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Effect of Enhanced Recovery After Surgery Protocol Combined with Preoperative Upper Limb Exercise on Length of Stay Following Modified Radical Mastectomy: A Randomized Controlled Trial

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ABSTRACT

Background: Modified radical mastectomy (MRM) is the primary surgical treatment involving the pectoralis muscles for early-stage breast cancer, the most prevalent cancer among women. The Enhanced Recovery After Surgery (ERAS) protocol may reduce the side effects associated with this intervention. Additionally, preoperative upper limb exercise has been shown to reduce postoperative complications. This study evaluates whether combining the ERAS protocol with upper limb exercise (ERAS-UE) reduces hospital stay for patients undergoing MRM.

Methods: This experimental study was a single-blinded randomized controlled trial design. Twenty-four patients who were scheduled for MRM at Prof. Dr. dr. R. D. Kandou General Hospital, Manado, and met the inclusion criteria were enrolled. Participants were randomly assigned either to the intervention group or the control group using a simple randomization sequence. The intervention group received the ERAS-UE, which included aerobic, strengthening, and stretching exercises for 4 weeks prior to surgery. The control group received standard care. The number of nights spent in the hospital from the end of surgery to being discharged home was compared between the two groups.

Results: Twenty-four participants were enrolled. The ERAS-UE group demonstrated a significantly shorter length of hospital stay compared to the control group ($P < .05$).

Conclusion: Implementation of the ERAS protocol combined with upper limb exercise significantly reduced the length of hospital stay in patients after MRM.

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INTRODUCTION

Breast cancer is a disease in which abnormal breast cells grow uncontrollably and form tumors.[1] Breast cancer represents a significant global health challenge and is the most frequently diagnosed cancer worldwide. In 2022, approximately 2.3 million new cases were reported according to the Global Burden of Cancer (GLOBOCAN), making it the leading cause of cancer-related mortality among women.[2] Surgical removal of breast tumors can be performed using mastectomy techniques, with or without axillary lymph node dissection for tumor tissue that has spread to the axillary lymph nodes, commonly referred to as modified radical mastectomy (MRM), and may be performed with or without breast reconstruction.[3,4] MRM is one of the most commonly performed surgical procedures for breast cancer.[5]

Applying Enhanced Recovery After Surgery (ERAS) principles to breast cancer patients facilitates safe outpatient management after mastectomy without increasing postoperative morbidity.[6] Upper limb exercise, which includes shoulder range-of-motion exercises, stretching, and strengthening exercises performed before breast cancer surgery, may help restore shoulder joint mobility.[7] These exercises are implemented concurrently with the ERAS protocol. According to an article by Donna Wilson, preoperative upper extremity and stretching exercises are effective in improving shoulder range of motion and reducing chest tightness and pain, thereby decreasing postoperative side effects and improving quality of life.[8]

Some studies in Indonesia have shown that the

mean length of stay for MRM remains variable, ranging from 4.6 to 7.5 days.[9,10] Several factors significantly influence the length of stay after MRM, including patient demographics, comorbidities, tumor characteristics and management, surgical interventions, surgical outcomes, and postoperative complications. ERAS has been shown to be beneficial in surgical care and can be applied to various types of breast surgery with promising outcomes.[11] This study aims to analyze the effect of the ERAS protocol combined with upper limb exercise (ERAS-UE) on length of stay after MRM and to compare length of stay between ERAS and non-ERAS care following MRM.

METHODS

Study design and setting

This study was a randomized controlled trial comparing the ERAS-UE group and the control group in patients scheduled for MRM surgery within 1 month. The study was conducted at Prof. Dr. dr. R. D. Kandou General Hospital, Manado, from October 2024 to March 2025. The study procedures were conducted in accordance with the Declaration of Helsinki's ethical standards. The first visit was used to inform the participants about the study and to sign the informed consent. Individual de-identified participant data, the data dictionary, study protocol, and statistical analysis code are available from the corresponding author upon reasonable request. The Health Research Ethics Committee of Prof. Dr. dr. R. D. Kandou General Hospital approved this study and it was registered at ClinicalTrials.gov (NCT07574372).

Participants and eligibility

Twenty-four patients who underwent MRM at Prof. Dr. dr. R. D. Kandou General Hospital, Manado, were randomized using a computer-generated simple randomization sequence generated by the Research Randomizer program (randomizer.org) with a 1:1 allocation ratio. The randomization sequence was provided by the physician in charge in the outpatient department, who was not involved in intervention delivery. Participants scheduled for MRM were randomly assigned to either the ERAS-UE group or the control group. Both the evaluator and the data analyst were blinded to group allocation.

The inclusion criteria were as follows: (1) female patients aged 30 to 65 years; (2) histopathologically confirmed breast cancer and scheduled for a first-time MRM; (3) scheduled to receive neoadjuvant chemotherapy (NAC); (4) hemodynamically stable, defined as systolic blood pressure <160 mmHg, diastolic blood pressure <100 mmHg, and heart rate 60 to 120 bpm; (5) Mini-Mental State Examination (MMSE) score >25; (6) controlled comorbid conditions; (7) corrected nutritional status; (8) no balance or coordination disorders; (9) normal or corrected vision; (10) normal hearing on the whisper test; and (11) willingness to participate until study completion and to provide written informed consent.

The exclusion criteria were: (1) presence of distant metastasis; (2) presence of lymphedema; (3) limited joint range of motion; and (4) cardiovascular conditions contraindicated for physical exercise per the American College of Sports Medicine (ACSM) guidelines.

Participants were withdrawn from the study if they missed 2 consecutive exercise sessions during the study period, chose to discontinue participation, failed to comply with the ERAS protocol, and experienced hemodynamic instability or required intensive care unit (ICU) admission after surgery.

Intervention

The intervention group (ERAS-UE) received preoperative oral nutrition for carbohydrate loading consisting of 50 g the night before surgery and 25 g 2 hours before surgery, exercise interventions consisting of aerobic, strengthening, and stretching exercises from the Department of Physical Medicine and Rehabilitation preoperatively, and a pectoralis nerve block II technique guided by ultrasonography (USG) and performed by an anesthesiologist. Aerobic exercise included walking for 30 minutes at moderate intensity (Borg scale 12 to 14) 2 times per week and cycling 3 times per week for 30 minutes, with an intensity of 40% to 60% of heart rate reserve (HRR), 64% to 76% of maximum heart rate (HRmax), or a rating of perceived exertion (RPE) of 12 to 14. Cycling was performed at the rehabilitation outpatient clinic 3 times per week, whereas home-based walking was performed 2 times per week and monitored using the Strava application. Adherence was defined as the percentage of completed prescribed sessions out of the total prescribed and was calculated separately for supervised center-based and home-based sessions. Lower limb strengthening exercises were performed 3 times per week at an intensity of 60% to 80% of 1-repetition maximum (1RM), consisting of 3 sets of 10 repetitions with 60 seconds of rest between sets, using a pulley machine. Upper limb exercises included shoulder range-of-motion exercises, shoulder stretching (3 times per week, 10-second hold, static stretching), and upper extremity strengthening exercises (3 times per week at an intensity of 60% to 80% of 1RM, 3 sets of 10 repetitions with 60 seconds of rest between sets), including bench press and cable front raise exercises. All exercise interventions were performed for 4 consecutive weeks under the supervision of the authors. Participants received standardized instructions on exercise intensity, technique, symptoms that require exercise termination, and the use of RPE. During supervised sessions, exercise was monitored using heart rate and RPE and the completion was recorded in an attendance log. If any side effect occurred and met the termination criteria, the exercise was stopped and the session was skipped. The preoperative exercise intervention was conducted after neoadjuvant chemotherapy and before surgery. The interval between neoadjuvant chemotherapy and planned surgery ranged from 1 to 4 months. The control group received neither preoperative exercise nor carbohydrate loading, and

underwent surgery under general anesthesia.

Mobilization, ambulation, shoulder range-of-motion exercises, and massage interventions were initiated within the first 24 hours postoperatively as part of standard care for both groups. The time interval from completion of surgery to the first ambulation was recorded, and the ambulation distance was measured on postoperative day 1.

Outcome measures

The primary outcome was the postoperative length of hospital stay, which was defined as the number of nights spent in the hospital from the end of surgery to being discharged home. Postoperative length of stay was selected as the primary outcome because it is an objective, routinely recorded, and clinically relevant indicator commonly used in studies evaluating ERAS and other perioperative recovery pathways. Length of stay is also relevant to hospital resource utilization and may reflect the time required to achieve clinical stability, adequate pain control, early mobilization, and discharge readiness.[11] Length-of-stay data were extracted from hospital medical records by an investigator who was not involved in intervention delivery and was unaware of group allocation at the time of outcome assessment.

Patients were eligible for discharge if they demonstrated: (1) hemodynamic stability; (2) absence of active bleeding; (3) no postoperative complications requiring continued inpatient care; (4) adequate pain control (resting pain score 0 to 3); (5) functional recovery, defined as full passive and at least minimally limited active shoulder range of motion; (6) a properly functioning surgical drain; and (7) independent mobilization and ambulation at JH-HLM Level 8, as assessed by physicians. The same criteria were applied to both groups.

Statistical analysis

The sample size was estimated using a formula for comparing mean differences between two independent groups. Because the intervention included a structured preoperative exercise program, functional capacity data were used to derive the standardized effect size, as functional capacity was considered a relevant physiological parameter responsive to exercise. However, postoperative length of stay remained the primary outcome. Based on previous studies of functional capacity assessed by the 6-minute walk test, a standard deviation of 58 m and a minimal clinically important difference of 66.5 m were used. Accordingly, the projected Cohen's d effect size was set at 1.16. This sample-size estimation was indirect and did not establish statistical power specifically for postoperative length of stay; therefore, findings should be interpreted as preliminary.[12,13] The 2-sided significance level was fixed at 0.05, and statistical power was set at 80% (β = .20). The primary analysis was conducted according to the intention-to-treat principle. All randomized participants were included in the analysis according to their originally assigned groups. Data analysis was performed using SPSS software version 29. Univariate analyses were conducted to obtain frequency tables, means, and standard deviations. Data normality was assessed using the Shapiro-Wilk test. Analysis was performed using the independent t test for normally distributed variables, whereas non-normally distributed variables were tested using the Mann-Whitney U test. Statistical significance was defined as a P value < .05.

RESULTS

Participant flow and baseline characteristics

Twenty-four women who were scheduled for MRM surgery were recruited (Figure 1). They were randomly assigned to the ERAS-UE group (n = 12) and the control group (n = 12). No participant discontinued the intervention or was lost to follow-up. In the ERAS-UE group, adherence to supervised center-based exercise sessions was 91.67% (91.67% to 100%), while adherence to home-based walking sessions monitored using the Strava application was 87.5% (87.5% to 100%). In the ERAS-UE group, the participants' ages ranged from 39 to 63 years, and ages ranged from 35 to 60 years in the control group. Baseline demographic and clinical characteristics are presented descriptively in Table 1.

Based on the Mann-Whitney U test results as shown in Table 2, the distribution of length of stay differed between the ERAS and non-ERAS groups. The non-ERAS group (n = 12) had a higher mean rank of 15.21 with a total rank sum of 182.50, whereas the ERAS group (n = 12) showed a lower mean rank of 9.79 with a total rank sum of 117.50, indicating shorter hospitalization in the ERAS group.

As shown in Table 3, median postoperative length of stay was 3 days in the ERAS-UE group and 3 days in the control group. Although the median was the same in both groups, the distribution of length-of-stay values was lower in the ERAS-UE group (P = .02). The mean length of stay was 2.75 days for the ERAS-UE group and 3.67 days for the control group. Graphically, the distribution for both interventions is illustrated in Figure 2, which shows that the length of stay in the ERAS group was lower than that in the non-ERAS group.

DISCUSSION

Although MRM is a widely used surgical technique and is considered the treatment of choice for breast cancer, a high incidence of complications may occur, such as infection, restricted shoulder mobility, chronic pain, psychological trauma, and arm lymphedema, which can prolong hospitalization.[14] Notably, shoulder dysfunction affects up to 67% of patients and is more prevalent than after breast-conserving therapy.[15,16] ERAS protocols have been shown to expedite postoperative recovery, reduce opioid requirements, and shorten hospital stays,[17,18] and when combined with early rehabilitation exercises following MRM, they further improve shoulder mobility and functional outcomes without increasing complication rates.[19] Furthermore, prehabilitation has evolved from a

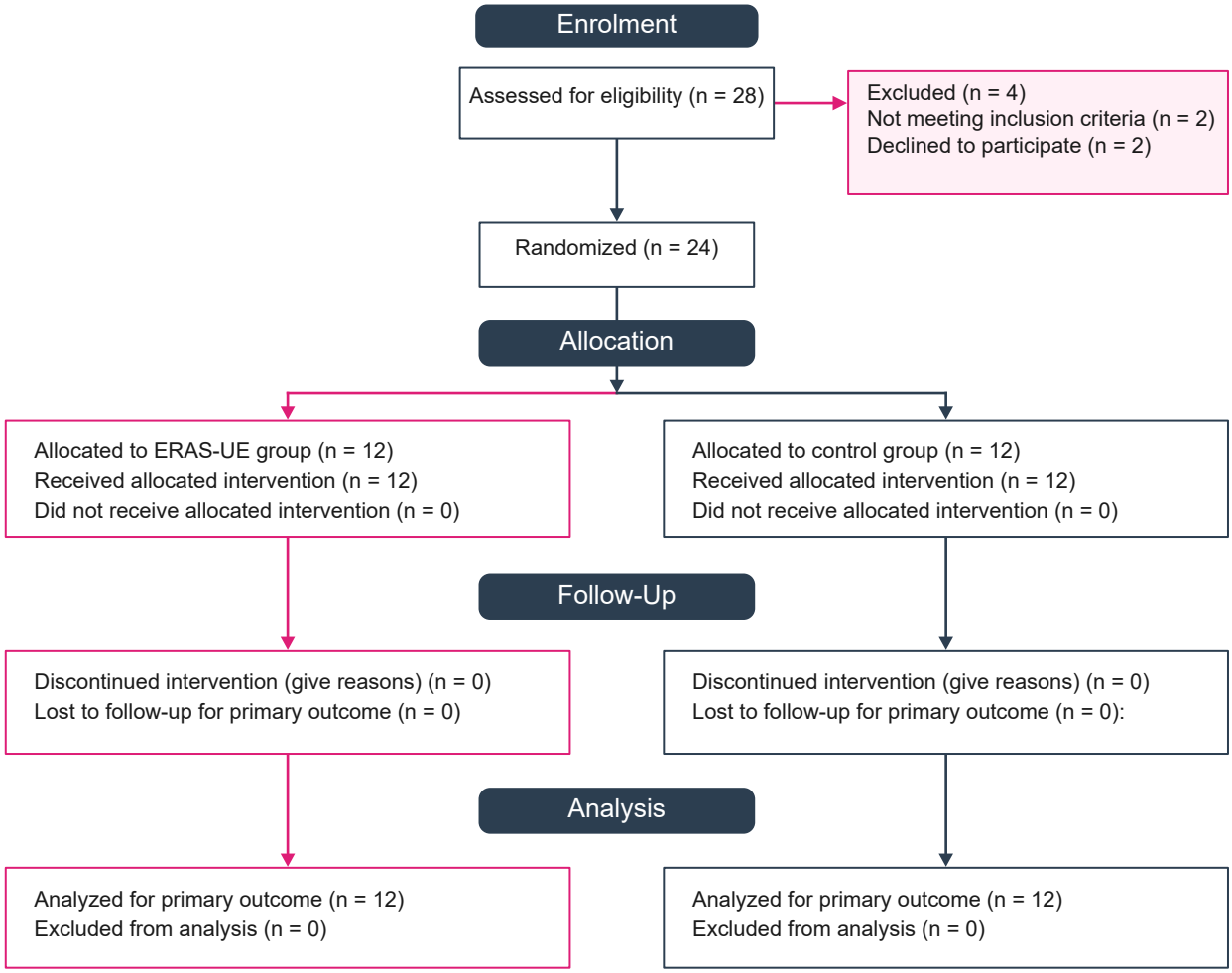


Figure 1. Participant flow through the randomized clinical trial
Twenty-four participants were randomized to the ERAS-UE and control groups (n = 12 each); all completed follow-up and were analyzed. ERAS-UE indicates enhanced recovery after surgery combined with preoperative upper limb exercise.

Table 1. Baseline demographic and clinical characteristics by study group

	ERAS-UE group (n = 12)	Control group (n = 12)
Age, y	51.33 ± 7.31	50.42 ± 8.66
Body mass index, kg/m^2[a]	24.23 ± 1.69	22.8 ± 2.22
Staging, n (%)		
1	1 (8.3)	0 (0)
2	4 (33.3)	2 (16.7)
3	7 (58.3)	10 (83.3)
6-minute walk distance, m[b]	373.5 (301-391)	305 (292-376)
Chemotherapy times, n (%)		
1	2 (16.7)	4 (33.3)
2	8 (66.7)	6 (50)
3	2 (16.7)	2 (16.7)

Values are presented as mean ± standard deviation, median (interquartile range), or n (%), as appropriate.
Abbreviation: ERAS-UE, enhanced recovery after surgery combined with preoperative upper limb exercise.
[a] Data are presented as mean ± standard deviation.
[b] Data are presented as median (first to third quartile).

purely physical approach into a multidisciplinary preoperative intervention. It not only improves strength and endurance but also reduces postoperative complications and the incidence of lymphedema, while enhancing immune function and attenuating inflammation; evidence suggests that implementing prehabilitation for 1 to 8 weeks prior to surgery,[20,21] with our study selecting a 4-week duration for optimal compliance, can significantly contribute to improved patient recovery.

Table 2. Mean ranks of postoperative length of stay by study group

	Intervention	n	Mean rank	Sum of ranks
Length of stay	**Control**	12	15.21	182.50
	ERAS	12	9.79	117.50
	Total	24		

Mean ranks and sums of ranks are from the Mann-Whitney U test. ERAS indicates enhanced recovery after surgery combined with preoperative upper limb exercise.

Table 3. Postoperative length of stay by study group

Outcome	ERAS-UE group (n = 12)	Control group (n = 12)	*P*[a]
Length of stay, d	3 (2-3)	3 (3-4)	.02

Values are presented as median (first to third quartile).
Abbreviation: ERAS-UE, enhanced recovery after surgery combined with preoperative upper limb exercise.
[a] Mann-Whitney U test.

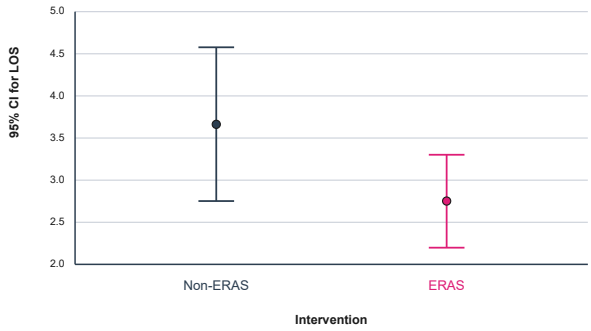


Figure 2. Postoperative length of stay by study group Points show mean length of stay (LOS), in days; error bars show 95% confidence intervals. ERAS indicates enhanced recovery after surgery plus preoperative upper limb exercise; non-ERAS, control.

The study used 2 primary implementation strategies: center-based and home-based approaches, which may involve aerobic training, resistance training, or a combination of both. Aerobic training often includes high-intensity protocols within these strategies. Center-based approaches offer increased supervision and facilitate adherence to session goals. Conversely, home-based strategies are generally more cost-effective and flexible for patients' schedules. Notably, patient preferences appear to be evenly divided between these options. To facilitate a clear assessment of effectiveness, our study therefore employed a center-based therapy protocol, supplemented by walking data collected via a mobile application, positioning this hybrid approach as a viable alternative.[22]

Our study demonstrated a reduction in the length of stay, consistent with positive outcomes reported in previous research, reporting that a 4-week preoperative exercise program for breast cancer patients improved quality of life, range of motion, strength, and reduced lymphedema. The exercise types included resistance training, aerobic exercise, and stretching.[23] Additional studies have also shown that preoperative exercise enhances physical function and functional capacity.[24] Implementing a 4-week preoperative exercise program may increase physiological reserve, thereby improving the body's ability to manage the physical demands of surgery and supporting postoperative recovery.[25] Furthermore, preoperative stretching of the shoulder muscles has been shown to be safe and effective in reducing postoperative pain and functional limitations in patients undergoing mastectomy.[26]

The results of this study showed that the mean difference in length of stay between the ERAS-UE and control groups was 1 day. This difference was statistically significant (P = .02, Mann-Whitney U test). The length of stay ranged from 2 to 5 days for the ERAS cohort, compared to 2 to 7 days for the non-ERAS cohort. Despite sharing the same median value (3 days), the two groups showed distinct distribution patterns; the ERAS group had a markedly higher concentration of length of stay values at the lower end of the spectrum (2 to 3 days), while the non-ERAS group demonstrated a broader distribution skewed toward longer durations. In the control group, conventional care may involve later initiation of mobilization within the first 24 hours after surgery, higher opioid doses, dietary restrictions for several days after surgery, and prolonged use of surgical drains. These practices may delay physiological recovery, increase the risk of complications, and prolong length of stay.[27] Based on evidence from the literature, Bonde *et al.* reported that implementing ERAS protocols in breast surgery reduced mean length of stay by approximately 1 day compared with conventional methods, without increasing complication risk. ERAS focuses on coordinated multidisciplinary care and procedure-specific elements to accelerate patient recovery and reduce complications, including shorter operative time, nutritional optimization, fluid management, effective pain control, and early mobilization. ERAS has consistently demonstrated reductions in length of stay across various surgical procedures, including breast surgery. Studies have shown that ERAS patients may be discharged earlier, even by postoperative day 3 following breast reconstruction with flap procedures.[28]

CONCLUSIONS

The findings of this study suggest that implementation of an ERAS protocol combined with preoperative upper limb exercise may contribute to a reduction in postoperative length of stay following MRM. However, because this study was conducted at a single

center with a small sample size, the results should be considered as preliminary. Further adequately powered multi-center trials are necessary to validate these findings and evaluate their impact on additional clinical outcomes.

ETHICAL CONSIDERATIONS

The study protocol was approved by the Health Research Ethics Committee of Prof. Dr. dr. R. D. Kandou General Hospital (200/EC/KEPK-KANDOU/X/2024), and it was registered at ClinicalTrials.gov (NCT07574372). All procedures were conducted in accordance with the Declaration of Helsinki and written informed consent was obtained from all participants.

DATA AVAILABILITY

The data generated and analyzed during the current study are available from the corresponding author upon reasonable request.

CONFLICTS OF INTEREST

None.

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AI DISCLOSURE

The authors declare that no artificial intelligence (AI) tools or services were utilized in the preparation of this research or text.

AUTHOR CONTRIBUTIONS

M: Conceptualization, Methodology, Investigation, Data curation, Writing – original draft. DS: Investigation, Resources, Supervision, Writing – review & editing. TK: Investigation, Project administration, Data curation, Writing – review & editing. KK: Investigation, Data curation, Validation, Writing – review & editing. RGS: Formal analysis, Data curation, Validation, Writing – review & editing.

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