|--------------------------|------------------|-----------------------------|------------------|-----------------------------|------------------|----------------------------|------------------|-----------------|------------------|-----------------|
| | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment |
| Observation group (n=38) | 53.19 ±2.52 | 61.22 ±3.15 ^a | 35.22 ±5.15 | 33.30 ±5.19 ^a | 1.29 ±0.51 | 1.81 ±0.67 ^a | 75.02 ±3.17 | 79.08 ±3.43 | 66.87 ±3.22 | 43.80 ±2.68 |
| Control group (n=38) | 53.22 ±2.51 | 56.80 ±3.08 ^a | 35.25 ±5.09 | 30.22 ±5.26 ^a | 1.27 ±0.49 | 1.40 ±0.70 ^a | 75.10 ±3.09 | 76.88 ±3.07 | 66.80 ±3.25 | 53.70 ±3.04 |
| t | 0.052 | 6.185 | 0.026 | 2.569 | 0.174 | 2.257 | 0.111 | 15 | 0.094 | 15.06 |
| P | 0.959 | <0.001 | 0.979 | 0.012 | 0.862 | 0.027 | 0.912 | <0.001 | 0.925 | <0.001 |

Table 3: Comparison of the psychological state before and after treatment

| Groups | HAMA(points) | | HAMD(points) | |
|--------------------------|------------------|-------------------------|------------------|-------------------------|
| | Before treatment | After treatment | Before treatment | After treatment |
| Observation group (n=38) | 25.22±3.82 | 12.23±1.58 ^b | 32.73±3.59 | 17.65±1.54 ^b |
| Control group (n=38) | 25.25±3.80 | 19.70±1.66 ^b | 32.75±3.60 | 26.34±2.12 ^b |
| t | 0.034 | 20.090 | 0.024 | 20.440 |
| P | 0.973 | <0.001 | 0.981 | <0.001 |

Note: b indicates that compared with before treatment, $P < 0.05$

Comparison of the psychological state before and after treatment

The HAMD and HAMA scores in the two groups were similar before treatment ($P > 0.05$); after treatment, the HAMD and HAMA scores in the observation group were significantly lower ($P < 0.05$, table 3).

Comparison of the quality of life before and after treatment

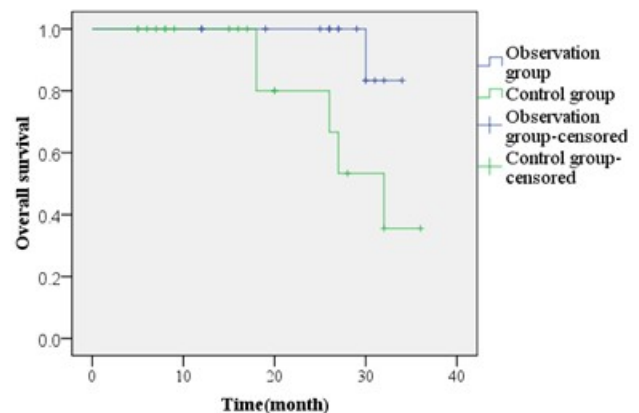
Before treatment, no noticeable difference was seen in the quality of life in the two groups ($P > 0.05$); after treatment, the observation group had lower physiological, emotional, family, functional and additional concerns scores in comparison to the control group ($P < 0.05$, table 4).

Comparison of the satisfaction of postoperative breast shape

The postoperative breast shape satisfaction rating of the observation group was higher (94.74% vs 73.68%) ($P < 0.05$, table 5).

Comparison of the survival rate

The follow-up was implemented for 3 years after discharge and found that 2 cases of relapse, 1 case of metastasis, and 1 death were in the observation group; 4 cases of relapse, 2 cases of metastasis and 4 deaths in the control group. The results of survival analysis by kaplan-meier method found that the overall survival rate of the observation group was 82.20%, and the control group was 38.59%, in which the difference was significant ($\chi^2 = 4.830$, $P = 0.028$) by Log-Rank test (fig. 1).

**Fig. 1:** K-M survival analysis of two groups of patients

DISCUSSION

Breast cancer is a relatively common malignant tumor disease in the oncology department and it prevails in middle-aged and elderly women. The incidence of breast cancer in women before and after menopause is higher (Xia *et al.*, 2016). However, with the development of society, the disease gradually tends to be younger.

There are many factors influencing the incidence of breast cancer, mostly accompanied by abnormal genetic or biological levels. Related studies have shown that abnormal immune function of breast cancer patients will affect the transcription of tumor cell DNA, allowing gene

regulated by them to express, proliferating and differentiating the white blood cells and further aggravating the progress of the disease (Kim *et al.*, 2016; Murata *et al.*, 2016). In the past, the treatment of breast

cancer mainly adopted resection therapy and it can indeed cure the tumor. However, the morphological defect or loss of the breast as the secondary sexual characteristics causes negative emotions for patients such as inferiority, depression and anxiety, affecting the physical and mental health and quality of life of patients (O'Brien *et al.*, 2015). With the continuous development of medical technology and surgery, many patients are accessible to breast-conserving surgery and it has been developed. Early breast-conserving surgery is a routine one, which can achieve aesthetics effects. However, since the residual cavity was not sutured in this surgery, the pressure of the residual cavity is likely to rise after filling the serum and fibrin, which seriously affects the healing of the incision and recovery (Soltani *et al.*, 2015). The plastic breast-conserving technique has been applied and obtained satisfactory outcomes. This surgical method uses the rearrangement of non-cancerous glands to reconstruct and repair the surgical cavity, which not only has the therapeutic effect of conventional breast-conserving surgery, reduces the incidence of surgical complications, but also maintains the original shape of the breast (Rajan *et al.*, 2014). Fluorouracil is a cycle-specific drug and has no anti-tumor activity itself. It enters the body and is decomposed into dihydrofluorouracil, Fluorouracil deoxynucleoside monophosphate (FdUMP), fluorouracil deoxynucleoside triphosphate (FdUTP) and fluorouracil triphosphate (FUTP). They can affect thymine nucleotide synthase through different mechanism and DNA synthesis, further inhibiting tumor cell growth and proliferation (Yu *et al.*, 2019).

This study revealed that the operation time and hospital stay of the observation group were shorter, and the intraoperative blood loss was less in comparison with the control group, indicating that plastic surgery can shorten the operation time and hospital stay of patients with early breast cancer, and can also reduce the operation time and blood loss. Studies have shown that the expression of immune levels of peripheral hematoma cells in the anti-tumor immune system in most tumor patients is low (Strnad *et al.*, 2016). The immune function of T lymphocyte subsets is extremely valuable in the detection of clinical efficacy of tumors, which can be clearly stated body's ability to directly resist the invasion of cancer cells. CD4+ has the function of immune memory and can directly kill tumor cells. The ratio of CD4+/CD8+ directly reflects the balance of cellular immunity. A decrease in the ratio indicates a decline in immune function (Morrow *et al.*, 2016). IL-8 and IL-10 are inflammatory factors that play an important role in fighting infection, anti-tumor and immune regulation (Yu *et al.*, 2019). After treatment

Table 4: Comparison of quality of life before and after treatment (x ± s)

| Groups | Physiological | | Emotional | | Family | | Functional | | Additional | |
|--------------------------|------------------|-------------------------|------------------|-------------------------|------------------|-------------------------|------------------|-------------------------|------------------|-------------------------|
| | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment |
| Observation group (n=38) | 30.25±3.88 | 14.38±1.55 ^c | 26.45±2.14 | 12.35±1.43 ^c | 31.01±3.50 | 14.68±1.26 ^c | 31.44±3.20 | 15.64±1.78 ^c | 38.70±3.67 | 19.25±2.01 ^c |
| Control group (n=38) | 30.27±3.85 | 23.24±1.85 ^c | 26.48±2.15 | 18.44±1.65 ^c | 29.98±3.53 | 22.11±2.37 ^c | 31.50±3.23 | 23.45±1.99 ^c | 38.74±3.70 | 25.43±2.52 ^c |
| t | 0.023 | 22.63 | 0.061 | 17.19 | 1.277 | 17.06 | 0.081 | 18.03 | 0.047 | 11.82 |
| P | 0.982 | <0.001 | 0.952 | <0.001 | 0.205 | <0.001 | 0.935 | <0.001 | 0.962 | <0.001 |

Note: c indicates that compared with before treatment, P<0.05

Table 5: Comparison of postoperative breast shape

| Groups | Satisfied | Fair | Unsatisfied | Satisfaction rate |
|--------------------------|-----------|-----------|-------------|-------------------|
| Observation group (n=38) | 25(65.79) | 11(28.95) | 2(5.26) | 36(94.74) |
| Control group (n=38) | 15(39.47) | 14(36.84) | 9(23.68) | 28(73.68) |
| χ^2 | | | | 6.633 |
| P | | | | 0.012 |

in this study, the CD4+/CD8+ ratio of the two groups declined, but the observation group was higher than the control group and the observation group's CD4+, CD8+, IL-10 were higher than the control group, suggesting that both operations will produce immunosuppressive effect, but plastic breast-conserving surgery can relatively mitigate the patient's immunosuppression and improve the recovery of the patient's immune function after the operation; the negative emotions such as anxiety and depression in the observation group after 3 years of follow-up were lower than the control group and the quality of life was better than the control group. Through follow-up communication, it can be seen that the control group feel inferior because of the lack of beauty of the postoperative breast and the inharmonious sexual life, which affects the psychological state and quality of life of the patients; while the observation group has obtained better breast morphological effects with higher satisfaction, fewer negative emotions such as low self-esteem, anxiety and depression, harmonious sex life, and higher quality of life. A study claimed that plastic breast-conserving surgery in Asian women with early breast cancer and small breasts had better breast aesthetic effects and higher patient satisfaction (Dahlback *et al.*, 2019). Some scholars pointed out that choosing the appropriate incision according to the size of the patient's breast and tumor can reduce the massive damage and effectively avoid the recurrence and distant metastasis (Langhans *et al.*, 2016). After follow-up in this study, there were 2 cases of relapse, 1 case of metastasis and 1 death in the observation group; 4 cases of relapse, 2 cases of metastasis, and 4 deaths in the control group; Kaplan-meier survival analysis found that observation had higher overall survival rate than the control group. It confirmed the control effect of plastic breast-conserving surgery on young patients with early breast cancer and stated that the application of plastic breast-conserving surgery can effectively prolong the survival time of patients. The reason for this may be that the research object of this study is young and in early stage, thus the surgical effect and surgical recovery are better.

CONCLUSION

In summary, use of fluorouracil and plastic breast-conserving surgery has a more satisfactory outcome on young patients with early breast cancer, which can promote the postoperative recovery of the patient,

maintain the normal shape of the breast and reduce the immune function damage following the surgery. Moreover, it can improve the psychological state and life quality of the patient and reduce the incidence of postoperative complications and deaths.

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