Original Article

The impact of early exercise intervention on the incidence and severity of lymphedema following axillary lymph node dissection in breast cancer

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Background: Breast cancer-related lymphedema (BCRL) is a chronic complication of axillary lymph node dissection (ALND) that impairs mobility and quality of life (QoL). This study evaluated the impact of early systematic exercise on BCRL incidence, severity, and functional recovery.

Methods: A retrospective cohort study analyzed 136 patients who underwent ALND between 2020 and 2024. The intervention group (n=70) participated in a therapist-guided, phased exercise program initiated within two weeks post-surgery. The control group (n=66) received conventional health education. The primary outcome was BCRL incidence within 12 months (defined as ≥10% or ≥200 mL volume increase). Secondary outcomes included shoulder range of motion (ROM), [Disabilities of the Arm, Shoulder, and Hand (DASH) score] scores, pain [Visual Analog Scale (VAS) score], and QoL [European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 and breast cancer module (EORTC QLQ-C30/BR23)].

Results: The overall BCRL incidence was 25.0%. The intervention group showed a significantly lower incidence compared to controls (17.1% *vs.* 33.3%, P=0.03). Multivariate analysis confirmed early exercise as an independent protective factor [odds ratio (OR) =0.42, 95% confidence interval (CI): 0.20–0.88, P=0.02] and significantly delayed the time to BCRL onset [hazard ratio (HR) =0.52, P=0.04]. In the intervention group, patients experienced significantly reduced severity of lymphedema, characterized by smaller limb volume differences (95±120 *vs.* 165±140 mL, P=0.01) and a lower proportion of moderate-to-severe cases (5.7% *vs.* 18.2%). These patients also demonstrated superior functional recovery, with greater shoulder flexion and abduction ROM (P<0.01) and lower DASH scores (12.4±8.6 *vs.* 18.1±10.3, P=0.002), alongside enhanced well-being evidenced by lower median pain scores (VAS 1 *vs.* 2, P=0.02) and higher QLQ-C30 QoL scores (78.5±12.0 *vs.* 72.0±13.5, P=0.008). Subgroup analysis revealed the greatest benefits for high-risk patients [radiotherapy, high body mass index (BMI), ≥15 lymph nodes dissected]. No serious exercise-related adverse events occurred.

Conclusions: Early, systematic exercise intervention after ALND is a safe and effective strategy to reduce BCRL risk and severity. It significantly enhances physical function and QoL, particularly in high-risk populations. These findings support integrating individualized exercise programs into routine postoperative rehabilitation pathways.

Keywords: Breast cancer; axillary lymph node dissection (ALND); lymphedema; early exercise intervention; upper limb functional recovery

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Introduction

Breast cancer is the most frequently diagnosed malignancy and a leading cause of cancer-related death among women worldwide (1). In recent global estimates, approximately 2.3 million new cases and 670,000 deaths were reported in a single year, and the incidence has more than doubled since 1990 (2,3). Although incidence remains higher in high-income countries, mortality disproportionately affects women in low-income regions, reflecting marked inequalities in access to care (4,5). Overall, the rising incidence, substantial mortality, and associated disability-adjusted life years (DALYs) highlight the urgent need for effective prevention, early detection, and timely treatment strategies for breast cancer (6).

Breast cancer-related lymphedema (BCRL) emerges as a prevalent complication following breast cancer treatment. The fundamental pathophysiology involves disruption of lymphatic drainage pathways postoperatively, leading to accumulation of protein-rich fluid within interstitial tissues (7). BCRL typically presents as persistent swelling and heaviness in the ipsilateral upper extremity (or corresponding breast/trunk region), frequently accompanied by pain. Chronic progression may lead to skin fibrosis and adipose deposition (8). These clinical manifestations can result in restricted arm mobility, impaired performance of daily activities, and substantially diminished quality of life (QoL) (9,10). Current evidence indicates that approximately 20% of breast cancer patients undergoing axillary lymph node dissection (ALND) develop BCRL (11). Extensive nodal dissection and regional lymphatic radiotherapy constitute major treatment-related risk factors, while patient-specific factors including elevated body mass index (BMI) and postoperative infection further contribute to risk elevation (12,13). Consequently, early surveillance and targeted intervention in high-risk populations are essential for BCRL prevention and mitigation of its physical and psychological consequences.

In recent years, the therapeutic potential of early postoperative exercise intervention in breast cancer recovery has garnered increasing scientific interest. From a physiological perspective, exercise-mediated skeletal muscle contractions promote lymphatic return and enhance clearance of tissue fluids (14), providing a mechanistic rationale for exercise in BCRL prevention. Substantial evidence confirms that appropriately prescribed exercise is both safe and effective for improving functional status in this population. One randomized controlled trial (RCT) demonstrated that patients initiating personalized home-based exercise regimens commencing on the first postoperative day exhibited significantly superior recovery of shoulder strength at 1 and 6 months compared to usual care recipients (15). Notably, the study reported equivalent BCRL incidence rates (3.6%) in both groups at 6 months, indicating that early exercise implementation did not increase edema risk (15). Furthermore, a recent systematic review highlighted that combined aerobic and resistance training regimens yield beneficial effects for both prevention and management of BCRL (16). Collectively, current evidence supports the safety and potential efficacy of early exercise interventions for improving postoperative function and possibly reducing

Highlight box

Key findings

- In 136 post-axillary lymph node dissection (ALND) breast cancer patients, early supervised progressive exercise (starting ≤2 weeks) was associated with lower 12-month breast cancer-related lymphedema (BCRL) incidence (17.1% *vs.* 33.3%; odds ratio =0.42), delayed onset, reduced limb volume/severity, and improved range of motion, function, pain, and quality of life. Benefits were greatest in high-risk subgroups; no serious adverse events occurred.

What is known and what is new?

- Exercise is known to be safe and to improve function after breast cancer surgery, but its role in preventing BCRL in high-risk ALND populations remained inconclusive due to heterogeneous protocols and adherence issues.
- This study provides real-world evidence from a systematic, supervised ALND-specific protocol, showing significant BCRL reduction, delayed onset, and multidimensional benefits. It quantifies protective effects in high-risk subgroups and demonstrates a dose-response with adherence.

What is the implication, and what should change now?

- Early, individualized exercise should be routine post-ALND, especially for high-risk patients. Clinical pathways must integrate early referral, supervision, and adherence monitoring. Future randomized controlled trials with longer follow-up and objective lymphatic assessment are needed to confirm findings and refine protocols.

BCRL incidence, though methodological variations across studies preclude definitive conclusions.

Despite established benefits of postoperative exercise, considerable controversy persists regarding optimal intervention parameters. Substantial heterogeneity exists in exercise timing, intensity, and modality across investigations. Some protocols advocate immediate postoperative initiation of passive or active movements, while others recommend delayed commencement following wound healing, employing varying training intensities (17). For instance, one meta-analysis suggested a transient elevation in BCRL risk [relative risk (RR) ≈3.7] with early vigorous exercise, though long-term risk demonstrated no significant difference compared to conventional care (15). Conversely, recent clinical trials (including the aforementioned *JAMA* study) reported no increased edema incidence with early exercise implementation (18). Additional complexity arises from adherence considerations, as evidenced by a multicenter trial (CALGB 70305) where only approximately 50% of early intervention participants consistently performed prescribed exercises, and fewer than one-third maintained regular compression sleeve use (19). The absence of standardized BCRL diagnostic criteria and assessment methodologies across studies, compounded by typically limited follow-up durations of 1–2 years, impedes comprehensive evaluation of long-term outcomes (20). These methodological challenges perpetuate ongoing scholarly debate regarding the precise role of exercise rehabilitation in BCRL prevention, emphasizing the necessity for larger-scale RCTs employing standardized protocols.

Currently, research specifically examining early exercise interventions for BCRL prevention following ALND remains relatively limited. The present study addresses this knowledge gap by implementing a rigorously designed early exercise protocol and evaluating its effects on BCRL incidence and severity in a high-risk cohort. This investigation possesses significant innovative merit, theoretically contributing to understanding exercise-mediated modulation of lymphatic function and inflammatory pathways. From a clinical perspective, the findings may inform evidence-based postoperative rehabilitation guidelines, facilitating development of optimized functional exercise strategies to reduce BCRL incidence, improve patient outcomes, and alleviate healthcare burdens. Thus, this study holds substantial value for advancing breast cancer rehabilitation science while offering potential societal and medical benefits. The primary aim of this investigation is to determine the effect of early exercise intervention following ALND on BCRL incidence and severity. We present this article in accordance with the STROBE reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-2025-1-597/rc).

Methods

Patients

This single-center retrospective cohort study analyzed the clinical data of patients who underwent radical mastectomy for breast cancer along with ALND (defined as ALND with removal of ≥10 lymph nodes) in the Department of Breast Surgery at West China Hospital between January 2020 and December 2024. Case screening and data extraction from the hospital's electronic medical record system were performed independently by two researchers, with dual verification to ensure data accuracy and completeness. A total of 136 patients meeting the eligibility criteria were enrolled, comprising 70 patients in the early exercise intervention group and 66 patients in the control group. All patients were followed up for at least 12 months postoperatively and possessed complete clinical data, including upper limb volume monitoring, imaging, and functional follow-up records. Group assignment was based on whether patients received therapist-guided upper limb rehabilitation within two weeks after surgery. This decision was made by the treating clinicians based on individual factors like wound healing and patient willingness, not by a predefined study protocol. Although a departmental rehabilitation SOP recommended that all clinically stable ALND patients be evaluated for early exercise, the actual referral and timing of initiation ultimately depended on physician judgment and shared decision-making with the patient; therefore, as in other observational cohorts, confounding by indication cannot be fully excluded. To ensure scientific rigor, a standardized case report form (CRF) was used for data collection. All continuous variables were recorded using uniform units (e.g., mL for volume, cm for circumference), and categorical variables were grouped according to standard medical definitions. Missing data, if any, were addressed through supplementary medical record retrieval or follow-up telephone verification. Data entry was followed by quality control and double-checking by an independent third-party statistician. This study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study protocol was reviewed and approved by the Ethics Committee of West China Hospital (Ethics approval No. 2019 Audit 512).

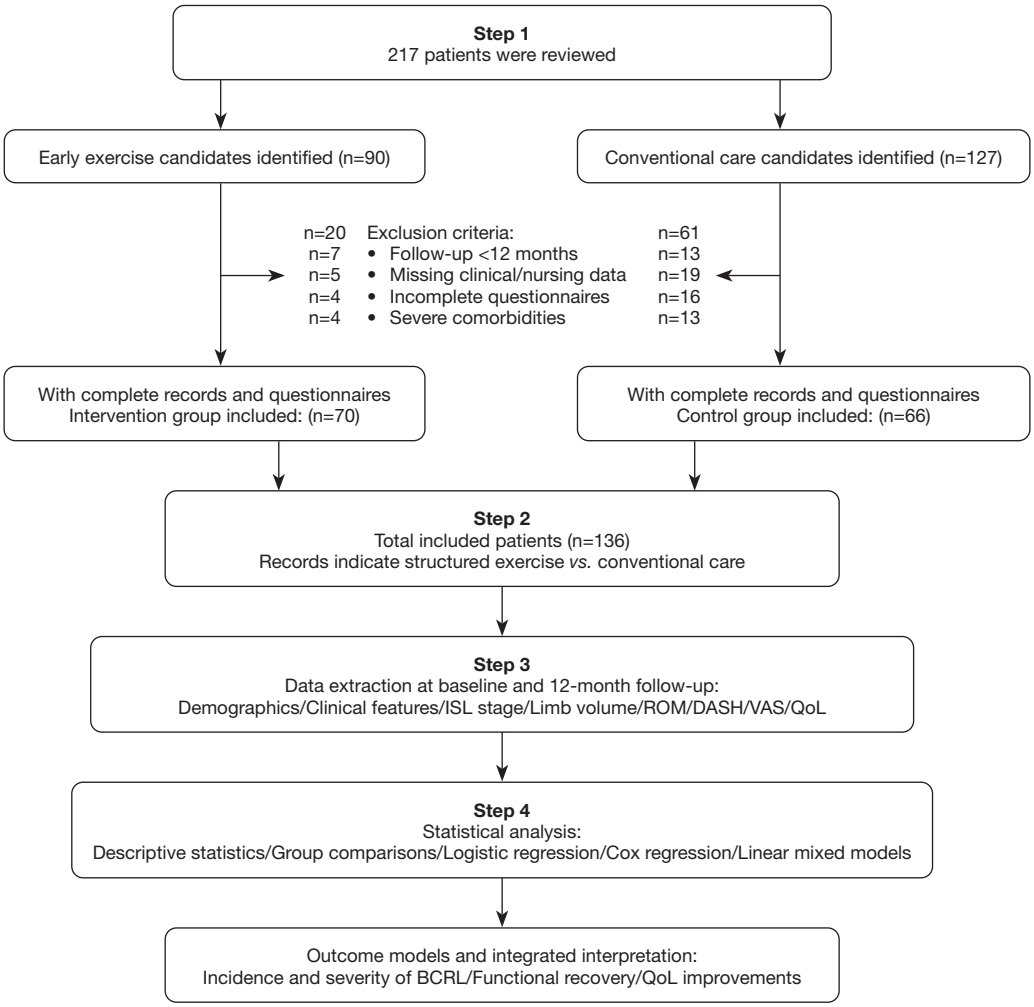

Figure 1 Study flowchart. A total of 217 patients who underwent radical mastectomy for breast cancer with axillary lymph node dissection were retrospectively screened. Based on exclusion criteria (follow-up <12 months, missing clinical/nursing data, severe comorbidities, etc.), 81 patients were excluded, resulting in 136 patients being ultimately enrolled. These comprised 70 patients in the Early Exercise Intervention Group and 66 patients in the Conventional Rehabilitation Group. All subjects were followed for 12 months, during which data on upper limb volume difference, ISL stage, shoulder ROM, upper limb function (DASH questionnaire), pain score (VAS), and quality of life (QoL, EORTC QLQ-C30/BR23) were collected. Statistical analyses included descriptive statistics, between-group comparisons, Logistic regression, Cox regression, and linear mixed models. BCRL, breast cancer-related lymphedema; DASH, Disabilities of the Arm Shoulder and Hand; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; ISL, International Society of Lymphology; QoL, quality of life; ROM, range of motion; VAS, Visual Analog Scale.

Patient privacy was protected through anonymization of all identifying information during data analysis, which was conducted solely for scientific research purposes without commercial interests or individual identification. Given the retrospective analysis of de-identified data, the requirement for written informed consent was waived by the Ethics Committee of West China Hospital.

The study flowchart is show in *Figure 1*.

Inclusion and exclusion criteria

Inclusion criteria

(I) Postoperative pathological confirmation of breast cancer and having undergone ALND as defined above, with ≥10 axillary lymph nodes removed.

(II) Postoperative follow-up duration ≥12 months.

(III) Availability of complete upper limb circumference or

volume monitoring data.

(IV) Patients were required to have good postoperative wound healing, defined as no infection, dehiscence, or delayed healing at the first rehabilitation assessment. Those with unresolved wound complications before postoperative week 2 were excluded prior to group assignment.

Exclusion criteria

(I) History of prior surgery, major trauma, or chronic lymphedema in the affected upper limb.

(II) Postoperative occurrence of severe infection, thrombosis, or other complications impairing upper limb function.

(III) Incomplete follow-up data or loss to follow-up during the study period.

(IV) Having undergone sentinel lymph node biopsy only without subsequent ALND, or having <10 axillary lymph nodes removed in total.

Intervention methods

Based on postoperative rehabilitation records and the actual rehabilitation protocols received by patients, all cases were retrospectively categorized into an early exercise intervention group (n=70) and a control group (n=66). The grouping criterion was whether, in the course of routine care, the patient received a systematic, therapist-guided upper limb exercise training program within 2 weeks post-surgery; decisions to initiate such early rehabilitation were made on the basis of wound healing, absence of serious postoperative complications (e.g., infection, thrombosis), and the patient's general condition and preferences, rather than predefined research-specific allocation rules, which implies a pragmatic, indication-based allocation that may favor patients perceived as healthier or more motivated and thus introduces potential confounding by indication. To ensure the reproducibility and consistency of the intervention, a departmental Standard Operating Procedure (SOP) for postoperative upper limb rehabilitation had been established before the study period and was routinely applied in clinical practice. All therapists and assessors had received unified training and passed competency assessments before the start of the study period and retrospective data collection. The same team carried out all interventions and assessments. Following data entry, verification was performed by two independent researchers. Assessors were blinded to patient group allocation during the statistical analysis phase to minimize observer bias. This intervention protocol was developed based on prior evidence that early muscle pump activation, improved upper limb venous and lymphatic return, and enhanced joint function may help prevent or delay BCRL onset and progression, while also reducing postoperative fluid retention and fibrosis. The underlying mechanisms, however, were not directly assessed in this study.

Intervention group

Patients in the intervention group commenced an early exercise intervention program within two weeks postoperatively, after confirmation of satisfactory wound healing and overall clinical stability, implemented and monitored by the same rehabilitation therapy team. The training content adhered to evidence-based rehabilitation principles and incorporated recommendations from the International Society of Lymphology (ISL) (21) and the National Comprehensive Cancer Network (NCCN) Breast Cancer Guidelines (22). The intervention goals were to: promote upper limb lymphatic return, improve shoulder joint range of motion (ROM), enhance muscle pump function, and prevent the onset of upper limb lymphedema and functional impairment. The overall training regimen was a phased, individualized, and progressive comprehensive rehabilitation plan, with the rehabilitation therapist dynamically adjusting the intensity and load based on the patient's recovery status.

During the early postoperative period (weeks 1–2), patients primarily underwent ROM training. This included shoulder flexion, extension, abduction, internal rotation, and external rotation exercises. Initially, these were performed as passive or active-assisted movements, twice daily for 10–15 minutes per session. Patients were positioned sitting or supine, with the therapist assisting in gradually increasing the ROM while avoiding wound strain or pain provocation. As wound healing progressed and tolerance improved, exercises gradually transitioned to active full-range movements to restore shoulder flexibility and prevent postoperative adhesions.

Starting from the second postoperative week, therapists instructed patients in self-manual lymph drainage (S-MLD) techniques and skin care. The drainage sequence proceeded from proximal to distal, encompassing the cervico-clavicular region, axilla, and proximal upper arm, using gentle, rhythmic strokes directed along lymphatic pathways. Each session lasted approximately 10 minutes and was performed once daily, focusing on promoting residual

lymph fluid return and reducing subcutaneous interstitial fluid accumulation. Concurrently, patients were educated on skin moisturization, avoiding trauma and insect bites, and refraining from wearing constrictive clothing to prevent infection and secondary cellulitis.

Once the patient's shoulder ROM approached that of the contralateral side and the surgical site showed no signs of exudate or infection (approximately postoperative week 3), progressive resistance training (PRT) was initiated. Using resistance bands or light dumbbells (initial load 1–2 kg), patients performed resistance exercises such as upper limb flexion, extension, abduction, forward elevation, and horizontal abduction. Each exercise session consisted of 2–3 sets of 10–15 repetitions, performed three times per week. Load progression was based on the patient reporting minimal to no pain and a perceived exertion rating of <5 on the Borg Scale, with the rehabilitation therapist reassessing and gradually increasing resistance every 2 weeks. The core objective of this phase was to strengthen the upper limb muscle pump, thereby improving the efficiency of venolymphatic fluid return and preventing chronic fluid stasis and fibrosis.

Additionally, patients concurrently engaged in functional and task-oriented training, which simulated activities of daily living such as donning and doffing clothing, washing hair, lifting, and reaching for objects. This aimed to enhance upper limb coordination and fine motor control. Therapists emphasized postural symmetry and involvement of the affected limb, assisting patients in safely resuming independent daily activities as early as possible. Follow-up outpatient appointments were scheduled at postoperative weeks 3 and 6, during which the rehabilitation therapist reassessed shoulder ROM, muscle strength, and pain levels (using the Visual Analog Scale, VAS), and adjusted the individualized exercise prescription based on recovery progress.

All intervention details were documented in a standardized CRF, including daily exercise type, duration, intensity, pain scores, and any adverse reactions. Therapists were required to complete and sign a training log after each session. Data were periodically reviewed by an independent research coordinator. To ensure intervention consistency and reproducibility, the research team established a SOP prior to project initiation and organized unified training and assessment for all rehabilitation therapists. An independent Quality Control Committee monitored adherence and consistency throughout the study period. Should significant pain, wound dehiscence, infection, or impaired lymphatic drainage occur, training was immediately suspended, and the attending physician was consulted for evaluation and management.

Control group

Patients in the control group received conventional postoperative health education and nursing guidance but did not undergo any systematic, phased, or therapist-supervised upper limb rehabilitation training. All educational activities were conducted by the responsible breast surgery nurse or a dedicated rehabilitation nurse before hospital discharge, utilizing a combination of face-to-face verbal instruction and written materials. Educational content primarily included: maintaining cleanliness and dryness of the affected limb, avoiding high-temperature or humid environments, avoiding tight-fitting clothing, prohibiting blood draws, intravenous access, or blood pressure measurements on the affected upper limb, and avoiding heavy lifting or strenuous upper body exercise. Nursing staff also provided basic knowledge on early prevention of upper limb edema, such as recognizing early signs (e.g., finger tightness, ring constriction, pitting edema) and appropriate pathways for seeking medical attention.

During the follow-up period, the research team did not provide any structured rehabilitation prescriptions or professional exercise guidance to the control group patients but permitted them to maintain their usual activities of daily living. Some patients might have engaged in mild self-directed activities (e.g., walking, light housework, or gentle stretching) based on their personal recovery. To ensure data completeness and control for potential confounding factors, the research team recorded the frequency, duration, and subjective intensity (using the modified Borg scale) of patients' routine physical activities during each follow-up visit via a standardized questionnaire. This information was used for subsequent covariate adjustment in statistical analyses to assess the potential influence of spontaneous activity on the study's primary outcomes.

All control group patients received standard outpatient follow-up assessments at 1, 3, 6, and 12 months postoperatively. Each assessment, conducted by the attending physician or a research assistant, evaluated upper limb swelling, skin changes, and shoulder joint mobility, with findings recorded in the CRF. If patients exhibited significant swelling, infection, or pain, they were managed according to standard clinical pathways but were not enrolled into the early exercise rehabilitation program.

To ensure consistency in nursing education, the research

team developed a standardized Health Education SOP. All nursing personnel received unified training before the study commenced, covering topics such as postoperative edema risk recognition, key health education points, and patient communication skills. Only those who passed the training were authorized to deliver patient education, thereby minimizing bias due to variations in education quality. After data entry, an independent quality controller performed verification checks. Assessors remained blinded to patient group assignment during the data analysis phase to ensure study objectivity and internal validity.

Monitoring indicators

Primary outcome measure

The primary outcome measure was the incidence of BCRL. BCRL was defined as a ≥10% increase in volume of the affected upper limb compared to the contralateral limb, or an absolute volume difference ≥200 mL, consistent with ISL diagnostic criteria (23). Upper limb volume was calculated using a standardized circumferential measurement method. Measurements were performed by the same assessor under consistent environmental conditions at 3, 6, and 12 months postoperatively. Measurement points were located 10 cm above the elbow, 10 cm below the elbow, and at the wrist, using the elbow crease as the reference point. Measurements were taken at 4 cm intervals, resulting in six segments. A flexible tape measure was used for all measurements, applied lightly to the skin without compressing underlying tissues. Each site was measured twice, and the average was recorded; measurements were repeated if the difference exceeded 0.2 cm. Volume was calculated using the Kuhnke formula: $V = \Sigma\pi \times (C_i + C_{i+1})^2 \times h / (16\pi^2)$, in which C_i represents the circumference of adjacent segments and h is the interval (4 cm). The percentage volume difference was calculated as: Volume difference (%) = [(V_affected – V_non-affected) / V_non-affected] × 100%. All measurements were scheduled between 9:00 AM and 11:00 AM, with room temperature maintained at 22–25 ℃. Patients rested for 15 minutes prior to measurement to minimize fluid fluctuation effects.

Secondary outcome measures

Lymphedema severity

Graded according to ISL criteria from stage 0 to III: stage 0 indicated a latent phase with no symptoms but impaired lymphatic function; stage I represented mild, reversible edema; stage II denoted partially reversible, moderate edema; and stage III indicated severe, irreversible edema accompanied by skin fibrosis or fat deposition. Two senior rehabilitation physicians independently performed the assessments. In case of discrepancy, a third physician arbitrated. Acceptable inter-rater reliability was defined as a Kappa coefficient ≥0.85.

Shoulder ROM

Measured using a standard goniometer (Baseline® Goniometer, Elmsford, NY, USA) for shoulder flexion, abduction, internal rotation, and external rotation (units: degrees). Patients were seated with the trunk vertical to avoid compensatory movements. Each movement was measured twice, and the average was recorded. Assessments occurred at 1, 3, 6, and 12 months postoperatively. Changes in ROM were used to analyze the temporal dynamic effects of the intervention on upper limb motor function recovery.

Upper limb function

Assessed using the Chinese version of the Disabilities of the Arm, Shoulder, and Hand (DASH) questionnaire (24). This 30-item scale yields a score ranging from 0 to 100, with higher scores indicating greater functional limitation. Patients completed the questionnaire independently, and research assistants checked for completeness. Internal consistency testing showed a Cronbach's α=0.92, indicating good reliability.

Pain intensity

Evaluated using the VAS (25), ranging from 0 to 10 cm, where 0 represented "no pain" and 10 represented "the most severe pain imaginable". Resting and activity-related pain intensity were assessed at 1, 3, 6, and 12 months postoperatively. Changes in VAS scores were used to analyze intervention safety and pain control efficacy.

QoL

Assessed using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) and its breast cancer-specific module (QLQ-BR23) (26). These instruments cover dimensions including physical functioning, emotional functioning, social role functioning, and breast cancer-related symptoms. Scores were linearly transformed to a 0–100 scale, with higher scores representing better QoL. Questionnaires were administered at 6 and 12 months postoperatively, and patients completed them independently on-site.

Complications and intervention adherence

All rehabilitation-related adverse events within 12 months postoperatively were recorded, including infection, delayed wound healing, deep vein thrombosis, increased pain, and exercise-related injuries. Adherence was assessed based on

therapist-completed training logs for supervised sessions, patient self-reported home-practice logs, and follow-up interview results. The completion rate was calculated as (actual number of training sessions / planned number of sessions ×100%). A completion rate ≥80% was defined as high adherence.

Statistical analysis

All data were analyzed using SPSS version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean ± standard deviation ($\bar{x}$ ± SD) or median (interquartile range). Group comparisons for continuous variables were performed using independent samples t-tests or Mann-Whitney U tests based on normality test results. Categorical variables are presented as counts (percentages) and were compared using the Chi-squared test or Fisher's exact test.

For the primary outcome (BCRL incidence), a Logistic regression model was employed to analyze the independent effect of early exercise intervention. Given the retrospective, non-randomized design and the possibility of confounding by indication, potential confounding variables, including age, BMI, radiotherapy, chemotherapy, postoperative infection, and number of dissected lymph nodes, were entered stepwise into the model as covariates. Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) are reported. To further address allocation bias, propensity scores for receiving early exercise were estimated using a Logistic regression model including the same covariates, and stabilized inverse probability of treatment weights (IPTW) were applied to construct propensity score-weighted Logistic and Cox models as sensitivity analyses.

For secondary outcomes (ROM, DASH, VAS, QoL, etc.), which involved repeated measures over time, linear mixed models (LMM) or repeated measures analysis of variance (ANOVA) were used to assess the interaction effects between intervention and time.

Subgroup analyses were conducted by stratifying variables such as radiotherapy (yes/no), chemotherapy (yes/no), BMI (<25 *vs.* ≥25 kg/m^2), and number of dissected lymph nodes (<15 *vs.* ≥15). Adjusted ORs for each subgroup and interaction P values were calculated.

Kaplan-Meier curves were plotted with the time to first BCRL diagnosis as the event endpoint. Between-group differences were tested using the log-rank test. The Cox proportional hazards model was used to calculate adjusted hazard ratios (HRs) with 95% CIs.

Cases lost to follow-up or with missing data were handled using multiple imputation. The robustness of the results was verified through sensitivity analyses [per-protocol (PP) and intention-to-treat (ITT)]. All tests were two-sided, and the significance level was set at P<0.05.

Results

Baseline characteristics

This study enrolled a total of 136 patients, with 70 in the early exercise intervention group and 66 in the control group. All patients completed a minimum follow-up of 12 months, with a median follow-up duration of 12 months. As presented in *Table 1*, the distribution of major clinical and demographic characteristics, including early postoperative wound complications, was balanced between the two groups, with no significant differences observed.

Primary outcome: BCRL incidence and risk analysis

At the 12-month follow-up, 34 patients in the entire cohort were diagnosed with BCRL, yielding an overall incidence of 25.0%. The incidence was significantly lower in the intervention group compared to the control group: 17.1% (12/70) *vs.* 33.3% (22/66) (χ^2=4.66, P=0.03, *Figure 2A*). The absolute risk difference between groups was 16.2 percentage points, corresponding to an approximate 49% reduction in relative risk.

Further logistic regression analysis was performed, adjusting for potential confounders including age, BMI, number of dissected lymph nodes, radiotherapy, chemotherapy, and postoperative infection. The analysis revealed that early exercise intervention was independently and inversely associated with BCRL occurrence (adjusted OR =0.42, 95% CI: 0.20–0.88, P=0.02). This suggests that the intervention reduced the risk of developing edema within 12 months post-surgery by approximately 58% (*Figure 2B*). Hosmer-Lemeshow test indicated a good model fit (P>0.05). In the Cox proportional hazards model, with time to first BCRL diagnosis as the endpoint, the intervention group demonstrated a higher edema-free survival rate (HR =0.52, 95% CI: 0.28–0.96, P=0.04), a finding directionally consistent with the logistic regression analysis. Kaplan-Meier survival curves further revealed that while group differences were not significant within the first 3–6 months, a clear divergence emerged from around the 9th month onward, with the intervention group maintaining a consistently lower cumulative incidence of BCRL (P=0.04;

Table 1 Baseline characteristics of patients in the early exercise and control groups (N=136)

Variable	Investigation (n=70)	Control (n=66)	P value
Demographic characteristics			
Age (years)	52.8±9.5	53.1±10.0	0.82
BMI (kg/m^2)	24.7±3.3	24.9±3.5	0.74
Postmenopausal status	39 (55.7)	38 (57.6)	0.82
Dominant hand = affected side	32 (45.7)	30 (45.5)	0.98
Diabetes mellitus	9 (12.9)	8 (12.1)	0.89
Hypertension	14 (20.0)	13 (19.7)	0.96
Tumor and surgical characteristics			
Tumor stage (I–II)	51 (72.9)	47 (71.2)	0.81
Tumor laterality (left)	34 (48.6)	33 (50.0)	0.88
Histologic type (invasive ductal)	60 (85.7)	55 (83.3)	0.70
Number of dissected lymph nodes	16.4±4.2	17.1±4.7	0.39
Positive lymph nodes	3 [1–6]	4 [2–6]	0.46
Tumor size (cm)	2.4±1.1	2.5±1.0	0.69
Surgical side lymphedema at baseline	0 (0.0)	0 (0.0)	–
Adjuvant treatment			
Radiotherapy	41 (58.6)	40 (60.6)	0.81
Chemotherapy	51 (72.9)	46 (69.7)	0.68
Endocrine therapy	28 (40.0)	25 (37.9)	0.80
Targeted therapy (HER2+)	10 (14.3)	9 (13.6)	0.91
Postoperative wound infection within 2 weeks postoperatively	6 (8.6)	6 (9.1)	0.92
Rehabilitation and follow-up variables			
Rehabilitation adherence (% completed sessions)	84.1±11.5	–	–
Follow-up duration (months)	12 [12–13]	12 [12–13]	0.77

Values are presented as mean ± standard deviation, n (%) or median [IQR]. P values were obtained using independent-samples t-tests for continuous variables and χ^2 or Fisher's exact tests for categorical variables. Postoperative wound infection refers to infections occurring within 2 weeks after surgery and before group categorization. BMI, body mass index; IQR, interquartile range.

Figure 2C).

Within the intervention group, an exploratory analysis showed that higher exercise adherence (≥80%) was associated with a lower BCRL incidence (13.9% *vs.* 24.7%, P=0.048; *Figure 2D*). However, this dose-response pattern is based on self-reported adherence and may reflect selection bias. Furthermore, sensitivity analyses using IPTW-weighted models consistently demonstrated that early exercise was associated with reduced BCRL risk (OR =0.43, P=0.03) and delayed onset (HR =0.49, P=0.03).

Limb volume difference and edema severity

At the continuous variable level, the volume difference between the affected and unaffected upper limbs at 12 months postoperatively was significantly smaller in the intervention group compared to the control group, with mean values of 95±120 *vs.* 165±140 mL, respectively. The between-group mean difference was −70 mL (95% CI: −124 to −16, P=0.01, *Table 2*), representing an approximate 42% relative reduction compared to the control group mean. After adjusting for baseline volume difference,

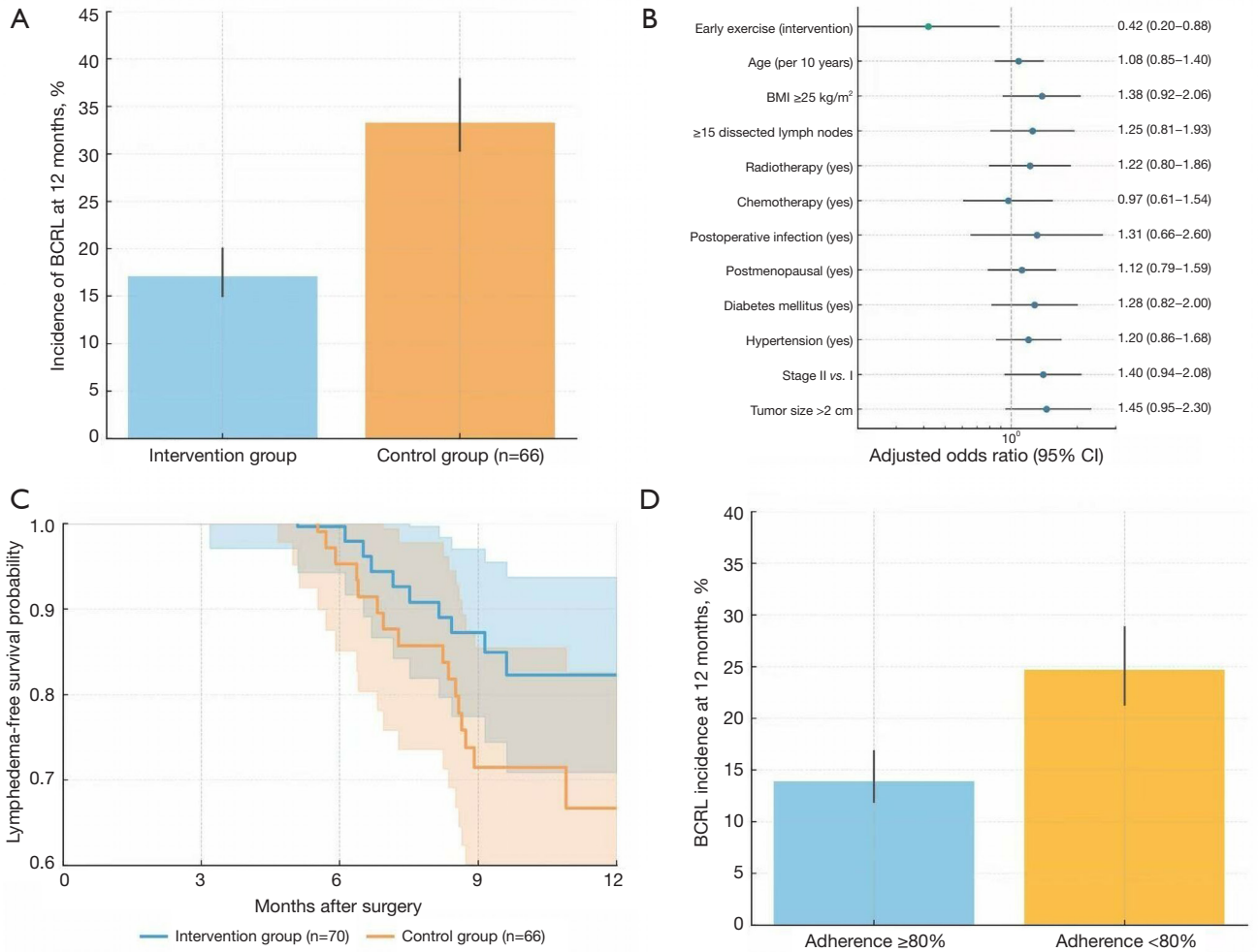

Figure 2 Impact of early exercise intervention on the incidence and risk of BCRL. (A) Comparison of BCRL incidence at 12 months postoperatively between the Intervention group and the Control group, reflecting the overall effect of early exercise intervention on the risk of edema development. (B) Forest plot from the multivariable Logistic regression analysis, displaying the adjusted ORs and 95% CIs for early exercise intervention and various clinical factors associated with BCRL risk. (C) Kaplan-Meier edema-free survival curves, comparing the probability of remaining free from BCRL over the 12-month postoperative period between the Intervention group and the Control group. The shaded areas represent the 95% CIs. (D) Subgroup analysis plot based on adherence, showing the difference in BCRL incidence at 12 months postoperatively between patients with different exercise adherence levels (≥80% *vs.* <80%), used to assess the association between intervention intensity and the protective effect. BCRL, breast cancer-related lymphedema; CI, confidence interval; ORs, odds ratios.

BMI, number of dissected lymph nodes, and radiotherapy using ANCOVA, the adjusted mean difference remained both statistically and clinically significant (adjusted mean difference: −65 mL, P=0.02). This suggests that the observed effect was not attributable to the known confounders. In clinical practice, a volume increase of ≥200 mL or ≥10% is often considered the threshold for perceptible lymphedema. Notably, a greater proportion of patients in the intervention group remained below this threshold, which typically corresponds to fewer reports of visible swelling, heaviness, and functional limitation in daily practice.

Regarding categorical severity, among the 34 patients diagnosed with BCRL, the proportion of patients with ISL stage II or higher was lower in the intervention group compared to the control group: 33.3% (4/12) *vs.* 54.5%

Table 2 Limb volume difference and edema severity between groups

Variable	Intervention group (n=70)	Control group (n=66)	Between-group difference (95% CI)	Unadjusted P values	Adjusted analysis[†]	Adjusted P values
Limb-volume difference at 12 months (mL)	95±120	165±140	−70 (−124 to −16)	0.01	−65 (ANCOVA adjusted)	0.02
Relative reduction *vs*. control (%)	–	Reference	≈42% lower	–	–	–
Patients with BCRL (ISL ≥ II)	4 (5.7%)	12 (18.2%)	ARR 12.5% (NNT ≈8)	–	–	–
Among BCRL cases (n=34): ISL ≥ II severity	4/12 (33.3%)	12/22 (54.5%)	–	–	–	–
Ordered logistic regression (ISL grade)	–	–	OR =0.48 (0.23–0.98)	0.044	–	–
Limb-volume growth rate (% *vs*. baseline)—3 months	+2.3%	+3.5%	–	–	–	–
Limb-volume growth rate (% *vs*. baseline)—6 months	+4.1%	+7.9%	–	–	–	–
Limb-volume growth rate (% *vs*. baseline)—12 months	+5.8%	+11.2%	–	–	–	–
Group × time interaction (mixed model)	–	–	–	–	F=5.76	0.02

Data are presented as mean ± standard deviation unless otherwise specified. [†], adjusted for baseline limb volume, BMI, number of dissected lymph nodes, and postoperative radiotherapy. ANCOVA, analysis of covariance; ARR, absolute risk reduction; BCRL, breast-cancer-related lymphedema; BMI, body mass index; CI, confidence interval; ISL, International Society of Lymphology; NNT, number needed to treat; OR, odds ratio.

(12/22). Although limited sample size affected precision, the direction consistently pointed towards reduced severity (*Table 2*). The intervention was associated with a markedly lower population risk for ISL stage ≥ II. The absolute risk was 5.7% (4/70) in the intervention group *vs.* 18.2% (12/66) in the control group, translating to an absolute risk reduction of 12.5% and a number needed to treat (NNT) of approximately 8 to prevent one case. Supporting this, an adjusted ordinal logistic regression confirmed the intervention was associated with lower overall severity grades (proportional OR ≈0.48, 95% CI: 0.23–0.98, P=0.044), aligning with the continuous volume measurements.

Observing the volume change trajectory over time, the volume increase rates in the intervention group at 3, 6, and 12 months postoperatively were +2.3%, +4.1%, and +5.8% respectively, compared to +3.5%, +7.9%, and +11.2% in the control group. LMM revealed a significant group-by-time interaction effect (P=0.02, *Table 2*), indicating that the intervention not only reduced the endpoint volume difference but also significantly slowed the rate of increase during follow-up. Taken together, these findings indicate that, compared with usual care, the intervention group had a smaller increase in limb volume and a lower proportion of moderate-to-severe edema during follow-up. Sensitivity analyses excluding patients with postoperative infections and those with adherence below 80% confirmed the direction and statistical significance of the between-group differences for both volume difference and severity.

Upper limb function and joint ROM

Postoperative upper limb function and shoulder joint ROM significantly improved over time in both groups, but the magnitude of improvement was greater in the intervention group. LMM analysis revealed a significant time-by-group interaction effect for shoulder flexion and abduction (P=0.02), suggesting that early exercise intervention not only accelerated the functional recovery process but also altered the improvement trajectory over time. As shown in *Figure 3A*, at the 12-month follow-up, the mean flexion ROM reached 167°±10° in the intervention group *vs.* 160°±13° in the control group (P=0.004); abduction ROM was 165°±11° *vs.* 158°±14°, respectively (P=0.006); external rotation was slightly higher (78°±9° *vs.* 75°±10°), approaching statistical significance (P=0.058). This sustained functional advantage suggests that early initiation of active and resistance training effectively prevents shoulder joint stiffness and soft tissue adhesion, maintaining joint mechanical flexibility.

Upper limb function assessment results aligned with the joint mobility trends. DASH scores decreased over time in both groups (lower scores indicate better function), but the decrease was faster and greater in the intervention group, with a significant time-by-group interaction effect (P=0.02).

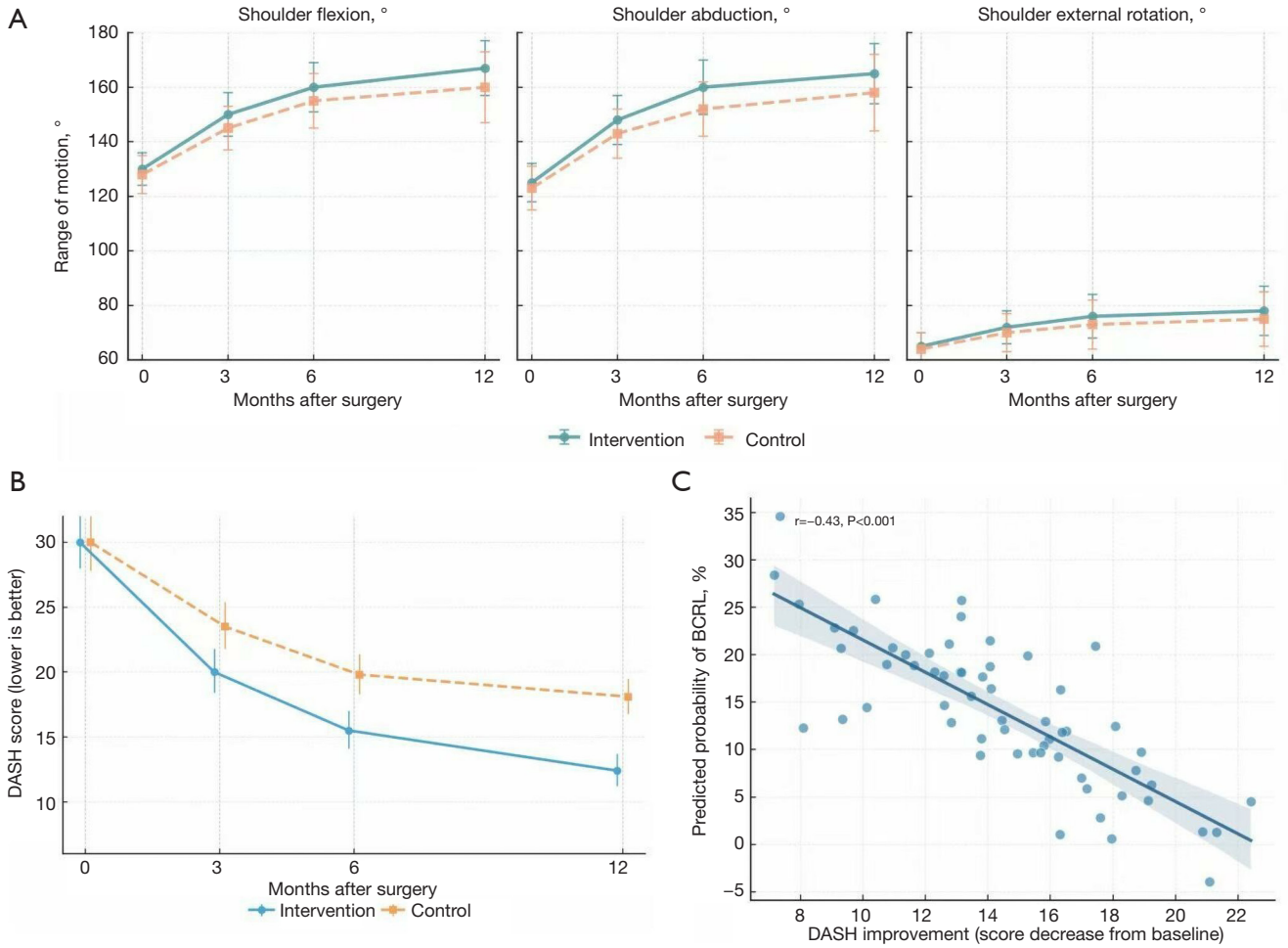

Figure 3 Impact of early exercise intervention on postoperative upper limb function and shoulder range of motion. (A) Displays the trends in shoulder flexion (left), abduction (middle), and external rotation (right) at 0, 3, 6, and 12 months postoperatively. The x-axis represents follow-up time, and the y-axis represents the range of motion (degrees, °). The graph compares the recovery trajectories of ROM in different planes between the Intervention group and the Control group, reflecting the influence of early exercise on shoulder flexibility and soft tissue compliance. (B) Shows the trend of upper limb function DASH scores at different postoperative time points. The x-axis represents postoperative months, and the y-axis represents the DASH score (lower scores indicate better function). The graph contrasts the speed and magnitude of functional recovery between the Intervention Group and the Control Group, reflecting the effect of early systematic exercise on improving activities of daily living (e.g., lifting, reaching, combing hair, dressing). (C) Illustrates the linear correlation between the magnitude of upper limb function improvement (decrease in DASH score) and the predicted probability of BCRL. The scatter plot reflects individual-level trends, and the fitted line with its 95% confidence interval (shaded area) suggests a negative correlation between functional improvement and the risk of edema. BCRL, breast cancer-related lymphedema; DASH, Disabilities of the Arm Shoulder and Hand; ROM, range of motion.

At 12 months postoperatively, the mean DASH score was 12.4±8.6 in the intervention group compared to 18.1±10.3 in the control group, with a mean difference of −5.7 (95% CI: −9.2 to −2.2, P=0.002, *Figure 3B*). Considering the longitudinal trend, the intervention group showed significant functional improvement as early as 3 months postoperatively, and this difference continued to widen later, suggesting a cumulative effect of early rehabilitation.

Further correlation analysis revealed a significant negative correlation between functional improvement and BCRL risk (r=−0.43, P<0.001; *Figure 3C*), suggesting that greater functional recovery was linked to a lower probability

of edema. This association persisted after adjustment for age, BMI, radiotherapy, and number of dissected lymph nodes in a multiple linear regression model (standardized β=–0.37, P=0.003). Together with the observed limb volume differences, these findings indicate a concurrent link between better functional recovery and more favorable volume outcomes in patients who received early exercise.

Pain and QoL

At 12 months postoperatively, both groups showed significant improvement from baseline in pain control and QoL, yet the intervention group demonstrated superior overall outcomes. Pain scores during activity (VAS) were significantly lower in the intervention group compared to the control group: 1 [interquartile range (IQR), 0–2] *vs.* 2 (IQR, 1–3), respectively (P=0.02). In contrast, the difference in resting pain did not reach statistical significance (P=0.11). As illustrated in *Figure 4A*, the distribution curve for activity-related pain was markedly left-shifted in the intervention group, with pain intensities concentrated in the lower range, whereas the control group exhibited a wider distribution. These distribution patterns are consistent with a greater reduction in activity-related pain in the intervention group, whereas between-group differences in resting pain were small. Patient interview records corroborated the quantitative findings, with the intervention group frequently reporting reduced "tightness" and alleviated "nocturnal pain" following active shoulder and upper limb training.

QoL assessments corroborated these benefits (*Figure 4B*). The intervention group reported a significantly higher global health status score on the EORTC QLQ-C30 (78.5±12.0) compared to the control group (72.0±13.5; P=0.008), indicating superior overall health perception, physical functioning, and emotional adjustment. In the BR23 module, scores for the "Arm Symptoms" dimension were significantly lower in the intervention group (15.0±11.2 *vs.* 22.1±13.8; P=0.01), reflecting a meaningful reduction in subjective complaints such as limb heaviness, numbness, and pulling sensations. Additionally, the intervention group showed positive, though non-significant, trends toward improved social function and self-image, which may relate to greater confidence in physical recovery and reduced limb-use avoidance. These results align with the trend depicted in the bar chart of *Figure 4B*, showing consistently rising QoL scores across both instrument dimensions in the intervention group.

Correlation analysis revealed intrinsic links between pain, functional recovery, and QoL (see *Figure 4C*). Improvement in QoL was significantly negatively correlated with the reduction in DASH scores (r=–0.49, P<0.001), indicating that better upper limb functional recovery was associated with stronger subjective health perception. Concurrently, QoL was positively correlated with pain reduction (r=0.42, P<0.001), suggesting that pain control may be an important mediating factor in improving QoL. The correlation matrix in *Figure 4C* clearly illustrates the synergistic relationship among functional improvement, pain alleviation, and QoL enhancement, with color gradients representing correlation strength and darker shades corresponding to significant correlations.

Further multiple linear model analysis, after controlling for age, BMI, radiotherapy, and chemotherapy, confirmed that both functional improvement and pain reduction remained independent predictors of global health scores (β=–0.38 and β=–0.29, respectively; both P<0.01). These associations are compatible with a potential pathway in which improvements in function and reductions in pain are related to better QoL, although formal mediation was not assessed in this study. An integrated summary of these multidimensional rehabilitation outcomes is visually represented in a radar chart (Figure S1), which combines key indicators such as pain, function, ROM, and QoL. The intervention group is depicted by a larger enclosed area, visually summarizing its superior profile across these domains. Clinically, this translates to patients in the intervention group reporting lower activity-related pain alongside higher global health and arm symptom scores compared to the usual care group.

Subgroup and sensitivity analyses

To further investigate the consistency of the early exercise intervention effect across different clinical contexts, subgroup analyses with multivariate adjustment were performed. The overall trend indicated that the intervention effect was numerically larger in high-risk populations. Specifically, patients in the radiotherapy subgroup derived the most substantial benefit, with the intervention group showing an approximately 64% reduced risk of BCRL compared to the control group (OR =0.36, 95% CI: 0.15–0.87, *Table 3*). These patterns indicate that the association between early exercise and lower BCRL risk was numerically stronger in patients who received radiotherapy, had BMI ≥25 kg/m^2, or had ≥15 lymph nodes

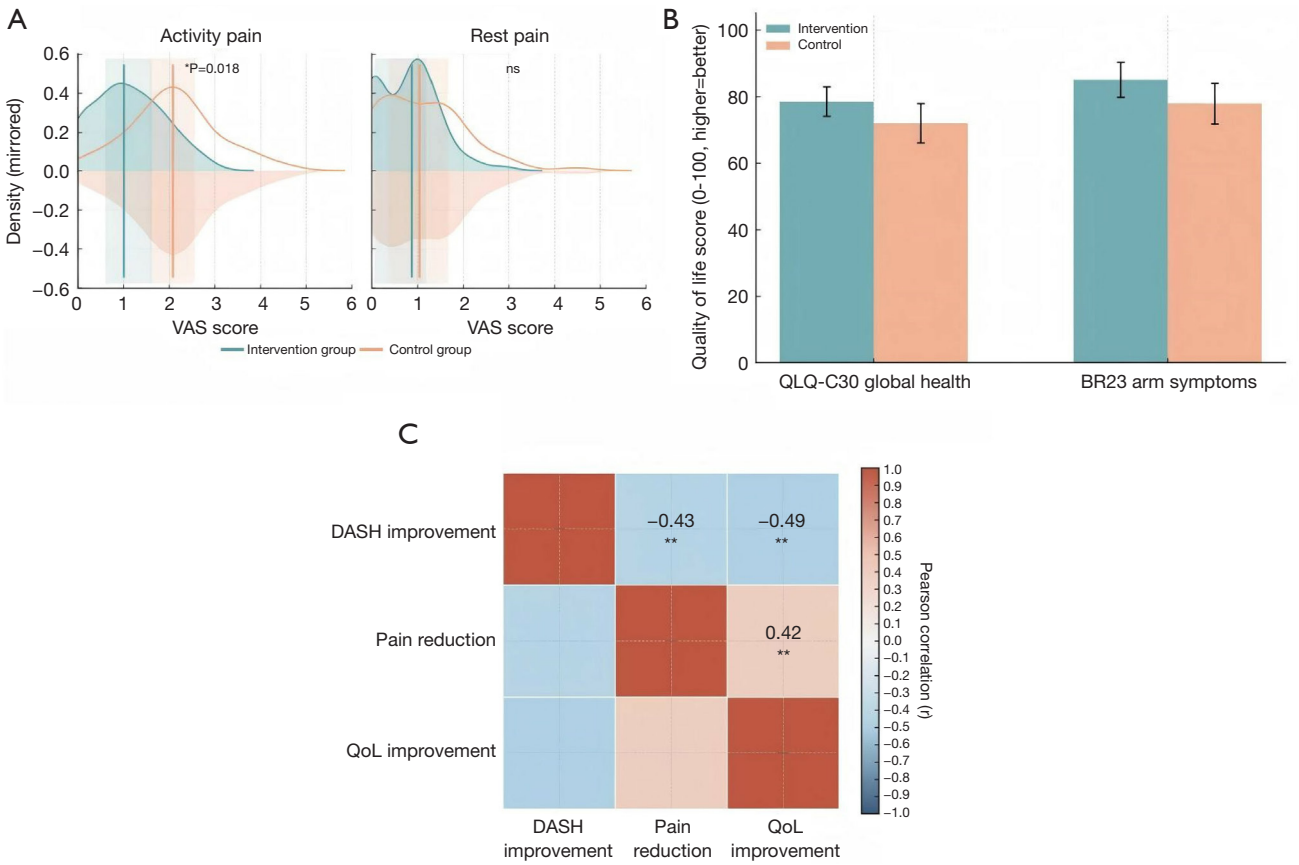

Figure 4 Impact of early exercise intervention on postoperative pain, quality of life, and their multidimensional correlations. (A) Displays the distribution of VAS scores for pain during activity (left) and pain at rest (right) at 12 months postoperatively in the Intervention group *vs*. the Control group. Bilateral kernel density curves are used to show the overall distribution of pain intensity and the median position, providing a visual comparison of the differences between the two groups in controlling functional activity-related pain and rest pain. (B) Compares quality of life scores between the two patient groups, including the "Global Health Status" dimension of the EORTC QLQ-C30 questionnaire and the "Arm Symptoms" dimension of the BR23 module, reflecting the impact of early exercise intervention on overall health perception and symptom relief in the affected limb. (C) Presents the Pearson correlation matrix among improvement in upper limb function (decrease in DASH score), pain reduction (decrease in VAS score), and enhancement of quality of life (increase in QoL score). Numbers within the squares represent correlation coefficients; color intensity represents the strength of the correlation, and shading indicates statistical significance. This figure is used to reveal the multidimensional relationships among functional recovery, pain control, and quality of life. ns, not significant; *, P<0.05; **, P<0.01. DASH, Disabilities of the Arm Shoulder and Hand; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; QoL, quality of life; VAS, Visual Analog Scale.

dissected. Among patients with ≥15 lymph nodes dissected, the BCRL risk was significantly lower in the intervention group compared to the control group (OR =0.40, 95% CI: 0.16–0.98; *Table 3*). This suggests that the benefits of systematic rehabilitation may be more pronounced when the axillary surgical scope is larger and lymphatic injury is more extensive. Interaction tests further revealed consistent effect directions across all subgroups, with no significant heterogeneity observed (all interaction P values >0.2). This indicates a stable protective effect of the intervention across different clinical subpopulations.

To verify the robustness of the primary analysis results, multiple sensitivity analyses were conducted (*Table 3*). In the PP analysis, which included only patients with intervention adherence ≥80%, the association between the intervention and reduced BCRL risk became more pronounced (adjusted OR =0.38, 95% CI: 0.17–0.86), consistent in direction with the primary analysis. The ITT analysis and models after

Table 3 Subgroup and sensitivity analyses of the association between early exercise intervention and BCRL risk

Analysis type	Subgroup or model	Adjusted effect size (95% CI)	P value/ interaction	Interpretation
Subgroup analyses	Radiotherapy (+)	OR =0.36 (0.15–0.87)	0.02	64% risk reduction in patients with post-radiation lymphatic impairment
	BMI ≥25 kg/m^2	OR =0.35 (0.14–0.88)	0.03	Significant protective effect in overweight patients prone to lymphedema
	≥15 lymph nodes dissected	OR =0.40 (0.16–0.98)	0.044	Greater benefit in extensive axillary dissection subgroup
	Interaction across subgroups	—	All P>0.20	No significant heterogeneity detected; consistent direction of effect
Sensitivity analyses	Per-protocol (adherence ≥80%)	OR =0.38 (0.17–0.86)	0.02	Stronger effect among highly adherent participants
	Intention-to-treat (all participants)	OR =0.44 (0.21–0.91)	0.03	Effect consistent with main analysis after imputation for missing data
	Cox model (time to first BCRL event)	HR = 0.50 (0.26–0.95)	0.03	Intervention delayed onset of lymphedema during 12-month follow-up
	Propensity score-weighted model (IPTW)	OR =0.43 (0.20–0.91); HR =0.49 (0.25–0.95)	0.03/0.031	Results remained robust after adjustment for treatment allocation bias
Safety assessment	Shoulder pain (mild, transient)	8.6% (self-limiting within 1 week)	–	No serious exercise-related adverse events reported
	Severe complications (infection, thrombosis, wound dehiscence)	None observed	–	Intervention deemed safe and well-tolerated

All ORs and HRs were adjusted for age, BMI, number of lymph nodes dissected, radiotherapy, and chemotherapy. Propensity scores were estimated using a logistic model with the same covariates and applied via stabilized IPTW. No significant effect modification was detected across subgroups (all interaction P>0.2). BCRL, breast-cancer-related lymphedema; BMI, body mass index; CI, confidence interval; HR, hazard ratio; IPTW, inverse probability of treatment weights; OR, odds ratio.

multiple imputation also showed similar trends (OR =0.44, 95% CI: 0.21–0.91, *Table 3*), indicating that the limited missing data and variations in adherence had minimal impact on the conclusions. Furthermore, sensitivity checks using a Cox model with "time to first BCRL occurrence" as the endpoint yielded stable results (HR =0.50, 95% CI: 0.26–0.95), supporting the sustained protective effect of the intervention against edema risk.

Regarding safety, no serious exercise-related adverse events occurred in the intervention group. The incidence of mild shoulder pain was 8.6%, and all cases resolved spontaneously within one week following short-term rest or adjustment of training intensity, without impacting the subsequent rehabilitation process. No serious complications such as infection, thrombosis, or wound dehiscence were observed. Integrating the results from all analyses, the main conclusions of this study remained consistent in direction across different populations, analytical methods, and statistical assumptions, indicating that the early exercise intervention has a robust and widely applicable clinical effect in reducing the incidence of BCRL and delaying its onset.

Overall, across the 12-month follow-up, patients in the early exercise intervention group had a lower incidence of BCRL, smaller limb volume increases, less frequent moderate-to-severe edema, greater improvements in shoulder ROM and upper limb function, lower activity-related pain, and better quality-of-life scores than patients receiving usual care, with consistent effect directions across prespecified subgroups and sensitivity analyses.

Discussion

BCRL is a common complication following breast cancer surgery, characterized by swelling, pain, and restricted joint mobility in the ipsilateral limb. It can be accompanied by recurrent infections, skin fibrosis, and chronic pain, significantly impairing patients' daily function and psychosocial QoL (27). As survival rates for breast cancer patients improve, the management of long-term complications becomes increasingly crucial. BCRL warrants

particular attention due to its often persistent and refractory nature once established. Effective rehabilitation concepts emphasize early symptom monitoring and intervention. International research indicates that preventive strategies, such as risk assessment, patient education, and early postoperative exercise, are important for alleviating lymphedema symptoms and improving patient QoL (28). In this single-center retrospective cohort, early postoperative, therapist-guided exercise after ALND was associated with a lower risk and milder clinical presentation of BCRL, better upper limb function, less activity-related pain, and improved QoL over 12 months.

Our results indicate that early exercise intervention was associated with a lower 1-year incidence of BCRL compared with usual care, with an effect size broadly comparable to that reported in a recent meta-analysis of exercise-based interventions (29). However, our findings contrast with several randomized trials and prospective surveillance studies in which early or progressive exercise did not significantly reduce BCRL incidence compared with usual care (15,19,30). Several methodological differences may help explain these discrepancies. First, our cohort consisted exclusively of women undergoing ALND, representing a higher-risk population than the mixed-surgery samples (including large proportions of sentinel lymph node biopsy or limited nodal surgery) enrolled in some randomized trials (15,31). In this context, the 33.3% 1-year incidence observed in our control group lies toward the upper end of the incidence range reported in meta-analyses (8–20%) (32,33), potentially providing greater scope to detect a risk reduction. Second, the key strength of our program lay in its supervised, therapist-guided, and progressive multi-component design, which explicitly targeted adherence. This stands in contrast to trials of unsupervised home-based interventions, which have often shown neutral results—a discrepancy likely linked to adherence challenges. For instance, adherence was only about 50% in the CALGB 70305 trial (19), which combined exercise with compression garments. Third, our study defined BCRL using circumferential limb volume measurement and ISL criteria. This differs from other studies, which have employed symptom-based criteria, bioimpedance ratios, or different volume thresholds. Such heterogeneity in diagnostic definitions and follow-up intervals (typically 6–18 months) may partly explain the discrepant incidence rates and effect sizes reported across the literature (20,32,33). In summary, while our data support a potential protective effect of early exercise in high-risk ALND populations, several limitations must be considered. These include the retrospective, non-randomized, single-center design and the potential for selection bias. Therefore, our findings should be interpreted alongside neutral or conflicting reports, and viewed as complementary rather than definitive evidence.

In addition to reducing overall incidence, time-to-event analyses indicated a delay in BCRL onset within the early exercise group, reflected by higher edema-free survival and a lower hazard of diagnosis within 12 months. Several mechanisms may explain this observation. First, early mobilization, self-administered manual lymph drainage, and PRT may enhance lymphatic transport and soft-tissue compliance, thereby postponing the point at which limb volume exceeds diagnostic thresholds. Alternatively, more frequent contact with rehabilitation therapists could have standardized measurement procedures, while milder symptoms in the intervention group might slow the progression from subclinical to clinically apparent edema. As limb volume was assessed only at discrete intervals (3, 6, and 12 months) without continuous bioimpedance or RVC-based surveillance, we cannot fully distinguish between a true biological delay in onset and detection-related factors. This finding should therefore be interpreted with caution.

Regarding severity, patients who developed BCRL in the intervention group presented with milder, predominantly reversible ISL stages compared to controls. This trend suggests that early, standardized exercise may help prevent progression from reversible to irreversible fibrotic stages. International literature indicates that BCRL often follows a progressively worsening course without early intervention. For example, one cohort study of patients undergoing mastectomy and radiotherapy (median follow-up: 35 months) found that about 74% of BCRL cases had advanced to ISL stage II–III (34). In contrast, most BCRL cases in our intervention group remained at stage I, aligning with the concept that timely intervention curbs progression. Supporting evidence also comes from prospective surveillance models, where immediate intervention upon detection of subclinical swelling resulted in only about 4% of high-risk patients progressing to chronic lymphedema (35). Mechanistically, regular active exercise may enhance the shoulder girdle's "muscle pump" action, reducing interstitial fluid accumulation and delaying fibroadipose transformation. This framework could also explain the more pronounced risk reductions observed in subgroups with radiotherapy or higher BMI, where improved lymphatic transport might partially offset treatment- or obesity-related damage—although these pathways were not directly measured.

Improvements in upper limb function (DASH score) and shoulder ROM represent another key finding. Although both groups improved over time, recovery was faster and greater in the intervention group, with clinically relevant between-group differences in DASH scores and shoulder flexion/abduction ROM at 12 months. These effect sizes are comparable to those reported in recent randomized trials of early or progressive resistance exercise. For instance, Stuiver *et al.* (36) observed significantly accelerated shoulder function recovery with personalized resistance exercise initiated immediately after surgery. Similarly, a meta-analysis of 20 RCTs concluded that exercise significantly improved shoulder ROM and upper limb function, with the greatest benefits seen when interventions started within two weeks postoperatively (37). Our findings thus reinforce, in a high-risk ALND cohort, the functional advantages demonstrated in randomized settings and extend them to a broader set of outcomes (DASH, ROM, pain, and QoL). However, the non-randomized design means residual confounding (e.g., by patient motivation or baseline health) cannot be excluded and may partly inflate the apparent benefit. Proposed mechanisms from prior research include the prevention of disuse atrophy, reduction of joint capsule contracture, and maintenance of soft tissue elasticity, although these were not directly evaluated in our study.

Significant improvements in pain and QoL further reflect the comprehensive benefits of early rehabilitation. Pain scores decreased in both groups, but the reduction was greater in the intervention group, particularly for activity-related pain at 12 months. In contrast, between-group differences in resting pain were not significant (P=0.11), suggesting that postoperative resting pain may be influenced more by factors such as nerve injury and less amenable to short-term exercise alone. Reductions in activity-related pain may stem from improved soft tissue pliability and decreased stretch pain related to joint stiffness—a mechanism consistent with prior rehabilitation literature, though not directly measured here (38). Regarding QoL, the intervention group showed better postoperative scores on both the global health status domain of the EORTC QLQ-C30 and the arm symptom domain of the QLQ-BR23, indicating fewer upper limb symptoms and better overall health perception. Positive, though non-significant, trends in social function and self-image were also observed, potentially linked to regained confidence and reduced limb-use avoidance following functional improvement (39). Taken together, the observed multidimensional benefits in function, pain, and QoL may contribute to a virtuous cycle of rehabilitation—a conceptual model generated from, but not formally tested in, this study. Our findings align with recent systematic reviews indicating that exercise can meaningfully reduce pain and improve QoL in postoperative breast cancer patients (29). While the absolute differences may be modest, their statistical and clinical significance underscores the substantive impact of early exercise on both subjective experience and objective function.

As a single-center observational study, this work has several important limitations. The lack of randomization introduces potential selection bias and confounding, meaning the relatively large risk reduction observed may reflect center-specific practices or unmeasured factors rather than purely causal effects. Therefore, these associations should be regarded as hypothesis-generating. Generalizability may be limited by the exclusion of patients with poor wound healing, and the use of cross-sectional limb volume differences (rather than preoperative-postoperative relative volume change, RVC) may have underestimated subtle, individual-level changes. The relatively small sample size and 12-month follow-up period further limit precision and the ability to assess long-term risk, as BCRL can develop beyond 1 year. Adherence was based on self-report, which is subject to bias; the observed dose-response relationship may thus reflect underlying patient factors rather than a direct causal effect. Finally, the absence of objective lymphatic function assessments (e.g., bioimpedance, lymphoscintigraphy) means our mechanistic interpretations remain speculative. Future research should prioritize multicenter, prospective designs with long-term follow-up, objective adherence monitoring, and direct physiological measurements to validate these findings, optimize exercise prescriptions, and clarify underlying biological pathways.

Conclusions

In this single-center retrospective cohort, the early implementation of a systematic, evidence-based exercise program following breast cancer ALND was associated with a reduced risk and milder clinical severity of BCRL over 12 months, with no clear safety concerns. Mechanistically—drawing on prior studies—this benefit is hypothesized to stem from activation of the shoulder and upper limb muscle pump, enhanced venous/lymphatic return, and maintenance of soft tissue compliance, potentially preventing fluid retention and fibrosis progression. It must be emphasized that these pathways were not directly assessed in our study. Compared to usual care, the intervention group

exhibited not only lower BCRL incidence and severity but also superior upper limb mobility and function, reduced activity-related pain, and higher QoL. However, given the non-randomized design, these associations warrant cautious interpretation. Exploratory analyses suggested greater relative benefit in higher-risk subgroups (e.g., those receiving radiotherapy, with higher BMI, or more extensive dissection), and no serious exercise-related adverse events were observed, supporting the protocol's feasibility in these populations. In conclusion, early, structured, and individualized exercise appears to be a beneficial component of post-ALND rehabilitation. Nevertheless, confirmation through multicenter RCTs with longer follow-up is essential to validate these findings, optimize exercise prescriptions, and elucidate the underlying mechanisms and long-term effectiveness across diverse risk groups.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://gs.amegroups.com/article/view/10.21037/gs-2025-1-597/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-2025-1-597/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study protocol was reviewed and approved by the Ethics Committee of West China Hospital (Ethics approval No. 2019 Audit 512). Given the retrospective analysis of de-identified data, the requirement for written informed consent was waived by the Ethics Committee of West China Hospital.

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