Comparative effectiveness of surgery for traumatic acute subdural hematoma

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PART I

CURRENT EVIDENCE

Chapter 2

Surgical management of traumatic brain injury – to operate or not

Adapted from:
Traumatic brain injury: integrated approaches to improve prevention, clinical care, and research.
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And

Surgical dilemmas in traumatic brain injury
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SUMMARY

Traumatic brain injury has a high mortality and those patients that survive often experience long-term disability due to physical, cognitive or psychological deficits. Neurosurgical interventions in traumatic brain injury can cause major reductions in mortality and morbidity. However, the precise indications of surgery in traumatic brain injury are not sufficiently clear. As a consequence, treatment varies among regions, hospitals and neurosurgeons. Recent, current and future research is rapidly changing this uncertainty. Pragmatic studies with a so-called comparative effectiveness design seem to be the most promising to increase the level of evidence of neurosurgical interventions in traumatic brain injury.

INTRODUCTION

One of the most vexing problems in the neurosurgical care for brain trauma patients is to determine which patients might benefit from surgical treatment for traumatic intracranial hematoma's and/or raised intracranial pressure. This is complicated by additional uncertainty regarding the optimal timing of surgery and the most effective technique, in particular in cases with large contusions and in patients considered for decompressive craniectomy (DC). The goals of the initial surgical treatment in TBI are to remove space-occupying intracranial hematomas, and to decrease pressure on the brain in order to prevent or minimize damage to important brain structures and to prevent life-threatening herniation events. Surgical decompression can be achieved by evacuation of a hematoma, by insertion of an external ventricular drain for drainage of cerebrospinal fluid (CSF), or by removing a large part of the skull to alleviate raised intracranial pressure resulting from swelling of the brain.[1-3] The latter procedure, called decompressive craniectomy (DC), may be performed in the same setting as the evacuation of a hematoma or later to treat diffuse brain swelling that is refractory to conservative medical management. Evacuation of an intracranial hematoma may be considered a causal approach, whilst DC is more symptomatic.

The majority of emergency TBI neurosurgery is directed at evacuating hematomas.[4] The hematoma may be located inside the brain (contusion) or outside the brain, above (epidural hematoma (EDH)) or below (acute subdural hematoma (ASDH, figure 1)) the outermost covering of the brain (dura mater).

ASDH and contusions, which are sometimes called intracerebral hematomas, represent the major clinical dilemmas. The occurrence of an ASDH is estimated to be up to 11% in patients with TBI and up to 49% of the patients with severe TBI (GCS < 9).[5,6] Large cerebral contusions are observed in 8% of all TBI, in up to 35% of severe TBI,[7] sometimes together with an ASDH, and in one study contusions were seen in 73% of patients with moderate and severe TBI as diagnosed on MRI.[8]

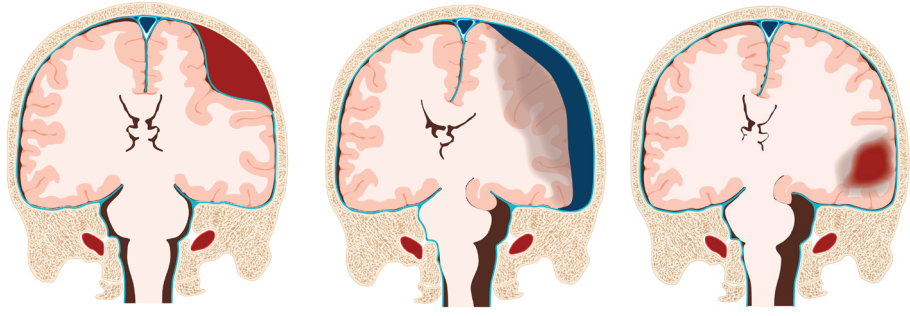

Figure 1. Different types of post-traumatic intracranial hematomas: A: epidural; B: subdural hematoma; C: intracerebral hematoma or contusion

Whereas international consensus exists with regard to the necessity for evacuation of a moderately sized or large EDH, heterogeneity exists in decision-making for ASDH, for contusions and for refractory raised intracranial pressure. This leads to considerable practice variation. The focus of this review is on the clinical specificities of the surgical indications and on the evidence underpinning these decisions.

FACTORS INFLUENCING SURGICAL DECISION-MAKING IN TBI

Many clinical factors may influence the choice and timing of surgical treatment, including patient related factors, surgeon preference, patient and family wishes, religion and cultural background, as well as logistic considerations. Patient factors include the initial GCS, pupillary size and reactivity, extracranial injuries, the severity of the injury, structural abnormalities on the CT scan and comorbidity as determinants of the balance between benefit and risk or futility. One of the most important factors, however, seems to be the preference and (lack of) experience of the treating neurosurgeon! When confronted with a patient with traumatic ASDH and/or contusion the neurosurgeon on-call is faced with several challenging management decisions.[2] Before choosing what type of surgery to perform, the first decision is whether or not surgery should be performed. Surgery might save a patient's life and preserve neurological function.[9] However, some patients may survive by surgery, but others may have an unfavorable functional outcome,[10-12] ranging from severe neurological and cognitive deficits to a persistent vegetative state. Conversely, surgery may not always be necessary and a substantial portion of patients managed conservatively have favorable outcomes.[13-15] Furthermore, certain subgroups may not benefit from surgery because the primary damage is simply too devastating. Too liberal surgical indications may lead to an increased number of survivors with severe disabilities, but inappropriate conservative management may result in unnecessary deaths. The decision to operate or not is not only based on medical considerations of expected mortality and functional outcome, but also on ethical considerations. The patient and relatives view towards a meaningful quality of life might be different from our medical perception of favorable outcome. Notably, the view on a worthwhile outcome can greatly differ between the clinician and the patient/relatives, not seldom due to cultural and religious standpoints. Sometimes, when there is enough time and opportunity to discuss the expected outcome with the relatives, this personal view on quality of life can be taken into account. Thus, the decision whether to operate or not does not merely depend on rational factors, but also involves several intuitive and ethical issues.

Furthermore, an important aspect of surgical approach is the timing of surgery. This relates specifically to intracerebral hematomas/contusions since it is generally agreed

upon that early surgery is better than delayed for ASDH and EDH. Sometimes, a contusion is initially managed conservatively, but may later be treated surgically by bony decompression or removal of contused brain tissue because of secondary deterioration. Indeed, a study conducted by the European Brain Injury Consortium reported that 73% of patients undergoing a delayed DC had developed raised ICP due to a contusion or intra-cerebral hemorrhage.[4]

These complex decisions often have to be made in difficult circumstances, constrained by time.[9] and in absence of peer consultation. As a result, the decision is often based on intuition and experience of the surgeon, which is not a rational evidence-based approach.

EVIDENCE UNDERPINNING SURGICAL DECISION-MAKING IN TBI

Surgical guidelines have been developed but lack robust scientific grounds.[1] The guidelines recommend that every ASDH with a thickness more than 10 mm and midline shift over 5 mm should be evacuated as soon as possible, irrespective of the neurological condition. For contusions the guidelines advocate to evacuate all lesions above 50 cm^3, and above 20 cm^3 in case of a GCS 6-8 with midline shift of at least 5 mm and/or cisternal compression on CT. These guidelines were based on low grade evidence (level III) derived from retrospective studies of small groups of selected patients, published more than 10 years ago. While additional studies have emerged,[6,10] these studies have only marginally improved the evidence base in this context.

Consequently, many different opinions exist between neurosurgeons as to what constitutes best surgical practice. Controversy is probably greatest with regard to the management of intracerebral contusions: in some countries contusions are routinely operated upon early to prevent deterioration (pre-emptive approach), whilst in others a conservative approach is preferred and patients only seldom operated.[4,16] The variation in surgery for ASDH lies not so much in the timing, since benefits of early surgery have been established, but more in the stance towards which subgroups of patients can benefit from evacuation.[5] Moreover, there is a large difference in point of view among neurosurgeons with respect to combining the evacuation of an ASDH with a DC.[17]

This paucity of high quality evidence on surgical management for TBI is partly explained by the difficulty of performing RCTs in TBI in general.[18] The heterogeneous study population, presence of other injuries, different mechanisms of injury, and the multitude of treatment variables, together with relatively low patient numbers per subgroup - due to rigid selection criteria - make the execution of RCTs of considerable power problematic. To include a sufficient number of patients, TBI trials generally

suffer from a considerable lag time between inception of the study and publication of results. This leads to high costs with a low yield of effect.

Besides these general methodological difficulties in TBI RCTs, specific additional constraints for surgical RCTs exist. Randomizing surgical treatments for TBI may be problematic because of ethical concerns of withholding a potentially lifesaving procedure. Although evidence is lacking, treating surgeons often do not have doubts about the "best" treatment. In case this treatment is surgery, a decision to randomize the patient and obtain informed consent is difficult to execute in the acute phase. And even if a trial succeeds it frequently has limited external validity since the treatment effect has been evaluated in selected populations, with prescriptive management protocols that are sometimes difficult to replicate in the real-world clinical setting.

Several studies have recently been conducted, or are still on-going that address several clinical uncertainties in neurosurgical decision-making (table). No RCTs have been published on the surgical treatment of TBI, until recently, the Decompressive Craniectomy in Patients with Severe Traumatic Brain Injury (DECRA) study was published.[19] In the DECRA trial, the investigators wanted to assess whether early/neuroprotective bifrontal DC can lead to better outcomes compared to standard ICU treatment for patients with diffuse TBI. At 6-month follow-up, a higher rate of unfavorable outcomes was observed in the DC group (OR 2.21; 95% CI 1.14–4.26; p = 0.02). However, 27% of patients in the DC arm had bilaterally unreactive pupils compared with only 12% in the medical arm. Following post-hoc adjustment for pupil reactivity at baseline, the between-group difference in terms of unfavorable outcome was no longer significant (adjusted OR 1.90; 95% CI 0.95–3.79).

Contrary to DECRA, the Randomised Evaluation of Surgery with Craniectomy for Uncontrollable Elevation of Intra-cranial Pressure (RESCUEicp) trial aims to assess the effectiveness of DC as a last-tier therapy for patients with refractory intracranial hypertension. The results (primary end point) are expected in late 2014.

Another surgical study is the Surgical Trial in Traumatic Intracerebral Haemorrhage (STITCH-Trauma), an international multicenter pragmatic randomized controlled trial exploring the value of surgery in patients with intracerebral hemorrhage and contusion. This study inclusion is based on clinical equipoise: only patients for whom the responsible neurosurgeon is uncertain about the benefits of either treatment are eligible. The study started in October 2009 but was halted due to concerns regarding the numbers of patients recruited in the UK. On analysis, a strong tendency towards benefit of early surgery was found, but non-significant due to low numbers.

Table. Recent and emerging studies on surgery for TBI

	Patients	Intervention	Controls	Outcome	Main findings
DECRA	Patients with diffuse TBI within 72 hours post-injury	(Early) secondary (Bifrontal) DC	Standardized ICU treatment	GOSE at 6 months post-injury	- DC greater risk of unfavorable outcome (OR 2.21) - No significant difference in unfavorable outcome (a composite death, vegetative state or severe disability) after post-hoc adjustment for pupil reactivity
RESCUE-ICP	Patients with refractory ICP	(Last resort) secondary DC (hemicraniectomy or bifrontal)	Standardized ICU treatment	-Outcome at discharge (GOS) - GOSE at 6 months post-injury	- Recruitment completed - Follow-up ongoing
STITCH-trauma	- Patients with intracerebral hematoma/ contusion - Based on equipoise of neurosurgeon	Early evacuation of the hematoma	Best medical treatment combined with delayed evacuation (if appropriate)	A prognosis based GOSE/ Modified Rankin Scale	- Halted - Non-significant benefit on primary efficacy analysis
CENTER-TBI/Net-QuRe	Patients with ASDH and/or intracerebral hematoma/ contusion	Non-experimental CER design: - Direct evacuation of the hematoma vs conservative management - Primary DC with evacuation of hematoma vs craniotomy with evacuation of hematoma		GOSE at 6 months post-injury	- Initiated 1st January 2015
RESCUE-ASDH	Patients GCS < 8 with ASDH	Primary DC with evacuation of hematoma	Craniotomy with evacuation of hematoma (only)	GOSE at 12 months post-injury	- Initiated September 2014

CENTER-TBI, Collaborative European NeuroTrauma Effectiveness Research in TBI; DECRA, Decompressive Craniectomy in Patients with Severe Traumatic Brain Injury; RESCUE-icp, Randomised Evaluation of Surgery with Craniectomy for Uncontrollable Elevation of Intra-cranial Pressure; STITCH-trauma, Surgical Trial in Traumatic Intracerebral Haemorrhage; Net-QuRe, Dutch Neurotraumatology Quality Registry; CER, comparative effectiveness research; RESCUE-ASDH, Randomised Evaluation of Surgery with Craniectomy for patients Undergoing Evacuation of Acute Subdural Haematoma; DC, decompressive craniectomy; ICU, intensive care unit; ICP, intracranial pressure; GOS, Glasgow Outcome Scale.

FUTURE PERSPECTIVES - COMPARATIVE EFFECTIVENESS RESEARCH

Clearly, there is a need for stronger evidence in the field of surgical treatment of TBI. Future studies in surgical strategies for TBI should focus on feasibility and generalizability, typical characteristics of comparative effectiveness research (CER).[20,21] Non-experimental CER, uses variability in treatment for comparison in real-world conditions and is increasingly used in medicine to compare the outcomes of different treatments.

This approach may allow us to link documented variation in surgical strategies to outcome variation in two promising studies now under development (Table). Specifically, for surgical strategies, the proven variation in surgical strategies will be linked to the outcome variation. Thereby, in CENTER-TBI, we expect to answer the burning clinical questions of this chapters' title: who to operate and when in certain subgroup of patients with ASDH and/or contusions. In addition, the Randomised Evaluation of Surgery with Craniectomy for patients Undergoing Evacuation of Acute Subdural Haematoma (RESCUE-ASDH) is an international multicenter, pragmatic, parallel group randomized trial of primary DC versus craniotomy for adult head-injured patients with an ASDH.[22] The new study is currently in the set-up phase and the internal pilot phase is expected to start in 2014.

With these innovative studies as forerunners, we strongly believe that the CER approach has the potential to create more clarity in the uncertainties in the neurosurgical treatment of TBI.[20,21]

Thus, confronted with a patient with TBI, neurosurgeons have to deal with multiple clinical and radiological variables, in a limited time frame and with a shortage of data or predictive outcomes, leading to a broad variation in current practice. We strongly believe that CER approaches and pragmatic trials have potential to create more clarity in the uncertainties in the neurosurgical treatment of TBI.[20,21]

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