Balkan Med J 2023;40:74-81

Acute Multidisciplinary Management of Aneurysmal Subarachnoid Hemorrhage (aSAH)

Kathleen R Ran[1], Andrew C Wang[2], Sumil K Nair[1], Ozan Akça[2], Risheng Xu[1]

[1]Department of Neurosurgery, Johns Hopkins School of Medicine, Baltimore, United States
[2]Department of Anesthesiology and Critical Care Medicine, Johns Hopkins Medical Center, Baltimore, United States

Aneurysmal subarachnoid hemorrhage is a life-threatening, neurological emergency characterized by accumulation of blood in the subarachnoid space due to a ruptured aneurysm. Over the past several decades, improvements in the clinical management of aneurysmal subarachnoid hemorrhage have led to better patient outcomes. However, aneurysmal subarachnoid hemorrhage is still associated with high morbidity and mortality. During the acute phase of aneurysmal subarachnoid hemorrhage and prior to the definitive management of the aneurysm, numerous medical emergencies, such as elevated intracranial pressure and cerebral vasospasm, must be effectively managed to ensure the best possible neurological outcome. Early and rapid open communication between the clinical specialties caring for the aneurysmal subarachnoid hemorrhage patient is vital for rapid data collection, decision-making, and definitive treatment. In this narrative review, we aim to present the current guidelines for the multidisciplinary acute management of aneurysmal subarachnoid hemorrhage.

Subarachnoid hemorrhage (SAH) following rupture of an intracranial aneurysm is a medical emergency with an estimated global incidence of 6 per 100,000 person-years.[1] During aneurysmal SAH (aSAH), blood accumulates between the arachnoid layer and pia mater, leading to a rapid increase in intracranial pressure (ICP), and depriving the brain tissue of oxygen. Recent studies have reported that aSAH has a 30-day case fatality rate of approximately 20%, and among survivors, the functional dependency rate is as high as 50%.[2,3] Patient outcomes following aSAH have improved over time. A recent study found a significant decrease in hospital mortality when comparing the years 2003-2008 with 2015-2019.[4] In addition, the 12-month case fatality rates of aSAH have declined over time.[4] This trend could be partially attributed to improvements in the clinical treatment of aSAH.[5] However, the overall aSAH morbidity and mortality rates remain high. Approximately 12% of patients experience sudden death before hospital arrival, 35% die within 3 months, and >50% of survivors experience an incomplete recovery.[6] Despite accounting for only 5% of stroke cases, the total loss of productive life years from aSAH is comparable to that of ischemic stroke.[7] Proper management of patients with aSAH during the acute phase prior to aneurysm securement is critical to increasing the chances of survival and improving functional outcomes. A recent international survey identified significant global variability in multiple aspects of aSAH management, including the timing and type of aneurysm repair, fluid management methods, and endovascular treatment of delayed cerebral ischemia.[8] Furthermore, studies have demonstrated that discharge outcomes for aSAH patients in the United States vary by geographic region and that this variability is at least partly attributable to differences in hospital management of aSAH.[9] Guideline-based practices are therefore critical for optimizing aSAH patient care and outcomes. This review aims to present the current recommendations for the acute multidisciplinary management of aSAH.

Assessment of Airway, Breathing, and Circulation

The first step in the acute management of aSAH is to ensure appropriate resuscitation and airway, breathing, and circulation control. Inadequate oxygen and ventilation can lead to hypoxia and exacerbate ischemic damage to brain tissue. Multiple studies have associated low brain oxygenation with poor neurologic outcomes and mortality after aSAH.[10,11] Proper airway management requires first responders to obtain a Glasgow coma score (GCS) to determine the patient's level of consciousness. Patients with a GCS $\leq$ 8 are typically unable to maintain a patent airway and thus require

Corresponding author: Risheng Xu, Department of Neurosurgery, Johns Hopkins School of Medicine, Baltimore, United States
e-mail: rxu4@jhmi.edu

Received: January 31, 2023 Accepted: February 13, 2023 Available Online Date: March 08, 2023 • DOI: 10.4274/balkanmedj.galenos.2023.2023-1-100

Available at www.balkanmedicaljournal.org

ORCID iDs of the authors: K.R.R. 0000-0001-5573-7534; S.K.N. 0000-0002-9937-7478; O.A. 0000-0002-7275-1060; R.X. 0000-0003-4288-1232.

Cite this article as:
Ran KR, Wang A, Nair SK, Akça O, Xu R. Acute Multidisciplinary Management of Aneurysmal Subarachnoid Hemorrhage (aSAH). *Balkan Med J.*; 2023; 40(2):74-81.

intubation and mechanical ventilation for proper oxygenation. In addition, sedation, intubation, and mechanical ventilation are indicated in aSAH patients presenting with severe agitation or respiratory failure. Approximately 38.5-65% of aSAH patients require mechanical ventilation.[12] Arterial blood gases are used to adjust ventilator settings to achieve upper normoxia levels, or a $PaO_2 \geq 100$ mmHg.[13] In case of acute respiratory failure, to prevent pressure-induced secondary lung injury, settings can be adapted to target a PaO_2 of 60-80 mmHg with the lowest possible FiO_2.[14]

Hypercapnia, defined as $PaCO_2 > 45$ mmHg, is detrimental in the context of aSAH. High levels of CO_2 in the blood can induce a vasodilatory response, which increases cerebral circulation but raises ICP, increases intracranial hypertension, and reduces cerebral perfusion.[15] Studies have associated higher than normal $PaCO_2$ values with poor outcomes for aSAH patients.[16] On the other hand, an association between significant hypocapnia, $PaCO_2 < 30$ mmHg, and poor outcomes has also been reported.[17] A study found that the optimal range of $PaCO_2$ for aSAH patients was 30-38 mmHg based on clinical outcomes.[18] Although there are no firm guidelines regarding the target $PaCO_2$ value in aSAH patients, neurointensivists generally attempt to maintain a low-to-normal $PaCO_2$ target of 35-40 mmHg.[19]

aSAH is also known to cause neurogenic stress cardiomyopathy also known as Takotsubo cardiomyopathy (TTC), and leads to impaired cardiac function.[20] A study found that 16% of aSAH patients developed TTC, and when present, TTC was associated with higher mortality and poorer long-term functional outcomes.[20] Severe TTC may be present in up to 8% of SAH cases, and TTC severity may independently predict aSAH long-term outcomes, including mortality.[21] To assess cardiac function, aSAH patients routinely undergo transthoracic echocardiography (TTE), and the TTE results enable neurointensivists to observe intracardiac abnormalities and determine the necessary treatments to support the circulatory system.[22]

Neurological Examination

A rapid neurological examination is essential for assessing aSAH severity and can guide treatment decisions. The GCS is a routine part of aSAH patient assessment and provides an objective measurement of a patient's level of consciousness following brain injury (Table 1). The total GCS score provides a summative report of the patient's condition and determines the patient's level of impairment. Moreover, cranial nerve functions are also assessed simultaneously with the GCS. These include tests for pupillary reflex, extraocular movement, intact facial sensation and motor function, palate elevation, gag reflex, and tongue deviation. Furthermore, the motor and language functions of patients are also evaluated.

Several other clinical grading systems are routinely used to assess SAH severity. The Hunt and Hess scale is one of the most widely used grading systems for SAH and predicts mortality based on clinical features (Table 2).[23] Although the Hunt and Hess scale is a quick and easy method of assessing SAH, it has several notable limitations. Patients may present with features on their initial neurologic examination that do not allow classification into a single grade. In such cases, the classification is left to the subjective decision of the clinician. The Hunt and Hess scale has also been found to have sizable interobserver variability.[24] Furthermore, several studies have found that incremental increases in the Hunt and Hess scale did not correlate with progressively worse outcomes following aSAH (i.e. no dose-response type relationship was observed).[25,26] In 1988, the World Federation of Neurological Surgeons developed a new grading scale for SAH patients that considers both the total GCS score and the presence or absence of motor deficits to predict mortality (Table 3). This method of classification enables clinicians to assign grades based on objective examination results.

In addition to clinical grading scales, a mental status examination is conducted for all patients with aSAH. The mental status examination assesses alertness and orientation to person, place, and time. A decreased level of alertness is a symptom of hydrocephalus,

TABLE 1. Glasgow Coma Scale.

Glasgow coma scale		
Response	Scale	Score
Eye-opening response	Eyes open spontaneously	4
	Eyes open to verbal command	3
	Eyes open to pain	2
	No eye-opening	1
Verbal response	Orientated to time/person/place	5
	Confused	4
	Inappropriate words	3
	Incomprehensible sounds	2
	No verbal response	1
Motor response	Obey commands	6
	Localizes pain	5
	Flexion response to pain	4
	Abnormal flexion (decorticate) to pain	3
	Abnormal extension (decerebrate) to pain	2
	No motor response	1
Brain injury severity based on total score: Minor =13-15, Moderate =9-12, Severe =3-8		

TABLE 2. Hunt and Hess Grading Scale.

Hunt and hess grading scale		
Grade	Clinical presentation	Predicted mortality (%)
I	Asymptomatic or mild headache and slight nuchal rigidity	11
II	Moderate to severe headache, nuchal rigidity, no motor deficit, and potential cranial nerve deficit	26
III	Somnolent or confused, may have mild motor or focal neurologic deficit	37
IV	Stupor, moderate to severe motor or focal neurologic deficit	71
V	Coma, decerebrate posturing, or no motor response	100

which is estimated to occur in 20% of aSAH patients.[27] Acute hydrocephalus is caused by the abnormal production and impaired drainage of cerebrospinal fluid (CSF), which rapidly accumulates. Pressure from excess CSF can damage brain tissue and be fatal if left untreated. If a decreased level of alertness or consciousness is found during the neurological assessment of a potential aSAH patient, further imaging is urgently needed to determine whether hydrocephalus is present.

In addition, routine bedside neurological assessments performed by neurocritical care nurses are an essential component of aSAH patient care throughout their hospital stay. According to the American Association of Neuroscience Nursing guidelines, aSAH patients require neurological assessments at least hourly while in the intensive care unit (ICU).[28] Certain symptoms, such as worsening headache, decreased level of consciousness, and new-onset focal neurological deficits, can raise suspicion of elevated ICP and aneurysm rebleeding.[29] Frequent bedside monitoring can also alert care team members to the occurrence of seizures, hemodynamic instability, or fever. Through early detection of patient clinical deterioration and regular communication of patient clinical status with neurointensivist and neurosurgical teams, neurocritical care nurses form an essential part of the multidisciplinary care team.

Diagnostic Imaging

Cerebral imaging is an essential step in the diagnosis of aSAH, and non-contrast computed tomography (CT) scan remains the most commonly used diagnostic tool. CT scans are particularly useful for the detection of aSAH during the acute period, with a reported sensitivity of approximately 100% in the first 3 days after ictus.[30] Failure to obtain a CT scan is the most common diagnostic error in the workup of aSAH.[31]

If a CT scan is negative for SAH but there remains a high clinical suspicion for aSAH, the American Heart Association (AHA) guidelines recommend confirming these results through a lumbar puncture (LP). CSF collected via LP can be tested for an elevated red blood cell count or xanthochromia, either of which suggests SAH.[32] Xanthochromia, which describes yellow or pink discoloration of CSF, is best detected 6-12 hours after aSAH and lasts at least 2 weeks in most patients.[33] The diagnostic specificity of LP is limited by the potential for traumatic needle placement. It is challenging to distinguish true SAH from a traumatic tap, mainly due to the lack of a definitive cut-off value for red blood cell count. While a decrease in red blood cell count from tube 1 to tube 4 of the LP samples may help distinguish true SAH from needle trauma, there are no definitive guidelines or established red blood cell ratios for this method.[34]

TABLE 3. World Federation of Neurological Surgeons Grading Scale.

World Federation of Neurological Surgeons grading scale			
Grade	Glasgow coma scale	Motor deficit	Survival (%)
I	15	Absent	70
II	13-14	Absent	60
III	13-14	Present	50
IV	7-12	Present or absent	20
V	3-6	Present or absent	10

If both non-contrast CT imaging and LP are negative, CT angiography (CTA) is the next step in the workup of aSAH. CTA uses intravenous contrast to visualize the cerebral vasculature, and non-contrast CT followed by CTA has been found to rule out aSAH with > 99% sensitivity.[35] Failure to detect an aneurysm via CTA may suggest a diagnosis of non-aneurysmal SAH, such as perimesencephalic non-aneurysmal SAH, which is hypothesized to result from venous bleeding around the midbrain and estimated to account for 6.8% of spontaneous SAH cases.[36] However, CTA scans may have a relatively low sensitivity for detecting small aneurysms.[37] The most updated AHA guidelines state that CTA may be considered in the workup of aSAH, but if CTA imaging results are inconclusive, DSA imaging is still recommended.[13]

Recent advances in brain magnetic resonance angiography (MRA) make it a potential tool for the investigation and diagnosis of aSAH. Unlike CTA, MRA enables visualization of the cerebral vasculature without contrast use and necessitates less radiation exposure. However, a meta-analysis found that while MRA and CTA have a comparable sensitivity of approximately 95% for aneurysm detection in SAH, MRA has a lower specificity than CTA, 89% versus 96.2%.[38] Furthermore, in the emergency setting of an aSAH, using MRA for diagnostic purposes remains challenging due to lengthy imaging periods, the logistical difficulties of scanning acutely ill patients, and potential delays to treatment. Therefore, MRA scans are currently not a routine part of the diagnostic workflow for aSAH at our institution.

According to the most recent AHA guidelines, DSA remains the gold standard for aneurysm detection and neurosurgical planning in definitive aSAH management.[13] In acute aSAH, small aneurysms may be compressed by the hemorrhage, resulting in negative CTA imaging. A study that compared DSA with CTA for the detection of ruptured aneurysms reported that CTA only detected 306 of the 431 total aneurysms detected by DSA.[37] In addition, repeat DSA imaging may be useful for aneurysm detection if the initial DSA imaging is negative but clinical suspicion of aSAH still exists.[39]

Intracranial Pressure Management

One of the most common causes of decreased consciousness during aSAH is elevated ICP. aSAH can lead to an abrupt rise in ICP, which can compromise cerebral perfusion and cause temporary intracranial circulatory arrest. Monitoring and treatment of elevated ICP during the acute management of aSAH is therefore critical for improving patient outcomes. Studies have reported that over 80% of aSAH patients experience an episode of elevated ICP, defined as ≥ 20 mmHg.[40] In addition, elevated ICP is strongly associated with poor outcomes and increased mortality after aSAH.[40] Current ICP treatment goals for aSAH are based on the traumatic brain injury guidelines of the Brain Trauma Foundation, which recommend maintaining ICP < 22 mmHg and cerebral perfusion pressure (CPP) between 60-70 mmHg for patients with GCS scores ≤ 8.[41]

For patients who display hydrocephalus on CT scan, ICP is managed via placement of an external ventricular drain (EVD). Proper EVD management has been shown to influence rates of delayed cerebral ischemia (DCI), length of stay in the hospital or ICU, and cognitive outcomes among survivors of SAH.[42] However, the abrupt lowering of ICP via an EVD can increase aneurysmal transmural pressures and precipitate re-rupture.[43] Furthermore, whether EVDs are continuously or intermittently opened to drainage prior to aneurysm securement varies by institution. A multicenter study found that the majority (81%) of institutions surveyed prefer continuous open drainage.[44] In addition, for unsecured aneurysms, 58% of institutions used a strategy that sought to minimize CSF drainage, whereas 42% of institutions used a strategy that sought to enhance CSF drainage.[44] At our institution, we employ a strategy that seeks to temporize ICP while minimizing the risk of re-rupture by initially setting EVDs to a pop-off pressure of 20 mmHg (i.e. drains only when ICP goes above 20 mmHg).

Electrolyte imbalances may also be an important cause of elevated ICP after aSAH. Hyponatremia, defined as a serum sodium level < 131 mEq/L, is the most common electrolyte abnormality observed in the context of aSAH and is estimated to affect about 30-56% of aSAH patients.[45] aSAH patients with hyponatremia have been found to have a longer length of stay, increased risk of vasospasm, and higher morbidity. Osmotically active agents, such as mannitol and hypertonic saline, are commonly used to manage elevated ICP in the setting of aSAH. These hyperosmolar agents decrease ICP by causing fluid to shift from the interstitial and intracellular spaces of the brain into the bloodstream.[46] However, the use of osmotically active agents may be associated with certain risks for the patient. For example, mannitol initially causes a rapid increase in intravascular volume, which may precipitate acute hypervolemia and cause pulmonary edema or heart failure in predisposed patients.[47] Following this initial increase in intravascular volume, mannitol exerts a strong diuretic effect, which can cause intravascular volume contraction.[47] Therefore, neuro-intensivists must carefully monitor parameters such as fluid balance, blood pressure, serum sodium, and serum osmolality to prevent secondary injury.

Clinically induced hyperventilation with subsequent hypocapnia can be considered as another method for rapidly reducing ICP. However, multiple studies have shown that hypocapnia can induce cerebral vasoconstriction, which may worsen cerebral ischemia and lead to poorer neurologic outcomes.[48] Therefore, induced hyperventilation is recommended only for short, temporary use to dramatically reduce elevated ICP. Moreover, we need to acknowledge that hypocapnia resulting in respiratory alkalosis will be compensated by renal-based metabolic responses. More research on the outcomes of clinical hyperventilation is required to determine whether it is useful in the setting of aSAH.

Blood Pressure Management

The blood pressure (BP) of aSAH patients must be maintained within a range that reduces the risk of rebleeding from the ruptured aneurysm while maintaining adequate CPP. Rebleeding is estimated to occur in 8-23% of aSAH patients within 72 hours after onset and has an extremely poor prognosis, with reported mortality rates as high as 60%.[49] Although proper BP control is important for the prevention of rebleeding, there are no firm guidelines on the magnitude of BP control necessary to reduce the risk of rebleeding. For most patients with acute SAH, the AHA recommends maintaining a systolic BP < 160 mmHg.[13] Our institution targets a systolic BP < 140 mmHg for patients with aSAH.

The risk of impaired cerebral perfusion due to elevated ICP is also an important consideration for BP management and may require paying attention to the lower limits of BP. There are no specific guidelines for optimum mean arterial pressure (MAP) values in aSAH patients, but maintaining a MAP between 70 and 90 mmHg is generally accepted.[50] Our institution targets an MAP > 75 mmHg for patients with aSAH. Since increasing MAP helps to maintain CPP, antihypertensive therapy is often withheld unless there is an extreme increase in BP.[13] Though uncommon in the setting of aSAH, hypotension is also undesirable and can exacerbate ischemic injury. Hypotensive patients should be initially assessed for appropriate intravascular fluid status, oxygen-carrying capacity, cardiac rate, and rhythm abnormalities, and treated appropriately. Vasopressor infusions, including norepinephrine or phenylephrine, may be required to maintain normal MAP values.

In addition, careful fluid management is a critical part of BP control and maintaining adequate CPP. Both hypovolemia and fluid loading beyond normal preload values have been associated with DCI and worse functional outcome.[51] Randomized controlled trials (RCTs) investigating the efficacy of prophylactic hypervolemic therapy for DCI prevention have found that patients who received a mean fluid intake of 4-5 l/day versus 3 l/day did not experience any clinical benefit and were more likely to experience complications, such as arrhythmias and congestive heart failure.[52,53] Current AHA and American Stroke Association (ASA) guidelines recommend targeting euvolemia to prevent DCI. Saline 0.9% is the most commonly used maintenance fluid, but repletion via albumin has demonstrated promising findings in animal models of brain injury and is currently being explored as a treatment for aSAH patients.[54] Data from the ALISAH (Albumin in Subarachnoid Hemorrhage) pilot clinical trial suggests that albumin administration is associated with a lower incidence of vasospasm and DCI.[54] However, this finding is yet to be validated in a phase III randomized controlled trial, and results from the SAFE (Saline versus Albumin Fluid Evaluation) trial associated fluid resuscitation via albumin with a higher mortality rate among patients with traumatic brain injury.[55] Therefore, most neurointensivists administer normal saline to achieve euvolemia for patients with aSAH.

Seizure Prophylaxis

Seizures are reported in up to 27% of aSAH patients and occur most commonly in the immediate posthemorrhagic period.[56] Studies have associated seizures with reduced cerebral blood flow, increased ICP, and increased hemorrhage severity.[56] Furthermore, early in-hospital mortality is significantly more

common among non-traumatic SAH patients who experience seizures.[57] The high risk of seizures and concerns about the possible consequences of a seizure in the setting of an unsecured aneurysm have led many centers to routinely administer prophylactic antiepileptic drugs (AEDs), such as phenytoin and levetiracetam, after SAH.[56]

Despite the frequent use of AEDs, the indications and duration of AED use following aSAH are often center-specific. Propensity score-matched analysis suggests that prophylactic AEDs do not significantly reduce the risk of seizure occurrence in patients with spontaneous SAH.[58] Furthermore, several recent studies have highlighted the adverse side effects associated with posthemorrhagic AED exposure. These include serious drug-related complications, such as impaired liver function, thrombocytopenia, rash, and Stevens-Johnson syndrome, and worse cognitive and functional outcomes.[58] A study by Naidech et al.[59] found that phenytoin exposure was associated with cognitive and functional disability following SAH. Therefore, whether AED prophylaxis should be initiated in patients with aSAH remains a challenging decision. AHA guidelines state that AED prophylaxis may be considered during the acute phase of aSAH, but do not recommend its long-term use unless patients are deemed to be at risk of delayed seizures.[13]

Vasospasm

Cerebral vasospasm is a phenomenon characterized by vasoconstriction of the intracranial arteries, which commonly occurs in the acute period following aSAH. Neurointensivists can monitor aSAH patients for vasospasm daily using transcranial Doppler (TCD) sonography, a non-invasive technique for measuring blood flow within the intracranial arteries. Commonly used benchmarks for blood flow velocity measured from the middle cerebral artery include < 120 cm/sec for normal blood flow, 120-150 cm/sec for mild vasospasm, 150-200 cm/sec for moderate vasospasm, and > 200 cm/sec for severe vasospasm. The Lindegaard ratio, which is calculated as blood velocity in the middle cerebral artery divided by that of the cervical internal carotid artery, is another method for measuring vasospasm risk. A ratio of 3-6 indicates mild vasospasm, while a ratio > 6 indicates severe vasospasm. TCDs have 90% sensitivity and 71% specificity for detecting vasospasm, but the diagnostic accuracy depends on the user's ability to obtain a proper insonation window.[60] Increased blood flow velocity detected via TCD can alert neurointensivists to the potential development of symptomatic vasospasm, which is characterized by clinical deterioration due to DCI and is estimated to occur in approximately 20-40% of aSAH cases.[61] The modified Fisher scale measures the risk of vasospasm after SAH. A grade is assigned based on the SAH thickness and the presence of intraventricular hemorrhage (IVH) (Table 4). A recent meta-analysis confirmed that higher scores on the modified Fisher scale are associated with an increased risk of DCI. Among SAH patients assigned a score of 0-1, 21% experienced DCI. For patients assigned modified Fisher scale scores of 2, 3, and 4, the overall occurrence of DCI was 26%, 30%, and 42%, respectively.[61]

Cerebral vasospasm leading to DCI is a major cause of morbidity for aSAH.[62] Neurointensivists may attempt to avoid vasospasm in the setting of acute aSAH via treatment with nimodipine. Nimodipine is a second-generation calcium channel blocker that was initially developed for the management of systemic hypertension. The current use of nimodipine is primarily limited to patients with SAH. Notably, nimodipine is the only pharmacologic treatment that has been demonstrated to improve neurological outcomes after aSAH.[63] Although nimodipine was originally hypothesized to be beneficial to aSAH patients by blocking vasospasm, other studies that used more potent calcium channel blockers to block vasospasm in patients with aSAH failed to show an improvement in neurological outcomes.[64] Therefore, the mechanism by which nimodipine benefits aSAH patients is not fully understood. Current guidelines recommend administering nimodipine as early as possible or within 96 hours of SAH diagnosis.[13]

Vasospasm may also be medically treated with triple-H therapy, which includes increasing BP (Hypertension), increasing intravascular volume (Hypervolemia), and reducing blood viscosity (Hemodilution).[65] The only H that is utilized frequently in current practice is Hypertension. Phenylephrine and norepinephrine are the commonly used pharmacological agents to induce hypertension.[66] A survey of current practices regarding triple-H therapy reported that therapeutic goals for systolic BP range from 140 to 240 mmHg, and therapeutic goals for MAP range from 70 to 210 mmHg.[66] Originally, for hypervolemia, a central venous pressure of 10 mmHg and a pulmonary artery occlusion pressure of 15 mmHg was generally recommended.[66] However, the current approach prioritizes normovolemia or euvolemia. Fluid management is commonly monitored by using stroke volume and cardiac output monitors, such as a pulse index continuous cardiac output (PiCCO).[67] While hemodilution may alleviate vasospasm by decreasing viscosity, decreased hemoglobin levels may compromise cerebral oxygen delivery in aSAH patients. Tertiary centers generally target an average hematocrit of 30, but the optimal hemoglobin goal is unknown.[66] Triple-H therapy also poses potential risks of pulmonary edema, dilutional hyponatremia,

TABLE 4. Modified Fisher Scale.

Modified Fisher Scale		
Grade	CT findings	Risk of symptomatic vasospasm (%)
0	No SAH or IVH	0
1	Minimal SAH (< 1 mm thin) and no IVH	24
2	Minimal SAH (< 1 mm thin) with bilateral IVH	33
3	Thick SAH (> 1 mm thick, completely filling one or more cistern or fissure) without bilateral IVH	33
4	Thick SAH (> 1 mm thick, completely filling one or more cistern or fissure) with bilateral IVH	40

SAH: Subarachnoid hemorrhage; IVH: Intraventricular hemorrhage

cerebral edema exacerbation, increased ICP, hemorrhagic infarction, and aneurysm rebleeding.[68]

In patients who fail medical treatments for vasospasm, endovascular/surgical treatments include intra-arterial (IA) calcium channel blockers and/or balloon angioplasty. Nicardipine and verapamil are calcium channel blockers that can be administrated intra-arterially and have been demonstrated to effectively treat vasospasm after aSAH.[69,70] Intravenous (IV) administration of other spasmolytics, such as the phosphodiesterase inhibitor milrinone, has also been demonstrated to safely treat vasospasm, and rescue IA milrinone can effectively treat vasospasm in cases that are refractory to IV milrinone.[71] Finally, for cases in which vasospasm is refractory to IA spasmolytic treatment, balloon angioplasty can be used as a safe and effective surgical intervention.[72] Endovascular therapies, such as balloon angioplasty, used to treat vasospasm have a longer-lasting effect and are associated with a reduced risk of in-hospital mortality.[73] Current AHA guidelines do not recommend endovascular prophylaxis for vasospasm, but state that such interventions may be considered for the treatment of refractory vasospasm.[13]

Ongoing research in detecting impaired autoregulation after aSAH holds promise for reducing rates of vasospasm and DCI. Personalized BP targets based on cerebral oximetry measurements may result in better patient functional outcomes when used instead of more general BP ranges. Our institution routinely uses optimal MAP (OptMAP) values derived from cerebral oximetry assessments to guide BP management. Preliminary findings indicate that targeting cerebral oximetry-derived OptMAP values is associated with decreased rates of DCI and mortality.[74] A recent prospective study that investigated the use of cerebral oxygenation-guided BP management found that limiting deviation from calculated autoregulatory goals was associated with improved functional outcomes.[75] In the future, personalized BP targets may become a routine part of aSAH management, especially as advances such as near-infrared spectroscopy (NIRS) make non-invasive continuous monitoring of cerebral oxygenation possible.[76] The utility of NIRS for the early detection of vasospasm is currently being studied in the COMOVA (Permanent Cerebral Oximetry Monitoring for Early Diagnosis and Treatment of Delayed Vasospasm After Subarachnoid Hemorrhage) clinical trial.

Time to Definitive Aneurysm Securement

Clinical guidelines from the AHA and ASA recommend aneurysm securement as early as feasible.[13] Currently, most patients with aSAH receive treatment within 24 hours of presentation. Historically, during the 1960s and 1970s, neurosurgeons waited for 2-3 weeks after hemorrhage to avoid performing surgery on aneurysms during peak vasospasm and brain swelling periods, which is known to increase the rates of perioperative complications and mortality.[77] A prospective randomized study that compared neurologic outcomes for aSAH patients who received surgical treatment during the acute (0-3 days), intermediate (4-7 days), and late period (8 or more days) after hemorrhage found that patients who underwent surgery during the acute period had the highest rate of functional independence (91.5%) at 3 months post-surgery, followed by patients treated during the late period (80.0%), and then those treated during the intermediate period (78.6%).[78] Similarly, the International Cooperative Study on the Timing of Aneurysm Surgery compared outcomes for ruptured aneurysms treated at 0-3 days, 4-10 days, and 11-14 days post-bleeding. Outcomes for early and late surgical treatment were similar, and mortality was the highest for aneurysms treated 7-10 days post-bleeding.[79] Notably, a more recent post-hoc analysis of the International Subarachnoid Aneurysm Trial, which compared surgical clipping and coiling of ruptured intracranial aneurysms, found that patients who received definitive aneurysm treatment within the first 4 days had improved neurological outcomes compared with patients treated 5-10 days or > 10 days after ictus.[77]

Although our article presents best practices for acute aSAH management based on current guidelines, medical decision-making must ultimately be guided by individual patient considerations. aSAH patients may present with other pathologies, such as concomitant hemorrhage in other intracranial compartments and cardiac dysfunction. Furthermore, certain hematological disorders, such as acute myeloblastic leukemia and congenital coagulopathies, can cause acute SAH.[80] Finally, our article focuses on the acute period of aSAH prior to aneurysm securement. While high-quality, multidisciplinary care during this period is necessary for favorable patient outcomes, ensuring optimal long-term neurological outcomes also depends on the care provided both during and after surgical treatment of the aneurysm.

In conclusion, aSAH is a medical emergency with high morbidity and mortality rates. Proper management during the acute phase and prior to aneurysm obliteration has the capacity to save lives and improve neurological outcomes. A multidisciplinary team comprising of staff in the neurocritical care unit, radiology department, and neurosurgery department play important roles during this time. Neurointensivists manage cardiopulmonary stability and patient comorbidities, radiologists obtain and interpret diagnostic imaging examinations, and neurosurgeons and neuro-anesthesiologists manage ICP with interventions such as EVD placement. In addition, neurocritical care nurses provide first-hand guidance for this multidisciplinary care via frequent neurological assessments, immediate management of patient care, and communication with neurointensivist and neurosurgery teams. Given that most centers secure ruptured aneurysms within 24 hours after SAH onset and that many patients present with other comorbidities that require the involvement of other medical specialty teams, collaboration among these different teams is very important. Furthermore, as new innovations in the treatment of SAH continue to emerge, including new monitoring techniques, drugs, and interventions, providers must remain informed about updates in best practice to ensure continued coordination of care. Therefore, the multidisciplinary approach is essential for the comprehensive and timely treatment of aSAH patients.

Authorship Contributions: Concept- K.R.R., A.C.W., S.K.N., O.A., R.X.; Design- K.R.R., A.C.W., S.K.N., O.A., R.X.; Data Collection or Processing- K.R.R., A.C.W., S.K.N., O.A., R.X.; Analysis or Interpretation- K.R.R., A.C.W., S.K.N., O.A., R.X.; Literature Search- K.R.R., A.C.W., S.K.N., O.A., R.X.; Writing- K.R.R., A.C.W., S.K.N., O.A., R.X.

Conflict of Interest: No conflict of interest was declared by the authors.

Funding: The authors declared that this study received no financial support

REFERENCES

1. Etminan N, Chang HS, Hackenberg K, et al. Worldwide Incidence of Aneurysmal Subarachnoid Hemorrhage According to Region, Time Period, Blood Pressure, and Smoking Prevalence in the Population: A Systematic Review and Meta-analysis. *JAMA Neurol.* 2019;76:588-597. [CrossRef]
2. D'Souza S. Aneurysmal Subarachnoid Hemorrhage. *J Neurosurg Anesthesiol.* 2015;27:222-240. [CrossRef]
3. Lantigua H, Ortega-Gutierrez S, Schmidt JM, et al. Subarachnoid hemorrhage: who dies, and why? *Crit Care.* 2015;19:309. [CrossRef]
4. Virta JJ, Skrifvars M, Reinikainen M, et al. Trends in Mortality after Intensive Care of Patients with Aneurysmal Subarachnoid Hemorrhage in Finland in 2003-2019: A Finnish Intensive Care Consortium study. *Neurocrit Care.* 2022;37:447-454. [CrossRef]
5. Dhandapani S, Singh A, Singla N, et al. Has Outcome of Subarachnoid Hemorrhage Changed With Improvements in Neurosurgical Services? *Stroke.* 2018;49:2890-2895. [CrossRef]
6. Macdonald RL, Schweizer TA. Spontaneous subarachnoid haemorrhage. *Lancet.* 2017;389:655-666. [CrossRef]
7. Nieuwkamp DJ, Setz LE, Algra A, Linn FH, de Rooij NK, Rinkel GJ. Changes in case fatality of aneurysmal subarachnoid haemorrhage over time, according to age, sex, and region: a meta-analysis. *Lancet Neurol.* 2009;8:635-642. [CrossRef]
8. de Winkel J, van der Jagt M, Lingsma HF, et al. International Practice Variability in Treatment of Aneurysmal Subarachnoid Hemorrhage. *J Clin Med.* 2021;10:762. [CrossRef]
9. Shah VA, Kazmi SO, Damani R, et al. Regional Variability in the Care and Outcomes of Subarachnoid Hemorrhage Patients in the United States. *Front Neurol.* 2022;13:908609. [CrossRef]
10. Rass V, Helbok R. Early Brain Injury After Poor-Grade Subarachnoid Hemorrhage. *Curr Neurol Neurosci Rep.* 2019;19:78. [CrossRef]
11. Gouvea Bogossian E, Diaferia D, Ndieugnou Djangang N, et al. Brain tissue oxygenation guided therapy and outcome in non-traumatic subarachnoid hemorrhage. *Sci Rep.* 2021;11:16235. [CrossRef]
12. Towner JE, Rahmani R, Zammit CG, Khan IR, Paul DA, Bhalla T, Roberts DE. Mechanical ventilation in aneurysmal subarachnoid hemorrhage: systematic review and recommendations. *Crit Care.* 2020;24:575. [CrossRef]
13. Connolly ES Jr, Rabinstein AA, Carhuapoma JR, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/american Stroke Association. *Stroke.* 2012;43:1711-1737. [CrossRef]
14. Hernández-Durán S, Salfelder C, Schaeper J, et al. Mechanical Ventilation, Sedation and Neuromonitoring of Patients with Aneurysmal Subarachnoid Hemorrhage in Germany: Results of a Nationwide Survey. *Neurocrit Care.* 2021;34:236-247. [CrossRef]
15. Rangel-Castilla L, Gopinath S, Robertson CS. Management of intracranial hypertension. *Neurol Clin.* 2008;26:521-541, x. Erratum in: Neurol Clin. 2008;26:xvii. Rangel-Castillo, Leonardo [corrected to Rangel-Castilla, Leonardo]. [CrossRef]
16. Reiff T, Barthel O, Schönenberger S, Mundiyanapurath S. High-normal PaCO2 values might be associated with worse outcome in patients with subarachnoid hemorrhage - a retrospective cohort study. *BMC Neurol.* 2020;20:31. [CrossRef]
17. Solaiman O, Singh JM. Hypocapnia in aneurysmal subarachnoid hemorrhage: incidence and association with poor clinical outcomes. *J Neurosurg Anesthesiol.* 2013;25:254-261. [CrossRef]
18. Darkwah Oppong M, Wrede KH, Müller D, et al. PaCO2-management in the neuro-critical care of patients with subarachnoid hemorrhage. *Sci Rep.* 2021;11:19191. [CrossRef]
19. Neumann JO, Chambers IR, Citerio G, et al. The use of hyperventilation therapy after traumatic brain injury in Europe: an analysis of the BrainIT database. *Intensive Care Med.* 2008;34:1676-1682. [CrossRef]
20. Kilbourn KJ, Levy S, Staff I, Kureshi I, McCullough L. Clinical characteristics and outcomes of neurogenic stress cadiomyopathy in aneurysmal subarachnoid hemorrhage. *Clin Neurol Neurosurg.* 2013;115:909-914. [CrossRef]
21. Molnár C, Gál J, Szántó D, et al. Takotsubo cardiomyopathy in patients suffering from acute non-traumatic subarachnoid hemorrhage-A single center follow-up study. *PLoS One.* 2022;17:e0268525. [CrossRef]
22. Komamura K, Fukui M, Iwasaku T, Hirotani S, Masuyama T. Takotsubo cardiomyopathy: Pathophysiology, diagnosis and treatment. *World J Cardiol.* 2014;6:602-609. [CrossRef]
23. Hunt WE, Hess RM. Surgical risk as related to time of intervention in the repair of intracranial aneurysms. *J Neurosurg.* 1968;28:14-20. [CrossRef]
24. Degen LA, Dorhout Mees SM, Algra A, Rinkel GJ. Interobserver variability of grading scales for aneurysmal subarachnoid hemorrhage. *Stroke.* 2011;42:1546-1549. [CrossRef]
25. Proust F, Hannequin D, Langlois O, Freger P, Creissard P. Causes of morbidity and mortality after ruptured aneurysm surgery in a series of 230 patients. The importance of control angiography. *Stroke.* 1995;26:1553-1557. [CrossRef]
26. Ogilvy CS, Carter BS. A proposed comprehensive grading system to predict outcome for surgical management of intracranial aneurysms. *Neurosurgery.* 1998;42:959-968; discussion 968-970. [CrossRef]
27. Chen S, Luo J, Reis C, Manaenko A, Zhang J. Hydrocephalus after Subarachnoid Hemorrhage: Pathophysiology, Diagnosis, and Treatment. *Biomed Res Int.* 2017;2017:8584753. [CrossRef]
28. LaBuzetta JN, Hirshman BR, Malhotra A, Owens RL, Kamdar BB. Practices and Patterns of Hourly Neurochecks: Analysis of 8,936 Patients With Neurological Injury. *J Intensive Care Med.* 2022;37:784-792. [CrossRef]
29. Preece A, Young S. Caring for Patients with Aneurysmal Subarachnoid Hemorrhage: Nursing Perspectives from the United Kingdom. *Crit Care Nurs Clin North Am.* 2021;33:47-59. [CrossRef]
30. Cortnum S, Sørensen P, Jørgensen J. Determining the sensitivity of computed tomography scanning in early detection of subarachnoid hemorrhage. Neurosurgery. 2010;66:900-902; discussion 903. [CrossRef]
31. Kowalski RG, Claassen J, Kreiter KT, et al. Initial misdiagnosis and outcome after subarachnoid hemorrhage. *JAMA.* 2004;291:866-869. [CrossRef]
32. Ichiba T, Hara M, Nishikawa K, Tanabe T, Urashima M, Naitou H. Comprehensive Evaluation of Diagnostic and Treatment Strategies for Idiopathic Spinal Subarachnoid Hemorrhage. *J Stroke Cerebrovasc Dis.* 2017;26:2840-2848. [CrossRef]
33. Dugas C, Jamal Z, Bollu PC. Xanthochromia. 2022. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022. [CrossRef]
34. Gorchynski J, Oman J, Newton T. Interpretation of traumatic lumbar punctures in the setting of possible subarachnoid hemorrhage: who can be safely discharged? *Cal J Emerg Med.* 2007;8:3-7. [CrossRef]
35. McCormack RF, Hutson A. Can computed tomography angiography of the brain replace lumbar puncture in the evaluation of acute-onset headache after a negative noncontrast cranial computed tomography scan? *Acad Emerg Med.* 2010;17:444-451. [CrossRef]
36. Hou K, Yu J. Current status of perimesencephalic non-aneurysmal subarachnoid hemorrhage. *Front Neurol.* 2022;13:960702. [CrossRef]
37. Philipp LR, McCracken DJ, McCracken CE, et al. Comparison Between CTA and Digital Subtraction Angiography in the Diagnosis of Ruptured Aneurysms. *Neurosurgery.* 2017;80:769-777. [CrossRef]
38. Sailer AM, Wagemans BA, Nelemans PJ, de Graaf R, van Zwam WH. Diagnosing intracranial aneurysms with MR angiography: systematic review and meta-analysis. *Stroke.* 2014;45:119-126. [CrossRef]
39. Agid R, Andersson T, Almqvist H, et al. Negative CT angiography findings in patients with spontaneous subarachnoid hemorrhage: When is digital subtraction angiography still needed? *AJNR Am J Neuroradiol.* 2010;31:696-705. [CrossRef]
40. Magni F, Pozzi M, Rota M, Vargiolu A, Citerio G. High-Resolution Intracranial Pressure Burden and Outcome in Subarachnoid Hemorrhage. *Stroke.* 2015;46:2464-2469. [CrossRef]
41. Carney N, Totten AM, O'Reilly C, et al. Guidelines for the Management of Severe Traumatic Brain Injury, Fourth Edition. *Neurosurgery.* 2017;80:6-15. [CrossRef]

42. Klopfenstein JD, Kim LJ, Feiz-Erfan I, et al. Comparison of rapid and gradual weaning from external ventricular drainage in patients with aneurysmal subarachnoid hemorrhage: a prospective randomized trial. J Neurosurg. 2004;100:225-229. [CrossRef]
43. Gigante P, Hwang BY, Appelboom G, Kellner CP, Kellner MA, Connolly ES. External ventricular drainage following aneurysmal subarachnoid haemorrhage. Br J Neurosurg. 2010;24:625-632. [CrossRef]
44. Chung DY, Leslie-Mazwi TM, Patel AB, Rordorf GA. Management of External Ventricular Drains After Subarachnoid Hemorrhage: A Multi-Institutional Survey. Neurocrit Care. 2017;26:356-361. [CrossRef]
45. Sherlock M, O'Sullivan E, Agha A, et al. The incidence and pathophysiology of hyponatraemia after subarachnoid haemorrhage. Clin Endocrinol (Oxf). 2006;64:250-254. [CrossRef]
46. Diringer MN, Scalfani MT, Zazulia AR, Videen TO, Dhar R, Powers WJ. Effect of mannitol on cerebral blood volume in patients with head injury. Neurosurgery. 2012;70:1215-1218; discussion 1219. [CrossRef]
47. Halstead MR, Geocadin RG. The Medical Management of Cerebral Edema: Past, Present, and Future Therapies. Neurotherapeutics. 2019;16:1133-1148. [CrossRef]
48. Zhang Z, Guo Q, Wang E. Hyperventilation in neurological patients: from physiology to outcome evidence. Curr Opin Anaesthesiol. 2019;32:568-573. [CrossRef]
49. van Donkelaar CE, Bakker NA, Veeger NJ, et al. Predictive Factors for Rebleeding After Aneurysmal Subarachnoid Hemorrhage: Rebleeding Aneurysmal Subarachnoid Hemorrhage Study. Stroke. 2015;46:2100-2106. [CrossRef]
50. Lee K, Choi HA, Edwards N, Chang T, Sladen RN. Perioperative critical care management for patients with aneurysmal subarachnoid hemorrhage. Korean J Anesthesiol. 2014;67:77-84. [CrossRef]
51. Vergouw LJM, Egal M, Bergmans B, et al. High Early Fluid Input After Aneurysmal Subarachnoid Hemorrhage: Combined Report of Association With Delayed Cerebral Ischemia and Feasibility of Cardiac Output-Guided Fluid Restriction. J Intensive Care Med. 2020;35:161-169. [CrossRef]
52. Egge A, Waterloo K, Sjøholm H, Solberg T, Ingebrigtsen T, Romner B. Prophylactic hyperdynamic postoperative fluid therapy after aneurysmal subarachnoid hemorrhage: a clinical, prospective, randomized, controlled study. Neurosurgery. 2001;49:593-605; discussion 605-606. [CrossRef]
53. Lennihan L, Mayer SA, Fink ME, et al. Effect of hypervolemic therapy on cerebral blood flow after subarachnoid hemorrhage : a randomized controlled trial. Stroke. 2000;31:383-391. [CrossRef]
54. Suarez JI, Martin RH, Calvillo E, et al. The Albumin in Subarachnoid Hemorrhage (ALISAH) multicenter pilot clinical trial: safety and neurologic outcomes. Stroke. 2012;43:683-690. [CrossRef]
55. SAFE Study Investigators; Australian and New Zealand Intensive Care Society Clinical Trials Group; Australian Red Cross Blood Service, et al. Saline or albumin for fluid resuscitation in patients with traumatic brain injury. N Engl J Med. 2007;357:874-884. [CrossRef]
56. Kodankandath TV, Farooq S, Wazni W, et al. Seizure Prophylaxis in the Immediate Post-Hemorrhagic Period in Patients with Aneurysmal Subarachnoid Hemorrhage. J Vasc Interv Neurol. 2017;9:1-4. [CrossRef]
57. Arboix A, Martí-Vilalta JL. Predictive clinical factors of very early in-hospital mortality in subarachnoid hemorrhage. Clin Neurol Neurosurg. 1999;101:100-105. [CrossRef]
58. Panczykowski D, Pease M, Zhao Y, et al. Prophylactic Antiepileptics and Seizure Incidence Following Subarachnoid Hemorrhage: A Propensity Score-Matched Analysis. Stroke. 2016;47:1754-1760. [CrossRef]
59. Naidech AM, Kreiter KT, Janjua N, et al. Phenytoin exposure is associated with functional and cognitive disability after subarachnoid hemorrhage. Stroke. 2005;36:583-587. [CrossRef]
60. Kumar G, Shahripour RB, Harrigan MR. Vasospasm on transcranial Doppler is predictive of delayed cerebral ischemia in aneurysmal subarachnoid hemorrhage: a systematic review and meta-analysis. J Neurosurg. 2016;124:1257-1264. [CrossRef]
61. van der Steen WE, Leemans EL, van den Berg R, et al. Radiological scales predicting delayed cerebral ischemia in subarachnoid hemorrhage: systematic review and meta-analysis. Neuroradiology. 2019;61:247-256. [CrossRef]
62. Rumalla K, Lin M, Ding L, et al. Risk Factors for Cerebral Vasospasm in Aneurysmal Subarachnoid Hemorrhage: A Population-Based Study of 8346 Patients. World Neurosurg. 2021;145:e233-e241. [CrossRef]
63. Allen GS, Ahn HS, Preziosi TJ, et al. Cerebral arterial spasm--a controlled trial of nimodipine in patients with subarachnoid hemorrhage. N Engl J Med. 1983;308:619-624. [CrossRef]
64. Feigin VL, Rinkel GJ, Algra A, Vermeulen M, van Gijn J. Calcium antagonists in patients with aneurysmal subarachnoid hemorrhage: a systematic review. Neurology. 1998;50:876-883. [CrossRef]
65. Archer DP, Shaw DA, Leblanc RL, Tranmer BI. Haemodynamic considerations in the management of patients with subarachnoid haemorrhage. Can J Anaesth. 1991;38:454-470. [CrossRef]
66. Meyer R, Deem S, Yanez ND, Souter M, Lam A, Treggiari MM. Current practices of triple-H prophylaxis and therapy in patients with subarachnoid hemorrhage. Neurocrit Care. 2011;14:24-36. [CrossRef]
67. Yoneda H, Nakamura T, Shirao S, et al. Multicenter prospective cohort study on volume management after subarachnoid hemorrhage: hemodynamic changes according to severity of subarachnoid hemorrhage and cerebral vasospasm. Stroke. 2013;44:2155-2161. [CrossRef]
68. Lee KH, Lukovits T, Friedman JA. "Triple-H" therapy for cerebral vasospasm following subarachnoid hemorrhage. Neurocrit Care. 2006;4:68-76. [CrossRef]
69. Linfante I, Delgado-Mederos R, Andreone V, Gounis M, Hendricks L, Wakhloo AK. Angiographic and hemodynamic effect of high concentration of intra-arterial nicardipine in cerebral vasospasm. Neurosurgery. 2008;63:1080-1086; discussion 1086-1087. [CrossRef]
70. Keuskamp J, Murali R, Chao KH. High-dose intraarterial verapamil in the treatment of cerebral vasospasm after aneurysmal subarachnoid hemorrhage. J Neurosurg. 2008;108:458-463. [CrossRef]
71. Abulhasan YB, Ortiz Jimenez J, Teitelbaum J, Simoneau G, Angle MR. Milrinone for refractory cerebral vasospasm with delayed cerebral ischemia. J Neurosurg. 2020;134:971-982. [CrossRef]
72. Newell DW, Eskridge JM, Mayberg MR, Grady MS, Winn HR. Angioplasty for the treatment of symptomatic vasospasm following subarachnoid hemorrhage. J Neurosurg. 1989;71:654-660. [CrossRef]
73. Johnston SC. Effect of endovascular services and hospital volume on cerebral aneurysm treatment outcomes. Stroke. 2000;31:111-117. [CrossRef]
74. Shah V, Humayun M, Radzik B, et al. 532: Cerebral Oximetry-Derived Optimal Blood Pressue Targets In Aneurysmal Subarachnoid Hemorrhage. Critical Care Medicine. 2023;51:253. [CrossRef]
75. Silverman A, Kodali S, Strander S, et al. Deviation From Personalized Blood Pressure Targets Is Associated With Worse Outcome After Subarachnoid Hemorrhage. Stroke. 2019;50:2729-2737. [CrossRef]
76. Zweifel C, Castellani G, Czosnyka M, et al. Continuous assessment of cerebral autoregulation with near-infrared spectroscopy in adults after subarachnoid hemorrhage. Stroke. 2010;41:1963-1968. [CrossRef]
77. Dorhout Mees SM, Molyneux AJ, Kerr RS, Algra A, Rinkel GJ. Timing of aneurysm treatment after subarachnoid hemorrhage: relationship with delayed cerebral ischemia and poor outcome. Stroke. 2012;43:2126-2129. [CrossRef]
78. Ohman J, Heiskanen O. Timing of operation for ruptured supratentorial aneurysms: a prospective randomized study. J Neurosurg. 1989;70:55-60. [CrossRef]
79. Kassell NF, Torner JC, Jane JA, Haley EC Jr, Adams HP. The International Cooperative Study on the Timing of Aneurysm Surgery. Part 2: Surgical results. J Neurosurg. 1990;73:37-47. [CrossRef]
80. Arboix A, Jiménez C, Massons J, Parra O, Besses C. Hematological disorders: a commonly unrecognized cause of acute stroke. Expert Rev Hematol. 2016;9:891-901. [CrossRef]