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Commentary

Imaging the Pathophysiology of Infarction in the Clinical Setting

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The article by Levy et al documents the case of a comatose patient with midbasilar artery occlusion who was treated with intraarterial urokinase. Xenon CT evaluation of cerebral blood flow (CBF) was done within 1 hour of onset and repeated after thrombolysis. The initial scan, obtained during the period of basilar occlusion, showed very low CBF levels (6 mL/100 g per minute) both in the brain stem and the posterior cerebral artery (PCA) distributions bilaterally.

Reopening of the vertebrobasilar circulation was accomplished, with the exception of the distal left PCA. Immediately after treatment, brain stem and right PCA CBF values rose to hyperemic levels (60 mL/100 g per minute). Areas of the distal left PCA that remained occluded continued to show very low CBF levels, in the range of 6 mL/100 g per minute, unchanged from pretreatment values. A delayed CT scan showed an infarction confined to the area of persistently reduced CBF involving the unopened distal left PCA.

The pattern of blood flow measurements obtained by the authors before and after intraarterial thrombolysis correlated well with outcome as measured by the later observation of infarction on CT scans. Initially, CBF was significantly reduced from its normal value of 50 mL/100 g per minute throughout the territories of the occluded arteries. Repeat CBF measurement following reopening of the basilar artery documented that hyperperfusion had developed within the brain stem, an area that showed no infarction on delayed CT scans. In contrast, areas supplied by the PCA that remained occluded continued to manifest very low levels of blood flow after treatment. Infarction was seen within these portions of the PCA distribution on CT scans. CBF imaging revealed the treatment effect in moving brain stem tissue from the low CBF state associated with ischemic penumbra to the acute hyperperfusion state associated with a good outcome.

The case illustrates how basic imaging that reflects parenchymal ischemia may be obtained in the clinical setting and used to interpret the physiology underlying ischemic stroke. In this case, the information provided a basis for understanding the spatial and temporal evolution of the ischemic process and for monitoring the effects of treatment.

The authors' use of this information is an important step in moving the evaluation of ischemic brain parenchyma from the laboratory into the clinical arena. The next step will be to routinely acquire and prospectively interpret meaningful physiological information to guide stroke treatment in individual patients.

Great strides have been made in understanding the chain of events that affects the CNS during ischemia. These events have significant implications for the time course of ischemic tissue viability and therefore for determining the usefulness and risk of stroke therapies. So far, this information has lacked clinical application in acute stroke treatment. The shortcoming has resulted from our evolving understanding and attitudes regarding both the imaging and treatment of acute stroke.

Imaging of CNS ischemia has been the object of considerable recent research. To date, however, the correlation between imaging findings and clinical outcome in stroke has consistently been relatively weak. Simple determination of blood flow values is important but has little impact in determining the salvageability of ischemic tissue. Other indexes, such as oxygen extraction fraction, cerebral metabolic rates, diffusion coefficients, and perfusion, are still investigational but require validation with clinical outcome. In the past, little in the way of acute stroke treatment was available, and such imaging issues were of largely academic interest without apparent clinical application.

The need for emergent treatment of acute stroke is now obvious, and the need for accurate, timely imaging assessment of ischemic parenchyma is apparent (1). As one of the newest areas in all of medicine, stroke treatment is truly in its infancy. Stroke intervention efforts have so far been limited in scope, focusing on single aspects of the overwhelmingly complex pathophysiology of brain ischemia. But stroke therapy is evolving to synthesize a more coherent and precise response to the dynamic physiology of ischemia. This will require multifaceted treatment protocols involving reopening of occluded vessels, neuroprotective agents, and potentially other pharmacologic and perfusional treatments all designed to salvage ischemic brain (2, 3).

To optimize therapy, we must know to what extent the ischemic pathophysiology is progressing or responding to treatment in the individual patient.

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Proper understanding of such data is important for assessing the potential of ischemic brain and for permitting risk-benefit analysis prior to treatment. Acquiring data during and after treatment is necessary for monitoring the effects of therapy and for determining a therapeutic end point. To date, our clinical determinations of brain viability and therapeutic end points have been crude at best, based on empirically determined "time windows," derived from estimated times of stroke occurrence and presumed rates of infarction development. Treatment decisions currently rely on application of these estimates of the progression of ischemia.

Considerable data indicate that rather than occurring in an all-or-none fashion, within a rigid time frame, progression from treatable ischemia to irreversible infarction occurs at rates that vary widely among stroke mechanisms and individuals, and even within the ischemic area of brain (4). In fact, the single important time window for a patient is related only to the progression of his or her pathophysiology and to the type of intended treatment. It is in the evaluation of that patient's progression of ischemia that physiological neuroimaging will be essential.

The guidance of stroke therapy provides neuroradiologists the opportunity to remain indispensable contributors to the management of this most common neurologic disease. Such guidance will also place increasing demands on physiological imaging techniques and require increased involvement by the neuroradiologist. If imaging is to be useful, however, it must not only be relevant to management and outcome but obtained in the clinical setting. This means in *real* time in *real* patients. The physiological information provided by positron emission tomography (PET) is impressive, but equally impressive is the difficulty in clinical PET scanning of the sick patient (5). Similarly, the xenon CT method so effectively used by the authors of the preceding article has been found by other investigators to be difficult to apply with as much accessibility and reliability. Single-photon emission CT using blood flow tracers has found clinical application in acute ischemia, and its use may warrant further investigation (6, 7). Functional MR imaging has made great strides in the past several years in the evaluation of ischemic brain parenchyma (8–10). These new techniques, combined with the widespread availability of MR imaging, may hold the most promise for obtaining real-time data on ischemia in the individual patient. Whatever the method, correlation with clinical outcome and availability will be major determinants of its usefulness.

The debilitating effects of stroke are well documented, and some of the most devastating are those of basilar occlusion. The work by Levy et al is perhaps the initial step in imaging the pathophysiology of infarction and in using the findings as a guide to clinical decision making in stroke therapy.

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