Anesthesia for Traumatic Brain Injury

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15.1 Introduction

Traumatic brain injury (TBI) is a significant public health issue and a leading cause of death and disability worldwide [1]. In the United States, TBI contributes to approximately 30% of all injury-related deaths and places a substantial burden on the healthcare system [2]. In 2013, roughly 2.8 million people in the United States were diagnosed with TBI, resulting in approximately 282,000 hospitalizations and 56,000 deaths [2]. TBI occurs most commonly in young children (age 0–4 years), adolescents and young adults (age 15–24 years), and the elderly (age ≥ 75 years) [2]. Across all ages, males are more likely to suffer TBI than females [2]. The most common mechanisms of TBI in the United States are falls, being struck by or against an object, and motor vehicle collisions [2]. Recently, there has been increased awareness and concern about concussions (also referred to as mild traumatic brain injury), especially in regard to athletes and the pediatric population [3]. In the United States, it is estimated that up to 3.8 million concussions occur per year during recreational activities and competitive sports [4], and as many as 50% of concussions may go unreported [4].

Given the prevalence of TBI and the significant morbidity and mortality associated with these injuries, anesthesia providers will frequently be faced with the management of these patients. The main goals of caring for this patient population are to stabilize the patient and prevent secondary neurologic injury [5]. This chapter will focus on the perioperative management of patients with traumatic brain injury, including initial evaluation, intraoperative management, prevention of secondary injury, and anesthetic considerations for patients with concussions. The critical care management of patients with traumatic brain injury is discussed in a separate chapter.

15.2 Pathophysiology

There are numerous mechanisms of TBI, including motor vehicle collisions, falls, gunshot wounds, athletics, and combat injuries [6]. TBI severity ranges from mild to severe, with variations in associated morbidity and mortality across this spectrum [7]. The severity of a head injury can be classified based on the Glasgow Coma Scale (GCS), which defines neurologic impairment in terms of eye opening, speech, and motor function (Table 15.1) [8]. Severe TBI is defined as an initial GCS score ≤8 persisting for 6 h or more [8]. Trauma may result in a variety of neurologic injuries, ranging from subtle changes in molecular

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Table 15.1 Modified Glasgow Coma Scale[a]

Feature	Point(s)
Eye opening	
Spontaneously	4
To verbal command	3
To pain	2
None	1
Best verbal response	
Oriented, conversing	5
Disoriented, conversing	4
Inappropriate words	3
Incomprehensible sounds	2
No verbal response	1
Best motor response	
Obeys verbal commands	6
Localizes to pain	5
Flexion or withdrawal	4
Abnormal flexion (decorticate)	3
Extension (decerebrate)	2
No response (flaccid)	1

From Phan RD, Bendo AA. Perioperative management of adult patients with severe head injury. In: Cottrell JE, Patel P, editors. Cottrell and Patel's neuroanesthesia. 6th ed. New York: Elsevier; 2017. Used with permission from Elsevier

[a]Total scores: mild head injury = 13–15 points; moderate = 9–12 points; severe ≤8 points

signaling and cellular function to extensive tissue injury, such as hemorrhage and contusions [6]. Primary brain injury is due to the mechanical impact itself, and when severe, results in increased intracranial pressure (ICP) and reduced cerebral perfusion [9]. TBI also causes blood-brain barrier (BBB) dysfunction and impaired neurologic homeostasis [5], which lead to inflammation, cerebral edema, and further increases in ICP and reductions in cerebral perfusion pressure (CPP) [9]. The primary neurologic injury can also lead to alterations in the function of other organ systems, such as acute kidney injury, respiratory failure, and cardiac injury (Table 15.2) [5, 9–11]. Trauma patients often have other injuries, such as orthopedic fractures, intra-abdominal injuries, and spinal cord compromise [5]. These coexisting injuries, coupled with BBB dysfunction and neurologic inflammation, contribute to the development of secondary neurologic injury [5, 6].

Table 15.2 Effects of traumatic brain injury on other organ systems

Cardiovascular
• Sympathetic nervous system overactivity – Hypertension, tachycardia, increased cardiac output – Electrocardiogram changes mimicking myocardial ischemia • Neurogenic stunned myocardium/Takotsubo stress cardiomyopathy – Left ventricular dysfunction – Electrocardiogram changes: ST-segment elevation, T-wave inversion – Elevated cardiac enzymes: CK-MB, troponin • Cushing response: hypertension, bradycardia • Arrhythmias • Hemorrhagic shock • Hypotension
Respiratory
• Upper airway obstruction/inability to protect airway • Abnormal respiratory patterns: apnea, hypoventilation • Neurogenic pulmonary edema • Acute respiratory distress syndrome (ARDS) • Pneumonia • Pulmonary embolism • Pulmonary injuries: pneumothorax, hemothorax, pulmonary contusion, flail chest, aspiration, atelectasis
Musculoskeletal
• Cervical spine injury • Long bone or pelvic fractures
Gastrointestinal
• Aspiration risk due to "full stomach" • Stress-induced gastric ulcers (Cushing's ulcers) • Intra-abdominal injuries • Alterations in mucosal permeability and gastrointestinal absorption
Metabolic/endocrine
• Hyperglycemia, insulin resistance • Hypokalemia • Hyponatremia • Pituitary dysfunction • Diabetes insipidus • Syndrome of inappropriate antidiuretic hormone secretion (SIADH) • Increased catecholamine levels • Increased caloric demand
Hematologic
• Coagulopathy • Disseminated intravascular coagulation (DIC)
Other
• Sepsis, septic shock • Acute kidney injury • Autonomic dysfunction: hypertension, tachycardia, tachypnea, fever

Table 15.3 Time course and mechanisms of secondary insults in traumatic brain injury (Reprinted from Perioperative management of adult traumatic brain injury. Sharma D, Vavilala MS, pages 333–46, 2012, with permission from Elsevier/Anesthesiology Clinics 2012 June;30(2):333–46)

Secondary insult	Early causes	Delayed causes
Hypoxemia	Aspiration Apnea Pneumothorax Pulmonary contusion Endobronchial intubation Neurogenic pulmonary Edema	Adult respiratory distress syndrome Ventilator-acquired pneumonia Transfusion-related acute lung injury Pulmonary embolism
Hypotension	Associated high spinal cord injury Long bone fracture Thoracic/abdominal bleeding	Shock Sepsis
Hypercarbia	Apnea Brainstem injury Inadequate ventilation	Iatrogenic (opioids) Pneumonia
Hypocarbia	Unwanted hyperventilation	Unwanted hyperventilation
Hyperglycemia	Stress	Persistent/new onset
Seizures	Electrolyte abnormalities Hypoglycemia	Syndrome of inappropriate antidiuretic hormone
Vasospasm	–	In patients with traumatic subarachnoid hemorrhage
Intracranial hypertension	Mass effect of hematoma Herniation	Cerebral edema

15.2.1 Secondary Neurologic Injury

Secondary neurologic injury is neurologic compromise not directly caused by the mechanical trauma of TBI but rather resulting from physiologic perturbations following the initial injury that result in cerebral hypoxia and ischemia [8, 9]. Hypotension and hypoxemia are the two most important secondary insults that can worsen patient prognosis [9]. Systolic blood pressure (SBP) <90 mmHg in adults and PaO_2 <60 mmHg are independently associated with increased morbidity and mortality in TBI patients [9]. Additional secondary insults include hyper- and hypoglycemia, hyper- and hypocapnea, and elevated ICP (Table 15.3) [9].

Secondary injury can occur hours to days to months after the initial trauma and adversely affects outcomes [5, 6, 8, 9]. While surgery and anesthesia are often necessary components of TBI management, they can also predispose to additional secondary insults [9]. Thus, the perioperative period is a critical time for optimizing outcomes in TBI patients. Goals in the perioperative period include resuscitation and stabilization of the patient, as well as correcting and preventing additional physiologic perturbations that can lead to secondary neurologic injury [5, 9].

15.3 Head Injury Guidelines

In 1995, in an effort to standardize care and improve outcomes in TBI, the Brain Trauma Foundation collaborated with the American Association of Neurological Surgeons to create guidelines for the management of patients with severe traumatic brain injury [12]. The fourth, and most recent, edition of these guidelines was published in 2016 [13]. It provides 28 evidence-based recommendations to help guide TBI management in regard to treatment, monitoring, and thresholds (Tables 15.4, 15.5, and 15.6). Recommendations were made only when there was sufficient evidence to do so, and as such, the guidelines are not meant to serve as a complete clinical protocol. Rather, these guidelines are meant to supplement consensus and clinical judgment in the development of treatment protocols [13]. Adherence to these guidelines is variable, but research has demonstrated a causal relationship between guideline adherence and improved outcomes [14]. With the

Table 15.4 Updated treatment recommendations[a] (From Carney M, Totten AM, O'Reilly C, Ullman JS, Hawryluk GW, Bell MJ, et al. Brain Trauma Foundation. Guidelines for the management of severe traumatic brain injury, fourth edition. Neurosurgery. 2017 Jan 1;80(1):6–15. Used by permission of Oxford University Press/Congress of Neurological Surgeons)

Topic	Recommendations
Decompressive craniectomy	Level IIA
	• **Bifrontal DC is not recommended to improve outcomes as measured by the GOS-E score at 6 month post-injury in severe TBI patient with diffuse injury (without mass lesions) and with ICP elevations to values >20 mmHg for more than 15 min within a 1-h period that are refractory to first-tier therapies. However, this procedure has been demonstrated to reduce ICP and to minimize days in the ICU**
	• **A large frontotemporoparietal DC (not <12 × 15 cm or 15 cm diameter) is recommended over a small frontotemporoparietal DC for reduced mortality and improved neurologic outcomes in patients with severe TBI**
	*The committee is aware that the results of the RESCUEicp trial were released soon after the completion of these guidelines. The results of this trial may affect these recommendations and may need to be considered by treating physicians and other users of these guidelines. We intend to update these recommendations if needed. Updates will be available at https://braintrauma.org/coma/guidelines
Prophylactic hypothermia	Level IIB
	• **Early (within 2.5 h), short-term (48 h post-injury), prophylactic hypothermia is not recommended to improve outcomes in patients with diffuse injury**
Hyperosmolar therapy	Recommendations from the prior (third) edition not supported by evidence meeting current standards
	Mannitol is effective for control of raised ICP at doses of 0.25–1 g/kg body weight. Arterial hypotension (systolic blood pressure <90 mmHg) should be avoided
	Restrict mannitol use prior to ICP monitoring to patients with signs of transtentorial herniation or progressive neurologic deterioration not attributable to extracranial causes
Cerebrospinal fluid drainage	Level III
	• **An EVD system zeroed at the midbrain with continuous drainage of CSF may be considered to lower ICP burden more effectively than intermittent use**
	• **Use of CSF drainage to lower ICP in patients with an initial GCS <6 during the first 12 h after injury may be considered**
Ventilation therapies	Level IIB
	• Prolonged prophylactic hyperventilation with $PaCO_2$ ≤25 mmHg is not recommended
	Recommendations from the prior (third) edition not supported by evidence meeting current standards
	Hyperventilation is recommended as a temporizing measure for the reduction of elevated ICP
	Hyperventilation should be avoided during the first 24 h after injury when CBF is often reduced critically
	If hyperventilation is used, SjO_2 or $BtpO_2$ measurements are recommended to monitor oxygen delivery
Anesthetics, analgesics, and sedatives	Level IIB
	• Administration of barbiturates to induce burst suppression as measured by EEG as prophylaxis against the development of intracranial hypertension is not recommended
	• High-dose barbiturate administration is recommended to control elevated ICP refractory to maximum standard medical and surgical treatment. Hemodynamic stability is essential before and during barbiturate therapy
	• Although propofol is recommended in the control of ICP, it is not recommended for improvement in mortality or 6-month outcomes. Caution is required as high-dose propofol can produce significant morbidity

Table 15.4 (continued)

Topic	Recommendations
Steroids	Level I
	• The use of steroids is not recommended for improving outcomes or reducing ICP. In patient with severe TBI, high-dose methylprednisolone was associated with increased mortality and is contraindicated
Nutrition	Level IIA
	• **Feeding patients to attain basal caloric replacement at least by the fifth day and at most by the seventh day post-injury is recommended to decrease mortality**
	Level IIB
	• **Transgastric jejunal feeding is recommended to reduce the incidence of ventilator-associated pneumonia**
Infection prophylaxis	Level IIA
	• Early tracheostomy is recommended to reduce mechanical ventilation days when the overall benefit is thought to outweigh the complications associated with such a procedure. However, there is no evidence that early tracheostomy reduces mortality or the rates of nosocomial pneumonia
	• **The use of PI oral care is not recommended to reduce ventilator-associated pneumonia and may cause an increased risk of acute respiratory distress syndrome**
	Level III
	• Antimicrobial-impregnated catheters may be considered to prevent catheter-related infections during extraventricular drainage
Deep vein thrombosis prophylaxis	Level III
	• LMWH or low-dose unfractioned heparin may be used in combination with mechanical prophylaxis. However, there is an increased risk for expansion of intracranial hemorrhage
	• In addition to compression stockings, pharmacologic prophylaxis may be considered if the brain injury is stable and the benefit is considered to outweigh the risk of increased intracranial hemorrhage
	• There is insufficient evidence to support recommendations regarding the preferred agent, dose, or timing of pharmacologic prophylaxis for deep vein thrombosis
Seizure prophylaxis	Level IIA
	• Prophylactic use of phenytoin or valproate is not recommended for preventing late PTS
	• Phenytoin is recommended to reduce the incidence of early PTS (within 7 days of injury), when the overall benefit is thought to outweigh the complications associated with such treatment. However, early PTS have not been associated with worse outcomes
	• **At the present time, there is insufficient evidence to recommend levetiracetam compared with phenytoin regarding efficacy in preventing early post-traumatic seizures and toxicity**

$BtpO_2$ brain tissue O_2 partial pressure, *CBF* cerebral blood flow, *CSF* cerebrospinal fluid drainage, *DC* decompressive craniectomy, *EEG* electroencephalogram, *EVD* external ventricular drainage, *GCS* Glasgow Coma Scale, *GOS-E* Glasgow Outcome Scale-Extended, *ICP* intracranial pressure, *ICU* intensive care unit, *LMWH* low-molecular-weight heparin, *$PaCO_2$* partial pressure of arterial carbon dioxide, *PI* povidone-iodine, *PTS* posttraumatic seizures, *RESCUEicp trial* Randomized Evaluation of Surgery with Craniectomy for Uncontrollable Elevation of ICP trial, *SjO_2* jugular venous oxygen saturation, *TBI* traumatic brain injury

[a]Bold: New or revised recommendations

Table 15.5 Updated monitoring recommendations[a] (From Carney M, Totten AM, O'Reilly C, Ullman JS, Hawryluk GW, Bell MJ, et al. Brain Trauma Foundation. Guidelines for the management of severe traumatic brain injury, fourth edition. Neurosurgery. 2017 Jan 1;80(1):6–15. Used with permission from Oxford University Press/Congress of Neurological Surgeons)

Topic	Recommendations
Intracranial pressure monitoring	Level IIB
	• **Management of severe TBI patients using information from ICP monitoring is recommended to reduce in-hospital and 2-week post-injury mortality**
	Recommendations from the prior (third) edition not supported by evidence meeting current standards
	ICP should be monitored in all salvageable patients with a TBI (GCS 3–8 after resuscitation) and an abnormal CT scan. An abnormal CT scan of the head is one that reveals hematomas, contusions, swelling, herniation, or compressed basal cisterns
	ICP monitoring is indicated in patients with severe TBI with a normal CT scan if ≥2 of the following features are noted at admission: age >40 years, unilateral or bilateral motor posturing, or SBP <90 mmHg
Cerebral perfusion pressure monitoring	Level IIB
	• **Management of severe TBI patients using guideline-based recommendations for CPP monitoring is recommended to decrease 2-week mortality**
Advanced cerebral monitoring	Level III
	• Jugular bulb monitoring of $AVDO_2$, as a source of information for management decisions, may be considered to reduce mortality and improve outcomes 3 and 6 months post-injury

$AVDO_2$ arteriovenous oxygen content difference, *CPP* cerebral perfusion pressure, *CT* computed tomography, *GCS* Glasgow Coma Scale, *ICP* intracranial pressure, *SBP* systolic blood pressure, *TBI* traumatic brain injury
[a]Bold: New or revised recommendations

Table 15.6 Updated recommendations: thresholds[a] (From Carney M, Totten AM, O'Reilly C, Ullman JS, Hawryluk GW, Bell MJ, et al. Brain Trauma Foundation. Guidelines for the management of severe traumatic brain injury, fourth edition. Neurosurgery. 2017 Jan 1;80(1):6–15. Used with permission from Oxford University Press/Congress of Neurological Surgeons)

Topic	Recommendations
Blood pressure thresholds	Level III
	• **Maintaining SBP at ≥100 mmHg for patients 50–69 years old or at ≥110 mmHg or above for patients 15–49 or >70 years old may be considered to decrease mortality and improve outcomes**
Intracranial pressure thresholds	Level IIB
	• **Treating ICP >22 mmHg is recommended because values above this level are associated with increased mortality**
	Level III
	• A combination of ICP values and clinical and brain CT findings may be used to make management decisions
	*The committee is aware that the results of the RESCUEicp trial were released after the completion of these guidelines. The results of this trial may affect these recommendations and may need to be considered by treating physicians and other users of these guidelines. We intend to update these recommendations if needed. Updates will be available at https://braintrauma.org/coma/guidelines

Table 15.6 (continued)

Topic	Recommendations
Cerebral perfusion pressure thresholds	Level IIB
	• **The recommended target CPP value for survival and favorable outcomes is between 60 and 70 mmHg. Whether 60 or 70 mmHg is the minimal optimal CPP, threshold is unclear and may depend upon the autoregulatory status of the patient**
	Level III
	• Avoiding aggressive attempts to maintain CPP >70 mmHg with fluids and pressors may be considered because of the risk of adult respiratory failure
Advanced cerebral monitoring thresholds	Level III
	• Jugular venous saturation of <50% may be a threshold to avoid in order to reduce mortality and improve outcomes

CPP cerebral perfusion pressure, *CT* computed tomography, *ICP* intracranial pressure, *RESCUEicp trial* Randomized Evaluation of Surgery with Craniectomy for Uncontrollable Elevation of ICP trial, *SBP* systolic blood pressure
[a]Bold: New or revised recommendations

Table 15.7 Canadian CT head rule (Reprinted from The Lancet, volume 357, Stiell IG, Wells GA, Vandemheen K, Clement C, Lesiuk H, Laupacis A, et al. The Canadian CT head rule for patients with minor head injury, pages 1391–6, 2001, with permission from Elsevier)

CT head rule is only required for patients with minor head injuries with any one of the following:
High risk (for neurologic intervention) – GCS score <15 at 2 h after injury – Suspected open or depressed skull fracture – Any sign of basal skull fracture (hemotympanum, "raccoon" eyes, cerebrospinal fluid otorrhoea/rhinorrhoea, Battle's sign) – Vomiting ≥2 episodes – Age ≥ 65 years
Medium risk (for brain injury on CT) – Amnesia before impact >30 min – Dangerous mechanism (pedestrian struck by motor vehicle, occupant ejected from motor vehicle, fall from height >3 ft or five stairs)
Minor head injury is defined as witnessed loss of consciousness, definite amnesia, or witnessed disorientation in a patient with a GCS score of 13–15

fourth edition of these guidelines, the Brain Trauma Foundation is transitioning to a "Living Guidelines model" in which the literature will be constantly evaluated and updates to the recommendations will be made as the evidence warrants, rather than publishing updated editions every few years [13]. Specific recommendations from these guidelines will be discussed throughout this chapter.

15.4 Evaluation

Trauma patients undergo initial assessment and stabilization upon arrival to the emergency department. Not all patients with minor head injuries (GCS 13–15) require radiographic evaluation. Two slightly different sets of criteria, the Canadian CT Head Rule and the New Orleans Criteria, are widely used to determine which of these patients require computed tomography (CT) scanning based on clinical findings, patient factors, and the mechanism of injury (Tables 15.7 and 15.8) [15, 16]. All patients with moderate or severe head injuries require radiographic evaluation. Noncontrast multidetector CT is the test of choice in TBI because it is widely available, fast, and highly accurate for detecting injuries that require urgent or emergent neurosurgical intervention, such as hemorrhage, herniation, and hydrocephalus [17]. MRI is generally not used for the initial evaluation of TBI because it is less widely available, less sensitive for fractures, more time-consuming, relatively

Table 15.8 New Orleans criteria [16]

CT is recommended for patient with head trauma and any of these factors
– Headache
– Vomiting
– Age > 60 years
– Drug or alcohol intoxication
– Short-term memory deficits
– Physical evidence of trauma above the clavicles
– Seizure

CT computed tomography

more expensive, and incompatible with some medical devices and metallic foreign bodies [17]. Intravenous contrast is only indicated in cases of suspected vascular injury. Risk factors for traumatic vascular injury, many of which can be identified on noncontrast CT, include skull base fractures, LeFort II and III facial fractures, high cervical spine fractures, epistaxis, GCS ≤8, and traumatic axonal injury [17].

Indications for neurosurgical intervention in TBI include evacuation of mass lesions (e.g., hematomas), repair of vascular injuries, removal of foreign bodies, and decompressive craniectomy for elevated ICP. "Primary" decompressive craniectomy is performed in the early phase after TBI for evacuation of intracranial hematomas. "Secondary" decompressive craniectomy is part of a tiered therapeutic protocol used in the intensive care unit (ICU) to control elevated ICP [18]. The 2016 Brain Trauma Foundation guidelines make two recommendations regarding decompressive craniectomy [13]. First, bifrontal decompressive craniectomy is not recommended to improve outcomes in patients with severe TBI with diffuse injury (without mass lesions) and ICP >20 mmHg for more than 15 min in a 1-h period that is refractory to first-tier therapy. This procedure has been shown to decrease ICP and minimize ICU length of stay, but there are no outcome benefits 6 months post-injury, as measured by the Glasgow Outcome Scale-Extended (GOS-E) score [13]. Second, a large frontotemporoparietal decompressive craniectomy (at least 12 × 15 cm or 15 cm diameter) is recommended over a small craniectomy for reduced mortality and improved neurologic outcomes in patients with severe TBI [13]. The RESCUEicp trial [18] was published shortly after the release of the 2016 TBI guidelines. This study compared outcomes of secondary decompressive craniectomy plus medical therapy versus continued medical management alone in patients with TBI and refractory intracranial hypertension. Patients with ICP >25 mmHg despite medical management were randomly assigned to last-tier secondary decompressive craniectomy or continued medical management. At 6 months post-injury, patients who had undergone craniectomy had significantly lower mortality but higher rates of vegetative state and severe disability than those managed medically. Rates of moderate disability and good recovery were similar between the two groups [18]. These results seem to bolster the findings of other studies that have shown that while secondary decompressive craniectomy reduces mortality, it does not translate into survival with good quality of life [19]. Whether living with severe disability or in a vegetative state is preferable to death is subjective. The authors of the 2016 Brain Trauma Foundation guidelines have not amended their recommendations regarding decompressive craniectomy in light of the findings of the RESCUEicp trial [13].

If it is determined that surgical intervention is warranted, another focused, rapid evaluation should be conducted by the anesthesia provider prior to surgery [9]. The patient's airway, breathing, and circulation should be assessed, in addition to a brief neurologic exam evaluating level of consciousness (via GCS score) and pupillary responses [5, 9]. The patient should be evaluated for the presence of anemia, coagulopathy, appropriate blood glucose control, and adequate vascular access [9]. The presence of extracranial injuries should be assessed and considered as factors in the development of hypoxemia, anemia, and hemodynamic instability in the perioperative period [9].

15.5 Management

15.5.1 Airway

Airway management in TBI patients can be challenging due to a number of complicating factors. Urgent intubation may be needed due to hypoxia

or a patient's inability to protect his airway [9]. It may be difficult to assess the airway due to altered consciousness, the presence of a cervical collar, facial injuries, or blood or debris in the oral cavity [9]. All trauma patients should be assumed to have a cervical spine injury until proven otherwise [5] and should be considered at risk for aspiration due to a full stomach [5, 9]. Many patients with TBI will have intracranial hypertension, and care must be taken to avoid further elevations in ICP while securing the airway [5]. Tenuous hemodynamic status must also be considering when selecting the method of intubation, as many anesthetic agents can cause hypotension and cardiovascular depression that may not be tolerated by hypovolemic patients [5].

The appropriate technique for endotracheal intubation depends on the patient's injuries, the practitioner's expertise, and available resources [9]. Most patients can be managed with a rapid sequence intubation (RSI) using cricoid pressure and manual in-line stabilization to maintain neutrality of the cervical spine [9]. Newer airway devices, such as video laryngoscopes and lighted stylets, may improve visualization of the glottis, especially in difficult airway scenarios [5, 9, 20]. Fiber-optic laryngoscopy remains the "gold standard" for difficult airway management, particularly in the setting of cervical spine injury [5]. Nasal intubation is contraindicated in patients with basilar skull fractures, sinus injuries, midfacial fractures, and bleeding diatheses [5, 9]. In some cases, proceeding directly to cricothyroidotomy without attempting to instrument the airway may be appropriate [5]. Regardless of the initial technique selected, a backup plan should also be established in the event of a difficult intubation, as TBI patients will poorly tolerate increases in cerebral blood flow (CBF) and ICP that accompany hypoxemia and hypercarbia [9].

As all trauma patients are assumed to have cervical spine injuries until cleared, manual in-line stabilization should be used regardless of intubation technique [5]. Once manual in-line stabilization is established, the anterior portion of the cervical collar can be removed to allow for greater mouth opening [21]. The goal during manual in-line stabilization is to apply forces that are equal in force and opposite in direction to those generated by laryngoscopy, thereby reducing overall movement of the cervical spine during airway manipulation [21]. However, care must be taken to avoid the application of traction forces, which can cause excess distraction at the site of ligamentous compromise [21].

The first step in selecting an appropriate technique for airway management is to determine if an awake intubation is necessary. Awake intubations may be possible in severely head-injured patients but will be challenging in combative or uncooperative patients [8]. If the need for an awake intubation is ruled out, careful consideration should be given to the appropriate pharmacologic agents for anesthesia induction and muscle relaxation. The main goal during induction of anesthesia is to maintain CPP by avoiding hypotension and reducing ICP [5]. Propofol and etomidate are two commonly used induction agents for RSI, which reduce the cerebral metabolic rate of oxygen ($CMRO_2$) and decrease ICP by inducing cerebral vasoconstriction and reducing cerebral blood flow [9]. Propofol causes hypotension, especially in hypovolemic patients. The resulting decrease in CPP may be worse for the patient than would be a transient increase in ICP as the result of intubation [5]. While etomidate maintains hemodynamic stability during induction, even single doses have been shown to cause adrenal suppression, which may result in delayed hypotension and increased need for vasopressors [22]. This finding led many institutions to curtail the use of etomidate for emergency airway management [23, 24]. However, subsequent research has failed to demonstrate worse outcomes with single-dose etomidate [23–25], and it remains an appropriate agent for RSI in hypovolemic and hemodynamically unstable TBI patients. Ketamine has become a popular induction agent for RSI, especially in emergency departments, as it has been shown to provide excellent intubating conditions while inducing limited cardiovascular compromise [23]. Traditionally, brain injury has been considered a relative contraindication to the use of ketamine due to its ability to increase mean arterial blood pressure (MAP), leading to increases in CBF and ICP [9, 26]. However, more recent

research has questioned this belief, and new data suggest that ketamine can safely be used in patients with intracranial hypertension [26, 27]. The judicious use of adjuvants, such as narcotics and antihypertensive agents, may be necessary to control tachycardia, hypertension, and increased ICP during intubation [5]. These agents should be used cautiously due to the risk of decreased CPP if hypotension ensues. Esmolol can be used to rapidly control heart rate with less potential for hypotension than longer-acting agents. Nicardipine is an easily titratable calcium channel blocker that is frequently used for blood pressure control in patients with brain injury [5].

A muscle relaxant should be administered to prevent coughing and facilitate intubation [5]. Use of neuromuscular blockade during airway instrumentation is associated with improved intubating conditions, including improved laryngeal view and fewer number of intubation attempts, as well as reduced procedure-related complications [28, 29]. The choices for neuromuscular blockade for RSI are rocuronium and succinylcholine [30]. Traditionally, succinylcholine has been the drug of choice for rapid sequence intubation due to its rapid onset of action and short duration of action [30, 31]. However, now that sugammadex is widely available for the rapid reversal of rocuronium, the superiority of succinylcholine is no longer obvious [32]. Nondepolarizing neuromuscular blockers have been shown to prevent significant increases in ICP during stimulation of the airway, such as endotracheal suctioning [33]. The effects of succinylcholine on ICP are less clear. Some studies demonstrate a transient increase in ICP with the use of succinylcholine [34, 35], possibly related to increased carbon dioxide production or cerebral stimulation from fasciculations [5]. Other studies show no effect of succinylcholine on ICP [31, 36, 37]. Additionally, the clinical significance of succinylcholine-related changes in ICP is questionable, and pretreatment with a defasciculating dose of nondepolarizing muscle relaxant has not been shown to influence outcomes [31]. The need to rapidly and effectively secure the airway in order to prevent aspiration, hypoxemia, and hypercarbia outweighs the risk of transient increases in ICP with the use of succinylcholine [5, 8, 9].

15.5.2 Maintenance of Anesthesia

The ideal anesthetic for TBI patients is one that maintains hemodynamic stability and CPP, preserves cerebral autoregulation and carbon dioxide reactivity, optimizes surgical conditions, and allows for a smooth and rapid emergence to facilitate early postoperative neurologic assessment [38]. A variety of anesthetic agents can be employed to meet these goals, including total intravenous anesthesia, volatile anesthetics, or a combination of the two. Under normal conditions, CBF is coupled to $CMRO_2$. When the metabolic demands of the brain increase, CBF increases to deliver more oxygen and glucose and to remove carbon dioxide. When cerebral metabolism decreases, so too does CBF [39]. In general, intravenous anesthetics decrease $CMRO_2$ and CBF in parallel, leading to a reduction in ICP [39]. The exception is ketamine, which increases both CBF and $CMRO_2$ [39]. As mentioned previously, despite the increase in CBF, ketamine does not appear to cause an increase in ICP [26, 27]. In fact, a recent review by Zeiler et al. [40] found no studies demonstrating an increase in ICP following ketamine administration and three that showed a reduction in ICP. Opioids do not affect cerebral hemodynamics when ventilation is controlled [9]. Volatile anesthetics are cerebral vasodilators and "uncouple" CBF from cerebral metabolism, resulting in an increase in CBF despite a reduction in $CMRO_2$ [39]. This increase in CBF has the potential to cause increased ICP. However, at <1 minimum alveolar concentration (MAC), the vasodilatory effects of volatile anesthetics are minimal, and low concentrations can be safely used in the setting of intracranial hypertension [9]. Nitrous oxide increases CBF, cerebral metabolism, and ICP [39] and thus should be avoided in brain-injured patients.

Several studies have investigated the impact of anesthetic technique on intraoperative and postoperative conditions; however, recent reviews of

the literature have failed to uncover evidence of the superiority of specific anesthetic agents [38, 41]. Equivalent brain relaxation can be achieved with either propofol or volatile anesthetics [38]. Time to emergence is similar with sevoflurane and propofol-based anesthetics [41]. Rates of postoperative nausea and vomiting are lower with propofol than volatile anesthetics, but other postoperative complications and recovery profiles are similar [38, 41]. There are insufficient data to determine the effects of anesthetic technique on neurologic morbidity and mortality in TBI [9, 38, 41]. Hence, selection of a specific anesthetic agent is less important than tailoring management to achieve the overarching principal of preventing secondary neurologic injury. The 2016 Brain Trauma Foundation guidelines do not make recommendations regarding the intraoperative use of anesthetic agents. However, barbiturates and propofol are recommended for control of ICP in the ICU (Table 15.4) [13].

15.5.3 Ventilation

Controlled ventilation can help avoid secondary neurologic injury by maintaining normocarbia ($PaCO_2$ 35–45 mmHg) and adequate oxygenation (PaO_2 > 60 mmHg) and, when necessary, by facilitating surgical exposure and the short-term treatment of intracranial hypertension via hyperventilation [9]. Arterial PaO_2 and $PaCO_2$ should be closely monitored to ensure adequate gas exchange and to evaluate the effectiveness of hyperventilation [9, 12]. End-tidal CO_2 may not accurately reflect arterial CO_2 if a large alveolar-arterial CO_2 gradient exists [8]. The 2016 Brain Trauma Foundation guidelines recommend against prolonged prophylactic hyperventilation with PaCO2 <25 mmHg due to the risk of cerebral ischemia from cerebral vasoconstriction [13]. Prophylactic hyperventilation should be avoided during the first 24 h after injury when CBF is often critically reduced [13]. When employing hyperventilation, cerebral oxygen delivery should be monitored via measurements of jugular venous oxygen saturation or brain tissue oxygen partial pressure [9, 13]. Normocarbia should be restored prior to dural closure to allow for an accurate assessment of cerebral swelling [9]. A temporary scalp closure with a loose dural patch may be required in the setting of persistently elevated ICP [8].

Most patients with TBI that require surgical intervention are taken to the intensive care unit intubated and sedated postoperatively. Postoperative brain swelling peaks 12–72 h after injury, and thus a period of postoperative controlled ventilation is reasonable even after uncomplicated craniotomy [8]. Postoperative sedation and controlled ventilation can also be helpful to avoid hypertension and coughing or bucking on the endotracheal tube, which can cause intracranial bleeding or increased ICP [8]. However, accurate neurologic examination is critical in the perioperative period, and thus sedative agents should be short-acting and easily titratable [5].

15.5.4 Monitoring

Standard American Society of Anesthesiology (ASA) monitors should be employed for all TBI patients that require surgical intervention. Additionally, arterial catheterization is recommended to allow for continuous blood pressure monitoring and sampling for blood gas analysis, glucose control, and monitoring of coagulation status [9]. Central venous catheterization can be considered to aid in resuscitation, but emergent surgery should not be delayed in order to obtain central access [9]. Adequate vascular access in the form of multiple large-bore peripheral intravenous catheters should be established prior to surgery.

The 2016 Brain Trauma Foundation guidelines make several recommendations for cerebral monitoring. ICP monitoring is indicated for all patients with severe TBI to reduce in-hospital and 2-week post-injury mortality. Treatment is recommended for ICP >22 mmHg, as this is the threshold for increased mortality. Management decision should be based on a combination of ICP values and clinical and brain CT findings. Additionally, CPP should be monitored in all

patients with severe TBI and maintained at a minimum threshold of 60–70 mmHg. Due to the risk of respiratory failure, practitioners may consider avoiding aggressive attempts to maintain CPP >70 mmHg with fluids and vasopressors [13].

Advanced cerebral monitoring allows for evaluation of global and regional blood flow and oxygenation. Modalities include transcranial Doppler (TCD) ultrasonography, measurement of arteriojugular venous oxygen content difference ($AVDO_2$), and measurements of focal cerebral oxygenation. Although rarely used outside of research settings, microdialysis can be employed to evaluate brain metabolism, and electrocorticography can determine cortical spreading depression [13]. The 2016 Brain Trauma Foundation guidelines recommend jugular bulb monitoring to assess global cerebral oxygenation and provide information for management decisions. Jugular venous saturations of >50% should be maintained to reduce mortality and improve outcomes [13]. Saturations of <50% indicate the need to improve cerebral oxygen utilization, either by increasing oxygen supply or decreasing cerebral metabolic demands. Cerebral oxygen delivery can be improved by increasing the inspired oxygen concentration (FiO_2), increasing hemoglobin via blood transfusion, and increasing CPP by increasing MAP or decreasing ICP [9, 42]. Based on new, higher-quality evidence, the 2016 Brain Trauma Foundation guidelines removed the previous recommendation for the use of local brain tissue oxygen monitors to assess for focal ischemia [13]. Despite insufficient evidence for a formal recommendation, the noninvasive nature of TCD and near-infrared spectroscopy (NIRS) monitoring leads to their frequent use in the ICU in the care of patients with severe TBI [9]. NIRS allows for assessment of regional cerebral oxygenation without the need for invasive probes. TCD ultrasonography provides information regarding cerebral autoregulation, vasospasm, and blood flow velocity [9]. Regardless of which monitoring modalities are chosen, it is important to remember that outcomes are not affected by the monitoring per se but rather by the treatment decisions based on the information generated from those monitoring techniques [13].

15.5.5 Blood Pressure Management and Vasopressors

Hypotension following TBI is known to contribute significantly to secondary neurologic injury and adversely affects outcomes [9, 43]. In patients with intact cerebral autoregulation, systemic hypotension results in a compensatory cerebral vasodilation in an attempt to maintain adequate brain perfusion. This results in increased cerebral blood volume and a resultant increase in ICP [13]. In patients with compromised autoregulation, adequate cerebral perfusion is dependent on systemic blood pressure, with hypotension resulting in ischemia [13]. Traditionally, hypotension has been defined as systolic blood pressure (SBP) <90 mmHg, and this was the minimum threshold recommended in previous editions of the Brain Trauma Foundation guidelines [13]. However, more recent research supports a higher SBP threshold that varies by age. The 2016 Brain Trauma Foundation guidelines recommend maintaining SBP ≥100 mmHg for patients aged 50–69 years old and ≥110 mmHg for patients aged 15–49 or ≥70 years old [13].

While hypotension can contribute to secondary neurologic injury at any point following TBI, anesthesiologists are most concerned about intraoperative blood pressure management. Research by Sharma et al. [43] revealed that intraoperative hypotension occurs commonly during craniotomy for TBI, and risk factors include multiple and large brain lesions on preoperative CT scan, subdural hematoma, and longer duration of general anesthesia. Hypotension commonly occurs at the time of dural opening and may be a result of the sudden reduction in ICP and cessation of the Cushing response [44]. Risk factors for hypotension following dural opening include low GCS score, lack of mesencephalic cisterns on preoperative CT scan, and bilateral dilated pupils [44]. Knowledge of the risk factors for intraoperative hypotension allows the anesthesiologist to anticipate, and hopefully avoid, this complication.

Data comparing the effectiveness of various vasopressors in TBI are limited. A few small studies comparing norepinephrine to dopamine found similar effects on cerebral blood flow

velocity [45, 46] and cerebral oxygenation and metabolism [47], but the effects of norepinephrine were more consistent and predictable [46]. Dopamine was also found to increase ICP [45]. A larger single-center retrospective study found that phenylephrine is commonly used in TBI patients and generates greater increases in MAP and CPP compared to dopamine and norepinephrine, without a concomitant increase in ICP [48]. There is insufficient evidence to recommend the use of a specific vasopressor in the setting of TBI, and the choice should be guided by individual patient characteristics and clinical circumstances.

15.5.6 Intravenous Fluids

Fluid resuscitation in TBI patients is a delicate balance between avoiding and treating hypotension, replacing intravascular losses, and avoiding cerebral edema and worsening intracranial hypertension. The BBB is relatively impermeable to sodium, and thus water moves between the serum and brain tissue depending on the osmolality of each. When serum osmolality is lower than that of the brain, water exits the vasculature and crosses the BBB, resulting in cerebral edema. While this process occurs even with an intact BBB, the risk of cerebral edema is worsened in the setting of TBI and BBB disruption [8]. In this setting, warm, non-glucose containing, isotonic crystalloid solutions, such as 0.9% saline, PlasmaLyte, or Normosol, are preferable. Hypotonic solutions, such as hypotonic saline or lactated Ringer's, should be avoided because they decrease serum osmolality and promote cerebral edema.

Peripheral tissue edema occurs with large-volume fluid resuscitation with isotonic crystalloids due to the reduction in colloid oncotic pressure. However, the colloid oncotic pressure gradients in cerebral vasculature are weaker than those generated by osmolar gradients, and cerebral edema does not occur in normal brain tissue in the setting of reduced colloid oncotic pressure as long as serum osmolality is maintained [8]. The use of colloids in TBI is controversial. A post hoc analysis of the Saline versus Albumin Fluid Evaluation (SAFE) study demonstrated increased mortality and worse neurologic outcomes at 24 months in TBI patients who were resuscitated with 4% albumin versus those who received 0.9% saline [49]. An additional post hoc analysis demonstrated that the use of albumin was associated with elevated ICP and an increased need for additional interventions to treat intracranial hypertension, which was postulated to be responsible for the increased mortality in this patient population [50]. Based on these findings, the use of albumin in TBI patients was widely discouraged. However, Van Aken et al. [51] questioned the validity of this conclusion. They evaluated the physicochemical characteristics of the albumin solution used in the SAFE trial and found it to be hypo-osmolar compared to serum. The authors suggest that, rather than avoiding all colloid solutions, a more appropriate conclusion to the SAFE trial is to avoid the use of hypo-osmolar solutions in patients with TBI.

Hypertonic saline may be considered for low-volume resuscitation of TBI patients due to its ability to improve cerebral perfusion while reducing ICP, replenish intravascular volume, improve tissue perfusion, and modulate the inflammatory response to trauma, which may reduce the development of multiorgan failure [52]. However, two randomized controlled trials of prehospital resuscitation with hypertonic saline versus conventional fluids in trauma patients showed no difference in survival or neurologic outcome at 6 months post-injury [52, 53].

In summary, the goals of fluid resuscitation of the head-injured patient include avoiding and treating hypotension, replenishing intravascular volume, and maintaining serum osmolality to prevent cerebral edema and worsening intracranial hypertension. Based on available evidence, glucose-free isotonic crystalloids should be administered to achieve these goals.

15.5.7 Management of ICP

The 2016 Brain Trauma Foundation guidelines recommend maintaining ICP $\leq$22 mmHg, as values above this threshold are associated with increased mortality [13]. ICP management intraoperatively is often very different than that

undertaken in the ICU setting. Patients with severe TBI may present emergently for decompressive craniectomy or hematoma evacuation without an indwelling ICP monitor. In these situations, evidence of intracranial hypertension may be evident from CT scan (e.g., midline shift, ventricular effacement) and physical exam findings (e.g., fixed and dilated pupils, posturing). For patients at imminent risk of cerebral herniation, the goal is to reduce ICP until the dura is opened, at which point ICP becomes zero. Intraoperative techniques that may be employed to acutely reduce ICP include hyperventilation, hyperosmolar therapy, CSF drainage, head elevation, and maintenance of venous cerebral drainage.

Hyperventilation reduces ICP by causing cerebral vasoconstriction, which results in reduced cerebral blood volume. While the prophylactic use of hyperventilation is discouraged by the 2016 Brain Trauma Foundation guidelines [13] due to the risk of cerebral ischemia, it is a reasonable technique for short-term, acute ICP management in patients with evidence of intracranial hypertension. Hyperosmolar therapy, using either mannitol or hypertonic saline, reduces ICP by creating an osmotic gradient that draws water from brain tissue, reduces cerebral edema, and stimulates osmotic diuresis. Additionally, these agents reduce blood viscosity, improve microcirculatory flow, and improve cerebral tissue oxygen delivery, which induces a reflexive vasoconstriction of cerebral arterioles, leading to reduced cerebral blood volume and ICP [13, 54]. Mannitol also decreases CSF production and reabsorption, thereby reducing ICP by decreasing CSF volume [54]. There is insufficient evidence on clinical outcomes for the 2016 Brain Trauma Foundation guidelines to make a specific recommendation or support a specific hyperosmolar agent for use in patients with severe TBI [13]. The authors of the 2016 guidelines state that "[the] Committee is universal in its belief that hyperosmolar agents are useful in the care of patients with severe TBI. However, the literature does not currently support recommendations that meet the strict criteria for contemporary evidence-based medicine approaches for guideline development" [13]. Despite the lack of a specific recommendation, existing literature suggests mannitol is effective at reducing ICP at doses of 0.25–1 g/kg body weight [9]. Hypovolemia and hypotension can result from osmotic diuresis, and practitioners should be prepared to treat this potential side effect.

An external ventricular drainage (EVD) system allows for both ICP measurement (while in the closed position) and CSF drainage (when in the open position). This can be advantageous for both the intraoperative and ICU management of patients with severe TBI. The 2016 Brain Trauma Foundation guidelines recommend continuous CSF drainage from an EVD leveled at the midbrain for more effective ICP control than that achieved with intermittent drainage [13]. The guidelines also recommend the use of CSF drainage to lower ICP during the first 12 h after injury in patients with an initial GCS <6 [13]. Care must be taken not to remove an excessive amount of CSF, which can lead to complications such as intracranial hemorrhage and brainstem herniation [55].

Simple techniques to aid in ICP reduction include head elevation and maintenance of cerebral venous drainage. Elevating the head of the bed up to 30° aids in venous drainage and reduces passive cerebral blood flow due to gravity. However, head elevation intraoperatively exposes the patient to the risk of venous air embolism during craniotomy, and proper precautions should be taken for the monitoring and treatment of this potential complication. Proper head and neck positioning should be ensured to maintain adequate cerebral venous drainage. Compromised jugular venous drainage, which can be caused by extreme neck flexion, external compression from malpositioned endotracheal tube or tracheostomy ties, or internal obstruction by venous catheters, can result in cerebral vascular congestion and increased ICP.

Barbiturates and other sedatives are routinely used to control ICP in the ICU setting. However, these drugs are not commonly used intraoperatively due to the preference for short-acting, easily titratable anesthetics that allow for accurate postoperative neurologic assessment. A detailed

discussion of the use of barbiturates and sedatives for ICP control in the ICU is outside the scope of this chapter.

15.5.8 Blood Transfusion

Anemia is common in patients with severe TBI and may contribute to secondary neurologic injury due to decreased cerebral oxygen delivery [56, 57]. The causes of anemia in critically ill patients include primary blood loss (e.g., trauma, gastrointestinal bleeding, surgical blood loss), hemodilution secondary to fluid resuscitation, phlebotomy, altered red blood cell production, and decreased red blood cell lifespan [58]. In the face of anemia, the body attempts to maintain cerebral oxygen delivery by increasing sympathetic tone via activation of aortic and carotid chemoreceptors, which results in increased heart rate and left ventricular stroke volume, leading to increased cardiac output and CBF [58, 59]. Anemia is associated with decreased blood viscosity, which improves microvascular perfusion and promotes venous return [58]. Additionally, tissue oxygen extraction is enhanced in the setting of anemia, and endothelial and neuronal production of nitric oxide increases, resulting in cerebral vasodilation and increased CBF [58]. At the cellular level, anemia stimulates the production of neuroprotective factors, such as hypoxia-inducible factor, erythropoietin, and vascular endothelial growth factor, which protect cells from ischemia and stimulate adaptation to chronic hypoxia [58, 59]. Despite these compensatory mechanisms, anemia is associated with increased in-hospital mortality [57] and poor outcomes in patients with severe TBI [58, 60]. Cerebral injury in anemic patients may be due to a number of factors, including tissue hypoxia, anemic cerebral hyperemia, embolic events, damage from reactive oxygen species, inflammation, and BBB disruption [59].

Twenty years ago, liberal transfusion parameters were commonly used in the ICU due to the belief that critically ill patients would poorly tolerate anemia [61]. More recent research, however, has shown improvements in morbidity and mortality with a more restrictive transfusion strategy [62, 63]. Blood transfusion is associated with complications such as infection, organ dysfunction, respiratory failure, increased ICU and hospital length of stay, and increased mortality [62, 63]. Current guidelines recommend a transfusion threshold of hemoglobin <7 g/dL for hemodynamically stable adult patients, including those who are critically ill [64]. For patients undergoing orthopedic or cardiovascular surgery or those with preexisting cardiovascular disease, the recommended transfusion threshold is hemoglobin <8 g/dL [64]. However, given how detrimental anemia is to patients with severe TBI, researchers have questioned whether these recommendations should be applied in the setting of acute brain injury. Theoretically, transfusion of red blood cells should increase oxygen delivery to the brain, thereby reducing the risk of secondary neurologic injury from hypoxia. However, studies have not consistently demonstrated that increased hemoglobin is associated with improved brain tissue oxygenation ($PbtO_2$) [65, 66]. Additionally, elevated hematocrit from blood transfusion may reduce CBF due to an increase in blood viscosity, potentially increasing the risk of cerebral ischemia [67]. Blood transfusion in patients with severe TBI is associated with poor long-term outcomes [56, 60, 68], including increased mortality [60]. Thus, the risks of anemia in the setting of TBI must be weighed against those of blood transfusion. There is insufficient evidence to recommend a specific transfusion threshold in this patient population. However, based on available data, a liberal transfusion threshold (hemoglobin <10 g/dL) is not recommended for most patients [58, 60]. Transfusion triggers should be individualized and guided by risk factors for poor tolerance to anemia (e.g., ischemic heart disease) or evidence of cerebral hypoxia. In patients without these characteristics, a restrictive transfusion strategy (hemoglobin <7 g/dL) is likely appropriate [58].

15.5.9 Glycemic Control

Hyperglycemia is common in critically ill patients and is associated with increased morbidity and mortality in patients with severe TBI [69–71].

Following head injury, circulating levels of catecholamines increase due to a systemic stress response. This, in turn, results in elevated serum glucose [70]. Additional causes of hyperglycemia in acute illness include insulin insufficiency, insulin resistance, and impaired glucose utilization [72]. Whether hyperglycemia is merely a marker of TBI severity or directly contributes to poor outcomes has been debated, with several studies identifying hyperglycemia as an independent risk factor for poor outcomes in TBI [70, 71]. Hyperglycemia contributes to secondary neurologic injury via a variety of complex mechanisms, including oxidative injury from free radical formation, activation of *N*-methyl-D-aspartate (NMDA) receptors, increased intracellular calcium, activation of inflammatory and apoptotic pathways, and altered lactate metabolism and tissue acidosis [69]. Additionally, BBB disruption leads to dysregulation of CBF, alterations in cerebral glucose transport and utilization, and excitotoxicity [72].

Given the association between hyperglycemia and poor outcomes in critically ill patients, researchers have sought to elucidate the optimal range of glycemic control for this patient population. An early study found that intensive insulin therapy to maintain blood glucose <110 mg/dL resulted in reduced morbidity and mortality for surgical ICU patients [73]. Subsequent studies, however, have demonstrated increased complication rates and no mortality benefit with intensive insulin therapy compared to conventional glycemic control (blood glucose <180 mg/dL) [74–76]. Hypoglycemia is of particular concern in brain-injured patients, as even moderate reductions in serum glucose may induce cerebral metabolic distress and neuroglycopenia [77]. Following TBI, there is a profound increase in glucose utilization (hyperglycolysis) and an inability to utilize ketone bodies as an energetic substrate [78]. As such, hypoglycemia could have devastating consequences in this setting. Several researchers have investigated the use of intensive versus conventional glycemic control in TBI patients [69, 77, 78]. In these studies, intensive insulin therapy was associated with more frequent episodes of hypoglycemia, although no differences in mortality or long-term neurologic outcomes were found [69, 77, 78]. There is a paucity of data regarding the best strategy for intraoperative glycemic control in TBI patients. As such, the previously cited data from ICU patients is extrapolated to the operative environment. Based on available data, no formal recommendation for glycemic control was included in the 2016 Brain Trauma Foundation guidelines [13]. Intermediate glucose control, avoiding both hyper- and hypoglycemia, appears to be a reasonable approach.

15.5.10 Temperature Control

Induced hypothermia has been successfully used to improve neurologic outcomes in the settings of cardiac arrest and neonatal hypoxic-ischemic encephalopathy [79]. Hypothermia has also been employed in the management of other types of brain injuries, such as ischemic strokes and TBI, although there is less evidence supporting its use in these settings [79, 80]. The mechanisms by which hypothermia provides neurologic protection include decreased cerebral metabolism, augmentation of apoptotic cell death, attenuation of inflammation and free radical production, decreased release of excitatory neurotransmitters, restoration of BBB integrity, and decreased vascular permeability [79, 81]. Hypothermia reduces cerebral metabolism by 5% for every 1 °C reduction in core body temperature, resulting in cerebral vasoconstriction, a reduction in cerebral blood volume, and a decrease in ICP [81]. Although induced hypothermia appears to offer several possible neurologic benefits, the technique is not without risks. Complications include coagulopathy, infection, hypotension, and cardiac dysrhythmias [13, 82], as well as complications associated with rewarming, including rebound intracranial hypertension and shock [82].

Despite its proven utility in other settings, hypothermia has not been consistently demonstrated to reduce mortality or improve outcomes in TBI. A Cochrane Review of 37 randomized trials found no high-quality evidence of benefit

from the use of hypothermia in patients with TBI [80]. Although hypothermia is often used as a method to control intracranial hypertension in the ICU, there is no evidence of improved neurologic outcomes in TBI compared to standard methods of ICP reduction [83]. There is insufficient evidence to recommend widespread use of hypothermia for neuroprotection after TBI [82]. In fact, the 2016 Brain Trauma Foundation guidelines recommend against the use of early (within 2.5 h), short-term (<48 h post-injury), prophylactic hypothermia [13].

Spontaneous temperature dysregulation is common in the setting of brain injury [84]. Fever following TBI is associated with increased mortality and worse neurologic outcomes [84, 85]. Both the degree and duration of post-injury pyrexia are correlated with long-term neurologic outcomes in TBI; even brief, mild hyperthermia (37.3–38 °C) is associated with worse outcomes and higher mortality [84]. Temperature regulation and avoidance of hyperthermia are an important aspect of TBI management.

15.5.11 Corticosteroids

BBB disruption following TBI can lead to the development of cerebral edema. Corticosteroids, particularly dexamethasone, are commonly used to control cerebral edema in other settings, such as intracranial tumors. In the case of tumor-induced cerebral edema, steroids act to regulate tumor mediators, stabilize the BBB, and decrease vascular permeability [86]. For decades, steroids were administered in head injuries with the goal of reducing cerebral edema via similar mechanisms, although there was little supporting evidence [13]. However, the Corticosteroid Randomization After Significant Head Injury (CRASH) trial demonstrated increased risk of 2-week and 6-month mortality, as well as severe disability, in TBI patients who had received high-dose methylprednisolone [87, 88]. Steroid administration in TBI is also associated with higher rates of infection and gastrointestinal bleeding [89]. According to the 2016 Brain Trauma Foundation guidelines, steroids are not recommended to improve outcomes or reduce ICP, and high-dose methylprednisolone is contraindicated in severe TBI [13].

15.5.12 Seizure Prophylaxis

Post-traumatic seizures are a common complication of TBI, affecting over 20% of patients in the ICU [90] and up to 25% of patients chronically [91]. Post-traumatic seizures promote secondary neurologic injury and are associated with poor outcomes [90]. Seizures increase ICP, promote cerebral edema, and result in cerebral metabolic crisis, which is characterized by reduced oxidative metabolism and increased glucose consumption, resulting in an increased lactate/pyruvate ratio and decreased extracellular glucose level [90]. Seizures also induce excitotoxicity, leading to cell membrane disruption and cell death [90].

Post-traumatic seizures are defined as immediate (occurring <24 h after injury), early (occurring 24 h to 7 days after injury), or late (occurring >7 days after injury). The majority of early seizures are nonconvulsive and thus go unrecognized unless continuous electroencephalography (EEG) is used [92, 93]. Prophylactic anticonvulsants are routinely administered following TBI in order to prevent post-traumatic seizures and reduce the potential for secondary neurologic injury and post-traumatic epilepsy. However, studies have shown that anticonvulsant prophylaxis is only effective in preventing early seizures and does not impact morbidity or mortality following severe TBI [94, 95]. Thus, the current recommendation is to discontinue prophylaxis 1 week after injury [13].

Traditionally, phenytoin has been the drug of choice for post-traumatic seizure prophylaxis. However, phenytoin is associated with numerous side effects, including significant drug-drug interactions due to its induction of the hepatic cytochrome P450 system [96]. Additionally, phenytoin is known to cause cutaneous hypersensitivity reactions, fever, and altered level of consciousness in some patients [97]. Phenytoin also has a narrow therapeutic window and

requires close monitoring of serum drug levels [96, 97]. Several studies have found levetiracetam to be equally effective as phenytoin at preventing early post-traumatic seizures [96–98]. Levetiracetam is an attractive alternative due to its better side effect profile and wider therapeutic index, which obviates the need to monitor serum drug levels [98]. Although the use of levetiracetam in this setting is increasing, the available comparative studies were insufficient for the Brain Trauma Foundation to recommend its use over phenytoin in the 2016 guidelines [13].

Data regarding intraoperative seizures following TBI is lacking. Prophylactic anticonvulsants should be continued for 7 days following injury, and care must be taken that scheduled doses are not missed while patients are in the operating room. Conversion of enteral dosages to intravenous administration may be required depending on surgical timing. Intraoperative prophylactic anticonvulsants may be indicated outside the window of early post-traumatic seizures in select patients. For example, a patient undergoing decompressive craniectomy >1 week after injury may be at risk of intraoperative seizures due to intracranial pathology and cerebral stimulation during surgery. The use of prophylactic anticonvulsants in such settings should be a collaborative determination between the surgeon and anesthesia provider. As discussed previously, phenytoin can alter the metabolism of many medications. Phenytoin use has been associated with resistance to the effects of nondepolarizing muscle relaxants, including pancuronium, vecuronium, and rocuronium [99]. Phenytoin may also precipitate in some electrolyte solutions [100] and should not be administered through the same intravenous line as continuous intravenous anesthetics.

15.6 Concussion

The terms mild traumatic brain injury and concussion are often used interchangeably. Mild traumatic brain injury is defined as a GCS score of 13–15 within 24 h of head injury. Concussion, on the other hand, is a clinical syndrome that describes the neurological, cognitive, and behavioral symptoms that result from a transient disruption of normal brain function by a biomechanical force [3]. Public awareness of the risks and ramifications of concussions, particularly in the setting of organized sports, has increased dramatically in recent years. It is estimated that between 1.6 million and 3.8 million athletes suffer concussions each year [101], and up to 50% of concussion may go unreported [4]. Studies have found that the vast majority of patients who visit the emergency department for sports- and recreation-related TBI are treated and released, suggesting that their injuries are mild [102]. However, up to 25% of such patients have persistent signs and symptoms 1 year after injury, which suggests that the term "mild TBI" may be a misnomer in these cases [102]. Risk factors for prolonged recovery after concussion include history of prior concussions; younger age; preexisting learning disability, attention deficit, or psychiatric diagnoses; symptoms of migraine headache, fogginess, or dizziness; and on-field mental status change [101].

Similar to the pathogenesis described for severe TBI, head injury in mild TBI results in a metabolic crisis due to a massive flux of ions and excitatory neurotransmitters within the brain. This crisis is characterized by transmembrane ion imbalance, hyperglycolysis, and mitochondrial dysfunction. Decreased cerebral perfusion exacerbates this process by creating a metabolic mismatch of high glucose demand and impaired delivery. The acute hypermetabolic state is followed by a prolonged subacute hypometabolic phase, characterized by inflammation and microstructural injury [3]. These changes result in a disturbance of brain function and produce symptoms from physical, cognitive, and emotional domains. Unlike severe TBI, however, gross structural injuries are absent [103]. It is theorized that the symptoms of concussion are related to the metabolic mismatch created by reduced cerebral blood flow in the setting of cerebral hypermetabolism [3, 103]. Symptoms of concussion include headache, dizziness, photophobia, phonophobia, nausea, drowsiness, difficulty concentrating, slowed processing, slowed

reaction time, and amnesia [3, 103]. Concussed patients are also at higher risk of subsequent concussions, a phenomenon known as "second impact syndrome" [103]. Repetitive concussions can result in cognitive and behavioral dysfunction, ranging from mild memory impairment to gross dementia, as well as pituitary dysfunction, most commonly hyposomatism and hypogonadism [101].

Given the prevalence of concussions, particularly in recreational activities that may be associated with other injuries, anesthesia providers may frequently encounter these patients. There is a lack of definitive experimental or clinical data regarding the impact of anesthesia on the concussed brain. Management of these patients requires a balance of concern regarding the potential for impaired neurologic recovery versus suboptimal surgical or orthopedic outcomes due to unnecessary surgical delays. Although the impact of anesthesia and surgery on concussion recovery is unknown, several physiologic changes have been shown to occur following concussion that may have ramifications for the administration of anesthesia. Within 3 days of injury, alterations in vascular myogenic tone and vagal tone occur [103]. Autonomic nervous system dysfunction, particularly in the first 7–10 days after injury, may lead to inappropriate hemodynamic responses and reduced capacity to appropriately react to increased metabolic demands [103]. Additionally, cerebrovascular response to CO_2 may be impaired [103]. Autoregulation of cerebral blood flow may be impaired or even abolished, exposing the injured brain to risk of secondary neurologic injury during periods of even mildly reduced cerebral perfusion pressure [104]. Thus, although it is not yet possible to definitively show the impact of anesthesia on concussion recovery, the injured brain is clearly vulnerable to additional harm. Avoidance of elective anesthetics, particularly in the acute postconcussive phase, seems prudent. Thus, it is reasonable to postpone elective procedures at least until postconcussive symptoms have resolved. When anesthesia cannot be avoided in these patients, utmost care must be taken to prevent secondary neurologic injury.

15.7 Summary

TBI is very prevalent and is associated with significant morbidity and mortality. Anesthesia providers will often be faced with the management of these patients, and the primary goals of care are patient resuscitation and avoidance of secondary neurologic injury. The 2016 Brain Trauma Foundation guidelines for the management of severe traumatic brain injury represent an effort to improve outcomes in this patient population through the implementation of evidence-based practices and standardized care. Anesthesia providers play a critical role in optimizing outcomes and decreasing mortality in these vulnerable patients. Further research is needed to elucidate additional means by which the care of patients with brain injury can be improved.

Key Points

- Traumatic brain injury (TBI) is an important public health concern associated with significant morbidity and mortality. In the United States, nearly three million people are diagnosed with TBI annually, and almost four million concussions occur each year.
- The primary goals of anesthetic care for patients with TBI are patient resuscitation and avoidance of secondary neurologic injury. Hypotension and hypoxemia are the two most important secondary insults that can worsen patient prognosis. Systolic blood pressure should be maintained ≥100 mmHg for patients aged 50–69 years old and ≥110 mmHg for patients aged 15–49 or ≥70 years old.
- The ideal anesthetic for TBI patients is one that maintains hemodynamic stability and cerebral perfusion pressure, preserves cerebral autoregulation and carbon dioxide reactivity, optimizes surgical conditions, and allows for a smooth and rapid emergence to facilitate early postoperative neurologic assessment.

- The goals of fluid resuscitation of the head-injured patient include avoiding and treating hypotension, replenishing intravascular volume, and maintaining serum osmolality to prevent cerebral edema and worsening intracranial hypertension. Glucose-free isotonic crystalloids should be administered to achieve these goals.
- Elective anesthetics should be avoided in patients with recent concussions. When anesthesia cannot be avoided in these patients, utmost care must be taken to prevent secondary neurologic injury.

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