Reviewer's report

Title: Perioperative blood transfusion adversely affects prognosis after resection of lung cancer: A meta-analysis

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Reviewer: Morgan LE GUEN

Reviewer's report:

This meta-analysis is the first about outcome of patients undergoing a lung resection and transfusion. This is a current interrogation with the theory of immunomodulation and even immunodepression during surgery, anaesthesia with opioids or with transfusion. For this concern, your study has caught my reviewer’s attention. Authors conclude to the negative impact of transfusion on postoperative mortality but they omit some interactions between patients’ disability (ASA, preoperative low haemoglobin…) and risk of transfusion.

1. Is the question posed by the authors well defined?
   The primary end-point is well defined in the introduction of the manuscript with a devoted paragraph in the result and in the discussion section.

2. Are the methods appropriate and well described?
   This is a meta-analysis as indicated in the title. This method is probably the only one to answer to the question because a randomized study would not be ethical as suggested in the manuscript.
   The authors follow the current international guidelines. Nevertheless, as required in the PRISMA methodology, it would be appreciable that authors mentioned in methodology section the need to contact some original writers to complete datasheet. In the opposite, just suggest it was not the case.

Major Compulsory Revisions

Authors should mention in methodology section the need to contact some original writers to complete datasheet. In the opposite, just suggest it was not the case.

About data extraction, some additional information is interesting in this specific population undergoing major non cardiac surgery. First, ASA (American Society of Anesthesiology) score is required because it is known to be directly and independently correlated to the postoperative outcome of patients. If there is a great unbalance with severe illness patients (ASA III or IV) in the group of transfusion, this leads to a confusing factor with an expected poor outcome. In the same way, the oncologic status may be interesting especially with preoperative chemotherapy which could modulate the immune system and may enhance immunodepression.
Minor Essential Revisions

As suggested in PRISMA guidelines, please mention “Systematic Review and Meta-analysis” in the title as followed: “Perioperative blood transfusion adversely affects prognosis after resection of lung cancer: A Systematic review and a Meta-analysis.”

3. Are the data sound?

The article is short and precise with a huge sample. The choice of a clear primary end-point with specific tables helps the reader to make his self-opinion.

Minor essential revisions:

It is surprising not to have included any Chinese studies. Is it really the case or is it a choice of the authors after the first selection of studies? Depending your answer, revision of method section may be required.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?

Yes it is except for the point detailed in the second point, mainly about communication with original authors of selected articles.

Major Compulsory Revisions

Authors did not describe the number of patients lost during the follow-up, neither the number of censured data especially for the secondary outcome as recurrence-free interval.

5. Are the discussion and conclusions well balanced and adequately supported by the data?

In my opinion, discussion needs some further revision. Many confounding factors are not discussed as the medical history (neoadjuvant chemotherapy, preoperative cardiac status as ischemic cardiopathy, preoperative haemoglobin, anticoagulant…). Moreover, the extended period of analysis make comparison between study really hard because surgery, anaesthesia and threshold for erythrocyte prescription have notably changed!

6. Are limitations of the work clearly stated?

Limit section is correct but insufficient in regard to the superficial analysis of this question. Some confounding factors are not analysed and this should be discussed in this section.

Major Compulsory Revisions

Authors did not discuss some critical point as the extended period of inclusion with changes in surgical, anesthesiology practice and in the trigger of transfusion. Moreover, less invasive surgery (video-thoracoscopy…) has probably changed the risk of bleeding but in the other side more patients receive now antiagregant or anticoagulant with a higher risk of exposure to transfusion for a similar disease many years before.
The authors should better define the primary outcome (the overall survival) in term of median follow-up with a detailed description of the follow-up duration for every study.

We are not sure of the homogeneity in the demographic data (rate of pneumonectomy varies from 1/30 patients to 1/1.5; ischemic cardiopathy is not given; histology of cancer…)

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?

This article is a meta-analysis and by essence, it is based on previously published article according to their power (number of patients, quality of the study: randomised controlled trial in comparison to observational cohort…..)

8. Do the title and abstract accurately convey what has been found? Title and abstract follows current guidelines.

Yes they follow current guidelines: PRISMA method for Preferred Reporting Items for Systematic Reviews and Meta-Analysis.

Minor Essential Revisions

As suggested in PRISMA guidelines, please mention “Systematic Review and Meta-analysis” in the title as followed: “Perioperative blood transfusion adversely affects prognosis after resection of lung cancer: A Systematic review and a Meta-analysis.”

9. Is the writing acceptable?

Yes it is.

Minor essential revisions:

Background section: replace “Inspite of” by “Despite improvements”, “need” by “needs” or “requires”. Add “postoperative outcome” in the following sentences.

Statistical analysis: you should define “SEs” before giving abbreviation.

Eligible studies: in the second sentence, a word is lacking: inclusion “criteria” miss.

Many references included more than 6 authors. Indicate into brackets the number of journals from the start of the year.

There is probably a mistake in the 25th reference with a double and consecutive author “Zhou Y“

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I declare that I have no competing interests.