

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	How common is isolated dysphasia among stroke patients treated with intravenous thrombolysis, and what is their outcome? Results form the SITS-ISTR
<b>AUTHORS</b>	Lundström, Erik; Zini, Andrea; Wahlgren, Nils; Ahmed, Niaz

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Michal Bar Faculty Hospital Ostrava Comprehensive stroke center Ostrava Czech Republic
<b>REVIEW RETURNED</b>	15-Jul-2015

<b>GENERAL COMMENTS</b>	<p>The authors present a manuscript entitled: Intravenous thrombolysis in acute ischemic stroke patients with isolated dysphasia: Results from the SITS-ISTR registry</p> <p>Thank authors for your paper. Title and Introduction : OK Methods and Discussion : The study has an excellent methodology. According to fig.1 the authors say "The Figure 1 illustrates the individual mRS scores at 3 month. Patients with isolated dysphasia had a more favorable prognosis than the SITS-ISTR registry in general"</p> <p>I would like to recommend to compare also your results to patients with NIHSS 2-7 and with 0 in item 9. It could be beneficial.</p> <p>Conclusion: OK , Very important for general medical practice. References: OK</p> <p>I recommend this manuscript "Intravenous thrombolysis in acute ischemic stroke patients with isolated dysphasia: Results from the SITS-ISTR registry" to accept to BMJ open after "minor revision"</p>
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<b>REVIEWER</b>	Dejana Jovanovic Clinical Center of Serbia, Neurology Clinic Medical Faculty, University of Belgrade Serbia
	Jovanovic has received lecture fees from Boehringer Ingelheim and Pfizer.
<b>REVIEW RETURNED</b>	20-Jul-2015

<b>GENERAL COMMENTS</b>	The reviewer also provided a marked copy with additional comments. Please contact the publisher for full details.
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### VERSION 1 – AUTHOR RESPONSE

#### Reviewer 1

The authors present a manuscript entitled: Intravenous thrombolysis in acute ischemic stroke patients with isolated dysphasia: Results from the SITS-ISTR registry

Thank authors for your paper.

Title and Introduction: OK

Methods and Discussion: The study has an excellent methodology.

According to fig.1 the authors say “The Figure 1 illustrates the individual mRS scores at 3 month. Patients with isolated dysphasia had a more favorable prognosis than the SITS-ISTR registry in general”

I would like to recommend to compare also your results to patients with NIHSS 2-7 and with 0 in item 9. It could be beneficial.

Conclusion: OK , Very important for general medical practice.

References: OK

I recommend this manuscript “Intravenous thrombolysis in acute ischemic stroke patients with isolated dysphasia: Results from the SITS-ISTR registry” to accept to BMJ open after “minor revision”

#### Answer

Thank you for reviewing our manuscript. The review is mainly positive and the reviewer suggests us to compare the results with 0 in item 9, referring to Table 2. Our understanding is that the reviewer suggests that we should compare patients with aphasia, with non-aphatic patients,

We have included SITS-ISTR data on patients without isolated dysphasia to provide an overview of this part of the SITS-ISTR population. A formal statistical comparison between the groups was not the aim of the study. We have now modified the text and hope this is clear now. In the Introduction, p 4, line 23-28 we wrote:

“We aimed to describe the frequency and outcome of isolated dysphasia among patients treated with IVT, as documented in the Safe Implementation of treatment in Stroke – International Stroke Thrombolysis Register (SITS-ISTR). We also presented the SITS-ISTR cohort without isolated dysphasia for an overview.” (Italic in this version, not in the manuscript.)

In addition, we have made a comment on patients in the range 2-7 on baseline NIHSS, see Results (page 9, line 4-8):

“Within the range of 2-7 points on baseline NIHSS, approximately 45% improved completely, whereas patients with score 1 on NIHSS, 75% were completely improved. Only 1 patient with 1 point on NIHSS worsened (Table 2).”

Please let us know if anything is unclear in our understanding of your review.

#### Reviewer 2 – major comments

1.It isn't clear if the authors wanted to compare or not the baseline characteristics and outcome of patients with isolated dysphasia with all the other SITS-ISTR patients.

2.In the Methodology section of the abstract the authors quoted "Parameters associated with any clinical improvement were identified by univariate analysis" - however there are no such data in the Results of the manuscript.

3. In the Statistical testing the authors pointed that they did not perform any formal statistical testing between these groups of patients. Then, why they presented the baseline characteristics, local (and remote) haemorrhages and outcome of both groups in Tables 1 and 4 and Figure, respectively.

4. I do not see any reason why univariate, even multivariate statistical analysis should not be performed in comparing two groups of patients.

#### Answers to reviewer 2 – major comments

Thank you for your comments. We have numbered the comments from 1-4 in order to easier answer the questions.

1. We agree with the reviewer that the current description is not clear. Initially, we considered leaving out any data from the rest of the SITS-ISTR since we consider this a descriptive study of isolated aphasia. However, we finally added the rest of the SITS-ISTR data just to provide an overview of the rest of SITS-ISTR population. A formal statistical comparison between the groups was not the aim of the study. We have now modified the text and hope this is clear now. In the Introduction, p 4, line 23-28 we wrote:

“We aimed to describe the frequency and outcome of isolated dysphasia among patients treated with IVT, as documented in the Safe Implementation of treatment in Stroke – International Stroke Thrombolysis Register (SITS-ISTR). We also presented the SITS-ISTR cohort without isolated dysphasia for an overview.”

2. We thank reviewer to notice the inconsistency.

In the Abstract: The text “Parameters associated with any clinical improvement were identified by univariate analysis” is not relevant for the current version of the manuscript and has been removed. We have replaced this sentence with “We performed descriptive statistics for baseline and demographic data, and ...”. This wording is in the line with the description of the the statistical section of the main body of the manuscript: “We performed descriptive statistics for baseline and demographic data”

3. Please see also the response 1. The main reason for not to do any formal statistical testing between the groups is that we can clearly assume that outcome would differ. Patients with isolated aphasia had 8 points lower NIHSS compared to rest of the population. Moreover, due to large number of patients in the rest of the SITS-ISTR cohort (>58 000) a small clinically insignificant difference could appear as a highly statistically significant and that could be misleading to the readers. Therefore, we chose not to perform any formal statistical comparison between the groups.

4. Please see answer to point 1 & 3 above.

#### Reviewer 2 – minor comments

1. Tables 2 and 3 are with too many details without obvious message.
2. Two or one decimals in the results presented in Tables?
3. Percentages not clearly presented in the Tables.
4. Abbreviations in the Tables should be explained.
5. English editing is desirable.

#### Answers to reviewer 2 – minor comments

1. We agree that the tables have a lot of information. The reason for the details is for making it possible for the reader to compare the outcome for different initial NIHSS, e.g. Table 2: The proportion of complete recovery seems to be the same for all NIHSS (the first column, although patients with NIHSS = 1 has 75 % recovery. Since this is the largest study of isolated aphasia treated

with IV thrombolysis, we do believe that such thorough information is of importance, and we argue for leaving Table 2-3 as they are.

- 2.Thank you. We would prefer only one decimal, and that has been changed accordingly.
- 3.This has been edited (marked with red in v2 of the manuscript)
- 4.This has been added. Thank you.
- 5.Some misspelling was found.

#### VERSION 2 – REVIEW

<b>REVIEWER</b>	Dejana Jovanovic Clinical Center of Serbia, Neurology Clinic Medical Faculty, University of Belgrade Serbia
<b>REVIEW RETURNED</b>	06-Oct-2015
<b>GENERAL COMMENTS</b>	The reviewer completed the checklist but made no further comments.