Author’s response to reviews

Title: Outcomes of General Anesthesia versus Conscious Sedation for Stroke Undergoing Endovascular Treatment: A Meta-analysis

Authors:

Teng-Fei Wan (15566109814@163.com)
Rui Xu (xuruiwade1@sina.com)
Zi-Ai Zhao (zhaoziai@hotmail.com)
Yan Lv (lana@323foxmail.com)
Hui-Sheng Chen (chszh@aliyun.com)
Liang Liu (18580763671@163.com)

Version: 1 Date: 13 Jan 2019

Author’s response to reviews:

Rebuttal letter

Dear Editors and Reviewers:

Thank you for your letter and the reviewers’ comments concerning our manuscript entitled “Outcomes of General Anesthesia versus Conscious Sedation for Stroke Undergoing Endovascular Treatment: A Meta-analysis”. Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction. The main corrections in the paper and the responds to the reviewers’ comments are as following:

Ozan Akça (Reviewer 1):

Authors aimed to assess the impact of general anesthesia versus conscious sedation on the outcomes of ischemic stroke patients who underwent endovascular treatment. They analyzed data from published trials and reported their meta-analysis results in this manuscript. Study question is somewhat original and represents a multidisciplinary interest topic. Please find detailed comments below.
Point 1:
How was general anesthesia (GA) defined? If GA was defined as all intubated patients, this would be an error, because many of those patients were possibly intubated due to their neurological status instead of a routine or elective choice. Such error may even lead to a type I error. This major issue can technically explain why there was a major statistical difference in the non-randomized studies, but not in the randomized controlled studies. In non-randomized studies, the choice of sedation/anesthetic was most likely due to either technical concerns (difficulty of interventional procedure) or safety concerns (airway patency). Please explain and provide discussion.

Reply 1:
Thanks for your questions. General anesthesia (GA) is often used to sedate and immobilize the patient to prevent wire-induced vessel injury; facilitate blood pressure control; provide adequate patient ventilation and airway protection; and make the procedure tolerable for patients. During the procedure general anesthesia, patients were intubated to prevent the possibility of asphyxiation or airway obstruction. However, GA was not just defined as all intubated patients. As you mentioned, in clinical practice, the choice of GA or CS for a given AIS patient were mainly decided by the technical concerns (difficulty of interventional procedure) or safety concerns (airway patency). As we have presented in discussion part (paragraph 5 in Discussion), the “medically indicated” highlights the problem of bias and may explain the reason that why the randomized and nonrandomized studies show marked discrepancy in results.

Point 2:
Were the patients in the GA group controlled for their baseline NIHSS scores? Please report the baseline neurological status of all patients (NIHSS, GCS). If the baseline NIHSS and/or GCS were higher (or lower, respectively), then this would provide explanation to this reviewer's first concern.

Reply 2:
Thanks for your questions. As you mentioned, the baseline neurological status of patients in different groups was a matter of concern. The baseline NIHSS scores of all patients were listed in Table S1. We found that the patients in the GA group showed higher NIHSS scores compared with CS group in 6 included studies (P < 0.05). And 5 studies showed no significant difference in the baseline NIHSS scores between GA and CS groups (P > 0.05). However, we could not pool all the baseline NIHSS scores of patients for all included trials, because these studies presented data in different forms [mean (SD) or mean (IQR)] and the individual data were unobtainable. Thus, we added this limitation into the Discussion part.
Point 3:

Two large trials included in the meta-analysis, Abou-Chebl et al. 2010 and Bekelis et al. 2017 which got quality scores of 5 and 6 included more than 2,000 patients to their analyses. Therefore, I'd suggest an additional separate meta-analysis, which excludes trials receiving quality scores less than 7.

Reply 3: Thanks for your questions. As you suggested, we have conducted an additional separate meta-analysis for high quality studies (quality scores ≥ 7). After excluding four trials [1-4], which receive quality scores less than 7, the results suggested GA patients also have lower odds of favorable functional outcome (mRS scores ≤ 2) compared with CS patients (OR = 0.64, 95% CI: 0.48-0.86) (Figure S1). Moreover, GA was also associated with a statistically significant higher risk of mortality (OR = 1.85, 95% CI: 1.57-2.18) (Figure S2). We added these results into the supplementary material.

Point 4:

Also, within the RCT reported in this meta-analysis manuscript, Abou-Chebl et al.’s 2017 trial was in fact not randomized for GA vs. CS. That study (and possibly some others) was randomized to a different intervention not for anesthesia vs. sedation. Therefore, this study (and other RCTs which did not randomly assigned the anesthesia/sedation approach) should be listed under the non-randomized retrospective category, because they did not randomly assigned the anesthetic approach, and instead they gathered the anesthesia approach in a secondary retrospective analysis.

Reply 4: Thanks for your questions. As you mentioned, Abou-Chebl et al.'s 2015 trial and Berkhemer OA. et al.’s 2017 trial were in fact randomized to a different intervention not for GA vs. CS. Abou-Chebl et al.’s 2015 trial was a post hoc analysis of the Interventional Management of Stroke (IMS) III trial which was the largest randomized open-label trial of endovascular therapy following intravenous thrombolysis for acute ischemic stroke. Berkhemer OA. et al.'s 2017 trial was post hoc analysis of the Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands (MR CLEAN) which was a multicenter, randomized, open-label trial of intra-arterial therapy (IAT) vs no IAT. Thus, we revised the characteristics of the included studies in Table 1. Moreover, we conducted the subgroup analysis according to the type of study design again (RCT or non-RCT). All of the results were presented in manuscript.
Point 5:

Abstract, Conclusions: CS was misspelled as "GS". Similar spelling errors can be found in the Conclusion statement of the manuscript. Please revise.

Reply 5: Thanks for your questions. We are very sorry for these spelling errors. We have modified these spelling errors according to your suggestion.

Point 6:

There are some grammatical errors throughout the text. Please revise.

Reply 6: Thanks for your questions. We are very sorry for the grammatical errors in our manuscript. We revised the English language within our manuscript carefully. Besides, we asked Dr. Xu for help to revise our manuscript again.

Sujoy Banik, MBBS, MD, DM (Reviewer 2):

I thank the editors and the journal for giving me the opportunity to review the work of the authors and I commend the authors on their efforts on their work and the manuscript. Overall this is a fine effort at looking at all the data regarding stroke interventions, however the paucity of data regarding the benefit of GA and the lack of anaesthesiologists in these trials is worth noting. Usually patients who are administered general Anesthesia are those who are already known to have possible poor outcome regardless of the intervention. Therefore further trials are already underway to assess this question and therefore the current retrospective review does not add to the literature in any new way nor does it reveal anything that has not already been revealed by previous studies.

Reply: Thanks for your questions. As you mentioned, in clinical practice, the choice of GA or CS for a given AIS patient were mainly decided by the patient’s physical status. Thus, in non-randomized studies, the AIS patients with underlying medical comorbidities or stroke severity may be performed with GA as “medically indicated”. However, in the subgroup analysis, we found marked discrepancy in results between non-randomized and randomized studies. The rate of favorable functional outcome (mRS scores ≤ 2) in non-RCT subgroup showed a statistically significant lower between CS and GA group but not in RCT subgroup. Moreover, GA was associated with significantly higher rate of mortality than CS in non-RCT subgroup, but there was no significant difference in the rate of mortality between GA and CS groups during RCT subgroup analysis. As we have stated in discussion part (paragraph 5 in Discussion), the “medically indicated” highlights the problem of bias and may explain the reason that why the randomized and nonrandomized studies show marked discrepancy in results.
Importantly, compared with previous meta-analysis, we first found the marked discrepancy in results between non-randomized and randomized studies. Besides, we first found GA may be associated with significantly higher rate of favorable functional outcome (mRS scores ≤ 2) in randomized studies. Our findings highlight that additional multi-center RCTs to definitively address these issues is warranted. Moreover, we are working on an individual patient-data meta-analysis of randomized clinical trials for anesthesia-related outcomes.

References:


