Author's response to reviews

Title: Exploring the impact of intravenous thrombolysis on length of stay for acute ischemic stroke: a retrospective cohort study

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Author's response to reviews: see over
Dear Professor Hengjin Dong,

We would like to submit our revised manuscript entitled “Exploring the impact of intravenous thrombolysis on length of stay for acute ischemic stroke: a retrospective cohort study” for your consideration for publication as an original article in the BMC Health Services Research. We are grateful for your comments. For clarity, we quote the comments verbatim, and then add our responses below.

Reviewer 1's report:

The finding of this paper is that IVT reduced the risk of prolonged LOS in patients with acute ischemic stroke. The, two questions appear:

1) Why is not the currently the standard treatment for patients with NIHSS scores of 5-7 should be add into discussion.

Response:
We fully understand the concerns you raised. According to the American Heart Association/American Stroke Association guidelines for the early management of patients with acute ischemic stroke (Stroke 2013;44:870-947), approximately one third of patients who are not treated with IVT because of mild or rapidly improving stroke symptoms on hospital arrival have a poor final stroke outcome. Therefore, the practice of withholding IVT because of mild or rapidly improving symptoms has been questioned. Stroke patients with gait disturbance, isolated aphasia, or isolated hemianopia, may have potentially disabling symptoms although their initial NIHSS score may be as low as 2 points.

According to a Delphi study on a group of international specialists in the field of IVT in acute ischemic stroke, all the participating specialists agreed on a minimal NIHSS score of 2 to 3 to warrant the use of IVT. (J Neurol Neurosurg Psychiatry 2007;78:685–689) At present, no specific lower limit of NIHSS score is mentioned in the treatment guidelines of acute ischemic stroke from Europe (Cerebrovasc Dis 2008;25:457–507) and the US (Stroke 2013;44:870-947). As mentioned in line 7 to line 11 on page 5, we treated stroke patients with IVT in our hospital if they fulfilled the American Heart Association guidelines and they paid the cost of tPA on their own. Therefore, we included patients with a low NIHSS score in our study. We have modified the text in line 9 and line 10 on page 5 to make this clear.

2) The paper discussed that IVT is not reimbursed by NHI in patients with NIHSS scores < 6, it there evidence for LOS and patients with NIHSS scores 6-7? (paper discussed patients with NIHSS scores of 5-7 had the lowest probability of prolonged LOS if they were treated with IVT). It could be evidence for reimbursement policy change.

Response:
Thank you for your very insightful comment. The decision to define minor stroke as an NIHSS score < 6 by NHI is arbitrary. A study found that an NIHSS score of ≤3 is more suited to the definition of minor stroke in terms of favorable short-term and medium-term outcomes (Stroke 2010;41:661–666). In our study, the patient group of an NIHSS score of 5 to 7 was...
not created by the authors. Instead, it was determined automatically by the CART algorithm to be the optimal cut-off points as mentioned in line 11 on page 10 of the manuscript.

In our study, 391 patients had an admission NIHSS score of 6 or 7. For patients treated with IVT, 20% had prolonged LOS. For those not treated, 54% had prolonged LOS. We have added this information in line 23 to line 25 on page 8.

**Reviewer 2's report:**

This is a relevant and generally well-written manuscript.

- Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)
  
  The Conclusion is brief and succinct to the point of uninformative, as it merely reiterates the main finding. Expansion of the Conclusion to consider the implications of this finding would be helpful.
  Occasional grammatical awkwardness.

**Response:**

Many thanks for your suggestion to help us improve the manuscript. We have expanded our conclusion.

**Reviewer 3's report:**

Overall
This paper is very well written.
There is a large data set, 3054 patients.
The statistical analysis is well justified and very detailed.
This is an important topic and highly relevant in the context of Taiwanese health care delivery and stroke care.
The background to the study is clearly justified by the authors in relation to funding models for acute stroke care and thrombolysis.
The data is sourced from the Taiwan Stroke Registry.
The statistical analysis seems appropriate and justified.
I am not familiar with CART analysis. In the limitations section, refer to the use of register data and retrospective nature of the data.
The results and data analysis are very detailed.

**Response:**

Thank you for your comments. We have included the use of register data and the retrospective nature of the study to the limitations of the study.

Other Minor changes suggested as follows;
Background section
page 3 line 2, change 3 to three

**Response:**

We have modified the text.
Response:
We agree with your opinion that these two references are quite old. However, the data of these references stemmed from two very important randomized trials on IVT, i.e., the European Cooperative Acute Stroke Study and the National Institute of Neurological Diseases and Stroke rt-PA Stroke Study. We failed to find more recent randomized trials that specifically discussed the relationship between LOS and intravenous thrombolysis.

Methods
page 4 line 24, when was functional status assessed using the mRS
Response:
The functional status was evaluated at discharge. We have changed the text accordingly.

Page 5 line 2 define NHI
Response:
NHI has been defined in line 9 on page 3 in the Background section. We have reworded line 2 on page 5 to avoid ambiguity.

Tables / figures
Review font size/style in Figure 1
Response:
We have increased the font size in Figure 1 to make it more legible.

We have revised and improved the manuscript according to the suggestions of the reviewers and we have highlighted the changes in the manuscript. Thank you again for all the valuable comments and help. We hope that the revised manuscript is suitable for publication in *BMC Health Services Research*.

Your favorable consideration will be highly appreciated.

Yours sincerely,

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