Cerebral perfusion in acute stroke prognostication

Go with the flow, or know with the quo?

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Most patients improve after stroke. But when dealing with individuals, clinicians are challenged to predict whether, how much, and how soon that particular patient will recover. The best predictive tool for at least 40 years has been the presenting clinical examination—the odds and the extent of recovery decrease roughly proportionally to the initial clinical severity.[1,2]

Newer technologies incorporated into the stroke workup have enabled neurologists to forecast more accurately individual stroke outcomes. Imaging and quantifying the "real estate factor"—infarct location and size—adds some confidence to stroke outcome prediction.[3] But how much does this information really tell us that we do not already know from examining the patient? More importantly, can we develop algorithms that not only improve prognostication, but also inform treatment?

Enter vascular- and flow-based imaging technologies. Visualizing acute large-vessel occlusion guides the use of thrombolytic and endovascular treatments, as well as downgrades the prognosis for recovery.[4] Visualizing at-risk brain tissue (ischemic penumbra), whether by MRI or CT-based perfusion imaging, also affects prognosis and management. A larger area of at-risk tissue (on perfusion-weighted imaging) than already infarcted tissue (on diffusion-weighted imaging) portends further deterioration, thereby providing justification for the risks of thrombolytic therapy, supportive hypertension, and (someday) neuroprotectant therapy.[5–7]

In this issue of *Neurology*®, Payabvash and colleagues[8] take a higher resolution look at brain blood flow in acute stroke—they examine differences in cerebral perfusion among 146 areas within each hemisphere, not just in peri-infarct penumbral areas. They use this information to predict recovery during the first week or 2 after stroke, thereby avoiding confounding factors such as different rehabilitation regimens that may affect 90-day outcomes. A previous study by the same group examined the relationship between regional cerebral perfusion and early improvement of aphasia.[9] The current study, using an overlapping set of patients, investigates the relationship between flow and early recovery of limb paresis.

Payabvash et al. retrospectively analyzed 80 patients with first-ever anterior circulation strokes who received CT angiography and CT perfusion scans within 9 hours of stroke onset. They analyzed which clinical factors and regional flow measurements correlate most strongly with early clinical improvement. "Early" was defined as the date of discharge from acute-care hospitalization, ranging from 3 to 23 days after stroke. "Clinical improvement" was based on whether or not the limb-specific NIH Stroke Scale component score decreased by the time of discharge. For example, if a patient presented with inability to lift the right arm against gravity (3 points), but was able to briefly get the arm off the bed (2 points) by the time of hospital discharge, this met the definition of early clinical improvement. Unlike more sensitive stroke scales such as the Fugl-Meyer Assessment, the NIH Stroke Scale does not account for fine motor skill, dexterity, or coordination.

Despite the diluting effect of these limitations, Payabvash et al. offer a multivariate predictive model that demonstrates over 80% sensitivity and specificity for accurately predicting early improvement in each limb. This is presented as an improvement in prognostic accuracy compared to the clinical examination alone.

The clinical findings of this study should surprise no one (e.g., less arm weakness at baseline correlates with early recovery). Many of the flow-based findings raise interesting questions, or perhaps raise eyebrows. For example, right arm recovery correlates partly with mean transit time of the left superior parietal

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lobule gray matter. Left arm recovery correlates partly with cerebral blood flow of the anterior lower insular cortex. In fact, most of the low-flow regions linked to early limb recovery are not in the expected motor-associated pathways, and are not identical on left and right. Furthermore, the group's previous study linked recovery from aphasia to flow in the angular gyrus and insular ribbon—two areas not known to be directly involved in language.[9]

Do these findings represent the never-ending complexity of the brain and its response to injury? fMRI studies lend support to this possibility. For example, within 48 hours after stroke, activation of 2 areas not thought of as directly motor-related, ipsilesional postcentral gyrus and cingulate cortex, correlates with motor recovery at 3 months.[10] But it is still hard to make sense of some of the observations noted by Payabvash et al. For example, why would flow in the precuneus white matter predict left leg recovery? Why would predictive areas of abnormal flow on the left not match those on the right? Why would mean transit time be the relevant flow factor in some regions, whereas cerebral blood flow takes precedence in others?

Could blood flow to these areas merely represent coincidental consequences rather than causal or predictive factors? A lot rides on the answer to this question. Better predictive tools would allow more accurate risk-benefit calculations in acute stroke management: a patient with a predicted excellent prognosis may not need to be rushed to the angiography suite for endovascular clot retrieval. But to base management decisions on such a predictive model, it would need to have a specificity of nearly 100%. Otherwise, if a patient were wrongly classified into the good-prognosis category, we would miss the window for aggressive thrombolytic intervention.

By going with the flow, Payabvash et al. undeniably shed light on a method with potential utility in stroke management and rehabilitation. But does the amount of insight gained by adding perfusion imaging to the traditional bedside evaluation justify the added time and money spent in the acute stroke setting? Until we have a truly specific and verified predictive imaging tool, we continue to rely on the clinical examination—Know with the status quo.

DISCLOSURE

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

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