Reviewer's report

Title: The Effect of Post Mastectomy Radiation Therapy on Breast Reconstruction with and without Acellular Dermal Matrix: A Systematic Review and Meta-analysis Protocol

Version: 0 Date: 25 Oct 2018

Reviewer: Ryckie Wade

Reviewer's report:

Dear Dr Chung and colleagues,

Thank you for the opportunity to review your work and please accept my apologies for the tardy submission.

Abstract

1. Re: "Implant-based breast reconstruction has undergone advancements including" - perhaps change to "Implant-based breast reconstruction has undergone several changes including...". You imply that ADMs are a positive/beneficial 'advancement' in the field and yet the literature does not support this conjecture (and indeed this is why you're doing this much needed review).

Intro

Very nice. One suggestion only Re: "Several studies have demonstrated additional benefits including: lower risk of capsular contracture and implant migration" - this isn't quite correct, the above review by Hallberg shows equipoise re: capsular contracture. The article you cite is a narrative review which should be replaced.

Methods

1. I fear if you build your searches using terms concerning radiotherapy then you will miss a great deal of information. Many articles concerning ADMs for implant-based breast reconstruction do not explicitly mention neoadjuvant or adjuvant therapy in the title and nor will these terms necessary be reflected in the keywords / MESH terms. I suggest your search is broadened to capture all studies using implant-based breast reconstruction with ADMs; you could then manually remove irrelevant papers and of those included they aren't obviously RT ADM vs. noRT ADM studies, extract subgroup data from broader articles pertaining to irradiated ADM patients. Thoughts?
2. "Only peer-reviewed papers written in English will be included." - It is good practice not to limit searches to a language; if you have funds for translation, helpful multilingual students in your institution or access to Google Translate, etc then articles should be translated where possible.

3. Re: "The types of study to be included are control trials, quasi randomized studies, cohort studies, case-control, case series" do you mean "The types of study to be included are randomised controlled trials, quasi randomized studies..."?

4. The primary outcome should be a single event. e.g., the most important end-point of failure of the reconstruction / implant loss. All other outcomes are of secondary interest (infection, seroma, haematoma, etc). At the moment I'm not clear what you will count as a "post operative complication" and this is critical, as the figures could be massaged (e.g., you choose not to include seroma as it shows ADMs unfavourably or vice versa). I suggest these outcomes are examined individually and you select one as the primary end-point.

5. You don't need to detail this "Dichotomous data will be analyzed using odds ratios (OR) with 95% CI. For continuous data, mean differences (MD) with 95% confidence interval (CI) will be calculated." as this is tacit. Your decision or whether to use fixed/random effects is not solely based on statistically heterogeneity as this fails to account for clinical heterogeneity (i.e., a study of using one brand of ADM may be statistically the same as another ADM but there are clearly important clinical differences which must be accounted for). I imagine there will be need for random effects given the expected clinical heterogeneity. Consequently you can remove reference 22 which is passe.

6. Cochrane recommends the use of the ROBINS-I tool for the risk of bias assessment in observational studies - please amend.

7. Please add methods on your GRADE assessment.

8. What will you do if data are missing? Will you contact authors? Exclude the paper? This should be detailed.

9. What will be your unit of analysis? The breast or patient? This is a hotly debated topic and the majority of clinicians, statisticians and the literature suggest that the patient should be the unit of analysis. None-the-less you must expect some studies to report the units differently and have a plan of how to deal with this data.
10. Will you consider 2-stage implant-based reconstruction or straight to implant only with ADM +/- RT studies? How will you handle immediate versus delayed reconstructions? And what is the evidence underpinning these decisions?

Throughout the protocol and within the letter to the Editor, there is an flavour of bias in favour of ADMs. My sincerest apologies if my observation is incorrect but still, I wonder if the authors could state their position/preference/biases/conflicts regarding ADMs and their clinical practice? Ideally, the author team is composed of individuals with equipoise on the matter and conflicts of interest/preferences, etc are stated upfront.

I do hope my comments are helpful in improving the review and would be delighted to clarify anything. This is a much needed piece of work and after these minor points are addressed, I am sure it will pave the way for a strong review.

With kind regards,

Ryckie G. Wade

NIHR Doctoral Research Fellow in Plastic & Reconstructive Surgery

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