Author's response to reviews

Title: Perioperative blood transfusions and survival in patients with non-small cell lung cancer: A retrospective study.

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Author's response to reviews: see over
Reviewer: Myong Cheol Lim

Reviewer's report:
This manuscript was described reasonably and dealt with an important issue. Several issues should be considered as below:

• Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)
  1. Median age in the current was more than 65 years. Therefore, overall survival might be influenced from intercurrent disease. Therefore, disease-specific survival outcome might be analyzed and be helpful to understand the real impact of disease for the readers. We agree with the reviewer, that the use of an outcome such as cancer-related mortality would be useful to discriminate the potential effect of concurrent disease on survival. However, at our institution the collection of data regarding vital status is in a significant large number of patient done as binary outcome death/alive without specification of cause of death. Our sample size would be significantly small if we exclude those patients with cause of death. In order to try to adjust for concurrent diseases that might have influenced outcomes we included the ASA physical score in the matching. In the discussion section, we added a comment (5th paragraph, 4rd sentence) regarding the issues rose by the reviewer.
  2. 5-year survival rate might be depicted in the two figures.
  3. Type of disease related to TRIM related disease progression could be specified in the section of introduction. As indicated by the reviewer, we added to the introduction XXXX number of sentences (end of first paragraph) regarding the immunologic background of TRIM with emphasis on lung cancer.

• Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
  1. From figure legends, “A p < 0.05 was considered statistically significant.” might be removed. As indicated by the reviewer, the sentence “A p < 0.05 was considered statistically significant.” was removed

• Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)
  1. Immunologic background of transfusion related with lung cancer might be specifically described in the section of introduction or discussion. As indicated by the reviewer, we added to the introduction 4 sentences (end of first paragraph) regarding the immunologic background of TRIM with emphasis on lung cancer.
  2. Percentage should be considered per each group for Table1. As indicated by the reviewer, we included the percentage of transfused and non-transfused patients.
  3. Figure legend for figure 2 is same to that of figure 1 and not appropriate. Figure legend for figure 2 should be written again. As indicated by the reviewer, the figure legends were corrected.
  4. Adequate referencing is required through the whole manuscript. e.g. Our findings are not fully in line with some of the results published by other authors. As indicated by the reviewer, adequate referencing was done.
Reviewer: Hirotaka Tashiro

Reviewer's report:

In the manuscript, Cata et al. concluded that perioperative blood transfusion is associated with decreased overall survival but not recurrence free survival after lung cancer surgery. These results using propensity score matching seem to be interesting, and clear well-written. However, there are some drawbacks.

1. The authors concluded that perioperative blood transfusion is associated with overall survival but not tumor recurrence. I wonder if postoperative complication is associated with overall survival. The authors should describe postoperative complications associated with postoperative deaths. The patients who received blood transfusions during operation might have complicated lung operations related to postoperative complications. As indicated by the reviewer blood transfusions appear to be related to worse postoperative outcomes. Unfortunately, in our databases postoperative complications were not captured systematically hence we cannot provide with the information that the reviewer asked. In the discussion section, we added a comment (5th paragraph, 3rd sentence) regarding the issues rose by the reviewer.

2. I think that it is ethically difficult to conduct a randomized control study. As indicated by the reviewer, a RCT might bring a lot of ethical considerations however, if patients were are into “standard of care/liberal transfusion” versus “conservative transfusions” the study would not be unethical if the conservative group is treated with an evidence-based medicine trigger.

Reviewer: Gildasio S De oliveira

Reviewer's report:
Cata and Colleagues have performed a retrospective study to evaluate the association between blood transfusions and lung cancer outcomes.

Major:
The major issue with manuscript is the novelty of the information described. As the authors know, several studies have evaluated the same question with contradictory results in lung cancer. I am not sure how another small retrospective study will add to the current literature. As indicated by the reviewer, the novelty of the study might be questionable in terms of the study population however a significant difference compared to other is the PMS analysis.
The authors should include in the propensity matching other variables such surgery duration and postoperative chemotherapy use. The decision on not adding surgical time as a variable is due to the fact that we adjust for another variable that is type of surgery (thoracoscopy versus thoracotomy). In our institution, thoracotomies are consistently longer in duration. Moreover, by adding a continuous variable we should have arbitrarily
decide short- and long-duration procedures and have significant problems with matching. In terms of adding postoperative chemo as a variable, we decided not included because postoperative chemo is dependent on postoperative tumor staging (at least in our institution). Moreover, current protocols are using for instance TKIs start adjuvant treatment immediately after surgery and in some patients remain as a “chronic medication.”

The author should focus the discussion to their findings since this is a original submission and not a review article. As indicated by the reviewer, we restructured the discussion section by adding paragraph (5th paragraph) and shortening the 3rd paragraph.

It is unclear how the author decided to interpret their findings on Figure 2 - since the p value was 0.05. The chance to reproduce of the authors findings is very small given that p value. The p value of the figure was a mistake the correct value was changed.