Hemicraniectomy
A Second Chance on Life for Patients With Space-Occupying MCA Infarction
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Hemicraniectomy for malignant MCA territory infarction is intended to prevent the death spiral by normalizing intracranial pressure, restoring compromised flow in the penumbra and adjacent vascular territories, and restoring the midline position of the brain stem and diecephalon. The procedure is not new, but was performed rarely for MCA infarction before the 1990s, primarily because of concerns that it would result in survival with overwhelming neurological impairment and handicap. With improvements in postoperative critical care, however, there has been a resurgence of interest in hemicraniectomy over the past 10 years. Several case series and nonrandomized case-control studies have suggested that hemicraniectomy can improve survival, but the evidence has been far from definitive, particularly regarding the extent of residual handicap in those who survive the procedure. Given the lack of evidence from clinical trials to date, hemicraniectomy has remained one of the most controversial and hotly debated topics in stroke care. Is it “radical surgery” that only leads to more pain and suffering, or a beneficial procedure that can give some patients a second chance on life?

In this issue of Stroke, the results of 2 of the 5 recently organized trials designed to evaluate the efficacy of hemicraniectomy for MCA infarction—the DESTINY and DECIMAL trials—are reported. But before we look into the results of these studies, it is important to review the recent history of hemicraniectomy clinical trials. The first trial to be reported was the phase II National Institute of Health-sponsored Hemicraniectomy And Durotomy On Deterioration From Infarction Related Swelling Trial (HeADDFIRST). HeADDFIRST randomized 26 patients between the ages of 18 and 75 between the years 2000 to 2003. Patients were enrolled if they presented with CT evidence of a massive (>180 mL) MCA infarction, with randomization to surgery or continued medical therapy triggered by the subsequent development of midline shift (defined as ≥7 mm septal or ≥4 mm pineal gland displacement). The investigators reported a nonsignificant reduction in mortality from 46% with medical therapy to 27% in the surgically treated group. Functional outcomes were not reported, however, leaving open to question the issue of quality of life in these survivors.

Somewhat unconventionally, 3 European hemicraniectomy trials, including the DESTINY and DECIMAL trials, reported a pooled analysis of their 1-year outcomes in March of 2007, before individual publication of their main results. This turn of events resulted from termination of enrollment in the DESTINY and DECIMAL trials last year after it became clear that survival was improved with surgery. The DESTINY and DECIMAL investigators combined their data with the ongoing HAMLET trial in an attempt to get the most definitive data to the scientific community as soon as possible. Importantly, all 3 of these studies restricted enrollment to patients ≤60 years of age, and the timing of surgery to <48 hours after stroke onset.

The aforementioned pooled analysis reported by Vahedi et al earlier this year is a landmark publication because it is the first to demonstrate that hemicraniectomy can be a life-saving procedure. A total of 93 patients were randomized to surgical or medical therapy and evaluated with the modified Rankin Scale (mRS) at 1 year. Hemicraniectomy more than doubled the chances of survival, from 29% to 78%. This staggering absolute risk reduction of 49% was highly significant and translates into a number needed to treat of 2 to avoid one fatality.

Thus, it seems clear that hemicraniectomy can save lives, at least in younger patients if the surgery is performed early. But what was the quality of recovery among those who survived? In the acute phase of a severe stroke the decision to proceed with hemicraniectomy is usually made by families, based on the patient’s wishes and best interests. In this regard the pooled analysis by Vahedi et al also provides useful information that cannot be gleaned from the individual trial results reported in this issue of Stroke. First, hemicraniectomy did not appear to increase the risk of complete dependency, misery, and hopelessness. Exactly 2 patients in the surgical and medical groups (≈5%) were bedbound and severely

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disabled (mRS level of 5) at 1 year. The proportion of patients alive with minimal-to-moderate disability (mRS 0 to 3), however, was significantly increased from 21% to 43%. Viewed another way, hemicraniectomy resulted in a 49% absolute risk reduction in death, and an absolute increase in the proportion of patients rated as mRS 2 of 12%, mRS 3 of 10%, and mRS 4 of 29%. Thus, for every 10 hemicraniectomies performed for MCA infarction, 5 patients will escape death, and at 1 year 1 of these patients will have mild disability, 1 will have moderate disability, and 3 will have moderate-to-severe disability (ie, unable to walk independently). This information may be helpful for explaining the anticipated outcome of this procedure to families.

With this backdrop, the more detailed reports of the DESTINY and DECIMAL trials in this issue of Stroke allow for a more nuanced and critical appraisal of the data reported in the pooled analysis. The most clinically pertinent issues involve patient selection and the timing of surgery. The fact remains that not every patient with an MCA infarct develops fatal brain edema, and the factors that contribute to a malignant course are poorly understood. The most consistently identified clinical risk factors for death after MCA infarction include a high initial National Institute of Health Stroke Scale (NIHSS) score, larger infarct volume, younger age, and early signs of transtentorial herniation.11,12 The DECIMAL investigators performed MRI preoperatively and used a diffusion-weighted imaging lesion volume of >145 mL as one of their inclusion criteria. Importantly, they noted that among the 8 patients screened but not randomized because their stroke was smaller than 145 mL, none died, which confirms a prior report identifying this threshold as a risk factor for malignant ischemic edema.13 Conversely, no patient with a baseline lesion volume exceeding 210 mL survived without a hemicraniectomy. Unfortunately, infarct volume cannot be quantified precisely without advanced image analysis tools. There is a need for larger imaging studies to systematically evaluate lesion volume, midline shift, cisternal effacement, vessel patency, and other potential predictors of malignant edema after MCA infarction.

The optimal timing of hemicraniectomy remains uncertain. There has been an ongoing debate over whether to operate as soon as the diagnosis of MCA infarction is made, or to wait for signs of early symptomatic mass effect, which might perhaps spare some patients the procedure if they have a stable course. The mean interval between onset and surgery in the DESTINY and DECIMAL trials was ≈24 hours, and the pooled analysis by Vahedi et al found no additional benefit with surgery performed within 24 hours compared with surgery performed later (both studies required that surgery take place no more than 6 hours after randomization).9 A systematic review of 129 published cases of hemicraniectomy for MCA infarction also found no difference in outcome if surgery was performed within 24 hours or at a later time point,4 in contrast to a single center study that reported better results with early surgery.4 These data indicate that for alert patients who lack significant shift or mass effect on imaging, careful clinical monitoring is appropriate until a change in level of consciousness or other signs of intracranial mass effect develop. In contrast to the classic teaching that brain edema peaks in intensity 3 days after stroke, some patients with MCA infarction deteriorate from mass effect several days later. Because the DESTINY and DECIMAL studies did not include patients enrolled beyond 48 hours, the benefit of hemicraniectomy as a late “salvage” procedure in patients who were initially managed medically remains uncertain.

Involvement of the dominant hemisphere has often been used in the past as an excuse to deny patients hemicraniectomy as a life-saving procedure, with the logic being that global aphasia is a fate worse than death.14 For several years there has been an increasing sentiment in the stroke community that this concept is outmoded.15 Neglect resulting from nondominant lesions is known to limit the degree of active participation in rehabilitation programs and is associated with poor functional recovery and social reintegration, thus making it just as disabling as aphasia.16 Moreover, significant improvement in aphasia can occur in dominant hemisphere stroke treated with hemicraniectomy.17 A prespecified subset analysis in the DECIMAL trial showed no difference in the mRS scores of survivors with or without aphasia,7 and the pooled analysis by Vahedi et al showed that the benefit of surgery for preventing death or moderate-to-severe disability (mRS) was similar regardless of the presence or absence of aphasia at baseline.9 In the DESTINY trial all surgical survivors agreed with the decision to undergo surgery in retrospect, including the slightly more than half of patients still experiencing aphasia.6 These data indicate that involvement of the dominant hemisphere is no longer an acceptable reason for withholding hemicraniectomy from otherwise appropriate candidates.

Perhaps the most common question that will vex clinicians in the near future will be the issue of age. In the aforementioned systematic review of published hemicraniectomy cases, younger age (in this case dichotomized at 50 years) was the only preoperative clinical determinant of survival with good functional outcome.5 A prespecified analysis in the DECIMAL trial confirmed that younger age was a stronger determinant of favorable outcome than infarct volume among surgically treated patients.7 However, the DESTINY and DECIMAL trials only provide us with information on the benefits of hemicraniectomy for patients younger than age 60. Given the striking survival benefit, it is now clear that studies to determine whether patients aged 60 to 80 can also benefit from hemicraniectomy are now urgently needed. Until that time, clinicians will need to struggle with where to “draw the line” in terms of offering hemicraniectomy as a treatment option for older patients, who clearly have worse functional outcomes after hemicraniectomy,18 and who are at increased risk for complications in the intensive care unit (ICU). The detailed data reported in the DECIMAL trial confirms that hemicraniectomy patients can experience a vast array of medical problems, including nosocomial infections, venous thromboembolism, and seizures. The importance of meticulous intensive care for restoring patients to health after hemicraniectomy cannot be emphasized enough. The ICU protocol provided in Table 2 of the DESTINY trial provides an excellent starting point in this regard.6

The DESTINY and DECIMAL trials are not without flaws, of course, including their small size, the presence of several
protocol violations, and the fact that approximately half of the patients in each trial was enrolled by a single center. The biggest doubt that remains, however, lies in the fact that the clinical management was unblinded to treatment modality. It is well established that survival in critically ill stroke patients is largely determined by decisions regarding whether to aggressively pursue care, or to withhold or withdraw support. It is entirely possible that unconscious biases among the investigators could have influenced this decision-making. It is notable that in the DECIMAL trial 100% of the surgically treated patients received mechanical ventilation, compared with only 61% of the medically treated patients,7 which suggests that decisions to withhold life support may have played a role in the early demise of some of these patients. This conundrum cannot be solved, unfortunately, because there is no practical way to blind caregivers in the ICU to treatment in a hemicraniectomy trial. What this points to is the importance of ICU support after surgery for determining who lives and who dies.

In terms of interpreting the results of the DESTINY and DECIMAL trials, however, the lack of blinding may not matter. Until now, massive MCA infarction has essentially been a guarantee of death or devastation. Let us agree that hemicraniectomy combined with aggressive ICU support can give many patients with MCA infarction a second chance on life, compared with supportive care alone combined with a possibly more nihilistic attitude. Tell this to your patients, and let them decide.

Disclosures
None.

References

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