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Original Article

Oncoplastic breast-conserving surgery improves cosmetic outcomes without increasing recurrence risk compared to modified radical mastectomy in early breast cancer patients: development and validation of a recurrence risk prediction model

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Abstract: In the quest for effective treatment of early-stage breast cancer, this study aimed to compare the clinical efficacy of modified radical mastectomy (MRM) and oncoplastic breast-conserving surgery (OBCS). Breast cancer remains a major health concern globally, where early detection and effective treatment strategies are crucial for improving the outcomes of patients. MRM and OBCS are two primary treatment modalities for breast cancer, each with its distinct benefits and challenges. Through a retrospective analysis, we found that although the patients in the OBCS group experienced a longer operation time, they had significantly less intraoperative bleeding, postoperative drainage, and hospitalization time compared to the MRM group. Furthermore, patients in the OBCS group demonstrated higher subjective satisfaction and quality of life scores, along with better objective outcomes. In terms of postoperative complications and recurrence rates, no significant difference was identified between the two groups. However, our multivariate Cox regression analysis identified lymph node metastasis and molecular type as independent prognostic factors for disease-free survival (DFS). Subsequently, we constructed a risk model based on these variables, which was proven to be effective in predicting recurrence, with an area under the risk score curve for recurrence prediction being 0.852. The group with a lower risk score demonstrated a significantly higher DFS rate. Our study suggests that compared with MRM, OBCS can significantly reduce surgical incision, improve patient satisfaction, and does not increase the risk of complications or recurrence. Our risk model, developed using Cox regression, also demonstrated high clinical value in predicting breast cancer recurrence, thereby aiding in personalized patient management and treatment planning.

Keywords: Modified radical mastectomy, oncoplastic breast-conserving surgery, early breast cancer, recurrence, risk model

Introduction

As the most common cancer among women worldwide, breast cancer (BC) shows an increasing incidence in many countries [1]. According to the latest statistics of the World Health Organization, in 2020, there were 2.3 million new cases of BC, accounting for 11.7% of all new cancer cases worldwide [2]. The latest data from the China National Cancer Center showed that the incidence of BC in China in 2020 was 41.55 cases per 100,000 women [3]. In recent years, thanks to the improvement in treatments and early detection, the mortality rate of BC has decreased slightly, but this disease is still a main cause of cancer-related death [4]. Despite the rapid advancement of systemic therapy for BC over the past few years, surgery is still irreplaceable in local treatment [5]. Given the relatively favourable therapeutic outcomes and long survival time of patients with BC, the preservation of the breast, while ensuring safe tumour resection, has become the centre focus of every breast surgeon, so as to improve the quality of life (QoL) of patients [6].

Traditional breast-conserving surgery for BC is mostly suitable for patients whose tumour is less than 2-3 cm and the volume of breast resection is less than 20% [7]. For a large tumour, in order to obtain a negative margin, the specimen requiring removal is often more than 20% of the breast volume, which changes the appearance of the breast [8]. It is urgent for clinicians to solve the problem for BC patients who want to conserve the breast but need removal of 20%-50% of it. In recent years, tumour plastic surgery has been applied to breast cancer surgery, which makes breast conservation possible for BC with larger tumours. This technique is called oncoplastic breast surgery [9]. It is the perfect combination of cancer resection (ONCO) and breast reconstruction (PLAST), that is, the idea of plastic surgery runs through the whole process of clean tumour resection [10]. In a narrow sense, oncoplastic breast surgery means the use of breast gland flap to repair the breast; broadly speaking, it can be classified into two types, breast gland flap and non-(breast) skin flap [11]. The latter includes almost all breast reconstruction operations, such as latissimus dorsi myocutaneous flap (LDMF), deep inferior epigastric perforator (DIEP), transverse rectus abdominis myocutaneous (TRAM), implant and other free flap [12]. It can be said that oncoplastic breast surgery is one of the most ideal, technical and artistic breast surgery at the current stage. Although breast-conserving surgery is effective for early BC, there is also the risk of cancer recurrence [13]. The risk of recurrence depends on several factors, including the size and location of the tumour, the characteristics of cancer cells and the adequacy of surgical margin [14]. However, whether oncoplastic breast-conserving surgery (OBCS) affects postoperative recurrence is still controversial. This study retrospectively analysed the clinical efficacy of modified radical mastectomy (MRM) and OBCS in patients with early BC, and explored the postoperative recurrence of patients to establish a recurrence risk model, aiming at providing reference for clinical therapy and prognosis observation of BC.

Materials and methods

Case selection

The medical data of 149 patients with early BC treated in The First People's Hospital of Changde City from January 2018 to January 2022 were retrospectively collected and analysed. Among them, 104 patients treated by MRM were assigned to a control group, and 45 patients treated by OBCS were assigned to an observation group. This study was approved by the Medical Ethics Committee of The First People's Hospital of Changde City.

Inclusion and exclusion criteria

Inclusion criteria: Patients who were diagnosed with stage I or stage II BC according to preoperative puncture pathology or intraoperative frozen pathology; patients whose tumour was a single lesion or in the same quadrant of the breast; patients whose tumour shrank and reached the condition of breast conservation after neoadjuvant therapy.

Exclusion criteria: Patient whose lesion was extensive, and the margin could not be guaranteed to be negative after extended resection; patients comorbid with liver or kidney insufficiency; patients with coagulation dysfunction; patients without detailed clinical data.

Therapeutic regimens for the patients

In the control group, each patient was given MRM. During the operation, the patient was required to take a supine position, and then given general anaesthesia. According to the shape and condition of the patient's breast, a transverse fusiform incision including nipple and areola complex was designed to preserve pectoralis major and pectoralis minor. After anaesthesia, the patient's back was cushioned. The affected upper limb of the patient was raised by 45°, with abduction of 90° to fully expose the armpit. A fusiform incision was taken. The skin flap was separated from the superficial surface of the patient's superficial fascia, and the free range was controlled between the inferior edge of the clavicle, the upper edge of rectus abdominis, the lateral edge of sternum and the front edge of latissimus dorsi. After reaching the free range, the breast was dissociated from the superficial surface of the patient's pectoralis major muscle, and then the anterior sheath of the rectus abdominis muscle was cut off. The breast and pectoralis major fascia were excised outward. Axillary lymph nodes were routinely dissected to grade II. After axillary lymph node dissection, a drainage tube was placed in the axilla and next to the sternum, separately.

Table 1. Baseline data

Factors	Observation group (n=45)	Control group (n=104)	X^2 value	*P* value
Age			1.877	0.170
≥ 50 years old	20	34		
< 50 years old	25	70		
BMI			0.843	0.358
≥ 25 kg/m^2	15	27		
< 25 kg/m^2	30	77		
Tumour diameter			0.382	0.536
≥ 20 mm	12	33		
< 20 mm	33	71		
Tumour staging			0.303	0.581
Stage I	26	55		
Stage II	19	49		
Lymph node metastasis			0.609	0.435
Yes	9	27		
No	36	77		
Molecular type			0.886	0.641
Triple negative	20	53		
Her-2 positive	9	15		
Luminal A+B type	16	36		

Note: BMI: Body mass index.

In the observation group, each patient was given OBCS. The lesion determination and resection operation were the same as above. For patients whose breast tissue resection was less than 20%, the gland was directly sutured after the lesion resection, and the breast was suspended, fixed and shaped. In addition, tissue filling was carried out by means of lifting and rotation, and whether the two nipples and areola were symmetrical was evaluated. The deviation was corrected and adjusted in time. For patients with 20%-50% of breast tissue resection, the defect needed to be repaired with the help of their own tissue. In the case of impossible application of direct suturing, the pedicled breast tissue repair method was used to dissociate the breast tissue from the fascia layer and subcutaneous fat layer of the pectoralis major muscle. The breast tissue was sutured intermittently after shifting and rotating the breast tissue flap. The repair of the inferior breast defect was to dissociate the subcutaneous adipose tissue in the submammary fold, flip the rectus abdominis sheath fat fascia flap, and then fill and suture it. All patients received radiotherapy after breast-conserving surgery.

Following surgery, all patients underwent comprehensive treatment according to CSCO-BC guidelines. This included assessing the necessity for postoperative radiotherapy intervention for the group undergoing MRM, devising a reasonable chemotherapy scheme according to the patient's condition (as per the recommended scheme in the CSCO-BC guidelines), and selecting suitable targeted drug therapy and endocrine adjuvant therapy based on the patient's pathological examination results.

Data collection

Based on the LIS system, patients' electronic medical records, outpatient re-examination records, and follow-up data were all collected, including age, body mass index (BMI), tumour diameter, tumour stage, lymph node metastasis, molecular type, operation indices (operation time, intraoperative blood loss, postoperative drainage, and hospitalization time), score of the QoL scale developed by the European Organization for Research and Treatment of Cancer (EORTC), objective response rate, subjective satisfaction rate of breast, and postoperative recurrence of patients. The patients were followed up till January 2023.

Subjective satisfaction rate: Subjective satisfaction refers to a patient's personal perception of their postoperative results, including the aesthetic outcome and psychological wellbeing, namely, their satisfaction with the appearance of their breasts and the psychological impact of the surgery. Different scales or questionnaires, such as the BREAST-Q or the EORTC QLQ-BR23, might be used to measure it. The rate is determined by the proportion of patients reporting satisfaction on these measures.

Objective response rate: The objective excellent and good rate typically refers to a clinical assessment of the postoperative results, often evaluated by the surgeons or a panel of experts. It is based on objective criteria like symmetry of the breasts, absence of surgical complications, and the quality of the scar. The 'excellent and good' rating is typically part of a scale that may also include 'fair' and 'poor' ratings. The rate is the proportion of patients whose treatment efficacy scored in the range of

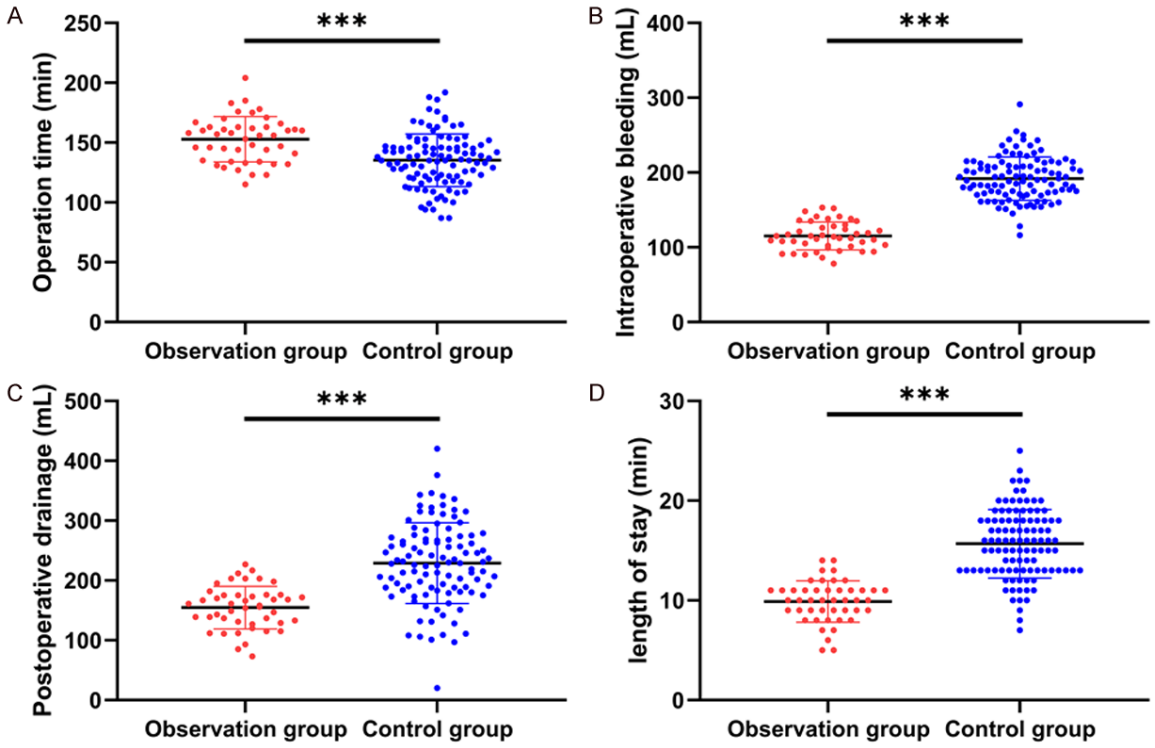

Figure 1. Comparison of patients' operation indices. A. Comparison of operation time between the observation group and control group. B. Comparison of intraoperative blood loss between the observation group and control group. C. Comparison of postoperative drainage between the observation group and control group. D. Comparison of hospitalization time between the observation group and control group.

Table 2. Comparison of subjective satisfaction rate and objective excellent and good rate after treatment

Group	Subjective satisfaction rate	Objective excellent and good rate	Quality of life score
Observation group (n=45)	42/3	39/6	81.04±8.51
Control group (n=104)	83/21	69/36	68.72±8.38
X^2/t value	4.252	6.859	8.260
P value	0.030	0.008	< 0.001

'excellent' or 'good' based on these objective measures.

The operation indices of patients and the influence of two operations on postoperative recurrence were primary outcome measures. Secondary outcome measures included the objective response rate, QoL score, postoperative complications and risk prediction model.

Statistical analyses

In the present study, SPSS20.0 software package was adopted for statistical analyses. Counting data (%) were analysed using the chi-square test, and expressed by X^2, and data were counted using Fisher's chi-square test when the number of cells with an expected frequency less than 5 was high. The measurement data were described by the mean ± SD. Their inter-group comparison was conducted using the independent-samples t test, and their intra-group comparison was conducted using the paired t test, and presented by t. Cox regression was conducted to analyse the prognostic factors impacting the disease-free survival (DFS) of patients. The Kaplan-Meier (K-M) survival curve was used to draw the DFS rate of patients in different risk groups. $P < 0.05$ implies a significant difference.

Results

Baseline data comparable between the two groups

The two groups were not significantly different in age, BMI, tumour diameter, tumour stage,

Table 3. Incidence of complications

Group	Haematoma	Infection	Poor incision healing	Skin necrosis	Fat necrosis	Total incidence rate
Observation group (n=45)	2	0	1	0	4	7 (15.56%)
Control group (n=104)	6	1	2	4	2	15 (14.42%)
X^2 value	0.108	0.436	0.014	1.779	3.559	0.032
P value	0.741	0.509	0.905	0.182	0.059	0.858

Table 4. The influence of different operations on patients' recurrence

Group	Recurrence	No recurrence
Observation group (n=45)	5	40
Control group (n=104)	5	99
P value	0.169	

Note: Statistics were performed using Fisher-square test.

lymph node metastasis, and molecular type (P > 0.05, **Table 1**), indicating comparability.

Comparison of operation indices

The operation time, intraoperative blood loss, postoperative drainage and hospitalization time were all compared between the two groups. According to the results, the observation group experienced a significantly longer operation time than the control group (P < 0.001, **Figure 1**), but the observation group showed a significantly lower amount of intraoperative blood loss and postoperative drainage than the control group, and also experienced a shorter hospitalization time than the control group (P < 0.001, **Figure 1**).

Comparison of subjective satisfaction rate of breast, objective response rate, and QoL

The control group showed significantly lower subjective satisfaction rate and objective excellent and good rate than the observation group (P=0.030, P=0.008, **Table 2**), and the observation group exhibited significantly higher QoL scores than the control group (P < 0.001).

Comparison of complications

No notable difference was revealed in the incidence of complications between the control group and observation group (P > 0.05, **Table 3**).

Statistics of postoperative recurrence

There were 10 patients with recurrence in the 149 patients. According to comparison, there was no significant difference between the observation group and control group in the postoperative recurrence (P=0.169, **Table 4**).

Statistics on postoperative recurrence and analysis of risk factors

According to the recurrence, Cox regression was conducted to analyse factors impacting the DFS of patients. First of all, univariate Cox analysis showed that age, tumour diameter, tumour stage, lymph node metastasis and molecular type were associated with DFS (P < 0.05, **Table 5**). According to multivariate Cox regression analysis, lymph node metastasis and molecular type were independent prognostic factors of DFS (P < 0.05 **Table 5**).

Establishment of recurrence prediction model

Based on the identified significant prognostic factors, we constructed a risk model to predict recurrence. The coefficients for each of these factors were determined through a Cox regression analysis. Specifically, the coefficient for lymph node metastasis was 1.175, and the coefficient for molecular type was -1.3. The risk score for each patient was then calculated using the following formula, derived from the Cox regression model: 1.175 * (lymph node metastasis) + (-1.3) * (molecular type). This formula allowed us to quantify the risk of recurrence for each individual patient based on their specific lymph node metastasis and molecular type data. According to comparison, the recurrence group showed notably higher risk scores than the non-recurrence group (P < 0.05, **Figure 2A**). In addition, according to the ROC curve-based analysis, the area under the curve (AUC) for predicting recurrence was 0.852 (**Figure 2B**), and the corresponding spec-

Table 5. Cox univariate and multivariate regression analysis

Factors	Cox univariate analysis			Cox multivariate analysis		
	P value	HR value	95% CI	*P* value	HR value	95% CI
Age	0.029	2.879	1.114-7.436	0.560	1.369	0.475-3.944
BMI	0.657	1.249	0.468-3.337			
Tumour diameter	0.019	3.059	1.202-7.783	0.293	1.727	0.623-4.787
Tumour stage	0.018	4.470	1.292-15.459	0.062	3.278	0.944-11.379
Lymph node metastasis	0.001	4.962	1.915-12.857	0.018	3.239	1.228-8.543
Molecular type	< 0.001	0.222	0.115-0.430	< 0.001	0.272	0.137-0.541
Operation mode	0.471	1.420	0.547-3.686			

Note: BMI: Body mass index.

ificity, sensitivity and critical values were 81.81%, 69.06% and < -0.712, respectively (**Figure 2B**). According to the cut-off-based grouping analysis, the low-risk group showed a notably higher DFS rate than the high-risk group (P < 0.001, **Figure 2C**).

Nomogram analysis

With R4.1.1 software, the factors impacting 3-year DFS in multi-factor Cox regression analysis were included to establish a functional model and draw a nomogram. The score of each number or category of these factors was added on the score scale, and corresponding total score was marked. A straight line was drawn down, and its intersection with the 3-year total DFS rate axis represented the DFS rate. According to the results, the C index of the nomogram prediction model was 0.760, 95% CI (0.615-0.906), indicating a good degree of model differentiation (**Figure 3**).

Discussion

The conventional breast-conserving surgery was to directly suture the tumour residual cavity or skin incision after local extended resection of the tumour, and to fill the tumour residual cavity with fibrin and serum exudation [15, 16]. Despite the good tumour removal effect, it still has its limitations. If the margin is positive, a second operation is needed and may increase surgical complications and hospitalization expenses for patients [17-20]. Additionally, MRM is prone to cause skin and gland defects, areola and breast asymmetry, which cannot meet the needs of breast aesthetics.

Over the past few years, OBCS has been gradually applied to patients with early and middle-stage BC. The effective repair of surgical residual cavity by interventional plastic surgery can well deal with breast droop, large breast volume, large tumour volume and special tumour site, and the surgery can effectively protect the aesthetics of patients' breasts with relatively high clinical efficacy and safety [21-23]. In the present study, OBCS greatly shortened the postoperative hospitalization time of patients with stage I-II BC, and effectively controlled the amount of bleeding and reduced the postoperative drainage, but its operation time was prolonged. This is because OBCS is a surgery that does not increase the surgical trauma of patients while effectively keeping the breast intact. This method can help reduce drainage and promote the recovery of patients. Moreover, MRM involves a large resection area, which may cause great trauma to patients, resulting in a longer recovery time after surgery. In addition, compared with traditional breast-conserving surgery, OBCS increases the steps of breast shape modification, which may prolong the operation time of patients. Grujic et al. [24] revealed that patients who received OBCS showed greatly improved psychological status and functional well-being, and a notably higher subjective satisfaction rate after operation than patients who underwent MRM. This is consistent with our research results. The results also demonstrated that OBCS effectively improved the subjective satisfaction rate and objective excellent and good rate for BC patients after treatment. This is because OBCS does not increase the surgical trauma and ensure the integrity of patients' breasts, which is conducive to the reduction of drainage and the rehabilitation of patients [25]. In addition, OBCS can completely preserve the appearance of the patient's breast. Plastic surgery technology can repair the defect by rotating and shifting the breast tissue flap after local resection

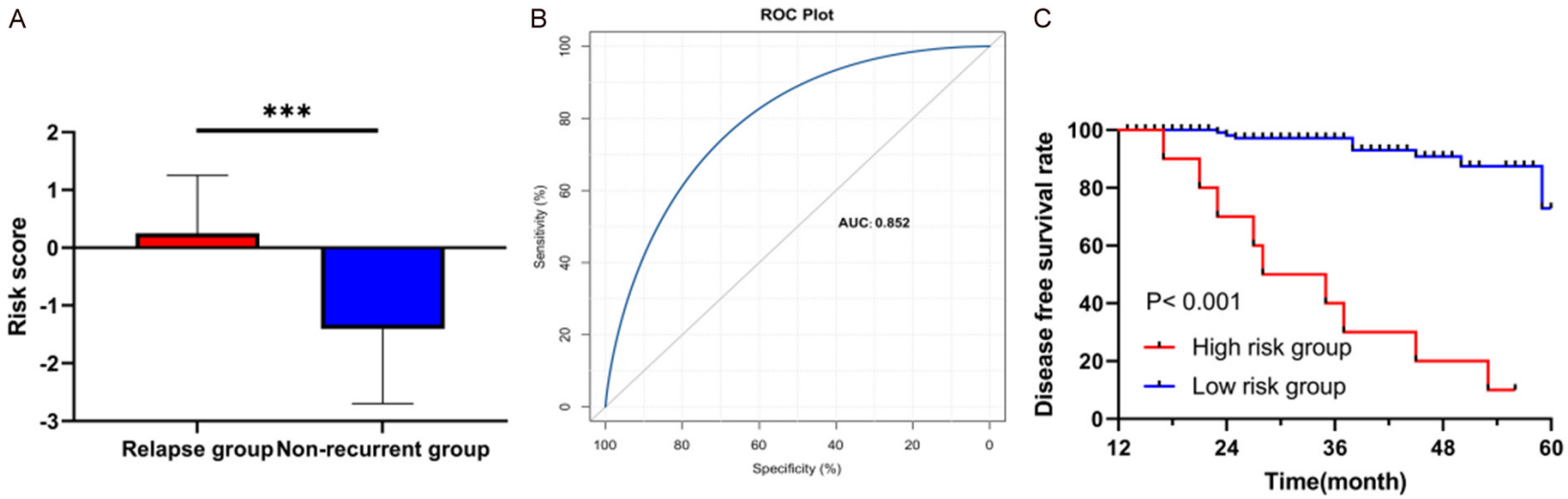

Figure 2. The predictive value of risk score for patients' recurrence. A. Risk score in patients with recurrence and patients without recurrence. B. ROC curve of risk score for prediction of patients' recurrence. C. K-M curve analysis of disease-free survival time of patients in different risk groups. ***P < 0.001, AUC: Area under the curve.

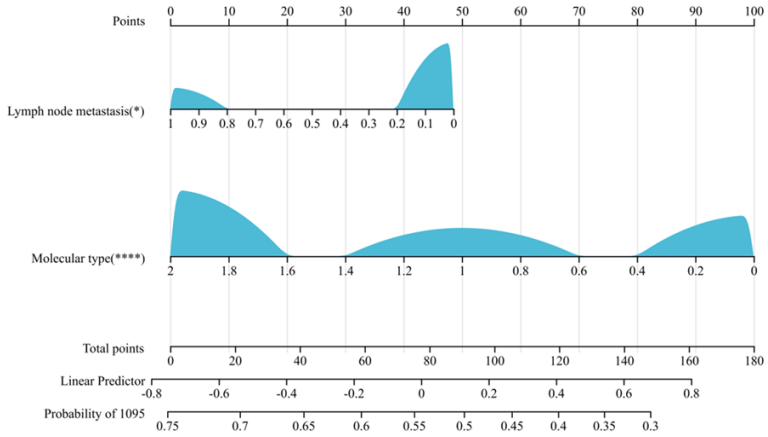

Figure 3. Construction of nomogram and survival prediction.

of the patient's breast, which effectively avoids asymmetric appearance of the breast after surgery and is conducive to maintaining the aesthetics of the breast [26]. Moreover, this study found that OBCS did not increase the incidence of postoperative complications, suggesting a high safety of OBCS.

Breast-conserving surgery is widely adopted in the treatment of early BC, and the breast-conserving rate in Europe and America has reached 50%-70%. However, recurrence after breast-conserving surgery is the main factor limiting its popularization [27]. Clough et al. [28] reported that the 5-year local recurrence rate and survival rate of BC patients who underwent OBCS were 9.4% and 95.7%, respectively. In addition, Cruz et al. [29] found that the DFS and the total survival time of 6011 patients with early BC treated by OBCS were 95.0% and 90.0%, respectively, while the local recurrence rate was 3.2%. These studies all imply a good oncological safety of OBCS. However, there is little research on the difference of local recurrence rate between OBCS and MRM. In this study, MRM and OBCS presented no difference in DFS. Di Leone et al. [30] found no difference in DFS between 87 patients undergoing plastic surgery and 210 patients undergoing mastectomy with immediate breast reconstruction during analysis of 297 patients with BC. Additionally, Sagiroglu et al. [16] found no difference in postoperative recurrence between patients undergoing OBCS and patients undergoing mastectomy. These studies suggest that OBCS does not increase the postoperative recurrence of patients with early BC.

A number of studies have revealed that age, tumour diameter, and lymph node metastasis are the influencing factors of local recurrence after breast-conserving surgery; namely, the patients with older age, large tumour diameter, and lymph node metastasis are at a high risk of local recurrence, distant metastasis, and poor prognosis [31, 32]. Similar to previous studies, lymph node metastasis and molecular subtypes were found to be independent prognostic factors for DFS in the present study. The results suggest that lymph node metastasis and molecular subtypes should be given special attention to before operation. Predictive risk models can help health care providers make informed decisions about patient care, such as identifying high-risk patients and providing targeted interventions to lower risks [33, 34]. In this study, a score for predicting recurrence was successfully constructed according to Cox regression coefficient. Comparison results showed that the recurrence group demonstrated notably higher risk scores than the non-recurrence group. ROC curve showed that the ACU of risk score for predicting recurrence was over 0.8.

Moreover, the included patients were divided into a high-risk group and a low-risk group according to the cut-off value. The DFS rate in the high-risk group was significantly lower than that in the low-risk group, suggesting that we have successfully constructed a risk model for predicting recurrence and a 3-year DFS nomogram.

This study has determined that OBCS can effectively improve the subjective satisfaction and objective excellent and good rate, without increasing the postoperative recurrence of patients. However, it still has some limitations. First of all, the data collection period in this study is limited, so we are unable to get longer survival data. Secondly, this is a single-centre study, so whether the risk model is universal needs external data for verification. Therefore, we hope to carry out more clinical experiments in the future to improve the conclusion of this study.

To sum up, compared with MRM, OBCS can substantially reduce the surgical incision and improve the satisfaction rate without increasing the complications and recurrence rate in patients with early BC. In addition, we have successfully constructed a risk model for predicting the recurrence of early BC based on Cox regression, which has high clinical value in predicting the recurrence of BC.

Disclosure of conflict of interest

None.

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