# Traumatic brain injury: an evidence-based review of management

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**Key points**

Traumatic brain injury is common and a major cause of morbidity and mortality worldwide.

Management is based on avoidance of secondary injury, maintenance of cerebral perfusion pressure, and optimization of cerebral oxygenation.

Evidence-based guidelines and management protocols help to guide target-driven care and are associated with better outcome.

Multimodality monitoring of the injured brain enables individualized therapeutic targets to be set to optimize patient management.

Patients with moderate or severe brain injury should be managed in a specialist neurosurgical centre.

## Epidemiology

Traumatic brain injury (TBI) is the leading cause of death and disability in young adults in the developed world. In the UK about 1.4 million patients per year suffer head injuries. Although the majority of injuries are mild, around 10.9% are classified as moderate or severe and many patients are left with significant disability.[1] The incidence is increasing in lower income countries, with the World Health Organization predicting that TBI and road traffic accidents will be the third greatest cause of disease and injury worldwide by 2020. In our ageing population the number of elderly patients presenting with TBI has increased and age appears to be an independent risk factor for poor outcome. Consequently TBI presents a major health and socioeconomic problem.[2]

TBI is a heterogeneous condition in terms of aetiology, severity, and outcome. The most useful classification of severity is based on the level of consciousness as assessed by the Glasgow Coma Scale (GCS) after resuscitation. The GCS comprises the sum score of the values from three components: eye, motor, and verbal scales (Table 1). TBI is classified as mild (GCS 15–13), moderate (GCS 13–9), and severe (GCS $< 8$). However, factors such as hypoxia, hypotension, and alcohol intoxication can all affect GCS, leading to diagnostic confusion. Therefore the patient should be resuscitated and reversible causes corrected before GCS assessment. The ability to assess eye opening and verbal response is influenced by sedative agents or tracheal intubation, leading some to suggest the use of the motor score alone.

TBI can be divided into primary and secondary brain injury. The primary injury occurs as a consequence of the initial physical insult. The pattern and extent of damage will depend on the nature, intensity, and duration of the impact. Compression and shearing forces may result in skull fracture, contusions, intracranial haematoma, cerebral oedema, and diffuse brain injury. Microscopically there is cell wall disruption and increased membrane permeability disrupting ionic homeostasis. Axonal tissue is particularly susceptible to injury.

Neurological injury progresses over hours and days, resulting in a secondary injury. Inflammatory and neurotoxic processes result in vasogenic fluid accumulation within the brain, contributing to raised intracranial pressure (ICP), hypoperfusion, and cerebral ischaemia. Much of this secondary injury may be amenable to intervention, as almost one-third of patients who die after a TBI will talk or obey commands before their death. Secondary injury also occurs as a result of further physiological insults. Hypoxia, hypotension, hyper- or hypocapnia, hyper- or hypoglycaemia have all been shown to increase the risk of secondary brain injury.

## Acute management

This is a crucial period when mortality and morbidity can be influenced by interventions to prevent secondary brain injury.[3] Targeted resuscitation and early specialist management have resulted in a decline in mortality over the last few decades.

### Pre-hospital care

This includes simultaneous assessment, stabilization, and therapeutic interventions. The priorities are to prevent hypoxia and hypotension, both common findings after trauma. Even a single episode of hypotension is associated with increased morbidity and a doubling of mortality.[4] The number and duration of episodes of hypotension are correlated with mortality.[5] Studies have also found an association between hypoxia and worse outcome.[4] In the USA this has led to pre-hospital guidelines, which include early tracheal intubation for patients unable to maintain their own airway or achieve a target $S_{p_{O_2}} > 90\%$ on supplemental oxygen.[6] However, suboptimal intubation and

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**Table 1** Glasgow Coma Scale

| Glasgow Coma Scale | Score |
|---|---|
| Eye opening | |
| Spontaneous | 4 |
| To speech | 3 |
| To pain | 2 |
| None | 1 |
| Best verbal response | |
| Orientated | 5 |
| Confused | 4 |
| Inappropriate | 3 |
| Incomprehensible | 2 |
| None | 1 |
| Best motor response | |
| Obeying | 6 |
| Localizing | 5 |
| Withdrawing | 4 |
| Flexing | 3 |
| Extending | 2 |
| None | 1 |

**Table 2** Summary of management goals in TBI

| Systems | Management goals |
|---|---|
| Airway | Early tracheal intubation if GCS $\leq$ 8 or unable to maintain respiratory goals |
| Respiratory | Avoid hypoxia, maintain $Sa_{O_2}$ >97%, $Pa_{O_2}$ > 11 kPa |
| | Maintain a $Pa_{CO_2}$ value of 4.5–5.0 kPa |
| | Hyperventilation, a $Pa_{CO_2}$ value of 4.0–4.5 kPa reserved for impending herniation |
| CVS | Avoid hypotension, maintain MAP > 80 mm Hg |
| | Replace intravascular volume, avoid hypotonic and glucose-containing solutions |
| | Use blood as necessary, reverse existing coagulopathy |
| | Vasopressor agents as necessary to maintain CPP |
| Brain | Monitor ICP, avoid ICP > 20 mm Hg |
| | Maintain CPP > 60 mm Hg |
| | Adequate sedation and analgesia |
| | Hyperosmolar therapy, keep $Na^+ < 155$ mmol $l^{-1}$, $P_{osm} < 320$ mosm $l^{-1}$ |
| | CSF drainage |
| | Treat seizures |
| | Barbiturate coma, decompressive craniectomy, hypothermia, all reserved for elevated ICP refractory to standard medical care |
| Metabolic | Monitor blood glucose, aim for blood glucose 6–10 mmol $l^{-1}$ |
| | Avoid hyperthermia |
| | DVT thromboprophylaxis |

CVS, cardiovascular; ICP, intracranial pressure; CPP, cerebral perfusion pressure; $P_{osm}$, plasma osmolarity; CSF, cerebrospinal fluid; DVT, deep vein thrombosis.

ventilation is associated with worse outcome. Patients with a moderate or severe TBI should be transferred to a designated trauma centre.[2]

## Management in the emergency department

There is a limited evidence base for much of the management of TBI. A summary of management based on existing consensus guidance and available evidence is shown in Table 2. In-hospital resuscitation begins with Advanced Trauma Life Support (ATLS®) priorities using an ABCDE approach. Assessment of neurological status is based on GCS, pupillary responses, and localizing signs. The mechanism and timing of injuries can provide valuable information and point towards associated injuries. Major extra-cranial injuries are present in 50% of those with severe TBI. Cervical spine injury is also common with the risk increasing with increasing severity of TBI. Cervical immobilization is required until clearance obtained.

Tracheal intubation remains the gold standard for airway management in patients with a GCS of $\leq$8. However, the risks, benefits, and timing must be carefully assessed. Pre-existing hypoxia, intracranial hypertension, a potential full stomach, and coexistent injuries including cervical spine instability and maxillofacial injuries may be present. Careful preparation and pre-oxygenation are mandatory. Airway devices and adjuncts such as laryngeal mask airway, Airtraq®, or Glidescope® may be useful, and alternative means of oxygenation and ventilation must be available. Anaesthetic agents should allow rapid control of the airway while attenuating increases in ICP and providing haemodynamic stability. Propofol and thiopental are commonly used but may cause hypotension. Etomidate has advantages in terms of cardiovascular stability but the possibility of adrenal suppression exists. Ketamine is popular in trauma patients and recent evidence suggests that its effect on ICP may be limited.[7] For rapid sequence intubation, succinylcholine or rocuronium may be used. Although succinylcholine may produce a small increase in ICP, this is not clinically significant. To obtund the response to laryngoscopy an opiate such as fentanyl is a useful adjunct but there is no evidence to support the use of lidocaine. Adequate sedation and muscle relaxation will reduce cerebral metabolic oxygen requirement ($CMRO_2$), optimize ventilation, and prevent coughing or straining.

Despite widespread agreement on the principles of early management there is less clarity on resuscitation endpoints, with expert panels offering differing guidelines for management. While the Brain Trauma Foundation (BTF) suggests targeting $Pa_{O_2}$ > 8 kPa to avoid hypoxia, the European Brain Injury Consortium (EBIC) targets $Pa_{O_2}$ > 10 kPa and the Association of Anaesthetists of Great Britain and Ireland (AAGBI) >13 kPa.[8–10] Hyper- and hypocapnia are both viewed as potentially avoidable secondary insults. UK guidelines suggest a $Pa_{CO_2}$ value of 4.5–5.0 kPa.[10]

Arterial blood pressure (ABP) targets also vary between guidelines. The BTF and EBIC advocate a mean blood pressure (MBP) of >90 mm Hg, while AAGBI targets >80 mm Hg.[8–10] As the most common cause of hypotension after trauma is haemorrhage, the initial treatment is fluid resuscitation. For most patients an isotonic fluid such as normal saline is suitable. There is some evidence that hypertonic saline may be useful as a resuscitation fluid, with one study showing increased survival in a subgroup of patients with TBI and GCS < 8.[11] However, definitive clinical trials are awaited. Hypotonic fluids must be avoided. Colloids confer no benefit, indeed the Saline or Albumin for Fluid Resuscitation in Patients with Traumatic Brain Injury (SAFE) study found an increased risk of death in patients who received albumin rather than saline.[12] After TBI there is a profound

**Table 3** Criteria for immediate request for CT scan of the head in adults

| |
|---|
| GCS < 13 on initial assessment in the emergency department |
| GCS < 15 at 2 h after injury on assessment in the emergency department |
| Suspected open or depressed skull fracture |
| Any sign of basal skull fracture (haemotympanum, 'panda' eyes, cerebrospinal fluid leakage from the ear or nose, Battle's sign) |
| Post-traumatic seizure |
| Focal neurological deficit |
| More than one episode of vomiting |
| Amnesia for events >30 min before impact |
| In addition, adult patients who have experienced some loss of consciousness or amnesia since the injury and: |
| Age > 65 yr |
| Coagulopathy (history of bleeding, clotting disorder, current treatment with warfarin) |
| Dangerous mechanism of injury (a pedestrian or cyclist struck by a motor vehicle, an occupant ejected from a motor vehicle or a fall from a height of >1 m or five stairs) |

catecholamine response, with cortisol release and glucose intolerance making hyperglycaemia common. Glucose-containing fluids should be avoided and blood sugar monitored. Sources of bleeding must be identified and controlled and blood products used early in the face of significant haemorrhage.

Increasing numbers of patients with TBI are elderly and frail. Many are taking anticoagulants or antiplatelet drugs, often for cardiac arrhythmias, cardiac stents, or prosthetic heart valves. Age and warfarin are independent predictors of mortality after TBI as reflected by specific advice for CT scanning after TBI (Table 3). The British Committee for Standards in Haematology recommends that patients on warfarin with a strong suspicion for an intracranial bleed after TBI should have this reversed immediately with prothrombin complex (PCC) before waiting for an INR result or CT scan.[13] As dosage regimes for PCC vary, local haematologists should be contacted for advice. Typically, doses range between 15 and 50 U $kg^{-1}$ dependent on INR. I.V. vitamin K is recommended in addition. The reversal of platelet dysfunction in patients with TBI on antiplatelet drugs has not been fully investigated and no guidelines currently exist. However, platelet infusions or desmopressin may be useful in those patients on aspirin and clopidogrel who require urgent neurosurgical intervention.

## Imaging

The investigation of choice is CT scanning. Early imaging reduces time to detection of life-threatening complications and is associated with better outcomes. The incidence of radiological abnormalities increases with the severity of injury, and various criteria, such as those recommended by the National Institute of Clinical Excellence (Table 3), have been developed to determine who requires CT scan.[14] CT imaging of the cervical spine should be performed at the same time. MRI studies are rarely used in the acutely ill, as they are logistically more complex and take longer. MRI is useful if a penetrating injury with a wooden object is suspected. Advanced MRI (diffusion tensor imaging) allows visualization of white matter tracts and quantification of axonal damage. Skull X-rays are useful only as part of a skeletal survey in children with non-accidental injury. Additional imaging may be necessary to identify occult life-threatening injuries. As brain injury evolves over time, repeat imaging is commonly indicated and always necessary if there is clinical deterioration or an increase in ICP.

## Transfer

National guidelines on the transfer of patients with TBI are available.[10] Initial resuscitation and stabilization of the patient should be completed before transfer. Although neurosurgical transfers are time-critical, the risks of delayed transfer must be balanced against that of an unstable patient or ill-prepared transfer team.

An experienced and appropriately trained doctor with dedicated and skilled assistance should accompany patients with TBI. There must be means of communication with the neurosurgical centre and base hospital, a suitable transfer vehicle, full monitoring, including invasive arterial pressure, capnography and urinary catheter, resuscitation equipment, necessary drugs, and back up supplies in case of ventilator or pump failure.

Management priorities remain maintenance of oxygenation and ABP and minimizing increases in ICP. Patients who are persistently hypotensive despite resuscitation should not be transferred until the cause established and the patient stabilized. Patients with a GCS of ≤8 should be intubated and ventilated, aiming for $Pa_{O_2}$ > 13 kPa and a $Pa_{CO_2}$ value of 4.5–5.0 kPa with adequate sedation, analgesia, and muscle relaxation. AAGBI indications for intubation and ventilation and a transfer checklist are shown in Tables 4 and 5.

Good communication between the referring clinician, transfer team, and the neurosurgical centre is paramount.

## Anaesthesia for trauma craniotomy

About one-third of patients with severe TBI need neurosurgical intervention. Rapid treatment is crucial. Acute subdural haematomas in patients with a severe TBI have 90% mortality if surgical evacuation occurs >4 h after injury compared with 30% for those evacuated earlier.

Perioperative management should be a seamless continuation of the resuscitation process already begun and an opportunity to correct pre-existing secondary insults. Surgery and anaesthesia predispose the patient to additional risks such as hypotension because

**Table 4** Indications for intubation and ventilation for transfer after brain injury

| |
|---|
| GCS ≤ 8 |
| Significantly deteriorating conscious level (i.e. decrease in motor score >2 points) |
| Loss of protective laryngeal reflexes |
| Hypoxaemia ($Pa_{O_2}$ < 13 kPa on oxygen) |
| Hypercarbia ($Pa_{CO_2}$ > 6 kPa) |
| Spontaneous hyperventilation causing $Pa_{CO_2}$ < 4.0 kPa |
| Bilateral fractured mandible |
| Copious bleeding into the mouth (e.g. from skull base fracture) |
| Seizures |

**Table 5** AAGBI check list for transfer of adult neurosurgical patients

| |
|---|
| Respiration |
| $Pa_{O_2} > 13$ kPa and $Pa_{CO_2} < 5$ kPa? |
| Airway clear? Airway protected adequately? |
| Intubation and ventilation required? |
| Circulation |
| MBP > 80 mm Hg, pulse < 100 $min^{-1}$? |
| Peripheral perfusion? Two reliable large i.v. cannulae *in situ*? |
| Estimated blood loss already replaced? |
| Arterial line? Central venous access if appropriate? |
| Head injury GCS? |
| GCS trend (improving/deteriorating)? |
| Focal signs? Skull fracture? Seizures controlled? |
| Raised ICP appropriately managed? |
| Other injuries |
| Cervical spine injury (cervical spine protection), chest injury, fractured ribs, pneumothorax excluded? Intrathoracic, intra-abdominal bleed? Pelvic, long bone fracture? Extracranial injuries splinted? |
| Escort doctor |
| Escort adequately experienced? Instructed about this case? |
| Transfer documentation prepared? Money in case of emergencies? |
| Adequate equipment and drugs? Can use equipment and drugs? |
| Sufficient oxygen supplies? Case notes and X-rays? |
| Where to go in the neurosurgical unit? The name and the bleep number of the receiving doctor? |
| Telephone numbers programmed into mobile phone? Mobile phone battery fully charged? |

of blood loss or the effect of anaesthetic agents. Essential monitoring includes ECG, $S\,p_{O_2}$, capnography, temperature, and urine output. Invasive arterial pressure allows beat-to-beat monitoring of ABP and regular assessment of arterial blood gases and glucose. Central venous access may be useful for resuscitation and administration of vasoactive drugs. ICP monitoring is recommended for patients with TBI who require non-neurosurgical intervention.

The goals of anaesthesia are

- optimization of cerebral perfusion pressure (CPP) and the prevention of intracranial hypertension;
- adequate anaesthesia and analgesia;
- prevention of secondary insults by adequate oxygenation, normocapnia, and avoidance of hyper- or hypoglycaemia and hyperthermia.

Anaesthesia and analgesia are essential, as surgical stimuli can increase cerebral blood flow (CBF), $CMRO_2$, and ICP. Despite important differences between the effects of i.v. and volatile anaesthetic agents on cerebral physiology there is little evidence to support the use of one over the other. All volatile agents reduce $CMRO_2$ and may produce cerebral vasodilation, resulting in increased CBF and ICP. They also impair $CO_2$ reactivity. However, at concentrations up to 1 MAC these effects are minimal. Sevoflurane appears to have the best profile. Nitrous oxide is best avoided. I.V. agents reduce $CMRO_2$, CBF, and ICP. However, propofol can cause significant hypotension and reduce CPP. Neuromuscular drugs are recommended to prevent coughing or straining.

Patient positioning is usually dictated by surgical access. However, flexion or rotation of the head and the Trendelenberg position may increase ICP in patients with impaired intracranial compliance. Overly tight tracheal tube ties or cervical collars can also obstruct venous drainage. Ventilation should be controlled to maintain oxygenation and normocapnia as confirmed by ABG analysis. Intraoperative hypotension is associated with a three-fold increase in mortality. As discussed previously, i.v. fluids are the primary means to control ABP but debate continues as to the type and volume of choice. There may be a temporary, sometimes severe, decrease in BP after surgical decompression, and administration of vasopressor agents may be necessary to maintain BP and CPP during periods of instability.

Several studies have shown an association between hyperglycaemia and poor neurological outcome in patients with TBI. The optimal target glycaemic range is yet to be defined but, currently, the literature supports targeting intermediate glucose levels in the range of 6–10.0 mmol $l^{-1}$.[15] Patients should have frequent glucose monitoring and hypoglycaemia must be prevented.

## Management of ICP

Intracranial hypertension reduces cerebral perfusion and results in cerebral ischaemia. Consensus guidelines recommend treatment of an ICP >20–25 mm Hg.[8] Measurement of ICP allows early detection of evolving mass lesions and enables the calculation of CPP from the relationship CPP = MAP − ICP. The primary goal of an adequate CPP is to maintain CBF and tissue oxygenation and its manipulation has become central to the management of TBI. BTF guidelines initially adopted a CPP of >70 mm Hg but this was subsequently reduced when studies confirmed a greater risk of pulmonary complications with aggressive fluid and vasopressor therapy. Current consensus is a target of >60 mm Hg.

ICP can be controlled by a variety of methods.

### Hyperventilation

A reduction in $Pa_{CO_2}$ causes cerebral vasoconstriction, reducing CBV and ICP. Although once widely used, hyperventilation has been shown to exacerbate cerebral hypoperfusion and may result in ischaemia.[16] Moderate hyperventilation to a $Pa_{CO_2}$ value of 4.0–4.5 kPa is reserved for those with intractable intracranial hypertension and should be guided by monitoring such as jugular venous oxygen saturation to ensure adequate cerebral oxygenation.

### Hyperosmolar therapy

This is particularly useful for acute increases in ICP. Mannitol remains the most commonly used agent. The effective dose is 0.25–1 g $kg^{-1}$, usually given as a 20% solution. Intermittent boluses appear to be more effective than continuous infusions. However, care must be taken to prevent serum osmolarity increasing above 320 mOsm $l^{-1}$, as this has been associated with neurological and renal complications. Other potential complications include hypotension, intravascular volume depletion, hyperkalaemia, and rebound intracranial hypertension.[17] The use of

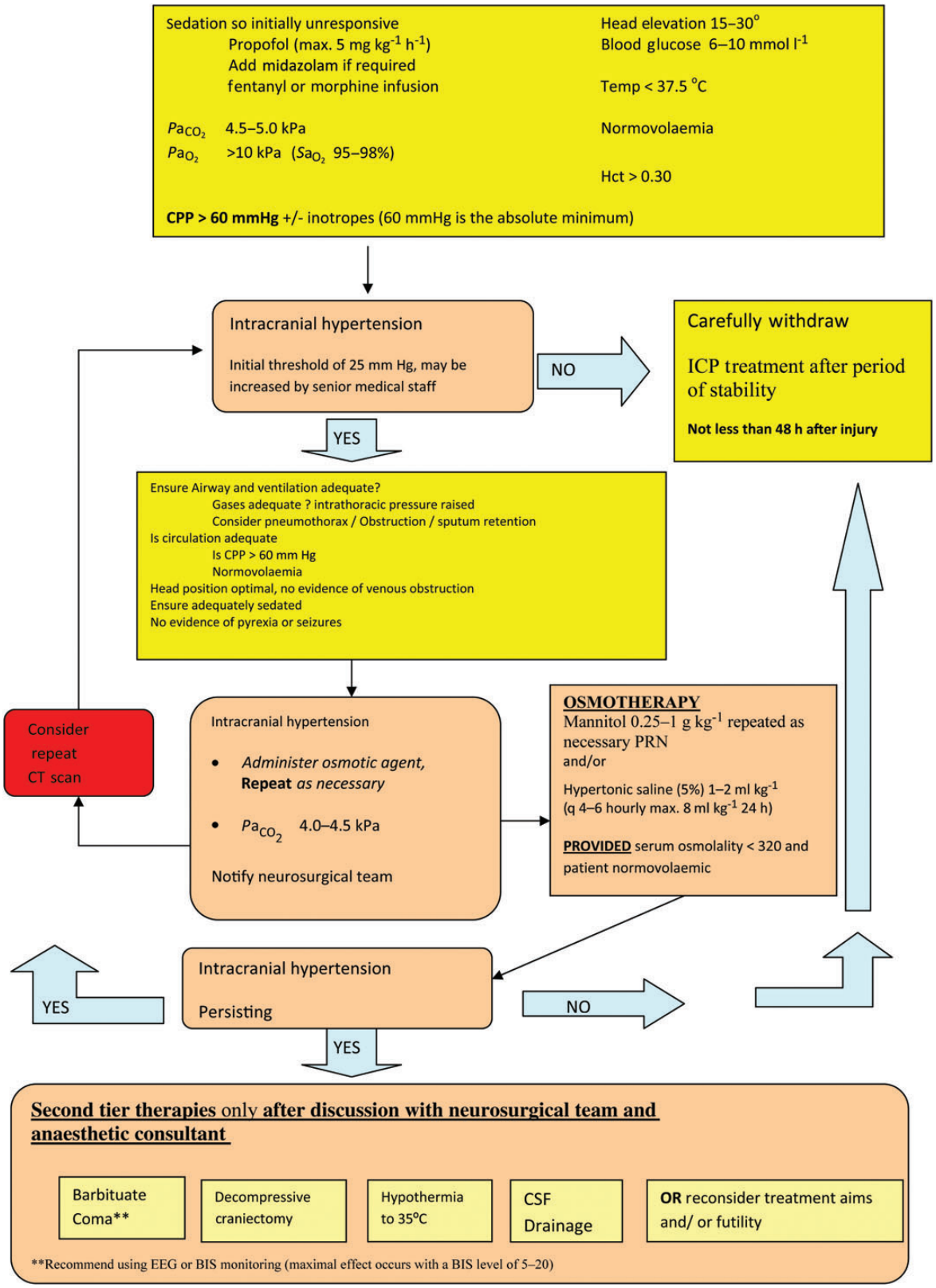


**Fig 1** St George's neurocritical care unit management algorithm for patients with severe traumatic brain injury. ICP, intracranial pressure; CPP, cerebral perfusion pressure.

hypertonic saline is increasing. It has fewer side-effects and may control ICP refractory to mannitol. Hypertonic saline acts predominantly through the osmotic shift of fluid from the intracellular to the intravascular and interstitial space. It may also improve CBF and myocardial performance and may have immune-modulatory effects. Various concentrations are available from 1.7 to 29.2% and numerous regimens described, although a dose of 2 ml $kg^{-1}$ of a 5% solution is typical. This can be repeated, providing the plasma osmolarity remains $<320$ mOsm $l^{-1}$ and serum sodium concentration $<155$ mmol $l^{-1}$.

### Hypothermia

Hypothermia has been shown to be neuroprotective in animal studies and has many theoretical benefits. However, evidence from studies has failed to demonstrate that it is associated with a consistent and statistically significant reduction in mortality.[18] Moderate hypothermia effectively reduces ICP and is often included in management algorithms.[17] The Eurotherm3235 Trial is currently investigating the effects of hypothermia, 32–35°C, titrated to reduce ICP $<$ 20 mm Hg (www.eurotherm3235trial.eu).

### Barbiturates

I.V. barbiturates lower ICP but there is little evidence that they improve outcome. They are associated with significant cardiovascular instability and so are reserved for refractory intracranial hypertension. Dosage is titrated to produce burst suppression with EEG.

### Neurosurgical interventions

Drainage of cerebrospinal fluid via an external ventricular drain is an effective method of reducing ICP. For intracranial hypertension refractory to medical therapy, decompressive craniectomy can be used. A section of skull vault is removed, allowing the brain to expand and ICP decrease. However, there is little consensus on its use. Results from the DECRA study did not resolve this uncertainty. Contrary to expectations, outcome was significantly poorer for patients randomly assigned to receive decompressive craniectomy compared with those who received standard care. Consequently, decompressive craniectomy is currently reserved for when other methods of ICP control have failed. It is hoped that the RESCUEicp trial, now ongoing, will provide further evidence (www.rescueicp.com).

## Continuing management

Advances in our understanding of the pathophysiology, monitoring, and imaging of brain injury have allowed the development of evidence-based intensive care management strategies and there is good evidence that this improves outcome.[17] Consequently many units now use protocol-driven algorithms (Fig. 1).

The purpose of continuing care is to provide optimum opportunity for brain recovery. Maintenance of oxygenation, normocapnia, and haemodynamic stability is essential. Adequate sedation and analgesia reduces pain, anxiety, and agitation and facilitates mechanical ventilation. Multimodality monitoring of the injured brain is useful to tailor individual patient care. Advanced monitoring may include cerebral oxygenation, measurement of CBF, microdialysis, and electrophysiological monitoring.[19]

Early nutritional support is associated with better outcomes and enteral administration is preferable. Appropriate metabolic monitoring is essential, as hyperglycaemia is associated with secondary ischaemic injury. Blood glucose should be monitored, but optimal targets for glycaemic control are yet to be defined. However, as with perioperative management, intermediate glucose levels in the range of 6–10.0 mmol $l^{-1}$ are usually targeted. Hypoglycaemia must be avoided.

Seizure activity is relatively common, occurring both early and late after TBI. Seizures increase $CMRO_2$ and are associated with increased ICP. Although there is little evidence for prophylactic anticonvulsants,[8] some advocate their use in high-risk groups such as those with depressed skull fractures.

Patients with TBI are at significant risk of thrombo-embolic events. Options for prevention include mechanical (graduated compression stockings or intermittent pneumatic compression), pharmacological (low-dose or low-molecular-weight heparin) prophylaxis, or a combination of both. Most would avoid pharmacological thromboprophylaxis for 24 h after neurosurgical intervention. Additional care includes peptic ulcer prophylaxis, physiotherapy, and full hygiene care.

## Summary

TBI is common and a major public health problem. Despite a progressive and significant reduction in mortality no single treatment has been shown to improve outcome. Management continues to be focused on prevention of secondary injuries and maintenance of CPP. National guidelines and management algorithms seem to be associated with better survival but ignore individual patient variability and injury-specific factors.

## Declaration of interest

None declared.

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**Please see multiple choice questions 1–4.**