Author's response to reviews

Title: Anemia status, hemoglobin concentration and outcome after acute stroke: a cohort study

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Author's response to reviews: see over
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Miss Angelina Ilievska MSc
The BioMed Central Editorial Team

Dear Miss Angelina Ilievska,

Re: MS: 1771551928307896
“Anemia status, hemoglobin concentration and outcome after acute stroke: a cohort study”

Thank you very much for your kind letter dated January 05, 2010. We have revised the manuscript in accordance with the useful suggestions made by both reviewers and have detailed the response to each of the comments of the reviewer in the following pages. We trust that this revised and improved manuscript may be of interest to the readers of BMC Neurol and thank you for the time and effort in considering it for publication.

Sincerely yours,

Prof. David Tanne.
Reviewer#1

This is a well-written manuscript describing the association between admission Hgb and outcome after stroke using a relatively large patient population. The authors demonstrated non-linear association with increased risk of death at both extreme low and high Hgb. The authors appropriately used the admission Hgb as the surrogate for baseline anemic status rather than using the mid-hospital course anemia status which could have been confounded by numerous variables.

Major Compulsory Revisions: None

Minor Essential Revisions:

• In table 2, I recommend putting the actual number of patients plus (%) as in Table 1 rather than just reporting the percentage.

  Actual number of patients plus (%) were added.

• In page 10, add “to” between “found” and “improve.” (i.e., Hemodilution therapy was not found “to” improve overall survival).

  Corrected

Discretionary Revisions:

• It would be appropriate to mention the institution’s Hgb threshold for transfusion if there is any institutional guideline.

  There was no strict institutional guideline for transfusion- determined based on overall clinical judgment. Discussed in limitations section (page 10).

• In the logistic regression model, the authors included age, gender, stroke type, stroke severity, prior disability, chronic kidney disease, other cardiac disease and malignancy. It would be more informative to also include whether or not the patient received transfusion in the model since transfusion itself is associated with poor outcome and increased risk of infection in the ICU. However, the authors discussed this limitation in Discussion.

  We agree with the reviewer, however, these data are unfortunately not available to adjust for. We have clarified in the limitations section that we did not document the use of blood transfusions, but that admission hemoglobin concentrations were rarely in the range leading to blood transfusion in our routine clinical practice (page 10).

• What were some of the reasons why 20% of the patients did not have a follow-up interview at 1 month, and 15% of the patients at 1 year? Are these the more disabled patients who might be important to be included in the final analysis? If the reason does not bias the population of the outcome group, the authors’ results should be OK to be published, but they should mention this in the Discussion.

  Mortality data, the main outcome of interest, were available for all patients. This is now clarified in page 6. Indeed 20% of the patients did not have a follow-up
interview at 1 month, and 15% of the patients at 1 year. The main reasons were that patients were not located or refused. The age, gender and stroke severity of patients with available follow-up data at 1-months and those with available data at 1-year were, however, comparable to the entire study cohort.
Reviewer#2

Reviewer appreciates the opportunity to review this original research. Authors addressed an important issue regarding anemia, Hb, and adverse outcomes in this population. There are many merits to this manuscript. However, my initial enthusiasm was dampened by the number of concerns I have for this manuscript.

Major Compulsory Revisions

1. The major concern is the selection of statistical methods. Authors should consider Cox model to examine the questions posed, and it is not clear to me why logistic regression is superior. Cox model would provide a much more rigorous method of evaluating the questions at hand.

   A Cox model was added to the outcome of all cause mortality (Methods-Page 6; Results- Page 7,8).

2. I applaud the authors for using Hb-sq to examine the spectrum. In addition, I would like to see categorical presentation of higher ranges of Hb compared with normal ranges, to provide further confirmatory evidence of the adverse outcome of the upper range Hb for mortality and NH placement.

   Categorical presentation of Hb was changed into quintiles (Figure 1).

3. It is not clear to me why NH placement and Mortality should be combined.

   Our main outcome of interest was all-cause death. In addition, we assessed a combined end-point of poor outcome i.e. disability or long-term nursing facility care or all-cause death.

4. References 1-5 should be separately out for each of the specific outcomes citations.

   Corrected

5. Briefly describe TOAST for readers who might not be familiar

   Added to Methods section (page 4). “Ischemic stroke etiology was determined by the TOAST classification, a system for categorization of subtypes of ischemic stroke mainly based on etiology, that has been developed for the Trial of Org 10172 in Acute Stroke Treatment.

6. MDRD needs reference

   Reference #13 was added.

7. Author should consider the role of other CBC markers in this analysis, especially the inflammatory markers and other anemia categorizations variables.

   Author should consider the role of cognitive function, nutritional status as potential confounds as well in the analyses.

   Categorical presentation of Hb by quintiles was added. We have also added to the limitation section that the effects of unmeasured confounding variables such
as nutritional status, frailty, cognitive function or complex interactions between covariates on the observed association cannot be ruled out (pages 9-10).