Chapter 10

DECOMPRESSIVE CRANIECTOMY FOR REFRACTORY POSTTRAUMATIC INTRACRANIAL HYPERTENSION:
INTERPRETATION AND IMPLICATIONS OF THE INTERNATIONAL RESCUEICP RANDOMIZED TRIAL

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ABSTRACT

Although decompressive craniectomy has been used for more than 100 years in neurosurgery, uncertainties still remain regarding the indications, optimal timing, and effects of decompressive craniectomy on the functional outcome of head-injured patients. In this chapter we discuss the role of decompressive craniectomy for refractory intracranial hypertension following severe traumatic brain injury.

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**INTRODUCTION**

One of the major determinants of outcome after traumatic brain injury (TBI) is the severity of the primary injury, which is irreversible. Primary injury, however, invariably leads to the activation of cellular and molecular processes, which mediate further (secondary) injury over the ensuing hours and days [1] and are therefore amenable to therapeutic intervention. These molecular cascades can lead to brain swelling within the confines of a fixed intracranial compartment, leading to increased intracranial pressure (ICP). This can, in turn, compromise the cerebral perfusion pressure (CPP), cerebral blood flow (CBF), and brain oxygenation [2, 3]. Ischemia and cell damage can exacerbate the swelling, forming part of a vicious circle that can lead to life-threatening brain herniation. TBI is associated with extracranial injuries in at least 35% of the cases, and these can further increase the risk of secondary injury due to hypotension, hypoxemia, hypercarbia, pyrexia, and/or coagulopathy [4, 5]. A considerable body of evidence links posttraumatic intracranial hypertension at levels above 20 to 25 mm Hg with excess mortality and worse functional outcomes [6-11]. Similar findings have been shown for reduced CPP at levels below 50 to 55 mm Hg [6, 7, 11].

The control of ICP and preservation of CPP has therefore been the mainstay of neuro-intensive care management of TBI for several decades. Tier-based protocols employing neuroprotective measures such as sedation, controlled hyperventilation, therapeutic hypothermia, hyperosmolar therapies, barbiturate coma, and ventricular drainage have been recommended and are widely used in intensive care units to control intracranial hypertension and facilitate cerebral perfusion and oxygenation [12, 13]. Measures such as hyperventilation, therapeutic hypothermia, and barbiturate-induced coma have been found to be effective in reducing ICP; however, subsequent clinical studies have failed to demonstrate clinical benefit, and in certain instances these therapies may have even caused harm [14-18], possibly due to unfavorable effects on cerebral perfusion [19, 20] or adverse extracranial effects [17].

**DECOMPRESSIVE CRANIECTOMY**

Decompressive craniectomy (DC) is an operative procedure whereby a large segment of skull (bone flap) is removed; the underlying dura is then opened and left unsutured or a wide nonconstricting duraplasty is performed. This procedure can reduce ICP and
maintain or improve cerebral compliance [21, 22]. In the context of TBI, DC can be used as the primary or a secondary procedure. Primary DC refers to leaving a bone flap out after evacuating an intracranial hematoma (mass lesion) in the early phase after the head injury either because of evident brain swelling (brain protruding beyond the margins of the inner table of the skull) or because there is a concern of impending brain swelling in the next few hours to days [23-26]. A secondary DC is performed as part of tiered therapeutic protocols, which aim to control intracranial hypertension. The operation can be undertaken as last-tier (life-saving) therapy when all other measures have failed to reduce ICP to levels below 25–35 mm Hg. Alternatively, it can be performed as a second-tier therapy in patients with less pronounced elevation of ICP (e.g., 20 mm Hg); this can be viewed as a neuroprotective measure [25].

From a physiological viewpoint, DC provides additional space for the swollen brain to decompress with beneficial effects on ICP [21]. The procedure was described by Theodor Kocher in 1901 [26]. Following his description, Harvey Cushing presented a case series of patients with head injury treated with subtemporal decompression [27]. Cushing reported a surgery-associated reduction in mortality from 50% to less than 15% and concluded that the brain edema and swelling that accompany severe cerebral contusions were best managed with a subtemporal DC. Renewed interest in DC emerged in the late 1960s and early 1970s in the context of TBI as well as ischemic stroke [28-30]. However, its utility was questioned in the late 1970s owing to the reports on poor clinical outcomes [31, 32] as well as animal studies that seemed to suggest that decompression may worsen cerebral edema [33]. With the significant improvements in the prehospital and neurointensive care management of TBI in the past 30 years, along with the widespread adoption of ICP monitoring and tier-based therapeutic protocols, the role of DC was re-examined. A resurgence of interest was seen throughout the 1980s and 1990s with a progressive increase in the number of publications describing its use in TBI as well as in other pathologies causing life-threatening intracranial hypertension [34, 35]. Although there were reports of the survival benefit of DC [35, 36], those studies were largely observational/uncontrolled, and the optimal timing and functional outcome of patients remained unclear.

The 2006 Cochrane Database Systematic Review on the use of DC for the treatment of refractory high ICP in TBI [22] identified only one randomized controlled trial [37]. In that study, 27 children (median age, 120.9 months; range, 13.6–176.4 months) with head injuries were randomly assigned to receive medical management alone or medical management plus bi-temporal DC (removal of a disc of temporal bone measuring about 3–4 cm, with extension of the craniectomy to the floor of the middle cranial fossa; dura mater was not opened). The study showed that DC was associated with a risk ratio of 0.54 (95% confidence interval, 0.29–1.01) for unfavorable outcome (death, vegetative status, or severe disability) at 6 months after injury (non-significant trend) [37].
With the continued dearth of good quality data from randomized controlled trials, questions about the utility of DC persisted, and DC did not feature in the 2007 Brain Trauma Foundation Guidelines for the Management of Severe Traumatic Brain Injury (3rd edition) [12]. Several reports have emerged in the past 10 years addressing differences in TBI surgical techniques, timing of DC, and patient populations [37-41]. While DECRA [42] examined the efficacy of early DC in patients with diffuse injury with an ICP threshold of 20 mm Hg for 15 minutes within 72 hours of injury, the role of DC in the treatment of raised and refractory intracranial hypertension was examined solely in observational studies [43, 44].

**RESCUEicp Trial**

The need for a good quality randomized controlled trial to examine the role of DC in the treatment of intracranial hypertension (> 25 mm Hg for 1–12 hours) refractory to medical treatment was widely recognized, and the RESCUEicp trial was launched in 2004 [45, 46]. This international, multicenter, parallel-group, superiority, randomized trial [46], compared last-tier secondary DC with continued medical management for refractory intracranial hypertension after TBI. The trial included patients with TBI aged between 10 and 65 years, with an abnormal computed tomography scan of the brain, an ICP monitor in place, and raised ICP of more than 25 mm Hg for 1 to 12 hours, despite applying stage 1 and 2 measures of the ICP protocol. All patients were treated in intensive care according to a stratified protocol (see Figure 1 in [46]) aimed at maintaining an ICP of 25 mm Hg or less. If, despite these measures, the ICP remained above 25 mm Hg for 1 to 12 hours, then at stage 3 of the protocol, patients were randomized to DC with medical therapy or to continued medical therapy with an option to use barbiturates to reduce the ICP.

The surgical treatment was either large unilateral frontotemporoparietal craniectomy (hemicraniectomy) or bifrontal craniectomy [46]. The primary outcome measure was the Extended Glasgow Outcome Scale (GOS-E) at 6 months after randomization. Table 1 lists the secondary outcome measures.

Four hundred and eight patients were recruited to this trial: 206 were randomized to the surgical and 202 to the medical group. No significant between-group variability was observed in terms of baseline characteristics and medical or surgical treatment given prior to randomization [46]. Looking at the primary outcome measure (GOS-E at 6 months), the surgical (DC) group had a significantly lower mortality rate than the medical group (26.9% versus 49.9%). Surgery was found to be associated with higher rates of vegetative state, lower severe disability, and upper severe disability than was medical management, but the rates of moderate disability and good recovery were similar between the groups (see Table 3 and Figure 2 in [46]). The trial pre-specified favorable outcome as upper
severe disability or better on the GOS-E and with such prespecified sensitivity analysis, 42.8% of surgical patients had a favorable outcome compared to 34.6% of medical patients (P = 0.12) [46]. Using the same prespecified sensitivity analysis at 12 months showed that 45.4% of surgical patients had a favorable outcome compared to 32.4% of medical patients (P = 0.01) (see Figure 2 in [46]).

**Table 1. RESCUEicp trial outcome measures. GOSE-Extended Glasgow Outcome Scale; GCS- Glasgow Coma Scale; ICU- Intensive Care Unit**

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<td>• Extended Glasgow Outcome Scale (GOSE) at 6 months</td>
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<th>Secondary outcome measure</th>
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<td>• GOSE at 12 and 24 months</td>
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<td>• Mortality at 6, 12 and 24 months</td>
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<td>• GCS at time of discharge from ICU</td>
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The trial also showed that the control of ICP was better in the surgical than the medical group. It is therefore not surprising that 37.2% of patients in the medical group eventually underwent a craniectomy and only 9.4% of patients in the surgical group required barbiturates as the failure to control ICP was greater in the medical group [46].

In contrast to the RESCUEicp trial, the DECRA trial [42] showed that patients undergoing craniectomy had worse ratings on the 6-month GOS-E than those receiving standard care (P = 0.03) with similar rates of death at 6 months (19% versus 18%). As we discussed in our correspondence that followed publication of the initial paper in the *New England Journal of Medicine* [47]:

The contrasting results of the DECRA and RESCUEicp trials are due to different hypotheses, inclusion criteria, and therapeutic protocols. The DECRA trial, as compared with the RESCUEicp trial, enrolled patients with a lower intracranial-pressure threshold (20 mm Hg vs. 25 mm Hg) for shorter intervals (15 minutes vs. 1 to 12 hours), after lower intensities of therapy (stage 1 interventions vs. stage 1 and 2 interventions), and within a shorter interval after injury (all patients enrolled within 72 hours after injury vs. 44% of patients enrolled >72 hours after injury). Patients with intracranial hematomas were enrolled in the RESCUEicp trial, but they were not enrolled in the DECRA trial. At enrollment, the populations also differed with respect to expected outcome; the requirement for stage 2 interventions increases the relative risk of death by 60%. Hence, at 6 months, the pooled mortality of 37.5% in the RESCUEicp trial versus 18.7% in the
DECRA trial is unsurprising. In addition, our primary analysis showed a significant between-group difference in the GOS-E distribution and a substantial reduction in mortality with surgery; this finding differed from that of the DECRA trial, in which mortality was similar in the two groups. The severity of injury in the RESCUEicp trial underpinned dichotomization in the prespecified sensitivity analysis at upper severe disability (independent at home) or better. Given the high expectation of a poor outcome, the use of a “conventional” dichotomy would be as inappropriate as the use of it in populations with mild TBI (in whom disability-free survival is often attainable).

The survival advantage of DC in the RESCUEicp trial was translated to both dependent and independent living, and this is something that clinicians and family members will need to be aware of when making decisions regarding treatment [46]. It is important to appreciate that the perspectives of patients and their families need to be respected when determining the degree of “acceptable” disability and subsequently whether a craniectomy should be considered. We believe that the concept of shared decision making can play a fundamental role to this end [11, 48].

**CONCLUSION**

Improved control of ICP with surgery may have accounted for mortality that was lower than that observed with medical management. With a large body of evidence showing that it drives mortality, the treatment of intracranial hypertension will remain important [43, 44]. Future research should also focus on cranial reconstruction and the role of primary craniectomy for acute subdural hematomas, which is the topic of the ongoing RESCUE-ASDH trial (rescueasdh.org). To close, we would like to quote an excerpt from our recently published correspondence in the *British Journal of Anaesthesia* [49]:

In the past, we never advocated for an indiscriminate use of craniectomy, and we are not doing so after the publication of the trial results. However, we believe that the RESCUEicp results have shown that craniectomy can be useful, as long as a thoughtful approach is adopted with involvement of the multidisciplinary clinical team and family members in the decision-making process.

**REFERENCES**


This chapter is partly based on the NEJM publication and subsequent correspondence (references (46, 47, 49).