

EARLY CAROTID ENDARTERECTOMY AFTER ISCHEMIC STROKE IMPROVES DIFFUSION/PERFUSION MISMATCH ON MAGNETIC RESONANCE IMAGING: REPORT OF TWO CASES

Satish Krishnamurthy, M.D., M.Ch.

Pennsylvania State University—Milton S. Hershey Medical Center, Hershey, Pennsylvania

David Tong, M.D.

Stanford University Medical Center, Stanford, California

Kevin P. McNamara, M.D.

Pennsylvania State University—Milton S. Hershey Medical Center, Hershey, Pennsylvania

Gary K. Steinberg, M.D., Ph.D.

Stanford University Medical Center, Stanford, California

Kevin M. Cockroft, M.D.

Pennsylvania State University—Milton S. Hershey Medical Center, Hershey, Pennsylvania

Reprint requests:

Kevin M. Cockroft, M.D., Division of Neurosurgery, Pennsylvania State University—Milton S. Hershey Medical Center, PO Box 850, MC H110, Hershey, PA 17033-0850.

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OBJECTIVE AND IMPORTANCE: The functional magnetic resonance imaging techniques of diffusion-weighted imaging and perfusion-weighted imaging allow for ultra-early detection of brain infarction and concomitant identification of blood flow abnormalities in surrounding regions, which may represent brain “at risk.”

CLINICAL PRESENTATION: We report two patients with acute ischemic stroke associated with ipsilateral high-grade carotid stenosis. The first patient, a 64-year-old woman with a remote history of ischemic stroke and a vertebral artery aneurysm, presented with worsening of her preexisting right hemiparesis. The second patient, another 64-year-old woman with known multiple intracranial aneurysms and bilateral high-grade internal carotid artery stenosis, was admitted for the elective microsurgical clipping of an enlarging giant left carotid-ophthalmic artery aneurysm. Postoperatively, she developed right hemiparesis and mild aphasia. Both patients showed progressive worsening of their neurological deficits in the setting of small or undetected diffusion-weighted imaging abnormalities and large perfusion-weighted imaging defects.

INTERVENTION: After prompt carotid endarterectomy, symptoms in both patients resolved or improved. Follow-up magnetic resonance imaging scans demonstrated resolution or significant improvement in the perfusion abnormalities in both patients.

CONCLUSION: Carotid endarterectomy in the setting of diffusion-weighted/perfusion-weighted imaging mismatch can lead to improvement in cerebral perfusion as evidenced by resolution of the perfusion-weighted imaging lesion. Diffusion/perfusion magnetic resonance imaging may be useful in identifying patients with severe neurological deficits but without large territories of infarction who may safely undergo early surgical revascularization.

KEY WORDS: Acute stroke, Carotid endarterectomy, Carotid stenosis, Diffusion-weighted magnetic resonance imaging, Perfusion-weighted magnetic resonance imaging

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Whereas computed tomography may not provide an accurate analysis of infarct size for several days, newer magnetic resonance imaging (MRI) techniques allow ultra-early detection of brain infarction. Diffusion-weighted imaging (DWI) can rapidly detect ischemic brain lesions, and a complementary technique, perfusion-weighted imaging (PWI), can identify blood flow abnormalities (1, 14). Such acute information may prove valuable in selecting patients for early surgery and predicting future neurological outcomes. We describe two patients with progressive ischemic symptoms leading to severe neurological deficits. Both patients had small

or nonexistent lesions as revealed by DWI but large lesions as revealed by PWI. After early carotid endarterectomy, neither patient had a significant complication. Both patients subsequently demonstrated resolution of their DWI/PWI mismatch with improvement in neurological function.

CASE REPORTS

Patient 1

A 64-year-old woman with a remote history of ischemic stroke and Hunt and Hess Grade IV subarachnoid hemorrhage from a right vertebral artery aneurysm presented with wors-

ening of her preexisting right lower extremity weakness. At baseline, her right lower extremity strength was graded as 4/5 and she was able to walk with a cane. At presentation, she barely had antigravity strength and had considerable difficulty walking. The patient's medical history also was remarkable for hypertension and non-insulin-dependent diabetes mellitus. A DWI scan obtained on her first hospital day did not reveal evidence of a new acute infarct. A magnetic resonance angiogram obtained at the same time showed high-grade (>90%) stenosis of the left internal carotid artery (ICA) just distal to the bifurcation (Fig. 1A). The patient's right lower extremity paresis fluctuated initially; then it progressively worsened on hospital Day 5 to the point that she no longer had antigravity strength and could not walk. A follow-up DWI scan obtained on hospital Day 5 revealed a small ischemic lesion in the left anterior cerebral artery distribution (Fig. 1B). However, a concomitant PWI scan revealed a much larger region of low perfusion in the same hemisphere (Fig. 1C). On the basis of the observed DWI/PWI mismatch, which suggested only a relatively small area of infarcted tissue, early surgical revascularization was recommended. Postoperatively, the patient's neurological deficit improved to baseline. A follow-up MRI scan obtained 1 week later demonstrated

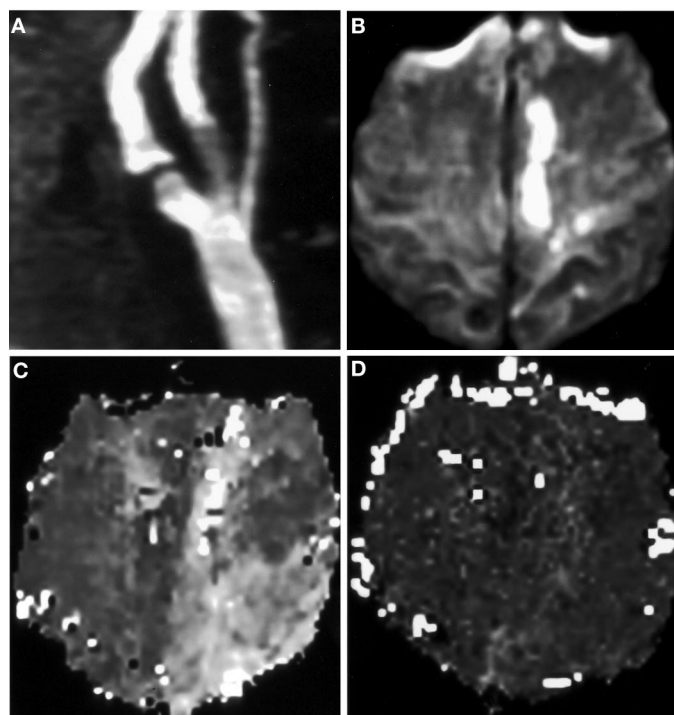


FIGURE 1. Patient 1. A, cervical magnetic resonance angiogram demonstrating greater than 90% stenosis of the left ICA. B, DWI scan obtained 5 days after the onset of symptoms, showing a small ischemic lesion in the left anterior cerebral artery distribution. C, PWI scan from the same series, revealing a much larger region of low perfusion in the left hemisphere. D, follow-up PWI scan obtained 1 week after emergent carotid endarterectomy, showing normal (symmetric) perfusion to the left hemisphere.

normal perfusion in the left hemisphere (Fig. 1D). There was no change in the diffusion abnormality.

Examination Technique

All MRI scans for Patient 1 were obtained using a 1.5-T GE Signa MRI scanner (General Electric, Milwaukee, WI) at the Stanford University Medical Center. DWI was performed using echo planar imaging (EPI) technique. Multislice whole-brain images were obtained in 12 slices: TR, 6000 milliseconds; TE, 110 milliseconds; field of view, 24 cm; slice thickness, 5 mm with a 2.5-mm skip between slices; image size, 128 × 128. The *b* values were 0 and 741. DWI images were acquired in *x*, *y*, and *z* planes, with and without an inversion pulse (fluid-attenuated inversion recovery sequence). EPI diffusion images were processed to generate average (trace) apparent diffusion coefficient maps. The *b* values (0 and 741) were measured twice to improve the accuracy of the apparent diffusion coefficient determination. PWI was performed using the same EPI MRI equipment after the injection of 30 ml of gadolinium (0.2 mmol/kg). PWI acquisition values were TR, 2000 milliseconds and TE, 40 milliseconds and 35 time points. Other parameters were the same as for DWI. The total imaging time was approximately 3 minutes. Perfusion images were processed to generate maps of time to bolus peak (TTP), which is the time from the start of the scan to the peak bolus effect, and regional cerebral blood volume, which is the integral of the area under the bolus transit curve. Approximately 400 individual scans were acquired within 3 minutes. The total scanning time for the entire protocol was 15 to 20 minutes.

Patient 2

A 64-year-old woman was admitted for elective clipping of an enlarging giant left carotid-ophthalmic artery aneurysm. Her medical history was remarkable for coronary artery disease, a previous myocardial infarction, and a previous coronary angioplasty, as well as multiple intracranial aneurysms and bilateral high-grade (80–90%) ICA stenoses. Preoperative neurological examination revealed a left visual field defect. Intraoperatively, temporary occlusion of the left ICA in the neck and suction decompression of the aneurysm were required. During this temporary occlusion procedure, a significant decrement in somatosensory evoked potentials from the patient's right arm (decreased amplitude >50%) was noted. This improved somewhat toward the end of the procedure, but it did not return to baseline. Postoperatively, the patient had mild expressive aphasia and mild right hemiparesis (right pronator drift with approximately 4+/5 strength). A computed tomographic scan obtained on the first postoperative day revealed no new infarcts. A postoperative cerebral angiogram obtained the same day demonstrated complete occlusion of her giant aneurysm without evidence of occlusion or stenosis of the adjacent intracranial carotid. In addition, there was no change in her high-grade cervical ICA stenosis (Fig. 2A). Her examination results initially fluctuated, then progressed to hemiplegia and a dense expressive aphasia on the

second postoperative day. A repeat computed tomographic scan obtained at that time revealed a small hypodensity in the left caudate (Fig. 2B). A subsequent MRI scan obtained the same day did not demonstrate a significant diffusion defect (Fig. 2C), although her numerous aneurysm clips generated considerable metallic artifact. PWI revealed decreased perfusion throughout the entire left hemisphere (Fig. 2D). On the basis of her deteriorating clinical condition and the DWI/PWI mismatch, she underwent emergent left carotid endarterectomy later that day. Postoperatively, she had no immediate change in her neurological function. A repeat MRI scan obtained 3 days after endarterectomy revealed a profound improvement in the perfusion of the left cerebral hemisphere and no new diffusion defect (Fig. 2E). During the next few days, the patient's aphasia and hemiparesis gradually improved. At the time of discharge, 19 days after her first operation, the patient had no demonstrable weakness on her right side.

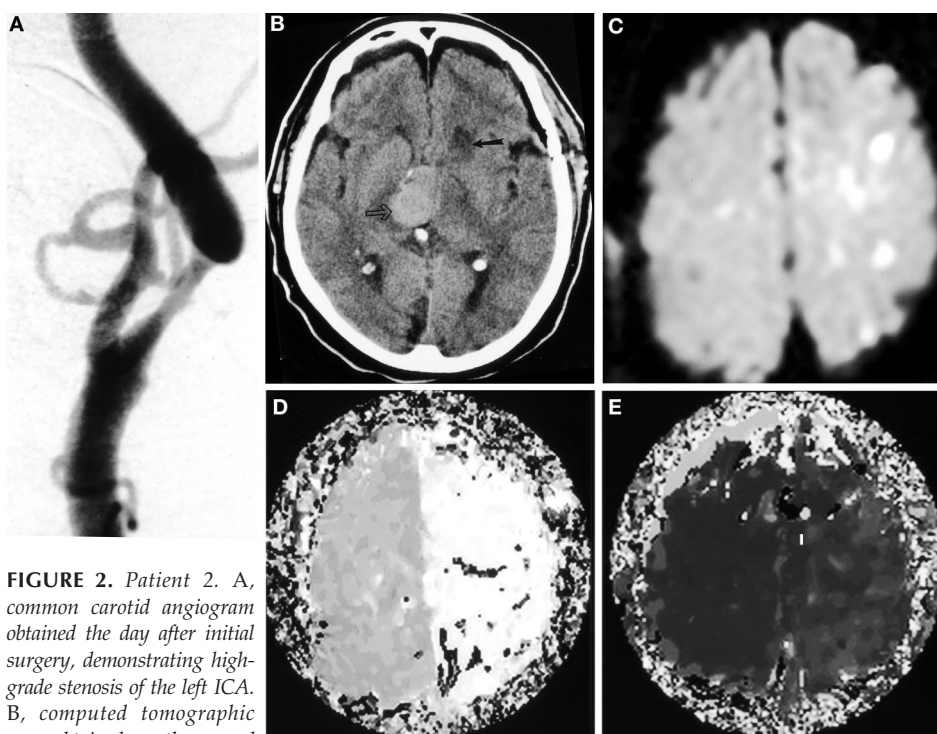


FIGURE 2. Patient 2. A, common carotid angiogram obtained the day after initial surgery, demonstrating high-grade stenosis of the left ICA. B, computed tomographic scan obtained on the second postoperative day, revealing a small hypodensity in the left caudate (solid arrow). The patient's giant basilar artery bifurcation aneurysm also is visible (open arrow). C, DWI scan obtained the same day, revealing no significant diffusion defect. D, concomitant PWI scan showing decreased perfusion throughout the left hemisphere. E, follow-up PWI scan obtained 3 days after emergent carotid endarterectomy, showing a profound improvement in perfusion to the left hemisphere.

Examination Technique

All MRI scans for Patient 2 were obtained using a 1.5-T Picker Eclipse MRI scanner (Picker International, Inc., Cleveland, OH) at Pennsylvania State University–Milton S. Hershey Medical Center. DWI was performed using spin echo (EPI) technique. Multislice whole-brain images were obtained in 19 slices: TR, 5629 milliseconds; TE, 110 milliseconds; field of view, 24 cm; slice thickness, 5 mm with a 1-mm gap between slices; image size, 128 × 128. The *b* values were 0 and 741. DWI images were acquired in *x*, *y*, and *z* planes. EPI diffusion images were processed to generate apparent diffusion coefficient maps. PWI was performed using field echo (EPI) technique after injection of 15 ml of gadolinium (0.1 mmol/kg). PWI acquisition values were TR, 1000 milliseconds and TE, 60 milliseconds and 40 time points. Other parameters were 128 × 128 matrix size and 5-mm slice thickness with a 5-mm gap for a total of 10 slices. The total imaging time was approximately 56 seconds. PWI scans were processed to generate maps of TTP and regional cerebral blood volume. The total scanning time for the entire protocol was 15 to 20 minutes.

DISCUSSION

DWI is of established value in detecting acute cerebral ischemia (3, 4). Lesion volumes visualized on early DWI scans in stroke patients have a strong correlation with final infarct

volumes and clinical neurological outcomes (2, 13, 15). Serial DWI scans obtained during the first several days after stroke onset frequently reveal progressive enlargement of the lesion. The eventual lesion volume as revealed by DWI correlates closely with the final lesion volume as revealed by T2-weighted MRI scans, which in turn correlates closely with the final volume of infarcted brain tissue (2, 13, 15).

PWI is a complementary technique to DWI. It uses a rapidly injected bolus of contrast agent to create a qualitative map of brain perfusion (3, 10, 11). A variety of hemodynamic maps can be created by use of PWI. In animal models, lesions can be observed with PWI immediately after vessel occlusion, and they resolve rapidly after successful thrombolysis or reperfusion (8, 16). In studies of acute stroke patients, the volume of the early lesion revealed by PWI correlates more closely with the acute neurological deficit, which suggests that PWI provides a more accurate estimate of the volume of dysfunctional brain tissue than does DWI (2, 13).

In both of the patients described herein, a large lesion revealed by PWI was associated with a severe neurological deficit and little or no lesion on DWI scans. Undeniably, both of these cases are complex. Whereas interpretation of neurological changes in the first patient was complicated by her preexisting deficits, the second patient's situation was confounded by her recent intracranial surgery and general anes-

thetia. Clearly, however, the traditional preference would have been to offer delayed carotid surgery to both of these patients. Yet, prompt surgical revascularization was followed by improvement in each patient's neurological deficit. Neither patient had a hemorrhagic complication as a result of early surgery, and repeat MRI scans in both patients revealed resolution of their perfusion deficits. The primary benefit of DWI/PWI in this situation is the ability to differentiate a severe neurological deficit caused by a large completed infarction (DWI) from a similar deficit associated with a large, potentially reversible area of ischemia (PWI).

Whether DWI/PWI will be useful in selecting patients who will benefit from early surgery remains to be learned. It is difficult to extrapolate, from only two cases, specific DWI/PWI risk factors that might predict a poor outcome and/or hemorrhagic conversion after early carotid endarterectomy. In addition, it is impossible to conclude that early surgical intervention in cases of significant DWI/PWI mismatch actually leads to improved neurological outcome. Without baseline perfusion data, it is impossible to ensure that the decreases in blood flow, presumably associated the PWI changes, were the cause of the neurological deficit. It is interesting, however, that the second patient had bilateral high-grade ICA stenosis but there remained a substantial difference between the perfusion images of the two hemispheres (Fig. 2C). This suggests that an acute alteration in cerebral hemodynamics between the two hemispheres may have occurred.

Furthermore, the present report does not include a quantitative measurement of cerebral blood flow or cerebral blood volume. PWI is a relative test of perfusion, and the PWI measurements used herein are based on a TTP analysis, which may reflect the duration of collateral blood flow pathways more than actual tissue perfusion. PWI maps usually are generated with at least a 1- to 2-second delay in perfusion between hemispheres. In our patients, a TTP delay of 1 second was used, because this was the standard at the time these patients were studied. However, this short delay may lead to an overestimation of the tissue at risk. Recently, Neumann-Haefelin et al. (9) reported that only severe perfusion deficits (TTP delays ≥ 6 s) correlated with final infarct volume. In the future, it may be important to view perfusion with various TTP delays when deciding whether significant brain remains at risk. Although a quantitative measure of cerebral blood flow may be ideal, techniques to acquire such information, such as positron emission tomography or xenon blood flow tomography, may not be readily available and therefore may be impractical for widespread use. Thus, several groups are investigating alternative methods of generating quantitative blood flow data from MRI and correlating these data with other, more traditional measures of cerebral blood flow and cerebral blood volume (5-7, 12).

CONCLUSION

Carotid endarterectomy in the setting of DWI/PWI mismatch can lead to improvement in cerebral perfusion as evidenced by resolution of the PWI lesion. Further study will be needed to determine whether DWI/PWI techniques are useful

in identifying patients with high-grade carotid stenosis and ipsilateral acute stroke who may be appropriate candidates for early carotid endarterectomy despite severe neurological deficit. In the future, functional MRI techniques using DWI and PWI may be helpful in differentiating which of these patients, if any, will derive improved neurological outcomes after early surgery.

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COMMENTS

Krishnamurthy et al. highlight the issue of early endarterectomy after small strokes with ongoing perfusion mismatch. They performed early endarterectomy and suggest that, in this subpopulation, they definitely would perform early surgery when defined by radiological criteria such as these.

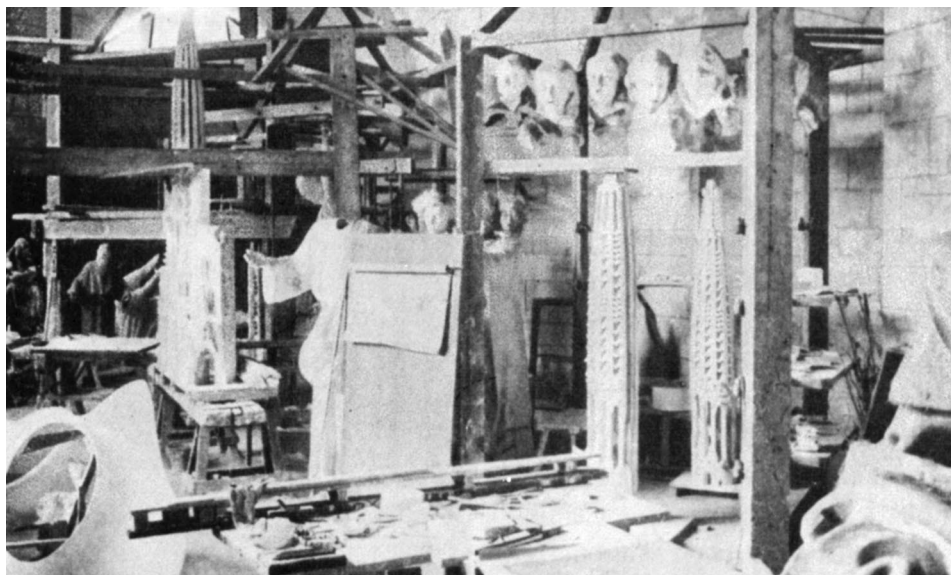
In our institution, both of these patients would have been offered early endarterectomy. Our tendency has been to move quickly in treating patients with small strokes and high-grade stenosis. The concept outlined in this report is not particularly controversial. However, this report raises the question of how such an approach might be used in patients with moderate-size infarcts and ongoing large perfusion/diffusion mismatch. In such cases, the risk of hemorrhage certainly is increased for early endarterectomy, yet there is the ongoing prospect of additional and sizable tissue loss.

We recently experienced a case similar to this latter scenario, in which an early endarterectomy was performed in the setting of a moderate-sized infarct as revealed by diffusion-weighted imaging. However, fluctuating symptoms (hemiplegia) and a large additional area of perfusion defect prompted us to proceed with endarterectomy. The feared hemorrhage into the stroke area occurred, but the eventual outcome was better than we would have anticipated if the area of perfusion mismatch had converted to frank infarction. In the end, we thought that we had walked a fine line between two very difficult clinical scenarios.

This report highlights the increasing amount of data made available by magnetic resonance imaging regarding cerebral blood flow and areas of tissue at risk. Additional compilation of results in these very specific scenarios is warranted to allow us to understand the overall risk-to-benefit ratio of our interventions.

Bob S. Carter
Christopher S. Ogilvy
Boston, Massachusetts

Robert J. Dempsey
Madison, Wisconsin



Gaudi's workshop in the Sacred Family Cathedral, showing innumerable plaster models.

In this article, the authors report two quite different cases that have the common thread of endarterectomy performed in a patient with a new or increasing neurological deficit and a diffusion/perfusion mismatch. The lack of large diffusion deficits suggests that a fixed stroke was not present. The patients improved both in clinical course and perfusion after endarterectomy. This is consistent with present thinking regarding acute thrombolysis after neurological deficit when a favorable perfusion/diffusion mismatch exists. As such, it is an interesting although not unique contribution.

The major questions here are twofold. First, can a perfusion/diffusion mismatch be reversed by a revascularization procedure such as endarterectomy? Not surprisingly, this is true, and it is observed in these patients. The larger questions remain: is there a safe time to proceed with an endarterectomy or other reperfusion technique, and is perfusion/diffusion mismatch useful in determining the safety of this procedure? This could be addressed if we knew the conditions that would predict worsening after an intervention, such as the diffusion-weighted imaging conditions that would predict which patients will have hemorrhagic conversion of a stroke area if endarterectomy is performed. These questions need to be answered to determine whether the timing of surgery needs to be restricted, and if so, in which cases. This article does not answer that question. As a result, it does not add information as to the best timing of surgery for a patient with an infarct, but it does, as the title suggests, provide information regarding the reversal of perfusion mismatch.

The results in these patients cannot be generalized to all patients undergoing endarterectomy. The article increases our understanding of perfusion/diffusion mismatch and the anatomic relationship to stenosis ipsilateral to the mismatch. However, our knowledge regarding safe timing of endarterectomy after neurological deficit has not been increased.