

ORIGINAL ARTICLE

Correlation between ultrasound guided staining margin and survival rate, recurrence rate and cosmetic effect of breast cancer patients

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Summary

Purpose: To analyze the effect of ultrasound-guided marking margin on cosmetic results, recurrence rate and survival rate of breast cancer patients.

Methods: 96 cases of early breast cancer admitted to Tumor Surgery Department of our hospital from January, 2017 to March, 2018 were treated by breast-conserving surgery. According to random number table method, 48 cases in the Control Group received routine surgical treatment. Forty-eight cases in the Research Group were treated with ultrasound guided staining and location of the mark and then surgical removal. The margin of incision, perioperative indexes and aesthetic effect of breast surgery were compared between the two groups. The patients were followed up for 3 years, the recurrence rate and survival rate were recorded, and the 3-year quality of life (QoL) was evaluated.

Results: 8.33% of patients in the Research group and 27.08% in the control group were positive for the first margin ($p < 0.05$); The volume of resected specimens in the Research Group was significantly smaller than that in the Control Group ($p < 0.05$); The proportion of maximum resection margin ≤ 2 cm in the Research Group was higher than that in the Control Group ($p < 0.05$). The operation time in the Research Group was higher than that in the Control Group, while the

hospital stay and intraoperative blood output in the Research Group were lower than those in the Control Group ($p < 0.05$). The excellent and good rate of postoperative breast beauty in the two groups was 75.00% and 39.58% in the Control Group. The beauty effect of the Research Group was higher than that of the Control Group ($p < 0.05$). The recurrence rate in the Research Group was 4.17% lower than 16.67% in the Control Group, and the tumor-free survival rate and distal metastasis free survival rate were significantly higher than those in the Control Group ($p < 0.05$). After 3 years of follow-up, the scores of QoL-46 in both groups were significantly higher than those before operation ($p < 0.05$); The scores of mental and psychological dimensions were significantly higher than those in the Control Group ($p < 0.05$).

Conclusions: In the operation of breast cancer, the use of ultrasound guided staining and location can improve the accuracy of surgical margin, reduce the volume of the removed specimen, reduce operative trauma, intraoperative blood loss, reduce the recurrence rate, improve the tumor-free and distant metastasis survival rate, and better meet the master's aesthetic needs and improve the patient QoL.

Key words: cosmetic effect, mammary cancer, breast conserving surgery, ultrasound guidance, staining mark

Introduction

Breast cancer shows an upward trend, which poses a serious threat to women's health. Surgery is a primary means to treat this disease (breast-con-

serving surgery, mastectomy, etc). Generally, for patients with early breast cancer, breast-conserving surgery is one important way. Combined with

adjuvant radiotherapy, this operation can achieve similar long-term results such as mastectomy, and can better preserve the appearance of breasts to meet the cosmetic needs of patients [1]. This operation has the advantages of good postoperative recovery and small surgical trauma, conforms to the concept of minimally invasive, and is widely used in the clinic and favored by the majority of doctors and patients. However, a large number of studies has shown that conventional breast-conserving surgery has a higher positive rate of margins and a higher recurrence rate after surgery [2,3]. Therefore, in breast-conserving surgical treatment of breast cancer, how to reduce excessive removal of disease-free lymph nodes, improve the accuracy of surgical resection, and meet patients' needs for breast beauty has become a key research issue for current clinical breast surgeons and experts [4]. In recent years, with the promotion and application of ultrasound-guided assisted positioning technology, new treatment options have been provided for breast cancer patients with breast-conserving surgery. In this study, 96 cases of early breast cancer treated in Tumor Surgery Department of our hospital from January, 2017 to 1 March, 2018 were chosen as observation group, and the application value of staining markers under ultrasound guidance was analyzed

Methods

General information

96 cases of early breast cancer treated in Tumor Surgery Department of our hospital from January, 2017 to 1 March, 2018 were chosen and the study was approved by the hospital ethics committee; random number table method was used for grouping. The Control

Group included 48 patients aged 28 to 64 years (mean 53.42 ± 10.64), TNM stage included 29 cases of stage I, 14 cases of stage IIA, 5 cases of stage, pathological types: 1 case of medullary carcinoma, 9 cases of invasive lobular carcinoma, 38 cases of invasive ductal carcinoma, maximum tumor diameter 0.5-2.7 cm (mean 1.42 ± 0.38) cm; the Research Group: 48 patients aged 25 to 62 years, (mean 54.10 ± 11.06); TNM stage: 30 cases of stage I, 16 cases of stage IIA, 2 cases of stage IIB; pathological types: 2 cases of medullary carcinoma, 10 cases of invasive lobular carcinoma, 36 cases of invasive ductal carcinoma, maximum tumor diameter 0.6-2.9 cm (mean 1.53 ± 0.40). The basic data of the two groups of patients were comparable ($p > 0.05$).

Inclusion criteria: (1) diagnosed as breast cancer by needle biopsy, ultrasonography, etc.; (2) know the study and sign the consent form to be included; (3) tumor diameter of the patient <3 cm (including burr range); (4) single lesion shown in preoperative imaging examination; (5) the patient met the indications for breast-conserving surgery; (6) age ≥ 18 years old.

Exclusion criteria: (1) lack of main information; (2) lost to follow-up; (3) no margin evaluation during operation; (4) neoadjuvant treatment before operation; (5) patient lesions have achieved TNM stages III or IV; (6) having history of radiotherapy and chemotherapy or other malignant tumors; (7) multifocal breast cancer and central breast cancer.

Methods

Both groups of patients underwent imaging examinations such as enhanced magnetic resonance, mammography, Color Doppler ultrasound, and preoperative co-localization. According to clinical examination, the conditions for breast-conserving surgery were judged. Color Doppler ultrasound technology checks the lesion boundary, depth, size, location, etc. If the lesion is beyond the visible range of Color Doppler ultrasound, a mammography target detection is performed on the basis of its positioning, and finally an enhanced mag-

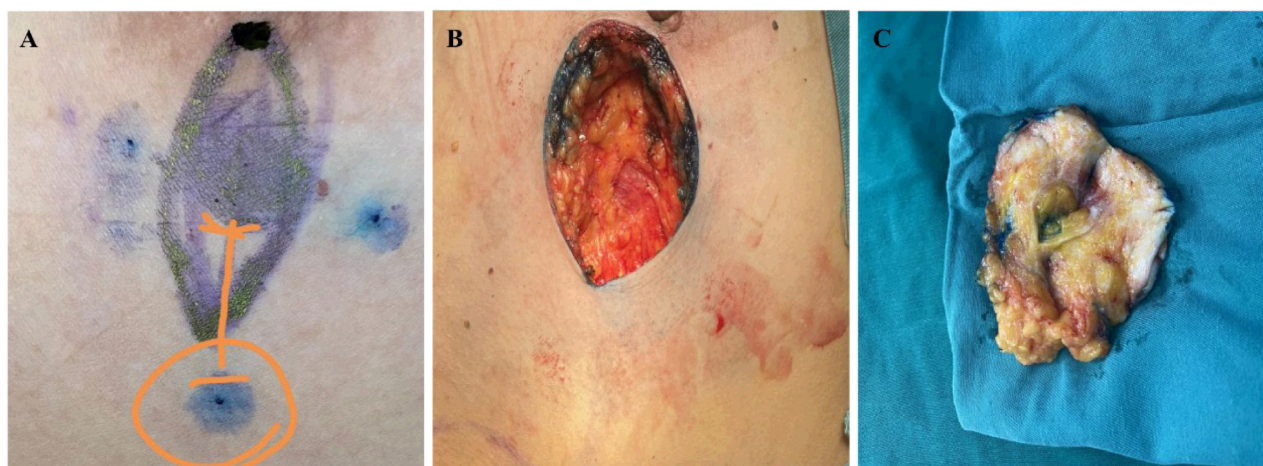


Figure 1. Preoperative and postoperative positioning map of breast cancer patients. **A:** Preoperative marking (arrow indicates the location of methylene blue, 1cm from the tumor edge). **B:** intraoperative findings. **C:** Anatomy of breast conserving specimens.

netic resonance scan is performed to determine whether the lesion area is the same as that confirmed based on Color Doppler ultrasound and molybdenum. If the target matches, check whether the lesion is single.

The patients in the Research Group were stained and positioned under the guidance of ultrasound, using methylene blue staining and 4-6 point method for positioning. One-two hours before the operation, under the guidance of ultrasound, 2 ml 0.25% methylene blue were injected into the surface of the breast at 1cm from the boundary of the lesion positioned by combined imaging method, and 0.2 ml per positioning point. A fusiform incision just above the tumor was chosen for surgery, and the skin from the projection area of the tumor body surface was removed. The postoperative suture should be performed without tension. The subcutaneous cut was perpendicular to the surface of the tumor along with the incision, and the free treatment was performed away from the center of the middle. When all 4-6 methylene blue positioning points could be seen, cutting vertically along the positioning points to the posterior breast space was performed. Note that in order to ensure the integrity of the natural barrier, the pectoralis major fascia does not need to be removed. If during the operation or preoperative imaging shows that the tumor involves the pectoralis major fascia, it needs to be removed. Surgical cancer specimens were excised and stained to mark the margins for examination (Figure 1).

Patients in the Control Group underwent conventional breast-conserving surgery. The surgical incision design and method were the same as those in the Research Group. During the operation, the lesion was resected according to the results of preoperative imaging and combined with the experience of the surgeon. One cm area of the lesion boundary was resected.

Observation indicators

The surgical margins of the two groups were evaluated. The surgical resection specimens were sent for examination. The volume of the resection specimens was measured first, and then the maximum resection margin was determined by dissection to determine whether the margin was greater than 2 cm. The positive rate of the resection margin was determined and analyzed based on the pathological frozen examination results of the specimens. The interpretation of specimen pathology was performed by two pathologists with deputy senior titles.

The perioperative indicators of the two groups of patients were recorded, including hospital stay, operation time, bleeding volume, etc.

Postoperative evaluation of the breast beauty effect of the two groups [5,6]; Excellent: postoperative breast skin, hand feel, appearance, etc., without significant difference between the unrejected side, nipple level difference ≤ 1 cm, double breasts are symmetrical; Good: postoperative breast skin without significant difference between the hand feel, shape, etc. and the healthy side, and the nipple level difference ≤ 2 cm; Middle: There is a difference between postoperative breast skin and the unrejected side, the nipple level difference is 2~3 cm; Poor: postoperative breast skin, feel, shape, etc. with significant difference from the healthy side, the level of the nipple is more than 3 cm, or the breasts are asymmetrical. Excellent rate (excellent + good) / total number of cases $\times 100.00\%$.

The two groups of patients were followed up for 3 years, and the recurrence rate, survival rate, tumor-free survival, and survival without distant metastasis were recorded.

The QoL after breast cancer - 46 (QOL-46) scale was used to evaluate the QoL of patients before and after surgery. The scale included 4 dimensions. The higher the score, the better the QoL [7].

Statistics

SPSS 22.0 software (IBM, Armonk, NY, USA) was used to complete the statistical analyses. Enumeration data was expressed in [case (%)], using χ^2 test; measurement data was expressed in mean \pm SD, using t-test. $P < 0.05$ was considered statistically significant.

Results

Comparing the margins of the two groups

Result analysis showed that 8.33% of patients in the Research Group had positive margins for the first time, and 27.08% in the Control Group. There was a significant difference between the two groups ($p < 0.05$); the volume of excised specimens in the Research Group was smaller than that of the Control Group, and the difference was significant ($p < 0.05$); The proportion of largest resection margin ≤ 2 cm in the group was higher than that in the Control Group, and the difference was statistically significant ($p < 0.05$) (Table 1).

Table 1. Comparison of the margins of the two groups (mean \pm SD)

Group	n	Positive margin for the first time (%)	Resection specimen volume (cm ³)	Swelling margin distance (%)	
				Maximum resection margin >2 cm	Maximum resection margin ≤ 2 cm
Research Group	48	4 (8.33)	86.10 \pm 21.02	2 (4.17)	46 (95.83)
Control group	48	13 (27.08)	97.21 \pm 25.63	25 (52.08)	23 (47.92)
t/x ²	-	5.790	2.322	27.259	
p	-	0.016	0.022	0.000	

Comparison of perioperative indicators between the two groups

The results showed that the operation time of the Research Group was larger than that of the Control Group, while the length of hospitalization and intraoperative blood loss were lower than those of the Control Group ($p < 0.05$) (Table 2).

Comparison of postoperative breast beauty effects between the two groups

The postoperative breast cosmetic excellent rate of the two groups of patients was 75.00%, and that of the Control Group was 39.58%. The cosmetic effect of the two groups was compared. The Research Group was higher than the Control Group, and the difference was significant ($p < 0.05$) (Table 3).

Comparison of follow-up survival rate and recurrence rate

Follow-up was conducted by consulting medical records, letter questionnaires, telephone inquiries, and patients' returning visit. The survey showed that there was no statistical difference in the survival rate between the Research Group and the Control Group ($p > 0.05$), while the recurrence rate of the Research Group was 4.17%, lower than that in the Control Group which was 16.67%, the tumor-free survival rate and the survival rate with-

out distant metastasis were significantly higher than those in the Control Group, and the difference was statistically significant ($p < 0.05$) (Table 4).

Comparison of the quality of life of the two groups of patients

The QOL-46 scale scores of the three-year follow-up showed that there was no statistical difference ($p > 0.05$) between the two groups in pre-operative mental, social support, psychological, physical, etc.; the QOL-46 scale scores of the two groups of patients on the three-year follow-up were significantly higher in various dimension, and the difference was significant compared with the pre-operative comparison ($p < 0.05$); the comparison between the two groups, the social support and physical scores of the Research Group were not statistically different from those of the Control Group ($p > 0.05$), but the mental and psychological dimensions scores were significantly higher than the Control Group ($p < 0.05$) (Table 5).

Discussion

Handling breast cancer is a difficult task in clinical breast surgery, which is more common in people aged 45-50. According to an IARC survey in 2018, about 24.2% of female cancer cases are breast cancer, ranking first among cancers in females [8].

Table 2. Comparison of perioperative indexes between the two groups (mean±SD)

Group	n	Hospitalization time (d)	Operation time (min)	Intraoperative blood loss (ml)
Research Group	48	10.45±3.62	32.14±10.02	67.24±15.36
Control group	48	14.37±5.88	26.85±7.15	75.83±22.12
t	-	3.933	2.977	2.209
p	-	0.000	0.003	0.029

Table 3. Postoperative breast cosmetic effect of the two groups, n (%)

Group	n	Excellent	Good	Fair	Poor	Rates of excellent and good
Research Group	48	10 (20.83)	26 (54.17)	9 (18.75)	3 (6.25)	75.00
Control group	48	2 (4.17)	17 (35.42)	19 (39.58)	10 (20.83)	39.58
χ^2	-					12.303
p	-					0.000

Table 4. Comparison of survival rate and recurrence rate between the two groups after 3 years of follow-up, n (%)

Group	n	Recurrence rate	Survival rate	Tumor-free survival	Survival without distant metastasis
Research group	48	2 (4.17)	47 (97.92)	44 (91.67)	46 (95.83)
Control group	48	8 (16.67)	45 (93.75)	35 (72.92)	39 (81.25)
χ^2	-	4.018	1.043	5.790	5.031
p	-	0.045	0.307	0.016	0.024

Table 5. Comparison of the quality of life of the two groups during the 3- year follow-up (mean±SD)

Grading	Research group (n=48)				Control group (n=48)			
	Preoperative	Follow-up for 3 years	t	p	Preoperative	Follow-up for 3 years	t	p
Spirit	22.10±7.34	43.36±12.42*	10.209	0.000	12.68±8.13	36.07±12.41	10.922	0.000
social support	25.57±10.32	52.46±15.31	10.090	0.000	26.03±8.16	49.13±11.45	11.382	0.000
psychology	58.26±23.60	119.17±32.01*	10.611	0.000	57.48±21.32	87.60±25.49	6.279	0.000
Body	27.41±11.09	63.45±13.06	14.573	0.000	28.01±10.26	64.14±15.05	13.742	0.000

*p<0.05.

With the development of radiotherapy and imaging technology, breast-conserving surgery came into being in the 1980s. Since its development, its surgical trauma is getting smaller and smaller, and the surgical treatment effect is almost the same as that of traditional total mastectomy [9-11]. With the clinical application, breast-conserving surgery in the treatment of breast cancer has a higher rate of positive resection margins, and problems such as easy recurrence after surgery, have gradually become prominent, which has become a key research topic in the current medical field.

The positive rate of resection margins is the key to the treatment effect and recurrence rate of breast-conserving surgery, and affects the long-term survival of patients. How to accurately locate the cancer foci and improve the minimally invasive and precise operation is the current problem to be continuously solved [12]. With the development and application of ultrasound technology, ultrasound-guided staining and positioning technology has appeared in the field of scholars and experts, and has received wide attention and recognition, providing new research directions for the development of minimally invasive tumor surgery [13,14].

This study shows that patients positive resection margin in the first Research Group patients (8.33%) was lower than that in the Control Group, (27.08%, etc). Resected specimen volume in Research Group was smaller than that in the Control Group, the maximum incision margin ≤ 2 cm in Research Group had a higher proportion than that in Control Group ($p < 0.05$), which shows that in the surgical treatment of breast cancer, the use of ultrasound-guided staining and marking can reduce the positive margin of the surgery, improve the accuracy of the surgery, and make the maximum resection margin of the surgery smaller than 2 cm as much as possible, and reduce the surgical mechanical damage to the surrounding healthy tissue. In this regard, foreign researchers believe that 1cm is enough for the maximum resection margin in surgery [15]. In clinical surgery, the surgeon mainly determines the range of the resection margin based on the imaging analysis of

the lesion, his own experience, and the feel of the lesion; the physician cannot predict the results of his own resection margins, so the actual margin results may be greater than 1cm or smaller than 1 cm [16,17]. From a theoretical point of view, when resection margin during surgery is greater than 1 cm, it will increase the damage to the healthy tissue around the cancer, but objectively this error is inevitable. In view of this, this study chose to adopt the maximum distance of the surgical margin not exceeding 2 cm as a minimally invasive standard for surgery, which is reasonable and scientific. The postoperative blood loss and length of hospital stay in the Research Group were lower than those in the Control Group ($p < 0.05$), suggesting that surgery according to this standard can help shorten the patient's hospital stay, reduce intraoperative blood loss, and reduce surgical trauma.

The postoperative breast cosmetic excellent rate of the two groups of patients was 75.00% and that of the Control Group was 39.58%. By comparison of the cosmetic effect of the two groups, the Research Group was higher than the Control Group ($p < 0.05$). The symmetry of the double nipple, breast shape, breast skin and hand feel are less destructive; by analysis, the conventional breast-conserving surgery can preserve the patient's breasts compared with mastectomy, but it cannot accurately locate the lesion during the operation. To ensure the surgical treatment effect and reduce the positive margin of the resection, excessive removal of the surrounding tissues of cancer may be performed by expansion surgery, which will damage the shape and structure of the breast [18,19]. The surgery is blind and will inevitably lead to problems such as local degeneration or partial depression of the breast, and displacement of the nipple and areola after the operation, affecting the beauty of breasts. Breast-conserving surgery after staining and marking under ultrasound guidance can more accurately locate the lesions and lymph nodes, prevent the surgeon from blindly removing the cancer surrounding tissues, prevent excessive damage to the breast structure and morphology, and better preserve the patient's breast beauty.

The recurrence rate of the Research Group was 4.17%, lower than that of the Control Group (16.67%). The tumor-free survival rate and the survival rate without distant metastasis were significantly higher than those of the Control Group ($p < 0.05$). The postoperative recurrence rate has a definite effect on improving the tumor-free survival rate of patients. By analysis, the past palpation may not be able to detect the deep tumors and small tumors in time; with the development of ultrasound technology, tumors below 0.5 cm can be detected, but for tumors with clear edge, irregular shape, and obvious blood flow pattern, low and uneven internal echo, positive rate of surgical margins is high. At the same time, it may be accompanied by fine calcification points and other undetectable lesions, resulting in a relatively high postoperative recurrence rate. By using methylene blue staining markers to locate before surgery, all inaccessible masses and microcalcifications can be marked to ensure the resection rate of the lesion and avoid excessive damage to the surrounding tissues, thereby improving the patient's tumor-free survival rate and survival rate without distant metastasis as well as reducing recurrence rate.

After 3 years of follow-up, the scores of all dimensions of the QOL-46 scale of the two groups of patients were significantly increased. Compared with preoperation ($p < 0.05$), it shows that surgical treatment is beneficial to improve the patient QoL. The scores of the mental and psychological dimensions of the Research Group were significantly higher than that of the Control Group ($p < 0.05$), sug-

gesting that compared with conventional breast-conserving surgery, ultrasound-guided staining and marking followed by breast-conserving surgery have improving effect on the mental health and mental state of patients, which may relate to tumor-free survival and that postoperative breast beauty is better.

Conclusions

In summary, the use of ultrasound-guided staining to mark the margins of breast cancer patients has a definite effect on reducing recurrence rate and improving survival rate. It is also helpful for postoperative breast cosmetic recovery and is worthy of clinical promotion.

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Conflict of interests

The authors declare no conflict of interests.

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