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# Factors influencing the incidence of postoperative lymphedema in patients with locally advanced triple-negative breast cancer

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**Factors Influencing the Incidence of Postoperative Lymphedema in Patients with Locally Advanced Triple-Negative Breast Cancer**

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**Running Head:** LYMPHEDEMA RISK IN TNBC SURGERY

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## Abstract

**Objective:** To analyze the risk factors for postoperative secondary upper limb lymphedema in patients with locally advanced triple-negative breast cancer (TNBC).

**Methods:** In this retrospective cohort study, a total of 176 patients with stage IIIB–IIIC TNBC treated at our hospital from January 2021 to December 2023 were included consecutively. The modified technique was introduced in 2022, and all procedures were performed by the same surgical team. They were divided into an experimental group (modified surgical technique, n=90) and a control group (standard technique, n=86) based on the surgical approach. The modified technique involved concurrent resection of the clavicular portion of the pectoralis major muscle fibers and the clavipectoral fascia in addition to standard axillary lymph node dissection (ALND). The incidence of postoperative upper limb lymphedema was compared between groups, and its association with obesity, cardiovascular cardiovascular disease, and metabolic syndrome was analyzed.

**Results:** The postoperative lymphedema incidence was 23.3% (21/90) in the experimental group, significantly lower than the 41.9% (36/86) in the control group (P=0.009). Lymphedema incidence in obese patients was 47.8% (43/90), markedly higher than the 16.3% (14/86) in non-obese patients (P<0.001). Multivariate logistic regression identified obesity (OR=4.80, 95% CI 2.38–9.68, P<0.001) and standard surgical technique (OR=2.45, 95% CI 1.23–4.88, P=0.011) as independent risk factors for lymphedema.

**Conclusion:** Obesity and surgical technique are independent risk factors for postoperative upper limb lymphedema in locally advanced TNBC patients. The modified ALND technique may help reduce lymphedema incidence, with a particularly pronounced benefit observed in obese patients. **However, the proposed mechanism remains speculative, and the findings require prospective validation.** Prospective randomized studies are needed before routine adoption.

**Keywords:** Breast cancer; Axillary lymph node dissection; Postoperative lymphedema; Obesity; Risk factors

## Introduction

Breast cancer is one of the most common malignancies in women worldwide, and surgery remains the cornerstone of treatment for locally advanced disease [1]. With improved survival, management of postoperative complications has gained increasing attention. Postoperative upper limb lymphedema is a common chronic complication after breast cancer surgery, with an incidence ranging from 15% to 40%. Severe cases can lead to impaired limb function, recurrent infections, and reduced quality of life, imposing long-term burdens on patients [2,3].

Lymphedema is influenced by multiple factors, including treatment-related aspects such as the extent of axillary lymph node dissection, radiotherapy, and chemotherapy, as well as patient-specific characteristics. Comorbidities such as obesity, metabolic syndrome, and cardiovascular disease may increase lymphedema risk by affecting lymphatic drainage, microcirculation, and inflammatory responses [4-7]. Recent advances in lymphatic biology and surgical anatomy have highlighted the potential for technique modifications to reduce morbidity [8-10]. Furthermore, emerging evidence supports the role of metabolic and genetic factors in lymphedema susceptibility [11-13]. While numerous studies have explored lymphedema risk factors, research on the impact of specific surgical techniques on lymphedema incidence in locally advanced breast cancer remains limited and findings are inconsistent [14-17]. **Recent work has also underscored the complex interplay between tumor biology, immune modulation, and surgical outcomes in TNBC 18.**

Therefore, this study aimed to retrospectively analyze the influence of a modified axillary lymph node dissection technique on the incidence of postoperative upper limb lymphedema in patients with locally advanced triple-negative breast cancer (TNBC), and to further investigate the role of obesity, cardiovascular disease, and metabolic syndrome. The findings may provide a basis for clinical risk stratification, surgical optimization, and individualized intervention.

## Materials and Methods

### 1. Study Design and Population

This was a retrospective, single-center cohort study. Patients were not randomized; the modified surgical technique was introduced in 2022, and all procedures were performed by the same surgical team to minimize surgeon-related bias. Consecutive patients meeting the inclusion criteria were included. We analyzed patients with locally advanced TNBC (stage IIIB–IIIC) treated at the Breast Diagnosis and Treatment Center of the First Affiliated Hospital of Gannan Medical University between January 2021 and December 2023. All patients are of Han ethnicity, which may limit generalizability.

All patients with stage IIIB–IIIC TNBC received neoadjuvant chemotherapy (anthracycline/taxane-based) per institutional guidelines. Postoperatively, all patients received standardized regional nodal irradiation (including supraclavicular field, 50 Gy/25 fractions) and adjuvant chemotherapy as per the same guidelines. No significant differences in chemotherapy cycles, regimens, or radiotherapy fields were observed between the two groups.

Inclusion criteria were: (1) pathologically confirmed TNBC; (2) clinical stage IIIB–IIIC; (3) underwent radical surgical treatment (mastectomy with ALND); (4) complete clinical and follow-up data available.

Exclusion criteria were: (1) pre-existing upper limb lymphedema; (2) other concurrent malignancies; (3) follow-up time less than 12 months; (4) lost to follow-up.

A total of 176 patients were included and categorized into an experimental group (modified technique, n=90) and a control group (standard technique, n=86) based on the surgical approach.



### 2. Surgical Methods

**Control group:** Underwent standard modified radical mastectomy or mastectomy with level I and II axillary lymph node dissection (ALND).

**Experimental group:** Underwent the same standard ALND plus concurrent resection of the clavicular portion of the pectoralis major muscle fibers covering the superior aspect of the axillary vein and the underlying clavipectoral fascia. This modification aimed to reduce postoperative scar compression on axillary lymphatic pathways by expanding the surgical field. **Perioperative outcomes including operative time, drainage duration, seroma rate, and wound complications were recorded and are presented in Table 11.**

### 3. Assessment Indicators

**Primary outcome:** Incidence of postoperative secondary upper limb lymphedema.

**Diagnostic criteria for lymphedema:** Increase in circumference of the affected limb by ≥2 cm compared to the contralateral limb at the same anatomical site (measured at 4 cm above and below the olecranon), or a volume increase ≥10%, persisting for over 3 months. Assessments were performed preoperatively and at 3, 6, and 12 months postoperatively by trained nurses blinded to group assignment.

**Secondary outcomes:** Severity of lymphedema (graded I–II using CTCAE v5.0 criteria), body mass index (BMI), and comorbidities (cardiovascular disease, metabolic syndrome). Obesity was defined as BMI ≥30 kg/m². Non-obese was defined as BMI <30 kg/m² (including normal weight and overweight). Metabolic syndrome was diagnosed using the International Diabetes Federation criteria [19].

### 4. Statistical Analysis

Data analysis was performed using SPSS software (version 26.0). Continuous data were presented as median (range) and compared using the Mann-Whitney U test. Categorical data were presented as number (percentage) and compared using the $\chi^2$ test or Fisher's exact test. Univariate and multivariate logistic regression analyses were used to identify risk factors for lymphedema, calculating odds ratios (OR) and 95% confidence intervals (CI). Variables with P<0.1 in univariate analysis were entered into the multivariate model. No formal sample size calculation was performed due to the exploratory nature of the study. A predictive model was constructed based on independent risk factors, and its discriminative ability was assessed using the receiver operating characteristic (ROC) curve, reported as the area under the curve (AUC). P<0.05 was considered statistically significant. **Formal interaction testing between obesity and surgical technique was not performed, which is acknowledged as a limitation.**

## Results

### 1. Patient Baseline Characteristics

Both groups completed over one year of postoperative follow-up. Median follow-up duration was 18 months (range 12–30 months). As described in Methods, chemoradiotherapy regimens were standardized and balanced between groups. There were no statistically significant differences between the two groups in age, residence, tumor stage, differentiation degree, or comorbidities (obesity, cardiovascular disease, metabolic syndrome) (all P>0.05), indicating balanced baseline characteristics (Table 1).



**Table 1. Comparison of Patient Baseline Characteristics**

| Characteristic | Control Group (n=86) | Experimental Group (n=90) | P-value |
|---|---|---|---|
| Urban Residents, n (%) | 67 (77.9%) | 65 (72.2%) | 0.415 |
| Age (years), median (range) | 53.5 (29–70) | 52.5 (31–68) | 0.725 |
| Tumor Differentiation Degree, n (%) | | | 0.938 |
| – Poorly Differentiated | 26 (30.2%) | 26 (28.9%) | |
| – Moderately Differentiated | 57 (66.3%) | 60 (66.7%) | |
| – Well Differentiated | 3 (3.5%) | 4 (4.4%) | |
| Cardiovascular Disease, n (%) | 43 (50.0%) | 42 (46.7%) | 0.659 |
| Obesity (BMI ≥30), n (%) | 46 (53.5%) | 44 (48.9%) | 0.542 |
| Metabolic Syndrome, n (%) | 26 (30.2%) | 26 (28.9%) | 0.846 |
| N3 stage, n (%) | 20 (23.3%) | 20 (22.2%) | 0.86 |

### 2. Lymphedema Incidence and Severity

Among all 176 patients, BMI distribution was as follows: 2 (1.2%) underweight (BMI <18.5), 40 (22.7%) normal weight (18.5–24.9), 44 (25.0%) overweight (25.0–29.9) , 53 (30.1%) grade I obesity (30.0–34.9), 24 (13.6%) grade II obesity (35.0–39.9), and 13 (7.4%) grade III obesity (≥40.0). For analysis of obesity as a binary variable, obese was defined as BMI ≥30 (n=90) and non-obese as BMI <30 (n=86), with overweight patients included in the non-obese group. The BMI distribution was comparable between the control and experimental groups (Table 2).

**Table 2. Comparison of Body Mass Index (BMI) Distribution Between Experimental and Control Groups**

| Characteristic | Control Group (n=86) | Experimental Group (n=90) | p-value |
|---|---|---|---|
| Median BMI (kg/m$^2$) | 30.1 | 29.7 | 0.738 |
| Underweight | 2 (2.3%) | 0 | >0.05 |
| Normal weight | 23 (26.8%) | 17 (18.9%) | |
| Overweight | 15 (17.4%) | 29 (32.2%) | |
| Grade I Obesity | 28 (32.6%) | 25 (27.8%) | |
| Grade II Obesity | 10 (11.6%) | 14 (15.6%) | |
| Grade III Obesity | 8 (9.3%) | 5 (5.5%) | |

**3. Effect of Obesity on Lymphedema**

Among all patients, 57 developed postoperative lymphedema: 36 in the control group (41.9%) and 21 in the experimental group (23.3%), a statistically significant difference (P=0.009). The severity of lymphedema was also higher in affected patients in the control group compared to the experimental group (P=0.049, Table 3).

The lymphedema incidence in obese patients (BMI ≥30) was 47.8% (43/90), significantly higher than the 16.3% (14/86) in non-obese patients (P<0.001). This trend remained consistent within both the control group (P<0.001) and the experimental group (P=0.005) (Table 4).

Among non-obese patients, there was no significant difference in lymphedema incidence between the two groups (P=0.145). Among obese patients, the lymphedema incidence in the control group (58.7%) was significantly higher than in the experimental group (36.4%) (P=0.034, Table 5). The severity of obesity (grades I, II, III) did not significantly affect lymphedema incidence in the overall sample or within either group (all P>0.05, Table 6).

Table 3 Comparison of Postoperative Lymphedema Severity in Affected Patients Between Groups

| Severity | Control Group (n=36) | Experimental Group (n=21) | P-value |
|---|---|---|---|
| Grade I | 16 (44.4%) | 15 (71.4%) | 0.049 |
| Grade II | 20 (55.6%) | 6 (28.6%) | |

Table 4 Lymphedema Incidence in Patients with Different Weight Status

| Group | Lymphedema Rate in Obese Patients | Lymphedema Rate in Non-obese Patients | P-value |
|---|---|---|---|
| Control | 27/46 (58.7%) | 9/40 (22.5%) | <0.001 |
| Experimental | 16/44 (36.4%) | 5/46 (10.9%) | 0.005 |
| Total | 43/90 (47.8%) | 14/86 (16.3%) | <0.001 |

Table 5 Comparison of Lymphedema Incidence Between Groups in Obese Patients

| Group | Lymphedema Cases/Total Cases | Lymphedema Rate | P-value |
|---|---|---|---|
| Control | 27/46 | 58.7% | 0.034 |
| Experimental | 16/44 | 36.4% | |

Table 6 Relationship Between Obesity Severity and Lymphedema

| Obesity Degree | Grade I | Grade II | Grade III | P-value |
|---|---|---|---|---|
| Control Group | 18/28 (64.3%) | 4/10 (40.0%) | 5/8 (62.5%) | 0.396 |
| Experimental Group | 8/25 (32.0%) | 5/14 (35.7%) | 3/5 (60.0%) | 0.493 |
| Overall | 26/53 (49.1%) | 9/24 (37.5%) | 8/13 (61.5%) | 0.361 |

**4. Effect of Cardiovascular Disease on Lymphedema**

The lymphedema incidence in patients with cardiovascular disease (40.0%) was significantly higher than in those without (25.3%) (P=0.037, Table 7). In the control group, the incidence was higher in patients with cardiovascular disease (P=0.029), whereas no significant difference was observed in the experimental group (P=0.549). Among patients with cardiovascular disease, the incidence in the control group (53.5%) was significantly higher than in the experimental group (26.2%) (P=0.011).



Table 7 Cardiovascular Disease and Lymphedema Incidence

| Group | Lymphedema Rate with CVD | Lymphedema Rate without CVD | P-value |
|---|---|---|---|
| Control | 23/43 (53.5%) | 13/43 (30.2%) | 0.029 |
| Experimental | 11/42 (26.2%) | 10/48 (20.8%) | 0.549 |
| Total | 34/85 (40.0%) | 23/91 (25.3%) | 0.037 |

**5. Effect of Metabolic Syndrome on Lymphedema**

Diagnostic criteria for metabolic syndrome were as follows [12]: 1. Central obesity; 2. Plus any two of the following four factors: a) Elevated triglycerides (≥150 mg/dl (1.7 mmol/l) or specific treatment for this lipid abnormality); b) Reduced HDL cholesterol (<40 mg/dl (1.03 mmol/l) in men, <50 mg/dl (1.29 mmol/l) in women, or specific treatment for this lipid abnormality); c) Elevated blood pressure (systolic ≥130 mmHg or diastolic ≥85 mmHg, or treatment of previously diagnosed hypertension); d) Elevated fasting plasma glucose (≥100 mg/dl (5.6 mmol/l) or previously diagnosed type 2 diabetes.

Analysis showed that the influence of metabolic syndrome on secondary lymphedema incidence did not reach statistical significance (P=0.069, Table 8). No significant association was found between metabolic syndrome and lymphedema incidence either in the control group (P=0.314) or the experimental group (P=0.107).

Table 8 Metabolic Syndrome and Lymphedema Incidence

| Group | Lymphedema Rate with MS | Lymphedema Rate without MS | P-value |
|---|---|---|---|
| Control | 13/26 (50.0%) | 23/60 (38.3%) | 0.314 |

| Group | Lymphedema Rate with MS | Lymphedema Rate without MS | P-value |
|---|---|---|---|
| Experimental | 9/26 (34.6%) | 12/64 (18.8%) | 0.107 |
| Total | 22/52 (42.3%) | 35/124 (28.2%) | 0.069 |

### 6. Univariate Analysis of Lymphedema Risk Factors

Results of univariate logistic regression analysis are shown in Table 9. Factors significantly associated with lymphedema occurrence included: Standard surgical technique (vs. modified) (OR=2.37, 95% CI 1.23–4.53; P=0.009), Obesity (OR=4.71, 95% CI 2.32–9.54; P<0.001), Cardiovascular disease (OR=1.97, 95% CI 1.04–3.74; P=0.038). The effect of metabolic syndrome was not statistically significant (P=0.070).

Table 9 Univariate Analysis of Lymphedema Risk Factors

| Factor | OR | 95% CI | P-value |
|---|---|---|---|
| Surgical technique (Standard vs. Modified) | 2.37 | 1.23–4.53 | 0.009 |
| Obesity (Yes vs. No) | 4.71 | 2.32–9.54 | <0.001 |
| Cardiovascular disease (Yes vs. No) | 1.97 | 1.04–3.74 | 0.038 |
| Metabolic syndrome (Yes vs. No) | 1.86 | 0.95–3.66 | 0.070 |

### 7. Multivariate Analysis and Prediction Model Construction

Multivariate logistic regression analysis showed that only Obesity (OR=4.80, P<0.001) and Surgical technique (Standard vs. Modified) (OR=2.45, P=0.011) were independent risk factors for lymphedema (Table 10).

A prediction model was constructed based on these results, with the formula: $P = 1 / (1 + e^{-(-2.122 + 0.896 \times X_1 + 1.570 \times X_2)})$. Where e is the base of the natural logarithm (=2.718); $X_1$ is the surgical technique (0=modified, 1=standard); $X_2$ is the obesity status (0=non-obese, 1=obese). The model was statistically significant ($\chi^2$=29.9, P<0.001). This model is exploratory and should not be used clinically without external validation. The area under the ROC curve (AUC) was 0.729 (95% CI 0.650–0.807), indicating moderate discriminative ability (Figure 1).

**Table 10. Multivariate Logistic Regression Analysis of Lymphedema Risk Factors**

| Risk Factor | β Coefficient | SE | Wald | P-value | OR (95% CI) |
|---|---|---|---|---|---|
| Cardiovascular Disease | 0.214 | 0.401 | 0.286 | 0.593 | 1.24 (0.57–2.71) |
| Metabolic Syndrome | 0.524 | 0.441 | 1.408 | 0.235 | 1.69 (0.71–4.01) |
| Surgical Technique | 0.896 | 0.353 | 6.454 | 0.011 | 2.45 (1.23–4.88) |
| Obesity | 1.570 | 0.368 | 18.192 | <0.001 | 4.80 (2.38–9.68) |
| Constant | -2.122 | 0.367 | 33.428 | <0.001 | |

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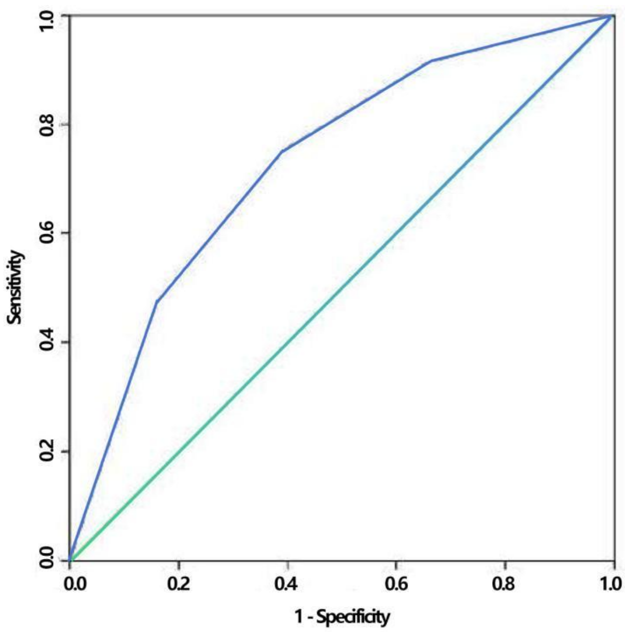


**Figure 1. ROC Curve** (AUC = 0.729, 95% CI 0.650–0.807)

**8. Oncological safety data**

The median number of lymph nodes removed was 18 (IQR 14–22) in the modified group vs. 17 (IQR 13–21) in the control group (P=0.34). The number of positive lymph nodes did not differ significantly between groups (P=0.62). These data suggest no compromise in oncological adequacy.

**9. Perioperative outcomes**

**Perioperative outcomes are summarized in Supplementary Table 1. There were no significant differences between the two groups in operative time, postoperative drainage duration, seroma formation rate, or wound complications (all P > 0.05).**

**Table 11. Perioperative Outcomes**

| Outcome | Control Group (n=86) | Experimental Group (n=90) | P-value |
|---|---|---|---|
| Operative time (min), median (IQR) | 125 (110–140) | 130 (115–145) | 0.32 |
| Drainage duration (days), median (IQR) | 7 (6–9) | 7 (5–9) | 0.58 |
| Seroma formation, n (%) | 12 (14.0%) | 10 (11.1%) | 0.56 |
| Wound infection, n (%) | 5 (5.8%) | 4 (4.4%) | 0.74 |

## Discussion

Postoperative upper limb lymphedema is a chronic complication that severely affects the quality of life of breast cancer patients. This retrospective study confirmed that modified axillary lymph node dissection (concurrent resection of the clavicular portion of the pectoralis major and the clavipectoral fascia) can significantly reduce the incidence of postoperative lymphedema (23.3% vs. 41.9%) in patients with locally advanced (stage IIIB–IIIC) triple-negative breast cancer. Furthermore, obesity and surgical technique were identified as two independent risk factors influencing its occurrence. These findings are consistent with those of Johnson et al. [20] and Vangsness et al. [21], who reported improved outcomes with less constrictive dissections.**Surgical technique modifications aimed at reducing axillary constriction have been previously explored[7], and our approach aligns with that concept without requiring lymphatic microsurgery, making it more accessible in resource-limited settings.** However, unlike those studies, our modification does not involve lymphatic reconstruction, making it more accessible in resource-limited settings.

**The proposed mechanism by which the modified technique reduces lymphedema risk is speculative.** It may involve releasing potential constrictive structures at the axillary apex. Resection of the clavicular portion of the pectoralis major and the clavipectoral fascia theoretically expands the axillary space, reducing postoperative scar contracture compression on lymphatic drainage pathways around the axillary vein. This may facilitate the establishment of lymphatic collateral circulation or functional compensation by residual lymphatic vessels, aligning with the concept of previous technical explorations aimed at reducing surgical trauma and protecting lymphatic vessels [20-21]. **Further experimental and imaging studies are needed to validate this mechanism.**

The most prominent finding of this study is the central role of obesity as an independent risk factor (OR=4.71). Adipose tissue is not only a mechanical burden but also an active endocrine organ. Obesity-related chronic low-grade inflammation, dysregulated adipokine secretion, lymphatic vessel dysfunction, and increased interstitial hydrostatic pressure collectively create a microenvironment conducive to lymph accumulation [22,23]. Importantly, the protective effect of the modified surgery was more pronounced in obese patients (lymphedema rate reduced from 58.7% to 36.4%), suggesting this high-risk subgroup can derive greater absolute benefit from surgical optimization, providing exploratory evidence for individualized surgical decision-making. **Although stratified analyses suggested a differential effect, formal testing for interaction between obesity and surgical technique was not performed, and this should be addressed in future studies.**

Our study also highlights the prevalence and clinical relevance of "menopausal metabolic syndrome" in this patient population. Approximately 40% of postmenopausal women have this syndrome. Its characteristic insulin resistance, dyslipidemia, and chronic inflammation, superimposed with breast cancer treatment (especially iatrogenic menopause), form a pathological basis promoting lymphedema [24,25]. Therefore, for perioperative management of patients with locally advanced triple-negative breast cancer, screening and intervention for metabolic syndrome (such as weight management, glycemic and blood pressure control) should be considered as potentially important adjuncts to surgical technique.

The prediction model constructed in this study (based on surgical technique and obesity status) has moderate discriminative ability (AUC=0.729). However, this model is exploratory; it does not include many known determinants of lymphedema (e.g., radiotherapy details, number of nodes removed, postoperative complications), and it lacks internal validation and calibration. Therefore, it should not be used as a clinical prediction tool without further prospective validation. Future prediction models could consider integrating more refined indicators, such as lymphangiography-assessed lymphatic function preoperatively (e.g., using indocyanine green). For patients with high BMI or clinically suspected aberrant lymphatic drainage, we recommend preoperative indocyanine green lymphography to guide reverse mapping, although this was not systematically performed in the present cohort. Specific genetic susceptibility markers (e.g., FLT4, FOXC2 gene polymorphisms), or dynamic changes in early postoperative inflammatory markers (e.g., IL-6, VEGF-C levels), to achieve earlier and more precise risk prediction [26,27].

Striking a balance between oncological safety and functional preservation is a perennial theme in breast cancer surgery. As reported in the Results, nodal yield and positive node counts did not differ between groups, suggesting no compromise in oncological adequacy. However, long-term tumor control outcomes still require confirmation through larger sample sizes and longer follow-up in prospective studies.

Limitations of this study mainly include: First, the retrospective design makes it difficult to completely avoid selection bias and information bias; second, no formal sample size calculation was performed; third, the sample size is relatively limited and from a single center, which may affect generalizability; fourth, the minimum follow-up of 12 months (median 18 months) may not capture late-onset lymphedema; **fifth, although radiotherapy protocols were standardized, they were not individually adjusted in the regression model, and residual confounding related to radiotherapy cannot be excluded**; sixth, the diagnosis of metabolic syndrome employed a simplified criteria based on medical records; seventh, the study did not deeply analyze the potential impact of surgical details (such as specific suture materials and techniques) on local fibrosis; eighth, surgeons were not blinded to technique; ninth, we did not separately record the frequency of level III lymph node dissection (although N3 stage proportions were similar); **tenth, perioperative outcomes (e.g., seroma rate, infection) were collected but not adjusted in the main analysis, and rehabilitation practices were not standardized**; **eleventh, formal interaction testing between obesity and surgical technique was not performed, which may have provided additional insight into the differential benefit observed.**

**Conclusion**

Obesity and surgical technique are independent risk factors for postoperative upper limb lymphedema in patients with locally advanced triple-negative breast cancer. Employing a modified axillary lymph node dissection technique involving resection of the clavicular pectoralis major and clavipectoral fascia may significantly reduce lymphedema incidence, with particular benefit observed for obese patients. **The proposed mechanism is speculative, and residual confounding (e.g., from radiotherapy) cannot be excluded.** Given the retrospective design and lack of external validation, these findings should be interpreted as hypothesis-generating. Prospective randomized studies are needed before this technique can be routinely recommended. Simultaneously, emphasis should be placed on perioperative metabolic management and the development of integrated prediction models to form a comprehensive prevention strategy.



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## Author Contributions

All authors contributed substantially to the manuscript's development, including conceptualization, writing, and editing. Conceptualization and design: Zhi-yong Liu, Ran Chen; part of the treating team and data collection and data analysis: Zhi-yong Liu, Ran Chen; revision of the manuscript drafts: Zhi-yong Liu, Ran Chen. The submitted version of the manuscript has been approved by all authors, who have also agreed to take responsibility for any aspect of the work.

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## Ethics Declaration

This study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of the First Affiliated Hospital of Gannan Medical University (Approval No.: GYYFY202500192). The retrospective review was approved in 2025. Patient consent was waived due to the retrospective nature of the study.

## Consent for Publication

Not applicable.

## Competing Interests

The authors declare no competing interests.

## Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request, as the data are not publicly available due to patient privacy restrictions.



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