Does the Merci Retriever Work?

For

Jeffrey L. Saver, MD

Technically, it works. And remarkably so. The Merci Retriever is a mechanical embolectomy device designed to reopen occluded vessels by extracting occlusive thrombi from the cerebral vasculature. In the Mechanical Embolus Removal in Cerebral Ischemia (MERCI) trial (parts I and II combined), among 151 patients enrolled in the intention-to-treat group; partial or complete recanalization by use of the device alone was achieved in 46%. This rate substantially exceeded that in the prespecified comparator group—patients enrolled in the control arm of the Prolyse in Acute Cerebral Thromboembolism (PROACT-II) trial (18%). The associated probability value of $<0.0001$ indicates a less than 1 in 10 000 chance that this result occurred by chance. The Merci Retriever indeed works.

And it works well where we most need it to work: on proximal occlusions for which there was previously no good therapy. Proximal carotid terminus and M1 middle cerebral artery thrombi respond poorly to IV or intra-arterial fibrinolytic therapy, likely attributable in large part to the sheer volume of the clot burden requiring enzymatic digestion. The average volume of carotid terminus thrombi (0.4 ml) is more than an order of magnitude larger than that of M2 middle cerebral artery division thrombi (0.03 ml). Such large clot burdens resist enzymatic digestion. For example, IV tissue plasminogen activator recanalizes only 10% of carotid terminus occlusions. In contrast, the Merci Retriever disposes of large proximal clots with comparative ease (53% recanalization rate in the MERCI Trial).

The Merci Retriever perfectly complements lytic therapy. The device’s size limits its deployment in distal vessels; it cannot currently be safely deployed beyond the proximal portion of the M2 middle cerebral artery. In contrast, lytics work best on small distal clots, in M2, M3 and higher order branches and in small penetrating arteries, inaccessible to the Retriever but highly responsive to enzymatic digestion.

Moreover, the Merci Retriever works where many a previous mechanical thrombectomy device has failed. Suspended or abandoned mechanical strategies to treat cerebral thromboemboli include clot maceration and aspiration by rheolytic thrombectomy (Angiojet, too damaging to vessel walls), primary angioplasty (spongy clots spring right back), laser (too ineffective at low energies, somewhat damaging at high energies), whirling roto-rooter clot maceration (X-ciser, too damaging to vessel walls), snare retrievers (too often fail to capture clots), and nitinol capture baskets (Neuronet, too bulky to deploy easily in cerebral vessels). The technical challenge in endovascular thrombectomy is not just getting clots out, but also leaving intact vessels behind. The Merci Retriever’s inwardly curved shape and avoidance of energy delivery permits it to capture thrombi without unduly injuring the delicate cerebral vasculature. Its development is a major advance in stroke care.

Does the Merci Retriever make patients better? I firmly believe that it does. The case for benefit is strong. The Merci Retriever achieves recanalization with a low rate of adverse effects. Recanalization is the single most powerful treatment for ischemic stroke. Recanalization will improve the clinical outcome of patients with persisting salvageable penumbra, albeit not patients who have already completed their infarct. As an end point, recanalization may meet criteria to serve as an acceptable surrogate end point in ischemic stroke clinical trials. Vessel recanalization is both biologically and statistically strongly related to stroke clinical outcomes. Across 33 studies enrolling 1094 acute cerebral ischemia patients, recanalization increased the odds of a good final functional outcome by 4.5-fold.

In the MERCI Trial, recanalization was dramatically associated with improved outcomes. The Merci Retriever achieves recanalization in one-half of all treated patients, and does so more quickly after arrival on clot than intra-arterial lytics and without exposing the patient to the hemorrhagic risk, neurotoxicity, and blood-barrier disruption of fibrinolysis.

In contrast, the adverse event rate with the Merci Retriever is low. Symptomatic intracranial hemorrhage occurs, but at a rate (7.8%) lower than that associated with lytic therapy (in patients of equivalent stroke severity) and below the 10.2% rate which was compatible with substantial net clinical benefit in PROACT II. Patients who fail to recanalize with the Retriever do die frequently. However, the observed mortality rate is exactly that expected in patients who have severe strokes and persisting proximal occlusions. Indeed, it is because the natural history of severe acute ischemic stroke is so dismal that the PROACT II trial identified so clear a benefit of recanalization despite its small sample size.
So, there is every reason to believe that the Merci Retriever works clinically, as well as technically—that it improves patient final outcomes just as it reopening occluded arteries and restores blood flow to ischemic but salvageable neural tissue.

Is a randomized trial of the Merci device needed? Absolutely. I have never had a stronger belief that a therapy helps acute ischemic stroke patients. Firmly grounded in physiology, surrogate end point data, and remarkable clinical experiences, my belief in the benefit of the device approaches absolute conviction. I feel disappointed when a patient of mine is randomized to supportive medical care rather than Merci Retriever intervention. However, belief is not knowledge and conviction is not proof. If there is one trait my generation of stroke researchers has acquired, it is a sense of humility. Over the course of my career, I have participated in trials of numerous promising treatments for acute ischemic stroke, each launched with high hopes and strong beliefs. My personal record for success is 1 win (aspirin) and roughly 39 losses. I have learned the hard way the difference between belief and knowledge. A first in class device like the Merci Retriever requires a randomized, controlled trial with a clinical end point to demonstrate benefit. Technical end point, uncontrolled trials are appropriate for 2nd, 3rd, and later in class devices that modify proven treatment strategies, but not for the first-ever test of a new treatment strategy.

Accordingly, it is imperative that randomized clinical trials of the Merci Retriever be performed. The ongoing National Institutes of Health (NIH)-funded MR RESCUE (Merci Retrieval versus conventional supportive care) and IMS 3 (IV tPA+endovascular intervention versus IV tPA alone) trials must receive the support and referrals of neurologists and neurointerventionalists. Only then will we know what I (and you, dear Reader) already believe—that the Merci Retriever works clinically as well as technically.

References

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