



Neuromonitoring in the Intensive Care Unit for Treatment and Prognostication

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Key Learning Points

- Describe the indications, risks, and benefits for invasive intracranial pressure (ICP) monitoring.
- Define vasospasm and delayed cerebral ischemia (DCI) in aneurysmal subarachnoid hemorrhage (aSAH) and describe the monitoring modalities used for early detection.
- Apply information gathered from continuous electroencephalograms (EEGs) to diagnose brain injury and monitor response to therapy.
- Interpret fluctuations in vital signs and laboratory values in patients with brain and spinal injury.
- Summarize the approach to neuroprognostication post cardiac arrest and identify the limitations of prognostication.

Case 1: Traumatic Brain Injury

A 42-year-old man presented to the emergency department following a motor vehicle accident with head trauma and loss of consciousness. On arrival he had a laceration over the left side of his head with a blood pressure (BP) of 170/65 mmHg, heart rate (HR) 42 bpm, oxygen saturation 95%, and irregular respirations. On his neurologic exam he was minimally responsive to noxious stimulation with a Glasgow Coma Scale (GCS) of 6 and had a fixed, dilated pupil on the right. He was intubated for airway protection, and non-contrast computed tomography (CT) scan of the head revealed bi-frontal contusions, a traumatic right-sided subdural hematoma (SDH), and traumatic subarachnoid hemorrhage (SAH) consistent with severe traumatic brain injury (TBI). He was treated with hyperventilation and mannitol 1 g/kg and taken to the operating room (OR) for SDH evacuation and placement of an intracranial pressure (ICP) monitor. In the Neurologic Intensive Care Unit (Neuro ICU), his initial ICP reading was sustained at 30 mmHg with a blood pressure of 110/55 mmHg (mean arterial pressure [MAP] 73 mmHg) and over 1 liter of urine output since arrival. A central line was placed, and he was given 23.9% hypertonic saline and started on continuous infusions of 2% hypertonic saline and sedation. Following this, his ICP normalized, he had equal and reactive pupils, and was localizing with his right upper extremity. In the following

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week he continued to have ICP elevations responsive to similar medical interventions. His ICP eventually stabilized and on neurologic exam he was awake, following simple commands and tolerating spontaneous breathing trials.

Clinical Application of ICP Monitoring

Elevated ICP is a frequent problem in TBI patients with the majority requiring medical intervention. The space within the skull is fixed and composed of three materials: brain, blood, and cerebral spinal fluid (CSF). An increase in volume of any of these components or addition of a new component, e.g., cerebral edema, results in displacement of the other components. Once a critical volume of displacement is reached, any further increase in volume will directly translate into an elevation in the intracranial pressure (see Fig. 39.1). The approach to managing high ICP is generally the same regardless of the pathology, with the aim being to decrease either cerebral spinal fluid (CSF), blood, or cerebral edema volume within the skull to relieve pressure on the brain.

To directly measure ICP, patients require surgical placement of either an intraparenchymal monitor or an external ventricular drain (a full discussion on ICP monitors can be found in Chap. 12). Severe TBI patients (GCS 3–8) and other comatose patients clinically suspected of having elevations in ICP should be considered for placement of one of these monitors [1]. Current recommendations are to target an ICP less than 22 mmHg, which is typically achieved using the

three-tiered approach to ICP elevations shown in Fig. 39.2 [2].

In the case above, high ICP was suspected given the clinical features of Cushing's triad that includes widened pulse pressure, bradycardia, and irregular respirations [3]. Although this response is not commonly observed, it represents decreased cerebral perfusion and increased carbon dioxide tension in the setting of elevated ICP [4]. Other clinical features suggestive of elevated ICP include abnormal mental status or coma, asymmetric pupils, and decorticate or decerebrate posturing of the extremities.

Hyperventilation is a strategy commonly employed in the initial treatment algorithm for ICP exacerbations. All patients with elevated ICP should be mechanically ventilated and have arterial levels of CO_2 (PaCO_2) monitored frequently. PaCO_2 is one of the major determinants of cerebrovascular autoregulation and the level in the blood directly correlates with cerebral blood flow (CBF). Lower levels of CO_2 in the brain cause vasoconstriction and can reduce blood flow while higher levels cause vasodilation and can increase blood flow. When ICP is elevated, hyperventilation reduces PaCO_2 levels, which leads to reduced blood volume in the brain and can aid in lowering the ICP. This should only be used as a temporizing measure as prolonged PaCO_2 below 20 mmHg leads to cerebral ischemia and has not been shown to provide any benefit [5, 6]. In patients at risk for ICP elevations, it is crucial to continue monitoring PaCO_2 levels and target normal values (35–45 mmHg) to prevent hyperemia or ischemia.

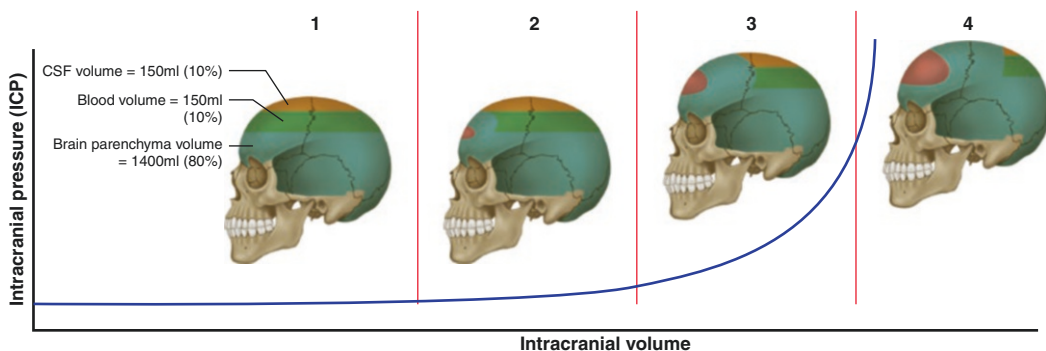
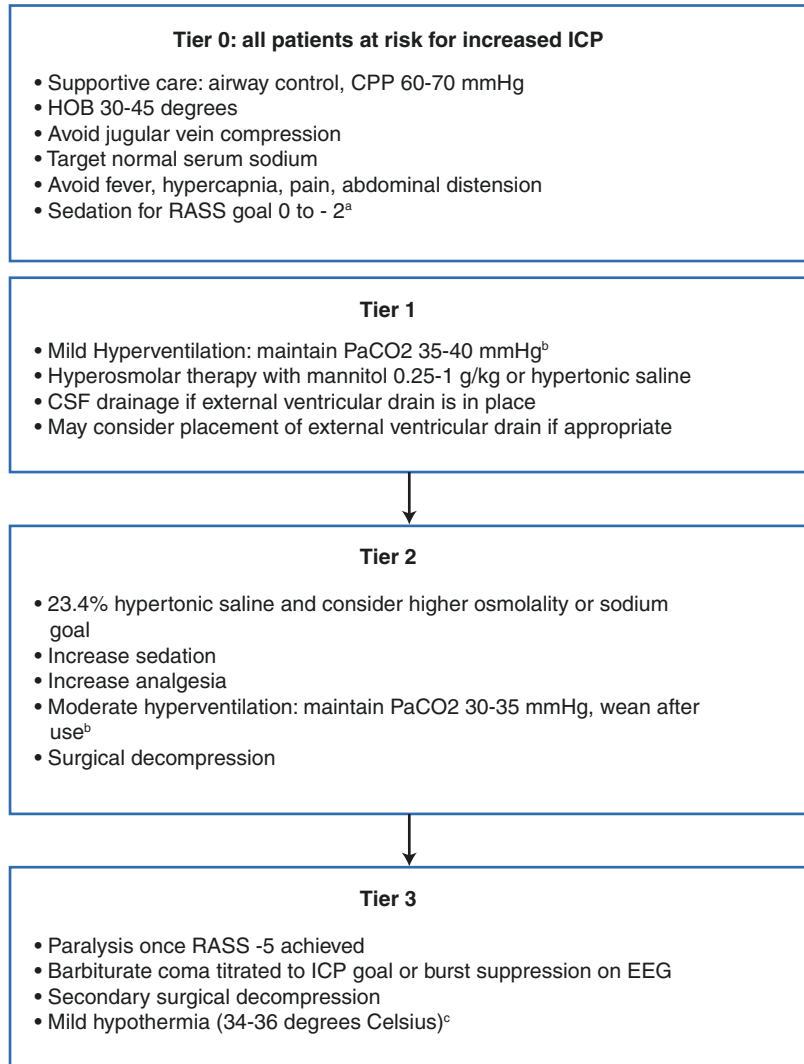


Fig. 39.1 Monro-Kellie doctrine

Fig. 39.2 A three-tiered approach to management of intracranial pressure (ICP) elevations. All at-risk patients should undergo tier 0 and, in the presence of elevated ICP, lower tier should be attempted before moving onto the next tier. Many examples of this algorithm have been developed based on information from clinical trials and professional guidelines. Institution of an algorithm like this has been shown to improve patient care and outcomes [1, 144, 145]



Cerebral Perfusion Pressure

When ICP is continuously monitored, it can be used to calculate the patient's cerebral perfusion pressure (CPP). CPP is the pressure gradient across the vasculature in the brain that drives cerebral blood flow (CBF) and subsequently oxygen delivery; it is proportional to the difference in MAP and the intracranial resistance, or ICP. It has been shown that a drop in CPP below 60 mmHg causes up to 35% reduction in cerebral blood flow and brain tissue hypoxia [7, 8]. Continuous monitoring of CPP is critical in patients with ICP elevations to prevent brain

ischemia when MAP may not be sufficient to provide adequate perfusion to the brain. Some studies suggest a benefit in mortality for augmentation of CPP to 70–75 mmHg in brain-injured patients; however, CPP > 70 mmHg has also been associated with an increased risk for acute respiratory distress syndrome [9–11].

Case 1 Continued: Paroxysmal Sympathetic Hyperactivity

Approximately 1 week later, the nurses noted that minimal stimulation of the patient resulted in

tachycardia, tachypnea, hypertension, and flushing. These episodes typically required small doses of sedation or anti-hypertensive medications. He was started on gabapentin and propranolol for likely paroxysmal sympathetic hyperactivity (PSH) and pre-medicated with morphine for nursing care with significant improvement in these fluctuations.

PSH is commonly seen in patients with significant brain injury, axonal shearing, and hypoxia due to disinhibition of sympathetic outflow in response to afferent stimulation [12, 13]. This phenomenon typically presents with sudden episodes of tachycardia, hypertension, tachypnea, hyperthermia, flushing, diaphoresis, and/or posturing. When compared to controls, TBI patients exhibit an increased response to noxious stimuli ranging from mild, self-resolving symptoms to dramatic sympathetic and motor hyperactivity indicating that this is likely a spectrum disorder. It can occur as early as the first week following injury and

can last for weeks to months [14]. This syndrome is often underrecognized and undertreated, as diagnosis requires continuous hemodynamic monitoring and a heightened suspicion in brain-injured patients. Lack of treatment has been associated with worse outcomes and increased mortality [15]. A standardized assessment method was proposed in 2014, which allows providers to determine the likelihood of PSH based on the clinical assessment (see Table 39.1) [16].

The goal of treatment is to avoid triggers and use pharmacotherapy to diminish the sympathetic response when triggers cannot be avoided (i.e., nursing care, procedures, etc.). Classes of drugs commonly used include opioids, intravenous (IV) anesthetics, beta blockers, alpha-2 agonists, neuromodulators, anti-psychotics, and benzodiazepines (see Table 39.2). The choice of agent depends on the predominant clinical features of the episodes with consideration of the agent’s side-effect profile.

Table 39.1 PSH assessment scale

	0	1	2	3	Score
HR	<100	100–119	120–139	>140	
RR	<18	18–23	24–29	>30	
SBP	<140	140–159	160–179	>180	
Temperature	<37	37–37.9	38–38.9	>39	
Diaphoresis	None	Mild	Moderate	Severe	
Posturing	None	Mild	Moderate	Severe	
				Subtotal:	
Score 1 point for each feature present:					
Clinical features occur simultaneously					
Episodes are paroxysmal in nature					
Sympathetic over-reactivity to normally non-painful stimuli					
Features persist >3 consecutive days					
Features persist >2 weeks post brain injury					
Medications administered to decrease sympathetic features					
>2 episodes daily					
Absence of parasympathetic features during episodes					
Absence of other presumed cause of features					
Antecedent acquired brain injury					
					Subtotal:
					Combined total:
PSH diagnostic likelihood	Unlikely		<8		
	Possible		8–16		
	Probable		>17		

Abbreviations: *HR* heart rate; *PSH* paroxysmal sympathetic hyperactivity; *RR* respiratory rate and rhythm; *SBP* systolic blood pressure

Table 39.2 Pharmacotherapy for PSH

Medication/class	Mechanism of action	Symptoms treated	Initial dosing
Baclofen	GABA _B agonist	Pain, rigidity	5 mg TID
Benzodiazepines	GABA _A agonist	Agitation, hypertension, tachycardia, posturing	Specific to agent used
Bromocriptine	Dopamine D ₂ agonist	Hyperthermia, dystonia, posturing	1.25 mg every 12 h
Clonidine	α ₂ receptor agonist	Hypertension	0.1–0.3 mg every 12 h
Dantrolene	Calcium ion blocker	Muscle rigidity, posturing	0.25–2 mg/kg every 12 h
Dexmedetomidine	α ₂ receptor agonist	Hypertension, agitation, tachycardia	0.1–1.2 µg/kg infusion
Gabapentin	GABA agonist	Spasticity, allodynic response	300–1200 mg TID
Morphine, oxycodone	µ-opiate agonist	Tachycardia, allodynic response, hypertension	1–8 mg
Propranolol	β-blocker	Hypertension, tachycardia, fever	10 mg every 8 h

Abbreviations: *GABA* gamma aminobutyric acid; *PSH* paroxysmal sympathetic hyperactivity; *TID* ter in die (three times a day)

Dosing regimen of these medications is based mostly on data from case series and small clinical trials and it is recommended to use combinations of drugs from different classes for better control of paroxysms [17]. Many intensive care units (ICUs) have protocols in place that allow a nursing-guided treatment strategy where hemodynamic response is recorded for various pharmacologic interventions and optimal treatment plans can be implemented.

Case 2: Subarachnoid Hemorrhage

A 37-year-old previously healthy woman presents with a sudden onset, worst headache of life associated with nausea/vomiting and mild confusion. A non-contrast CT of the head shows early hydrocephalus, diffuse subarachnoid hemorrhage, and intraventricular blood. A CT angiogram (CTA) reveals a 7 mm aneurysm in the anterior communicating artery. Her initial blood pressure is 185/110 mmHg. She is treated with labetalol for blood pressure reduction and a loading dose of levetiracetam for seizure prophylaxis. After an emergent external ventricular drain (EVD) is placed, she is taken for conventional angiogram where the aneurysm is successfully coiled. Postoperatively, her exam

Table 39.3 Hunt Hess scale

Grade	Characteristics	Mortality rate (%)
0	Unruptured aneurysm, no symptoms	0
1	Asymptomatic or minimal HA and nuchal rigidity	1
2	Moderate to severe HA, nuchal rigidity, no neurologic deficit except CN palsy	5
3	Drowsy, confused, focal deficit	19
4	Stupid, hemiparesis, early decerebrate	42
5	Deep coma, decerebrate	77

Abbreviations: *CN* cranial nerve; *HA* headache

is neurologically intact, and she is transferred to the Neuro ICU for close monitoring.

Several grading scales have been developed to aid in the prediction of mortality and complications in aneurysmal subarachnoid hemorrhage (aSAH). The most frequently used scale to predict 30-day mortality is the Hunt and Hess scale where higher scores are associated with higher levels of mortality (Table 39.3) [18, 19]. The modified Fisher Grading Scale is calculated to predict the development of vasospasm and is based purely on radiographic appearance of the subarachnoid hemorrhage (Table 39.4) [20, 21].

Table 39.4 Modified Fisher Grading Scale

Modified Fisher score	CT findings	DCI risk (%)
0	No SAH or IVH	0
1	Thin SAH, no IVH	6
2	Thin SAH, IVH present	15
3	Thick SAH, no IVH	35
4	Thick SAH, IVH present	34

Abbreviations: *CT* computed tomography; *DCI* delayed cerebral ischemia; *IVH* intraventricular hemorrhage; *SAH* subarachnoid hemorrhage

Blood Pressure Monitoring

Tight blood pressure control is of critical importance in aSAH. Although there is little evidence for the degree of reduction, it is reasonable to keep systolic blood pressure (SBP) below 160 mmHg to minimize the risk for aneurysm re-rupture prior to surgical securement [22]. Most patients initially present with elevated blood pressure due to a sympathetic surge in response to the intracranial injury [23]. To counteract this, we use continuous infusions of anti-hypertensives with intra-arterial monitoring of blood pressure to rapidly titrate these medications. Post aneurysm securement, patients remain in the ICU for vasospasm watch where blood pressure goals change. During this time, augmentation of blood pressure can aid in increasing cerebral perfusion to the areas of the brain experiencing decreased flow due to vasospasm. Patients experiencing new neurologic deficits due to vasospasm should have a trial of blood pressure augmentation with vasopressors. Blood pressure should be increased in a stepwise fashion with a neurologic exam assessed to determine the optimal blood pressure goal. Maintaining this goal can become especially difficult as patients are receiving nimodipine for its neuroprotective properties, which may result in hypotension. Intra-arterial blood pressure monitoring allows nursing to assess for hypotensive responses to nimodipine and titrate vasopressors to keep the blood pressure at goal. Further monitoring and treatment of vasospasm is discussed later in this chapter.

Case 2 Continued: Sodium and Fluid Shifts

On post-bleed day 4, the nurse notes that the patient's urine output has increased to 300 cc/h and labs reveal sodium of 132 mEq/dL. She is started on a hypertonic saline infusion and sodium is monitored every 6 h. Sodium improves to 135 mEq/dL, but urine output remains brisk requiring significant fluid boluses to keep her euvolemic. She is started on fludrocortisone with further improvement in her sodium to 138 mEq/dL while urine output slows to 150 cc/h.

Fluid Monitoring

Up to 50% of patients with aSAH experience some level of natriuresis and subsequent decreased plasma volume, which have been shown to lead to worse outcomes, higher rates of vasospasm, and increased risk for delayed cerebral ischemia (DCI) [24–27]. Previously, prophylactic hypervolemia, hemodilution, and hypertension, or triple H therapy, was thought to increase cerebral perfusion resulting in reduced vasospasm and improved overall outcomes [28]. In the early 2000s, it was shown that compared to euvolemia, hypervolemia does not result in an increase in CBF and, furthermore, hypervolemia leads to increased cardiopulmonary complications and decreased brain tissue oxygen [25, 29, 30]. Any improvement in neurologic function or restoration of CBF has been shown to be mostly driven by concomitant hypertensive therapy [31]. Current standard of practice for SAH is to strictly target euvolemia to reduce risk of DCI and systemic fluid overload. Historically, assessment of fluid status in ICU patients has been difficult and many studies have been done to investigate the best method for determining euvolemia in SAH. Invasive monitoring like Swan-Ganz catheterization does reliably predict fluid status but is associated with many complications outweighing any potential benefit [32]. Central venous pressure (CVP) and non-invasive arterial pressure-based cardiac output monitors have been shown to be unreliable, specifically in non-intubated patients,

and inferior to assessment with vigilant fluid management [33, 34]. In mechanically intubated patients with ventilator synchrony and absence of arrhythmias, stroke volume variation from non-invasive cardiac monitoring has been shown to accurately assess fluid responsiveness. Current guidelines are to rely mainly on clinical assessment and net fluid balance with strict monitoring of urine output to estimate intravascular fluid status in SAH [35].

Sodium Monitoring

As previously discussed, natriuresis in SAH is very common and, in addition to hypovolemia, results in hyponatremia that has been associated with poor outcome [26]. Typically, this natriuresis is in the setting of either a syndrome of inappropriate secretion of antidiuretic hormone (SIADH) or cerebral salt wasting (CSW). CSW seems to be more common than SIADH as vasopressin levels are reduced within 1 week of SAH [36]. In patients without SAH, differentiating between the two is important as the treatment for CSW is replacement of volume and sodium whereas treatment for SIADH is fluid restriction. In SAH patients where the goal is euvolemia, treatment of SIADH with fluid restriction has been shown to lead to stroke, making management of this complication very difficult [37]. Typically, the approach is to replace sodium with oral supplementation of intravenous hypertonic saline (2–3%), with frequent sodium monitoring up to every 4–6 h. In some situations, patients continue to experience worsening natriuresis refractory to sodium and volume replacement; this is especially seen in CSW where urine output tends to be very high. Corticosteroids like fludrocortisone (0.1–0.3 mg twice a day) have been studied and shown to be very effective at decreasing natriuresis and decreasing the amount of fluids and supplemental sodium needed to maintain euvolemia and prevent hyponatremia in SAH [24, 38, 39]. Glucose and potassium should also be monitored frequently in patients receiving corticosteroids for natriuresis as these can cause hyperglycemia and hypokalemia. The use of

vasopressin-receptor antagonists has also been studied with excellent control of hyponatremia by increasing free water excretion, however, at the cost of significantly increased urine output and severe volume contraction in patients with CSW [40, 41]. Given this, they are generally avoided in SAH patients within the vasospasm time window.

Case 2 Continued: Vasospasm

Daily, transcranial Dopplers (TCDs) are performed and on post-bleed day 6 the mean velocity in the left middle cerebral artery (MCA) increased to 140 cm/s from 70 cm/s the day prior. In the afternoon the patient exhibits new right-sided weakness, which improves with blood pressure augmentation. A CTA with perfusion is done and confirms left MCA vasospasm with decreased perfusion in the left frontal lobe. She is taken for a repeat angiogram where she receives intra-arterial verapamil. Postoperatively, her weakness is resolved, she is weaned off the pressors with a stable exam, and TCDs the next day are improved.

Vasospasm

During the first 3–21 days following an aneurysmal subarachnoid hemorrhage, patients are at risk for vasospasm of the cerebral blood vessels. Narrowing of the blood vessels causes decreased blood flow to that vascular territory and can lead to irreversible cerebral ischemia or stroke [25]. Vasospasm is often erroneously used interchangeably with the term delayed cerebral ischemia (DCI), which is historically poorly defined with overlapping terminologies. While vasospasm is the physical constriction of arteries, DCI is the neurologic deterioration due to cerebral ischemia and secondary brain injury [42]. Occurring in roughly 30% of SAH patients, DCI is thought to result from multiple factors in addition to vasospasm, such as spreading cortical ischemia and microcirculatory spasm and microthrombosis [25, 43]. Although DCI should be

thought of as a distinct process from vasospasm, the two are highly correlated and monitoring and treatments are similar. Nimodipine is given prophylactically to prevent DCI, and, like vasospasm, treatment of DCI includes blood pressure augmentation and balloon or pharmacologic angioplasty [35, 44, 45]. Rapid identification and treatment of vasospasm and DCI is crucial during this period to prevent permanent neurologic deficits.

Monitoring for Angiographic Vasospasm

Transcranial Dopplers of the large blood vessels in the brain are typically performed daily as a non-invasive monitor for vasospasm. A full description of TCD ultrasonography and its clinical applications is discussed in Chap. 14; although briefly, mean velocities below 120 cm/s and above 200 cm/s are commonly used thresholds for absence and presence of vasospasm [35]. Elevated mean velocities have been shown to be highly correlated with radiographic vasospasm on CTA with high specificity and, in many instances, can diagnose vasospasm before it becomes symptomatic [46, 47]. TCDs, however, do have some limitations. The reliability of values obtained from transcranial Dopplers are operator dependent, and areas of narrowing can be easily missed resulting in a low sensitivity when screening for vasospasm [48]. In addition, some patients have poor temporal bone windows and TCD values cannot be obtained. It should be noted that in instances of high flow states such as severe anemia, we can see diffusely elevated velocities that reflect global hyperemia rather than vasospasm. To quantify how much of the intracranial velocity is due to the vasospasm itself, we use the Lindegaard ratio (LR). This is the ratio of the mean velocity in the middle cerebral artery to the mean velocity in the extracranial internal carotid artery [49]. In general, Lindegaard ratios <3 would be consistent with absent to mild vasospasm, 3–6 moderate vasospasm, and > 6 severe vasospasm.

To confirm the presence of vasospasm, digital subtraction angiography (DSA) is the gold standard and provides the opportunity for therapeutic interventions if vasospasm is present. However, this is an invasive and costly procedure that should only be considered when intervention is likely. CTAs are more widely used for vasospasm screening with good specificity and, when performed with perfusion, can quantify the area of at-risk tissue [44]. Since these scans do involve contrast administration and radiation, they should only be done on patients who are symptomatic and being considered for treatment. Patients experiencing asymptomatic vasospasm should continue monitoring with close neurologic exams and daily TCDs.

Case 2 Continued: Worsening Vasospasm

On post-bleed day 7, TCD velocities have started to trend back up into the 150 s with LR now 4.5 on the right and 5.2 on the left indicating moderate vasospasm. On post-bleed day 8, she develops progressively worsening mental status and becomes difficult to arouse; her ICP at that time is normal and CPP is 60 mmHg. She is emergently intubated for airway protection and taken to angiogram, which confirms diffuse vasospasm for which she receives intra-arterial verapamil with bilateral MCA balloon angioplasty. Post angiogram, her exam remains poor despite increasing her CPP to 70 mmHg, so the team decides to pursue multimodality monitoring with an intracranial brain tissue oxygen monitor and continuous electroencephalograms (EEGs). Her initial brain oxygen partial pressure (P_{btO_2}) is 14 mmHg and after confirmation that the probe is correctly placed and functioning, her CPP goal is increased to 70–80 resulting in improvement in P_{btO_2} to 23 mmHg. On EEG, there are no seizures or epileptiform discharges, but diffuse slowing is noted. On quantitative analysis of the EEG, an alpha-delta ratio (ADR) is calculated and noted to also increase when CPP is above 70. On post-bleed day 12, the brain oxygenation and ADR both drop precipitously with

no change in ICP. CT angiogram with perfusion is done and shows again worsened vasospasm with decreased perfusion in the bilateral frontal lobes. She is taken for angiogram and given intra-arterial verapamil with normalization of her brain oxygen and ADR. By post-bleed day 20, her brain oxygenation and ADR have both stabilized and her exam has improved to following simple commands in the upper extremities when off sedation. Her blood pressure goals are slowly liberalized with normal brain oxygenation and no changes in exam. TCDs show down-trending mean velocities. Her brain oxygen monitor is removed, sedation is weaned, and she is extubated.

Brain Oxygenation Monitoring

Monitoring brain tissue oxygen and oxygen consumption is a promising technology and has been of great interest in neurocritical care. While neurologic assessment provides the best basis for clinical decision-making, a poor neurologic exam can preclude identification of new injury and therefore additional physiologic monitoring is often needed. Brain tissue oxygen can be used as a surrogate monitor to assess adequacy of cerebral perfusion and provides data complementary to bedside examination and other physiologic parameters [50]. Small observational studies suggest that patients with brain tissue oxygen guided therapy have decreased mortality, improved outcomes, and earlier detection of DCI [51–55]. There is insufficient evidence to support a strong recommendation for use of these monitors in subarachnoid hemorrhage; however their utility in TBI patients is being investigated in the multicenter randomized controlled trial BOOST-3 (Brain Oxygen Optimization in Severe TBI, Phase 3) [56, 57]. Brain oxygenation monitors come in many forms with varying levels of evidence including intraparenchymal monitors, subdural probes, near-infrared spectroscopy (NIRS), and jugular vein bulb oxygen catheters, which can assess brain oxygen consumption. Intraparenchymal monitors are the most frequently used and continuously measure

the brain oxygen partial pressure (PbtO₂). They are placed in the white matter of preferably at-risk brain tissue via a bedside procedure much like an ICP monitor. PbtO₂ levels <15 mmHg are associated with cerebral hypoxia and <20 mmHg with impaired cerebral blood flow [50, 53]. Generally, practitioners target PbtO₂ > 20 mmHg using therapies to improve brain tissue perfusion or decrease oxygen demand [58]. These probes do have several limitations. They are only able to provide information about the brain tissue directly surrounding the end of the probe and may not identify other focal areas of hypoxia. In addition, they are invasive procedures and require very advanced monitoring typically in a highly specialized ICU with neurocritical care trained personnel. NIRS uses technology similar to the pulse oximeter and is placed across the forehead giving an estimation of the brain tissue oxygen of the frontal lobes [59]. While this gives a more global assessment of brain oxygenation, it has not been shown to capture hypoxic events as well as intraparenchymal monitors [60].

Continuous EEG as a Monitor for Vasospasm

It is well known that patients with SAH are at a higher risk for seizures due to the presence of subarachnoid blood [61, 62]. Continuous EEG is generally recommended to evaluate for non-convulsive seizures or abnormal discharges in SAH patients with a poor neurologic exam [44]. Outside of seizure detection, EEG is being increasingly studied for its utility in neuromonitoring using quantitative analysis where raw EEG data are condensed into a spectral array that can display EEG trends over time. The software required for this is typically only available in highly specialized Neuro ICUs and requires epileptologists and neurointensivists with specific training to correctly interpret the data. Quantitative EEG (qEEG) can generate large volumes of data that highlight electrographic events and patterns of slowing that would not be detected from the traditional method of reading [63, 64]. In general, slowing is indicative of under-

lying cortical dysfunction and associated with a degree of encephalopathy, although not specific for etiology. By monitoring the amount and variability of faster waves (alpha, 8–12 Hz) and slower waves (delta, 0–4 Hz), it is possible to identify areas of worsening cerebral function due to decreased perfusion. The most widely used parameter, the alpha-delta ratio (ADR), is the ratio of alpha waves to delta waves. Worsening slowing (increased delta) or suppression of faster frequencies (decreased alpha) results in a decreasing ADR that has been shown to occur during DCI in SAH [65]. Some studies have shown that using ADR and other quantitative EEG parameters accurately predicts DCI and can detect it before it is evident on clinical exam or CT imaging [66–68].

Case 3: Cardiac Arrest

A 75-year-old man with a past medical history of atrial fibrillation, hypertension, hyperlipidemia, and stage 2 chronic kidney disease is brought into the emergency room for sudden onset non-exertional chest pain. On arrival to the emergency room, he becomes unresponsive due to onset of pulseless ventricular tachycardia. He received immediate high-quality cardiopulmonary resuscitation (CPR) for 45 min before a perfusing cardiac rhythm was restored. Electrocardiogram (EKG) is significant for ST elevations in V1–4 and a new right bundle branch block. He is taken emergently for cardiac catheterization where he undergoes successful thrombectomy and stenting of the left anterior descending coronary artery (LAD). Post procedure he is brought to the medical ICU where he remains unresponsive, and targeted temperature management (TTM) is initiated to 36 °C. After initiation of TTM his nurse notices shivering of his extremities, which improves slightly when surface counter warming is started. He is also started on a magnesium infusion, increased sedation, and buspirone treatment, with complete resolution of the shivering. Repeat laboratory evaluation showed a potassium level of 2.9, which is aggressively corrected.

Temperature Monitoring

During cardiac arrest, the brain experiences significant endothelial cell damage and a subsequent reperfusion syndrome where high levels of inflammatory mediators further potentiate ischemia and cell damage [69]. The extent of brain injury incurred from global ischemia and these secondary processes drives outcomes and return of consciousness. During this time there is potential for recovery, but this is highly dependent on perfusion, arterial oxygen levels, temperature, and other metabolic demands, making the post arrest period of crucial importance for monitoring [70, 71]. Preliminary data have shown that higher temperatures are associated with worsening injury, which has led to the use of therapeutic hypothermia in post cardiac arrest care. Data for TTM post cardiac arrest are rapidly evolving, resulting in highly variable practice. Historically, patients who remained unresponsive were cooled to 33 °C for 24 h [72]. Patients who did not tolerate 33° due to complications such as bradycardia, significant bleeding, or shock/hypotension were cooled to 36°. One trial compared 33–36° and showed that 36° was non-inferior in out-of-hospital cardiac arrest patients [73]. Current American Heart Association (AHA) guidelines are to target 32–36° post arrest for a minimum of 24 h, but this does not account for recent data that suggest that targeted normothermia compared to 33° is non-inferior [74, 75]. While some neurointensivists no longer pursue TTM, many centers and individuals still recommend TTM in select cases. When performed, TTM must be initiated rapidly within the first 6 h following the arrest with the goal to achieve target temperature within 1 h [76]. Methods of cooling can include ice packs to the groin and axilla, cold saline infusions (4 °C), and advanced temperature modulating intravascular and surface devices [77]. Advanced techniques not only achieve target temperature faster but also maintain that temperature better and are preferred over cold saline or cooling packs [78–80]. Intravascular devices have less temperature variability compared to surface devices but are associated with more procedural complications [80]. After 24 h at the chosen target temperature, patients are rewarmed at a rate of

Table 39.5 Bedside Shivering Assessment Scale

Score	Severity	Location
0	None	No shivering detected
1	Mild	Localized to neck and thorax only
2	Moderate	Involves gross movement of the upper extremities in addition to neck and thorax
3	Severe	Involves gross movements of the trunk and upper and lower extremities

0.1° per hour to minimize consequences of inflammatory and vasodilatory effects [81]. It is important to continuously monitor an accurate core body temperature via an esophageal or bladder temperature probe. Shivering, one of the most important complications to monitor for, not only mitigates the effects of TTM but also induces a hypermetabolic state and propagates secondary brain injury [82]. Many institutions have post cardiac arrest care bundles that include shivering protocols using the Bedside Shivering Assessment Scale (BSAS) shown in Table 39.5 [83].

Surface counter warming is a simple method to reduce the incidence of shivering and does not result in increased core body temperature [84]. When surface warming is not sufficient, pharmacotherapy including magnesium supplementation, analgesics, opioid receptor agonists, cholinesterase inhibitors, *N*-methyl-*D*-aspartate receptor antagonists, alpha-2 receptor agonists, and anti-serotonergic agents should be considered [76, 85]. In cases refractory to these interventions, paralysis with neuromuscular blocking agents may be required. Many medications have been investigated for efficacy in decreasing shivering with varying results, leading to some heterogeneity in practice. General recommendations are to prioritize non-sedation interventions with careful consideration of the pharmacodynamics of chosen medications [74, 76, 85].

Laboratory Monitoring: Potassium, Creatinine Clearance, Arterial Blood Gas, and Coagulation

TTM has considerable effects on physiology, making interpretation and management of certain

laboratory tests distinctive. Hypothermia causes an intracellular shift in potassium, which can result in hypokalemia proportional to the degree of temperature reduction. It must also be noted that during rewarming this process is reversed and hyperkalemia can develop, especially if aggressively replenished during TTM. Targeting potassium levels of 3–3.5 mmol/L has been shown to be safe and prevents hyperkalemia in the post rewarming period [86, 87]. In addition, partial pressures of oxygen and carbon dioxide change with temperature thus decreasing the accuracy of arterial blood gas (ABG) values. ABGs should be corrected for the patient's actual body temperature for the most accurate assessment of oxygenation and ventilation. Renal function can also be difficult to assess during hypothermia as both creatinine and creatinine clearance are reduced by up to 40% [88]. Because of this, creatinine is not completely reflective of renal clearance and the expected reduction may require adjustments in medications that are renally excreted. Hypothermia also affects the coagulation cascade and platelet function, resulting in prolonged prothrombin and partial thromboplastin times [89]. When patient populations who underwent cooling for various pathologies were evaluated for complications of the induced coagulopathy, it was found that there was no difference in the rates of clinically significant bleeding [90–93]. Prolonged coagulation times should not be used to guide management with respect to thrombosis prevention or treatment of thrombotic disease [76].

Case 3 Continued: Myoclonus

Once the neuromuscular blockade is weaned off, the patient begins to exhibit new movements characterized as sudden, non-sustained muscle jerks involving all four extremities. The nurses note that these movements seem to increase with any physical stimulation. He is connected to continuous EEG that shows generalized discharges that correlate with the movements. He is treated with a loading dose levetiracetam for cortical myoclonus and the movements initially improve.

Later that evening the myoclonus worsens and the epileptologist notes that the discharges are now approaching 2.5 Hz in frequency. The patient is given 4 mg midazolam and treated with a loading dose of valproic acid, which significantly improves his EEG and movements.

Post Hypoxic Myoclonus

Myoclonus is defined as sudden, involuntary, and irregular muscular jerks involving the body and/or face and occurs in up to one-third of post arrest patients [94, 95]. It has been previously associated with poor functional outcome but with improving management of post arrest patients, many have been treated and achieved a neurologic recovery [96–98]. It is not well understood whether post hypoxic myoclonus serves as a marker of poor prognosis or reflects an ongoing source of secondary brain injury that should be treated [99]. The classification of post hypoxic myoclonus is also highly variable in the literature, but it is commonly differentiated based on the origin of the discharge as cortical (having a preceding epileptiform discharge on EEG indicating) or subcortical (having no correlating EEG discharges) [100–102]. Regardless of the origin, it is commonly stimulation induced and can be highly refractory to pharmacologic interventions. The term “myoclonic status epilepticus” (MSE) is a misnomer as it refers to repeated myoclonic jerks with EEG correlates rather than a true form of status epilepticus. Lance Adams Syndrome refers to myoclonus in post arrest patients occurring with the emergence of consciousness and typically only requires symptomatic treatment [96]. There are no specific guidelines for the treatment of post hypoxic myoclonus and the medical necessity of fully suppressing these movements is not well understood. It is not unreasonable to base the decision for treatment on whether these movements are distressing to family or interfering with nursing care or ventilator synchrony [100]. In general, many neurointensivists treat cortical myoclonus more aggressively, with common agents being levetiracetam, valproic acid, and benzodiazepines.

Some studies have suggested that cortical myoclonus responds best to levetiracetam while subcortical myoclonus responds better to benzodiazepines [103, 104].

Case 3 Continued: Prognostication

It is now 3 days after the patient’s cardiac arrest, and he has not yet regained consciousness despite minimal sedation, nor is he able to be weaned from the ventilator. His family is considering tracheostomy placement but would first like to know what his prognosis for recovery is.

Prognostication

In patients who survive cardiac arrest, prognostication becomes one of the most important components of care as answers to these questions guide families making difficult decisions regarding code status, tracheostomy, and escalation of care. Despite the large body of high-quality literature pertaining to this topic, there remains significant controversy over the methods for determining neurologic prognosis [105]. This is largely related to the high rates of withdrawal of life-sustaining treatment (WLST) in this population based on a perceived poor prognosis by medical teams and families. WLST is the leading cause of death post cardiac arrest and contributes to prognostication studies as a poor outcome creating a self-fulfilling prophecy bias [106]. Providers need to be aware of this bias when interpreting studies evaluating methods of prognostication, as results can be skewed toward a more negative outcome. The introduction of TTM has also introduced many confounders to early prognostication with increased use of sedating medications and decreased cerebral metabolic rate [107]. The inconsistencies in prediction and reports of patients with delayed awakening despite perceived poor prognoses make prognostication post cardiac arrest a challenging and sometimes intimidating task to many providers. When evaluating a comatose survivor of cardiac arrest, it is best to base final determinations on

multiple pieces of data rather than relying on one sole method. Common tests used to determine likely outcomes include the bedside neurologic exam, somatosensory-evoked potentials (SSEPs), EEG, chemical biomarkers, and neuroimaging [108].

Bedside Examination

The neurologic exam in a comatose patient includes assessment of brainstem reflexes (pupillary, corneal, oculocephalic, cough, and gag), motor response to noxious stimuli, presence of abnormal movements such as myoclonus, and evidence of emerging consciousness such as eye opening, tracking with eyes, and following commands. Consciousness can be quantitatively reported using the Glasgow Coma Scale with a score < 9 representing coma. Absence of bilateral pupillary reflexes accurately predicts poor outcomes but has poor sensitivity [109]. Using motor response alone is not advised as this has a high false-positivity rate of poor outcome, especially in patients who received sedation [110]. The presence of myoclonus within 72 h of return of spontaneous circulation (ROSC) and myoclonic status within 48 h of ROSC both predict poor outcomes, however should be used in concert with other prognostication factors, as good neurologic recovery has been observed in these patients [96, 99].

Neurophysiology

Somatosensory-evoked potentials assess the brain's response to sensory stimuli and bilateral absence of this response (N20 peaks) has been shown to accurately predict death or persistent vegetative state [108, 111]. Prognostication studies have shown that SSEPs are the most frequently used test used by physicians to estimate prognosis and tend to be ordered for sicker patients with the highest rates of WLST [112, 113]. Current guidelines recommend using SSEPs >72 h from ROSC in TTM patients and >24 h from ROSC in survivors not treated with

TTM for prognostication [105]. Immediately following cardiac arrest, comatose patients frequently undergo EEG monitoring to evaluate for seizures as a treatable cause of altered mental status. In addition, this information can be used in prognostication. Findings of status epilepticus, lack of reactivity to stimuli, and burst suppression >72 h following ROSC can be used in combination with other variables to predict poor outcomes [105, 114, 115]. Isoelectric or low-voltage EEG is not recommended for use in prognostication given its dependence on other factors such as skin temperature, adequate electrode connection, and medications [116, 117]. The main limitation with EEG for prognostication is the lack of interrater reliability and standardized definitions of reactivity.

Neuron-Specific Enolase

Neuron-specific enolase (NSE) is a chemical biomarker released from injured neurons and glial cells and is typically measured on days 1–5 post cardiac arrest. Prior to TTM, a threshold of >33 mcg L⁻¹ was used to predict poor outcomes; however, numerous studies since then have demonstrated considerable variability [105, 108, 118]. In general, peak values greater than 60 are rarely associated with good outcomes [118]. Current recommendations suggest using high NSEs on days 2–3 combined with other factors to predict poor prognosis [105].

Neuroimaging

Data for using imaging to prognosticate are lacking and contain many confounders. Initial work-up for etiology of cardiac arrest typically includes a CT of the head, which can also be useful to look for early signs of anoxic ischemia. Loss of differentiation between gray and white matter on initial CT is associated with poor outcomes and has been shown to be up to 81% sensitive [119]. Magnetic resonance imaging (MRI) of brain is also often performed in the subsequent days following cardiac arrest to evaluate for diffusion

weighted restriction due to anoxic damage. High, multilobar, diffuse diffusion-weighted imaging (DWI) burden on days 2–5 may also be used to predict poor outcomes [120, 121]. Findings on neuroimaging should never be relied on alone as there are many high false-positives and variability in interpretation, especially in centers with little experience in neuroprognostication [105].

Case 4: Spinal Cord Injury

A 56-year-old man with morbid obesity and coronary artery disease is brought to the emergency room after a motor vehicle accident and is found to have a C6 burst fracture with American Spinal Cord Injury Association A (ASIA), i.e. a complete spinal cord injury (SCI), at the level of C5. He is taken to the OR for anterior decompression and fusion. He underwent total intravenous anesthesia (TIVA) with propofol and sufentanil infusions in addition to continuous vasopressor support and aggressive fluid resuscitation. Postoperatively his hemoglobin is 10.1 g/dL, lactate 3.6 mmol/L, and phenylephrine drip is continued at 0.8 mcg/kg/min. Vitals are BP 105/63 mmHg, HR 53 bpm, and oxygen saturation 93% on face mask with a nasal trumpet. On exam he awakens to voice and is notably agitated and restless. He is yelling with unintelligible speech and not voluntarily following commands but moving all extremities with good strength. Per the neurosurgeon's report, his estimated blood loss was 1.5 L and they would like to target mean arterial pressure (MAP) greater than 85 mmHg.

Neurologic Assessment

Clinical neurologic assessment generally includes level of alertness, orientation, grading of motor function, and sensory deficits. When assessing the patient's postoperative neurologic status, especially mentation, it is important to also consider their preoperative evaluation. Etiology for changes in mental status can include drug intoxication, stroke, seizures, and worsening of preexisting medical problems such as diabetic ketoacidosis (DKA) or electrolyte disturbances. Early attribution of abnormal mental status to residual anesthesia should be avoided.

Respiratory Monitoring

The monitoring of the respiratory system includes, at minimum, respiratory rate and pattern, pulse oximetry, capnography, and supplemental oxygen requirement. If mechanically ventilated, positive end-expiratory pressure (PEEP), FiO_2 , tidal volume, minute ventilation, maximal inspiratory pressure (MIP), and maximal expiratory pressure (MEP) should also be monitored. This information is used to independently assess three components of respiration: respiratory drive, airway patency, and pulmonary function. Respiratory drive can be evaluated based on these two components: respiratory pattern (respiratory rate and rhythm [RR]), and neuromuscular function. In an intact brain, the respiratory drive is directly stimulated by the pH in the cerebrospinal fluid, and indirectly related to the arterial partial pressure of carbon dioxide (PaCO_2) [122]. The respiratory drive can be suppressed under pathologic states, such as opiate intoxication or severe brain damage. Respiratory drive can be increased during pain, anxiety, hypermetabolic states, diaphragmatic weakness, and residual paralysis. Airway reflexes can be evaluated using the mnemonic GCS (gag, cough, swallow). One easy bedside test to evaluate neuromuscular function includes asking the patient to take a deep breath (diaphragmatic strength), hold the breath (vocal cord function), and forceful expiration (abdominal strength). The diaphragm is the main muscle during inspiration and is innervated by phrenic nerves arising from C3–C5. Diaphragmatic dysfunction should be suspected in any SCI involving the cervical levels. Key signs of diaphragm involvement are rapid shallow breathing and hypercapnia. Strength of the abdominal muscles on expiration is important for developing a strong cough.

To evaluate airway patency, we must rule out obstruction at three levels: supraglottic, glottic, and infraglottic (see Table 39.6). Supraglottic obstructions can include a large tongue in a narcotized patient, soft tissue edema after prolonged prone position, or perioperative hematoma formation especially when an anterior approach was used. Etiologies of glottic obstruction include laryngeal edema due to traumatic intubation or excessive resuscitation. Possible infraglottic obstructions include airway hyperreactivity or

Table 39.6 Monitoring of the respiratory system

Neurorespiratory function	Airway patency	Lung function
Respiratory rate and rhythm (medulla and pons) <ul style="list-style-type: none"> • Tachypnea: Pain, anxiety, hypermetabolic, residual anesthesia paralysis, diaphragm denervation, lung dysfunction • Bradypnea: Intoxications, residuals opioids • Abnormal patterns: Cheyne-Stokes, hyperventilation syndrome, apneustic breathing Airway protection (brainstem) <ul style="list-style-type: none"> • Gag (CN IX) • Cough (CN X) • Swallow (CN XII) Neuromuscular function (diaphragm and abdominal muscles) <ul style="list-style-type: none"> • FVC: <20 mL/kg (normal 50) • MIP: <30 cmH₂O (normal, M, >100; F, >70) • MEP: <40 cmH₂O (normal M, >200; F, >140) 	Supraglottic <ul style="list-style-type: none"> • Edematous/large tongue • Retropharyngeal hematoma formation (surgical anterior approach) • Anesthesia-related (bite blocks, gauzes, nasal/oral airways) Glottic <ul style="list-style-type: none"> • Laryngeal edema due to traumatic intubation or poor venous drainage in prone position • Laryngospasm (triggered by direct laryngeal stimulation from secretions in the setting of poorly protected airway) Infraglottic <ul style="list-style-type: none"> • Plugging • Intrabronchial endotracheal tube • Bronchospasm 	Pulse O ₂ , Capnography, ABG Physiologic shunting <ul style="list-style-type: none"> • Atelectasis • Pulmonary edema <ul style="list-style-type: none"> – Cardiogenic – Neurogenic – Negative-pressure – TACO • Pulmonary inflammation <ul style="list-style-type: none"> – TRALI – ARDS • Pneumonia Alveolar deadspace • Pulmonary embolism • High PEEP • Emphysema

Note: Evaluation of three main aspects: neurologic function (respiratory drive and neuromuscular function), airway patency (anatomical or pathophysiological obstructions), and lung function (adequate gas exchange)

Abbreviations: *ABG* arterial blood gas; *ARDS* acute respiratory distress syndrome; *CN* cranial nerve; *FVC* functional vital capacity; *MIP* maximal inspiratory pressure; *MEP* maximal expiratory pressure; *PEEP* positive end-expiratory pressure; *TACO* transfusion-associated circulatory overload; *TRALI* transfusion-related acute lung injury

bronchospasm and mucous plugging. Pulmonary pathology should be suspected when supplemental oxygen or tachypnea is required to maintain normal saturation and/or prevent hypercarbia in the setting of normal neuromuscular function and airway patency. In the context of a postoperative SCI, a weak cough and rapid shallow breathing are concerning for abdominal and diaphragmatic weakness localizing to cervical and thoracic spinal cord dysfunction. However, postoperative atelectasis, and pulmonary edema should remain high on the list of differential diagnoses.

Cardiovascular Monitoring

Cardiovascular monitoring should include telemetry, blood pressure, and volume status. Volume status can be assessed clinically by evaluating skin turgor, capillary refill time, oral mucosa, and response to intravenous fluid boluses. Other monitoring parameters such as net fluid balance, blood urea nitrogen (BUN)/creatinine ratio, inferior vena

cava (IVC) diameter, and variability during respiration, central venous pressure (CVP), and pulmonary artery occlusive pressure (PAOP) using a pulmonary arterial catheter may also be used to determine volume status. Our patient was admitted requiring a phenylephrine drip to achieve normal blood pressure. In the setting of significant intraoperative blood loss, elevated lactate, and altered mental status, the patient should be evaluated for etiologies of shock. The following algorithm is a diagnostic approach to the hypotensive patient (Table 39.7).

A good starting point when evaluating a patient in shock is the heart rate. Bradycardia is characteristic for neurogenic shock; however, it is important to rule out other causes of bradycardia including beta blockers, narcotics, and electrolyte abnormalities, particularly calcium and potassium. Types of shock presenting with tachycardia include anaphylactic, septic, hypovolemic, hemorrhagic, and obstructive. Cardiogenic shock presents with variable heart rate depending on the etiology (myogenic, arrhythmogenic, or valvular). The

Table 39.7 Systematic approach for the evaluation and treatment of shock

<p>Systolic blood pressure (SBP) < 90 mmHg, Mean arterial pressure (MAP) < 65 mmHg</p> <p>Confirm hypotension, evaluate invasive versus non-invasive. Decide if relevant, depending on clinical context and additional findings such as depressed mentation and low urinary output.</p>	
<p>How is the heart rate?</p>	
Bradycardia	Tachycardia
<p>How is the volume status? Evaluate inferior vena cava (IVC) and central venous pressure (CVP)</p>	
<ul style="list-style-type: none"> • IVC diameter collapsible • Respiratory variation >50% • CVP low 	
<p>How is the peripheral vasculature (dilating or constricting)? Evaluate skin and mucosa</p>	
<p>Cold and pale</p>	
<p>Warm and dry</p>	
<p>Distributive shock</p>	
Neurogenic shock	Septic shock
	Anaphylactic shock
	Hypovolemic shock
	Hemorrhagic shock
	Hypovolemic shock
	Tension Pneumothorax
	Cardiac tamponade
	Pulmonary embolism
	Cardiogenic shock
	Systolic/diastolic dysfunction
	Arrhythmias
	Valvular dysfunction
<p>Fluid responsive 😊</p>	
NE	Epi
Atropine	NE
	Blood products
	Fluids
	Needle decompression, chest tube
	Pericardiocentesis
	Thrombectomy
	Thrombolysis
	ACS protocol
	ACLS
	IABP/ECMO

Note: Three questions to initial evaluation: Heart rate, volume status, and vasculature status. Fluid responsiveness and further interventions based on presumed diagnosis
 Abbreviations: *ACLS* advance cardiovascular life support; *ACS* acute coronary syndrome; *ECMO* extracorporeal membrane oxygenation; *Epi* epinephrine; *IABP* intra-arterial balloon pump; *NE* norepinephrine

combination of neurogenic shock from SCI and hemorrhagic shock from trauma is difficult to differentiate and treat because the expected tachycardia and vasoconstriction from hemorrhagic shock are obscured by the loss of sympathetic tone from the neurogenic shock. Not uncommonly, up to 10 L of crystalloids, colloids, and blood products may be required to address the hemorrhagic shock. Essential distinctions between the two etiologies are fluid responsiveness and ruling out obstructive causes that require advanced management. When fluids and pressors fail to normalize blood pressure, careful evaluation for obstructive or cardiogenic shock should be performed.

Case Continued: Spinal Cord Perfusion

The patient receives additional fluids and phenylephrine is transitioned to norepinephrine. Several hours later the patient is fully awake and following commands, blood pressure normalized, and is noted to be in sinus bradycardia with a heart rate in the low 50s. Now that he is stabilized, his blood pressure goal is MAP goal greater than 85 mmHg for spinal cord perfusion.

Blood Pressure Augmentation

The rationale for this practice is to prevent secondary neurologic injury through improved perfusion to the spinal cord. In 2017, Saadeh et al. analyzed nine retrospective and two prospective studies to conclude that there are no high-quality data regarding optimal BP goals and duration for acute management of SCI [123]. However, MAP greater than 85 mmHg for 7 days post injury has been advocated by different societies, including The American Association of Neurological Surgeons (AANS) and the Congress of Neurological Surgeons (CNS) [124, 125]. Common practice is to achieve this goal with the use of norepinephrine. This is based on strong alpha-receptor-mediated vasoconstriction and direct inotropic effect on the heart. Phenylephrine can complicate the clinical picture due to the side

effect of reflex-bradycardia, and dopamine increases the risk of arrhythmias. Alternative oral approaches include pseudoephedrine or midodrine for blood pressure goals and enteral albuterol for heart rate control [126]. Pressure natriuresis refers to the concept that increased renal perfusion pressure leads to a decrease in tubular reabsorption of sodium and an increased sodium excretion [127]. Therefore, increases in urinary output during blood pressure augmentation are expected and attention should be paid to prevent hypovolemia or hyponatremia. In addition to replacing fluids for increased urinary output, potassium, magnesium, and phosphate should also be strictly monitored and replaced.

Case 5: Stroke

A 51-year-old man with history of polysubstance abuse is admitted to the Neuro ICU following a large right middle cerebral artery (MCA) stroke not suitable for thrombolytics or thrombectomy. The night before admission he was drinking heavily and was last known to be normal around 1:00 am. At 1:30 pm he woke up with left arm paralysis and called emergency medical services (EMS). Imaging revealed hypodensity in the right MCA distribution with large ischemic core on perfusion. On physical exam, his eyes open spontaneously with a right gaze preference; he follows commands but with fluctuating attention and is noted to be dysarthric and flaccid in the left upper extremity. Vitals are BP 200/109 mmHg, HR 135 bpm, RR 26/min, and oxygen saturation 97% on room air. Initial work-up reveals atrial fibrillation on EKG, dilated left ventricle with an ejection fraction (EF) 25% on transthoracic echocardiography (TTE), sodium 124 mEq/L, bicarbonate 18 mEq, glucose 48 mg/dL, beta-hydroxybutyrate 60.1 mg/dL, ammonia 154 mg/L, blood alcohol (EtOH) > 15 mg/dL, creatinine 1.6 mg/dL, aspartate transaminase/alanine transaminase (AST/ALT) ratio 54/89 units/L, lactate 2.3 mmol/L, International Normalized Ratio (INR) 1.9, and platelets 110,000/mcL. His sodium was slowly normalized; he was started on lactulose and rifaximin and allowed for permissive hypertension up to SBP 220 mmHg.

Neurologic monitoring at this point is focused on changes in the neurologic exam, particularly evaluating for signs of hemorrhagic transformation and cerebral edema due to hepatic encephalopathy or ischemia. This patient is also at increased risk for seizures, malignant cerebral edema, and progression to cerebral herniation based on his large hemispheric stroke. Other problems that can cause neurological deterioration include alcohol intoxication and withdrawal, delirium tremens, symptomatic hyponatremia, uremic encephalopathy, hepatic encephalopathy, hypoglycemia, ketoacidosis, and cardiogenic shock.

Cardiovascular Monitoring

Cardiovascular monitoring may include telemetry, invasive arterial blood pressure, and central line placement for CVP. General practice post stroke is to allow permissive hypertension; however, in the event of hemorrhagic transformation, blood pressure goals should be reduced to limit the risk of further hematoma expansion. The decision to use invasive arterial monitoring is based on the high risk for clinical deterioration and need for frequent laboratory monitoring. Strict control of blood pressure using invasive arterial monitoring is especially helpful as most patients require rapid titration of continuous antihypertensive medications. Central line placement is also preferred in anticipation of ICP crisis and impending herniation requiring hypertonic saline. CVP monitoring may also be helpful in guiding therapy in the setting of suspected dilated cardiomyopathy and systolic failure.

Case Continued: Abnormal EEG

Hours after admission, the patient becomes obtunded and requires intubation for airway protection. Repeat imaging shows significant cerebral edema, but no herniation. On exam he is unresponsive despite lack of sedation with symmetric pupils that are sluggishly reactive. Continuous electroencephalogram (EEG) monitoring is placed to rule out new onset seizures. The next morning the EEG report is read as no seizure, but high-voltage delta-

theta background activity with lateral periodic discharges (LPD) with triphasic morphology.

EEG Monitoring

One of the most common applications of EEG in critical care is to rule out seizure activity in the setting of a patient with altered mental status. In this case, the study did not show seizures, but a pattern consistent with encephalopathy. An EEG report typically includes a description of the background, state changes, continuity, symmetry, reactivity, and presence of any abnormal features [128]. Two key components of the background are the predominant frequency, described as delta (<4 Hz), theta (4–7 Hz), or alpha (8–12 Hz), and continuity based on interruptions of the background. Different patterns for encephalopathy have been described correlating with certain etiologies, but a common finding is slowing of the background [3]. Epileptiform findings can be categorized into sporadic epileptiform discharges and rhythmic and periodic patterns. Rhythmic and periodic patterns are described based on their location of origin and distinctive electrographic features [129] (see Table 39.8). For example, a lateralized periodic discharge refers to an epileptiform finding originating from either the right or left side of the brain occurring periodically. The technical definitions of the various EEG findings are inconsistently defined and commonly disputed and therefore a more in-depth discussion of this is out of the scope of this chapter.

Triphasic waves were initially described in hepatic encephalopathy, but later they have also been described in other metabolic encephalopathies. Other metabolic disorders presenting triphasic waves include uremic encephalopathy, Hashimoto's encephalopathy, and drug-induced encephalopathy [3]. They are composed of a high-voltage (>70 mV), downward-oriented sharp wave that are preceded and followed by upward-oriented sharp waves of relatively lower amplitude. They tend to be diffuse and bilateral, with a degree of frontal predominance, and repeat every 1–2 s [130]. Triphasic waves can be interpreted as a marker of severe encephalopathy rather than a finding that should be directly suppressed. Like triphasic waves, other common EEG findings and

Table 39.8 Basic electroencephalogram (EEG) terminology

EEG background	Epileptiform findings		
<ul style="list-style-type: none"> • Symmetry (left versus right side) • EEG frequency (delta, theta, alpha) • Posterior dominant rhythm (evaluated with eyes closed and attenuated with eye opening) • Continuity (ranges from continuous to completely suppressed) • Reactivity (present, absent, or unclear based on changes on EEG after stimulation) • Voltage (normal/low/suppressed) 	Sporadic epileptiform discharges	Rhythmic and periodic patterns (RPPs)	
	Prevalence	Main term 1	Main term 2
	<ul style="list-style-type: none"> • Abundant • Frequent • Occasional • Rare 	<ul style="list-style-type: none"> • Generalized • Lateralized independent • Unilateral independent • Multifocal 	<ul style="list-style-type: none"> • Periodic discharges (PD) • Rhythmic delta activity (RDA) • Spike and wave (SW)

Table 39.9 Common electroencephalogram (EEG) findings based on etiology of altered mental status

Diagnosis	EEG findings
Hepatic encephalopathy	Slow background + triphasic waves
Uremic encephalopathy	Slow background + triphasic waves
Disequilibrium syndrome	High-voltage rhythmic delta + bilateral spike-slow wave complexes
Hypoglycemia	Slowing of the background, mostly in the theta frequency range
Hyperglycemia	Diffuse delta slowing, and sporadic spike with glucose >400 mg/dL
Hyponatremia	Slowing in delta–theta range
Hypernatremia	Diffuse slowing
Hypothyroidism	Low-voltage activity, theta frequency range
Hyperthyroidism	Increased alpha activity with prominent central beta activity
Central nervous system (CNS) infections	Both generalized and focal epileptiform discharges with the corresponding slowing

patterns are more frequently seen in certain etiologies and can aid in forming a targeted differential diagnosis for encephalopathy (see Table 39.9).

Pupillometry

In a comatose patient, the evaluation of the pupils is paramount to identify early neurologic decline. Most recently, the use of automatic pupillometry is increasing in critical care units. Pupillary assessment is subject to interrater variability, has very low consistency, and relies

on subjective and imprecise descriptions such as “brisk” or “sluggish.” Quantitative pupillometry provides maximum size, minimum size, constriction velocity (CV), constriction amplitude (CA), response latency, and Neurological Pupil index (NPI). The NPI is the most widely used parameter and represents an algorithm integrating multiple measurements into a single number that reflects overall pupillary reactivity [131]. Changes on pupillometry have been shown to precede transtentorial herniation and increase intracranial pressure [132, 133]. In general, an NPI > 3.0 reflects brisk pupillary function and attention should be paid to not only the absolute values but also the trend over time and any evidence of asymmetry [134].

In summary, patients with large MCA stroke are at high risk for sudden neurological deterioration due to cerebral edema and seizures. EEG and pupillometry can assist to diagnose ongoing seizures, metabolic encephalopathies, and early identification of increased ICP and herniation. Invasive hemodynamic monitoring including intra-arterial catheters and central lines is encouraged due to the potential for neurologic deterioration requiring emergent surgical intervention, tight blood pressure goals, administration of hypertonic solutions, and cardiovascular infusions.

Case 6: Seizure

A 45-year-old woman is admitted to the Neuro ICU with a diagnosis of subarachnoid hemorrhage secondary to rupture of an anterior communicating artery aneurysm and is scheduled for aneurysm coiling. She arrived in the operating

room with a GCS of 14 and underwent uneventful induction of general anesthesia and successful coiling of the aneurysm. During emergence from anesthesia she had a generalized tonic-clonic seizure that was aborted with lorazepam and a propofol infusion. Antiepileptic treatment with levetiracetam was initiated with a loading dose. Emergent CT head showed new placement of coils in the anterior communicating artery and unchanged subarachnoid hemorrhage. Labs at this time did not show hypoglycemia or other electrolyte disturbances. She was transported back to the ICU where her exam remained poor. Therefore, continuous EEG was placed.

Non-convulsive seizure should be considered in any patient presenting with acute brain injury and subsequent decline in neurologic status. Non-convulsive seizures have been reported in up to 10–25% of patients with acute brain injury and are associated with worse outcome [135]. Proinflammatory states are prevalent after acute brain injury, particularly among pathologies with the highest risk for seizures, such as intracranial hemorrhage and infections. In subarachnoid hemorrhage, seizures are prevalent and typically occur 3–7 days after onset of bleeding [136].

Duration of EEG Monitoring

In patients being evaluated for non-convulsive seizures, the first question is typically whether to request a routine or continuous EEG? The answer to this question is highly dependent on the patient population, and the answer is not clearly defined. Continuous EEG is more time and labor intensive compared to routine EEG and not available at all centers, thus may necessitate transfer to a facility with higher level of care. A study analyzing 242 hospitalized patients with altered mental status but no prior seizure found that in patients without epileptiform abnormalities in the first 4 h of recording, no seizures were subsequently reported [137]. A recent randomized controlled trial evaluated unconscious patients without prior seizure with either routine or continuous EEG and found that both groups had similar 6-month outcomes. The group with continuous EEG, how-

ever, had more seizure and ictal feature detection as well as medication adjustments [138]. In a general critical care population, a routine EEG may suffice for the purpose of evaluating non-convulsive seizures and appears to be safe. In patients with acute brain injury, however, the risk for non-convulsive seizures is much higher and many studies suggest that routine EEG would be inadequate to make this diagnosis [139–141].

Table 39.10 shows the American Clinical Neurophysiology Society (ACNS) updated terminology for seizure and status epilepticus. Illustrative figures can be found on cited reference (129).

Table 39.10 Seizure and status epilepticus terminology

EEG recording	
Electrographic seizures (ESz)	Electroclinical seizure (ECSz)
Either: (A) epileptiform discharges averaging >2.5 Hz for ≥ 10 s (>25 discharges in 10 s), or (B) any pattern with definite evolution and lasting ≥ 10 s	Any EEG pattern with either: (A) definite clinical correlate time-locked to the pattern (of any duration), or (B) EEG and clinical improvement with a parenteral anti-seizure medication
Status epilepticus (ESE)	Status epilepticus (ECSE)
An electrographic seizure for either: (A) ≥ 10 continuous minutes, or (B) a total duration of >20% of any 60-min period of recording	An electroclinical seizure for either: (A) ≥ 10 continuous minutes, or (B) a total duration of >20% of any 60-min period of recording, if (C) ≥ 5 continuous minutes if the seizure is convulsive (i.e., with bilateral tonic-clonic motor activity). Possible ECSE: An RPP that qualifies for the IIC (below) that is present for ≥ 10 continuous minutes or for a total duration of >20% of any 60-min period of recording, which shows EEG improvement with a parenteral anti-seizure medication <i>but</i> without clinical improvement

Note: Adapted from American Clinical Neurophysiology Society (ACNS) Standardized Critical Care EEG Terminology 2021

Abbreviations: ECSE electroclinical status epilepticus; ECSz electroclinical seizure; EEG electroencephalogram; ESE electrographic status epilepticus; ESz electrographic seizures; IIC ictal interictal continuous; RPP rhythmic and periodic pattern

Management of Seizures and Status Epilepticus

The rapid recognition and treatment of new onset seizure is critical to prevent progression to status epilepticus. Early treatment of seizures and status has been shown to improve outcomes, necessitating a standardized therapeutic approach for management [142]. Status epilepticus is defined as 5 min or more of continuous seizure activity or recurrent seizure activity without return to baseline [143]. Benzodiazepines remain the first line of treatment. The agent of choice is intravenous lorazepam at 0.1 mg/kg (which can be repeated after 5 min) with an alternative agent of intramuscular midazolam 0.2 mg/kg (up to 10 mg). If seizures continue 10–20 min after initial therapy, a second-line antiepileptic should be added. Second-line therapies include fosphenytoin (20 mg/kg), valproic acid (40 mg/kg), or levetiracetam (60 mg/kg loading dose). The definition of refractory status epilepticus is controversial but most guidelines consider failure of benzodiazepines and a second-line agent to be refractory necessitating IV anesthetics. Recommended medications include midazolam (0.2 mg/kg IV bolus, followed by 0.1–2 mg/kg/h infusion), propofol (1–2 mg IV bolus, followed by 20–200 mcg/kg/min infusion), or ketamine (1–2 mg/kg IV bolus, followed by 0.5–10 mg/kg/h infusion). Ideally, continuous EEG should be placed within an hour of suspected non-convulsive status epilepticus.

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