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## Diffusion-weighted Imaging as a Surrogate Marker for Stroke as a Complication of Cerebrovascular Procedures and Devices

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*AJNR Am J Neuroradiol* 2001, 22 (7) 1234-1235

<http://www.ajnr.org/content/22/7/1234>

This information is current as of June 25, 2025.

sence of descent of the cerebellar tonsils or dural enhancement. Given the proper clinical setting, the ancillary findings of CSF hygroma, epidural venous collections, paraspinal fluid collections behind the C1-C2 level, and intracranial and extracranial venous dilatation are clues to the diagnosis. If one remembers that the epidural space is a gutter within which extrathecal CSF can travel long distances from the site of egress, an understanding of the MR imaging appearance of CSF hypovolemia becomes clear.

A search for the leak must first begin with fat-suppressed fast spin-echo imaging of the spine. In the absence of a frank leak, plain-film myelography, performed while the patient is in the decubitus position, is helpful because CT myelography, obtained after a low-dose injection of contrast material, is often insufficient for identification of the site of a small CSF fistula. We've had the occasion to watch the epidural contrast leak several vertebral body segments away from the site of CSF fistula in the course of 3 to 5 minutes. Our approach to these difficult patients who do not respond initially to epidural blood patch include a simultaneous puncture for myelography as well as isotope cisternography. Myelography is performed, preferably from the lumbar region, with attention to the tho-

racic spine. The patient is placed in a decubitus position and cross-table anteroposterior films are obtained every minute for 5 minutes. When the radiologist is satisfied a leak is not occurring, the patient is repositioned on his opposite side, and the films are repeated. CT myelography (3–5 mm) is then performed from the cervical through the lumbar region.

Because the imaging manifestations of SIH have become well known, many patients have been diagnosed who otherwise would have been misdiagnosed with migraine, headache of unknown origin, aseptic meningitis, or subdural hematomas. Attention to the myriad manifestations of CSF hypovolemia both intracranially and extracranially will prevent such errors of diagnosis and facilitate prompt treatment of CSF fistula.

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## Diffusion-weighted Imaging as a Surrogate Marker for Stroke as a Complication of Cerebrovascular Procedures and Devices

Ischemic stroke may occur as a complication of any vascular intervention from the heart to the head. These interventions include diagnostic arteriography, coronary revascularization, valve repair, carotid endarterectomy or angioplasty, and endovascular obliteration of aneurysms by use of detachable coils. Nearly all strokes associated with these procedures are attributable to embolic material lodging in distal cerebral arteries.

Efforts to reduce the stroke risk from cerebrovascular interventions are limited by several complicated factors. First, the nature of the embolic material generated during these procedures varies widely and, consequently, the potential for causing ischemic injury to the brain is variable. Embolic material can range from air bubbles, microscopic cholesterol or lipid particles, to larger fragments of atherosclerotic plaque and organized thrombus (1–3). Second, the embolic insult can vary in the total number of particles in the temporal profile of the particle shower. A slow trickle of microscopic particles may have less potential for ischemic injury than the same number of particles delivered in a sudden shower. Third, the potential for an embolic event to result in injury depends on the condition of the cerebral tissue. Given an identical embolic insult, cerebral tissue with reduced perfusion pres-

sure (due to proximal stenosis or occlusion, for example) has a greater risk of permanent ischemic injury than does brain with normal perfusion pressure. Finally, the low frequency of stroke in these procedures makes it difficult to perform studies with adequate power to detect changes in stroke risk with different devices or pharmacological adjuncts.

A surrogate marker for clinical stroke that occurs at a greater frequency would have considerable utility in studies of stroke risk reduction during neurointerventional procedures. At present, there are two complementary methods that have potential for this application: transcranial Doppler (TCD) (4) and, as discussed by Jaeger et al in this issue of the *AJNR* (page 1251), diffusion-weighted imaging (DWI).

The primary advantage of TCD is its capability for real-time monitoring of embolic events during the procedure. Embolic signals, with no clinical sequelae, have been detected by TCD in the middle cerebral artery stem among patients with symptomatic carotid stenosis, artificial heart valves, and polycythemia rubra vera. Asymptomatic signals have also been recorded during diagnostic arteriography, carotid endarterectomy or angioplasty, and endovascular treatment of aneurysms. The sen-

sitivity of TCD to small, clinically benign, embolic particles and the potential for real-time monitoring has been exploited in studies of right-to-left cardiac shunts, such as patent foramen ovale. Microbubbles injected in an arm vein can be identified with similar sensitivity in the middle cerebral artery among patients with patent foramen by use of TCD as with cardiac echocardiography. The real-time monitoring capability of TCD could be used to determine which steps during a procedure are associated with the greatest number of embolic events. Some evidence suggests that a large number of cerebral emboli during coronary bypass surgery occur with cross-clamping of the aorta. In carotid angioplasty and stenting, this could be during predilation or stent deployment or post stent angioplasty. Information regarding the relative embologenic potential of each step could guide the development or use of devices to prevent this occurrence. The primary drawback to TCD, with current technology, is its inability to distinguish either the nature or size of the embolic material as well as the effect of the emboli on the brain itself. Dual-frequency TCD techniques to distinguish air bubbles from solid material are under development.

DWI, as reported in this issue and prior studies, offers important complementary information: a quantitative assessment of ischemic injury (5, 6). DWI lesions can be quantified by size and number. The frequency of these lesions is in great excess to frequency of ischemic stroke. In these regards, DWI may serve as a useful surrogate endpoint for clinical stroke. Jaeger and colleagues report new DWI lesions in eight of 25 vascular territories after angioplasty of atherosclerotic lesions of the carotid, vertebral, or innominate arteries. They performed DWI before and 24 hours after the procedure. No clinical neurologic deficits were observed. Similar results were reported by Rordorf et al (5) after endovascular treatment of 14 intracranial aneurysms by means of Guglielmi detachable coils. DWI lesions were found at 48 hours in eight patients. One of the eight patients had clinical evidence of a stroke. Bendszus et al (6) reported new DWI lesions in 17 of 66 patients undergoing diagnostic cerebral arteriography.

One could argue that clinically silent lesions may not matter or that clinical stroke is a different entity than these small, silent lesions. However, it is much

more likely that clinically evident stroke represents the tip of the iceberg of embolic ischemic events. The literature concerning significant neuropsychological changes in the absence of clinical stroke occurring with cardiopulmonary bypass procedures and strongly associated with probable microembolic events support this hypothesis (2, 7).

In summary, DWI may serve as a useful surrogate endpoint for ischemic stroke in the investigation of new devices, drugs, and techniques for cerebrovascular intervention. The frequency of new lesions by discovered by DWI appears to be quite high for angioplasty and aneurysm treatment. The DWI lesions are measurable in both size and number. These factors will provide good statistical power for the detection of differences in event rates between control and experimental groups. The evidence linking DWI lesions with ischemic injury is strong. TCD also plays a useful and complementary role in these investigations with its capability for real-time monitoring of embolic events.

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## The Missing Element

Progress in the development of effective stroke therapies has been generally disappointing. The results of initially promising neuroprotective drugs applied in large clinical trials have been unimpressive (1), and the results of large thrombolysis ther-

apy trials have been inconclusive. A missing element in the development of effective stroke therapies has been the lack of available diagnostic tools capable of assessing the viability of brain tissue during the acute stages of evolving stroke. The