

Peer Review File

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Reviewer A

It was a pleasure to review this interesting manuscript entitled: “Barcelona lymphedema algorithm for surgical treatment of breast cancer-related lymphedema” from Pomata’s group. At first glance the authors explored a very controversial topic in breast surgery, how to standardise the interventional approach to lymphoedema and where successful in demonstrating an algorithmic approach. On the other hand, I would suggest minor revision of few areas that also caught my attention.

Comment 1: Abstract

Please consider review this affirmative: “the bases of an appropriate clinical and imaging evaluation of BCRL”. To my eyes although the authors brilliantly suggest a thorough way to assess lymphoedema, they also mention the lack of consensus.

Therefore, the rewording might be advisable.

Reply 1: We have reworded this sentence.

Comment 2: Introduction

Please consider writing a few lines about the progressively reduction of lymphoedema incidence due to less invasive axillary staging/treatment when feasible. In my opinion since the advent of sentinel lymph node technique, reducing the lymphoedema incidence significantly, and the recent trials supporting new radiotherapy protocols, also associated with significant less lymphoedema, worth mentioning at some stage.

Reply 2: We have written a few lines about the potential progressive reduction in the incidence of lymphedema due to less invasive axillary treatment and less aggressive radiotherapy protocols.

Comment 3: On main text, please consider:

Highlighting in the text that the staging/treatment approach were based on clinical trials and specially when the authors made extrapolation for upper lymph node chain was considered (eg. Yoshida et al 2020) and when significant complications were seen (eg. blood transfusion for ~ 25%, according to Brorson H 1997). Although this seems irrelevant at first look, this is a potential bias not mentioned on the future limitation section. Referencing the part of the text when the authors write the spectrum of “it is recommended”. In case no reference is available, the authors can consider writing “we recommend”. Reviewing some sections of the text where the wording “extremely important” could be substituted for a formal writing to express that an emphasis is required. On the same line, consider rephrasing “ideal” for preferable. Adding more description about the T-LAR (Targeted-Lymphatic Axillary Repair), for instance if it was a clinical trial, how many patients, adverse events. I sadly could not find a publication about this but would be advisable if there is, to reference after the last paragraph.

I would strongly consider adding the limitations the broad use of this algorithm (eg. validation, resources, adverse events) as mentioned previously. Finally, since several articles have been published in this topic, please consider to highlight in the text how this article add to the current literature in the view of the available evidence.

Reply 3: Regarding the main text we have added a section explaining broadly the basis of each technique, and we have improved the explanation of the algorithm so that the reader can better understand the stage/treatment approach. This updated algorithm is based on studies previously published by the co-authors of this article (Masia 2016, Masia 2017).

Regarding the complications of the liposuction technique, we approached the description of the technique just to understand the concept. In any case, Brorson had described the need for transfusion in 8 patients who had aspirated more than 2000 ml. In contrast, Boyages 2015 does not refer any complications in his publication and Hoffner 2018 does not refer complications when dry liposuction is performed distally and tumescent proximally. Please let us know your opinion.

We have changed the words "recommended" and "ideal" and the expression "extremely important".

Regarding the TLAR approach, it is a recent work and is in the process of being published. Anyway, this work was already presented at the 32nd EURAPS annual meeting in Naples, Italy, on May 26-28, 2022, we have added this reference (see the book abstract, abstract number 281: (<https://www.euraps.org/wp-content/uploads/2022/05/EURAPS-ABSTRACT-BOOK.pdf>)).

Regarding limitations, this algorithm is an update based on two previously published papers (Masia 2016: Combined Surgical Treatment in Breast CancerRelated Lymphedema, Masia 2017: Barcelona Lymphedema Algorithm for Surgical Treatment in Breast Cancer–Related Lymphedema). Regarding adverse events, I think they are more related to the techniques themselves than to the algorithm. In the final part of the introduction, we also have highlighted what this article could add to the current literature. We would appreciate it if you could give us some suggestions about these topics.

Reviewer B

The authors are to be commended on their clinical approach for treating BCRL with current trends for lymphedema treatment. This article is important in sharing their experiences for readers. I have some comments below to be answered.

Comment 1: Page 3, line9. ISL is miss introduced as ILS. Correction is required.

Reply 1: we have corrected

Comment 2: References are not enough to cover the authors' comments. At least, references below should be added.

Reply 2: Page3, Line 15:

- Mihara M, Hara H, Hayashi Y, et al. Pathological steps of cancer-related

lymphedema: histological changes in the collecting lymphatic vessels after lymphadenectomy. PLoS One 2012;7:e41126.

And/or

- Yamamoto T, Yamamoto N, Yoshimatsu H, Narushima M, Koshima I. Factors

associated with lymphosclerosis: an analysis on 962 lymphatic vessels. Plast Reconstr Surg 2017;140:734-41.

Comment 3: Page5, Line 15:

Ito R, Zelken J, Yang CY, Lin CY, Cheng MH. Proposed pathway and mechanism of vascularized lymph node flaps.

Reply 3: We have added the corresponding references for the comments of the authors.

Comment 4: Page4, line2. Three sessions of lymphatic drainage should be described with more details compared to recommended reference below. Is this same with the article below? And how the drainage changed the ICG pattern?

Seki Y, Yamamoto T, Kajikawa A. Lymphaticovenular anastomosis for breast cancer treatment-related lymphedema: Three-line strategy for an optimal outcome.

Reply 4: To avoid confusion on the subject, we have removed this part

Comment 5: In Image 1, figure (D) diffuse is not seemed to be typical diffuse pattern. It looks like stardust pattern. It should be changed to diffuse image.

Reply 5: we have changed the image 1D

Editorial Comments

Comment 1: Abbreviations

(1) P. 4, L10: Please add the full name "MR Lymphangiography" when first used "MRL".

Reply 1.1: done

(2) And, the full names of the abbreviations only need to be specified once, for example, please just save the statement once "lymphatic-venous anastomosis (LVA)" in the manuscript.

Reply 1.2: done

(3) Please also provide the full names of the abbreviations in the Figures footnote.

Reply 1.3: done

Comment 2: We suggest the authors consider adding the detailed descriptive information in the Figure 1, which would more clearer for the readers. For the authors' kind reference, consider specifying the important information in the four situations in the footnote.

Reply 2: we have added detailed descriptive information in the main text.

Comment 3: Table formatting

Please pay attention to the Table 1's format. Normally, researchers choose to use the trilinear table to present experimental data.

Reply 3: this is a staging table, what do you advise us to do?