In this issue, Baker and colleagues (1) review the available evidence for using neurothrombectomy devices to treat acute ischemic stroke. This review, performed by the University of Connecticut/Hartford Hospital Evidence-based Practice Center (funded by the Agency for Healthcare Research Quality of the U.S. Department of Health and Human Services), identified 87 primary studies of neurothrombectomy devices. Of the studies, 62 were case reports or series and only 18 were prospective cohorts; 3 of these reported blinded assessments of clinical outcomes. Existing studies have focused on recanalization end points rather than final health outcomes. The authors conclude that there is uncertainty about the types of patients who are most likely to derive clinical benefit from mechanical revascularization, and they call for randomized trials of neurothrombectomy. The field of acute ischemic stroke is at a critical juncture, with a dire need for more therapies established by randomized trials.

Currently, we have just 1 established therapy: intravenous administration of recombinant tissue plasminogen activator (rt-PA) within 4.5 hours of ischemic stroke symptom onset (2, 3). Although this therapy has a substantial effect on clinical outcomes by leading to 1 fewer disabled patient for every 8 patients treated within 3 hours, it still leaves more than half of treated patients disabled. It is linked to Centers for Medicare & Medicaid Services (CMS) reimbursement of approximately $16 000 to hospitals (4). In addition, 1 small, randomized trial and a meta-analysis of 3 independent trials suggest clinical benefit associated with intra-arterial administration within 6 hours of stroke onset of a lytic that is no longer commercially available (recombinant prourokinase) (5, 6). On the basis of these data, endovascular delivery of a different lytic agent, rt-PA, is now used as a treatment option without specific additional reimbursement from CMS beyond that of intravenously delivered rt-PA. Finally, we have neurothrombectomy devices, the subject of Baker and colleagues’ review, which offer great hope for more effectively and more rapidly achieving recanalization of occluded proximal cerebral arteries.

Unfortunately, we lack randomized trials to document that neurothrombectomy devices improve patient outcomes. Single-group prospective studies of both the MERCI Retriever (Concentric Medical, Mountain View, California) and the Penumbra System (Penumbra, Alameda, California) have shown reasonable safety and possibly improved outcomes compared with historical controls treated with heparin alone (7–9). Both have received 510(k) clearance from the U.S. Food and Drug Administration (FDA), based on similarity to predicate devices, as a way to restore blood flow in previously occluded arteries and are linked to CMS hospital reimbursement of approximately $28 000 (4).

The literature on the use of endovascular device therapies for acute ischemic stroke leaves us with more questions than answers. Both FDA-cleared devices are labeled for initiation within 8 hours of stroke symptom onset, on the basis of uncontrolled studies. Yet, we do not know when ischemia becomes irreversible in most patients, and no data support a clinical benefit of initiating recanalization beyond 6 hours by any method. Eight hours is probably far too late to derive benefit for at least some patients (10, 11). Some clinicians advocate using multimodal imaging studies to identify patients who present more than 8 hours after stroke onset with potentially reversible injury, but these methods remain unvalidated (12). Although available data suggest that recanalization is helpful, we do not know whether the patients in whom recanalization is attempted but fails, or is achieved too late, are harmed. Furthermore, recanalization alone, a common study end point, is certainly only 1 piece of the puzzle. Current data show a striking discrepancy between technically successful recanalization (43% to 100%) and good clinical outcome (21% to 48%) at 3 months. It should also be noted that the quality of available studies is difficult to ascertain and is believed to vary.

Despite uncertain evidence, use of endovascular device therapies is increasing in the United States. According to Medicare Provider Analysis and Review databases, the use of embolectomy has more than doubled from 2007 to 2009 and now comprises 11% of acute stroke treatments (13). At the same time, ongoing randomized studies are struggling to meet recruitment goals (14, 15). Physicians may decline to participate in randomized studies for various reasons.

Individual physicians may be so convinced that a given treatment works that they see randomization as unethical. Further education is needed to help clinicians understand how to choose among therapies in an evidence-based manner. A hierarchy for choosing among treatment options has been proposed: 1) standard care based on high-level evidence (from randomized trials); 2) a randomized clinical trial, if no standard is proven; 3) a nonrandomized registry, if no trial is available; or 4) consensus-based guidelines and personal experience, if no registry is available (16).

Yet, even physicians who understand evidence-based medicine may find that participation in trials can create administrative, political, and financial challenges. A hospital administrator who has just developed a neurointerventional program for his or her cutting-edge stroke center may find that supporting randomization of patients to medical therapies is counterproductive for referrals and
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requests a confusing message to the community regarding the necessity of the program. From a financial perspective, current randomized trials of acute stroke lead to hospital reimbursement based on the treatment group of randomization. Thus, the hospital may turn away the neurothrombectomy-related payment of $28,000 in favor of either the stroke-with-thrombolysis–related payment of $16,000 or the stroke-without-thrombolysis–related payment of $10,000. Device registries, in contrast, allow collection of the neurothrombectomy-related payment for each case, in addition to further payment for data collection.

The uncertainty about the effectiveness of neurothrombectomy is unsettling. If neurothrombectomy is clinically effective, then current rates of use are distressingly low, and resources must be devoted to making this therapy available to all who would benefit. There are good reasons to believe that neurothrombectomy devices may be superior to intravenous rt-PA during the 4.5-hour window or medical management beyond 4.5 hours. Baker and colleagues (1) show that technically successful recanalization is the strongest predictor of good clinical outcome and that the FDA-cleared devices seem to achieve this more frequently. However, if neurothrombectomy devices do not provide net benefit beyond that of intravenous rt-PA, then the current use of these devices is wasteful and perhaps even harmful. Medicine provides many examples of promising therapies based on strong nonrandomized data that ultimately fail to fulfill their promise when subjected to rigorous randomized trials (17, 18). Delays in recanalization related to mobilization of neurointerventional teams may diminish its benefits compared with thrombolytic therapy. Stroke may mimic the myocardial infarction experience such that if the time from door to endovascular treatment is greater than 90 minutes, intravenous thrombolysis alone is of greater benefit than any attempt at endovascular treatment before 6 hours. Baker and colleagues (1) show that technically successful recanalization is time-dependent. Neurology. 2009;73:1066–72.

Instead of adding patients to further case series or registries, we should devote efforts to conduct definitive randomized trials. It is premature to compare different devices until we first establish the clinical benefit of neurothrombectomy over thrombolysis. Until then, expansion of the necessity of the program. From a financial perspective, current randomized trials of acute stroke lead to hospital reimbursement based on the treatment group of randomization. Thus, the hospital may turn away the neurothrombectomy-related payment of $28,000 in favor of either the stroke-with-thrombolysis–related payment of $16,000 or the stroke-without-thrombolysis–related payment of $10,000. Device registries, in contrast, allow collection of the neurothrombectomy-related payment for each case, in addition to further payment for data collection.

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Instead of adding patients to further case series or registries, we should devote efforts to conduct definitive randomized trials. It is premature to compare different devices until we first establish the clinical benefit of neurothrombectomy over thrombolysis. Until then, expansion of the use of neurothrombectomy is unjustified.

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Potential Conflicts of Interest: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M11-0028.

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