

## Surgical Management of Traumatic Brain Injury – Evidence, Controversies and Perspectives for the Future

Süleyman Sener,<sup>1</sup> Bob Roozenbeek<sup>1</sup> and Andrew IR Maas<sup>2</sup>

1. Resident in Neurosurgery; 2. Professor of Neurosurgery and Chairman, Department of Neurosurgery, Antwerp University Hospital

### Abstract

The surgical treatment of traumatic brain injury is challenging. Evidence-based recommendations provide guidance, but the underpinning evidence is relatively weak. This lack of strong evidence has been quoted to emphasise the need for more clinical trials. Clinical trials should, however, not be seen as the only approach. The existing variability in surgical management offers opportunities for comparative effectiveness research (CER) based upon large-scale observational studies. CER has the potential to provide high-quality evidence in a cost efficient way. Controversies are greatest concerning the surgical management of contusions and indications for decompressive craniectomy (DC). Lesion progression is frequent in contusions and mainly occurs within six–nine hours after injury. Surgical treatment can be motivated by both mass and toxic effects. On-going studies, such as the Surgical trial in traumatic intracerebral hemorrhage (STITCH), will hopefully provide further guidance on ‘best surgical approaches’. Currently, early computed tomography (CT) follow-up is recommended with surgical decisions based on CT evolution and risk assessment. The increasing enthusiasm for DC has been tempered by the results of the recent multicentre prospective randomised trial of early decompressive craniectomy in patients with severe traumatic brain injury (DECRA) study, showing more unfavourable outcome following DC. It is unlikely though that these results will change clinical practice, as the study population was highly selected and focused only on diffuse injuries. The results cannot be extrapolated to patients with focal or mass lesions. DC should not be considered a risk-free procedure. Complication rates of up to 50 % have been reported. Major complications include subdural effusions, hydrocephalus and syndrome of the trephined. Early cranioplasty is preferred following DC, as complications may resolve more rapidly and recovery is enhanced.

### Keywords

Traumatic brain injury, surgery, guidelines, contusions, decompressive craniectomy

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**Correspondence:** Andrew IR Maas, Department of Neurosurgery, Antwerp University Hospital, Wilrijkstraat 10, 2650 Edegem, Belgium. E: andrew.maas@uza.be

### Surgery for Traumatic Brain Injury

The surgical treatment of traumatic lesions in head injury can be challenging and complex, both in terms of indication and technique. Most procedures in neurotrauma are, however, performed by young surgeons and residents, often in their junior years. The availability of guidelines and expert coaching are essential to delivery of high-quality surgical care. The importance of surgery in head injury should not be underestimated; an immediate priority following injury is the early detection and rapid evacuation of intracranial mass lesions. Indications for emergency surgery in closed<sup>1</sup> and penetrating traumatic brain injury (TBI)<sup>2</sup> are summarised in evidence-based guidelines. More controversial issues concern surgery for contusions and indications and timing for decompressive craniectomy (DC). The adverse effects of DC reported in the recently published multicentre prospective randomised trial of Early decompressive craniectomy in patients with severe traumatic brain injury (DECRA) trial on DC in diffuse brain injury<sup>3</sup> have further highlighted a relatively high incidence of complications, emphasising that a DC should not be considered a procedure without risk. In this article we aim to discuss the

interpretation and use of guidelines for surgical treatment in closed and penetrating TBI and to address in detail the more controversial topics of surgery for contusions and DC. We will further highlight ‘best procedures’ for the future to increase the level of evidence underpinning guidelines and recommendations.

### Guidelines

Evidenced-based guidelines for the surgical management of non-penetrating TBI were based on a literature search of clinical studies published between 1975 and 2000.<sup>1</sup> In total, this search resulted in 700 manuscripts that were reviewed by the author group. None of the studies concerned a randomised controlled clinical trial or high-quality comparative clinical study. Consequently, the level of evidence underpinning the surgical guidelines is limited to the class III level (see *Table 1*). Likewise, the guidelines on penetrating brain injury – based on a literature search including studies published between 1966 and 2000 – are solely based on Class III evidence.<sup>2</sup> A summary overview of the guidelines for surgical management of closed and penetrating TBI is presented in *Table 2*. Much of the evidence underpinning the

surgical treatment for penetrating brain injury (PBI) has originated from experiences during military conflicts.

For example, Cushing<sup>4</sup> reported an approximately 50 % decrease in mortality during experiences on the battlefield in World War I after introduction of aseptic conditions and thorough debridement. The introduction of antibiotics later decreased mortality further by decreasing the infection rate. Throughout the Korean and Vietnam War however, radical debridement was recommended, primarily for prevention of infections.<sup>5</sup> Subsequent studies revealed that repeated craniotomy to remove retained fragments did not always succeed in achieving complete removal and, moreover, frequently resulted in significant morbidity and mortality.<sup>6–8</sup> Encouraging results were reported from less aggressive management policies.<sup>9–12</sup> Taha<sup>13</sup> reported good results in 32 patients treated by simple wound closure. Also in the civilian experience possible advantages of less aggressive approaches have been reported.<sup>14,15</sup> Consistent with these reports the guidelines for PBI do not recommend extended or repeated procedures for debridement, but rather recommend treatment of small entrance wounds by local wound care and closure and only superficial debridement with more extensive wounds in the absence of mass effect. Emergency surgery is recommended in the presence of mass effects and recommendations further include more extensive repairs of open air sinus injuries. Particular attention to the risk of a traumatic intracranial aneurysm is required in patients with an intracerebral haematoma following PBI. In these regards there are therefore clear differences between surgical approaches to closed and penetrating brain injuries.

### Alternative Sources of Evidence

The lack of high-quality evidence underpinning the guidelines reflects the many uncertainties about the benefit/risk of surgical approaches in TBI and has been used appropriately to emphasise the necessity of clinical trials to address these uncertainties. It may be argued, however, that in many cases such as for the surgery of patients with epidural haematomas and deteriorating level of consciousness clinical trials are not required and would even be unethical. As illustrated with appropriate humorous sarcasm by Smith and Pell,<sup>16</sup> when evaluating the evidence underpinning efficacy of parachutes in preventing mortality when jumping from an airplane, clinical trials are not the appropriate methodology to answer all questions; moreover we should realise that we will never be able to conduct sufficient adequately powered trials to answer all the outstanding questions in TBI. Furthermore, clinical trials address efficacy generally under tightly controlled conditions and may not reflect real-world practice; other approaches providing high-quality evidence should not be neglected and perhaps even preferred. A recent workshop organised by the National Institutes of Health (NIH) and the EU have pointed to a paradigm shift in the focus of clinical TBI research and concluded that improved clinical care in TBI will likely depend on a range of research approaches including systems biology and comparative effectiveness research.<sup>17</sup> Such approaches have great potential for TBI research but will require the collection of high-quality clinical databases.

### Management of Contusions

Focal cerebral contusions are the most common intracranial lesions occurring after injury.<sup>18</sup> They are more frequent in older patients and then usually arise from contact impact subsequent to a fall. The incidence of contusions varies by severity of TBI and has been reported in up to 35 % of patients with severe TBI<sup>19</sup> and in up to 55–80 % of

**Table 1: Classification of Evidence in Surgical Guidelines**

Class I	Evidence from one or more well-designed, randomised, controlled clinical trials, including overviews of such trials
Class II	Evidence from one or more well-designed comparative clinical studies, such as non-randomised cohort studies, case-control studies and other comparable studies
Class III	Evidence from case series, comparative studies with historical controls, case reports and expert opinion

patients with fatal head injury.<sup>20,21</sup> From a clinical perspective it is important to recognise that contusional brain injury is a dynamic process and that an increase in volume occurs frequently in up to 40 % of patients.<sup>22</sup> In addition, follow up computed tomography (CT) scanning may reveal new lesions in approximately 16 %. Lesion progression occurs mainly within the first six–nine hours after injury<sup>23</sup> and is more pronounced if the first CT was performed within two hours of initial head injury.<sup>24</sup> Various factors are associated with an increased risk of lesion progression, such as the use of anticoagulant therapy, platelet aggregation inhibitors, larger initial size of lesions and the presence of subarachnoid or subdural haemorrhage. From a pathophysiological perspective, contusional brain injury represents a different type of disease than diffuse injury. In particular, inflammatory responses are more pronounced and pericontusional ischaemia (penumbra) may be a prominent feature worsened by local intravascular thrombocyte aggregation. Both the pathophysiological characteristics and the frequent lesion progression illustrate that reasons for surgical treatment of contusional brain lesion should not only include mass effect but also the toxic effect. The importance of this toxic effect was demonstrated by Katayama et al.<sup>25</sup> in experimental studies. Rapid evacuation of experimental lesions prevented in these experiments the occurrence of brain oedema and subsequent development of raised intracranial pressure.

### Indications and Timing of Surgery for Contusions

Major controversies exist in the surgical treatment of contusions particularly with regard to indication and timing; this is reflected in widely different approaches to management between countries, as demonstrated in surveys conducted by the European Brain Injury Consortium.<sup>26,27</sup> In some countries contusions are only very seldom operated upon; in others much more frequently. The main discussion is whether pre-emptive surgery should be preferred with the intent of preventing deterioration (but at a certain risk) or of delaying intervention until deterioration has occurred (when it may be uncertain that the patient can still recover). Advocates of early surgery base this policy upon combined relevance of mass and toxic effects of contusions and upon the observation that most neurosurgeons will have experienced patients with initially milder injuries who deteriorate and die following lesion expansion. Chang et al.<sup>22</sup> state that delayed enlargement of intraparenchymal contusions and haematomas is the most common cause of clinical deterioration and death in patients who suffered from a traumatic brain injury. Yamaura et al.<sup>28</sup> are even more explicit, reporting that all treatments are futile once a patient has deteriorated and a terminal stage of conservative therapy has been reached.

Adversaries of surgical approaches to contusions, however, emphasise the risks involved with surgery, the fact that viable neurons may be sacrificed during the procedure and that no

**Table 2: Summary of the Guidelines for Surgical Management of Closed and Penetrating Traumatic Brain Injury**

Diagnosis	Indication for Surgery	Timing	Method
Acute epidural haematoma	EDH >30 cm <sup>3</sup> should be surgically evacuated regardless of GCS score EDH <30 cm <sup>3</sup> and <15 mm thickness and <5 mm midline shift in patients with GCS score >8 without focal neurological deficit: non-operative treatment serial CT scanning observation in neurosurgical centre	As soon as possible	There are insufficient data to support one surgical treatment method. However, craniotomy provides a more complete evacuation of the haematoma
Acute subdural haematoma	Acute SDH >10 mm thick or with >5 mm midline shift on CT scan should be surgically evacuated regardless of GCS score. All patients with acute SDH in coma (GCS score <9) should undergo ICP monitoring. A comatose patient (GCS score <9) with an SDH <10 mm thick and a midline shift <5 mm should undergo surgical evacuation of the lesion if the GCS score decreased between the time of injury and hospital admission by 2 or more points and/or the patient presents with asymmetric or fixed and dilated pupils and/or the ICP exceeds 20 mmHg	As soon as possible	If surgical evacuation of an acute SDH in a comatose patient (GCS <9) is indicated, it should be performed using a craniotomy with or without bone flap removal and duraplasty
Traumatic parenchymal lesion	Patients with parenchymal mass lesions and signs of progressive neurological deterioration referable to the lesion, medically refractory intracranial hypertension or signs of mass effect on CT scan should be treated operatively Patients with GCS scores of 6–8 with frontal or temporal contusions >20 cm <sup>3</sup> in volume with midline shift of ≥5 mm and/or cisternal compression on CT scan and patients with any lesion >50 cm <sup>3</sup> in volume should be treated operatively Patients with parenchymal mass lesions who do not show evidence of neurological compromise, have controlled ICP and no significant signs of mass effect on CT scan may be managed non-operatively with intensive monitoring and serial imaging	Craniotomy with evacuation of mass lesion is recommended for those patients with focal lesions and the surgical indications listed above, under Indications Bifrontal DC within 48 hours of injury is a treatment option for patients with diffuse, medically refractory post-traumatic cerebral oedema and resultant intracranial hypertension Decompressive procedures, including subtemporal decompression, temporal lobectomy and hemispheric DC, are treatment options for patients with refractory intracranial hypertension and diffuse parenchymal injury with clinical and radiographic evidence of impending transtentorial herniation	
Posterior fossa mass lesions	Patients with mass effect on CT scan or with neurological dysfunction or deterioration referable to the lesion should undergo operative intervention Mass effect on CT scan is defined as distortion, dislocation or obliteration of the fourth ventricle; compression or loss of visualisation of the basal cisterns; or the presence of obstructive hydrocephalus Patients with lesions and no significant mass effect on CT scan and without signs of neurological dysfunction may be managed by close observation and serial imaging	In patients with indications for surgical intervention, evacuation should be performed as soon as possible because these patients can deteriorate rapidly, thus worsening their prognosis	Suboccipital craniectomy is the predominant method reported for evacuation of posterior fossa mass lesions, and is therefore recommended
Depressed skull fractures	Patients with open (compound) cranial fractures depressed greater than the thickness of the cranium should undergo operative intervention to prevent infection Patients with open (compound) depressed cranial fractures may be treated non-operatively if there is no clinical or radiographic evidence of dural penetration, significant intracranial haematoma, depression greater than 1 cm, frontal sinus involvement, gross cosmetic deformity, wound infection, pneumocephalus or gross wound contamination Non-operative management of closed (simple) depressed cranial fractures is a treatment option	Early operation is recommended to reduce the incidence of infection	Elevation and debridement is recommended as the surgical method of choice Primary bone fragment replacement is a surgical option in the absence of wound infection at the time of surgery. All management strategies for open (compound) depressed fractures should include antibiotics
Penetrating brain injury	Treatment of small-entrance bullet wounds to the head with local wound care and closure in patients whose scalp is not devitalised and have no 'significant' intracranial pathologic findings is recommended Treatment of more extensive wounds with non-viable scalp, bone or dura with more extensive debridement before primary closure or grafting to secure a watertight wound is recommended. In patients with significant fragmentation of the skull, debridement of the cranial wound with either craniectomy or craniotomy is recommended In the presence of significant mass effect, debridement of necrotic brain tissue and safely accessible bone fragments is		

**Table 2 (Cont.):**

Diagnosis	Indication for Surgery	Timing	Method
	recommended. Evacuation of intracranial haematomas with significant mass effect is recommended		
	In the absence of significant mass effect, surgical debridement of the missile track in the brain is not recommended, on the basis of class III evidence that outcomes are not measurably worse in patients who do not have aggressive debridement.		
	Routine surgical removal of fragments lodged distant from the entry site and reoperation solely to remove retained bone or missile fragments are not recommended		
	Repair of an open-air sinus injury with watertight closure of the dura is recommended. Clinical circumstances dictate the timing of the repair. Any repairs requiring duraplasty can be at the discretion of the surgeon as to material used for closure		

CT = computed tomography; DC = decompressive craniectomy; EDH = epidural haematoma; GCS = Glasgow Coma Scale; ICP = intracranial pressure; SDH = subdural haematoma.

evidence exists that early surgery will lead to better outcome. Various retrospective studies have reported benefits of surgery as compared with conservative approaches,<sup>29-31</sup> but randomised studies are lacking. These uncertainties formed the incentive for initiating the Surgical trial in traumatic intracerebral hemorrhage (STITCH) trial, which concerns an international multicentre pragmatic randomised controlled trial (<http://research.ncl.ac.uk/trauma.stitch>). The trial is based upon equipoise in that the treating neurosurgeon is uncertain whether a conservative or operative approach is preferable. Eligible patients with a lesion volume >10 ml can be randomised within 48 hours of injury. Exclusion criteria include the co-existence of an acute subdural or epidural haematoma, posterior fossa lesions and severe co-morbidities. The study was initiated in October 2009 and aims to recruit over 800 patients. Recruitment is on-going.

Current approaches should aim to identify patients at risk early in the disease process<sup>32</sup> and surgical decisions should be made for each individual case based on CT evolution and risk assessment for clinical deterioration and increased intracranial pressure (ICP).

### Decompressive Craniectomy

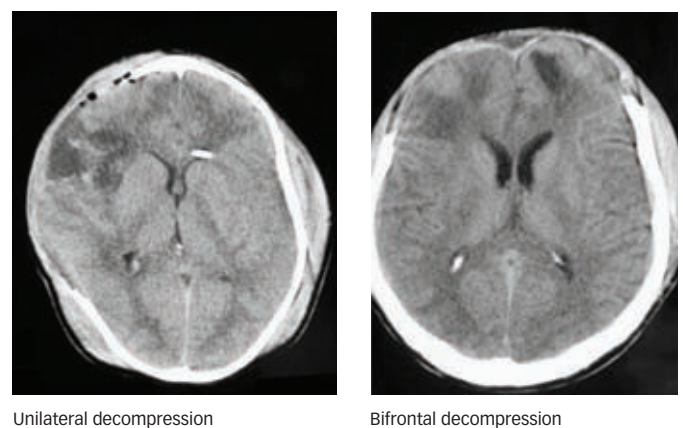
DC is an effective approach to decrease raised ICP. Over recent years it has been performed with increasing frequency and is no longer reserved as a third-tier treatment approach. Early generous DC has also been advocated in victims of cranial blast injuries in conflict zones.<sup>33,34</sup> Many different techniques are used to perform DC: uni- and bilateral hemicraniectomy, bifrontal craniectomy, circumferential craniectomy, bilateral temporal craniectomy and hinge craniectomy.<sup>35,36</sup> No evidence exists to support a preference for any specific technique and choice will depend on patient circumstances (unilateral or bilateral pathology) and doctor preference. Consensus exists that, if performed, a large craniectomy (diameter >12 cm) is required with opening and enlargement of the dura (see *Figure 1*). Substantial controversy, however, exists on indications, timing and benefit in terms of clinical outcome. Interpretation of reported studies is confounded by relatively small numbers, different techniques, variability in indications, additional evacuation of mass lesions and by reporting mixed results of early and late DC.

The growing enthusiasm for DC has recently been tempered by the unexpected findings of the DECRA study demonstrating an increased rate of unfavourable outcome in patients with diffuse brain injury treated by DC.<sup>3</sup> In this study, patients with refractory intracranial hypertension (defined as an ICP  $\geq$ 20 mm Hg for a cumulative period of 15 minutes during a one-hour period) were randomly assigned to receive standard care or to undergo a bifrontal craniectomy. Despite efficacy in reducing ICP and absence of an effect on mortality, the number of patients with unfavourable outcome was significantly higher in the surgically treated

**Table 3: Reported Frequency of Complications after Decompressive Craniectomy**

	Qiu et al., 2009 <sup>40</sup> n=74	Seung et al., 2010 <sup>39</sup> n=89	Akyuz et al., 2010 <sup>41</sup> n=76	Cooper et al., 2011 <sup>3</sup> n=73
External herniation	10.8 %	14.6 %	NR	NR
Delayed haematoma	7.4 %	5.6 %	5.2 %	4 %
Subdural effusion	5.4 %	32.6 %	14.5 %	NR
Hydrocephalus	NR	11.2 %	11.8 %	10 %
Intracranial infection	1.35 %	4.5 %	6.6 %	6 %

NR = not reported.

**Figure 1: Decompressive Craniectomy**

group. These findings were unexpected. The trial has been criticised for lacking generalisability as only 4.5 % of screened patients were enrolled and because of inadequate surgical technique, not including division of the falx and sagittal sinus as recommended by Polin et al.<sup>37</sup> More importantly, however, it should be recognised that the threshold for randomisation in this study was low, well below values of ICP at which most neurosurgeons would start to think about the possibility of a DC. Thus, patients may have been exposed to the risks of decompression without really having a clear prospect of benefit.

### Complications of Decompressive Craniectomy

The DECRA study has clearly demonstrated that DC is not a risk-free procedure and that in fact the rate of complication is fairly high. Even higher rates of complications (up to 50 %) have been reported in various studies originating from the Far East.<sup>38,39</sup> Reported rates of procedure-related complications following DCs are summarised in *Table 3*.<sup>3,39-41</sup>

Complications often arise in a sequential fashion at specific time periods following decompressive surgery.<sup>42</sup> They may occur early

**Table 4: Overview of Frequently Used Alloplastic Materials for Cranioplasty after Decompressive Craniectomy**

	Advantages	Limitations
Titanium	Rigid Very good cosmetic results with prefabricated implants	Artefacts on post-operative CT and MRI Difficult to adapt intra-operatively
Polymethyl-methacrylate (PMMA)	Easy free-hand modelling of the implant Low cost	Heats to high temperatures during application process Prone to fracture
Hydroxy-apatite cement (HA)	Similar to natural bone: promotes osteoblast	High cost Prone to fracture progression and mineral resorption Sufficient rigidity

CT = computed tomography; MRI = magnetic resonance imaging.

(external herniation with subsequent venous infarction, most commonly due to inadequate decompression; contusion expansion; post-operative haematoma), in the subacute phase (subdural effusions, infection) or late (hydrocephalus, syndrome of the trephined). Syndrome of the trephined is defined by onset of new neurological symptoms and a sunken parenchymal contour on CT with the absence of the bone flap. It can occur a few weeks to several months after a large DC.<sup>43,44</sup> It is poorly understood, but presumed to be caused by changes in cerebrospinal fluid (CSF) circulation and cerebral blood flow as a result of the effect of atmospheric pressure on the brain. Syndrome of the trephined, hydrocephalus and subdural effusions may resolve following cranioplasty.

### Cranioplasty – Timing and Technique

Historically, an interval of more than three months has been common for cranioplasty reconstruction. Currently, most neurosurgeons agree that early cranioplasty is recommended (weeks rather than months) when ICP control so permits.<sup>45</sup> Earlier cranioplasty is motivated not only to restore cranial integrity and protect against further trauma, but also to enhance rehabilitation. However, active systemic infection and multiple cranial procedures increase the risk of infection with early cranioplasty.

Cranioplasty may be performed by reimplantation of the autologous bone flap or by using alloplastic bone substitutes. The original bone flap is preferred for cranioplasty by most surgeons, because of its good fit, replacement of host cells and high cost-effectiveness. Alloplastic implants have, however, become more popular and are currently used almost as frequently as autologous bone. Preference for use of an alloplastic implant may be strictly medical (e.g. when the original bone flap cannot be used because of complex skull fractures or contamination of the flap due to open wounds), or logistic (complexity of cryopreservation according to regulations imposed by bone tissue banks). Different materials – both prefabricated and free-hand mouldable – are available, such as titanium, polymethyl-methacrylate (PMMA), hydroxy-apatite (HA) cement and polyetheretherketone (PEEK).<sup>46</sup> The main advantages and limitations of different frequently used alloplastic implants are summarised in *Table 4*. Osteoconductive bioresorbable materials, osteoinduction by growth factors and gene therapy have shown promising experimental results, but their added value in the clinical setting still has to be proven.<sup>47</sup>

Infection is the most frequent complication after cranioplasty, both for alloplastic implants as for original bone flaps. A recent meta-analysis by Yadla et al.<sup>48</sup> did not find any association between the bone graft storage method (abdominal space or cryopreservation in tissue bank) and the post-cranioplasty infection rate. Nor was any difference found in the rate of infection between early versus late cranioplasty. Other important complications include resorption of the bone flap, which can lead to scalp depression and may require secondary corrective surgery.

### Reflection and Future Perspective

A clear need is identified for stronger evidence in support of surgical treatment in TBI. Existing controversies are most pertinent with regard to the surgical management of contusions and indications and timing for performing a DC as treatment for raised ICP.

Wide variability exists in indications for the surgical treatment of contusional brain injury. Some neurosurgeons advocate early 'pre-emptive' surgery aiming to prevent deterioration; others only consider contusion evacuation following deterioration; while yet others prefer a more conservative approach, limiting surgical procedures to an external bony decompression without evacuation of the contusion. The on-going STITCH trial will hopefully shed some light on the dilemma concerning surgical indications for contusions. Interpretation of results may, however, be difficult as the trial is based on the principle of 'equipoise', according to which patients are only randomised when the treating surgeon is uncertain about the indication for surgery. Without knowledge of the disease course in patients not randomised, generalisability may be limited.

Expectations that the recently completed DECRA and on-going Randomised Evaluation of Surgery with Craniectomy for Uncontrollable Elevation of Intra-cranial Pressure (RESCUEicp – www.rescueicp.com) studies might resolve some of the controversies on DC were high. The results of the DECRA study have been met by general disappointment. It should be noted, however, that adverse effects of DC reported in this study only relate to a highly selected population of patients with diffuse injuries and cannot be extrapolated to other traumatic lesions, such as contusions with mass effect or acute subdural haematoma. The study population included in the on-going RESCUEicp study is broader, targeting all patients with refractory intracranial hypertension. RESCUEicp further differs from DECRA in terms of ICP threshold (25 mmHg versus 20 mmHg), in timing of surgery (any time after injury versus within 72 hours post injury) and longer follow-up (two years). Some concerns exist, however, that variability in surgical techniques, timing of surgery and approaches to the management of intradural lesions within recruiting centres, as well as cross-over between groups, may confound interpretation of study results.

These considerations illustrate the complexity of clinical trials in TBI and raise the question of whether classical clinical trials based on a hypothesis-driven reductionistic approach should always be the preferred approach to resolve controversies and to provide evidence in support of treatment recommendations. Moreover, we will never be able to conduct sufficient adequately powered trials to answer all the outstanding questions in TBI. Alternative approaches should be considered. The existing variability in medical and surgical

treatment approaches provides a major opportunity for comparative effectiveness research in TBI, in which alternative interventions/management strategies/care organisation that can all be considered possible best practices, are compared and related to outcome. This approach is facilitated by the availability of robust risk adjustment models specific for TBI<sup>49,50</sup> and by currently available advanced

statistical techniques, including random effect models, facilitating analysis of differences at different levels (country/centre/individual).

We argue that improved care for TBI patients will likely depend on a range of research approaches, including comparative effectiveness research. ■

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