

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Impact of a compression garment, on top of the usual care, in breast cancer patients with early disturbance of the lymphatic transport: protocol of a randomized controlled trial.
AUTHORS	Thomis, Sarah; Devoogdt, Nele; Bechter-Hugl, Beate; Nevelsteen, Ines; Neven, P.; Fourneau, Inge

VERSION 1 – REVIEW

REVIEWER	Takumi Yamamoto National Center for Global Health and Medicine Japan
REVIEW RETURNED	07-Aug-2020

GENERAL COMMENTS	<p>This is a study protocol of a randomized controlled trial on breast cancer-related lymphedema (BRCL). Patients with breast cancer who undergo axillary lymph node dissection (ALND) or sentinel node biopsy (SNB) in the lymphedema center are screened for participation in this study, and followed until 36 months postoperatively. This study is of clinical significance to clarify indication of lymphedema treatment for subclinical BCRL cases; optimal therapeutic strategy can be established with early diagnosis and early treatment, while avoiding overtreatment. Although methodology seems sound and well documented in the manuscript, the manuscript can be improved by revising the following points before considering publication.</p> <ol style="list-style-type: none">1. Previous studies already reported significance of subclinical lymphedema, and possibility of early or prophylactic treatment for subclinical lymphedema cases to achieve cure. As patient subjective symptoms and extremity volume can be changed between morning and evening thus not reliable for lymphedema diagnosis, subclinical lymphedema should be diagnosed with lymphatic imaging. This point should be emphasized in the Introduction with appropriate citations.2. There are many protocols of fluorescent lymphography, and differences of abnormal findings, dermal backflow patterns, are reported to be related to different prognosis of lymphedema. Severity stage based on lymphography findings can be used to categorize lymphedema patients, and should be applied in this study for secondary outcome assessment.
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REVIEWER	Didem KARADIBAK Dokuz Eylul University /Turkey
REVIEW RETURNED	17-Aug-2020

GENERAL COMMENTS	<p>Lymphedema that develops after breast cancer treatment approaches is one of the most common complications. Lymphedema can be controlled, but there is no cure. Also, follow up is very important. Therefore, I think, This study will make a great contribution to the literature.</p> <p>Key words The number of keywords may be less (4 is enough)</p> <p>Methodology Methodology explained in detail. I will only have a few suggestions</p> <ul style="list-style-type: none"> • The authors were specified as over 18 years of age in the inclusion criteria. It is not necessary to state under 18 years of age in the exclusion criteria. • There are compression garments of different companies. It would be good not to give a name (JUZO) to avoid a relationship of competing interest. • The strengths and limitations of the study should be given. <p>References</p> <ul style="list-style-type: none"> • There is a very old source... It would be better to use more up-to-date references. <p>For example; *Thomis S, Dams L, Fourneau I, De Vrieze T, Nevelsteen I, Neven P, Gebruers N, Devoogdt N. Correlation Between Clinical Assessment and Lymphofluoroscopy in Patients with Breast Cancer-Related Lymphedema: A Study of Concurrent Validity. <i>Lymphat Res Biol.</i> 2020 Mar 25. doi: 10.1089/lrb.2019.0090. *Abbaci M, Conversano A, De Leeuw F, Laplace-Builhé C, Mazouni C. Near-infrared fluorescence imaging for the prevention and management of breast cancer-related lymphedema: A systematic review. <i>Eur J Surg Oncol.</i> 2019 Oct;45(10):1778-1786. doi: 10.1016/j.ejso.2019.06.009.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 1

Reviewer Name: Takumi Yamamoto

Institution and Country:

National Center for Global Health and Medicine Japan Competing interests: None declared

Please leave your comments for the authors below This is a study protocol of a randomized controlled trial on breast cancer-related lymphedema (BRCL). Patients with breast cancer who undergo axillary lymph node dissection (ALND) or sentinel node biopsy (SNB) in the lymphedema center are screened for participation in this study, and followed until 36 months postoperatively. This study is of clinical significance to clarify indication of lymphedema treatment for subclinical BCRL cases; optimal therapeutic strategy can be established with early diagnosis and early treatment, while avoiding overtreatment Although methodology seems sound and well documented in the manuscript, the manuscript can be improved by revising the following points before considering publication. Thank you

1. Previous studies already reported significance of subclinical lymphedema, and possibility of early or prophylactic treatment for subclinical lymphedema cases to achieve cure. As patient subjective symptoms and extremity volume can be changed between morning and evening thus not reliable for lymphedema diagnosis, subclinical lymphedema should be diagnosed with lymphatic imaging. This

point should be emphasized in the Introduction with appropriate citations. Thank you for this remark, indeed this is an important issue and is added in the introduction.

2. There are many protocols of fluorescent lymphography, and differences of abnormal findings, dermal backflow patterns, are reported to be related to different prognosis of lymphedema. Severity stage based on lymphography findings can be used to categorize lymphedema patients, and should be applied in this study for secondary outcome assessment. Indeed, it will be interesting to evaluate the change in the severity of the disturbance in the two groups. I have added this as a secondary outcome in the text and table 3.

Reviewer: 2

Reviewer Name: Didem KARADIBAK

Institution and Country: Dokuz Eylul University /Turkey Competing interests: None

Please leave your comments for the authors below Lymphedema that develops after breast cancer treatment approaches is one of the most common complications. Lymphedema can be controlled, but there is no cure. Also, follow up is very important. Therefore, I think, This study will make a great contribution to the literature. Thank you

Key words

The number of keywords may be less (4 is enough) This is changed.

Methodology Methodology explained in detail. I will only have a few suggestions

- The authors were specified as over 18 years of age in the inclusion criteria. It is not necessary to state under 18 years of age in the exclusion criteria. This is changed
- There are compression garments of different companies. It would be good not to give a name (JUZO) to avoid a relationship of competing interest. This is removed.
- The strengths and limitations of the study should be given. This is added.

References

- There is a very old source... It would be better to use more up-to-date references. I have changed some references.

For example;

*Thomis S, Dams L, Fourneau I, De Vrieze T, Nevelsteen I, Neven P, Gebruers N, Devoogdt N. Correlation Between Clinical Assessment and Lymphofluoroscopy in Patients with Breast Cancer-Related Lymphedema: A Study of Concurrent Validity. *Lymphat Res Biol*. 2020 Mar 25. doi: 10.1089/lrb.2019.0090.

*Abbaci M, Conversano A, De Leeuw F, Laplace-Builhé C, Mazouni C. Near-infrared fluorescence imaging for the prevention and management of breast cancer-related lymphedema: A systematic review. *Eur J Surg Oncol*. 2019 Oct;45(10):1778-1786. doi: 10.1016/j.ejso.2019.06.009. Added as a reference

VERSION 2 – REVIEW

REVIEWER	Yamamoto, Takumi NCGM, Japan
REVIEW RETURNED	03-Nov-2020
GENERAL COMMENTS	Well revised manuscript worth publication