Surgical Decompression of Patients With Large Middle Cerebral Artery Infarcts Is Effective

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The Syndrome and Its “Natural” Course
Early mortality after acute ischemic stroke is most frequently caused by space-occupying ischemic brain edema. In case of complete middle cerebral artery territory (MCA) infarction, including the basal ganglia, a large space-occupying postischemic edema that finally leads to herniation and brain death may occur. These patients present with almost complete hemiplegia, head- and eye-turning progressive deterioration of consciousness over the first 24 to 48 hours, and a reduced ventilatory drive. Prognosis of large MCA or hemispheric infarctions is poor: in prospective case series, 80% died from herniation despite maximum conservative therapy.1

The Failure of Medical Intervention
General measures of treatment of increased intracranial pressure (ICP) after acute ischemic stroke include elevation of the head to a 30-degree angle to improve venous drainage and avoidance of both hyperthermia and hyperglycemia. As part of the specific anti-edematous pharmacological treatment, osmotherapy using glycerol, mannitol, or hyperosmolar saline solutions is used to reduce brain edema. All substances work by means of lowering ICP, but only for a limited time. The same is true for barbiturates, which may reduce critically elevated ICP reading massively, but only for a short period.2,3

Decompressive Surgery
Decompressive surgery for malignant MCA infarction is not a new invention. Actually, the first studies date back as early as 1935. Over the past decades, several case reports and smaller retrospective case series have suggested that decompressive surgery is a possible treatment option for massive hemispheric stroke. However, no controlled data were available to support its superiority. The rationale of decompressive surgery is to allow extracranial expansion of the edematous brain tissue to avoid ventricular compression and horizontal as well as vertical tissue shifts. This concept is supported by experimental studies indicating dramatic decrease in mortality and substantial tissue salvage with decompressive surgery. However, it was not until 1995 that a large prospective case series was published. This series also included a concurrent control group, which, sadly enough, was not a randomized control group. Nevertheless, in this control group the well-known 80% mortality with maximum conservative treatment was demonstrated, while the mortality rate in the surgically treated group was only 34.4%. Among the survivors, the quality of survival was a surprisingly good modified Rankin score of 2.6 (range, 1 to 4).4

When to Operate?
This is probably the most important question for those who support this treatment. In the past, the treatment was frequently offered only in cases that were already herniating—it is no surprise that that outcome was not very good. In our first case series, we waited for first signs of reversible herniation and a major middle shift on CT, before surgery was considered.

Over the past 7 years, our prospective treatment protocol has been substantially changed in order to allow early recognition of candidates who maybe at risk for malignant MCA symptom and early intervention. We do not wait any more for the first signs of herniation or for elevated ICP readings to indicate the intervention. Early repeated CT scanning and, more recently, immediate diffusion and perfusion MRI studies allow very early identification of the size of the infarct, and, combined with the clinical syndrome of a complete MCA infarction, the diagnosis may be made long before the life-treating swelling occurs. Using the strategy of early identification of patients at risk for malignant MCA symptoms, a second series of 32 patients has been published, in which the intervention took place on average in the first 24 hours after stroke onset. Mortality in this cohort was down to 20%, and quality of survival was even better with a mean modified Rankin score of 2.4 (range, 2 to 4).5

The Drawbacks
Unfortunately, no study has a control group involved, yet.6 Therefore, comparison of mortality rates is difficult, because we are dealing with a historical control that was assembled 7 to 8 years ago. There may have also been shifts in our general
The Call for Randomized Trials
There are several randomized trials on the way both in the United States and in Europe. We are very supportive of the idea of performing a randomized trial. In hospitals, where at the present time no special treatment is offered to the victims of malignant MCA infarction, randomization would offer at least 50% of the patients a chance of receiving treatment; that allows decent survival. Of course, mortality is an important but not the only issue in such a randomized trial. Everyone is concerned about allowing survival in a completely dependent, noncommunicative state, although our experience does not support this concern.

We are aware of several randomized trials in planning stages to address this important issue.

What to Do in the Meantime?
What shall physicians do, meanwhile, now that we are waiting for controlled trials to start? If centers have not yet performed this type of treatment, they should send experienced neurologists and neurosurgeons to institutions to get trained. Centers in which 30 or more patients have been treated successfully, however, may continue with their treatment efforts and help the others to get the experience needed for a good study. This, by the way, is also true for another interesting option for the treatment of malignant MCA infarction, controlled moderate hypothermia of 33°C.7

References

Surgical Decompression of Patients With Large Middle Cerebral Artery Infarcts Is Effective: Not Proven

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Middle cerebral artery territory infarction is an important cause of disability and death after stroke. Mortality associated with middle cerebral artery infarcts is usually caused by the complications of severe stroke, eg, pneumonia or pulmonary embolism. Death in a small proportion of cases is caused by coning secondary to malignant cerebral edema. Initially, ischemic cytotoxic edema causes only limited cell swelling, but the subsequent development of vasogenic edema can result in significant enlargement of the volume of infarcted tissue. Typically, patients destined to develop malignant edema present with symptoms of ischemia in the middle cerebral artery but initially remain alert. After a delay of 24 to 48 hours, as the infarct swells there is a rapid decline of consciousness from herniation leading to unresponsiveness and often death. It is logical to consider surgical decompression by craniectomy in these cases. Removal of a large portion of the skull vault allows the edematous hemisphere to expand out through the defect in the skull, relieving the mass effect. There is no doubt that this treatment appears to be life-saving in some cases. However, the syndrome of malignant cerebral edema is seen only in large infarcts, often resulting from internal carotid artery occlusion associated with poor collateral supply. Usually, the patients are young, presumably because cerebral atrophy with aging provides space for expansion of the brain and protects against a rise in intracranial pressure. Generally, most centers have limited treatment to younger patients with nondominant hemisphere infarction because of the assumption that residual aphasia would not be an acceptable outcome. This means that the proportion of patients currently thought suitable for decompressive surgery is small, and the exact indications have not been established.

One rationale for decompressive surgery argues that edema compresses adjacent tissues, causing secondary damage and extension of the infarction into the ischemic penumbra, and it has therefore been suggested that susceptible patients should be treated as early as possible.1,2 It is logical that the earlier patients are decompressed, the less likely secondary damage, but it is not clear that malignant cerebral artery edema can be reliably predicted. Better outcomes reported in patients...
treated early could simply reflect the selection of patients who were destined to do well. Moreover, the experience from thrombolysis suggests that penumbral tissue remains viable for only a few hours. One can argue that it is therefore unlikely that decompression will have an effect on the eventual size of cerebral infarction. Hence, even if decompressive surgery prevents death, it may not prevent disability, except in the rare patient otherwise destined to develop additional nonfatal infarction in the territories of the anterior or posterior cerebral arteries or brain stem perforators, secondary to herniation.

Reducing mortality may seem an obvious benefit of craniectomy, but this is likely to be acceptable only if the rate of disability is also reduced. Patients with malignant middle cerebral artery edema invariably have large infarcts, and the patient is therefore bound to be left with some impairment. In particular, recovery of arm function is unlikely and a degree of cognitive impairment is inevitable. Depression and poor integration into society are common. One of the early and influential randomized trials of acute stroke treatment studied dextran infusions and concluded that reduction of cerebral swelling reduced mortality in patients with severe stroke, but as more survivors were severely disabled, this was considered a negative outcome. Other treatments that reduce mass effect, including glycerol, mannitol, dexamethasone, and surgical evacuation of hematomas, have also failed to show convincing benefit on functional outcome in clinical trials.

These trials argue that treating cerebral edema is treating dead tissue to little avail. Even the impression from case series that craniectomy is beneficial in terms of mortality may be misleading. Randomized trials have often shown that logical surgical treatments, eg, extracranial-intracranial bypass surgery, fail to deliver significant benefit when properly tested, because the risks outweigh the benefits.

Although some previous case series of decompressive surgery have reported encouraging results, these must be treated with caution. Other series have reported disappointing results with high mortality rates and poor functional outcome. Moreover, surgery has risks, including intracranial hemorrhage, intracranial infection, wound infection, and bone flap infection. Overall, there are only a small number of patients reported in the literature and the results have been compared with poorly matched or historical controls. The problem with comparing any case series with historical controls is that the routine care of stroke improved in the intervening period. Only randomization provides a cohort of patients in whom decompressive surgery can be compared with best medical management alone, in patients matched for baseline characteristics, severity of stroke, and other treatments. There were no completed randomized trials of decompressive surgery for middle cerebral artery infarc-

In summary, craniectomy looks like a hopeful treatment, but one should conclude that its benefits have not been proven. We need the results of prospective randomized studies to establish the magnitude of benefit, optimum time for surgery, and the factors predicting severe residual disability despite surgery. Finally, economic studies are needed to establish the cost effectiveness of the treatment, with quality-of-life measures to establish the acceptability to patients of various degrees of long-term disability. For an expensive and invasive treatment, the number needed to treat to obtain benefit will need to be relatively small to be cost effective and to avoid exposing substantial numbers of patients to unnecessary surgery.

References


Key Words: brain edema □ craniectomy □ decompression □ infarction, middle cerebral artery □ intracranial pressure
Surgical Decompression for Malignant Middle Cerebral Artery Infarction: A Challenge to Conventional Thinking

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Early mortality after large middle cerebral artery (MCA) infarcts is most often due to acute brain swelling, with midline shift and transtentorial herniation. This is particularly relevant in younger stroke patients, with the syndrome of “malignant MCA infarction.” Conversely, neurological recovery may be better after a life-saving intervention. Medical management of ischemic brain edema is limited and at best may result in only temporary reduction in intracranial pressure. Hence, the logic of craniectomy with surgical decompression is appealing, although the concern has always been that a reduction in mortality might be outweighed by major disability in survivors. It seems likely that a driving force in early anecdotal reports of hemicraniectomy was the more obvious benefit seen in posterior fossa decompression with acute cerebellar infarction, although this is also an unproven management strategy.

One barrier to clinicians’ willingness to embrace the procedure is the daunting prospect of what appears to be major surgery in patients with a perceived poor prognosis. In fact, this type of surgery is commonly performed in trauma centers in cases with malignant cerebral edema and is technically relatively simple. Another issue relates to the inclusion of patients with dominant hemisphere infarction. We are not convinced that these should be excluded from clinical trials, since improvement may be just as dramatic in either hemisphere.

Both protagonists have pointed out that there are no definitive trials, although a number are fortunately in progress. In the HEADDFIRST study, patients are randomized to hemicraniectomy with durotomy versus control with death and disability measured at 21 days, 3 months, and 6 months. In the HAMLET study, Hoffmeijer et al plan to randomize about 100 patients under the age of 60 years to hemicraniectomy and duraplasty, with outcomes measured at 6 months. Obviously, more trials may be needed to refine patient selection, timing of intervention, and surgical approach, even if these initial trials are positive.

One of the most puzzling aspects of the management of patients who develop acute middle cerebral artery infarction is the development of malignant edema in only a subset. Clearly, better clinical and imaging selection criteria need to be defined. Some attempts have been made to identify those with a poor prognosis using strategies such as sonographic monitoring of midline shift, and SPECT. Possibly, as Schwab and Hacke mentioned, newer techniques such as perfusion and diffusion MRI may be more reliable, given their greater sensitivity in imaging acutely ischemic tissue.

What should the practicing clinician do in the meantime? While Brown is a little more cautious than Schwab and Hacke, all agree that more data are required from prospective randomized trials. We suggest that in younger patients with large MCA infarcts who are developing obvious edema with clinical deterioration, decompressive surgery should be considered earlier rather than later based on the limited information available to date. It would seem pointless to us to suggest surgery in patients with established signs of transtentorial herniation where the likelihood of recovery is remote. For stroke clinicians able to be involved in a prospective trial, we would encourage use of the uncertainty principle to randomize patients to surgical or medical management. Once we considered thrombolysis a radical possibility for stroke therapy. We should continue to challenge conventional thinking.

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