

Timing, testing, and standardization of endovascular therapy

Joseph P. Broderick,
MD

Correspondence & reprint
requests to Dr. Broderick:
joseph.broderick@uc.edu

Neurology® 2012;79 (Suppl 1):S117–S118

The Society of Vascular & Interventional Neurology (SVIN) roundtable meeting concerning endovascular therapy highlights the rapid advances in technologic approaches to revascularization in acute stroke patients. Although the new technology is exciting, the road to scientifically proven advances that improve outcomes for patients will depend upon minimizing the time to revascularization, scientific testing of the technology in clinical trials, and standardization of training and delivery of endovascular therapy.

One consistent theme from the single-arm clinical trials of endovascular therapy is that the clinical outcome after revascularization is highly dependent upon the time from stroke onset to revascularization. The IMS (Interventional Management of Stroke) I and II Trials,¹ the Penumbra Trial,² and the French Recanalize Study³ demonstrated a strong relationship between time to revascularization and a good functional outcome, as measured by a modified Rankin Scale score of 0–2 at 3 months. In the IMS I and II pilot trials, revascularization beyond 6 hours resulted in outcomes similar to those for patients without revascularization. The discrepancy between increasingly higher rates of recanalization with the new endovascular devices and relatively disappointing clinical outcomes at 90 days, in comparison with findings in the NINDS tPA (National Institute of Neurological Disorders and Stroke tissue plasminogen activator) trial and PROACT (Prolyse in Acute Cerebral Thromboembolism) II trial,^{2,4–7} also reflects the importance of time to revascularization. The most recent technologic advance, self-expanding retrievable stents, temporarily restores blood flow and then removes the occluding thrombus. It is not surprising that a number of companies are pursuing this particular technology, which appears to represent an advance over previous devices cleared by the US Food and Drug Administration for thrombus removal in acute stroke. Using imaging to determine a physiologic time window to perform endovascular therapy is under study, but imaging is most likely to

be helpful as a guide to futility and the decision not to proceed with endovascular treatment.

Testing and comparison of devices in animals and humans must focus not only on revascularization and safety but clinical outcomes as compared to standard therapy. Eventually, these devices must be tested in randomized trials comparing endovascular therapy to IV tPA within 4 1/2 hours and against standard therapy beyond 4 1/2 hours. Long-term acceptance, use, and reimbursement for these devices in clinical practice must be based upon demonstration of clinical effectiveness, not just revascularization. In addition, clinical and angiographic outcomes in pilot studies of these devices must be standardized if we are to truly compare devices. All trials should use the thrombolysis in cerebral ischemia (TICI) designation^{8,9} as well as recanalization of the primary occluded vessels. The use of imaging to select patients should also be noted and described, because the included populations of patients may vary substantially between trials. Finally, assessment of devices must recognize that the quality of data varies greatly by source (from highest to lowest): randomized controlled trials against standard therapy > single-arm trials > registries > case series. The latter 2 categories are extremely susceptible to reporting bias and less reliable outcome measurements. Thus, it is not surprising that the clinical outcomes in registries and case series as described in the roundtable articles are often much better than outcomes in clinical trials.

Finally, we are still in the infancy of endovascular therapy for acute stroke. As the technology begins to be better defined, the stroke community will need to define and standardize the overall training of stroke endovascular specialists, training and experience with given devices, and the angiographic procedure itself, including sedation and anesthesia. Recent reports indicate that conscious sedation, rather than routine general anesthesia, is associated with improved outcomes.^{10,11} This requires further study. With regard to standardization, the field of cardiology is far ahead of us in that current national American Heart Association guidelines speak to all parts of the pre- and

From the Department of Neurology, University of Cincinnati Neuroscience Institute, University of Cincinnati Academic Health Center, Cincinnati, OH.
Go to Neurology.org for full disclosures. Disclosures deemed relevant by the author, if any, are provided at the end of this article.

post-angiographic procedure and recommend criteria for ongoing experience and volume of cases, both by operator and by center. As our field moves forward, improved patient outcomes—not reimbursement, turf issues, or technology per se—should be the principle that guides our journey.

AUTHOR CONTRIBUTIONS

J.P.B. participated in drafting/revising the manuscript, study concept or design, analysis or interpretation of data, acquisition of data, and editorial writing.

DISCLOSURE

Dr. Broderick has served on scientific advisory boards for Johnson & Johnson, Wyeth, and PhotoThera; served on the steering committee for Novo Nordisk and Genentech (all consulting fees and honoraria are placed in an education/research fund in Dr. Broderick's department of his institution); has received honoraria for speaking from Oakstone Publishing (paid to Department of Neurology's educational/research fund); received study medication from Genentech, Novo Nordisk, and Schering Plough; received catheters from Concentric, EKOS, and Johnson & Johnson; and received research funding from NINDS, NIH-NINDS, and FDA. **Go to Neurology.org for full disclosures.**

Received July 10, 2011. Accepted in final form August 17, 2011.

REFERENCES

1. Khatri P, Yeatts SD, Broderick J, Tomsick T, for the IMS I and II Investigators. Good outcome after technically successful intra-arterial therapy is time-dependent. *Neurology* 2009;73:1066–1072.
2. The Penumbra Pivotal Stroke Trial Investigators. The Penumbra Pivotal Stroke Trial: safety and effectiveness of a new generation of mechanical devices for clot removal in intracranial large vessel occlusive disease. *Stroke* 2009;40:2761–2768.

3. Mazighi M, Serfaty JM, Labreuche J, et al. Comparison of intravenous alteplase with a combined intravenous-endovascular approach in patients with stroke and confirmed arterial occlusion (RECANALISE study): a prospective cohort study. *Lancet Neurol* 2009;8:802–809.
4. Smith WS. Safety of mechanical thrombectomy and intravenous tissue plasminogen activator in acute ischemic stroke: results of the Multi Mechanical Embolus Removal in Cerebral Ischemia (MERCi) Trial, part I. *AJNR Am J Neuroradiol* 2006;27:1177–1182.
5. Smith WS, Sung G, Saver J, et al. Mechanical thrombectomy for acute ischemic stroke: final results of the Multi MERCI Trial. *Stroke* 2008;39:1205–1212.
6. Furlan A, Higashida R, Wechsler L, et al. Intra-arterial prourokinase for acute ischemic stroke: the PROACT II Study: a randomized controlled trial: Prolyse in acute cerebral thromboembolism. *JAMA* 1999;282:2003–2011.
7. NINDS rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. *N Engl J Med* 1995;333:1581–1587.
8. Higashida RT, Furlan AJ, Roberts H, et al. Trial design and reporting standards for intra-arterial cerebral thrombolysis for acute ischemic stroke. *Stroke* 2003;34:e109–e37.
9. Tomsick T. TIMI, TIBI, TICI: I came, I saw, I got confused. *AJNR Am J Neuroradiol* 2007;28:382–384.
10. Nichols CW, Khatri P, Yeatts S, et al. Periprocedural sedation during intervention for acute stroke. *Stroke* 2008;39:69.
11. Abou-Chebl A, Lin R, Hussain MS, et al. Conscious sedation versus general anesthesia during endovascular therapy for acute anterior circulation stroke: preliminary results from a retrospective, multicenter study. *Stroke* 2010;41:1175–1179.

Neurology[®]

Timing, testing, and standardization of endovascular therapy

Joseph P. Broderick

Neurology 2012;79;S117-S118

DOI 10.1212/WNL.0b013e3182695939

This information is current as of September 24, 2012

Updated Information & Services	including high resolution figures, can be found at: http://n.neurology.org/content/79/13_Supplement_1/S117.full
References	This article cites 11 articles, 6 of which you can access for free at: http://n.neurology.org/content/79/13_Supplement_1/S117.full#ref-list-1
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): All Cerebrovascular disease/Stroke http://n.neurology.org/cgi/collection/all_cerebrovascular_disease_stroke All Clinical trials http://n.neurology.org/cgi/collection/all_clinical_trials
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://www.neurology.org/about/about_the_journal#permissions
Reprints	Information about ordering reprints can be found online: http://n.neurology.org/subscribers/advertise

Neurology® is the official journal of the American Academy of Neurology. Published continuously since 1951, it is now a weekly with 48 issues per year. Copyright © 2012 by AAN Enterprises, Inc.. All rights reserved. Print ISSN: 0028-3878. Online ISSN: 1526-632X.

