Need to Clarify Thrombolysis In Myocardial Ischemia (TIMI) Scale Scoring Method in the Penumbra Pivotal Stroke Trial

To the Editor:

We congratulate the Penumbra Investigators on the successful completion of the Penumbra Pivotal Stroke Trial.1 The addition of the Penumbra System to the therapeutic armamentarium is an important advance in acute stroke care.

A major defect of the report is that the investigators do not specify how they measured the primary trial outcome, angiographic revascularization. They state without further elaboration that the core laboratory used the Thrombolysis In Myocardial Ischemia (TIMI) scale to assess revascularization. However, the TIMI scale was developed for the myocardial circulation and cannot be applied in the more complex cerebrovascular arterial tree without the creation of additional operational rules. A recent review found no fewer than 7 different operationalized versions of the TIMI scale being used across different stroke trials.2 The Stroke Therapy Academic Industry Roundtable (STAIR) has for this reason recommended abandonment of the TIMI in future cerebral revascularization clinical trials and use of one or more of the more transparent and uniformly applicable scales that have been developed for the brain.3 For past studies that did use the TIMI, like the Penumbra Pivotal Trial, it is absolutely essential that the idiosyncratic rules used by the trial core laboratory to apply the TIMI to the brain circulation be specified in full, as was done in the reporting of the Mechanical Embolus Removal in Cerebral Ischemia (MERCI), Multi-MERCI, and Interventional Management of Stroke IMS 1 and 2 trials.4–6 It is difficult to determine whether the reported higher recanalization rate in the Penumbra Trial compared with the MERCI, Multi-MERCI, IMS 1, and IMS 2 trials is an artifact of different angiographic scoring methods or a genuine difference in device technical efficacy. The similar clinical outcomes of the Penumbra patients and the MERCI/Multi-MERCI patients suggest that, when scored with the same method, the actual revascularization rates likely were similar. To complete their trial report, the Penumbra trialists should provide a full specification of how they applied the TIMI scale to their cerebral angiograms. If the scoring method did indeed differ in the Penumbra trial from those used in the MERCI, Multi-MERCI, IMS 1, and IMS 2 trials, we would encourage all of these trial investigators to collaborate on having a single core laboratory reread all angiograms using a uniform method and reporting the results. This collaborative effort would allow genuine comparisons to be drawn that could inform clinical decision-making and provide a benchmark for future revascularization clinical trials.

Disclosures

J.L.S. is an employee of the University of California, which holds a patent on retriever devices for stroke; is a scientific consultant regarding trial design and conduct to Concentric Medical (modest); is a site investigator in the NINDS Award K23 NS054084, P50 NS044378, and U01 NS 44364. R.G.N. is a scientific consultant regarding trial design and conduct to Concentric Medical (modest); is a site investigator in the NIH Combined Approach to Lysis Utilizing Eptifibatide and rt-PA in Acute Ischemic Stroke-Enhanced Regimen (CLEAR-ER), IMS 2, IMS 3, and MR and REcanalization of Stroke Clots Using Embolectomy (MR RESCUE) multicenter clinical trials and the Concentric Merci registry for which the University of California Regents received payments based on the clinical trial contracts for the number of subjects enrolled; and is funded by NIH NINDS Awards K23 NS054084, P50 NS044378, and U01 NS 44364. D.S.L. is a scientific consultant regarding trial design and conduct as well as research and development to Concentric Medical, ev3 Neurovascular, CoAxia, and Rapid Medical (all modest); is a site investigator in the NIH IMS 3 and MR RESCUE multicenter clinical trials and the Concentric Merci registry for which Massachusetts General Hospital received payments based on the clinical trial contracts for the number of subjects enrolled. R.J. is an employee of the University of California, which holds a patent on retriever devices for stroke; is a scientific consultant regarding trial design and conduct to Ev3 and Talecris (all modest); received devices for use in an NIH multicenter clinical trial from Concentric Medical (modest); is a site investigator in the NIH CLEAR-ER, IMS 2, and IMS 3 multicenter clinical trials and the Concentric Merci registry for which the University of California Regents received payments based on the clinical trial contracts for the number of subjects enrolled; and is funded by NIH NINDS Award P50 NS044378.

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