Decompressive Hemicraniectomy for Malignant Hemispheric Infarction

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Current Treatment Options in Neurology 2009, **11:**113–119
Current Medicine Group LLC ISSN 1092-8480

Opinion statement

Malignant middle cerebral artery infarction is associated with up to 80% mortality due to ischemic edema and brain herniation. No medical therapy has proven its efficacy in efficiently and durably reducing brain edema and improving patients' outcome. Decompressive surgery by a large hemicraniectomy with durotomy has been suggested as a life-saving emergency procedure. However, because of the lack of established prognostic criteria, the fear of severe and "unacceptable" residual disability in surviving patients, and the impossibility of considering the opinion of the patient at the time of decision, there was no consensus regarding this surgery. Recently the results of a pooled analysis of three European randomized trials (DECIMAL, DESTINY, and HAMLET) of early (≤ 48 hours) decompressive large hemicraniectomy in patients less than 60 years of age showed that, compared with medical therapy alone, there was a 50% (95% CI, 33%–67%) absolute risk reduction (ARR) of death, with more patients surviving with a slight to moderate disability (modified Rankin score of 2 or 3) (ARR of 23% [95% CI, 5%–41%]) or with a slight to moderately severe disability (modified Rankin score of 2, 3, or 4) (ARR of 51% [95% CI, 34%–69%]). About 5% of all patients in each therapeutic group were left with a severe residual disability (Rankin 5). These data indicate that early decompressive hemicraniectomy should be considered and fully discussed with the relatives of selected patients with a malignant hemispheric infarction.

Introduction

Stroke is one of the leading causes of death and long-term disability worldwide. In the acute phase of brain hemispheric infarctions, neurologic deterioration is the major cause of early death. Neurologic deterioration may be the consequence of either hemorrhagic transformation or progression of brain ischemic edema. Both situations result from dysfunction of cerebral capillaries and progressive alteration in the permeability of the blood–brain barrier [1•]. Brain edema has a progressive course during the first hours and days after a focal ischemia, with a maximum on days 3 to 5 [2]. It causes mass effect with midline shift, raised intracranial pressure, damage to normal brain tissues, and, finally, brain herniation and brain death in some cases of large middle cerebral artery (MCA) infarction. This type of stroke has been called malignant MCA or hemispheric infarction; its mortality ranges between 50% and 80% in observational studies [2]. Almost all deaths are related to brain herniation and occur during the first days after stroke onset. The underlying mechanism of malignant MCA infarction is either a carotid occlusion or a proximal MCA occlusion [2,3, Class IV]. In young patients, the most frequent etiologies identified are carotid dissection and emboli from a cardiac source, but the stroke remains cryptogenic in half of the patients [2,4••, Class I]. In patients older than 55 years, emboli from a cardiac source (particularly atrial fibrillation) may be more prevalent [5, Class IV].

Standard antiedema drugs include osmotic agents such as mannitol and glycerol, corticosteroids, and diuretics. None of these agents have been shown to

Table 1. Score description of the modified Rankin scale

Score	Description
0	No symptoms at all
1	No significant disability despite symptoms; able to carry out all usual duties and activities
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability; requiring some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent, and requiring constant nursing care and attention
6	Dead

prevent brain herniation or improve functional outcome after malignant hemispheric infarctions. In addition, all of these drugs have potentially serious adverse effects that limit their routine use.

Observational studies of decompressive surgery in malignant MCA infarction suggest that hemicraniectomy with durotomy can be associated with increased survival and good outcomes [6, Class IV]. Until recently, however, data from randomized, controlled trials were missing for nonbiased comparison between surgery and standard medical therapy. Thus, the decision to perform a hemicraniectomy was controversial, as questions regarding the outcome of patients were considered unanswered. A main concern was whether patients could have "acceptable" residual disability and a good quality of life. In addition, because of the very sudden onset of a malignant MCA infarction, it is impossible to consider the preference of the patient at the time of decision.

Recently, the effect of decompressive surgery on functional outcome in patients with malignant hemispheric infarction has been studied in three European randomized controlled trials: the French DECIMAL (Decompressive Craniectomy in Malignant Middle Cerebral Artery Infarcts) trial, the German DESTINY (Decompressive Surgery for the Treatment of Malignant Infarction of the Middle Cerebral Artery) trial, and the Dutch HAMLET (Hemicraniectomy After Middle Cerebral Artery Infarction with Life-Threatening Edema Trial) [7••,8••,9•, Class I]. A pooled, prospective analysis of the individual data from the three trials (including a total of 93 patients) showed at 1 year follow-up that more patients in the surgery group were alive with a moderate residual disability (Rankin score of 2 or 3) (Table 1) than in the medical therapy–only group, with an absolute risk reduction of 23% (95% CI, 5%–41%) [7••] (Table 2). In total, hemicraniectomy reduced mortality by 50% (95% CI, 33%–67%). Also, there were more patients alive with a moderately severe residual disability (Rankin 4) after surgery, whereas the number of patients with a severe residual disability was not increased and remained small (about 5%) [7••, Class I].

Table 2. Clinical outcome after decompressive hemicraniectomy and standard medical treatment for malignant hemispheric infarction*

Outcome measures at 1 y	Surgery group, %	Medical group, %	Absolute risk reduction, % (95% CI)	Number needed to treat
MRS ≤ 4	75	24	51 (34–69)	2
MRS ≤ 3	43	21	23 (5–41)	4
Survival	78	29	50 (33–67)	2

*Pooled analysis of three randomized controlled trials (n = 93).
MRS—modified Rankin scale.
(*Data from* Vahedi et al. [7••].)

The DECIMAL trial showed that younger patients had better outcome on the Rankin score in the hemicraniectomy group. Without surgery, the best predictor of death was the volume of infarction measured on diffusion-weighted imaging (DWI) within 24 hours of the onset of symptoms. No patients with a volume more than 210 cm^3 survived without surgery, whereas all patients screened but not included because of a DWI infarct volume less than 145 cm^3 survived [4••, Class II]. In the surgery group, baseline infarct volume on DWI was also a prognostic factor, with a nonsignificant trend toward better outcome with lower infarct volume [4••, Class II].

HOW TO RECOGNIZE A MALIGNANT MCA INFARCTION BEFORE SIGNS OF HERNIATION

Any impairment in level of consciousness during the first 24 hours of a hemispheric ischemic stroke is a powerful independent predictor of mortality [10]. Higher scores (≥ 15) on the National Institutes of Health Stroke Scale (NIHSS) and an infarct volume on DWI ≥ 145 cm^3 within the first 24 hours are other predictors of a malignant course of the infarction [4••,11]. On CT scan, predictors of fatal outcome within 48 hours of stroke onset are midline shift ≥ 5 mm, pineal shift ≥ 2 mm, hydrocephalus, temporal lobe infarction, and involvement beyond the MCA territory [12].

In the DECIMAL and DESTINY trials, patients were included on the basis of either early large hypodensity on CT scans (> 50% MCA territory) or large diffusion restriction on MRI (≥ 145 cm^3) before signs of mass effect [4••,8••, Class I].

The combination of both clinical and radiologic signs can predict a malignant course early in the progression of a hemispheric infarction. These signs include early impairment in level of consciousness (< 24 hours), high baseline NIHSS score, severe hemiplegia, and large volume of ischemic lesions on CT scan or diffusion MRI. Clinical signs of brain herniation, such as anisocoria, oculomotor nerve palsy, coma, decerebration, tachycardia, and mass effect on

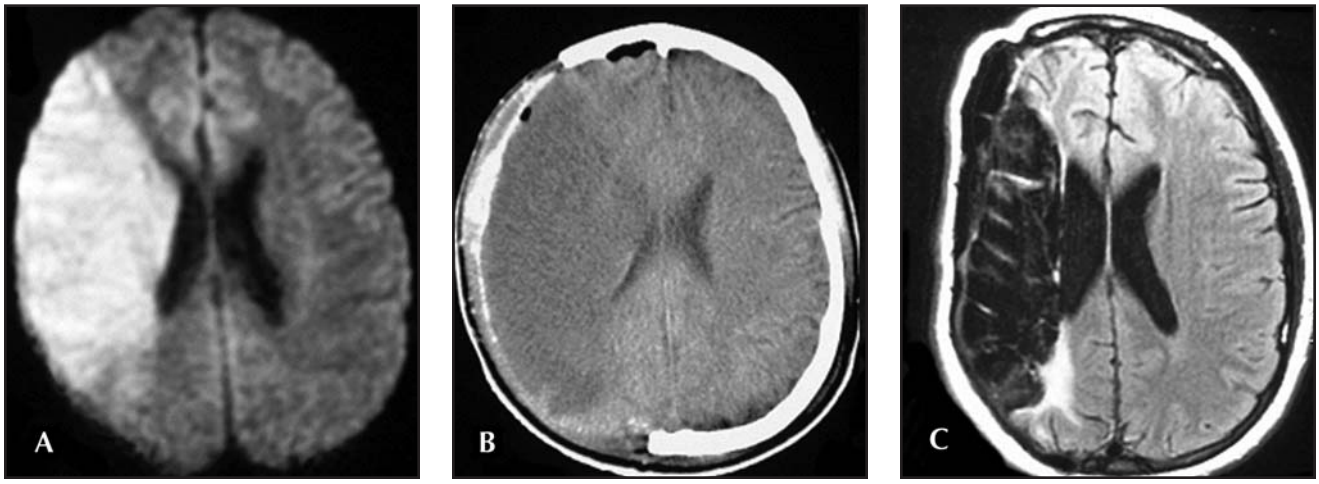

Figure 1. A, Baseline MRI scan of a 22-year-old woman with an infarct volume on diffusion-weighted imaging of 173 cm^3. **B,** A large right hemicraniectomy was performed at 20 hours from stroke onset. **C,** At 1 year follow-up (6 months after reconstruction of the bone defect), her Rankin score was 3 and fluid-attenuated inversion recovery (FLAIR) imaging revealed right-hemisphere atrophy.

brain imaging, were not selective criteria for the evaluation of decompressive hemicraniectomy in randomized trials, as they appear late in the course of the ischemic edema and may shortly precede brain herniation and death [7••].

LONG-TERM OUTCOME AFTER HEMICRANIECTOMY

Although the results of the randomized trials show a very significant increase in the probability of survival without increasing the number of very severely disabled survivors, the decision to perform decompressive hemicraniectomy should be made on an individual basis for every patient [7••, Class I]. Indeed, a favorable outcome after a malignant hemispheric infarction does not mean complete recovery, but rather recovery with "acceptable" disability. In deciding whether to perform decompressive surgery, prognostic factors such as young age, absence of any preexisting disability or severe comorbid disease, and the presence of strong family support should always be considered. More studies on patients' and family members' perception of surviving with a substantial disability may improve long-term follow-up of the patients.

Treatment

- Therapeutic management of a large hemispheric infarction should be started by an early admission of the patient to an intensive stroke unit [13, Class I] for a sequence of assessment and treatment:
  - Medical assessment and emergency brain imaging with CT or MRI; MRI with DWI has the advantage of higher sensitivity for early ischemic changes than CT. The neuroradiologist should have a written procedure for the measurement of the infarct volume in the diffusion-weighted images [4••, Class II] (Fig. 1).
  - Continuous monitoring of neurologic status, pulse, blood pressure, temperature, and oxygen saturation.
  - Standard medical treatment.
  - Multidisciplinary consideration of early decompressive surgery in selected patients based on time from stroke onset, the presence of clinical and radiologic criteria of malignant hemispheric infarction, age, associated severe diseases, and the willingness of the patient or relatives.
  - Rehabilitation by a specialized, multidisciplinary team.

Standard medical treatment

- The aims of standard medical treatment in the acute phase of a large hemispheric infarction are to prevent general complications and neurologic

deterioration secondary to the stroke. Therapy is based on established stroke treatment guidelines [14••,15••, Class I].

- It is recommended to avoid factors that may exacerbate brain edema (eg, hyperthermia, hyperglycemia) and to keep the head of the bed elevated at 30 degrees to help venous drainage.
- Intravenous fluid restriction (500 mL/d) using normal saline (0.9%) is recommended; the use of intravenous glucose solutions is discouraged unless necessary.
- The administration of intravenous mannitol (0.25–0.5 g/kg) or furosemide is recommended only for patients whose condition is rapidly worsening.
- In an acute ischemic stroke, blood pressure must be sufficient to perfuse the brain, but excess blood pressure may promote edema and may help to increase intracranial pressure in cases of malignant MCA infarction [1•]. On the other hand, lowering blood pressure too far may also promote edema if tissue perfusion is reduced too much. It is thus recommended to maintain a systolic blood pressure ≤ 220 mm Hg and a diastolic blood pressure ≤ 100 mm Hg, using intravenous antihypertensive drugs and repeated measures of blood pressure.
- There is no evidence that the prophylactic use of anticonvulsants in the acute phase of an ischemic stroke is beneficial.
- If oxygen saturation falls below 96%, administration of 2 to 4 liters of oxygen via a nasal tube is recommended. Endotracheal intubation and ventilation may be necessary to maintain adequate tissue oxygenation in patients with severely increased intracranial pressure, seizures, or inhalation pneumonia.
- Continuous invasive intracranial pressure monitoring is not recommended.

Cost/cost-effectiveness Although not specifically studied in patients with a malignant hemispheric infarction, it has been shown that increased costs of care in a dedicated stroke unit in the acute phase of stroke are counterbalanced by improved function and markedly reduced costs to society late after stroke [13, Class I].

Surgery

Decompressive hemicraniectomy with durotomy

Decompressive surgery in a malignant hemispheric infarction has three aims: 1) to decrease intracranial pressure by increasing the intracranial volume; 2) to prevent brain herniation and subsequent brain death; and 3) to decrease mortality and improve functional outcome in selected patients.

Standard procedure Decompressive surgery for a malignant hemispheric infarction consists of a large hemicraniectomy, removing (ipsilateral to the stroke) as large a bone flap as possible, including temporal, frontal, parietal, and (partly) occipital bones. The dura must be widely open to give more volume to the swollen brain. Duraplasty for dural expansion by implantation of various materials depends on the choice of the neurosurgeon; there is no standard recommendation. No resection of swollen ischemic brain is performed.

Contraindications Any severe coagulation disorders, any severe coexistent disorders that may interfere with short-term or long-term outcome, any significant preexisting disability that may interfere with functional outcome, the wish of the patient not to remain alive with a moderate or severe disability.

Complications Collection of cerebrospinal fluid (CSF) under the scalp, CSF collection within the brain, hydrocephalus, local infection (empyema and cerebral abscess), extradural hemorrhage, intracerebral hemorrhage, CSF hypotension.

Cranioplasty

Once the intracranial hypertension is resolved, the cranial defect should be closed by means of a cranioplasty, which has two aims: 1) restoration of a normal intracranial pressure, and 2) aesthetic cranial reconstruction for an improved clinical and psychological outcome.

Standard procedure Different procedures may be used, including the use of autologous bone, different types of synthetic resins, and titanium. The best time for the closure of the bone defect is not well known, but the cranioplasty should be performed as soon as possible during the first months after stroke, to normalize cerebral hemodynamics and intracranial pressure and for psychological and aesthetic reasons.

Contraindications Any contraindications to general anesthesia.

Complications Dural tear with CSF effusion, CSF collection under the scalp, CSF collection within the brain, communicating hydrocephalus, local infection (empyema, cerebral abscess), extradural hemorrhage, aesthetic concerns.

Cost/cost-effectiveness Cost depends on which procedure is used. Some implants, such as titanium, may require costly, high-tech equipment.

Physical/Speech Therapy and Exercise

After hemicraniectomy, patients will need early and long-duration rehabilitation by a multidisciplinary team with expertise in severe stroke [14••,15••, Class I]. The interventions should include speech therapy, physiotherapy, occupational therapy, and nursing.

Specific therapy Assistive devices and orthoses are usually needed to help gait and walking ability. Spasticity in the chronic phase requires posture and movement therapy, as well as botulinum toxin or neurotomy to improve range of movements, balance, and gait.

Special points It is important to maintain rehabilitation for at least 5 to 10 years after the stroke.

Cost/cost-effectiveness There are long-term functional benefits of care in a dedicated multidisciplinary stroke unit for patients with stroke; the risk of deterioration in function is reduced and activities of daily living are improved [14••,15••, Class II].

Pharmacologic therapy

Antithrombotic agents

- Aspirin is safe and effective when started within 48 hours after stroke [14••,15••, Class I] but it has not been evaluated when administered before surgery in patients undergoing hemicraniectomy for a malignant hemispheric infarction. When its administration has been delayed, aspirin should be started as soon as possible after surgery.
- Patients with hemicraniectomy are at high risk of deep venous thrombosis and should have all proven prophylactic measures that decrease this risk, including early mobilization and low-dose heparin (subcutaneous low molecular weight heparin) [14••,15••, Class I].

Antidepressant drugs

- Depression has been reported in up to 50% of patients with malignant hemispheric infarction, and it may even be more prevalent. Antidepressant drugs such as selective serotonin reuptake inhibitors can improve poststroke depression [14••,15••, Class I]. Their primary administration has also been proven to reduce the incidence of poststroke depression at 1 year [16•, Class II].

- There are no data on the incidence of mood disorders in close relatives or caregivers of patients with hemicraniectomy and no evidence to recommend specific prophylactic therapy for prevention of such disorders. However, psychotherapy may help relatives to better understand and support the patient.

Antiepileptic drugs

- The risk of late epilepsy in malignant MCA infarction is high (about 50%) [4••, Class I]. Recurrent seizures require the prolonged use of anticonvulsants [14••,15••, Class IV].
- There is no evidence that one antiepileptic drug is more beneficial than another for these patients. Standard antiepileptic drugs should be used according to general principles of seizure management.

Emerging therapies

- Moderate hypothermia (32°–33°C) has been found to reduce intracranial pressure in malignant MCA infarction, but intracranial pressure increases during rewarming [17, Class IV]. There are no randomized trials comparing hypothermia with standard medical therapy or decompressive hemicraniectomy.
- A small, randomized clinical trial compared a combination of moderate hypothermia (35°C) and hemicraniectomy versus hemicraniectomy alone in patients within the first 24 hours of a brain infarction involving more than two thirds of one hemisphere. There was no difference between the two groups in overall mortality and no severe adverse events related to hypothermia [18, Class IV].

Pediatric considerations

- Experience with hemicraniectomy in children with malignant hemispheric infarction is limited. One study reported on four children who underwent decompressive hemicraniectomy for malignant infarctions [19, Class IV]. At the time of follow-up, all patients were alive and able to walk and speak.
- Because of the very rare incidence of malignant hemispheric infarction in children and the results of randomized trials in young adults, randomized trials evaluating decompressive surgery in children with this disorder would be unfeasible and unethical. Thus, decompressive hemicraniectomy with durotomy should be considered in children with this disorder, as in adults.

Disclosure

No potential conflict of interest relevant to this article was reported.

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have been highlighted as:
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