EDITORIAL



## **Decompressive Hemicraniectomy in the Age of Personalized Medicine**

Michael N. Diringer<sup>1</sup>

Published online: 1 July 2016 © Springer Science+Business Media New York 2016

Ever since the pooled analysis of three randomized controlled trials of early decompressive surgery in malignant infarction of the middle cerebral artery was published in 2007 [1], the consideration of decompressive hemicraniectomy for large hemispheric stroke patients has become widespread. That paper reported on the pooled results of three small randomized trials: DECIMAL [2], DESTINY [3], and HAMLET [4]. While the analysis indicated that the procedure clearly can reduce mortality, considerable controversy persists over whether it improves functional outcome. The essence of the dispute is philosophical and essentially can be distilled down to whether one considers a modified Rankin score of four as a good or a bad outcome.

For those who maintain decompressive surgery is a reasonable intervention, careful consideration must be given to patient selection, timing of intervention, and medical alternatives. Following its publication, selection of candidates was based on the inclusion criteria for the pooled analysis: age 18-60 years, National Institutes of Health Stroke Scale (NIHSS) score >15, decreased level of consciousness ( $\geq 1$  on item 1a of the NIHSS), computtomographic scan (CT) signs of infarct erized involving  $\geq 50$  % of the middle cerebral artery territory, and inclusion within 45 h of onset of symptoms. Over the ensuing years, the age limit has been pushed higher; and in 2014, a randomized trial enrolling patients aged 61-82 years found that hemicraniectomy increased survival without severe disability [5].

Once a patient has been identified as a potential candidate for surgery, two different approaches to timing are possible. The early surgery, or preemptive, approach moves forward with hemicraniectomy as soon as the patient is identified, ideally within 24 h of onset. The alternative strategy espouses postponing surgical intervention until evidence of increased radiographic edema and/or clinical deterioration manifests and, in the interim, instituting medical management of cerebral edema.

There is little in the literature to assist in determining which approach is better. Timing of surgery varied across the trials included in the pooled analysis. In DECIMAL, patients were enrolled on average 15.8 h after onset, while in DESTINY and HAMLET, the average was 24 and 29.5 h, respectively. In Juttler's study of older patients, surgery was performed a median of 26 h after onset. While the early surgery approach intervenes before patients deteriorate further, not all of them are destined to do so. What remains unknown in that time window is whether an individual patient will continue to swell and ultimately herniate, whether the swelling is already at its peak, or whether it will respond to medical interventions and not progress to herniation. Without this information, patients may unnecessarily undergo hemicraniectomy and subsequent cranioplasty, procedures that carry complication rates as high as 30 % [6, 7].

The question of timing is further confounded by the wide variation in medical management. In HAMLET, medical management was at the discretion of the treating physician and could be provided in either an intensive care or stroke unit. In DESTINY, all patients were ventilated and treated in an intensive care unit. In DECIMAL,

Michael N. Diringer diringerm@neuro.wustl.edu

<sup>&</sup>lt;sup>1</sup> Department of Neurology, Neurocritical Care Division, Washington University, Box 8111, 660 S. Euclid Ave., St. Louis, MO 63110, USA

treatment location was not defined. Use of osmotic therapy also varied; DESTINY used osmotic therapy prophylactically, while HAMLET deferred its use until patients rapidly worsened due to brain edema.

Akins and colleagues [8] report their experience managing patients who, based on the criteria used by the pooled analysis, would have been candidates for early decompressive surgery. They were all managed by a team of neurointensivists in an ICU using a standard approach to medical management; and surgery was offered only if they deteriorated further. The management included hourly neurologic assessment, daily head CT scans, neurosurgical consultation, and additional CT imaging as clinically indicated. Patients who developed mass effect were monitored through post-stroke day 4, and a head CT was repeated prior to transfer off the unit. The use of osmotic therapy was determined by the treating neurointensivist, but no details are provided.

Using this approach, 60 % of the cohort avoided surgery without any increase in mortality or severe dependency compared to the pooled analysis results. Outcome tended to be worse in those who ultimately underwent hemicraniectomy, yet it was still better than those reported in the literature. These results speak to the role of a standardized approach to aggressive medical management, close clinical monitoring, and frequent imaging in maximizing outcome in this population.

This suggests that a subset of patients who meet the pool study criteria may do well without surgery. Patients with moderate-sized hemispheric infarcts, those who do not require osmotic therapy within the first 24 h of stroke [9], and younger patients [10] may be such subsets. By refining medical therapy through the optimization of osmotic administration and the development of new specific antiedema agents [11], the need for surgery could be reduced even further.

We need additional tools to help identify which patients will not develop malignant edema to avoid the risks of unnecessary surgery. Possibilities include increasing the sensitivity of imaging in detecting early edema, assessing blood-brain-barrier integrity, and identifying genetic markers of those more likely to develop edema. With better patient selection and aggressive medical management, surgical decompression can be reserved for those who stand to benefit the most.

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