For years after the US Food and Drug Administration approved intravenous recombinant tissue-type plasminogen activator (rtPA) for acute ischemic stroke, my friend, Lou Caplan, argued eloquently that thorough knowledge of each patient’s vascular anatomy must be obtained before administering a potentially dangerous thrombolytic; I argued the opposite in countless hallway, pub, and platform debates with Lou and others. Because time is brain, I believed, nothing should delay prompt thrombolysis. Jeff Saver estimated that for every 1-minute delay, an ischemic brain loses 1.9 million neurons. Because vascular imaging involved invasive angiography, or time-consuming transcranial Doppler, it was easy to oppose vascular imaging before thrombolysis. However, then rapid, reliable CT angiography and CT perfusion came along, and I succumbed—who could ignore those beautiful perfusion images? It appeared that finally we had the means to select patients for thrombolytic therapy rationally and thus perhaps to reduce the risk of hemorrhage and simultaneously to increase the chance of benefit. After reviewing hundreds of CT angiography/CT perfusion scans, however, my experience now suggests that the decision to administer intravenous rtPA still requires only 3 things: a well-known time of onset, a noncontrast head CT showing no blood, and a blood pressure in the target range. (Other criteria remain the subject of ongoing debate.) Vascular imaging before 3 hours (4.5 hours in medically advanced countries) does not routinely alter the thrombolytic decision—although the odds of benefit decline with each passing minute. Analysis of the original National Institute of Neurological Disorders and Stroke data showed no clinically identifiable subgroup that should be deprived of intravenous thrombolytic therapy, so vascular imaging is unlikely to refine patient selection for either intravenous, or more tempting, for intraarterial intervention. Although breathlessly advocated during myriad slide shows—“Here’s another case …”—the value of invasive intervention has no substantiation from rigorous, controlled clinical trials. Consider the talismanic carotid “T” or proximal M1 occlusion: despite assurances from our interventional colleagues that intravenous rtPA will “never open that,” I have many anecdotes of my own to the contrary. How does a puny intravenous infusion lyse a long segmental occlusion? In some cases, the large clot burden may be “fresh” and easily amenable to intravenous lytics; in other cases, a relatively small clot may simulate a larger clot by impeding contrast flow into the proximal arterial segment. In the interest of time, therefore, the patient should receive the proven therapy without delay. Once the rtPA is running, however, vascular imaging might very well alter the next few hours—and hopefully long-term outcome—for the patient. After standard therapy has begun, persistent lack of clinical response could prompt careful characterization of the occlusion location and the extent and sources of collateral flow in hopes of designing an effective next step. For example, documented M1 occlusion might justify consideration of a clinical trial of intra-arterial therapy after the intravenous treatment. Until and unless the Interventional Management of Stroke (IMS) 3 trial is completed, however, the appropriate management of proximal occlusions remains speculative and thus patients should be offered the trial or be informed of the unproven nature of the proffered “rescue” treatment. Similarly, collateral flow augmentation benefits some patients anecdotally, but enrollment in a trial would be a more ethical strategy. After vascular imaging, one might consider perfusion imaging, but like vascular imaging, the value of “penumbra” imaging remains in doubt until other well-designed trials such as MR and Recanalization of Stroke Clots Using Embolectomy (MR RESCUE) are completed. Mismatch between perfusion images and tissue destruction images may identify salvageable tissue eventually, but we not only lack definitive proof, but many examples exist to show that current techniques lack sufficient positive and negative predictive value. Thus, like with vascular imaging, perfusion imaging should be delayed until after standard therapy has begun and then offered preferably as part of a randomized clinical trial. To consider the case specifically, after 4 hours, the patient has a low and declining odds of good outcome; additional delay reduces even further her chance of benefit. Neither identification of the vascular occlusion site nor characterization of...
the perfusion status can influence decision-making that is guided by rigorous data. Once standard therapy has begun, however, further imaging might very well aid the critical physician in tailoring further therapy to her benefit.

Disclosures
None.

References

Key Words: safety ■ stroke ■ thrombolysis ■ treatment
Advanced Brain Imaging Studies Should Not Be Performed in Patients With Suspected Stroke Presenting Within 4.5 Hours of Symptom Onset
Patrick D. Lyden

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