Hemicraniectomy is a Promising Treatment in Ischemic Stroke

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The most devastating form of ischemic stroke is the large cerebral infarction. This type of infarction is commonly associated with cerebral edema which produces mass effect. If this mass effect is extensive enough, brain herniation and death can result. Hacke et al. have coined the term ‘malignant’ middle cerebral artery (MCA) territory infarction to describe the complete MCA territory infarction resulting in significant space occupying effect. In a large neuroprotective trial, LUB-INT-9, 25% of all stroke mortality was patients with ‘malignant’ MCA syndrome who developed brain herniation. Clinically, ‘malignant’ MCA infarction results in the early depression of consciousness that deteriorates to coma and brain death within two to five days in almost 80% of patients when treated with medical therapy alone. The incidence of this form of infarction is estimated at 3%-5% of all ischemic stroke. Neurologic deterioration from large cerebral infarction is known to correlate with horizontal displacement of the anterior septum and the pineal gland rather than with intracranial pressure (ICP) elevation. Recent evidence suggests that ICP elevation is a terminal and, most likely, an irreversible circumstance that results when mass expansion exceeds intracranial compliance. Medical therapy aimed at reducing ICP primarily contracts healthy brain tissue volume and may aggravate pressure differentials, causing devastating shifts in brain tissue. Ideal therapy should prevent the formation of brain edema and the subsequent displacement of tissue. Current medical therapies largely fail to prevent either. Decompression surgery is a controversial approach to decreasing the devastating consequences of mass effect and tissue shifts caused by intracranial mass lesions.

Hemicraniectomy and durotomy describe a neurosurgical decompressive approach to hemispheric masses and swelling. This was first performed as a treatment for acute subdural hematoma. Hemicraniectomy involves removal of bone on one side of the skull and simultaneous generous dural opening. The minimal adequate decompression is defined by the following bony boundaries (Figure 1):

1) anterior, frontal to midpupillary line
2) posterior, approximately 4 cm to the external auditory canal
3) superior, to the superior sagittal sinus
4) inferior, to the floor of the middle cranial fossa

Bone removed during a hemicraniectomy can be saved in a bone bank in antibiotic solution at –80°C. The bone flap can also be stored in the peritoneum by surgical implantation. Bone is replaced after the swelling has subsided in one to three months. Cruciate or circumferential durotomy must be performed over the entire region of bony decompression to insure that nothing resists the expanding brain from being able to herniate outward. Dural grafting is recommended. No brain amputation or ventriculostomy is required or necessary. This complete procedure achieves a new pathway of least resistance for the swelling brain ipsilateral to the lesion and causes less compression of the brain structures such as the brain stem, which are not otherwise involved in the primary disease process. The brain acts as a sphere rather than a cylinder when herniating through the surgical opening. The size of the bone flap determines the magnitude of decompression achieved and significantly increases when the diameter exceeds 12 cm. Small bone flaps do not achieve the desired decompression needed.

Animal studies of a form of hemicraniectomy called trephination surgery show promising results. The day seven mortality rate in the nonsurgical group (controls) was 35%, but with trephination surgery this mortality rate fell to 0%. Neurologic behaviors and infarct volumes were better in those treated with ultra-early surgery (four hours after occlusion), implying the potential role of preserving valuable collateral circulation. A recent MRI study revealed clear evidence of infarct size reduction with surgery. The hemispheric lesion volumes derived by a six-hour diffusion weighted-MRI showed significantly smaller infarcts in the craniectomy group (23.0+/-.4% of hemisphere) compared to the control group (44.1+/-.5% of hemisphere). Cranietomy led to higher perfusion in the cortex compared with the control group but not higher perfusion in the basal ganglia. Cranietomy decreased infarction volume by improving cerebral perfusion with regions of cortical ischemia spared by the surgery.

In human studies, decompression surgery for swelling due to large hemispheric infarction has been haphazardly applied, with anecdotal reports of good results. In a small series of 14 cases, decompressive hemicraniectomy was able to prevent death secondary to transtentorial herniation in all cases. Eleven patients experienced long-term survival. Eight of the 11 surviving patients were at home, functioning with minimal to moderate assistance. The remaining three patients were severely disabled. Seven of the 11 survivors were able to walk at one year after undergoing the procedure. Depression and failure to reintegrate socially were experienced by most patients. Fifty-five
percent agreed they would definitely have the procedure again if necessary, while 18% would not have the procedure done again. A recent open, nonrandomized, controlled trial of hemicraniectomy in large hemispheric infarction enrolled 53 patients with significant midline shift, basal cistern compression, or uncal herniation. Thirty-two of the 53 patients underwent hemicraniectomy and dural patch enlargement. The in-hospital mortality rate was 34.4% in the surgically treated group and 76.2% in the nonsurgical group. The morbidity rate among survivors was lower in the surgically treated group. A follow-up study at the same institution performed “earlier” (less than 24 hours from symptom onset) hemicraniectomy. This early surgery was associated with an in-hospital mortality rate of only 16% and a reduction in ICU stays with reasonable long-term outcomes.

This study was the first to report “acceptable” outcomes in several patients with dominant hemisphere stroke. Patients in this group had clinical deficits of hemiparesis and only mild to moderate aphasia. Figure 2 represents such a case of hemicraniectomy in the setting of a dominant hemisphere stroke.

A recent retrospective multicenter study evaluating hemicraniectomy in clinical practice identified a reduction in mortality compared to the “control” medical therapy only group. This mortality reduction remained significant after correcting for baseline differences in groups. The hemicraniectomy patients did tend to be younger with fewer vascular risk factors. The hemicraniectomy group did, however, have higher National Institute of Health Stroke Scores (NIHSS) and more abnormal initial CT ischemic changes. Mortality remained high despite hemicraniectomy if patients had early CT changes of hypodensity involving more than just the MCA territory, such as the anterior cerebral (ACA), posterior cerebral (PCA) or anterior choroidal artery territories. The explanation for this finding may be the additional infarct volume added to tissue shifts that could not be prevented by a reasonably sized bone flap.

Comparing published surgical outcomes with standard medical therapy is difficult. No randomized trials have been performed to date. Previous publications examining outcome with standard medical therapy suggest a poor result. Berrouschot et al published 53 patients with a slightly older mean age than other hemicraniectomy series. Mortality exceeded 70% despite aggressive medical management in neurointensive care units. All possible medical approaches were used, including osmotherapy, and...
tromethanol and mild hyperventilation. All patients went on to require mechanical ventilation and became comatose. Wijdicks et al. published a similar series of 42 patients. In this group, 33 of these patients went on to deteriorate with diencephalic herniation developing in 19 and uncal herniation in 11. The mortality was 70% in the group with deterioration. Patients older than 45 years (20/22=91%) were much more likely to die than younger patients (3/11=27%).

Critics of hemicraniectomy suggest that standard medical therapy may not have received a “fair shake” in published series. A selection bias in favour of hemicraniectomy is quite possible, younger patients with less severe comorbidity may have been more likely to receive hemicraniectomy than elderly patients with comorbidities. Wijdicks et al. published an interesting case report of a young patient with clinical signs of uncal herniation, obstructive hydrocephalus and increased ICP who responded dramatically to “aggressive” mannitol therapy. Most hemicraniectomy centers would have taken such a patient to surgery. We have had similar experience with mannitol therapy in a young patient with a large left middle cerebral artery stroke who was treated medically despite severe midline shift (13 mm of anteroseptal shift). Not only did this individual survive but he is now independent and returning to university! We considered hemicraniectomy but were apprehensive because the dominant hemisphere was involved. The benefit of hemicraniectomy appears less certain in dominant hemisphere stroke due to a smaller experience with surgery in this group and a fear that hemicraniectomy might result in very disabling severe aphasia. The lesson we have learned in young patients is to never underestimate the amount of clinical recovery possible despite the odds against it. Unilateral brain injury seems to have a much more favourable outcome than bilateral injury such as in head trauma. Regions of adjacent normal brain or opposite hemisphere structures do appear to take over important functions such as language. This must be taken into consideration before a “rush to judgement” on prognosis is made especially in young stroke patients with large unilateral and even dominant hemisphere infarction.

Many advances have been made recently in the medical approach to ischemic cerebral edema which put into question whether we can draw conclusions from the previous literature examining the effects of standard medical therapy alone. Hypertonic saline seems to be particularly effective as a short term measure to reduce edema. Standard therapies such as mannitol have been challenged because of concerns that rebound edema can develop with repeated use. Recent studies refute this concern, by showing no aggravation of cerebral edema with repeated uses of mannitol. Similarly, prolonged hyperventilation treatment has been discouraged because it may reduce the brain’s ability to tolerate ischemia. New literature, however, suggests that although acute hyperventilation may reduce cerebral blood flow, no global cerebral ischemic effects are seen. More recently, induced systemic hypothermia has been attempted with some evidence for success. Schwab et al. published a case series of patients with severe MCA stroke undergoing moderate hypothermia (33°C). This study showed that treatment can significantly reduce intracranial pressure. However, herniation by a secondary rise in ICP after rewarming was the cause of death in 11/25 (44%) patients receiving this treatment. Pneumonia was the most frequent complication (40%). Graffagnino et al. reported similar mortality in 11 patients. The major criticism of current hemicraniectomy literature is the lack of data regarding long-term outcome and quality of life. Medical therapy is advancing and we may now be able to reasonably manage this otherwise fatal complication.

At this time, in my opinion, hemicraniectomy has a role in the management of large MCA infarction. The age limit for such a procedure is not clear but no hard cutoff should be adhered to since many patients over 70 are otherwise in exceptional health. The goal should be early surgery with generous bone flap removal. If surgery is late, brain stem injury may occur and if the bone flap is too small, dangerous medidal displacement against the brain stem may also occur. Recent literature has identified early clinical predictors of eventual brain herniation and death to help us better identify the group that probably would benefit from early hemicraniectomy. The initial CT (less than six hours from symptom onset) can be very useful. Von Kummer was the first to determine that early ischemic CT changes in greater than 50% of MCA territory strongly correlates with mortality, a finding confirmed predictive of brain herniation by our group. A follow-up study also corroborated this finding. Additional early hypodensity in the posterior cerebral and anterior cerebral artery territories also predicted brain herniation. Angiography can also help by identifying an occlusion of the distal internal carotid...
artery and accompanying middle cerebral or anterior cerebral arteries (so called carotid ‘T’ occlusion). Such an occlusion has a high mortality rate and is predictive of brain herniation. Imaging of brain perfusion is very helpful. The absence of flow on early imaging strongly correlates with brain herniation. Berrouschot et al demonstrated six hours from onset single photon emission tomography (SPECT) to predict herniation if complete lack of tracer activity was identified in the entire MCA territory. In fact, brain herniation occurred in all cases with no MCA territory activity on SPECT. Our group recently identified other clinical predictors of herniation. Nausea or vomiting early in the clinical course should be considered an ominous sign of potential brain herniation particularly in patients with severe clinical deficits as identified in two studies. Using this information I propose a simple algorithm of risk stratification and management for this form of severe stroke (Figure 3). The use of such an algorithm, however, remains very controversial as long as we lack level 1 evidence of benefit for hemicraniectomy.

A randomized clinical trial is under way to determine the efficacy of hemicraniectomy in hemispheric infarcts with massive ischemic brain edema. This pilot study will seek to determine whether such randomization is possible and whether outcomes such as quality of life and burden of care can be appropriately evaluated. This study will assess several quality of life and burden of care scales. There is ample literature supporting the further evaluation of hemicraniectomy against 21st century standard medical therapy.

REFERENCES