Endovascular Thrombectomy for Treating Acute Ischemic Stroke

Using the Merci and Penumbra systems to restore flow to ischemic brain.

BY JOHN P. DEVEIKIS, MD

Intravenous recombinant tissue plasminogen activator (IV tPA) is the standard of care for acute ischemic stroke within the first 3 hours after symptoms onset based on positive data from the National Institute of Neurological Disorders and Stroke rtPA Stroke Study.[1] More recently, data also supported the use of IV tPA for selected patients with acute stroke in the 3- to 4.5-hour time window.[2] A prospective randomized trial involving endovascular administration of a thrombolytic agent in middle cerebral artery occlusion 3 to 6 hours after symptom onset (PROACT II) resulted in complete flow restoration in 66% of treated patients compared with 18% of control patients treated with heparin.[3] However, there are contraindications to thrombolytics (recent surgery, elevated coagulation parameters, known aneurysm or arteriovenous malformation, etc.), large thrombus burden may not respond to these agents, and there is a limited time window during which they can be used. Theoretical concerns about the neurotoxicity of tPA also exist.[4]

Mechanical disruption of thrombus can aid transcatheter thrombolysis. Gentle manipulation of guidewires and catheters into the thrombus may break it up, adding to the pharmacological effect of the fibrinolytic agent.[5] A snare can be deployed distal to the occlusion and pulled back to engage the thrombus. Snare thrombectomy has been successful in isolated cases of intracranial thrombi.[6] Mechanical thrombectomy may therefore be a possible means of treating stroke, with or without the use of thrombolytic agents. Two systems developed for intracranial thrombectomy are approved by the Food and Drug Administration (FDA) for use in the United States: the Merci retriever (Concentric Medical, Inc., Mountain View, CA) and the Penumbra System (Penumbra Inc., Alameda, CA).

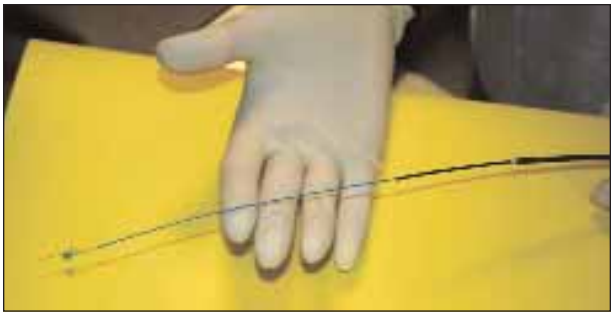

Figure 1. Merci system. Distal, working end of a V-series Merci retriever deployed via an 18-L microcatheter, inserted via a distal access catheter (DAC), which is advanced through a balloon guide catheter.

MERCI RETRIEVER

The Merci system was approved by the FDA in August 2004. It consists of a retriever used to extract clot, a microcatheter that delivers the retriever to the clot, a balloon-tip guide catheter that allows for flow arrest during clot retrieval, and a coaxial distal access catheter that stabilizes the microcatheter-retriever assembly during positioning and retrieval. The Merci retriever is a flexible nitinol wire that forms a multiloop helix as it is advanced out of the microcatheter (Figure 1).

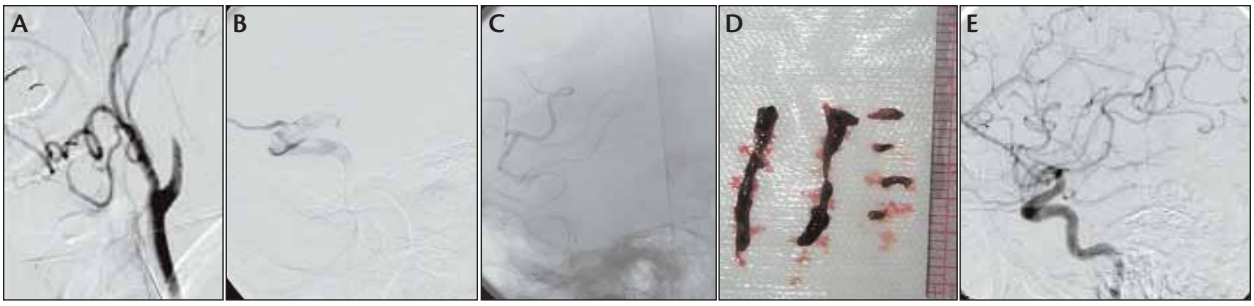

Figure 2. Merci retrieval case. The patient was an 83-year-old man with acute-onset aphasia and right hemiplegia 1 week after coronary artery bypass graft surgery. Left common carotid arteriogram confirms occlusion of the left internal carotid (A). A Merci microcatheter was navigated to the intracranial carotid. Contrast injection via the microcatheter shows clots with no flow distally (B). The microcatheter was advanced into the distal middle cerebral artery. Contrast injection shows patent distal branches (C). The Merci retriever was deployed to extract the thrombus. Multiple clot fragments were retrieved (D). Lateral view of a left internal carotid injection shows immediate restoration of flow throughout the intracranial circulation (E). The patient recovered fully.

The first iteration of the system was the X-series, which had a corkscrew-shaped tapering helix. The smaller distal loops engage the clot and allow extraction. The L-series is a nontapering helix with attached loops of suture to augment thrombus entrapment. The newest V-series incorporates aspects of both earlier series, with small, distal, helical loops to engage clot; looser winding of larger proximal loops to hold on to the clot; and suture fibers to assist capturing clot. The Merci microcatheters include the 3-F 14-X tapering to 2.4 F with a lumen of 0.017 inches, designed for the X-series and the 18-L with the same outer dimensions but a 0.021-inch lumen designed to deploy the L- and V-series retrievers. The Merci balloon guide catheters have both an 80- and 95-cm working length and are available in 8- and 9-F sizes with lumens of 0.078 and 0.085 inches, respectively. There is also a 7-F, 95-cm balloon guiding catheter available with a lumen of 0.059 inches. The larger balloon guides are for larger vessels with larger clots. The DAC has a 0.056-inch (4.3 F) outer diameter and can be advanced via any Merci balloon guide catheter; it has a lumen of 0.044-inch (3.3 F) and can accept either Merci microcatheter. The DAC line has recently been expanded to include both a smaller and larger diameter. The new DAC 038 has a 3.9-F (0.05 inches) outer diameter with a 0.038-inch inner diameter. The DAC 057 has a 5.2-F (0.068) outer diameter with a 0.057-inch inner diameter.

MERCI AND MULTI MERCI TRIAL RESULTS

The MERCI trial was a prospective, single-arm study to determine safety and efficacy of the Merci system using the X-series retriever in acute stroke.[7] Patients presenting with symptoms from large-vessel intracranial arterial occlusion within 8 hours of symptom onset were included but only if not eligible for IV tPA. Recanalization was achieved in 48% of the cases by the device alone and in 60% of the cases with a combination of device and adjunctive intra-arterial (IA) lytic. Procedural complications occurred in 7.1% of patients, and symptomatic intracranial hemorrhage occurred in 7.8%. Successful recanalization was associated with better outcomes and lower mortality rates. The Multi MERCI trial involved the use of L-series retrievers within 8 hours of symptom onset and allowed patients who failed IV tPA.[8] The results showed that 55% of patients were successfully recanalized with the retriever alone, but this increased to 68% when adjunctive IA tPA was used. Procedural complications were in 5.5%, and symptomatic hemorrhages occurred in 9.8%.

MERCI RETRIEVER TIPS

The 8- and 9-F balloon guides are optimal for larger patients, and the 7-F guide is recommended for small women or in vertebral arteries. The microcatheter is advanced over a soft, flexible neurovascular wire, such as the 0.014-inch Synchro soft (Boston Scientific Corporation, Natick, MA) or the 0.012-inch J-tip Headliner (Terumo Interventional Systems, Somerset, NJ). The J-tip shape avoids damaging the vessel. The DAC can be used to support the microcatheter by loading the microcatheter into the DAC and advancing the entire assembly through the balloon guide catheter as a unit. The wire and microcatheter system are carefully advanced through the clot into the vessel beyond. Positioning distal to thrombus is always confirmed by gentle contrast injection. A Merci retriever, selected to match the diameter of the occluded vessel, is advanced through the microcatheter and deployed distal to the clot. Withdrawal of the microcatheter-retriever assembly into the clot engages it, and combinations of rotation and gentle pulling will help dislodge it. Fluoroscopic visu-

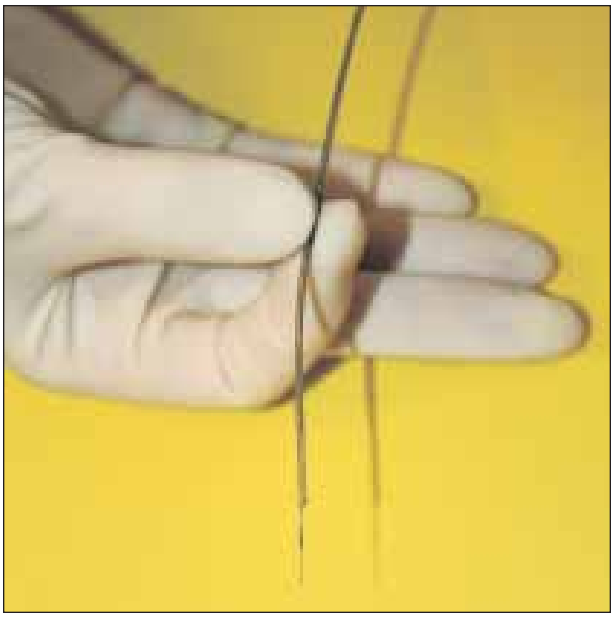

Figure 3. Penumbra system. Distal, working end of a 041 Penumbra reperfusion catheter with its matching Separator.

alization during withdrawal will confirm if the system is pulling back easily or, if the curves in the system straighten, suggesting the clot remains adherent to the vessel. If distal loops of the retriever straighten, it suggests the retriever is not fully engaging the clot. Patience is necessary because it often takes slow, steady pulling for some time before the retriever releases. Once it begins to move easily, the balloon of the guide catheter is inflated, and aspiration from the lumen of the guide catheter reverses flow and facilitates extraction of all thrombus. Aspiration continues as the entire assembly is withdrawn into the balloon guide catheter. The retriever, microcatheter, and DAC are all removed, and if blood cannot be freely aspirated from the guide catheter lumen, then the balloon must be deflated and the guide removed from the patient. Clots retracted using the Merci system can sometimes be quite substantial and may clog the guide catheter lumen (Figure 2). Multiple passes of the Merci device may be needed if thrombus remains in the vessel. Persistent occlusion after six attempts was considered treatment failure in the Multi MERCI trial.[8]

PENUMBRA SYSTEM

The Penumbra system received 510(k) clearance by the FDA in December 2007. It involves clot aspiration through reperfusion catheters navigated to the site of occlusion. The Penumbra reperfusion catheters are available in three sizes: 026 (150-cm long, 0.026-inch inner lumen, 3.9-F outer diameter tapered to 2.8 F distally), 032 (150-cm long, 0.032-inch inner lumen, 4.1-F outer diameter tapered to 3.4 F distally) and 041 (137-cm long, 0.041-inch inner lumen, nontapered 4.1-F outer diameter). The catheters have a stainless steel hypotube proximally to assist pushability of the catheter. Size selection depends on vessel size and accessibility. Each catheter must be used with a matching Separator (Penumbra Inc.), which is a soft guidewire with a teardrop-shaped swelling 6-mm proximal to the tip (Figure 3). Gentle movement of this teardrop in and out of the reperfusion catheter helps break up clot and allows aspiration without clogging of the catheter tip. The catheter is attached to suction tubing that is connect-

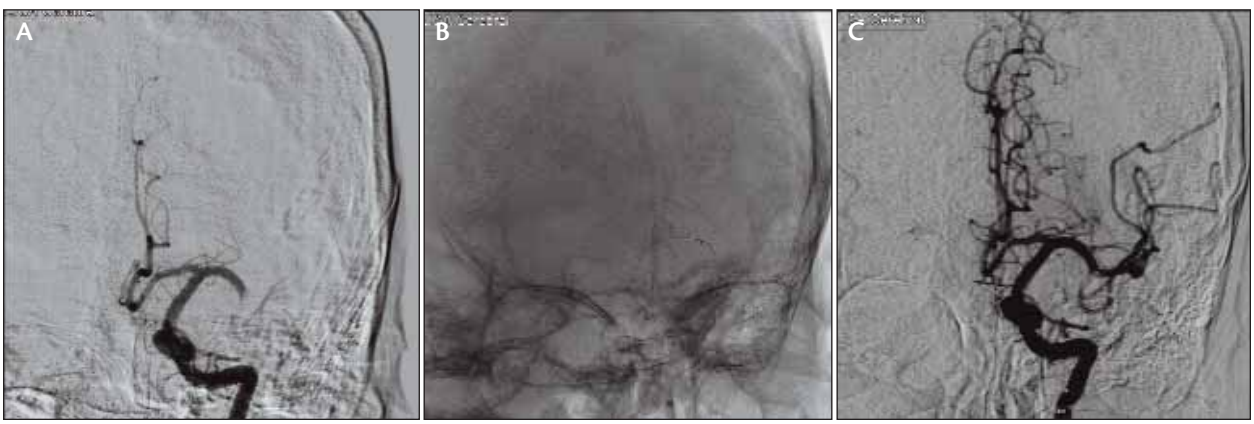

Figure 4. Penumbra system case. The patient was an elderly woman with atrial fibrillation on warfarin who had developed acute aphasia and right-sided weakness. Coagulation parameters were abnormal due to warfarin, so she could not receive tPA. Frontal view of left internal carotid shows complete occlusion of middle cerebral trunk (A). The Penumbra reperfusion catheter was navigated into the middle cerebral artery. Fluoroscopic image shows the catheter and the radiopaque distal marker of the Separator as clot aspiration was begun (B). After several minutes of clot aspiration, follow-up left internal carotid injection confirms that the artery is now patent (C).

ed to an aspiration pump that delivers 25 mm Hg of suction. This system works by aspiration beginning at the proximal face of the occluding thrombus, which can sometimes be quite an advantage over the Merci system, which requires catheterization distal to the clot.

PENUMBRA PIVOTAL TRIAL

A pilot trial of the Penumbra system in Europe showed the system to be 100% effective at restoring flow in the 87% of cases in whom microcatheter access to the lesion could be obtained.[9] The larger Penumbra pivotal trial was a single-arm prospective trial of 125 patients with severe stroke symptoms presenting within 8 hours of onset and ineligible for IV tPA.[10] Target vessel revascularization occurred in 81.6% of cases, with procedural complications in 12.8% and 2.4% of patients having serious adverse events. Symptomatic hemorrhage occurred in 11.2%. The system appears to be similar in safety and efficacy to the Merci system.

PENUMBRA SYSTEM TECHNIQUE

Penumbra reperfusion catheters are compatible with 6-F guide catheters, which are positioned in a stable position in the target vascular territory. The reperfusion catheters are advanced over a suitable soft neurovascular microwire to the site of thrombus. The 041 catheter is sometimes difficult to advance through tortuous vessels, but this can be facilitated by inserting a small microcatheter such as an Excelsior SL-10 (Boston Scientific Corporation) into the 041 and leading with the more flexible microcatheter. This technique has allowed positioning of the 041 through circuitous pathways, such as across the posterior communicating artery.[11] When the catheter reaches the clot, the wire is removed, and the matched Separator is inserted (Figure 4). Clot aspiration is then performed with the aspiration pump. The system is working if blood slowly aspirates back through the tubing. If the column of blood stops, pulling the Separator or reperfusion catheter back slightly may free up clot clogging the tip. When these maneuvers fail, the catheter may need to be removed and replaced with a new, possibly larger reperfusion catheter. Patience is required using the Penumbra system, because it may easily take 30 to 50 minutes to fully aspirate a clot.

WHEN MECHANICAL THROMBECTOMY FAILS

When, even after multiple passes with the Merci or after extensive use of the Penumbra system, the vessel remains occluded, other strategies may be attempted. One approach is to try the Penumbra system if Merci is not working—or vice versa. Low-dose tPA may be used if there are no contraindications to its use. Glycoprotein IIb/IIIa inhibitors such as abciximab or eptifibitide may facilitate recanalization, although, when used as a protocol violation in the Multi MERCI trial, these agents were associated with a dramatic increase in hemorrhage, albeit generally asymptomatic.[8] Placement of self-expanding stents across the occluding thrombus has been proven more effective than balloon angioplasty in rapidly restoring flow.[12] Stent placement may be an option to rescue failed thrombectomy.[13,14]

CONCLUSION

Both the Merci and Penumbra systems are reasonable methods of treating acute stroke patients with large-vessel intracranial occlusion. Choosing between systems depends on operator preference, although it should be remembered that catheter access distal to the clot is required with Merci. The ongoing IMS-III trial may provide further evidence as to the clinical effectiveness of endovascular treatment compared with standard IV rtPA.[15] ■

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1. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. N Engl J Med. 1995;333:1581-1587.
2. Hacke W, Kaste M, Bluhmki E, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. N Engl J Med. 2008;359:1317-1329.
3. 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.
4. Oka F, Fujisawa H, Nomura S, et al. Mechanistic insight into neurotoxicity of tissue plasminogen activator-induced thrombolysis products in a rat intraluminal middle cerebral artery occlusion model. J Neurotrauma. September. 2009;26:577-1584.
5. Barnwell SL, Clark WM, Nguyen TT, et al. Safety and efficacy of delayed intra-arterial urokinase therapy with mechanical clot disruption for thromboembolic stroke. AJNR Am J Neuroradiol. 1994;15:1817-1822.
6. Kerber CW, Barr JD, Berger RM, et al. Snare retrieval of intracranial thrombus in patients with acute stroke. J Vasc Interv Radiol. 2002;13:1269-1274.
7. Smith WS, Sung G, Starkman S, et al. Safety and efficacy of mechanical embolectomy in acute ischemic stroke: results of the MERCI trial. Stroke. 2005;36:1432-1438.
8. 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.
9. Bose A, Henkes H, Alfke K, et al. The Penumbra System: a mechanical device for the treatment of acute stroke due to thromboembolism. AJNR Am J Neuroradiol. 2008;29:1409-1413.
10. 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.
11. Hui FK, Narayanan S, Cawley CM. Posterior-to-anterior circulation access using the Penumbra Stroke System for mechanical thrombectomy of a right middle cerebral artery thrombus. Surg Neurol. Published online ahead of print July 28, 2009.
12. Brekenfeld C, Tinguely P, Schroth G, et al. Percutaneous transluminal angioplasty and stent placement in acute vessel occlusion: evaluation of new methods for interventional stroke treatment. AJNR Am J Neuroradiol. 2009;30:1165-1172.
13. Levy EI, Mehta R, Gupta R, et al. Self-expanding stents for recanalization of acute cerebrovascular occlusions. AJNR Am J Neuroradiol. 2007;28:816-822.
14. Brekenfeld C, Schroth G, Mattle HP, et al. Stent placement in acute cerebral artery occlusion: use of a self-expandable intracranial stent for acute stroke treatment. Stroke. 2009;40:847-852.
15. Khatri P, Hill MD, Palesch YY, et al. Methodology of the Interventional Management of Stroke III Trial. Int J Stroke. 2008;3:130-137.