

## CORRESPONDENCE



## Craniectomy in Diffuse Traumatic Brain Injury

**TO THE EDITOR:** On behalf of the Section on Neurotrauma and Critical Care of the American Association of Neurological Surgeons and the Congress of Neurological Surgeons, we register our concern with the recently published article “Decompressive Craniectomy in Diffuse Traumatic Brain Injury” by Cooper et al. (April 21 issue).<sup>1</sup> We have identified the following problems with the trial design: first, inclusion limited to a small subset of patients with traumatic brain injury (no mass lesions); second, choice of operative technique (bifrontal procedures without division of the sagittal sinus and falx cerebri, limiting the procedural efficacy for lowering intracranial pressure)<sup>2</sup>; third, a long accrual time (over which major differences in treatment may have evolved); fourth, differences in study groups (significantly more patients with bilaterally unreactive pupils included in the surgical group, expected to negatively skew results)<sup>3</sup>; and fifth, minimal mean elevations in intracranial pressure leading up to randomization (median for both groups during the 12 hours before randomization at the upper limit of normal, 20 mm Hg).<sup>4</sup>

It is therefore our view that no conclusions regarding management of the use of decompressive craniectomy in patients with traumatic brain injury should be drawn from this trial, and clinical practice should not be changed on the basis of these results.

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**TO THE EDITOR:** Cooper et al. found that early bifrontotemporoparietal decompressive craniectomy decreases intracranial pressure and length of stay in the intensive care unit but increases the proportion of patients with an unfavorable outcome. Interestingly, this study focused exclusively on the monitoring of intracranial pressure and focused all its interventions on control of intracranial hypertension. However, there is evidence showing that even when intracranial pressure and cerebral perfusion pressure are normalized, patients with traumatic brain injury may continue to have severe cerebral hypoxia, with reduced oxygen tension in brain tissue, which may explain

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their poor outcome.<sup>1,2</sup> Strategies to improve cerebral oxygenation suggest the benefit of multiple approaches to monitoring for these patients.<sup>3</sup> In this context, the only point the Decompressive Craniectomy (DECRA) trial may demonstrate, in a select group of patients with severe traumatic brain injury, is that early bifrontotemporoparietal decompressive craniectomy may be harmful when its exclusive goal is to reduce intracranial pressure. It would be interesting to know why the investigators did not incorporate any system for the evaluation of cerebral oxygenation.

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No potential conflict of interest relevant to this letter was reported.

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**TO THE EDITOR:** The DECRA trial will probably cause consternation among neurosurgeons and neurointensivists. An important issue inadequately addressed in the trial is the role of medical management in the treatment of elevated intracranial pressure. The trial's quick-trigger criterion for the use of decompressive craniectomy (an increase in intracranial pressure of >20 mm Hg for >15 minutes in any single hour after injury, despite the use of "optimized first-tier interventions") does not give sufficient time to optimize management of intracranial pressure. First-tier protocols, including the use of sedation, maintenance of a normal carbon dioxide level, optimization of blood pressure, use of osmotherapy, and drainage of cerebrospinal fluid,<sup>1</sup> should be implemented in a standardized, escalated manner before proceeding to decompressive craniectomy. Advancements in critical care have led to clinically significant improvements in outcomes in traumatic brain injury.<sup>2</sup> Before exploring a possible niche for decompressive craniectomy in the treatment of traumatic brain injury, we first must ensure that patients receive the best available medical therapies. Moreover, new medical therapies

aimed at preventing the early secondary events in patients with traumatic brain injury that cause elevated intracranial pressure (e.g., hemorrhagic transformation or contusion "blossoming")<sup>2</sup> should be given equal attention in future randomized, controlled trials.

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**TO THE EDITOR:** We read with interest the study by Cooper et al. to assess the use of decompressive craniectomy for adult patients with diffuse traumatic brain injury. However, in addition to supporting the concerns raised in the accompanying editorial,<sup>1</sup> we believe that this study shows that the normalization of intracranial pressure as achieved with decompressive craniectomy is probably not the key issue in managing the care of patients with traumatic brain injury whose injury is diffuse. It is indeed unfortunate that no concomitant measurements of cerebral blood flow were performed while intracranial pressure was increasing. The normalization of intracranial pressure does not mean that brain perfusion has been adequate, as has been shown with the use of severe hyperventilation.<sup>2</sup> Information about cerebral blood flow is readily obtained with the use of transcranial Doppler ultrasonography or a probe to monitor the oxygen tension in brain tissue at the bedside, or possibly with the use of brain perfusion computed tomography. Because brain ischemia is the key factor in determining neurologic outcome after brain injury, measurements of cerebral blood flow should be considered together with measurements of intracranial pressure in order to properly assess the value of aggressive approaches such as decompressive craniectomy in patients with traumatic brain injury.

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**TO THE EDITOR:** The DECRA study showed that the use of decompressive craniectomy for patients in whom intracranial hypertension develops after traumatic brain injury can ultimately have a negative effect on their functional status. The authors suggest that axonal stretch, caused by shifting brain bulk, could be responsible. Although this suggestion is plausible, it is important to consider the possibility that the release of pressure, in and of itself, may have aggravated the development of brain edema that would otherwise have been self-limiting (as suggested by Fig. 1 of the article and by the fact that mortality remained unaffected). Particularly when the response of the brain to variations in infusion pressure is impaired and the blood-brain barrier is leaky, the sudden increase in transcapillary hydrostatic pressure after decompression can promote the development of vasogenic edema.<sup>1</sup>

Unfortunately, there is still no good evidence that aggressive efforts to reduce intracranial pressure can improve outcome. Previous studies have shown that the use of hypothermia and barbiturates in the treatment of brain injury did not have a positive effect on outcome despite clear evidence that these interventions could effectively reduce the burden of intracranial pressure.<sup>2,3</sup> Craniectomy has become an example of yet another intervention that is effective in reducing intracranial pressure but not in improving outcome.

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**TO THE EDITOR:** The DECRA trial did not show improved outcome with craniectomy, and in particular showed no reduction in mortality despite lowering intracranial pressure. However, although intracranial pressure was lowered through decompression, intracranial pressure was not excessively high in the medical group.

Recordings of intracranial pressure after head injury show that thresholds of 25 mm Hg determine outcome.<sup>1</sup> Therefore, patients likely to benefit from decompression are those with uncontrollable intracranial pressure above 25 mm Hg.

The protocol for the RESCUEicp (Randomized Evaluation of Surgery with Craniectomy for Uncontrollable Elevation of Intracranial Pressure) trial differs from that of the DECRA trial in terms of intracranial pressure threshold, timing of surgery, acceptance of contusions, and duration of follow-up. The cohort profiles and criteria for entry and randomization in the two studies are therefore very different. Hence, the DECRA results should not deter recruitment into other surgical evaluation studies. As of June 30, 309 of the target of 400 patients had been recruited for the RESCUEicp trial.

We believe that other patients should be studied in trials incorporating multicenter randomization, focused imaging, and the monitoring of intensive care to increase our understanding of the pathophysiology of the brain's response to decompressive craniectomy.

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No potential conflict of interest relevant to this letter was reported.

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**THE AUTHORS REPLY:** To respond to the issues raised by Timmons et al.: First, we excluded patients with mass lesions because outcomes for these patients are different from outcomes among patients without lesions, and findings from clinical series with mixed types of traumatic brain injury have been misleading. Further investigation is required to determine the generalizability of findings from the DECRA trial to conditions other than diffuse traumatic brain injury. Second, different surgical approaches to traumatic brain injury are preferred by different neurosurgeons; there is no consensus. The DECRA procedure, a modified version of the Polin procedure,<sup>1</sup> significantly decreased intracranial pressure without evidence of injury caused by leaving the falx intact or by dividing it. Third, we are not aware of any major differences in the treatment of patients with traumatic brain injury that have accrued over the time frame of our study; such differences are not evident in practice guidelines.<sup>2</sup> Furthermore, we stratified randomization according to center and performed randomization in small blocks, such that changes in practice would have applied to both groups. Fourth, there was baseline balance between groups for the two most important prognostic factors: age and motor score on the Glasgow Coma Scale. The treatment effect was still significant after adjustment for four prespecified covariates. In accordance with the protocol, patients with fixed dilated pupils were excluded. IMPACT<sup>3</sup> algorithms make it clear that pupil reactivity is less important than other covariates, and the baseline imbalance was exaggerated due to missing values: after adjustment for pupils alone in all patients, those who had craniectomy had worse outcomes (odds ratio, 2.00; 95% confidence interval, 1.02 to 3.94;  $P=0.04$ ). Finally, there was a rising trend in intracranial pressure to 23 mm Hg before randomization.<sup>1</sup> Pilot data supported the use of an application of intracranial pressure of 20 mm Hg, as recommended in the practice guidelines.<sup>2,4</sup> We know of no mechanism that would support the suggestion that patients might benefit from a delay in effective intracranial pressure control and acceptance of pressures greater than 20 mm Hg for longer periods before craniectomy.

Six large North American centers agreed to the DECRA protocol before deciding to participate and did not raise concerns about the design. We believe the conclusions derived from the DECRA trial should lead to practice change.

Romero asks about monitoring oxygenation of brain tissue, and Hautefeuille et al. ask about the measurement of cerebral blood flow. Although both procedures are routine in some centers, neither is a standard of care. Patients in the DECRA trial had better functional outcomes when standard care was provided (including inducement of coma with a barbiturate in 77% of patients receiving standard care) than when more effective control of intracranial pressure was provided through craniectomy. It would be interesting to see the result of a randomized trial in which the effect of intracranial-pressure monitoring itself is assessed.

Simard et al. suggest that insufficient time was allowed for the optimization of first-tier therapies. However, a tiered suite of therapies was defined, and after heavy sedation, paralysis was induced in 78% of patients, external ventricular drainage was used in 100%, and barbiturates were used in 77% before randomization. Most (86%) did not require second-tier therapies.

We agree with Cremer and Slooter that vasogenic edema may have contributed to adverse results. In addition, clinicians used fewer intracranial pressure interventions after craniectomy, whereas brain edema may have actually been increasing.

In the RESCUEicp trial, Hutchinson and Kirkpatrick use an intracranial pressure threshold of 25 mm Hg, although this threshold is not recommended in practice guidelines,<sup>2,4</sup> and is not used in routine practice. Their results will complement ours and are eagerly awaited.

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Since publication of their article, the authors report no further potential conflict of interest.

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