

## Review report

### Final title: Combined manual lymphatic drainage and exercise for lymphedema in breast cancer survivors: A randomised controlled trial

Title at submission: Combined manual lymphatic drainage (MLD) and exercise versus exercise alone for lymphedema in breast cancer survivors: A randomized controlled trial

#### Round 1



Reviewer C: SM Mazharul Islam, ORCID: [0009-0006-1902-1452](https://orcid.org/0009-0006-1902-1452)

#### Overview

The study investigates the effectiveness of combining manual lymphatic drainage (MLD) with exercise versus exercise alone for treating lymphedema in 42 breast cancer survivors in Bangladesh. Participants were split into two groups: one receiving only supervised exercise (Group A) and the other receiving MLD plus the same exercises (Group B) for six weeks. The results showed that the combined therapy group (Group B) experienced significantly greater reductions in limb swelling and a more substantial improvement in quality of life, as measured by limb circumference and the B-LLIS v2 scale. The conclusion supports integrating MLD into standard rehabilitation for better patient outcomes.

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#### Publication history

Received: 5 Oct 2025  
Accepted: 28 Dec 2025  
Published online: 30 Dec 2025

#### Responsible editor

Rijwan Bhuiyan  
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#### Reviewers

C: S. M. Mazharul Islam  
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D: Anonymous

#### Keywords

manual lymph drainage,  
lymphedema, breast cancer,  
exercise

#### Funding

None

#### Ethical approval

Approved by IRB of Khwaja Yunus  
Ali Medical College (No. KYAMC/  
IERB/2022/04,  
Dated 1 Jan 2022).

#### Trial registration number

Not available

#### 1. Comment Major redundancy between text and tables/figures in the results section.

Have redundancy between text and tables. Author should reduce the text from results section and refer appropriate table.

**Response** We revised the text from the results section as advised (Lines 200–222).

#### 2. Comment Pertinence of the discussion section whether it justify the main message of the manuscript without repeating the results.

Discussion is poorly written. In-depth revision based on objectives of the study with proper justification is required. Author needs to clarify why other study findings is similar or dissimilar to their findings.

**Response** We have totally rewritten the discussion section as advised (Lines 225–266).

#### 3. Comment Whether strength(s) and limitation(s) are well described.

The document does not explicitly describe the study's strengths. However, its limitations are acknowledged in the conclusion.

**Response** We have added strength and limitation in separate paragraphs under discussion section (Lines 255–266).

#### Reviewer D: Anonymous

#### Overview

This manuscript presents a well-structured randomised controlled trial evaluating the effectiveness of manual lymphatic drainage (MLD) combined with exercise versus exercise alone in managing breast cancer-related lymphedema. The study demonstrates significantly greater reductions in limb circumference and improvements in quality of life among patients receiving combined therapy. The methodology is clearly described, and the use of a validated Bangla LLIS tool strengthens the findings. Despite some baseline group imbalances and the absence of long-term follow-up, the work contributes valuable local evidence supporting MLD integration into rehabilitation protocols. Overall, it is a clinically relevant and meaningful study with publishable potential.

#### 4. Comment Appropriateness of the title.

"Combined manual lymphatic drainage and exercise versus exercise alone for lymphedema in breast cancer survivors: A randomised controlled trial" is an appropriate and accurate title for your manuscript.

**Response** We have revised the manuscript according to your comments.

#### 5. Comment Completeness and accuracy of the Abstract.

Your abstract includes all essential components expected in a scientific abstract. The abstract accurately reflects the content of the full manuscript.

One minor issue, since groups differed significantly in age, BMI, socioeconomic status, and chemotherapy history, a brief note such as "Groups were generally comparable at baseline except for a few demographic differences" would improve accuracy and transparency.

<b>Response</b>	We highly appreciate your concern. We have added about the baseline differences between groups in the abstract.
<b>6. Comment</b>	<p>The methods are described in sufficient details so that the study can be reproduced. Whether ethical concerns have been well described.</p> <p>Overall, the methods section provides sufficient detail for another researcher to reproduce the study.</p>
<b>Response</b>	We highly appreciate your concern. We have added about the baseline differences between groups in the abstract.
<b>6. Comment</b>	<p>The methods are described in sufficient details so that the study can be reproduced. Whether ethical concerns have been well described.</p> <p>Overall, the methods section provides sufficient detail for another researcher to reproduce the study.</p> <p>Suggestion: Add more details on allocation concealment (e.g., sealed opaque envelopes) for full reproducibility.</p>
<b>Response</b>	We have revised the methods section to explicitly describe allocation concealment. Also added CONSORT flowchart (See figure 1).
<b>7. Comment</b>	<p>Clarity and appropriateness of the design to achieve the objective(s).</p> <p>The study design is clear, logical, and well-suited to achieving the stated objectives.</p> <p>It provides a robust framework for evaluating the added value of MLD in BCRL management. With minor improvements in reporting allocation concealment and addressing baseline imbalance, the design would fully meet high-level clinical research standards.</p>
<b>Response</b>	Allocation concealment has been explicitly clarified in the methods section, and baseline group differences have been acknowledged in the abstract and discussed as a study limitation.
<b>8. Comment</b>	<p>Appropriate and thorough description of the statistical methods.</p> <p>Overall, the chosen tests are suitable for the type of data and study objectives. To meet publication standards, the manuscript should include additional details.</p> <p>No use of paired t-tests for within-group comparisons: Since the study measured outcomes at baseline and 6 weeks, paired t-tests (within each group) are expected for limb circumference change, B-LLIS score change instead, only between -group comparisons are reported. This misses important statistical information.</p> <p>Baseline imbalance not adjusted statistically; Significant baseline differences exist (age, BMI, chemotherapy history).</p> <p>Using only T-tests does not account for these confounders.</p> <p>ANCOVA (analysis of covariance) would be more appropriate to adjust outcomes for baseline values.</p>
<b>Response</b>	We re-analysed and provided paired analysis along with ANCOVA.
<b>9. Comment</b>	<p>Major redundancy between text and tables/figures in the results section.</p> <p>Yes — there is major redundancy between the results text and the tables.</p> <p>The Results section frequently repeats numerical values, percentages, and p-values that are already fully presented in the tables. This repetition is unnecessary and reduces the clarity and conciseness of the manuscript.</p> <p>What the results section should do instead.</p> <p>Summarise key findings:</p> <p>"Group B showed significantly greater circumference reduction across all anatomical sites compared to group A (Table 3)."</p> <p>Highlight patterns and significance, not exact values</p> <p>"The combined therapy group demonstrated superior improvement in all B-LLIS domains compared with exercise alone."</p> <p>Refer readers to tables for details</p> <p>"Detailed numerical values and percentage changes are presented in tables 3 and 4."</p>
<b>Response</b>	The results section has been revised to eliminate numerical repetition and focus on summarizing key findings and overall patterns. Detailed values are now presented exclusively in the tables (Lines 200 – 2022).
<b>10. Comment</b>	<p>Pertinence of the discussion section whether it justify the main message of the manuscript without repeating the results. issues with repetition of results</p> <p>Despite its relevance, the discussion repeats several numerical values and descriptive results already provided in the results and tables. Examples: Re-mentioning exact percentages of circumference reduction. Repeating specific baseline differences between groups.</p> <p>Restating domain-wise B-LLIS scores</p> <p>Narrating data that is already detailed in tables</p> <p>This repetition is not necessary in a discussion section and reduces readability.</p> <p>What the discussion should do:</p> <p>Interpret findings, explain possible mechanisms, compare with other studies, identify strengths and limitations, and discuss clinical relevance.</p>
<b>Response</b>	We have totally revised discussion section as advised (Lines 225 - 266).
<b>11. Comment</b>	<p>Whether strength(s) and limitation(s) are well described.</p> <p>Strengths and limitations are not sufficiently described in the current manuscript.</p>
<b>Response</b>	We have added a separate Strengths and limitations section in the manuscript.

<b>12. Comment</b>	<b>Whether the manuscript is supported by appropriate and up-to-date references.</b> Yes, the manuscript is generally supported by appropriate, relevant, and high-quality references, but it would benefit from slightly more recent citations in certain areas.
<b>Response</b>	Recent and relevant studies have been added to the Introduction and Discussion sections to strengthen the contextualisation of our findings and ensure up-to-date referencing.
<b>13. Comment</b>	<b>Straightforward, clear, and logical Storytelling.</b> The manuscript presents a logically organized and scientifically coherent story, but the storytelling could be made clearer, more concise, and more impactful with targeted refinement.
<b>Response</b>	Recent and relevant studies have been added to the Introduction and Discussion sections to strengthen the contextualisation of our findings and ensure up-to-date referencing.
<b>13. Comment</b>	<b>Straightforward, clear, and logical Storytelling.</b> The manuscript presents a logically organized and scientifically coherent story, but the storytelling could be made clearer, more concise, and more impactful with targeted refinement.
<b>Response</b>	The manuscript has been revised to improve clarity and conciseness by reducing redundancy, streamlining the results section, and sharpening the focus of the discussion to better emphasize key findings and their clinical implications.
<b>Responsible editor: Rijwan Bhuiyan, ORCID: <a href="https://orcid.org/0000-0003-0005-8889">0000-0003-0005-8889</a></b>	
<b>14. Comment</b>	Introduction: The rationale of the study is not clearly articulated. Please revise this section to align more closely with the study objectives. You may reduce some content from the first three paragraphs and provide a more focused explanation based on the objectives. Additionally, a few statements are not fully supported by the cited references (e.g., References 16, 17). Please review and update the introduction and discussion sections with appropriate and recent references.
<b>Response</b>	The Introduction was revised to better articulate the study rationale and align it more closely with the study objectives. Redundant content in the first three paragraphs was reduced to provide a more focused and coherent background. Statements not fully supported by the cited literature, including those associated with references 16 and 17, were carefully reviewed and revised to reflect the strength of the evidence. In addition, the introduction and discussion were updated with appropriate and recent references.
<b>15. Comment</b>	Methods: Revise the methods section in accordance with the CONSORT checklist ( <a href="https://www.equator-network.org/">https://www.equator-network.org/</a> ). Please include a CONSORT participant recruitment flow diagram as required by the journal's guidelines ( <a href="https://www.consort-spirit.org/">https://www.consort-spirit.org/</a> ). Ensure that the methodological details are sufficiently clear and reproducible. The descriptions of the interventions need improvement. If manual lymphatic drainage (MLD) and the exercise program followed standard protocols, please cite supporting references. If a customised protocol was used, elaborate on the steps and procedures so other researchers can replicate them.
<b>Response</b>	The methods section was revised in line with the CONSORT checklist. A CONSORT participant flow diagram was added as Figure 1. Methodological details, including study design, recruitment, randomisation, blinding, and adverse event monitoring, were clarified. The intervention descriptions were expanded, with standard references cited for manual lymphatic drainage and detailed exercise protocols provided to ensure reproducibility.
<b>16. Comment</b>	Ethical issues: Please clarify any ethical issues encountered during the study and explain how these were mitigated. Describe the ethical challenges faced, how they were addressed, and what measures were taken to prevent potential ethical concerns.
<b>Response</b>	The ethical considerations section was revised accordingly.
<b>17. Comment</b>	Statistical analysis: This section should be more specific to the study. Clearly mention which statistical tests were used for which variables or hypotheses, and how the normality of data was assessed. In addition to the between-group comparison (Group A vs. Group B), please address within-group analyses. A multivariable analysis (e.g., modeling) is recommended.
<b>Response</b>	The statistical analysis section was revised to specify the statistical tests used for each comparison, including within-group (paired T-tests) and between-group (unpaired T-tests) analyses. We also clarified how data normality was assessed prior to analysis. While multivariable modeling was considered, it was not performed has been acknowledged as a limitation.
<b>18. Comment</b>	Results: There is redundancy between text and tables. Present only the key findings in the text and refer to the respective tables for details. Combine the "unemployed" category with another suitable group. Additionally, please explain how socio-economic status was measured in the methods section under "Variable Assignment." If socio-economic status was not robustly assessed, it is advisable to remove this variable from table 1. Please merge table 2 into table 1 and present them as one table with appropriate subheadings.
<b>Response</b>	The results section was revised accordingly. The "unemployed" category was merged with the housewife group due to the small cell size. A separate "Variable Assignment" section was added to the methods to clarify how socio-economic status and other variables were assessed. tables 1 and 2 were retained separately to maintain clarity, with table 1 presenting sociodemographic characteristics and table 2 presenting clinical variables.

**19. Comment** Discussion: The discussion section currently repeats the results. Please interpret the findings with support from relevant literature and provide potential explanations where evidence is limited. Ensure that updated and highly relevant references are cited.

**Response** The discussion section was revised accordingly.

## Round 2

**Responsible editor: Rijwan Bhuiyan, ORCID: 0000-0003-0005-8889**

**1. Comment** The Introduction should be more clearly centered on this combined approach for lymphedema. Recent evidence regarding the effectiveness of manual lymphatic drainage (MLD), exercise, and particularly their combined use in lymphedema management has not been sufficiently discussed and reported.

The rationale for selecting a combination therapy requires clearer justification, including an explanation of the physiological mechanisms through which MLD and exercise may act synergistically. Specifically, it would be helpful to clarify what limitations of MLD may be addressed by exercise and how their combination may lead to improved outcomes. We recommend revising the Introduction with a focused discussion on combined interventions for lymphedema.

**Response** We have revised the introduction focusing on the objectives and highlights the interventions. Strengthen the rationale (Lines 59–94).

**2. Comment** Methods: The current description of the methods lacks a clear, step-by-step narrative, which affects reproducibility. For example, the manuscript states that “a total of 46 patients were recruited and randomised equally.....” while the flow diagram indicates that 50 patients were eligible.

For the benefit of readers, we recommend restructuring the methods section to describe the study procedures sequentially, clearly outlining each step from participant eligibility and recruitment to randomisation and intervention delivery.

**Response** We totally revised the methods section according to CONSORT checklist and improved the flow of storytelling. A flowchart of subject recruitment has been added (Lines 96–197).

**3. Comment** Results: As Groups A and B are not homogeneous with respect to economic status, body mass index, and most clinical variables. Therefore, unadjusted analysis raises concerns regarding the validity and generalisability of the main findings. reporting results without appropriate adjustment may be misleading to readers.

**Response** We re-analysed and revised all tables. To address the confounding factors we did multivariate analysis (e.g. ANCOVA). According to the findings we revised the text of results section (Lines 200–222).

## Round 3

**Responsible editor: Rijwan Bhuiyan, ORCID: 0000-0003-0005-8889**

**1. Comment** To further enhance the quality of the article, the editorial team has conducted additional statistical analyses and comprehensive language editing to improve clarity and flow. The following revisions have been made for your information:

Revised the title, abstract, keywords, statistical analysis, and results sections

Added an outcome measures section

Re-analysed and revised tables 2 and 3

Revised the CONSORT flow diagram

Please review the manuscript carefully and ensure that all changes are appropriate and accurately reflected.

**Response** Such changes improve the quality of the manuscript. We have checked and ensuring that all changes are correctly done and appropriately placed.

**2. Comment** In addition, kindly provide the following information:

Details of any ethical issues or challenges encountered during the study and how they were addressed

Revised author contributions in accordance with the journal's guidelines for research articles

A copy of the ethical approval letter

Point-by-point response file compiling all previous comments including current one.

**Response** The ethical issues are detailed out as requested (see the methods section). Revised the author contribution section. Attached the image copy of the ethical approval letter and also attached the all point-by-point response in a doc file.