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Approach to Severe Hemispheric Stroke

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Severe hemispheric stroke represents a minority of ischemic strokes, yet is responsible for a disproportionate share of morbidity and mortality. It frequently results from occlusion of the proximal middle cerebral artery (MCA), but can also involve the distal internal carotid artery and anterior (ACA) or posterior cerebral arteries (PCA). Malignant infarction occurs in 10% of stroke victims, and formation of cerebral edema is a common cause for secondary neurologic deterioration. Despite intensive medical and surgical care, prognosis is often poor and mortality may be as high as 60%–80%. Surgical intervention can reduce that mortality compared to medical therapy alone,¹ but necessitates a careful exploration of patient preference for acceptable outcomes.

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IS IT AN ACUTE STROKE AND WHAT ARE THE IMMEDIATE TREATMENT OPTIONS?

The first step in assessing the patient with an acute neurologic deficit is to ascertain the cause and rapidly institute the appropriate therapy. TIA, intracerebral hemorrhage, or seizure with a postictal Todd paralysis can all be mistaken for an acute hemispheric stroke, particularly in the immediate setting when the dynamic nature of these alternatives may not yet be apparent. The NIH Stroke Scale (NIHSS) score and a rapid CT or MRI scan can be used to aid in the diagnosis. Assuming no contraindications are present, IV thrombolysis should be initiated within 3 hours of the last seen well time and should be considered for patients presenting between 3 and 4.5 hours. For emergency departments that do not possess primary stroke center certification, telemedicine systems may be available to assist with the decision regarding IV thrombolysis. For large hemispheric ischemic stroke, referral to a primary stroke center for intra-arterial and investigational treatment options, neurointensive care expertise, and potential neurosurgical consultation is strongly recommended.

WHAT ARE THE CLINICAL FEATURES OF LARGE HEMISPHERIC STROKES?

The clinical features of severe hemispheric infarction are well-described. Key clinical bedside tests can interrogate the areas of dysfunction and circumscribe the regions of the brain that are affected. Contralateral hemiplegia

“Surrogate decision-makers may underestimate the patient’s willingness to survive with disability”

gia and hemianesthesia are characteristic findings of severe hemispheric infarcts. Involvement of the contralateral leg is common, due to the interruption of the descending white matter fibers in the internal capsule, even when the cortical gray matter subserving this functional region is spared. Hemianopia develops from interruption of the optic radiations. The frontal eye fields frequently define the anterior extent of the typical severe infarction, and cause gaze deviation to the side of the infarct. In dominant hemispheric stroke, there is global aphasia. The posterior extent of the infarct is often demonstrated by the presence of neglect, but can be difficult to assess in the setting of aphasia. Alternatively, diminished optokinetic nystagmus can identify involvement in the parieto-occipital gaze centers, and does not require the ability to follow commands to perform the test. In nondominant hemispheric stroke, dense neglect and apraxia reliably define the posterior extent. The NIHSS score captures many of these clinical features, and dominant severe hemispheric infarctions tend to exhibit scores >20 and nondominant infarctions >15.

In addition to defining the neuroanatomic correlates of the stroke, particular attention should be paid to additional clinical and radiographic features that are associated with early cerebral edema and poor neurologic outcomes (table 1). Secondary neurologic deterioration typically ensues within 2 to 5 days after presentation. Key clinical findings that portend poor outcome include young age,² a high initial NIHSS score, an elevated systolic blood pressure >180 mm Hg at 12 hours, the development of nausea and vomiting within the first 24 hours,³ and a progressive decline in the level of arousal over the first couple of days.⁴ Late findings include unilateral or bilateral pupillary dilatation. A radiographic feature that predicts malignant cerebral edema and poor prognosis includes hypodensity on head CT within the first 6 hours and >50% of the MCA territory.⁵ The involvement of multiple vascular territories (i.e., MCA and either ACA or PCA),⁵ or midline shift >5 mm within the first 2 days, are also associated with early mortality.⁶ Additional clinical and radiographic factors such as history of congestive heart failure⁵ and collateral vessel status⁷ have been associated with the development of the malignant syndrome as well, but these and other clinical variables require further prospective validation. More recently, diffusion-

Table 1 Clinical and radiographic predictors of poor outcome or death in severe hemispheric stroke

Clinical
Nausea, vomiting
Reduced arousal
NIHSS >20 (dominant hemisphere)
NIHSS >15 (nondominant hemisphere)
Elevated SBP >180 mm Hg
Congestive heart failure
Radiographic
Hyperdensity >50% MCA territory on CT scan <6 h
Swelling visible on initial CT scan
Multiple vascular territories involved (ACA or PCA and MCA)
Incomplete circle of Willis
Midline shift >5 mm

Abbreviations: ACA = anterior cerebral artery; MCA = middle cerebral artery; NIHSS = NIH Stroke Scale; PCA = posterior cerebral artery; SBP = systolic blood pressure.

weighted imaging (DWI) has been used to identify those patients at highest risk of developing the malignant syndrome.⁸ In those patients with known vessel occlusion, DWI volume of 82 mL within 6 hours of symptom onset predicted the development of malignant infarction with high specificity, although with low sensitivity. Because no single factor can predict who will develop secondary neurologic deterioration in severe hemispheric stroke, intensive neuromonitoring is indicated until the peak period of cerebral edema has passed after day 5 or 6. Future studies evaluating the utility of advanced neuromonitoring such as brain tissue oxygen or cerebral microdialysis may assist in identifying those patients at highest risk of deterioration.

WHAT GENERAL CRITICAL INVESTIGATIONS AND TREATMENTS SHOULD BE PERFORMED IN THE SUBACUTE SETTING?

Patients with large hemispheric stroke frequently are intubated due to impending loss of airway protection. If possible, avoiding endotracheal intubation assists with the ability to monitor the neurologic examination in the critical first few days. Maintenance of airway patency, however, is a foremost priority, and when patients are intubated, ventilatory strategies should aim for normocarbica while minimizing positive end-expiratory pressure (PEEP). Increased PEEP may diminish venous return to the heart and lower cardiac output, leading to impaired cerebral perfusion. It may also reduce cerebral venous drainage and exacerbate elevations in intracranial pressure.

Vessel occlusion status, perfusion-based neuroimaging, and the presence of a fluctuating neurologic

examination can inform blood pressure goals. Published guidelines suggest an upper limit of 220 mm Hg in patients who have not received thrombolytic therapy, or 180 mm Hg in those patients who have received IV tissue plasminogen activator.⁹ After the first 24 hours, it is reasonable to reduce those blood pressure goals, although the exact target is an area under active investigation. The optimal hemoglobin concentration in acute ischemic stroke is not known; it is reasonable to transfuse patients with packed red blood cells to maintain values above 7 or 8 mg/dL based on current transfusion thresholds in critical care. Some patients with large stroke may have an elevated international normalized ratio due to prior warfarin use. Because the risk of hemorrhagic conversion may be increased in large hemispheric strokes, warfarin should be discontinued and reversal with vitamin K is indicated. In selected circumstances where the risk of hemorrhagic conversion is deemed to be very high, more immediate reversal with FFP can be considered. If anticoagulation is subsequently needed during the acute hospitalization, IV heparin can achieve that goal with the added ability of rapid reversal.

Fever is another common complication in patients with large stroke. The diagnosis of “central fever” should be one of exclusion, after infection, thrombosis, and adverse drug effect have been ruled out. While there is an association between fever and poor outcome in patients with large stroke, there are little prospective data to guide temperature management. Still, because fever may exacerbate cerebral edema, achieving normothermia is an important goal of management. In the setting of fever, standing acetaminophen and cooling blankets are first-line agents. If fever persists, advanced surface cooling techniques and peripheral administration of chilled saline (4°C) may be used. Any strategy for temperature lowering should include vigilant monitoring for shivering. Untreated shivering may increase cerebral metabolic requirements and diminish brain tissue oxygenation. Surface counterwarming, IV magnesium infusion, and buspirone can all be used to suppress shivering. Due to a variety of technological advances and improved understanding in hypothermia and shivering,

there has recently been renewed interest in cooling for acute stroke, and this will remain an important area of investigation.

Because of fluid resuscitation, blood transfusions, medication effects, or critical illness, acute stroke patients are at risk for electrolyte derangements. These abnormalities can also contribute to delirium, seizures, and cardiac complications. In particular, extra vigilance is needed to make sure that sodium and glucose levels are within appropriate ranges. Isotonic fluids should be used for maintenance and resuscitation to achieve the goal of eunatremia. Sodium levels should be monitored frequently in order to avoid an unanticipated drop in serum sodium concentration; however, there is no evidence to support the administration of “prophylactic” hypertonic saline. After the publication of several trials for intensive insulin therapy in the general critical illness population, there has been great enthusiasm for applying insulin infusions and strict glycemic protocols to neurocritically ill patients. The application to ischemic stroke was appealing particularly since hyperglycemia associates with poorer neurologic outcomes.¹⁰ However, intensive glycemic control may also lead to increased hypoglycemic episodes and a recent trial of tight glycemic protocol in ischemic stroke has met disappointing results.¹¹ The National Institute of Neurological Disorders and Stroke–sponsored Stroke Hyperglycemia Insulin Network Effort study aims to determine the efficacy of insulin infusion therapy for glucose control in acute stroke patients presenting with hyperglycemia. While the optimal glucose range remains uncertain, excessive hyperglycemia (i.e., glucose >180 mg/dL) should be avoided, and may require the use of an insulin infusion.

Several other principles apply in the intensive care unit management of large ischemic stroke. Antiepileptic therapy is not indicated for any patient with ischemic stroke including after decompressive craniectomy, unless there is evidence of a clinical seizure. Continuous EEG monitoring has raised the possibility of subclinical electrographic seizure activity, but it is unclear whether its detection and treatment has an impact on outcomes. The use of glucocorticoids should be avoided, since it is not effective in treating edema from cerebral infarction and does not improve outcomes. Acute stroke patients are at risk for stress ulcers, and should receive prophylaxis with either a proton pump inhibitor or H-2 blocking agent. Similarly, stroke patients are at risk for deep vein thrombosis and should be placed on chemical prophylaxis with low molecular weight heparin 0.5 mg/kg once daily. Patients treated with IV recombinant tissue plasminogen activator should defer deep vein thrombosis chemoprophylaxis for 24 hours after admission

Severe Hemispheric Stroke

- Severe hemispheric stroke occurs in 10% of stroke patients.
- Cerebral edema is common cause of secondary deterioration.
- Referral to primary stroke center may be helpful.
- Risk of multiple medical complications exists.
- Mannitol and hypertonic saline are first-line options for cerebral edema.
- In progressive malignant infarction, urgent decompressive craniectomy should be offered.

Table 2 Recommendations for surgical approach

1. A large, low, fronto-temporo-parietal craniectomy is required
2. The scalp flap is made using a large "question-mark" incision from the widow's peak, proceeding posteriorly toward the vertex, then curving inferiorly above the pinna and down to the zygoma
3. A large fronto-temporo-parietal bone flap with a minimum diameter of 12 cm is removed.¹² The bone flap is positioned to avoid violating the frontal sinus, unless the frontal sinus is huge. The medial limit of the craniectomy is ~2 cm from the midline, and the posterior limit is ~5 cm posterior to the external auditory canal. The temporal squama is resected down to the floor of the middle cranial fossa
4. A cruciate dural opening with stepwise expansive duroplasty¹³
5. A subgaleal drain, placed to bulb suction, is used to prevent the accumulation of blood in the subgaleal space that could compromise the decompression
6. It is left to the discretion of the surgeon whether to resect hemorrhagic or necrotic tissue

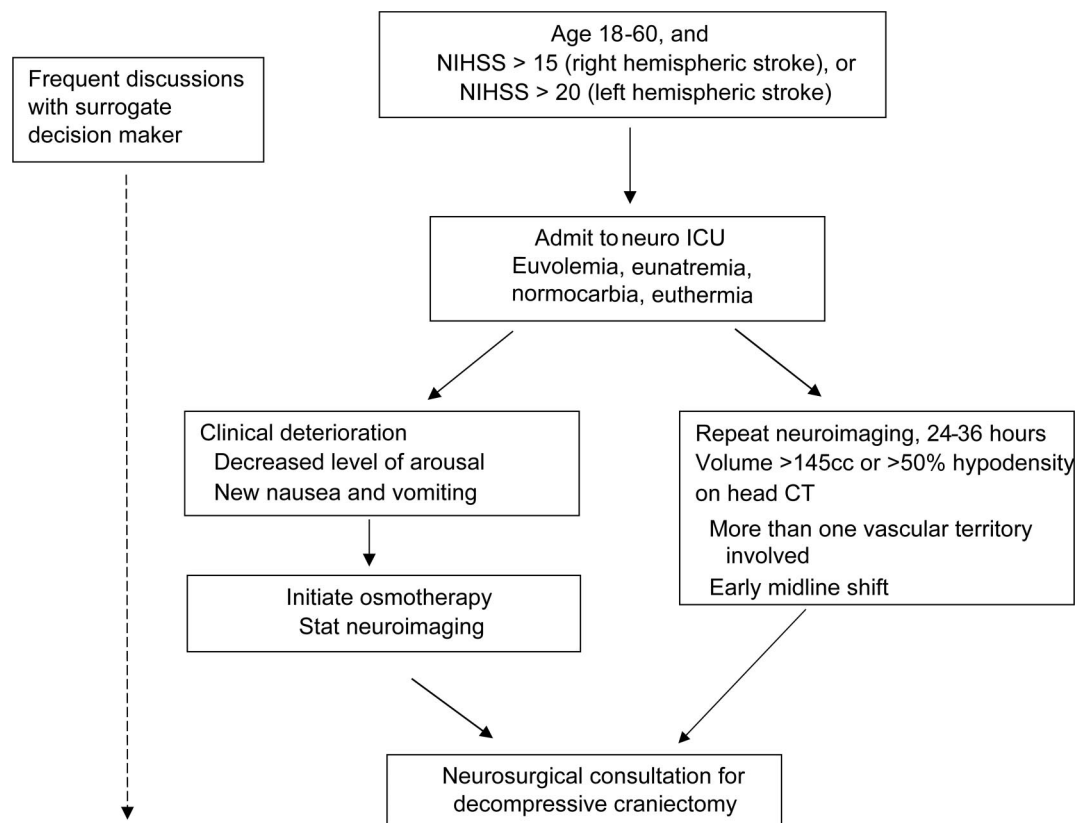
until a follow-up head CT has shown no evidence for hemorrhage.

WHAT APPROACH SHOULD BE USED IN MANAGING CEREBRAL EDEMA AFTER HEMISPHERIC STROKE? While there is no role for prophylactic osmotherapy, patients exhibiting diminished level of arousal or nausea and vomiting are appropriate candidates for treatment (figure 1). In patients less than 60 years of age and within 48 hours of onset, osmotherapy should not delay or take the

place of decompressive craniectomy and rather be administered concurrently with preparations for surgery. When osmotherapy is used to treat a patient with a declining neurologic examination, neuroimaging should be performed to evaluate midline shift, infarct expansion, and to exclude alternative causes such as hemorrhagic conversion.

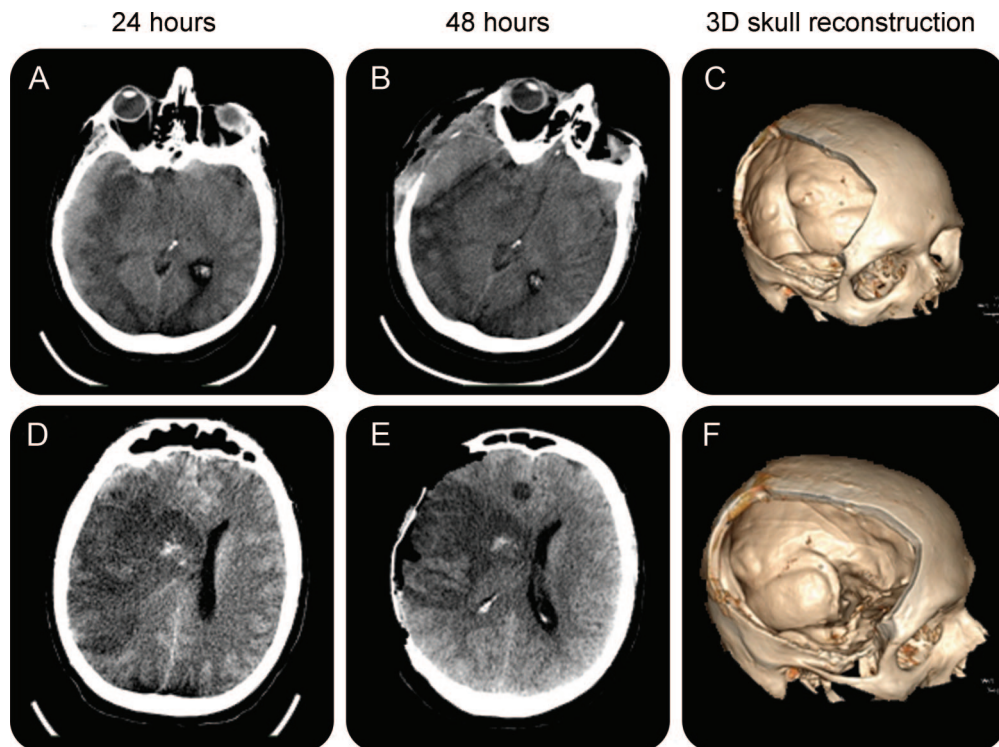
Both mannitol and hypertonic saline are first-line medical treatment options for cerebral edema in malignant infarction. While neither of these treatments has been subjected to a high level of evidence-based scrutiny, certain considerations are useful. Mannitol administration should be weight-based, approximately 1 g/kg IV, and repeated every 4–6 hours, only in the setting of symptomatic brain edema. Since it acts as a diuretic, major complications include hypovolemia and hypotension. Strict fluid goals and volume replacement are essential. Impaired mannitol clearance may manifest as nephrotoxicity. Following serum osmolality and holding repeat doses above a level of 320 is common practice; however, monitoring the osmol gap is a more sensitive method for discerning mannitol clearance. A gap greater than 10 indicates that mannitol remains in the bloodstream and has

Figure 1 Suggested treatment pathway for severe hemispheric stroke



ICU = intensive care unit; NIHSS = NIH Stroke Scale.

Figure 2 Head CTs on admission and after decompressive craniectomy of a patient with severe hemispheric infarction



The slices are located at the level of the pineal gland (A, B) and of the septum pellucidum (D, E). C and F: Oblique 3-D images looking from the right side of the patient, revealing the size and extent of the decompressive craniectomy.

not been cleared fully by the kidneys. The osmol gap can be calculated by subtracting the calculated osmolality from the measured osmolality. The calculated osmolality is obtained by the following equation:

$$\begin{aligned} \text{Calculated osmolality} &= 1.86 (\text{Na} + \text{K}) \\ &+ \text{glucose}/18 + \text{BUN}/2.8 \end{aligned}$$

Hypertonic saline (HS) avoids the diuretic effect of mannitol and is also effective at reducing brain water. Although various concentrations are used clinically, a 30-mL bolus of 23.4% saline is a standard dose for emergent reduction in intracranial pressure (ICP). Rapid increases in sodium in this context do not appear to cause other neurologic complications that can occur in the setting of rapid correction of hyponatremia. Sodium levels as high as 160 may be acceptable, beyond which point persistent hypernatremia may lead to worsening delirium, seizures, and overall poor outcome. HS has a higher reflection coefficient compared to mannitol, and this may allow HS to extract water from both the injured and uninjured brain. While there is no definitive data to promote the use of one osmotic agent over another, individual patient characteristics may play a role in agent selection. For example, mannitol may be pre-

ferred in patients with congestive heart failure and avoided in patients with renal failure.

Hyperventilation reduces ICP by reducing cerebral blood flow. Carbon dioxide is a potent cerebral vasodilator, and so vasoconstriction is induced by rapidly decreasing the paCO_2 . The effect is almost immediate, reducing ICP typically within minutes. However, it is short-lived, and can result in worsening of cerebral infarction volume due to the reduced delivery of blood. Furthermore, there is also a risk of rebound vasodilation and worsening ICP when the paCO_2 returns to normal. The use of hyperventilation is generally not recommended, although it is occasionally used as a bridge toward a more definitive treatment in an acutely herniating patient.

In light of the recent pooled analyses for decompressive craniectomy (DC) (figure 2), there is increased support to recommend DC for severe hemispheric infarction.¹ This multicenter European analysis of 93 patients focused on patients who were treated within 48 hours after a space-occupying MCA territory infarction associated with change in level of consciousness. All patients had at least 50% involvement of the MCA territory by head CT or 145 mL DWI lesion. The primary outcome measure,

proportion of patients with a favorable modified Rankin scale of 0–4, was observed in 75% of the group treated with surgical decompression compared to 25% in the group that received medical management. Patients who received craniectomy were more than twice as likely to survive at 1 year. This benefit seems to be most evident for patients under the age of 60, and more data are needed to determine the efficacy of this treatment strategy in older patients. As previously mentioned, patients with an NIHSS > 15, younger age, and clinical signs of herniation are at high risk for poor outcome. These patients should be identified early as potential candidates for DC, and neurosurgical consultation is essential. Repeat neuroimaging is helpful to determine the trajectory of infarct volume and edema formation, particularly in cases of high NIHSS but lower DWI- or CT-based “infarct” volumes. If there is evidence of clinical and radiographic progression of evolving malignant infarction, evidence suggests DC should be offered urgently, ideally within 48 hours of symptom onset. The surgical technique may vary from center to center but we suggest important considerations here (table 2).

Future studies are likely to address the utility of prophylactic decompression or surgery prior to neurologic deterioration as well as the efficacy of this strategy in patients above the age of 60.

WITHDRAWAL OF CARE AND QUALITY OF LIFE ISSUES

The natural history of large hemispheric stroke is poor and case fatality rates are high. Most patients with malignant infarction require intubation and ventilatory support, so decision-making regarding aggressiveness of care is a consistent component of management that will, in part, determine outcome. DC is the only treatment option demonstrated to improve mortality rates. However, since survivors are often left with considerable disability, both clinicians and family members often express concern about quality of life. Surrogate decision-makers may underestimate the patient’s willingness to survive with disability. Individual reports such as one written by an intensivist after a left hemisphere stroke treated with DC support the notion that some patients prefer survival with disability as compared to death.¹⁴ This notion is reinforced by a recent decision analysis that suggests DC is associated with more quality-adjusted life-years when compared with medical treatment, and this is independent of hemispheric dominance.¹⁵ Ultimately, any plan for surgical decompression must include active and comprehensive communication with family members.

DISCLOSURE

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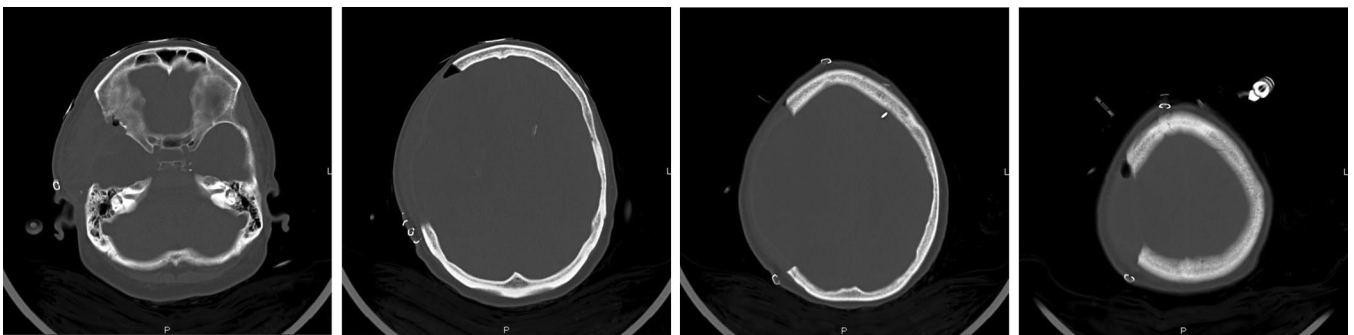
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Craniotomy to alleviate pressure from severe hemispheric stroke. Images from Robert Breeze, MD.

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