

Group Title: Functional outcomes among patients with acute ischemic stroke after mechanical thrombectomy with or without intravenous thrombolysis

In their randomized clinical trial, Suzuki and colleagues¹ reported that mechanical thrombectomy alone failed to demonstrate noninferiority when compared to combined intravenous thrombolysis and mechanical thrombectomy with regard to favorable functional outcome at 90 days. We have some concerns about this study.

First, several baseline characteristics of the patients were not well balanced in the treatment groups, as shown in the Table 1. For example, 55% of the patients in the mechanical thrombectomy alone group were men vs 70% in the combined intravenous thrombolysis and mechanical thrombectomy group. Although imbalances between groups can occur by chance in a randomized clinical trial, it is unusual to have imbalances for several baseline variables simultaneously, particularly for important prognosis factors in patients with stroke, such as blood pressure, stroke severity and stroke location. Therefore, we are concerned about systematic bias from the randomization process in this open-label trial.

Second, although the discrepancy between the primary outcome selection in the initial and final protocol was explained in the publication, the study hypothesis was not clearly stated in the protocol, and did not follow the SPIRIT guidance.² Additionally, the sample size description in both final protocol and statistical analysis plan indicated that 178 patients were required, assuming a favorable outcome in 48.6% with mechanical thrombectomy alone and 35.2% with combined intravenous thrombolysis and mechanical thrombectomy. The non-inferiority margin for the primary outcome was not predefined or considered in the sample size calculation for this “non-inferiority” trial but was compared against an odds ratio of 0.74, derived from a previous meta-analysis. Also, the

non-inferiority margin was not clearly prespecified but was tested for the secondary outcome of modified Rankin Scale score reduction.

Finally, the percentage of patients projected to drop out of this study decreased from 33% in the initial study design to 11% in the final study design. Due to the above concerns, we believe further clarifications and justifications are needed to avoid misinterpreting the findings of this trial.

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Conflict of Interest Disclosures: None reported.

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