

# Decompressive hemicraniectomy for malignant MCA territory infarction

Erion Musabelliu, Yoko Kato, Shuei Imizu, Junpei Oda, Hirotohi Sano

**Abstract:** A number of patients with ischemic cerebrovascular stroke suffer a progressive deterioration secondary to massive cerebral ischemia, oedema, and increased intracranial pressure (ICP). The evolution is often fatal. Stroke is the second leading cause of death worldwide. Life-threatening, complete middle cerebral artery (MCA) infarction occurs in up to 10% of all stroke patients, and this may be characterized as massive hemispheric or malignant space-occupying supratentorial infarcts.<sup>35,50</sup> Malignant, space-occupying supratentorial ischemic stroke is characterized by mortality up to 80%, several reports indicated a beneficial effect of hemicraniectomy in this situation, converting the closed, rigid cranial vault into a semi open.

The main cause of death encountered in these patients is severe postischemic brain oedema leading to raised ICP, clinical deterioration, coma, and death.<sup>20,44</sup> The result is dramatic decrease in ICP and a reversal of the clinical and radiological signs of herniation. For these reasons, decompressive craniectomy has been increasingly proposed as a life-saving measure in patients with large, space-occupying hemispheric infarction.

Recent successes with intra-venous<sup>(52)</sup> and intra-arterial<sup>(11)</sup> thrombolytic therapy have resulted in an increased awareness of stroke as a medical emergency.<sup>52</sup> Thus, increasing numbers of patients are being evaluated in the early hours following the ictal event. In the process of gaining more experience in the early management of patients with acute ischemic stroke, it has become clear that in a number of these patients a progressive and often fatal deterioration secondary to mass effect from the oedematous, infarcted tissue occurs. An increasing body of experimental and clinical evidence suggests that some of these patients may benefit from undergoing a decompressive craniectomy but the timing and indications for this potential lifesaving procedure are still debated. Early hemicraniectomy based on radiographic and clinical criteria, but before signs of brainstem herniation, has been proposed as a means of improving outcomes.

The objectives of the review are to help better define the selection criteria for performing the surgery in case of supratentorial infarctions, to assess the immediate outcome in terms of time conscious recovery and survival and to assess long term outcome using standard and functional assessment scales. (p9-18)

**Key words:** Ischemic stroke, decompressive surgery and craniectomy.

## Historical background

Decompressive craniectomy procedures have been used to relieve increased ICP and cerebral oedema caused by a variety of pathological events. This technique (decompressive craniectomy) first applied in 1905.<sup>6</sup> In 1905, Cushing reported the use of this procedure to relieve the pressure

caused by the growth of an intracranial tumor.<sup>1,28,49</sup> Since then, surgical decompression has been reported as a treatment option for traumatic head injury<sup>(16,18,38,32)</sup>, subdural haematoma<sup>(5,39)</sup>, oedema resulting from vasospasm secondary to subarachnoid haemorrhage<sup>(12)</sup>, encephalitis<sup>(29,46)</sup>, intracerebral haematoma<sup>(8)</sup>, cerebral venous and dural sinus thrombosis<sup>(51)</sup>, cerebellar infarction<sup>(21,23)</sup> and supratentorial cerebral ischemia.<sup>48</sup>

As no randomized control data are currently published, we reviewed the literature and analyzed the data, enrolling results abstracted from recent and earlier studies.

In the 1950s and 60s, a number of reports were published in which the authors described cases of massive cerebral ischemia accompanied by acute and severe brain swelling.<sup>1</sup> These cases were often fatal, with the oedema caused by the

Department of Neurosurgery  
Fujita Health University  
Toyoake  
Japan

**Correspondence:**

Dr. Erion Musabelliu  
Department of Neurosurgery  
Fujita Health University Hospital  
1-98, Dengakugakubo, Kutsukake  
Toyoake, Aichi 470-1192  
Japan  
Email: erionmusabelliu@yahoo.com

infarct producing a “pseudotumour” increasing in pressure within the cranial vault.<sup>33</sup> In 1968, Greenwood used surgical intervention in the treatment of such cases, which decreased the mortality rate to below 50% as reported.<sup>17</sup> In Greenwood’s series of 9 patients with acute infarction involving the MCA or ICA, decompressive hemicraniectomy as well as resection of the necrotic parenchyma were performed. Six of these patients survived, although 3 suffered postoperatively from severe disability. In their report in 1971, Kjellberg and Prieto described a bifrontal decompressive craniectomy procedure for the treatment of a massive infarction; however, the patient did not survive.<sup>30</sup> In 1981, Rengachary and co-workers reported the first cases in which straightforward craniectomy were undertaken, without removal of necrotic brain tissue.<sup>41</sup> Since that study, more than 100 additional cases of hemicraniectomy and two of bilateral craniectomy have been reported in the treatment of massive cerebral ischemia (Table 1).

**“Malignant” cerebral infarction**

Ischemic cerebral infarction is associated with a high rate of morbidity and mortality. Mortality rates are highest when lesions involve the trunk of one or more of the main cerebral vessels. In fact, occlusion of either the distal ICA or proximal MCA trunk has been characterized as a “malig-

nant” stroke in both clinical and animal studies.<sup>10,20</sup> Of all cases with supratentorial infarctions in which an autopsy is performed, 13% are shown to suffer from severe brain swelling after an infarction involving the entire distribution of the ICA or MCA.<sup>36</sup> Severe cerebral oedema can lead to herniation of cerebral structures through the tentorium or falx, as well as the brainstem structures through the foramen magnum. In fact, transtentorial herniation has been cited as the probable cause of death in many of these cases of malignant stroke. Bounds et al<sup>(2)</sup> reviewed 100 autopsy cases of patients in whom an infarction involving the ICA distribution had been diagnosed.<sup>2</sup> Thirty-one patients died of tentorial herniation, which was the only neurological cause of death in all the cases reviewed.

The prognosis for patients who suffer a “malignant” cerebrovascular accident (CVA) is poor, with death occurring usually within the first 4 to 5 days. In this subset of patients, a mortality rate of 78% (estimated to be between 50% - 78%) was observed by Hacke, et al.<sup>20</sup> All deaths were attributed to transtentorial herniation, which occurred within 2 to 7 days (median 4 days). Similarly, Schwab and co-workers have found that 81% of patients with malignant CVA died, and all deaths occurred within 5 days and were caused by herniation.<sup>45</sup> Given the poor prognosis in these

**Table 1** - Clinical studies in years: Summary of large case series with massive supratentorial infarct.

Author, year	No. of cases	Mean age / y	Patients with early surgery n (%)	Patients with brain-stem signs, n (%)	Mean time to follow-up, mo	Patients with good outcome n (%)	Patients died n (%)	Patients with severe disability n
Greenwood 1968	9	49.8	Not given	Not given	Not given	3 (33)	3 (33)	3 (33)
Kjellberg and Prieto 1971	1	Not given	1 (100)	1 (100)	Not given		1 (100)	
Ivamoto et al, 1974	1	49	0	1 (100)	7	1 (100)	0 (0)	NA
Rengachary et al, 1981	3	31	0	3 (100)	21	1 (33)	0 (0)	NA
Young et al, 1982	1	59	0 (0)	1 (100)	9	0 (0)	0 (0)	NA
Hacke et al, 1985	54	56	Not given	45 (82)	1	Not given	43 (78)	Not given
Ojeman et al, 1988	2	Not given	Not given	Not given	Not given	Not given	Not given	Not given
Kondziolka et al, 1988	4	42	2 (50)	4 (100)	20	4 (100)	0 (0)	NA
Delashaw et al, 1990	9	57	3 (33)	7 (78)	15	4 (44)	1 (11)	8/9
Jourdan et al, 1993	7	43.8	7 (100)	Not given	Not given	3 (43)	0 (0)	4/7
Kalia and Yonas 1993	4	34	1 (25)	2 (50)	17	3 (75)	0 (0)	2/4
Rieke et al, 1995	32	49	8 (25)	24 (75)	13	16 (50)	11 (34)	NA
Carter et al, 1997	14	49	5 (36)	14 (100)	12	8 (57)	3 (21)	6/11
Sakai et al, 1998	24	63.6	15 (62)	18 (75)	2	0 (0)	8 (33)	16 (67)
Schwab et al, 1998	31	50.3	31 (63)	4 (31)	3	26 (31)	5 (31)	NA
Yoo et al, 1999	2	29	Not given	Not given	Not given	2 (100)	0 (0)	NA
Mori et al, 2001	19	67	Not given	Not given	3	4 (21)	3 (16)	12 (63)
Koh et al, 2000	7	45	NA	NA	7	2 (29)	1 (14)	NA
Holtkamp et al, 2001	12	65	4 (33)	0 (0)	7	1 (8)	4 (33)	NA
Leonhardt et al, 2002	26	50	11 (42)	NA	12	11 (42)	6 (23)	14/20
Walz et al, 2002	18	50	9 (50)	NA	14	6 (33)	6 (33)	11/12
Gupta et al, 2004	9	53	2 (22)	6 (66)	8	1 (11)	1 (13)	3/8
Kastrau et al, <sup>(27)</sup> 2005	14	39 ± 7	Not given	Not given	*			
Pillai A et al, <sup>(37)</sup> 2007	26	48.4 ± 3.2	Not given	9 (35%)	6	60%	7 (28%)	2/ 19 (12%)

\*Recovery from aphasia after hemicraniectomy for infarction of the speech-dominant hemisphere.

patients, it is of critical importance to recognize imaging or clinical characteristics suggestive of such a progressive and rapid deterioration. In patients who suffer a malignant CVA the clinical course is generally predictable. The clinical course in these patients is uniform, with clinical deterioration developing within the first 2 to 3 days after stroke. Presenting symptoms may include the sudden onset of hemiplegia, homonymous hemianopsia, forced eye and head deviation toward the lesion side, and aphasia. Precipitous coma and papillary dilation usually occur together following the initial symptoms.<sup>4,7</sup> In the absence of further intervention, death occurs.

To establish objective criteria for aggressive intervention, many investigators have measured ICP once significant clinical deterioration is apparent. In an early study the authors showed that patients in whom ICP values were greater than 15 mm Hg did not survive the malignant infarct.<sup>44</sup> In subsequent studies other authors have shown that a fatal outcome occurred in most cases when the level was greater than 30 mm Hg.<sup>4,22,36,42,45</sup> In addition to clinical findings, neuroimaging criteria can help to identify those patients at particular risk for a malignant infarction in the early phase of their stroke. In patients with malignant CVA, a large area of parenchymal hypodensity in the MCA territory is often visualized on the admission CT scans.<sup>43,47</sup> With progressive clinical deterioration, CT-demonstrated signs may also include mass effect, effacement of the basal cisterns, compression of the ventricular system, a shift of midline structures,<sup>(55)</sup> and herniation of tissue through the falx, foramen magnum, or tentorium. These patients present clinically with 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.<sup>54</sup> As no model of medical treatment has been proven superior to the others, treatment options may vary, depending on each clinic protocol. The value of conventional therapies in this condition, as in others of raised ICP, consisting of artificial ventilation, osmotherapy, and barbiturate administration, has been a subject of debate.

### **Rationale for decompressive craniectomy and experimental studies**

Cerebral ischemia results in oedema formation in and around the ischemic area. The larger the area of the infarction, the greater the extent of oedema. In the case of malignant CVA, the entire vascular distribution of the MCA, and possibly the anterior cerebral artery, is compromised. A severe oedematous response ensues throughout a large area.<sup>44</sup> Oedema is responsible for the parenchymal hypodensity that is demonstrated on CT scanning.<sup>28,40</sup> Progressive brain oedema and the exacerbating effect it has

on increasing ICP can cause the area of damaged brain to extend. Within the confined cranial vault, the oedematous tissue places pressure against surrounding normal parenchyma. This is evidenced by the changes seen on CT scanning. Intracranial hypertension results in decreased cerebral perfusion pressure and therefore decreasing blood supply throughout the cerebrum. Because of the increase in mechanical pressure and ICP, other major cerebral vessels may be compressed by the expanding tissue, against dural edges or against the skull. The result is secondary ischemia and a further expansion of the infarcted area.<sup>3</sup>

Although originally proposed as a life-saving procedure, increasing experimental and clinical evidence indicates that an early decompressive craniectomy can limit the extension of the infarcted area. From a mechanical perspective hemicraniectomy provides an immediate opening in the otherwise closed cranial vault. Therefore, compression of normal tissue is prevented or limited. The additional space created allows the tissue to expand through the bone defect, away from midline structures, so that CT-demonstrated changes normally observed when surgery is not performed like midline shift, decreased ventricular size, and herniation are minimized or completely resolved postoperatively.<sup>28,31,44</sup> As the cranial vault has essentially been expanded during surgery, there is an immediate decrease of ICP. Jourdan et al, found that initial ICP values of 25 to 60 mm Hg decreased by 15% once the bone flap was removed, and by 70% once the dura was opened, resulting in the normalization of the ICP after surgery.<sup>24</sup> Similar findings were demonstrated in a more recent study in which the authors reported performing a bilateral craniectomy.<sup>56</sup> In 2 patients with ischemic CVA whose initial ICP values were 54.8 mm Hg and 20 mm Hg, respectively, removal of the bone flap caused a decrease in ICP to 35.5 mm Hg and 10 mm Hg, and opening of the dura caused a reduction to 4.4 mm Hg and 3 mm Hg, respectively. In the immediate postoperative period, the ICP values were recorded as 4.4 mm Hg and 10.2 mm Hg. A decrease in ICP allows for an increase in cerebral perfusion pressure, aiding blood flow to the ischemic area, optimizing circulation to the damaged area through collateral vessels. Because hemicraniectomy alone may improve blood flow in the ischemic area, surgical resection of the infarcted tissue should not be conducted in these patients. Although such resection or "strokectomy" has been associated with postoperative improvements in some cases, it is impossible to differentiate at surgery between ischemic tissue and necrotic tissue.<sup>26,41</sup> Being poorly delineated from necrotic tissue, the ischemic area may possibly be damaged or removed upon resection of the infarct.

### **Timing and indications**

Hemicraniectomy has for a long time been used as a last resort to prevent impending death after all medical therapies

have been attempted. The surgical procedure certainly preserves life, as evidenced by decreased mortality rates when compared with patients who undergo medical therapy alone.<sup>44</sup> In many of the reported cases, the symptoms of a severe herniation syndrome, fixed, dilated pupils, precipitous coma, cardiorespiratory difficulties and decerebrate posturing,<sup>28</sup> were used to indicate the need for decompressive surgery.

Patients suffering malignant CVA receive antioedema medical treatment (steroids, mannitol) and hyperventilation, before considering a decompressive craniectomy. Usually, an initial reversal of symptoms, such as the degree of pupillary dilation, occurs with aggressive medical treatment. After its initial effectiveness, however, additional medical therapeutic efforts often fail to control or prevent herniation. In the case of massive cerebral ischemia, the effectiveness of such medical therapy is severely limited, at best, as evidenced by the high mortality rates observed in the absence of surgical intervention. As Rengachary et al, have noted in the case of stroke, which is typically not treated surgically, physicians may wait too long to intervene surgically.<sup>40,41</sup> Once the pupils are fixed and a deep coma has indicated an irreversible decline of cerebral function, surgery should not be performed.

Evaluation of experimental findings suggests that, early surgical decompressive surgery for the treatment of massive cerebral ischemia may limit the extension of the infarction and reduce morbidity.<sup>9,13</sup> Forsting et al, have demonstrated that craniectomy can decrease the infarct volume and improve neurological outcome in a rat model of MCA occlusion when surgery is completed early (1 hour postictus).<sup>13</sup> Doerfler et al, found similar results in the same model when surgery was completed 4 hours postictus.<sup>9</sup> In the 4-hour treatment group, outcome and infarct volume were significantly better as compared with those observed in control animals and animals surgically treated at 12, 24 and 36 hours postictus. Animals treated at these later time periods improved, but no significant differences were reported among these three groups and the control group. The results of recent clinical studies support this notion.<sup>9,10,13</sup> When patients who suffer malignant CVA were surgically treated on average 21 hours postictus, there was a greater decrease in mortality rate and length of stay in the intensive care unit as compared with patients who underwent surgery an average 39 hours postictus. There was also a trend of improved Barthel Index scores demonstrated at follow-up for patients in the earlier surgical group. Several factors need to be considered to optimize both the timing and the indication for decompressive craniectomy (Table 2).

**Intracranial pressure monitoring**

Intracranial pressure monitoring has been recommended as

a guide to surgical timing.<sup>57</sup> Carter et al, have used an ICP measurement of greater than 25 mm Hg<sup>(4,42,43)</sup> and Rieke et al, a measurement of greater than 30 mm Hg, despite attempts at medical therapy, as an indicator for surgical intervention.<sup>42</sup> Increased ICP measurements are preceded by the constellation of clinical signs and symptoms constituting the “malignant CVA syndrome;” thus, the usefulness of ICP monitoring in these cases has been questioned. But, brain tissue shifts rather than raised ICP are probably the most likely cause of the initial decrease in consciousness.

**Table 2 -** Clinical and instrumental criteria used in evaluation of the patients.

Parameter	Time of surgery	Patient's outcomes. 1, 3, 6 months
Age	Mean ± SD	Survival after one month (in percentage - of enrolled patients)
Sex	Percentage	
Territory of infarction • MCA • MCA/ ACA • MCA/ PCA	Number	• Barthel Index • NIHSS score • MRS score
Hemisphere	Left / Right	
Pathological mechanism (if known) • Emboli • Dissection • Other	Number	• Functionally independent • Mild to moderate disability • Severely disabled
Other related disease/ conditions		
On admission • Barthel Index score • SSS score • GCS	Mean ± SD	
Time to surgery	Mean	
Imaging findings CT/ MRI Signs of herniation before surgery	Percentage	
Mortality rate (after surgery)	Percentage	
Time on NCU	Day	
Time of recovery		

**Neuroimaging studies**

Extensive MCA infarction with oedema in greater than 50% of the MCA territory can be identified early after the ictal event on CT scans, and it is observed on the initial CT scan in approximately 69% of the reviewed cases by Hacke et al.<sup>20</sup> Parenchymal hypodensity in greater than 50% of the MCA territory is highly indicative of a progressive clinical course, leading to severe morbidity or death. With current, newer CT scanners, parenchymal hypodensity can be seen and followed soon after symptom onset.

In all series of Schwab et al, most of the patients had at least two CT scans, one, within first 4 days after stroke and in some series within the first 12 hours after symptom onset, and the second one with the deterioration of symptoms and or after surgery.<sup>45-48</sup>

A midline shift of the cerebral structures is another phe-

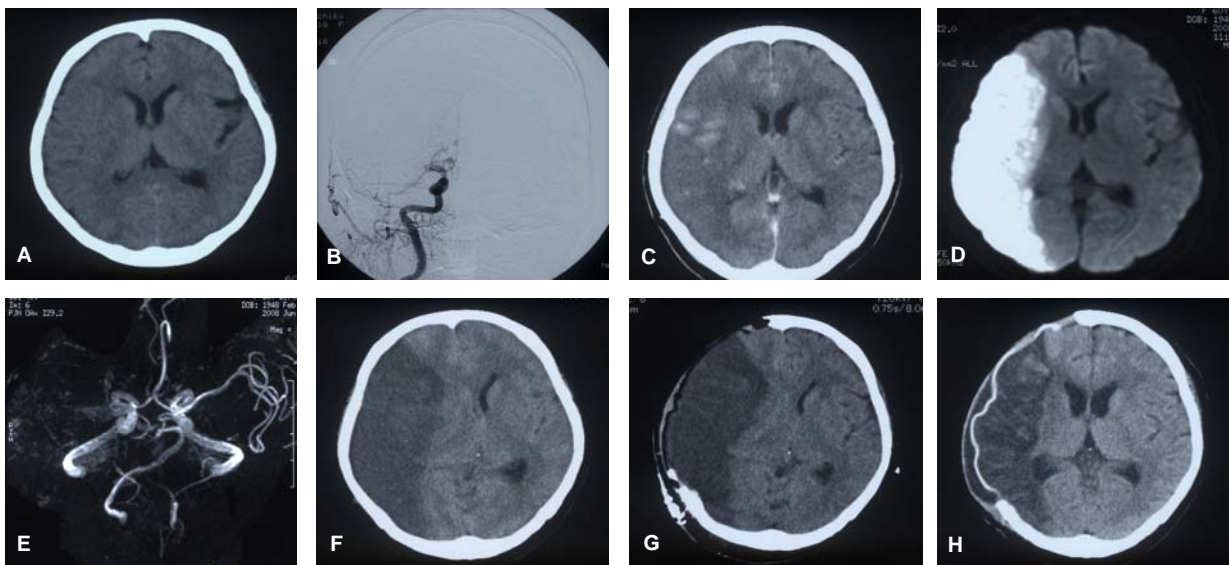
nomenon of increasing unilateral cerebral oedema that can be identified on CT scanning. Rieke et al,<sup>(42,43)</sup> have found that the amount of midline shift was significantly different between survivors and nonsurvivors of malignant CVA. In a recent study conducted to examine only the prognostic value of midline shift, it was suggested that at 32 hours after the occurrence of cerebral infarction, a shift of the third ventricle greater than 4 mm was indicative of a fatal outcome.<sup>15</sup> Regardless of its potential for prognostic significance however, midline shift is not visualized as early on CT scanning as is parenchymal hypodensity. Early changes demonstrated on CT scans are also an indicator of the viability of collateral circulation. In their study von Kummer et al,<sup>(9,20,54)</sup> performed cerebral angiography in patients in whom stroke was demonstrated early with CT scanning. Comparing the angiographic findings with those obtained using CT scanning, the authors observed that parenchymal hypodensity in greater than 50% of the MCA territory was predictive of poor collateral circulation, as evidenced by the angiographic study. These findings are important, because in patients with adequate collateral circulation, decompressive hemicraniectomy may not be necessary.

From neuroradiological studies it has been well recognized

that “early visual radiolucency” in the CT examination is a negative outcome predictor. Continued refinements of newer imaging techniques such as diffusion / perfusion magnetic resonance will lead to an earlier identification of those patients more likely to benefit from early decompressive craniectomy.

### Patient age

The age of patients undergoing surgical intervention reported in the reviewed series ranged from 11 to 70 years of age. Based on data provided in the literature, it was impossible to determine if a certain age range of patients benefits more from surgical decompression. Most investigators, however, noted that they are more aggressive in performing hemicraniectomy in young patients in whom CVA has occurred and that the young seemed to benefit more from the procedure. Carter and co-workers specifically divided their patients by age in those younger than and older than 50 years of age.<sup>4</sup> They found that 5 of 5 patients under the age of 50 years made a good functional outcome (Barthel Index scores > 60 [100 = independent, 60-95 minimum assistance, and < 60 = dependent]), whereas only in 3 of 6 patients over 50 years of age was this observed at follow-up examination. In theory and in practice, it would



**Figure 1** - Brain images from a 60 year-old woman, with malignant R MCA infarction, admitted in our clinic within one hour from the acute onset of clinic, she was found with disturbances of consciousness and severe weakness in her left extremities. (a) CT scan demonstrating early CT findings of acute ischemic stroke (within 3 hours from onset) - slight changes, right sulci and Sylvian fissure effacement - effacement of R insular islands and structures of basal ganglia. Recombinant tissue plasminogen activator (RTP) treatment failed. (b) R ICA AP angiogram after RTP failure reveals absence of R MCA - proximal occlusion. (c) CT scan demonstrating the R MCA territory infarction, immediately after the mechanical removal of thrombus (recanalization) failed. (d) MRI T2-weight diffusion, revealing R MCA territory infarction with early cytotoxic oedema. (e) MR angiography revealing the absence of flow - related enhancement in the R MCA. Confirming persistent proximal occlusion of R MCA. (f) CT scan on day one, demonstrating evolving R MCA infarction with mass effect and compression of the ventricular system, the day that surgery was completed. Clinical examination revealed right midriazis. (g) CT scan, one day after hemicraniectomy (in which large fronto-parieto-occipital bone was removed), revealing the presence of midline shift. (h) CT scan, one month posthemicraniectomy, with resolution of previous midline shift.

seem that younger patients with ischemic stroke would benefit from early decompressive surgery for the following reasons:

- Their brains are less atrophied, allowing less room for oedematous expansion within the cranial vault. Individuals aged 50 years and younger have been identified as benefiting more from bilateral decompressive craniectomy in cases of subarachnoid haemorrhage because of their unatrophied brains, as compared with those over 50 years of age.
- The ventricular system in younger persons is smaller than in older persons.
- It has been proposed that the oedematous response to ischemia is greater in younger individuals.

### Dominant hemisphere infarction

As a rule, investigators in the past did not undertake surgery in patients with dominant hemisphere infarctions. The loss of communicative abilities and a plegic dominant upper extremity were judged to be too damaging. Analysis of recent evidence suggests that considering a dominant hemisphere infarction to be a contraindication to surgery may be too harsh a criterion. A recent study, by Rieke and co-workers, included 7 patients who experienced massive dominant hemisphere CVA and who underwent hemispheric craniectomy.<sup>42,43</sup> One of those patients died. Good functional outcome was achieved in the remaining 6 patients (Barthel Index scores ranging from 60-100). All surviving patients were able to understand and communicate despite some aphasia, and one patient suffered no aphasic deficits. In another study, by Schwab et al, involving 5 hemispheric craniectomy treated patients who suffered dominant hemisphere CVA, no patients were diagnosed as being globally aphasic at follow-up.<sup>48</sup> Three patients sustained communication deficits that were so minor as to allow them to return to work. Functionally, the patients with the dominant hemisphere infarct who underwent hemispheric craniectomy were not significantly different from those patients who underwent craniectomy after CVA in the nondominant hemisphere. Therefore, surgery can be considered in patients with dominant hemisphere infarction, especially if some residual language function is present at admission.

There has been interest in identifying which patients will develop malignant cerebral oedema after massive infarcts, patients at high risk (Table 3).

### Technique, results and complications

#### Operative technique

Hemispheric craniectomy for supratentorial infarction usually involves aggressive bone removal to alleviate better the symptoms of malignant cerebral oedema. The need for a radical approach, extension of bone removal, was recognized by Guerra et al, in the event of severe posttraumatic cerebral

oedema.<sup>18</sup> His observation was echoed in the case of massive cerebral ischemia by Rieke and co-workers, who found that a few of their initial surgically treated patients harboured a bone defect that was too small, not providing adequate space for decompression and resulting in brain herniation through the skull opening.<sup>42,43</sup> Prolapse of the oedematous brain through the edges of the craniectomy defect, with possible exacerbation of brain damage is one of the possible limitations of decompressive craniectomy. In the case of cerebral infarction, however, this phenomenon does not result in significant increased cerebral damage or venous stasis, because most likely the protruding tissue is already necrotic.

**Table 3** - Criteria proposed to use for inclusion/ exclusion of patients and clinical outcome.

Inclusion criteria	Exclusion criteria
Age 18 - 60 years	Prestroke mRS score $\geq$ 2
NIHSS score nondominant hemisphere > 18 dominant hemisphere > 20	Prestroke score Barthel Index < 95
Imaging - documented unilateral infarction. • MCA at least 2/3 of territory and at least part of basal ganglia. • $\pm$ Additional infarctions in ACA or PCA territory. Ipsilaterally.	GCS < 6
Time - onset of symptoms	Bilateral - pupils fixed and dilated
	Other brain related diseases
	Haemorrhagic transformation of the infarct
	Life expectancy < 3 years
	Other related disease/ conditions - affecting outcome. Especially coagulopathy/ systemic bleeding disorders. Pregnancy.
	Contraindication for anaesthesia

In the event of massive cerebral ischemia, the frontal, temporal, and parietal bones overlying the infarcted hemisphere are removed. The dura is incised and reflected. A dural expansion graft of pericranium, lyophilized cadaver dura, homologous temporal fascia, or synthetic material is loosely sutured to the dura edges to prevent cortical adhesions. The dura is fixed to the craniectomy edges to prevent or limit epidural bleeding, and the temporal muscle and skin flap are reapproximated and sutured or stapled into place. The bone flap may be frozen or preserved in a subcutaneous pocket overlying the abdomen. Cranioplasty is then performed at a later date, when functional recovery has stabilized. Artificial flaps have also been used to close the bone defect.

### Results

For more than 20 years, more than 250 patients have been selected from case reports or series; range age 10 to 76 years, predominantly male patients, with a good outcome for up to 60% of the patients, several studies have shown that decompressive surgery is a possible treatment strategy

for increased ICP after severe supratentorial stroke.

Although increasing numbers of studies have reported encouraging results after decompressive craniectomy for ischemic stroke, these studies are mostly limited to case series without a control group. A summary of some of these studies is shown in Table 1. Rieke and co-workers have recently reported the results of a prospective, nonrandomized, single-institution, and control study involving 32 patients selected for surgical treatment and 21 patients with space-occupying cerebral infarction treated medically.<sup>42,43</sup> Entry criteria into the control group included extensive left hemispheric infarction presenting with global aphasia on admission (14 patients), additional severe medical complications (2 patients), and lack of informed consent from the relatives (5 patients). Although other clinical characteristics did not differ significantly between the two groups, patients in the control group were older (mean age 58.4 years) than patients who underwent surgical treatment (mean age 48.8 years). In this study, the mortality rate was 76.2% in the control group and 34.4% in the surgically treated group. Functional outcome, as reflected by the Barthel Index scores obtained 4 to 36 months after surgery, was consistent: excellent level of activity in 1 patient, minimal assistance required by 15 patients, and a severe disability in 5 patients. In the control group, 4 of the only 5 survivors had global aphasia.

As decompressive craniectomy can be a life-saving procedure in patients who will most likely be left with a significant neurological deficit, the operation has important ethical and psychological implications. Because of their altered level of consciousness, patients cannot directly provide consent and in such cases, informed consent has to be obtained from the relatives. Psychological disturbances in this patient population were addressed by Carter and co-workers.<sup>4</sup> In their series of 14 patients who underwent decompressive craniectomy after right-sided hemisphere ischemic stroke, they found mood disturbance to be significant in all survivors. Four of 11 patients suffered severe depressive symptoms, whereas in the remaining 7 mild to moderate impairment was demonstrated. When asked if they would have chosen to undergo the operation given the choice, 6 patients answered affirmatively, 3 were uncertain, and 2 would have declined the operation.

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 oedema;<sup>(44)</sup> 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.<sup>14</sup>

Even under full supportive therapy, the mortality rate is roughly 80%, and recently the effectiveness of many medical therapies such as chronic hyperventilation, osmotherapeutics, barbiturate therapy, has been challenged.<sup>9,13,22,25,53</sup> The clinical course of patients with severe supratentorial stroke is highly predictable, therefore, waiting for mesencephalic signs to occur potentially worsens prognosis. It was hypothesized that through decompressive surgery, the vicious circle of extensive oedema, which by elevation of ICP causes ischemia of neighbouring brain tissue and further infarction, may be interrupted.<sup>9</sup> This may then increase cerebral perfusion pressure and optimize retrograde perfusion of leptomeningeal collateral vessels, thus allowing functionally compromised but viable brain to survive.<sup>13</sup>

In 2004, Gupta and Connolly, et al, in a systemic review of 15 studies screened, in 13 studies described, 138 patients met the criteria for analysis.<sup>19</sup> In a 4 months follow-up period, 10 patients (7%) were functionally independent, 48 (35%) were mildly to moderately disabled, and 80 (58%) died or were severely disabled. Of 75 patients who were > 50 years of age, 80% were dead or severely disabled compared with 32% of 63 patients ≤ 50 years of age ( $P < 0.00001$ ), however early surgery (< 24h) did not show benefit, but a greater proportion of patients (64%) had signs of herniation before surgery. The timing of surgery, hemisphere infarcted, presence of signs of herniation before surgery, and involvement of other vascular territories did not significantly affect outcome. To identify the patients most likely to benefit from hemicraniectomy they concluded that age may be a crucial factor in predicting functional outcome after hemicraniectomy in patients with large MCA territory infarction.<sup>18</sup> There were several limits to their review. The individual data analyzed were obtained from uncontrolled, retrospective data; thus, formal meta-analysis techniques could not be applied. Such an analysis cannot control for data heterogeneity, which limits the scope of this study. The patients reviewed also lacked a uniform approach and follow-up time. In addition, all data were not always provided for all cases, and 13 of the 138 patients (9%) were assigned a functional category on the basis of clinical descriptions provided in the literature. Publication bias may also exist within the literature, with an overrepresentation of patients with good outcome. Although there are limitations to this approach, it may provide some useful hypotheses for future clinical trials. Age may be the most important factor when deciding on surgery, whereas laterality and additional vascular territory involvement may not affect outcomes. Future trials or standardized protocols may consider focusing on hemicraniectomy in younger patients or early surgery before signs of herniation.

In one of the largest case series, Schwab et al, postulated

that waiting for signs of herniation may worsen prognosis because of irreversible mesencephalic injury.<sup>20,43,48,53</sup> In addition, early decompressive surgery may further improve outcomes in these patients, considering for surgery nondominant hemisphere or incomplete aphasia before deterioration. The patients were treated with decompressive surgery before the occurrence of clinical signs of herniation, within the first 24 hours after stroke onset. They found hemicraniectomy to be an effective therapy for the condition of malignant MCA infarction. Most related complications associated with the operation were epidural haematoma, subdural haematoma, and hygromas. However, whether and when decompressive surgery is indicated in these patients is still a matter of debate. Patients undergoing decompressive craniectomy of the dominant hemisphere were younger but, had better functional outcome in general.

Five randomized trials have been designed to investigate the efficacy of decompressive surgery: The Hemicraniectomy and Durotomy on Deterioration from Infarction-Related Swelling Trial (HeADDFIRST) randomized 26 patients between 2000 and 2003. The final results have not been published yet.<sup>14</sup> Between 2001 and 2004, 4 other studies were initiated: one trial, the Hemicraniectomy for Malignant Middle Cerebral Artery Infarcts (HeMMI) performed in the Philippines, and 3 European trials. HAMLET (Hemicraniectomy after Middle Cerebral Artery Infarction with Life-Threatening Edema Trial)<sup>(22)</sup> is being performed in the Netherlands, DECIMAL (Decompressive Craniectomy in Malignant Middle Cerebral Artery Infarcts) has been conducted in France, and DESTINY (Decompressive Surgery for the Treatment of Malignant Infarction of the Middle Cerebral Artery) has been performed in Germany.<sup>34</sup> Meanwhile, a pooled analysis of data from DECIMAL, DESTINY, and HAMLET has been published that included 93 patients.<sup>53</sup> Results for the dichotomized end points, mRS score  $\leq 4$ , mRS score  $\leq 3$ , and survival showed a pooled absolute risk reduction of 51%, 23%, and 50%, respectively. DESTINY, a prospective, multicentre, randomized, controlled, clinical trial, showed that hemicraniectomy reduces mortality in large hemispheric stroke. With 32 patients included, the primary end point failed to demonstrate statistical superiority of hemicraniectomy, and the projected sample size was calculated to 188 patients. Despite this failure to meet the primary end point, the steering committee decided to terminate the trial in light of the results of the joint analysis of the three European hemicraniectomy trials.<sup>25</sup>

### Surgery-related complications

Few complications have been reported in the literature when hemicraniectomy has been completed after cerebral infarction. Although postoperative epidural and subdural haemorrhage as well as hygromas has occurred in a few

cases, none of these complications led to additional neurological deficits.<sup>4,21,22,25,33,43,48,53</sup>

### Conclusions

Malignant cerebral ischemia occurs in a significant number of patients who undergo emergency evaluation for ischemic stroke. The mortality rate in these patients is very high. Fatal outcome is usually related to progressive, severe cerebral oedema with brain herniation and compression of critical brainstem structures. This patient population can be identified by early clinical and neuroimaging characteristics. In some of these patients, decompressive craniectomy appears to be a life-saving procedure. If craniectomy is performed early, especially in young patients, a satisfactory functional outcome can be achieved in a significant proportion of cases. Questions persist regarding the indications for such a procedure in patients with dominant infarctions. Clinical experience, however, demonstrates that even in such patients, an acceptable functional outcome can be achieved after surgery if some preservation of speech is present at the time of intervention.

We hope that our findings will add to existing information on decompressive hemicraniectomy to serve as guidelines until further data are available from the ongoing randomized control trials. However, there are some unanswered questions: which subset of patients will benefit maximally? Which patients will survive with an unacceptable degree of functional dependency? What is the optimal timing for surgery? Additional studies will have to be executed to analyze in more detail these implications.

**Acknowledgement:** To our patients, to whom we dedicate a very important part of our lives.

### References

1. Adams JH, Graham DI: Twelve cases of fatal cerebral infarction due to arterial occlusion in the absence of atherosclerotic stenosis or embolism. *J Neurol Neurosurg Psychiatry* 1957, 30(6): 479-488
2. Bounds JV, Wiebers DO, Whisnant JP, Okazaki H: Mechanism and timing of deaths from cerebral infarction. *Stroke* 1981, 12(4): 474-477
3. Camarata PJ, Heros RC, Latchaw RE: "Brain attack": the rationale for treating stroke as a medical emergency. *Neurosurg* 1994, 34(1): 144-57; Discussion 157-8
4. Carter BS, Ogilvy CS, Candia GJ, et al: One-year outcome after decompressive surgery for massive nondominant hemispheric infarction. *Neurosurg* 1997, 40(6): 1168-75; Discussion 1175-6
5. Cooper PR, Rovit RL, Ransohoff J: Hemicraniectomy in the treatment of acute subdural hematoma: a re-appraisal. *Surg Neurol* 1976, 5(1): 25-28
6. Cushing H. The establishment of cerebral hernia as a decompressive measure for inaccessible brain tumors; with the description of intermuscular methods of making bone defect in temporal and occipital regions. *Surg Gynecol Obstet* 1905, 1: 297-314

7. Delashaw JB, Broddaus WC, Kassell NF, et al: Treatment of right hemispheric cerebral infarction by hemicraniectomy. *Stroke* 1990, 21(6):874-881
8. Dierssen G, Carda R, Coca JM: The influence of large decompressive craniectomy on the outcome of surgical treatment in spontaneous intracerebral haematomas. *Acta Neurochir (Wien)* 1983, 69: 53-60
9. Doerfler A, Forsting M, Reith W, Staff C, Heiland S, Schäbitz WR, von Kummer R, Hacke W, Sartor K: Decompressive craniectomy in a rat model of "malignant" cerebral hemispherical stroke: experimental support for an aggressive therapeutic approach. *J Neurosurg* 1996, 85(5): 853-859
10. Engelhorn T, Doerfler A, Kastrup A, et al: Decompressive craniectomy, reperfusion, or a combination for early treatment of acute "malignant" cerebral hemispheric stroke in rats? Potential mechanisms studied by MRI. *Stroke* 1999, 30: 1456-1463
11. Furlan A, Higashida RT, Wechsler L, et al: Intra-arterial pro-urokinase for acute ischemic stroke. The PROACT II study: a randomized controlled trial. *Prolyse in Acute Cerebral Thromboembolism. JAMA* 1999, 282(21): 2003-2011
12. Fisher CM, Ojemann RG: Bilateral decompressive craniectomy for worsening coma in acute subarachnoid hemorrhage. Observations in support of the procedure. *Surg Neurol* 1994, 41(1): 65-74
13. Forsting M, Reith W, Schäbitz WR, et al: Decompressive craniectomy for cerebral infarction: an experimental study in rats. *Stroke* 1995, 26(2): 259-264
14. Frank JI, Krieger D, Chyatte D: Hemicraniectomy and durotomy upon deterioration from massive hemispheric infarction: a proposed multicenter, prospective, randomized study. *Stroke* 1999, 30: 243
15. Gerriets T, Stolz E, Modrau B, et al: Sonographic monitoring of midline shift in hemispheric infarctions. *Neuro* 1999, 52(1): 45-49
16. Gower DJ, Lee KS, McWhorter JM: Role of subtemporal decompression in severe closed head injury. *Neurosurg* 1988, 23(4): 417-422
17. Greenwood J Jr: Acute brain infarctions with high intracranial pressure: surgical indications. *Johns Hopkins Med J* 1968, 122 (5): 254-260
18. Guerra WK, Gaab MR, Dietz H, et al: Surgical decompression for traumatic brain swelling: indications and results. *J Neurosurg* 1999, 90(2):187-196
19. Gupta R, Connolly ES, Mayer S, Elkind MS: Hemicraniectomy for massive middle cerebral artery territory infarction. A systematic review. *Stroke* 2004, 35(2): 539-543
20. Hacke W, Schwab S, Horn M, Spranger M, De Georgia M, von Kummer R: 'Malignant' middle cerebral artery territory infarction: clinical course and prognostic signs. *Arch Neurol* 1996, 53(4): 309-315
21. Heros RC: Surgical treatment of cerebellar infarction. *Stroke* 1992, 23: 937-938
22. Hofmeijer J, Amelink GJ, Algra A, van Gijn J, Macleod MR, Kappelle LJ, van der Worp HB, HAMLET investigators: Hemicraniectomy after middle cerebral artery infarction with life-threatening edema trial (HAMLET). Protocol for a randomised controlled trial of decompressive surgery in space-occupying hemispheric infarction. *Trials* 2006, 7: 29
23. Iwamoto HS, Numoto M, Donaghy RM: Surgical decompression for cerebral and cerebellar infarcts. *Stroke* 1974, 5(3): 365-370
24. Jourdan C, Convert J, Mottolese C, et al: Evaluation of the clinical benefit of decompression hemicraniectomy in intracranial hypertension not controlled by medical treatment. *Neurochirurgie* 1993, 39(5): 304-310 (Fr)
25. Jüttler E, Schwab S, Schmiedek P, et al: for the DESTINY Study Group. Decompressive Surgery for the Treatment of Malignant Infarction of the Middle Cerebral Artery (DESTINY) A Randomized, Controlled Trial. *Stroke* 2007, 38(9): 2518-2525
26. Kalia KK, Yonas H: An aggressive approach to massive middle cerebral artery infarction. *Arch Neurol* 1993, 50(12): 1293-1297
27. Kastrau F, Wolter M, et al: Recovery from aphasia after hemicraniectomy for infarction of the speech-dominant hemisphere. *Stroke* 2005, 36(4): 825-9
28. King AB: Massive cerebral infarction producing ventriculographic changes suggesting a brain tumor. *J Neurosurg* 1951, 8(5): 536-539
29. Kirkham FJ, Neville BG: Successful management of severe intracranial hypertension by surgical decompression. *Dev Med Child Neurol* 1986, 28(4): 506-509
30. Kjellberg RN, Prieto A Jr: Bifrontal decompressive craniotomy for massive cerebral edema. *J Neurosurg* 1971, 34(4): 488-493
31. Kondziolka D, Fazl M: Functional recovery after decompressive craniectomy for cerebral infarction. *Neurosurg* 1988, 23 (3): 143-147
32. Kunze E, Meixensberger J, Janka M, et al: Decompressive craniectomy in patients with uncontrollable intracranial hypertension. *Acta Neurochir Suppl* 1998, 71: 16-18
33. Lanzino JD, Lanzino G: Decompressive craniectomy for space-occupying supratentorial infarction: rationale, indications, and outcome. *Neurosurg Focus* 2000, 8(5): E3
34. Major ongoing stroke trials. *Stroke* 2006, 37(2): e18-e26
35. Moulin DE, Lo R, Chiang J, Barnett HJM: Prognosis in middle cerebral artery occlusion. *Stroke* 1985, 16(2): 282-284
36. Ng LKY, Nimmannitya J: Massive cerebral infarction with severe brain swelling: a clinicopathological study. *Stroke* 1970, 1(3): 158-163
37. Pillai A, Menon SK, et al: Decompressive hemicraniectomy in malignant middle cerebral artery infarction: an analysis of long-term outcome and factors in patient selection. *J Neurosurg* 2007, 106(1): 59-65
38. Polin RS, Shaffrey ME, Bogaev CA, et al: Decompressive bifrontal craniectomy in the treatment of severe refractory posttraumatic cerebral edema. *Neurosurg* 1997, 41(1): 84-92; Discussion 92-4
39. Ransohoff J, Benjamin MV, Gage EL Jr, Epstein F: Hemicraniectomy in the management of acute subdural hematoma. *J Neurosurg* 1971, 34(1): 70-76
40. Rengachary SS, Batnitzky S, Moranz RA, et al: Hemicraniectomy for acute massive cerebral infarction. *Neurosurg* 1981, 8 (3): 321-328
41. Rengachary SS: Surgery for acute brain infarction with mass effect. In: Wilkins RH, Rengachary SS (eds), *Neurosurgery*. New York, McGraw-Hill 1985, Vol 2, pp 1267-1271
42. Rieke K, Krieger D, Adams HP, et al: Therapeutic strategies in space-occupying cerebellar infarction based on clinical, neuro-radiological and neurophysiological data. *Cerebrovasc Dis* 1993, 3(1): 45-55
43. Rieke K, Schwab S, Krieger D, et al: Decompressive surgery in space-occupying hemispheric infarction: results of an open, prospective trial. *Crit Care Med* 1995, 23(9): 1576-1578
44. Ropper AH, Shafran B: Brain edema after stroke. Clinical syndrome and intracranial pressure. *Arch Neurol* 1984, 41(1): 26-29
45. Schwab S, Aschoff A, Spranger, et al: The value of intracranial pressure monitoring in acute hemispheric stroke. *Neuro* 1996, 47(2): 393-398
46. Schwab S, Junger E, Spranger M, et al: Craniectomy: an aggressive approach in severe encephalitis. *Neuro* 1997, 48 (2): 412-417
47. Schwab S, Rieke K, Aschoff A, et al: Hemicraniectomy in space-occupying hemispheric infarction: useful early intervention or desperate activism? *Cerebrovasc Dis* 1996, 6(6): 325-329
48. Schwab S, Steiner T, Aschoff A, et al: Early hemicraniectomy in patients with complete middle cerebral artery infarction. *Stroke*

- 1998, 29(9): 1888-1893
49. Shaw CM, Alvord EC Jr, Berry RG: Swelling of the brain following ischemic infarction with arterial occlusion. *Arch Neurol* 1959, 1: 161-177
  50. Silver FL, Norris JW, Lewis AJ, Hachinski VC: Early mortality following stroke: a prospective review. *Stroke* 1984, 15(3): 492-496
  51. Stefani R, Latronico N, Cornali C, et al: Emergent decompressive craniectomy in patients with fixed dilated pupils due to cerebral venous and dural sinus thrombosis: report of three cases. *Neurosurg* 1999, 45(3): 626-630
  52. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group: Tissue plasminogen activator for acute ischemic stroke. *N Engl J Med* 1995, 333(24): 1581-1587
  53. Vahedi K, Hofmeijer J, Juettler E, Vicaut E, George B, Algra A, Amelink GJ, Schmiedek P, Schwab S, Rothwell PM, Bousser MG, van der Worp HB, Hacke W, DECIMAL, DESTINY, HAMLET investigators: Early decompressive surgery in malignant infarction of the middle cerebral artery: a pooled analysis of three randomised controlled trials. *Lancet Neurol* 2007, 6(3): 215-222
  54. von Kummer R, Meyding-Lamadé U, Forsting M, Rosin L, Rieke K, Hacke W, Sartor K: Sensitivity and prognostic value of early CT in occlusion of the middle cerebral artery trunk. *Am J Neuroradiol* 1994, 15(1): 9-15; Discussion 16-18
  55. Wijdicks EFM, Schievink WI, McGough PF: Dramatic reversal of the uncal syndrome and brain edema from infarction in the middle cerebral artery territory. *Cerebrovasc Dis* 1997, 7(6): 349-352
  56. Yoo DS, Kim DS, Cho KS, et al: Ventricular pressure monitoring during bilateral decompression with dural expansion. *J Neurosurg* 1999, 91(6): 953-959
  57. Young PH, Smith KR, Dunn RC: Surgical decompression after cerebral hemispheric stroke: indications and patient selection. *South Med J* 1982, 75(4): 473-474