Imaging-based selection of patients for acute stroke treatment

Is it ready for prime time?

Emmanuel Carrera, MD
Max Wintermark, MD

Correspondence to
Dr. Carrera:
Emmanuel.Carrera@hcuge.ch

Neurology® 2017;88:2242–2243

Historically, brain imaging in acute stroke has sought to exclude brain hemorrhage in order to allow therapy aiming at recanalization of the occluded intracranial artery. The National Institute of Neurological Disorders and Stroke study, published in 1995, found a clinical benefit of IV thrombolysis in acute stroke after exclusion of brain hemorrhage based on noncontrast CT (NCCT).[1] More than 20 years later, the decision at most centers whether to give thrombolysis within the first 4.5 hours remains based on NCCT; often, the bolus of recombinant tissue plasminogen activator (rt-PA) is administered in the CT scanner suite even before vascular and perfusion imaging is performed to avoid any delay. While acknowledging that time is brain, the experienced stroke neurologist often feels that a more precise selection of patients, at the time of the decision for acute revascularization therapy, would be clinically beneficial. The publication of trials demonstrating higher rates of functional independence at 3 months in 2 studies (SWIFT PRIME[2] and EXTEND-IA[3]) that required the demonstration of substantial ischemic penumbra for inclusion (60% and 71%, respectively) compared to those that did not (MR CLEAN, 33%[4]; REVASCAT, 44%[5]; and ESCAPE, 53%[6]) underscores the dilemma. Better selection can improve patient outcome and avoid futile and costly endovascular treatments.

The imaging-based selection of acute stroke patients relies on the physiologic concept that part or the totality of the ischemic brain tissue may escape infarction if perfusion is restored quickly enough.[7] The challenge, at time of treatment, is to distinguish tissue that can be potentially salvageable (the ischemic penumbra) from the definitively infarcted tissue (the ischemic core). A patient with a large penumbra and a small core could benefit more from reperfusion. Despite a clear concept and great interest in the field, no consensus exists regarding how and when to base therapeutic decisions on perfusion imaging.

In this issue of *Neurology*®, Demeestere et al.[8] compared the value of 2 CT-based techniques to identify the ischemic core, and found that perfusion CT identifies the ischemic core better than the Alberta Stroke Program Early CT Score (ASPECTS) (based on NCCT).[9] In their study, the gold standard was the lesion delineated on a diffusion-weighted sequence (MRI), acquired within 1 hour of CT. Because of its use in many hospitals worldwide, investigation of the value of CT-based measures is particularly relevant. In the current study, the authors focused on 2 imaging techniques that have never been compared head-to-head in this setting.

Brain perfusion imaging (using CT or MRI) can reliably identify the ischemic penumbra and the ischemic core.[10] Different measures extracted from the time curves depicting the wash-in and wash-out of a bolus of contrast medium can describe brain perfusion (figure). The most reliable thresholds for determining the core infarction are an absolute cerebral blood volume of <2.0–2.2 mL/100 g and a decrease in cerebral blood flow (CBF) by 38%–50% relative to the normal hemisphere.[11–14] In the current study, the authors defined the infarct core as the brain region with a relative CBF of less than 30% (compared to the contralateral hemisphere) in an area with a delay time of more than 3 seconds.

One of the common mistakes in the interpretation of perfusion maps is to forget that the viability of the tissue is not directly assessed but inferred from the perfusion measures, used as a surrogate of brain metabolism. As an example, an occlusion of an artery may induce a severe alteration of the perfusion in the corresponding territory, which will not evolve into infarction if recanalization occurs early enough. The duration of occlusion is an important factor that affects the volume of the ischemic core and its evolution to final infarct.

The ASPECTS ranges from 10 to 1 depending on the extent of the hypodensity on NCCT.[9] Hypodensity caused by an increased net water uptake corresponds to severe ischemia that results in infarction. As the authors point out, the issue of intersubject variability in the assessment of ASPECTS remains unresolved.

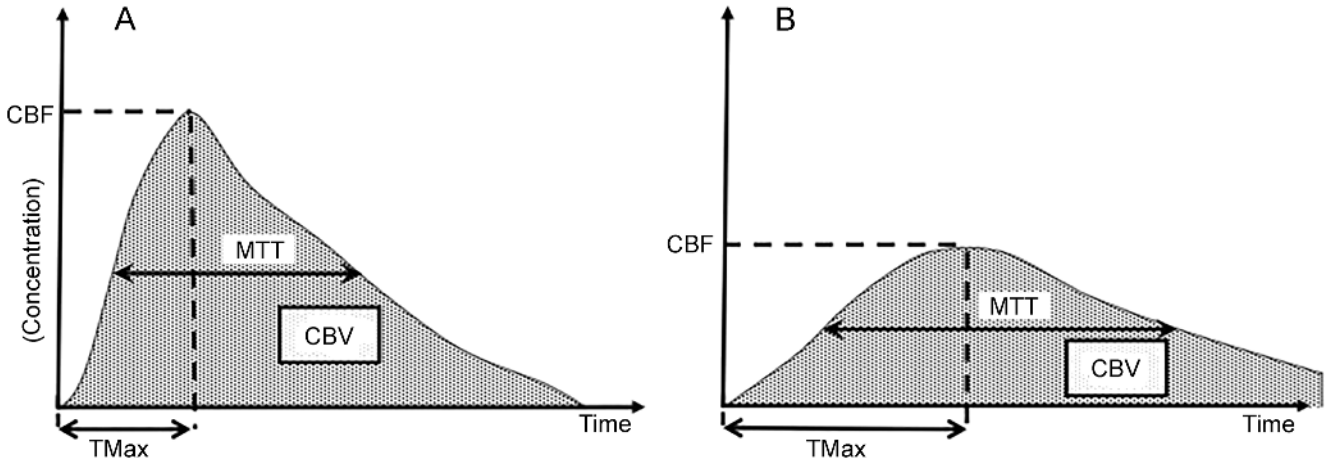
Should we change our practice based on the results of this study? No doubt, this study represents an important step towards a better understanding of the CT imaging parameters that can help identify the ischemic

See page 2248

From the Department of Neurology (E.C.), Geneva University Hospital, Switzerland; and Department of Radiology, Neuroimaging and Neurointervention Division (M.W.), Stanford University Hospital, CA.

Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the editorial.

Figure Perfusion curves in normally perfused and hypoperfused brain tissue



(A) Normally perfused and (B) hypoperfused brain tissue. In hypoperfused tissue, the mean transit time (MTT) and the TMax are increased, whereas the cerebral blood volume (CBF) is decreased. Depending on the severity of the ischemia, the CBV (area) can be decreased (ischemic core), unchanged, or increased (ischemic penumbra).

core. However, the implementation of these results in clinical practice is challenging because of the retrospective nature of the study, the low number of included patients, and the use of an older-generation CT scanner. Future comparisons should also include multiphase CT angiography, adopted by many centers as part of their evaluation protocols for large vessel occlusion.

Within the established time window, there is no evidence today that would support excluding patients for acute IV or endovascular treatment based on perfusion imaging or ASPECTS. Beyond the established time window and in patients with unknown onset of symptoms, randomized trials, such as the Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution Study (DEFUSE) 3, still need to determine whether acute endovascular treatment also benefits patients with a favorable penumbral pattern (target mismatch) and a concordant ASPECTS.

STUDY FUNDING

No targeted funding reported.

DISCLOSURE

The authors report no disclosures relevant to the manuscript. Go to Neurology.org for full disclosures.

REFERENCES

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. Saver JL, Goyal M, Bonafe A, et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. N Engl J Med 2015;372:2285–2295.
3. Campbell BC, Mitchell PJ, Kleinig TJ, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. N Engl J Med 2015;372:1009–1018.
4. Berkhemer OA, Fransen PS, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med 2015;372:11–20.
5. Jovin TG, Chamorro A, Cobo E, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. N Engl J Med 2015;372:2296–2306.
6. Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. N Engl J Med 2015;372:1019–1030.
7. Baron JC. Mapping the ischaemic penumbra with PET: a new approach. Brain 2001;124:2–4.
8. Demeestere J, Garcia-Esperon C, Garcia-Bermejo P, et al. Evaluation of hyperacute infarct volume using ASPECTS and brain CT perfusion core volume. Neurology 2017;88:2248–2253.
9. Barber PA, Demchuk AM, Zhang J, Buchan AM. Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy: ASPECTS Study Group: Alberta Stroke Programme Early CT Score. Lancet 2000;355:1670–1674.
10. Warach SJ, Luby M, Albers GW, et al. Acute Stroke Imaging Research Roadmap III imaging selection and outcomes in acute stroke reperfusion clinical trials: consensus recommendations and further research priorities. Stroke 2016;47:1389–1398.
11. WIntermark M, Flanders AE, Velthuis B, et al. Perfusion-CT assessment of infarct core and penumbra: receiver operating characteristic curve analysis in 130 patients suspected of acute hemispheric stroke. Stroke 2006;37:979–985.
12. Wintermark M, Reichhart M, Thiran JP, et al. Prognostic accuracy of cerebral blood flow measurement by perfusion computed tomography, at the time of emergency room admission, in acute stroke patients. Ann Neurol 2002;51:417–432.
13. Campbell BC, Christensen S, Levi CR, et al. Cerebral blood flow is the optimal CT perfusion parameter for assessing infarct core. Stroke 2011;42:3435–3440.
14. Cereda CW, Christensen S, Campbell BC, et al. A benchmarking tool to evaluate computer tomography perfusion infarct core predictions against a DWI standard. J Cereb Blood Flow Metab 2016;36:1780–1789.