**Severe traumatic brain injury in adults - A review of critical care management**

**Abstract**

This second of a two-part review on traumatic brain injury (TBI) describes current management for adult patients with a severe TBI (post-resuscitation Glasgow Coma Scale (GCS) score ≤ 8) who require critical care based on current evidence and recommendations. Evidence based standardised practice aims to limit secondary injury in patients with TBI. Critical care management is based on maintaining optimal physiology so as to minimise secondary injury in the early acute phase. The aim is to save lives and improve the quality of outcome for survivors.

**Keywords**

Severe traumatic brain injury, head injury, critical care, management

**Introduction and background**

Globally, 10 million people are affected by Traumatic Brain Injury (TBI) and is an increasing cause of death and disability, especially in low-middle income countries (Medical research council, 2022). In the UK, head injury is responsible for over 1 million accident and emergency attendances each year. Between 33% and 50% of these people are aged under 15. Approximately, 200,000 are admitted to hospital with the majority being classified as mild and are discharged directly from accident and emergency (NICE, 2023). The rate of ‘severe’ TBI is 10-20%. TBI is the most common cause of death and disability in the under 40s age group in high income countries and costs are in the region of £15 billion per year in the UK (Medical research council, 2022).

TBI is an alteration in brain function, or other evidence of brain pathology caused by an external force of sufficient magnitude (NICE, 2023). Severe TBI (post-resuscitation Glasgow Coma Scale (GCS) score ≤ 8) has high rates of mortality and disability (Raith et al, 2020).

Prehospital health care professionals treating patients with TBI have to make critical decisions regarding where and how to transport them (Lulla et al, 2023). All regions should have an organised trauma care system with protocols in place to direct destination decisions for patients with suspected TBI (Lulla et al, 2023). People who have sustained a TBI require transport directly to a major trauma centre (MTC) or trauma unit that has the age-appropriate resources to further resuscitate them, and to investigate and initially manage multiple injuries (NICE, 2023; Lulla et al, 2023). MTCs enable early rapid resuscitation and targeted interventions that maximise survival. Since their introduction, patient flow and mortality have improved, particularly for those most severely injured (Moran et al, 2018; Li et al, 2021). While direct transport to a trauma center is preferable, in the event that this is not possible, stabilization at a non-trauma center with subsequent transfer within an established trauma system to a neuroscience unit, irrespective of the need for neurosurgery is recommended (Lulla et al, 2023). If transfer is not possible, for those that do not need neurosurgery, ongoing liaison with the neuroscience unit regarding ongoing management is essential (NICE,2023).

The aim of this review is to provide clinicians working in critical care with an overview of current management and care based on research, guidelines, and recommendations. Little can be done about the extent of primary injury to the brain when patients present to critical care following TBI, but the detrimental contribution to outcome from secondary injury processes can be substantial (Mc Lernon 2023). Critical care management is aimed to attenuate the effects of ongoing secondary injury processes and prevent secondary insults to optimise neurological outcomes.

**Critical care management**

Over recent decades advances in management and the development of guidelines which have evolved from international consensus, have improved outcome and reduced mortality (Lawrence et al, 2016; Carney et al, 2017; NICE, 2023). Guidelines from the Brain Trauma Foundation (BTF) are constantly in review to incorporate new trial data and are aimed at providing high quality care and improvements in outcomes for patients hospitalised with severe TBI (Carney et al, 2017). Adherence and compliance to evidence-based guidelines in both adults and children results in improved mortality, functional outcomes and reduced length of hospital stay (Dheansa et al, 2023). **Table 1** summarizes key elements of targets and thresholds for the management of severe TBI in critical care based on current recommendations and guidelines (Carney et al, 2017; Nathanson et al, 2020; NICE, 2023).

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| Ventilation | PaO2 ≥11kPa (avoid hyperoxia)  Normocapnia PaCO2 4.6-6.00 kPa  PaCO2 4.5-5.0 kPa **when ICP<22-25mmHG.**  PEEP (≤15 cmH2O) to maintain oxygenation  Lung-protective ventilation strategies |
| Cardiovascular | Systolic blood pressure (SBP): ≥100mmHg for patients 50-69 years old or ≥110 mmHg for patients aged 15 to 49 years or ≥70 years  MAP≥80mmHg  Normovolaemia  Vasopressors/inotropes if required |
| ICP targets and management | ICP<22-25mmHG  *Tiered treatment of raised ICP (intracranial hypertension)*  ***First line measures:***  Positioning: Elevate head of bed up to 30-45o,avoid neck/hip flexion. Removal of possible obstructions to central venous return e.g., hard collar  Maintain PaCO2 4.5-5.0 kPa  Maintain adequate sedation (Propofol (2-4 mg/kg/hr) and analgesia  Seizure control  Normovolaemia |
| ***Second line measures:***  Increase analgesia and sedation, normothermia, neuromuscular blockade  Hyperosmolar agents (mannitol or hypertonic saline if impending uncal herniation  Cerebrospinal fluid drainage via an external ventricular catheter  Short-term, temporising moderate hyperventilation (PaCO2 4.0-4.5 kPa) guided by multimodal neuromonitoring  ***Extended measures:***  Therapeutic hypothermia  Barbiturate coma  Decompressive craniectomy |
| CPP targets and management | CPP 60-70mmHg  Euvolaemia plus norepinephrine to maintain CPP |
| Temperature control | Prophylactic hypothermia not recommended  Normothermia |
| Glycemic control | Intermediate glucose concentrations as per hospital protocol (e.g., 7.0-10.0 mmol/ l) |
| Seizure control | Phenytoin or levetiracetam to decrease the incidence of early post traumatic seizures (> 7 days) when benefit is felt to outweigh complications  Optimal dose unclear |
| Nutritional | Achieve basal caloric replacement at least by the fifth day and at most by the seventh day post injury |

*Table 1. TBI management targets and thresholds in critical care*

**Respiratory and ventilatory support**

In patients with TBI the effects of hypoxia, hypocapnia and hyperventilation are considered as secondary insults to the brain (Geeraerts, 2021).Tracheal intubation and ventilation is required immediately when the person has a GCS score of 8 or less, loss of protective laryngeal reflex, ventilatory insufficiency, as judged by blood gases: hypoxemia (PaO2 less than 13 kPa on oxygen) hypercarbia (PaCO2 more than 6 kPa), and irregular respirations (NICE, 2023). Once the airway is secured, the priority that follows is to ensure adequate ventilation.

The current recommendations for patients with severe TBI with or without polytrauma is to maintain normoxia (PaO2 60-100mmHg or 8kPa-13kPa) and normocapnia (PaCO2 35-45mmHg or 4.6 kPa-6.0 kPa) when ICP is normal and in the absence of cerebral herniation. However, when ICP is raised current thresholds are; PaCO2 4.5-5 kPa (Carney et al, 2017; Picetti et al, 2019). Patients with TBI with PaO2 <60 mmHg within 6 h after admission are more likely to have poor outcomes (Wu et al, 2021). Maintain SpO2 ≥ 94% and a target PaO2 of ≥11 kPa (>80 mmHg) (Carney et al, 2017). High PaO2 increases the risk of hyperoxic cerebral vasoconstriction and hyperoxic lung injury. However, the upper limit value of PaO2 that affects the outcome of TBI in patients has not been found (Wu et al. 2021).

Hyperventilation, with partial pressure of carbon dioxide in arterial blood (PaCO2) of 25 mm Hg (3.3kPa) or less is not recommended as this results in an increased risk of vasoconstriction and increased tissue hypoxia which should be avoided as patterns of CBF alter and is reduced in the injured brain (Carney et al, 2017). The high prevalence of cerebral ischemia in this patient population suggests safety in providing normoventilation so as to prevent further cerebral ischemia and cerebral infarction. Hyperventilation may be used as a temporizing measure to treat evidence of cerebral herniation and for the reduction of elevated intracranial pressure (ICP). However, if hyperventilation is used, jugular venous oxygen saturation (SjO2) or brain tissue O2 partial pressure (BtpO2) measurements are recommended to monitor oxygen delivery.

Pneumonia and acute respiratory distress syndrome frequently occur after TBI and require careful management using lung protective strategies (Raith et al, 2020). Moderate positive end expiratory pressure up to 15 cmH2O may be used without compromising ICP. Avoidance of high tidal volumes are essential after TBI with modifications based on individualised clinical assessment.

*Percutaneous tracheostomy*

Patients who have suffered severe TBI often require ventilatory support on critical care for a prolonged period. The reasons for this are multifactorial and include: prognostic uncertainty in the acute phase; impairment of bulbar function, high incidence of pulmonary infection due to poor cough (Wiles, 2022). The incidence of ventilator acquired pneumonia in patients with TBI is 36% and is associated with an increase in duration of mechanical ventilation and critical care stay (Li et al, 2020). Early insertion of a tracheostomy is associated with a reduction in the incidence of ventilator acquired pneumonia, duration of mechanical ventilation, critical care and hospital stay (de Franca et al, 2020). Indication and timing for tracheostomy in TBI patients are still debated and should be considered on an individual basis.

**Cardiovascular support**

Hypotension after TBI requires immediate intervention as it is a predominant contributing factor in the secondary brain injury cascade and is associated with poor outcome (Carney et al, 2017; Raith et al, 2020; El-Swaify et al, 2021). There are several pathophysiologic mechanisms when considering blood pressure thresholds after TBI. The interrelationship between systolic blood pressure (SBP), mean arterial pressure (MAP) and cerebral perfusion pressure (CPP) in the face of intracranial hypertension and autoregulation is important.

Cerebral autoregulation is a homeostatic and protective mechanism that occurs in large and small arterioles and involves the constriction or dilation of cerebral blood vessels in response to changes in transmural pressure detected by stretch receptors (Hickey, 2019). This enables the brain to maintain relatively constant cerebral blood flow (CBF) between 50 and 150mmHg MAP despite changes in perfusion pressures (Silverman & Petersen, 2023). For example, if autoregulation is intact a drop in SBP triggers an autoregulatory vasodilation of cerebral blood vessels in an attempt to maintain adequate brain perfusion. Conversely, if there is rise in SBP, this triggers an autoregulatory vasoconstriction of cerebral blood vessels. Following severe TBI, autoregulation may be impaired regionally and/or globally during the acute period, therefore CBF is largely dependent on systemic blood flow to prevent cerebral ischemia (Jain et al, 2019). Additionally, patterns of cerebral blood flow (CBF) alter following TBI and is reduced by extrinsic and intrinsic mechanisms in the first 72 hours following injury, with resultant global and regional ischemia (Wang et al, 2016). Thus, the causes of hypotension should be identified rapidly, and the provision of appropriate treatment and fluid resuscitation is imperative to prevent a drop in blood pressure. While hypotension following TBI in the setting of multisystem trauma is often the result of hypovolemia and blood loss from other injuries, hypotension after isolated TBI may also be as a result of extracranial complications such as a maladaptive catecholamine excess state.

Current SBP thresholds are described in Table 1 (Carney et al, 2017). However, there is a growing initiative to consider higher SBP thresholds (e.g., SBP targets of >100 mmHg and >120 mmHg in patients with TBI aged ≤60 and >60 years, respectively) because of the potential for better outcomes (Raith et al, 2020; El-Swaify et al, 2021). Further research is required to elucidate if higher thresholds result in better outcomes.

Hypertension may be a sign of worsening neurological status, or of inadequate sedation and should be reported. There are currently no guidelines for the management of hypertension after severe TBI, despite observational data which suggests that early hypertension is also associated with an increased risk of mortality after severe TBI (Krishnamoorthy et al, 2017).

Blood pressure thresholds are augmented through a combination of fluid administration aiming for euvolaemia and the judicious use of inotropes or vasopressors. Since saline (0.9 % NaCL) is isotonic, it has a negligible effect on brain water and has become the crystalloid of choice in the management of TBI (Wiegers et al, 2021). However, there may be adverse effects of excessive administration of 0.9% saline, such as hyperchloraemic acidaemia (Wiles, 2022). Currently, it is not possible to recommend the optimal intravenous fluid, as well as how to assess precisely what volume to deliver and at what time-point.

Alongside fluid resuscitation, vasopressors may be initiated to increase blood pressure through the increase of systemic vascular resistance. Their vasoconstrictive effect on the venous system also contributes to an increase in venous return and subsequently increases cardiac output (Legrand & Zarbock, 2022). No randomised controlled trials have compared choice of vasopressors for either improving neurological outcomes or reducing mortality however the use of norepinephrine is commonly used. Clinicians need to be aware of side effects such as excessive vasoconstriction caused by noradrenaline, which may result in hypoperfusion and hypoxia in other organs (Wiles, 2022).

*Management of Cerebral Perfusion Pressure (CPP)*

Cerebral perfusion pressure is representative of cerebral blood flow (CBF) and is defined as the difference between mean arterial and intracranial pressures (CPP = MAP - ICP). TBI management involves consideration of CPP thresholds which can be directly monitored and targeted in the neurocritical care setting. The arterial pressure transducer should be referenced at the tragus of the ear, which is the same level as ICP, which corresponds approximately to the foramen of Monro (Raith et al, 2020). A CPP of 60-70 mmHg should be targeted; exceeding this threshold may be associated with worsening ICP in the setting of impaired cerebral autoregulation (Carney et al, 2017). Additionally, induced hypertension to raise CPP >70 mmHg can cause adult respiratory distress syndrome (ARDS) and should be avoided (Constant et al, 2001; Carney et al, 2017). CPP directed therapy is primarily related to [fluid resuscitation](https://www.sciencedirect.com/topics/medicine-and-dentistry/fluid-resuscitation) and/or vasoactive support. SBP thresholds must be optimised in an attempt to maintain adequate CPP and ultimately oxygen delivery.

Current guidelines do not address the utility of individualised goals for CPP (Carney et al, 2017). Technologies that aim to quantify the optimal CPP include the pressure reactivity index (PRx) which is a tool for monitoring autoregulation and can possibly calculate individualised, patient-specific CPP thresholds (Rozanek et al, 2022). Utilising PRx monitoring, a feasibility randomised control trial (COGiTATE) concluded that individual cerebral autoregulation (CA) guided CPP is feasible and safe for TBI patients (Tas et al, 2021). However, to date its use is not routinely used in clinical practice.

*Brain tissue oxygenation measurement*

Direct measurement of brain tissue oxygenation can be obtained to guide intracranial and cerebral perfusion pressure management. Direct measurement can be obtained via multi-lumen probes inserted in an area considered at risk (e.g., peri-lesional) or non-eloquent brain parenchyma. In addition to ICP, these record brain tissue oxygen tension (PbtO2) which is defined as the partial pressure of oxygen in the interstitial space. PbtO2 management strategies often aim to achieve an arbitrary threshold greater than 20 mmHg. Ischaemia is suspected if < 20mmHg. Brain tissue oxygenation measurementcan serve as an ancillary tool to ICP/CPP-guided therapy and is associated with improved long-term outcomes (Raith et al, 2020).

**ICP monitoring and management**

A mainstay of the care of patients with severe TBI is the monitoring of and treatment of intracranial pressure (ICP). Sustained ICP elevations at levels above 22 mm Hg (i.e., intracranial hypertension) are not well tolerated by the injured brain since it alters tissue perfusion causing cerebral ischaemia and potential infarction which is associated with poor neurological outcomes. The current threshold for treatment is to treat ICP above 22 mmHg (Carney et al, 2017). Controlling ICP in isolation may not be sufficient to achieve adequate brain tissue perfusion hence other ICP lowering strategies need to be considered as outlined in **Table 1** in a stepwise manner. First line measures are instituted and then progressing to higher risk options for patients with refractory intracranial hypertension and/or at imminent risk of cerebral herniation (Raith et al. 2020).

**Box 1** describes the criteriafor intracranial pressure (ICP) monitoring (Carney et al, 2017; NICE, 2023). Interest in the use of optic nerve sheath measurement as a non-invasive assessment method for the detection of raised ICP has emerged as an alternative technique (Koziarz et al, 2019). However, currently its use is not widely used in routine clinical practice.

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| In all salvageable patients with a severe TBI (GCS 3-8 after resuscitation) and an abnormal computed tomography (CT) scan (i.e., an abnormal CT scan of the head is one that reveals hematomas, contusions, swelling, herniation, or compressed basal cisterns) |
| Patients with severe TBI with a normal CT scan if two or more of the following features are noted at admission: age over 40 years, unilateral or bilateral motor posturing, or episodes of systolic blood pressure (BP) <90mmHg. |

*Box 1.**Describes the criteria**for intracranial pressure (ICP) monitoring.*

*Positioning*

As the jugular venous system has no valves, gravity facilitates drainage of blood from the cranium thus lowering ICP. Thus, head rotation, neck and hip flexion should be avoided as this decrease’s jugular venous return, thus raising ICP. Head elevation between 30-450 decreases ICP by promoting venous return via the jugular veins. This is common practice provided the patient has an adequate mean arterial blood pressure and therefore positioning should be individualised. Position the patient in neutral alignment and turn as required for pressure area and chest care. Minimise head down positions especially when being transported always being aware of the effects of raised ICP on CPP. Subclavian neck lines are usually avoided due to the need to have the patient head down during insertion therefore femoral lines are usually preferred.

In the case of traumatic spinal cord injury and the need for collars, ensure they are fitted correctly and are not occluding venous flow via the jugular veins. A meta-analysis which examined the effect of cervical collar application on ICP showed that application of a cervical collar increased ICP by approximately 4.4 mmHg, despite the collars only being applied for a short time period (3–20 min)(Maschmann et al, 2019).

*Sedation, Analgesia and Neuromuscular Blockade*

Maintaining an adequate level of sedation and analgesia plays a key role in the management of TBI (Godoy et al, 2021). Adequate sedation and analgesia are required to facilitate ventilation as well as manage anxiety, pain, restlessness and agitation all of which can exacerbate increased intracranial pressure (Hickey, 2019; Godoy et al, 2021). Pain is a common symptom after acute TBI and analgesia is required through the administration of opioid infusions and regular paracetamol (Kim et al, 2022). Regular assessment by the medical team is required. Sedation also has neuroprotective properties such as reducing cerebral metabolic demand, and consumption of oxygen in a dose-dependent manner that, in turn, decreases CBF and leads to a reduction in ICP. Achieving an adequate level of sedation is paramount because it minimizes the length of hospital stay, ventilator days, incidence of delirium and helps in early mobilization (Dash & Cavali, 2018). Anesthetics such as propofol are commonly used as a sedating agent as it is titratable and effective at reducing ICP. Does should not exceed 3mg/kg/hr in order to avoid propofol infusion syndrome which is associated with hyperkalemia, metabolic acidosis, myocardial failure, rhabdomyolysis, and death (Mirrakhimov et al, 2015). Midazolam may be used (0-20 mg/ h) to minimise total propofol dose. Deep sedation (Richmond Agitation-Sedation Scale -5) should be pursued until ICP is adequately controlled. Sedation holds are not appropriate in patients with uncontrolled ICP (Raith et al, 2020). Barbiturate coma may be required as part of tiered therapy to manage ICP refractory to maximum standard medical and surgical treatments, however continuous electroencephalographic (cEEG) monitoring is required to assess for burst suppression(Carney et al, 2017). Neuromuscular blocking agents are not used routinely and are mainly reserved for patients with refractory intracranial hypertension. Their use needs to be carefully weighed against the potential to harm with continuous paralysis.

*Hyperosmolar therapy*

Hyperosmolar therapy such as mannitol 20% and hypertonic saline (HTS) 3-7.5% are widely used for the management of TBI. Mannitol is a sugar alcohol and is filtered through the renal tubules and is not reabsorbed, acting therefore as an osmotic diuretic. It lowers intracranial hypertension by two main mechanisms. The immediate effect is through reducing blood viscosity and leading to improved microcirculatory flow of blood constituents and increase in intravascular volume. The late, more persistent effect is due to the osmotic gradient generated between the intravascular and interstitial compartments. Doses are between 0.25 and 1g/kg body weight are recommended (Rossi et al, 2018).

Hypertonic saline administration produces an osmotic gradient between the intravascular and intracellular/interstitial compartments, leading to shrinkage of brain tissue (where blood brain barrier is intact) and therefore a reduction in ICP. It also augments volume resuscitation and increases circulating blood volume, mean arterial blood pressure and cerebral perfusion pressure. Some evidence suggests that although both hypertonic saline and mannitol can effectively reduce intracranial pressure, hypertonic saline has a more sustained effect on intracranial pressure and effectively increases CPP (Gu et al, 2019; Shi et al, 2020).

When administering hyperosmolar therapies, it is important to understand any side effects. While mannitol induces osmotic diuresis, the initial rapid increase in intravascular volume may cause an acute hypervolaemia which could affect heart failure or cause pulmonary oedema. It may also cause hypovolaemia, hypotension and electrolyte disturbances (Schwimmbeck et al, 2019). Mannitol may also induce renal failure because of renal vasoconstriction, intravascular volume depletion, and hyper-osmolarity (Rossi et al, 2018). Hypertonic saline can raise serum sodium concentrations rapidly, leaving the CNS at risk of central pontine myelinolysis. Fortunately, this devastating condition has been rarely observed. Hypertonic saline is also a volume expander so it may cause volume overload with heart failure and pulmonary oedema. Therefore, the use of hypertonic solutions in patients with impaired cardiac function should be performed under close cardiac monitoring (Shi et al, 2020). In addition, disruption of the blood brain barrier (BBB) can result in accumulation of osmotically active molecules which can lead to local oedema or rebound increases in ICP (Rossi et al, 2018).

Repeated and prolonged osmotic therapy needs to be avoided as this may have detrimental effects. Thus, osmotherapy should only be used as a temporising measure, not a definitive treatment (Wiles, 2022). Specific circumstances may prompt selection of a specific agent, and this is usually individualized to each center and patient.

The most recent meta-analysis showed no significant difference between hypertonic saline and mannitol in terms of mortality or neurological outcome (Schwimmbeck et al, 2021). A UK multicentre, randomised controlled trial (Sugar or Salt (SOS) trial registered with [ISRCTN Registry](https://www.isrctn.com/) 16075091 is currently investigating the relative long-term clinical and cost effectiveness outcomes of mannitol and hypertonic saline (Rowland et al, 2019). Results from this trial will assist clinicians to guide practice in the use of osmotherapy for patients with severe TBI.

Targeted Temperature Management (TTM)

Targeted temperature management involves controlling core body temperature at a specific level to achieve a desired temperature to prevent fever, maintain normothermia, or induce hypothemia. The aims are to minimise further secondary brain injury and improve patient outcome (Lavinio et al, 2023).

*Therapeutic hypothermia*

Therapeutic hypothermia management remains controversial for patients with TBI despite animal studies showing that hypothermia is profoundly cerebroprotective during or after a central nervous system (CNS) insult (Jackson & Kochanek, 2019). However, despite large-scale randomized controlled studies in humans (Andrews et al, 2015; Cooper et al, 2018) the efficacy and safety have not been demonstrated (Chen et al, 2019).

Some studies have shown that hypothermia sometimes has an adverse role. Eurotherm3235 Trial was terminated early due to safety concerns (Andrews et al, 2015). Long-term hypothermia is considered a form of immunosuppression that increases the infection rate of pneumonia and sepsis (Geurts et al, 2014). Other risks are coagulopathy and cardiac dysrhythmia.

Nevertheless, therapeutic hypothermia may help reperfusion/ischemic injury prevention after surgery in the case of mass lesions, such as acute subdural hematoma, and it has also been shown to be effective in intracranial pressure control (Jo, 2022). This strategy may still be at the centre of neuroprotective therapeutic studies regarding TBI when more positive efficacy can be confirmed. Current guidance for people with TBI, recommend normothermia and to target the avoidance of fever (defined as a core temperature ≥ 38 °C) (Chestnut et al, 2020).

*Management of fever*

The patient may have a fever due to a central (neurogenic) (non-infectious) cause as a direct consequence of the brain injury (Lavinio et al, 2023). Alternatively, it may be as a result of complications such as aspiration pneumonia due to decreased consciousness and diminished protective reflexes (Polderman, 2015). Brain temperature exceeds core temperature by 1–2 °C in patients with severe brain injury. High brain temperatures are a secondary cause of brain injury especially if it coincides with a period of ischemia. Fever causes a generalized increase in metabolic rate (7–10 % per °C increase in core temperature), with corresponding increases in minute ventilation and oxygen consumption. This can be detrimental depending on the patient’s condition. Clinically, it is important to correctly diagnose central fever vs fever of infectious origin because of the consequences of failing to identify a treatable condition, the negative consequences of antibiotic overuse, and the detrimental effect of fever on brain-injured patients (Lavinio et al, 2023).

Recent recommendations on targeted temperature management after stroke for those who require admission to critical care have been formulated (Lavinio et al, 2023). Core temperature should be maintained between 36.0C and 37.5C and monitored continuously and using automated feedback-controlled devices, where possible. Recommendations also advise the commencement of targeted temperature management within 1 h of first fever identification with appropriate diagnosis and treatment of infection, maintained for as long as the brain remains at risk of secondary injury, and rewarming should be controlled. Shivering should be monitored and managed to limit risk of secondary injury. Although these recommendations relate to people with all stroke subtypes, management of strict fever control with monitoring is also required when treating TBI patients due to its detrimental effects and association with unfavourable clinical outcomes.

*Seizure prophylaxis*

Seizures are common after TBI. Convulsive activity reflects disordered electrical discharges in the damaged brain and results in local loss of autoregulation, increased metabolic activity with concomitant increases in cerebral blood flow and tissue lactic acidosis. This results in increased ICP and altered oxygen supply to the injured brain causing secondary brain injury (Dash & Chavali, 2018).

Early post traumatic seizures (PTS) are classified as early when they occur instantaneously or within 7 days of injury or late PTS when they occur after 7 days (Carney et al, 2017; Fordington & Manford, 2020). The risk factors for early PTS include: Glasgow Coma Scale (GCS) score of ≤10; immediate seizures; post-traumatic amnesia lasting longer than 30 minutes; linear or depressed skull fracture; penetrating head injury; subdural, epidural, or intracerebral haematoma; cortical contusion; age ≤65 years; or chronic alcoholism (Fordington & Manford, 2020). PTS during acute hospitalisation have been shown to be an independent risk factor for PTS within 12 and 24 months following TBI. Late PTS within 24 months can have a negative impact on quality of life, return to work, return to driving, and can even result in death.

Within the UK the prophylactic use of anti-epileptic drugs (AEDs) varies between centers however when given, levetiracetam appears to be favoured (Kolias et al, 2019). Currently the optimal dose of levetiracetam is unclear and each center must evaluate the efficacy and overall benefit, as well as potential harms, of AEDs used for the prevention of PTS. The results from the Management of Seizures after Traumatic Brain Injury (MaST) trials(https://clinicaltrials.gov/ct2/show/NCT04573803) aim to define best practice in the use of anti-epileptic drugs for patients following TBI.

*Glycemic control*

Blood glucose levels that are too high (hyperglycemia) or too low (hypoglycaemia) after severe TBI can exacerbate secondary brain injury and independently predict a poor neurological outcome (Zhu et al, 2018; Yuan et al, 2022). Early control of blood glucose levels is important due to its direct relationship with prognosis. An elevated stress and inflammatory response seem to be the major causes of hyperglycemia after TBI (Shi et al, 2016). The stress response is thought to represent a complex interplay between endogenous catecholamines, cytokines and activation of the hypothalamic-pituitary-adrenal axis resulting in excessive cortisol secretion and induction of gluconeogenesis (Hermanides et al, 2018). Short-acting insulin therapy administered as a continuous infusion titrated to maintain systemic blood glucose within target ranges is used to control the dramatic increase in blood glucose levels following TBI (Hermanides et al, 2018).

Insulin increases glucose utilization and reduces the damage of hyperglycemia to brain cells. Strict glycemic control with a low target range carry a risk of inadvertent hypoglycemia episodes (van den Berghe et al, 2001; Zhu et al, 2018).  Therefore, care should be taken to avoid decreased glucose levels with insulin as this can induce and aggravate secondary brain injury (Shi et al, 2016). To date the optimal glycaemic target range is uncertain and may vary between individuals at different time points during the clinical course. A single “one size fits all” blood glucose target may not be possible due to the heterogeneous nature of the TBI patient population.

*Nutrition*

Patients with severe TBI are usually in catabolic and hyperglycemic states and may have gastrointestinal dysfunction (Zhu et al, 2018).Malnutrition is associated with a higher mortality rate in severe TBI patients, and early effective nutritional support may improve insulin resistance and patient prognosis (Shi et al, 2016). Enteral nutrition via tube feeding is the preferred way of feeding as it is an important means of counteracting the catabolic state induced by severe TBI (Bischoff et al, 2020). Recommendations suggest that TBI patients should be fed to achieve basal caloric replacement at least by the fifth day and at most by the seventh day post injury to decrease mortality. Early transgastric jejunal feeding may also reduce the incidence of ventilator-associated pneumonia ([Carney et al, 2017](https://www.frontiersin.org/articles/10.3389/fnins.2020.00190/full#B12)).

Patients with severe TBI frequently have gastric feeding intolerance, which may be attributed to dysfunctional gastric emptying secondary to increased ICP and the use of opiates. Prokinetic agents may improve feeding tolerance (Dash & Chavali, 2018). Delays in starting nutrition therapy must be avoided as much as possible to preserve skeletal muscle mass, optimise vital organ function, and cerebral metabolic homeostasis (Kurtz & Rocha, 2020). In the future substrate supplementation for brain energy production may change the way patients with severe brain injury are fed.

*Decompressive craniectomy (DC)*

Decompressive craniectomy (DC) is a surgical procedure in which a large section of the skull is removed and the underlying dura mater is opened widely. The temporary removal of a large portion of skull is an extended measure for treating ICP elevation resulting from severe TBI. Primary decompressive craniectomy (DC) occurs when the bone flap is not replaced when an intracranial mass lesion such as a traumatic acute subdural haematoma is evacuated early after a head trauma. This is the most common indication for DC as acute subdural haematoms are often associated with underlying parenchymal brain injury with brain swelling occurring intraoperatively or postoperatively. The RESCUE-ASDH (Randomised Evaluation of Surgery with Craniectomy for Patients Undergoing Evacuation of Acute Subdural Hematoma) trial compared the outcomes of craniotomy (bone flap replaced) and decompressive craniectomy (bone flap left out) in adult patients with traumatic acute subdural hematoma (Hutchinson et al, 2023). In this study, adult patients undergoing evacuation of traumatic acute subdural haematoma, decompressive craniectomy and craniotomy yielded similar results with respect to overall outcomes at 12 months. Additional craniectomies were performed more frequently in the craniotomy group, but wound complications and surgical-site infections occurred more frequently in the decompressive craniectomy group. The authors suggest that if the bone flap can be replaced without compression of the brain after removal of the haematoma, then surgeons may consider this rather than performing a pre-emptive craniectomy (Hutchinson et al, 2023).

Secondary DC involves removal of the bone flap later in the patient’s course to treat post traumatic intracranial hypertension refractory to other medical treatments and is considered a last-tier treatment (Hawryluk et al, 2020). The procedure has been shown to reduce mortality but is associated with higher rates of vegetative state and severe disability in survivors (Cooper et al, 2011;Hutchinson et al, 2016).

Technical aspects of DC, timing and patient selection require further clarification and are controversial (Cooper et al, 2020). The decision to offer a DC to alleviate intracranial hypertension has to be balanced against great uncertainty in regard to functional outcomes and quality of survival via shared decision-making taking patient preferences and values into consideration(Lazaridis et al, 2022).

**Other considerations**

*TBI patients on anticoagulants or antiplatelet agents*

A greater number of people who are older who sustain TBI are frequently on antiplatelet therapy, such as aspirin and clopidogrel, at the time of their injury. They may also be on anticoagulants, with an increasing proportion on direct oral anticoagulants (DOAC) rather than vitamin K antagonists such as warfarin. Anticoagulation reversal and discontinuation of antiplatelet therapy as per hospital protocols is therefore an important consideration when considering those that require emergency neurosurgery. The use of these medications should be relayed to consulting neurosurgeons as these patients are susceptible to a higher risk of intracranial haemorrhage (Wiles, 2022). Prothrombin complex concentrate should be used in hospital settings immediately in adults (16 or over) with major trauma who have active bleeding and need emergency reversal of a vitamin K antagonist (NICE, 2023). Consultation with a haematologist for advice on the need for the reversal of any anticoagulant agent is recommended. Patients with severe TBI can also develop a coagulopathy as a direct result of the initial trauma and should also be considered (Zhang et al, 2018).

*Early diagnosis of hypopituitarism (underactivity of the pituitary gland)*

TBI of any severity can cause pituitary dysfunction which can occur immediately, hours, weeks or months after the injury. Therefore, any suspicion of hypopituitarism should be investigated in people admitted to hospital if they have clinical symptoms (NICE, 2023). Hypopituitarism may present with central (neurogenic) diabetes insipidus (**Box 2** )as well as a wide variety of symptoms such as persistently abnormal low sodium levels (hyponatraemia) or hypoglycaemia and/ or low blood pressure that requires persistent high doses of vasopressors (Raith et al, 2020).

Hydrocortisone may be required for refractory hypotension and supplemented with a mineralocorticoid if hyponatraemia persists (Raith et al, 2020). Close monitoring of electrolytes and fluid balance is required.

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| *Causes of neurogenic diabetes insipidus after TBI*  Dysfunction of the hypothalamic-pituitary axis (i.e., damage of the hypothalamic-ADH-producing neurones, their axons or the posterior pituitary gland).Damage may be due to direct mechanical impact at the time of injury and/or as a secondary injury process such as ischaemia, hypoxia, raised ICP and changes in cerebral metabolism (Capatina et al , 2015).  *Physiological effect*  Decreased secretion or action of antidiuretic hormone (ADH) at the distal nephron inhibiting the reabsorption of water.  *Clinical features*  Large volumes of dilute urine (polyuria) in the presence of normal or high plasma osmolality.  Hypovolaemic hypernatremia  Signs of dehydration (e.g., decreased skin turgor, dry mucous membranes, hypotension, tachycardia, low central venous pressure )  *Diagnosis*  Blood levels of electrolytes (sodium, potassium, calcium) plasma and urine osmolalities. urinary sodium  Check urine specific gravity (report if between 1.001-1005)  *Treatment*  Replace fluids  Frequent monitoring of fluid and electrolyte balance  Hormonal replacement with desmopressin (DDAVP) as per hospital protocol |

***Box 2****:* Central (neurogenic) diabetes insipidus after TBI

*Systemic (extra-cranial) effects of TBI*

There is a complex interaction between the brain and systemic physiology. The aetiology of extra-cranial complications can be neurogenic in origin as a result of a complex interplay of multiple factors involving: the autonomic nervous system, neuroendocrine dysfunction, neuronal immune and inflammatory responses, systemic immune response, and biochemical cascades (Gundappa, 2019). The high levels of sympathetic activity and circulating catecholamines and neuroinflammation that occur following the primary injury affects extra-cranial organs and systemic physiology (Raith et al, 2020). **Table 2** describes some of the extra-cranial complications related to severe TBI which affect the respiratory, cardiac, renal and other systems (Gundappa, 2019). These extra-cranial complications increase morbidity as well as mortality after TBI (Goyal et al, 2018; Robba et al, 2020).

Extra-cranial complications can also occur because of brain directed therapies such as induced hypertension with vasopressors to target cerebral perfusion pressure (CPP), therapeutic hypothermia and pharmacological therapies.

Treatment of these complications is beyond the scope of this review; however it is important for early recognition and management which is like that of any other critically ill patient.

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| Respiratory complications which may be multifactorial (e.g., trauma, low GCS score, catecholamine release coupled with systemic inflammation and increased endothelium permeability). | Acute respiratory distress syndrome (ARDS)  Neurogenic pulmonary oedema (NPO)  Pneumonia  Atelectasis  Aspiration pneumonitis |
| Cardiovascular complications due to raised ICP and sympathetic overactivity | Blood pressure instability  Arrhythmias  Neurogenic stunned myocardium syndrome (Takotsubo’s cardiomyopathy) |
| Renal complications | Acute Kidney Injury (AKI) |
| Gastrointestinal complications | Peptic Ulceration and Ileus |
| Haematologic complications (High concentrations of thromboplastin released from the brain into the systemic circulation are related to coagulopathy) | Platelet dysfunction  Coagulopathy (including Disseminated intravascular coagulation (DIC)  Thromboembolic disease |
| Systemic inflammation disrupts neuroendocrine and autonomic pathways causing immunosuppression | Sepsis  Thermoregulatory dysfunction (e.g., fever) |
| Post-traumatic hypopituitarism (pituitary ischaemia from local and systemic insults) | Posterior pituitary dysfunction (Syndrome of inappropriate antidiuretic hormone secretion (SIADH); Diabetes insipidus (DI) (Box 2)  Anterior pituitary dysfunction (GH deficiency, Hypothyroidism, ACTH deficiency)  Adrenal insufficiency  Cerebral salt wasting (CSW) syndrome |
| Metabolic derangements | Hypo/hyper glycaemia  Hypermetabolism |

*Table 2. Systemic (extra-cranial) complications associated with severe TBI. Growth Hormone (GH); adenocorticotropic hormone (ACTH)*

*Nursing role*

Critical care management and care is focused on preventing secondary brain injury by optimising cerebral perfusion pressure, early recognition of complications and management of extracranial complications. Bedside nurses are required to have a good knowledge and understanding of related pathophysiology after TBI and are able to detect complications and /or potential problems so that they can provide prompt interventions See checklist in **Box 3** for basic bedside nursing measures to treat a sudden rise (>22mhg) or change in ICP from baseline.

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| Ensure proper positioning: Elevation of the head of bed to 30-45 degrees, to keep the head in midline position to promote jugular venous drainage (as BP tolerates),  Avoid neck/hip flexion to avoid jugular venous outflow obstruction-keep patient in neutral alignment when nursing on side  Ensure cervical hard collars are not obstructing jugular venous outflow |
| Ensure adequate pain and sedation guided by sedation scores (e.g., Richmond Agitation-Sedation Scale -5) |
| Check pupil size, shape, and reaction to light. anisocoria (unequal pupils with greater than 1 mm of difference) may indicate progression of a mass lesion resulting in trans-tentorial herniation possibly that may require emergent evacuation. |
| Limit any unnecessary external stimulation and space nursing activities to avoid further sudden rises in ICP which compromises CPP below targeted thresholds |
| Check arterial blood gases to check Pa02 and PaCo2 levels, acid base balance, electrolyte and blood sugar levels  Check core and/or brain temperature is within normal range |
| Suction as required to prevent a build-up of secretions (pre oxygenate with 100% before suctioning) |
| Observe for any seizure activity |
| Check all IV lines are patent and all infusions are running as prescribed |
| Check ICP monitor connections and ICP trace to ensure that readings are reliable |
| Check abdomen for any signs of distention that may increase intrathoracic pressure and impede venous return (e.g., constipation, bladder distension, bowel obstruction) |
| Document the change in ICP such as was the change spontaneous or following a intervention such as: transport to CT scan, turning, physiotherapy etc. Record any associated changes in CPP thresholds and/ or neurological deterioration |

**Box 3**. *Basic bedside nursing measures to treat a sudden rise (>22mhg) or change in ICP from baseline*

Families need attention, education and emotional support in the early acute phase. Clear, honest, transparent and consistent communication with the clinical team is imperative at a time of extreme uncertainty(Hayes et al, 2023). Families need to be supported in preparing for ongoing uncertainty in the hours, days, weeks and months ahead. Emotional support is shown by caring, listening and respecting the family in all communication. Involvement in patient care as the patient stabilises may be requested and should be supported where possible. Saving lives is of the utmost importance in the early acute phase. However, ongoing specialist care and rehabilitation is required to restore lives and achieve good functional outcomes after TBI. The introduction of a specialist interdisciplinary traumatic brain injury team, led by a neurosciences-trained brain injury consultant for the NHS (Li et al, 2021) may lead to reduced personal, societal and economic burden of TBI.

**Conclusions**

TBI is a devastating heterogenous disease that has life changing consequences not just for the individual but for the family and society. Management is aimed at avoiding secondary brain injury by the management of intracranial pathology and optimising systemic physiology. Clinicians need to consider the extracranial complications that can ensue following severe TBI and attenuate their detrimental effects that can contribute to poor outcome. Care of the patient with severe TBI in critical care requires a collaborative interdisciplinary and evidence-based approach to optimise outcome.

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| **Key Key points** |
| * Maintenance of adequate cerebral perfusion pressure and oxygenation in the early acute phase |
| * Aim to keep ICP ≤22mm Hg |
| * Rapid anticoagulation reversal if clinically indicated |
| * Seizure management if clinically indicated |
| * Aim for normothermia |
| * Neurosurgery if clinically indicated |

*Table 3:**Key priorities for acute management*

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| **Reflective Questions** |
| 1: What are the tiered treatments in the management of intracranial hypertension? |
| 2: How do I reverse anticoagulant/antiplatelet treatment if required? |
| 3: Do I need to increase the patient’s mean arterial blood pressure and if so when, by how much and with what agent, dose and route of administration? |
| 4: Does the patient fulfil criteria for emergency neurosurgery? |
| 5: What are the key priorities for the critical care nurse in the acute management of severe TBI to optimise patient outcome ? |

*Table 4: CPD Reflective questions*

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