Early Hemicraniectomy in Patients With Complete Middle Cerebral Artery Infarction

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Background and Purpose—Malignant, space-occupying supratentorial ischemic stroke is characterized by a mortality rate of up to 80%. Several reports indicate a beneficial effect of hemicraniectomy in this situation. However, whether and when decompressive surgery is indicated in these patients is still a matter of debate.

Methods—In an open, prospective trial we performed hemicraniectomy in 63 patients with acute complete middle cerebral artery infarction. Initial clinical presentation was assessed by the Scandinavian Stroke Scale (SSS) and the Glasgow Coma Scale (GCS). All survivors were reexamined 3 months after surgical decompression, with the clinical evaluation graded according to the Rankin Scale (RS) and Barthel Index (BI). We analyzed the influence of early decompressive surgery (<24 hours after symptom onset, based on clinical status at admission and initial CT findings) versus late surgery (>24 hours after first reversible signs of herniation) on mortality, functional outcome, and the length of time of critical care therapy was needed.

Results—In total, 46 patients (73%) survived. Despite complete hemispheric infarction, no survivor suffered from complete hemiplegia or was permanently wheelchair bound. In patients with speech-dominant hemispheric infarction (n=11), only mild to moderate aphasia was present. The mean BI score was 65, and RS score revealed severe handicap in 13% of the patients. In 31 patients with early decompressive surgery, mortality was 16% and BI score 68.8. Early hemicraniectomy led to a significant reduction in the length of time critical care therapy was needed (7.4 versus 13.3 days, P<0.05).

Conclusions—In general, the outcome of patients treated with craniectomy in severe ischemic hemispheric infarction was surprisingly good. In addition, early decompressive surgery may further improve outcome in these patients. (Stroke. 1998;29:1888-1893.)

Key Words: brain edema ■ cerebral infarction ■ hemicraniectomy ■ intracranial pressure ■ rehabilitation

Life-threatening, complete middle cerebral artery (MCA) infarction occurs in up to 10% of all stroke patients.1,2 The main cause of death encountered in these patients is severe postsischemic brain edema leading to raised intracranial pressure (ICP), clinical deterioration, coma, and death.1-7 This distinct syndrome was recognized long ago and is described in several older clinicopathological studies.3,4 The clinical course in these patients is uniform, with clinical deterioration developing within the first 2 to 3 days after stroke. A recent study1 has described the natural course and the neurological and neuroradiological findings in “malignant” MCA infarction. These patients present clinically with severe hemispheric stroke syndrome, including hemiplegia, forced eye and head deviation, and progressive deterioration of consciousness within the first 2 days. Thereafter, symptoms of transtentorial herniation occur within 2 to 4 days after onset of stroke. This clinical presentation is accompanied by early CT signs of major infarct during the first 12 hours after stroke.3,8 The prognosis of these patients is poor, and the mortality rate may be as high as 80%.3,4 The value of conventional therapies in this condition, as in others of raised ICP, consisting of artificial ventilation, osmotherapy, and barbiturate administration, has been subjected to scrutiny.9-11 Because of the limitations of medical therapies, there have been proposals for decompressive surgery in patients with elevated ICP for a variety of neurological disorders, such as head trauma, space-occupying hemispheric infarction, encephalitis, or subdural hematoma.12-17 The surgical management of intracranial hypertension is directed toward improving cerebral perfusion and preventing ischemic damage and mechanical compression of the brain against the rigid intracranial structures, such as the falx, tentorium, and the sphenoid ridge. We recently described17 a series of 32 patients who underwent craniectomy for space-occupying MCA stroke compared with 21 control patients who, because of missing informed consent or dominant hemispheric infarction, did not. The mortality rate for these 32 patients treated with decompressive surgery was 32% (11/32). However, particularly in patients with cerebrovascu-
lar accidents, there is still controversy about when and how to implement this invasive therapeutic procedure.\textsuperscript{14,15} We present the results of our ongoing open trial and discuss the indications and timing of surgical intervention in a prospective series of 63 patients treated with decompressive surgery after malignant MCA stroke, including our first 32 patients, who were treated after the first signs of herniation had occurred.

**Subjects and Methods**

Over the past 6 years we performed an open prospective, noncontrolled trial on the value of decompressive surgery in patients with malignant MCA infarction. Preliminary results of this trial have already been reported.\textsuperscript{17} The study was approved by the local ethics committee. Since we reported our first results, one major inclusion criterion for enrollment into our study has changed. In the ongoing trial, patients were treated with decompressive surgery before the occurrence of clinical signs of herniation, within the first 24 hours after stroke onset. To clarify this point, the inclusion criteria to both parts of this trial were spelled out. The initial inclusion criteria consisted of the following: patients younger than 70 years with clinical and CT evidence of acute, complete MCA infarction (which consisted of an early, large parenchymal hypodensity [ie, >50\% of the MCA territory] and signs of local brain swelling, such as effacement of the sulci and compression of the lateral ventricle); on follow-up CT, complete space-occupying MCA infarction with midline shift and compression of the basal cisterns and/or further neurological deterioration compared with the baseline clinical status on admission to the neurocritical care unit (NCCU).

For the group of patients treated within the first 24 hours, inclusion criteria were as follows: patients younger than 70 years with clinical and CT evidence of acute, complete MCA infarction (which consisted of an early, large parenchymal hypodensity [ie, >50\% of the MCA territory] and signs of local brain swelling, such as effacement of the sulci and compression of the lateral ventricle); on clinical follow-up, further neurological deterioration compared with the baseline clinical status on admission to the NCCU. Neurological deterioration consisted of a further decrease of consciousness to somnolence and stupor.

Patients with any previous disabling neurological disease, secondary parenchymal hemorrhage, coma, or terminal illness were excluded from both protocols. CT scans were obtained on admission and after clinical deterioration. Cranial CT scans were unenhanced and obtained with a Picker scanner (Picker International) with a slice thickness of 8 mm.

**Conservative Treatment**

The patients were kept euvoletic and received mannitol to achieve a serum osmolality of 300 mOsm. To reach mean arterial blood levels above 90 mm Hg, vasopressors (0.2 mg/kg/min norepinephrine via infusion pump) were used. The hemoglobin concentration was maintained above 90 g/L. Hyperventilation or barbiturates were not used in our treatment regimen. Invasive monitoring of ICP was not part of routine management in these patients.

Hemicraniectomy was considered only for patients with stroke in the nondominant hemisphere or for patients with only incomplete aphasia before deterioration. In all patients the decision to perform craniectomy was made in consultation with the patient and/or the patient’s family. Full written consent was obtained. Clinical data were obtained daily from all patients and assessed with use of the Scandinavian Stroke Scale (SSS) and Glasgow Coma Scale (GCS).\textsuperscript{19,20} Four weeks and 3 months after stroke, clinical outcome was assessed with the SSS and the Rankin scale (RS). Activities of daily living were rated with the Barthel Index (BI).\textsuperscript{21,22} In this study, scores of <60 indicated severe disability, scores of 60 to 70 indicated moderate disability, and scores from 70 to 99 indicated mild disability; a score of 100 indicated no disability identifiable with the BI. The length of stay in the NCCU was analyzed as an important indicator of the level of short-term dependency and medioeconomics.

For further analysis, the initially reported group of patients was compared with the following patients, who were treated according to the same protocol but received craniectomy considerably earlier (<24 hours), before the clinical signs of reversible herniation had become evident. For comparison with these patients, the data of the natural course of patients with malignant MCA infarction are given, but no statistical analysis was performed.\textsuperscript{1}

**Surgical Technique**

In brief, the technique for decompressive surgery required that a large bone flap with a diameter of 12 cm (including the frontal, parietal, temporal, and parts of the occipital squama) be removed so that the floor of the middle cerebral fossa could be explored.\textsuperscript{18} The dura was fixed at the edge of the craniotomy to prevent epidural bleeding. The dura was then opened, and an adjusted, biconvex dural patch made of lyophilized cadaver dura or homologous temporal fascia was placed into the incision. The size of the dural patch varied, but we usually used patches 15 to 20 cm in length and 2.5 to 3.5 cm in width. An artificial bone flap was implanted 6 to 12 weeks after the operation.

**Statistical Analysis**

All values are expressed as mean±SD. The physiological measurements within groups were analyzed by the Student t test for paired data. To compare both treatment groups, the Mann-Whitney rank sum test was used. Significance was assigned for P<0.05.

**Results**

**Patients**

A total of 63 patients were enrolled in this trial (23 women and 40 men). The mean age was 49.7±10.8 years. On admission, the mean SSS score was 19.5±9.2 (median, 17) and the mean GCS score was 8 points (range, 4 to 13). All patients presented with severe dense hemiparesis and forced eye and head deviation. Forty-one patients had complete MCA territory stroke; 22 had an additional anterior or posterior artery territory infarction. The etiology of stroke was cardioembolism (present atrial fibrillation, valvular disease, cardiomyopathy) in 41 patients, internal carotid artery dissection with secondary MCA embolization in 19 patients, and unknown in 3 patients. Of the 63 patients enrolled in the trial, 46 (73\%) survived. The ischemic stroke affected the dominant hemisphere in 11 patients and the nondominant hemisphere in 52 patients. The mean time between onset of symptoms and surgery in the initially reported group was 39 hours (range, 6 to 112 hours) versus 21 hours (range, 8 to 42 hours) in the present group. Even though this difference did not reach statistical significance (P<0.07), we identified this as the only major difference in patient management during the ongoing trial. For further analysis, the initially reported group of patients was compared with the following 31 patients who were treated according to the same protocol but received craniectomy considerably earlier (see the Table).

Mortality was 16\% (5/31) in the presently treated group versus 34.4\% (11/32) in the initially treated group and 78\% (43/55) in the historical controls. The comparison of the clinical conditions of the 2 patient groups revealed signs of uncal herniation in 24 of 32 patients (75\%) in the initially treated group, whereas in the presently treated group only 4 of 31 patients (13\%) had signs of uncal herniation with a unilaterally fixed and dilated pupil. Clinical deterioration in
the presently treated group consisted of a further decrease in consciousness to somnolence or sopor. None of the patients treated with craniectomy in the speech-dominant hemispheric stroke were left with a global aphasia. All patients were able to communicate and understand; 3 patients had only minor aphasic deficits, which allowed them to resume their occupation.

Length of stay on the NCCU was 7.4 days for the presently treated group versus 13.3 days in the initially treated group (*P*, 0.05). Functional outcome assessed with the BI revealed a mean score of 70, with scores from 80 to 90 in 2 patients, 70 to 80 in 15 patients, and 60 to 70 in 9 patients. All patients in the presently treated group were able to walk short distances without assistance. Compared with the initially treated group, with a mean BI of 62.6, this difference showed a trend toward better outcome in the presently treated group. However, it failed to reach statistical significance (*P* = 0.06).

All patients reported a good reintegration into their families and social environment.

Neuroradiological Data

All patients had at least 2 CT scans within the first 4 days after stroke, the first of which was obtained within the first 12 hours after symptom onset (Figures 1 and 2). All 63 patients received their first CT within the first 4 to 6 hours after stroke, and all already showed early signs of infarction, such as local swelling and parenchymal hypodensity. In all presently treated patients, parenchymal hypodensity in >50% of the MCA territory was observed on the initial CT. In 6 patients additional involvement of the anterior cerebral artery and in 5 patients involvement of the posterior cerebral artery was described. The comparison of neuroimaging results in the presently treated and initially treated groups showed that early signs of infarction described before were present to the same extent. Midline shift as measured on CT in the initially treated group was at the septum pellucidum level, with a median of 10 mm (range, 6 to 15), and at the level of the pineal gland, 5 mm (range, 4 to 10). In the presently treated group, midline shift as measured at the septum pellucidum level was obviously less often seen: only 6 patients showed midline shift, with a median of 3 mm (range, 0 to 5), 2 mm at the pineal body level (range, 0 to 3).

Complications associated with the operation were seen twice in the initially treated group of patients (epidural and subdural hematoma) and in 2 patients in the presently treated group (epidural hematoma). Three patients developed space-occupying subarachnoid hygroma over the trepanation site, but none of these complications led to an additional neurological deficit.

Discussion

Over the past 15 years, several studies have shown that decompressive surgery is a possible treatment strategy for otherwise uncontrollable increased ICP after severe hemispheric stroke. Surgical decompression seems to be effective in lowering increased ICP and preventing transtentorial herniation. It is being tested extensively in head trauma patients, with varying results, as well as in patients with space-occupying cerebellar infarctions, with a significant decrease in mortality and morbidity in comatose patients. It is well recognized that cerebral edema after large MCA infarcts occurs in up to 10% of all patients. Within this group

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Late Hemicraniectomy</th>
<th>Early Hemicraniectomy</th>
<th>Natural History</th>
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<tr>
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<tr>
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<td>SSS score on admission, mean±SD*</td>
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<td>19.5±7.6</td>
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<td>21 h</td>
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<td>Signs of herniation before surgery</td>
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<td>13% (4/31)</td>
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<tr>
<td>Mortality rate</td>
<td>34.4% (11/32)</td>
<td>16% (5/31)</td>
<td>78% (43/55)</td>
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<td>Time on NCCU, (d)</td>
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<td>7.4</td>
<td>12.6</td>
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<td>Barthel Index score, mean</td>
<td>62.6</td>
<td>68.8</td>
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</table>

*Of a possible 58 points.

Comparison of Parameters Among Late and Early Hemicraniectomy and Historical Control Groups

Natural history data from Hacke et al. 3
a certain proportion of patients develops space-occupying cerebral edema with subsequent irreversible herniation and death. Even under full supportive therapy, the mortality rate for this distinct syndrome of malignant MCA infarction is roughly 80%.3,4 Recently, the effectiveness of many medical therapies for brain edema has been challenged.30 Vigorous chronic hyperventilation has been discouraged because it may reduce the brain’s ability to tolerate ischemia and may therefore be more harmful than beneficial.10 The use of osmotherapeutics such as glycerol or mannitol may actually hasten tissue shifts and aggravate brain edema.9 Barbiturate therapy has failed to be of any benefit in the treatment of edema after severe brain injury.11

Studies in several cohorts of patients with large MCA infarction have shown that decompressive surgery can reduce mortality to less than 50%.14,16,17,23,24 Our previously reported first results revealed a mortality of 34%, with the majority of survivors only mildly to moderately disabled.17 This is especially important, because 75% of the patients in this series already showed clinical signs of uncal herniation. The clinical course of patients with severe MCA stroke is highly predictable. Therefore, waiting for a pupillary dilation causes an unnecessary delay, since allowing mesencephalic ischemia to occur potentially worsens prognosis. Further support for earlier intervention in these patients comes from 2 recent experimental stroke studies on the value of decompressive surgery,31,32 in which the authors showed that animals operated on within 4 hours after MCA stroke had a significantly better outcome than those treated within 12, 24, or 36 hours and, moreover, had a significant reduction in infarction size.
compared with controls. Compared with untreated animals, the neurological scores and behavior of all treated animals were also significantly better. It was hypothesized that through decompressive surgery, the vicious circle of extensive edema, which by elevation of ICP causes ischemia of neighboring brain tissue and further infarction, may be interrupted. This may then increase cerebral perfusion pressure and optimize retrograde perfusion of leptomeningeal collateral vessels, thus allowing functionally compromised but viable brain to survive.

From neuroradiological studies it has been well recognized that “early visual radiolucency” in the CT examination is a negative outcome predictor. Von Kummer et al demonstrated that large (>50%) or total hypodensity in the MCA territory predicted fatal outcome in 85% of cases (11/13), with a high specificity (94%) but moderate sensitivity (61%). In the ECASS trial, signs of early, major infarction were prognostic with respect to the development of space-occupying edema and death due to herniation, even in the placebo group.

In deciding when surgery is indicated, it is important to know that in general, clinical signs precede critically raised ICP. Ropper and Shafran suggest that drowsiness is the major clinical symptom of developing brain edema; thus, ICP monitoring of this condition might be helpful in guiding further therapy. However, Frank has demonstrated that elevated ICP is not a common cause of initial neurological deterioration from large hemispheric stroke. Because in most patients cerebral edema contributes to the gradual build-up of a mass, displacing the brain stem rather than globally increasing ICP, Wijdicks and colleagues suggest that ICP in younger patients might rise rather quickly due to less reserve to compensate for the increase in volume. Our own data from patients in whom ICP was monitored during severe MCA infarction showed a correlation of high ICP and poor clinical outcome. However, initial ICP values were not suitable to provide early information on the further clinical course.

Taking into consideration both clinical course and neuroradiological data in the early selection of our patients for decompressive surgery led to a further reduction in mortality, to only 16%. Also, the rating of clinical outcome showed a trend toward better functional performance as measured with the BI. One could argue that this further reduction in mortality is attributable to the fact that we operated on the spontaneous clinical course of some patients. However, all patients who underwent surgery early showed further clinical deterioration compared with initial assessment and fulfilled the neuroradiological criteria of complete MCA infarction. Taking these 2 major points together, the further clinical course in these patients without surgical intervention is highly predictable. Moreover, several groups have reported that the clinical decline in these patients is often so steep that the operation is just a life-saving maneuver and cannot prevent a more severe neurological deficit than might have been expected had surgery been instituted earlier.

Further support for earlier intervention is the fact that the length of time needed for critical care therapy is significantly reduced in the group of patients treated early after severe stroke. It is easy to understand that patients with anisocoria as sign for a frank herniation syndrome will have need of more (and more advanced) critical care support than those who are treated before mesencephalic ischemia can occur. This fact may also account for the relatively better outcome in the patient group treated early. For the future, integration of the clinical examination with early CT findings and new imaging techniques, such as perfusion- and diffusion-weighted MRI, might permit determination of the clinical significance of brain edema early after onset, thereby allowing us to gauge aggressive treatment forms such as decompressive craniectomy before life-threatening brain swelling and herniation occur.

In conclusion, we found hemicraniectomy to be an effective therapy for the condition of malignant MCA infarction. In our series of 63 patients, in those treated before the first and often still-reversible signs of herniation had occurred, the mortality rate was lower, there was a trend toward better outcome, and the patients were dependent on critical care for a shorter length of time. From this open trial we suggest that early hemicraniectomy can further the improve clinical outcome of patients in whom clinical deterioration is evident along with the neuroradiological signs of complete MCA stroke. To answer the question of when to perform surgical treatment of malignant space-occupying hemispheric infarctions, further prospective and controlled studies are required.

References


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