Reduction of Diffusion-Weighted MRI Lesion Volume After Early Moderate Hypothermia in Ischemic Stroke

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**Background**—Large areas of restricted diffusion in the middle cerebral artery (MCA) territory are highly predictive of severe and potentially space-occupying MCA stroke. A reduction of diffusion-weighted MRI (DWI) lesions occurs in 20% to 40% of acute stroke patients with early reperfusion.

**Methods**—We report of a patient with a severe stroke syndrome who was treated with early moderate hypothermia but not thrombolysis.

**Results**—The initially large DWI deficit of the whole MCA territory contrasted to the relatively small final lesion restricted to the basal ganglia on MRI and computed tomography scan.

**Conclusion**—This case describes an unexpected reduction of a DWI lesion after early moderate hypothermia and spontaneous recanalization 3 days after stroke onset. We discuss potential reasons for the unexpected DWI lesion reduction. *(Stroke. 2005;36:e56-e58.)*

**Key Words:** glutamates ■ magnetic resonance imaging ■ stroke ■ stroke, ischemic

Life-threatening middle cerebral artery (MCA) infarction occurs in ≤10% of all stroke patients. Clinical deterioration in this patient group is mainly attributable to formation of brain edema and increasing intracranial pressure (ICP).1,2 Because of a mortality rate of 80%, various rescue therapies are currently being evaluated. Moderate hypothermia for 48 to 72 hours in selected patients may be associated with a potential benefit on mortality, although higher class evidence is still lacking.3–6

Diffusion-weighted MRI (DWI) in combination with perfusion imaging as documented on a relative mean transit time map has become a potential modality for the identification of those patients who may develop massive space-occupying MCA infarctions.7 It is based on the diagnostic power of DWI to diagnose acute stroke, to identify the ischemic penumbra (the mismatch area between the DWI and perfusion imaging lesion), and to predict clinical outcome.

We report of a patient who was admitted with a severe MCA stroke and was treated with early moderate hypothermia after arrival. The initial DWI deficit was in contrast to the relatively small final lesion volume on MRI and computed tomography (CT) scan.

**Case Reports**

This 52-year-old man presented with a right-sided severe MCA stroke with onset during sleep (National Institutes of Health [NIH] Stroke Scale of 19) because of a newly diagnosed atrial fibrillation. Multiparametric MRI was performed 4 hours after awakening. DWI and perfusion MRI suggested a complete MCA infarction (Figure 1). On magnetic resonance angiography, the M1 segment of the MCA was occluded. As the patient’s consciousness deteriorated, he had to be intubated and mechanically ventilated. He was sedated with fentanyl and midazolam. On arrival in our emergency room, his spontaneous rectal temperature was 35.6°C. In knowledge of the large DWI lesion, the pronounced stroke severity, and the unknown onset time, we refrained from thrombolysis but instead decided to continue treatment with moderate hypothermia. The target temperature of 33°C was reached at 6 hours after symptom onset by an intravascular cooling catheter (Coolgard; Alsius). Routine neuromonitoring, including ICP measurement and cerebral microdialysis, was performed frontal to the infarct core in the ipsilateral hemisphere as described previously.8

Neuromonitoring revealed uneventful ICP values with only 1 short ICP increment beyond 20 mm Hg that was not accompanied by papillary disturbances. Glutamate concentrations declined to normal values during the first 12 hours, whereas glycerol concentrations and the lactate pyruvate ratio remained within normal ranges, indicating normal brain tissue (Figure 2). No association between neurochemical parameters and temperature was noticed (data not shown).

After 72 hours of hypothermia, the patient was actively rewarmed at a rate of 0.1°C per hour. Transcranial ultrasound showed a recanalization of the MCA on day 3 after stroke onset. The patient could be extubated 4 days later. Before he went to a rehabilitation unit, he was awake, had incomplete gaze palsy to the left, a plegia of the left arm, and a severe paresis of the left leg (NIH Stroke Scale 15). A CT scan on
day 6 and an MRI on day 11 revealed only a basal ganglia infarct (Figure 3).

**Discussion**

We report on a patient with an apparently complete MCA infarction on DWI and perfusion MRI at 4 hours after symptom presentation that resulted in a pure basal ganglia infarct on CT and MRI scan 6 and 11 days later. Previous reports indicate that DWI performed within 14 hours of stroke onset may predict malignant edema. Oppenheim et al reported that initial diffusion deficient volume $>145 \text{ mL}$ accurately predicted malignant MCA infarction in 10 patients. Even within the first 6 hours, quantitative analysis of DWI and perfusion imaging parameters allowed prediction of a malignant course of the MCA infarction. A volume $>82 \text{ mL}$ of an apparent diffusion coefficient (ADC) $<80\%$ had a sensitivity of 87% and a specificity of 91%.

It is known from the literature that DWI lesions may continue to grow even after the first 6 hours, although early application of thrombolysis may also reduce DWI lesion in a small proportion of patients. However, because of the severity of initial stroke symptoms and unknown time window, we refrained from thrombolysis. The reduction of DWI lesion volume in our case raises 2 potential explanations.

First, the DWI lesion in the very early stroke MRI may overestimate the final infarct size. This is supported by a comparative study with positron-emission tomography (PET) and MRI in that false-positive prediction was higher for the DWI variables and ADC than flumazenil PET. Reperfusion, whether spontaneous or induced by thrombolysis, may be a precondition for reduction of high tissue signal on DWI. However, the MCA in this case remained occluded until day 3. Because the previous studies are small in numbers, a prospective study with larger sample size is warranted to validate the predictive value of DWI MRI.

Second, pseudonormalization of DWI is occasionally observed 10 days after stroke. However, this is an unlikely explanation in this case because the follow-up CT scan was well in line with the lesion volume on MRI.

Third, the patient presented with a spontaneous hypothermia, which we continued at 33°C for 72 hours. Although his body temperature at the time of stroke onset is not known, the early reduction of temperature may have delayed deleterious ischemic processes, as indicated by normal neurochemical parameters, until spontaneous recanalization of the MCA on day 3. Subsequently, the final infarct volume was smaller.
than predicted on initial DWI. This explanation would be in line with numerous experimental data, which all show a reduction of infarct size using early moderate hypothermia.

In conclusion, increased signal on early DWI may not necessarily indicate irreversibly injured brain tissue. It may be reduced spontaneously, after reperfusion, or by neuroprotective measures such as hypothermia. One should be cautious to use distinct DWI lesion volumes as sole exclusion criterion for acute stroke studies.

References
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