Author’s response to reviews

Title: One-year Versus Five-year Hospital Readmission after Ischemic Stroke and TIA

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Author’s response to reviews:

To

Benjamin Tan, MBBS, MRCP
BMC Neurology

We thank you for the opportunity to submit the revised version of our manuscript. We have addressed the issues and suggestions made by the reviewers in the manuscript.

Reviewers’ Comments to Author:

Kajetan L. von Eckardstein, M.D. (Reviewer 1):

I congratulate the authors for this excellent analysis of readmission data after stroke, comparing the first year to the subsequent four years. Based on a large cohort of nearly 1500 patients, the authors were able to draw the relevant conclusion, that aggressive hypertension therapy might
lower the risk of readmission, as this was regarded an independent risk factor. The very homogenous Kaplan-Meyer curve serves as an example for the quality of the data evaluated.

Additional information: Needs some language corrections before being published.

Answer to reviewer: We thank the reviewer for the nice commentaries. A fluent English-speaking person have read the manuscript and we have corrected the language according to her advises.

Xiayan Shen (Reviewer 2):

- Paper explored the factors for readmission within a year as opposed to that within the first 2-5 years and that the predictors for readmission were largely similar between both groups because of the vascular risk profile

- Under Methods, Page 3, Line 40, please re-define TIA as the following: A brief episode of neurological dysfunction caused by focal brain or retinal ischemia, with clinical symptoms typically lasting less than one hour, and without evidence of acute infarction

Answer to reviewer: We acknowledge that the definition proposed by the reviewer is more in line with the new definition from the AHA/ASA. According to our study protocol, TIA is defined as the original description in the methods of the manuscript, and this definition is more comparable to other studies investigating readmission after ischemic stroke or TIA. We therefore choose to maintain the original definition in our manuscript.

- Under Methods, Page 4, Line 23-33: Will like the authors to clarify as to how they determined hemorrhagic transformation of ischemic stroke as opposed to it being a treatment related complication from anti platelet and anti coagulation. Will also like clarification as to how the authors decide that a readmission is for seizure unrelated to stroke as opposed to seizure from scar epilepsy
Answer to reviewer: We have used the diagnoses made by the treating doctors during the readmission for deciding the cause of the readmission. These were found in the discharge summaries. However, the two readmissions that were caused by hemorrhagic transformation happened within 15 days after discharge from the index admission, and both readmissions were to our stroke unit. The decision of hemorrhagic transformation as opposed to medical treatment complication was made by an experienced stroke neurologist (Professor Halvor Næss). In our stroke unit, hemorrhagic transformation is defined as petechial or confluent hemorrhage in the same area as the primary infarction. For clarification in the manuscript, we have now added the following sentence in the methods on how we determined hemorrhagic transformation of ischemic stroke: “Hemorrhagic transformation was defined as petechial or confluent hemorrhage in the same area as the primary infarction”

We have not explored whether any seizures were related to scar epilepsy or unrelated to the stroke, as we do not have information on this. Furthermore, as risk factors and differences in baseline characteristic is the focus of the article and rather few patients were readmitted with seizures, we have not mentioned seizures or epilepsy elsewhere in the article. We therefore choose not to add a comment on this in the manuscript.

- Under Results, Page 6, Line 32, does the author refer to Table 2? There has been no Table 5 appended

Answer to reviewer: The correct table that was referred to was Table 3, and we have added the correction to the manuscript. We thank the reviewer for this observation.

- Under Results, Page 7, Lines 17-27, is there a table for the causes of readmission?

Answer to reviewer: A table for the causes of the first readmission for patients readmitted within one year and between year two and five has been added to the manuscript. We originally chose to only include this information in the text and not as a table, as we already had four tables and a figure in the manuscript, and the focus on the article was on risk factors for readmission and comparison of patients that experienced the first readmission after stroke within one year versus
between years 2-5 after stroke. As we have now added this table, we have removed the percentages from the text.

- As smoking is also a known cardiovascular risk factor for both stroke and cardiac disease, does ever-smokers who continue to smoke after stroke as compared to those who stopped after stroke as opposed to smokers who stopped prior to admission predict for re-admission within 1 year as opposed to 2-5 years? This is a modifiable risk factor that can be looked into.

Answer to reviewer: We already had collected information by medical chart review of smoking status at the time of the first readmission, and have now added this to Table 2. We agree with the reviewer that if smoking cessation after stroke resulted in a lower risk of readmission, then this would be a modifiable risk factor. Unfortunately, we do not have information on smoking status after the index admission in patients that were not readmitted, and therefore cannot include this in the baseline characteristic of the entire study cohort or in the analyses where we investigate risk factors for readmission.

We found significant difference in smoking status between patients that were readmitted during the first year and patients that were readmitted between year 2-5. A higher percentage of patients had stopped smoking prior to the index admission in the group that was readmitted within one year, whereas a higher percentage stopped smoking after the index admission in the group that was readmitted between years 2-5. However, we did not find any difference between the two groups of readmitted patients in smoking status at the time of the first readmission in patients that were still smoking at the time of the index stroke. We have now added the following sentence to the results:

“A higher percentage of patients readmitted within the first year had stopped smoking before the index admission, whereas more patients had quit smoking after the index admission in patients that were readmitted between years 2-5. Of the patients that were smoking at the time of the index stroke, 37% of the patients that were readmitted between years 2-5 had stopped smoking compared to 28% of patients readmitted during the first year (p=0.144).”
- As obesity is a known cardiovascular risk factor, does Body Mass Index/ body fat percentage affect rate of re-admissions? Again, this is a modifiable risk factor that can be looked into but not addressed in the current paper

Answer to reviewer: We agree with the reviewer that this would be very interesting to look into, but unfortunately, we have no information on BMI or body fat percentage.

- Will also like the authors to explore if compliance to medical therapy predict for re-admission within 1 year as opposed to 2-5 years as opposed to no readmissions. This is another modifiable risk factor that can be potentially addressed

Answer to reviewer: We did not find any difference in antiplatelet, anticoagulation, antihypertensive drugs, or statin treatment between patients that were readmitted within one year and patients that were readmitted during year 2-5 after discharge. This is shown in Table 2 and already stated on page 6. Unfortunately, we have no information on treatment received after discharge in patients that were not readmitted. This have now been added to the limitations of the study.

- Under Discussion, will like the authors to explain why cardiac diseases is a more frequent cause of admission for stroke in 2-5 years as opposed to at the 1 year time point whereas stroke related event and recurrent strokes become a less frequent cause of admission for stroke in 2-5 year as opposed to the 1 year time point as the risk factors for both stroke as well as cardiac diseases are similar

Answer to reviewer: Cardiac disease was a more frequent cause of the first readmission in patients that were readmitted between years two and five, whereas stroke-related events and recurrent strokes were more frequent causes of the first readmission in patients that were readmitted within one year. However, we have only studied the timing and cause of the first readmission in this paper, and not the timing of all unplanned readmissions. We therefore cannot conclude that cardiac diseases is a more frequent cause of readmission in the 2-5 year as opposed to the first year, and that recurrent stroke and stroke-related events are more frequent during the
first year after stroke, as patients may have more than one unplanned readmission. We have now added the following paragraph on this subject to the discussion:

“Even though cardiovascular risk factors did not differ significantly between patients readmitted within one year and patients readmitted during years 2-5, recurrent stroke and stroke-related events were more frequent causes of readmission within one year, whereas cardiac disease was a more frequent cause of readmission for patients that were readmitted during years 2-5. Although we do not have data on all unplanned readmissions after stroke, studies have shown similar results in relation to recurrent stroke and cardiac disease, with the highest incidences of recurrent stroke observed in the early period after stroke, and lower, yet more stable, yearly incidences of myocardial infarction and congestive heart failure.”

Manuscript changes have been highlighted in the manuscript. We have also submitted a clean version to improve ease of read. We hope that you will consider the manuscript "One-year Versus Five-year Hospital Readmission after Ischemic Stroke and TIA", for publication in BMC Neurology.

Sincerely

(for the authors)

Anna T. Bjerkreim
Research fellow, Neurovascular section