8 Anesthesia for Aneurysmal Subarachnoid Hemorrhage

Nicolas Bruder, Salah Boussen, and Lionel Velly

8.1 Introduction

SAH is a rare disease explaining that the European Medicines Agency has given the status of orphan disease to SAH. Despite its relative rarity, SAH is still a subject of considerable interest explaining an extensive literature on the subject. However, there is a paucity of large, prospective, randomized trials explaining a large variability of clinical practice throughout the world [1, 2]. As expected, a number of retrospective studies have shown decreased mortality and improved neurologic outcome in high-volume centers compared to low-volume ones [3–5]. The definition of high volume is very variable in the literature. In the 2012 American guidelines, high volume is defined above 35 aneurysmal SAH cases per year. However, in a recent study, a relatively stable mortality was obtained above 60 cases/year [4]. There may be multiple reasons to explain these findings as availability of interventional neuroradiologists for coiling; increased experience of neurosurgeons, radiologists, anesthesiologists, and intensivists; better availability of complex procedures as cerebral angioplasty; and dedicated neuro-intensive care units. Except coiling and angioplasty, no magic treatment has appeared in the last 20 years. Nevertheless, there has been a clear trend toward a constant decrease in mortality and improved neurologic outcome in survivors. Despite increasing age of patients admitted for SAH, case-fatality rates have decreased by 17% between 1973 and 2002 [6]. In more recent years, mortality has still declined in the same proportion [7], but 90-day mortality remains around 30%, leaving room for further improvement [8, 9].

The main complication after SAH is cerebral ischemia that may have multiple causes. These causes may be divided between early and late cerebral ischemia (Fig. 8.1). Very early ischemia occurs in the first hours after aneurysm bleeding. It is due to intracranial hypertension, acute cerebral vasoconstriction, microvascular thrombosis, heart failure related to myocardial injury, or neurogenic pulmonary edema. Delayed cerebral ischemia (DCI) develops several days after SAH. DCI and cerebral infarction are the most important prognostic factors for neurologic outcome [10]. DCI has been linked to cerebral vasospasm. However, the absence of causal relationship between angiographic vasospasm and DCI in some studies and the absence of significant improvement in clinical outcome with drugs that have a potent effect against vasospasm have raised other hypotheses to explain DCI [11]. These hypotheses are cerebral vasoconstriction and thrombosis, cortical spreading ischemia, cerebral inflammation, and blood-brain barrier

N. Bruder (✉) · S. Boussen · L. Velly
Department of Anesthesiology and Intensive Care, CHU Timone, AP-HM, Aix-Marseille University, Marseille, France
e-mail: Nicolas.BRUDER@ap-hm.fr

H. Prabhakar, Z. Ali (eds.), *Textbook of Neuroanesthesia and Neurocritical Care*,
https://doi.org/10.1007/978-981-13-3387-3_8

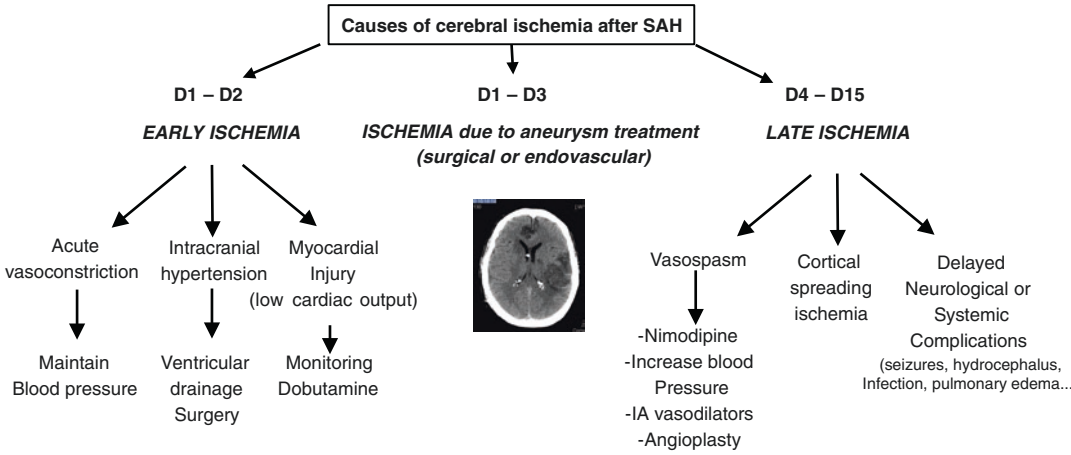

Fig. 8.1 Causes of cerebral ischemia after SAH depending on time after aneurysm rupture

disruption [12]. This chapter will focus on early management of SAH for anesthesia for neurosurgical clipping or endovascular embolization.

8.2 Preoperative Assessment

8.2.1 Central Nervous System (CNS)

The severity of CNS injury is the main predictor of long-term outcome. Several clinical scales have been used. The World Federation of Neurological Surgeons (WFNS) grading scale, based on the Glasgow coma score scale, is widely used (Table 8.1). The amount of blood in the subarachnoid space or in the ventricles has also been associated with the risk of DCI. Several scores have been published, the most popular being the modified Fisher scale (Table 8.2) [13]. Several scores associating clinical, radiological, or biological variables are able to predict mortality or neurologic outcome after SAH. For example, the HAIR score combining Hunt and Hess score, age, intraventricular hemorrhage, and rebleeding was strongly associated with in-hospital mortality [14]. The ABC score, which integrated the Glasgow coma score, troponin I, and protein S100beta at admission, predicted 1-year mortality [15].

Among several causes of impaired consciousness due to SAH, increased intracranial pressure (ICP) is the most relevant one for the anesthetist.

Table 8.1 Grades of the World Federation of Neurological Surgeons (WFNS) and relation to mortality

Grade	Glasgow coma scale score	Motor deficit	Mortality
1	15	Absent	1–5
2	13–14	Absent	5–10
3	13–14	Present	5–10
4	7–12	Present or absent	20–30
5	3–6	Present or absent	30–50

Table 8.2 Modified Fisher scale with an estimation of the associated risks of delayed cerebral ischemia (DCI) and new infarct on CT scan (unrelated to initial bleeding or aneurysm securing procedure)

Grade	Description	DCI %	New infarct on CT %
0	No SAH or IVH	0	0
1	Thin SAH, no IVH in lateral ventricles	12	6
2	Thin SAH, IVH in both lateral ventricles	21	14
3	Thick SAH, no IVH in lateral ventricles	19	12
4	Thick SAH, IVH in both lateral ventricles	40	28

Data from [13]

At the onset of SAH, loss of consciousness occurs in 40% of patients [16]. It is related to the abrupt bleeding into the subarachnoid space, increasing intracranial volume and ICP. In hospitalized

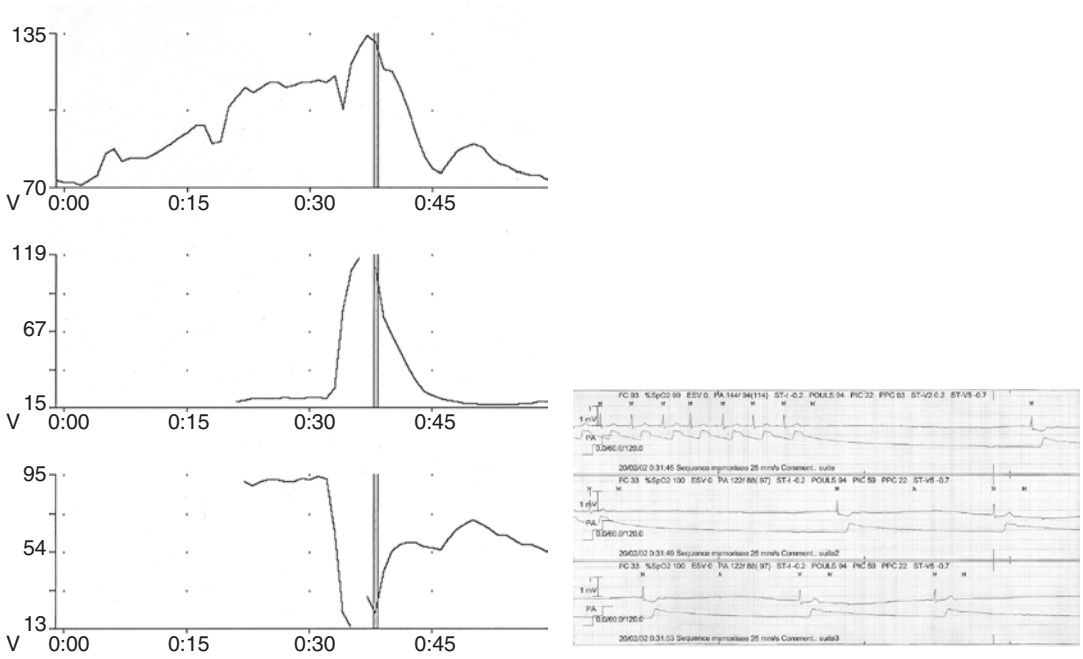

Fig. 8.2 Trends in mean arterial pressure (MAP), intracranial pressure (ICP), and cerebral perfusion pressure (CPP) in a patient in the intensive care unit after subarachnoid hemorrhage. A ventricular drain was placed in order to monitor ICP and treat hydrocephalus. Soon after 0:30 am, the patient suffered a severe headache immediately followed by a rapid decrease in consciousness requiring tracheal intubation. The ICP increased to 120 mm Hg and CPP below 10 mm Hg. Immediate ventricular drainage allowed a return toward normal ICP values in approximately 10 min. The aneurysm was treated by endovascular coiling, and the patient recovered without any neurologic impairment. The EKG trace shows severe bradycardia at the time of rebleeding (Cushing's response)

patients, rebleeding may be associated with a sudden and large increase in ICP, resulting in a severe reduction in cerebral perfusion pressure (CPP) and thus explaining loss of consciousness (Fig. 8.2). As such, assessment of ICP and CPP and control of increased ICP before the aneurysm securing procedure are critical to maintain cerebral homeostasis and prevent cerebral ischemia. Severe intracranial hypertension can be excluded in WFNS 1–2 grades. WFNS 4–5 patients are at highest risk of intracranial hypertension and reduced CPP. Except in the most severe cases with clinical signs of brain herniation (unilateral or bilateral mydriasis), clinical examination cannot help to evaluate the level of ICP or CPP. The amount of blood in the lateral ventricles (more than 50% of each ventricle filled with blood) and the amount of blood in the subarachnoid space are an indication of increased ICP [17, 18]. Transcranial Doppler (TCD) is probably the most convenient and easy to use monitoring device at the bedside to give a qualitative noninvasive access to the cerebral circulation. The decrease in diastolic flow velocity is associated with the decrease in CPP. When ICP increases toward arterial diastolic pressure, diastolic flow velocity progressively disappears. Zero-diastolic velocity is a critical value indicating that any further decrements of CPP are associated with rapid CBF decrease and cerebral ischemia (Fig. 8.3) [19]. In addition, bilateral failure of cerebral autoregulation with TCD has been associated with DCI and unfavorable outcome [20].

8.2.2 Cardiovascular System

Cardiovascular consequences of SAH had first been described long ago [21]. ECG changes may mimic coronary artery ischemia, but studies on

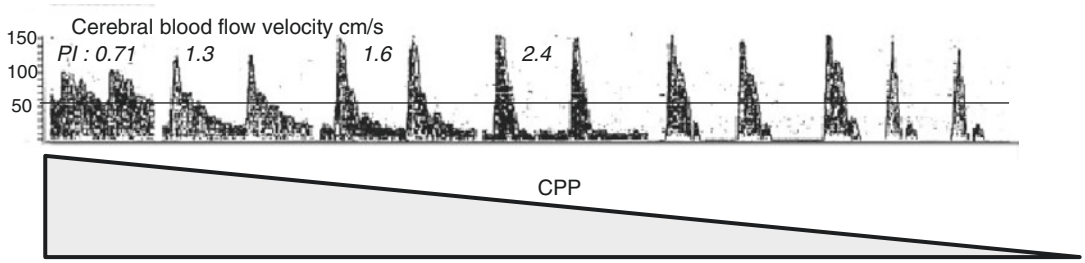

Fig. 8.3 Transcranial Doppler recordings in several patients with decreasing values of cerebral perfusion pressure. The decrease in diastolic blood flow is easily recognized at low CPP values. A diastolic velocity below 20 cm/s is usually associated with impaired CPP (<60 mm Hg)

the coronary circulation ruled out this hypothesis. Arrhythmias are frequent, affecting 35% of patients with life-threatening arrhythmias in 5–8% [22]. Biomarkers of myocardial injury like troponin are frequently elevated and are associated with myocardial dysfunction and outcome.

Echocardiography frequently reveals regional wall motion abnormalities (8–28% of patients), diastolic dysfunction, or global hypokinesia [23]. The most severe clinical presentation of myocardial injury is Takotsubo cardiomyopathy. It is associated with a critical decrease in cardiac output and has to be diagnosed as soon as possible because any attempt to increase blood pressure with vasopressors would further decrease cardiac output and CBF. This acute ventricular dysfunction associated with SAH is generally reversible within 2 or 3 days after admission.

8.2.3 Respiratory System

Pulmonary complications are frequent after SAH and contribute significantly to mortality [22]. As myocardial dysfunction, the incidence of pulmonary complications is related to the clinical grade. Pneumonia occurs in approximately 20% of patients and pulmonary edema in 8–28% of cases. The prevalence of ARDS in retrospective studies is reported to be 4–18% [23]. Neurogenic pulmonary edema (NPE) is less frequent, but the true incidence is difficult to assess because pulmonary edema may be due to heart failure or excessive fluid loading. NPE usually improves within a few days after SAH, but it may be a real problem for anesthetic management. The balance between the risk of surgery in patients with NPE and the risk of rebleeding if surgery is postponed needs a case-by-case discussion.

8.2.4 Other Medical Complications of SAH

Hypernatremia and hyponatremia are common after SAH. Hyponatremia is the most common electrolyte imbalance and usually develops a few days after the hemorrhage with the onset of vasospasm. The mechanisms of hyponatremia are cerebral salt wasting (CSW) and the syndrome of inappropriate secretion of antidiuretic hormone (SIADH). CSW is more frequent leading to excessive urine excretion of sodium. Hence, CSW is associated with volume contraction. In this case, patients should be given fluids before induction of anesthesia to avoid hypotension. Conversely, SIADH is associated with free water retention and normal or expanded intravascular volume. Hyponatremia may be treated by the infusion of hypertonic saline solution with frequent monitoring of blood sodium. Some studies have used fludrocortisone or hydrocortisone to treat hyponatremia, but the benefit of these treatments is unclear [24].

Hyperglycemia is common after SAH and has been associated with poor clinical outcome. The increased glucose level is due to the activation of the sympathetic system and the hypothalamic-pituitary-adrenal axis giving rise to an increase in the level of stress hormones (catecholamine,

cortisol, and growth hormone). The release of pro-inflammatory cytokines further increases the stress response and promotes insulin resistance. Patients with hyperglycemia have approximately a three-fold increased risk of poor outcome [25]. Some studies have shown a benefit of glycemic control on neurologic outcome or a decrease in the rate of infection [26, 27]. However, overly strict glycemic control may lead to brain hypoglycemia and metabolic crisis, even when serum glucose decreases to levels within the normal range [28, 29].

8.3 Timing of Aneurysm Treatment and Rebleeding

Preoperative rebleeding is an independent predictor of unfavorable outcome [30]. In recent studies, reported rates of rebleeding were between 6% and 17% [9, 31, 32]. Most rebleeding occur in the first 24 h, mainly in the first 6 h after hospital admission. In one study, the peak time of rebleeding was within 2 h [31]. The risk factors for rebleeding are a high clinical grade, a high modified Fisher grade, high systolic blood pressure, and external ventricular drainage. Modifiable risk factors include a tight control of blood pressure, provided that CPP is maintained, and emergency treatment of the aneurysm. Retrospective studies show that emergency treatment of the aneurysm reduces the risk of in-hospital rebleeding and improves clinical outcome [9, 33]. Poor-grade patients also deserve an early treatment despite a high mortality rate because a favorable clinical outcome may be obtained in approximately one-third of patients [34, 35]. However, the aneurysm securing procedure requires the presence of a highly specialized team that may not be available 24/7. Each center has to weigh the benefit of an early procedure with the emergency team versus waiting a few hours to perform the procedure in a better environment. In all instances, waiting for more than 24 h to secure the aneurysm does not seem reasonable. For the anesthetist, hemodynamic control is a main goal to prevent rebleeding. In the past, induced hypotension has been used. However, even short periods of induced hypotension have been related to an increased risk of neurologic deficits [36, 37]. In WFNS 1–2 patients, a systolic blood pressure < 140 mm Hg may be recommended before securing the aneurysm, although it does not eliminate the risk of early rebleeding. In WFNS 3–5 patients, the management of blood pressure is more difficult because the level of ICP is difficult to predict. After external ventricular drainage, ICP monitoring allows to determine the best arterial pressure range. A CPP > 60 mm Hg is probably reasonable to limit the risk of cerebral ischemia. Without ICP monitoring, transcranial Doppler may help the management of blood pressure. A low diastolic velocity and high pulsatility index are an indication of impaired cerebral blood flow. Treatments to decrease ICP or increase blood pressure have to be considered. In contrast, systolic hypertension with normal TCD recordings indicates that reduction of blood pressure is probably safe.

8.4 Anesthetic Management

Emergency anesthesia is necessary in all cases to secure the aneurysm and prevent rebleeding either by the endovascular approach or for surgical clipping of the ruptured aneurysm. There are general principles that apply to both procedures and specificities to each approach. The main determinant of anesthetic management is preoperative patient status. Patients in good clinical grades (WFNS 1–2) do not have intracranial hypertension and are usually free of significant hemodynamic, respiratory, or metabolic complications. In this case the priority is to prevent aneurysm rerupture through adequate hemodynamic control, especially during painful procedures (laryngoscopy and intubation, craniotomy). For surgery, anesthetic management should follow the general principles of anesthesia for intracranial surgery (maintain cerebral homeostasis, brain relaxation to improve the quality of surgical exposure, early emergence allowing early neurologic examination). Patients in bad clinical grades (WFNS 3–5) are more difficult to manage due to intracranial hypertension and concurrent major medical complications.

8.4.1 General Principles of Anesthesia for Surgery or Interventional Neuroradiology After SAH

8.4.1.1 Monitoring

Hemodynamic Monitoring

Invasive blood pressure monitoring is mandatory in order to obtain hemodynamic stability, preferably before induction of anesthesia and laryngoscopy. Central venous catheterization is useful in most patients undergoing surgery. It allows central venous pressure monitoring in order to detect preexisting hypovolemia or hypovolemia induced by mannitol or hemorrhage during aneurysm rupture. Ultrasound-guided central venous catheter insertion is strongly recommended because carotid artery puncture needing manual compression would be particularly deleterious in patients with impaired CBF. Myocardial dysfunction and hemodynamic instability may need a continuous infusion of catecholamine. A pulmonary artery catheter is seldom used now to monitor cardiac output. Another option is to use transpulmonary thermodilution allowing monitoring of cardiac output and preload. In bad-grade SAH patients, bedside transpulmonary thermodilution monitoring decreases the consequences of delayed cerebral ischemia, reduces the incidence of pulmonary edema, and improves clinical outcome [38, 39].

Monitoring of Brain Function

ICP monitoring is easy to perform in all patients with intraventricular drainage. This is particularly useful in grade IV–V patients who often have intracranial hypertension. In surgical patients, ICP and CPP may be monitored from induction of anesthesia until dura-mater opening. Afterwards, cerebrospinal fluid (CSF) drainage improves brain relaxation. In patients treated by the endovascular approach, ventricular drainage allows monitoring of ICP and CPP throughout the procedure. In case of aneurysm rupture, cerebrospinal fluid drainage is the best method to rapidly decrease ICP and restore CPP (Fig. 8.2).

Monitoring brain oxygenation would certainly be useful. Cerebral venous oxygen saturation ($SjvO_2$) reflects the balance between cerebral metabolic supply and demand. It is obtained by the placement of a catheter in the jugular bulb through retrograde jugular vein catheterization. Matta and colleagues found this monitoring useful for intracranial surgery in general and for aneurysm surgery in more than half of their patients [40]. An acute decrease in $SjvO_2$ may be a sign of aneurysm rupture. However, frequent $SjvO_2$ changes occur without obvious causes, most often leading to an increased $SjvO_2$ [41]. Near-infrared spectroscopy (NIRS) allows continuous monitoring of brain regional oxygen saturation. However, this monitoring is not reliable enough to guide therapeutic management in the operating room during neurosurgery. Extracranial contamination of the signal may lead to spurious changes in NIRS values especially during vasopressor treatment [42].

Other Monitoring

Standard monitoring includes ECG monitoring, pulse oximetry, end-tidal capnography, monitoring of neuromuscular blockade, and temperature monitoring. In addition, a urinary catheter and at least one 14- or 16-gauge peripheral catheter should be inserted. Blood glucose monitoring is useful because hyperglycemia has been associated with cerebral ischemia and poor outcome after SAH [25]. Tight blood glucose control with intensive insulin therapy is potentially dangerous by increasing the risk of hypoglycemia. The optimal blood glucose level is still unknown, and the objective to maintain it below 10 mmol/L (2 g/L) seems reasonable.

8.4.1.2 Management of Increased ICP

With hemodynamic control, reduction of increased ICP is a major goal of anesthetic management. There are several methods to reduce ICP or improve brain relaxation during surgery. CSF drainage is the most effective treatment. However, excessive drainage should be avoided because it has been associated with a risk of aneurysm rupture. Osmotic agents are another option to reduce ICP by reducing brain water content. Typically, 0.5–1 g/kg mannitol (150–400 mL 20% mannitol) infused over 20 min once

or twice before surgery has a rapid onset of action, with a peak effect after 30–45 min, lasting for 2–3 h. Hypertonic saline is an alternative to mannitol. Equiosmolar doses of hypertonic saline and mannitol have similar effects on brain relaxation and brain metabolism [43]. Urinary losses due to mannitol have to be replaced with normal saline to prevent hypovolemia. Hyperventilation and hypocapnia reduce cerebral brain volume and ICP and improve operating conditions during craniotomy [44]. However, this effect is related to cerebral vasoconstriction and may lead to cerebral ischemia depending on the balance between improved CPP and constriction of cerebral blood vessels. It should be used for only short periods of time. It may be particularly useful during surgery to limit brain bulk and provide better operative conditions. Intravenous anesthetics reduce brain metabolism, CBF, cerebral blood volume, and ICP if flow-metabolism coupling is maintained. Inhaled anesthetics are cerebral vasodilators and may increase ICP. Thus, in patients with intracranial hypertension, total intravenous anesthesia is a better option.

8.4.1.3 Induction of Anesthesia

The objectives of the induction period are to avoid both hypotension giving rise to cerebral ischemia and hypertension increasing the risk of aneurysm rerupture. Propofol and thiopental with sufentanil or remifentanil are the mostly used agents. Etomidate (0.2–0.3 mg/kg) may be an interesting alternative in patients with depressed myocardial function because this agent is associated with minimal hemodynamic effects. Remifentanil is very effective to blunt the hemodynamic response to laryngoscopy or pin head-holder application. Bolus infusion is associated with a significant risk of bradycardia and hypotension. Using a target-controlled infusion system, the concentration of remifentanil to blunt the hemodynamic response to noxious stimuli is usually between 4 and 6 μg/L. The concentration has to be decreased rapidly upon cessation of the painful stimulus to avoid hypotension. A continuous infusion of remifentanil is particularly useful when a difficult airway is anticipated because it allows long-lasting laryngoscopy with hemodynamic stability. If low-doses of sufentanil are used during induction of anesthesia, esmolol (1 mg/kg) can be used to blunt the hemodynamic response to laryngoscopy in patients without myocardial injury. Cisatracurium, vecuronium, and rocuronium can be used for muscle relaxation, but atracurium may be hypotensive.

In patients with a full stomach, the priority is to prevent tracheal aspiration and at the same time prevent the hypertensive response to tracheal intubation. Propofol or thiopental with succinylcholine (1.5 mg/kg) or rocuronium (1.2 mg/kg) may be used. In patients with preserved myocardial function, we use either a small bolus of remifentanil (0.25–0.5 μg/kg) or esmolol (1 mg/kg) before intubation.

8.4.1.4 Maintenance of Anesthesia

Depending on the preoperative neurological condition, either total intravenous anesthesia with propofol and remifentanil or sevoflurane with remifentanil or sufentanil can be used. Sevoflurane is a better choice than isoflurane because it is associated with faster recovery, especially after long-lasting procedures. Desflurane may be used but is a more potent cerebral vasodilator than sevoflurane [45, 46]. Nitrous oxide is a cerebral vasodilator and may increase ICP. In one study, nitrous oxide was associated with a greater risk of delayed ischemic neurologic deficits [47]. Thus, a mixture of air/oxygen is most often preferred either during inhalation or intravenous anesthesia. If sufentanil is used during anesthesia, total doses should be less than 2 μg/kg in order to allow rapid awakening and neurologic assessment. After a continuous propofol infusion, the dose or the target concentration has to be reduced toward the end of surgery (wound closure) to avoid accumulation of the drug leading to delayed recovery. Hypertension and tachycardia related to light anesthesia may be controlled by low-dose esmolol (0.5 mg/kg) or labetalol (5–15 mg).

Movement or coughing should not occur during neurosurgery or interventional neuroradiology. Continuous neuromuscular blockade with monitoring is the best option to prevent

movement. High-dose remifentanil may also be used at the expense of systemic hypotension [48].

A lung-protective ventilation strategy with low tidal volume (6–8 mL/kg) and positive end-expiratory pressure (PEEP) has been demonstrated to improve clinical outcome and reduce lung complication after anesthesia [49, 50]. However, neurosurgical patients were systematically excluded from the studies on lung-protective ventilation because recruitment maneuvers or high levels of PEEP may have deleterious effects on the brain. The application of low tidal volume is not a problem during neurosurgery because the respiratory rate can be increased to decrease $PaCO_2$. But low tidal volume without PEEP gives rise to atelectasis, especially when it is sustained for a few hours. High levels of PEEP and recruitment maneuvers have not shown beneficial effects compared to lower PEEP levels and no recruitment maneuvers [51, 52]. In addition, changes in the level of PEEP that result in an increase in driving pressure (plateau pressure—PEEP) are associated with more postoperative complications [53]. In neurosurgical patients, increasing PEEP was not associated with a substantial increase in ICP or decrease in CBF when blood pressure was maintained [54, 55]. In the operating room, low levels of PEEP (5–8 cm H_2O) associated with low tidal volume and no recruitment maneuver seem to be the best option for intraoperative ventilation in neurosurgery. Higher level of PEEP may be needed in patients with neurogenic pulmonary edema needing to find a compromise between oxygenation, deleterious hemodynamic effects of PEEP, and ICP.

8.5 Anesthesia for Neurosurgical Clipping

Specific objectives of anesthesia for ruptured intracranial aneurysms are to obtain an optimal state of brain relaxation to facilitate brain dissection, protect the brain from ischemia, and be prepared to manage aneurysm rupture. The methods to obtain brain relaxation are similar to those used to decrease ICP before skull opening. During surgery, positioning has a major impact on brain tension. A 10° reverse Trendelenburg position lowers ICP with minimal effects on blood pressure [56]. The head is usually turned laterally, and care must be taken to avoid jugular vein compression. Hyperflexion or hyperextension of the head also impairs cerebral venous return. In patients who do not have external ventricular drainage, lumbar CSF drainage is a good option to obtain brain relaxation. Care should be taken to minimize CSF loss during insertion of the drain and to close the drainage system until dura-mater opening because an abrupt decrease in ICP may lead to aneurysm rupture. A volume of 100–150 mL of CSF can usually be removed until the surgeon is able to clip the aneurysm.

Prevention of hemodynamic response to painful stimuli is important both to limit ICP increases and maintain hemodynamic stability. Pin headholder application and surgical incision are two critical times. A small bolus of remifentanil (0.5–1 μg/kg) or an increase in target blood concentration to 6.5 μg/L (EC90 to blunt cardiovascular responses to head fixation) [57] is effective. Other methods are injection of a bolus of esmolol (1 mg/kg) or local anesthetic infiltration of the pin site [58]. Brain dissection is painless, and the depth of anesthesia and analgesia is usually decreased to avoid hypotension. In this case, close monitoring of neuromuscular blockade is mandatory.

8.5.1 Anesthesia Management During Temporary Clipping of the Parent Vessel

Temporary clipping of the aneurysm parent vessel has become standard practice and is used in more than 50% of patients. The safety of this procedure has been demonstrated for short-lasting clipping times and was not associated with an increase incidence of DCI [59]. The duration of safe temporary clipping is very variable. Retrospective studies have shown that an occlusion less than 10 min long was safe [60, 61]. Temporary clipping lasting more than 20 min and multiple clipping episodes were significantly associated with cerebral ischemia [61]. An increase in blood

pressure to improve collateral brain blood flow during temporary clipping is recommended although the evidence to support it is scarce [62]. Thiopental-, etomidate-, or propofol-induced burst suppression in order to provide brain protection has been used. Some retrospective data suggested a decrease in postoperative brain infarction rates, especially for clipping duration above 10 min [60]. Hypothermia for intraoperative neuroprotection has been tested in the IHAST trial, a prospective randomized trial including 1001 patients [63]. Intraoperative hypothermia did not improve the neurologic outcome. A post hoc analysis of this trial did not show any effect of drugs used for neuroprotection on long-term clinical outcome [64].

Optimization of clip placement is essential for good long-term results. Microvascular Doppler ultrasonography has been used to assess the quality of the surgical procedure. One study demonstrated ongoing flow in the aneurysm in 12% of patients and occlusion of an adjacent vessel in 28% of cases [65]. Doppler was found to be more convenient and as effective as intraoperative angiography. Indocyanine green video angiography is a convenient method to confirm aneurysm occlusion and assess the cerebral circulation in the operative field [66]. However, it does not seem to be 100% reliable compared to conventional angiography [67]. Adenosine-induced cardiac arrest has been used as an alternative to limit the necessity of temporary clipping with good results [68].

8.5.2 Management of Intraoperative Rupture

Intraoperative rupture is a relatively frequent event. It occurred in 13% of cases in an international multicenter study published in 1990 [69]. More recently, an intraoperative rupture rate between 10.7 and 18% has been reported during surgery after SAH [70, 71]. Large aneurysms, clinical grade, anatomic location on the posteroinferior cerebellar artery, and the anterior or posterior communicating arteries have been associated with an increased risk of rupture. Intraoperative rupture is associated with a bad clinical outcome [70]. However, the difficulty to manage aneurysm bleeding is related to the timing of rupture during the surgical procedure. When the rupture occurs early during cerebral dissection, the time needed to gain access to the aneurysm and stop bleeding may be long and associated with significant blood losses, hypotension, and brain damage. In contrast, rupture during manipulation of the aneurysm is easily controlled by temporary clipping followed by aneurysm clipping with little consequences.

Aneurysm rupture with significant hemorrhage obscures the operative field under the microscope, making surgery impossible. Thus, the priority is to stop or minimize the hemorrhage. If possible, this is best achieved with temporary clipping [72] because even short periods of hypotension have been associated with poor outcome [36, 37]. Hypotension may be used as a rescue treatment to allow surgery. The adequate blood pressure level is the highest value providing an acceptable view in the operating field. Isotonic crystalloid solutions are the first choice to replace blood losses. Perioperative autologous blood transfusion may be used if prepared from the beginning of the procedure. Homologous transfusion is seldom necessary, but blood and plasma must be available rapidly in the case of major bleeding.

8.6 Anesthesia for Endovascular Treatment

In most centers, intracranial aneurysms are now frequently treated by the endovascular than the surgical approach. A large trial (ISAT trial), comparing endovascular coiling or surgical clipping of the aneurysm, concluded to a better outcome with the endovascular approach [73]. The relative risk reduction in dependency or death with the endovascular treatment was 22.6% in 2143 patients. This study was criticized because it included mostly patients with anterior cerebral artery aneurysms. However, it demonstrated that endovascular treatment may be considered a valid alternative to surgery.

8.6.1 Specific Objectives of Anesthesia for Interventional Neuroradiology (INR)

– Immobility

The placement of superselective intravascular catheters has to be very accurate. This is achieved by using "roadmapping." Even slight movement of the head can markedly degrade the image. In addition, forceful movement of the head (e.g., coughing) when a microcatheter is in situ may cause arterial dissection and thrombosis.

– Prevention of hypothermia

The environment in the INR suite is cold and large volume of contrast media may be used. The risk of hypothermia remains high. There is limited access to the patient to allow efficient warming during the procedure. It is suggested that preoperative surface warming be used to prevent hypothermia.

– Avoid patient injury

It is very imperative to secure the head and arms because the radiology table is often moved which may result in patient injury. The tracheal tube must be secured properly and any conflict with the radiology machine should be prevented.

– Radiation safety

Exposure by the anesthesia team to radiation hazards should be avoided as much as possible. A remote anesthesia monitor in the radiation safe area is useful.

8.6.2 Problems Associated with Anesthesia Outside the Operating Room

The problems associated with remote anesthesia location should not be underestimated. The anesthesia equipment should be checked regularly and before each anesthesia because another one (monitoring, ventilator, gas supply, etc.) may not be available rapidly in case of failure. Some specific features may compromise patients' security. For example, the access to the patient in INR facilities is limited due to bulky equipment. The personnel are often less familiar with anesthesia than the one working in the operating room. In emergency situations, it may be difficult to obtain valuable help. At any time, help must be speedily and effortlessly available. The INR location should be close to other remote anesthesia locations (vascular interventional radiology, endoscopy, interventional cardiology, etc.) in order to improve anesthetic organization and safety.

8.6.3 Morbidity and Mortality of INR

The range of morbidity in INR procedures is between 10% and 20% and mortality between 1% and 4% [74–76]. The two main complications are cerebral hemorrhage and cerebral artery thrombosis.

8.6.4 Cerebral Hemorrhage

In a meta-analysis in 2002, the risk of intraprocedural aneurysm perforation was 4.1% for the endovascular treatment of ruptured aneurysms [77]. The combined risk of permanent neurologic disability and death associated with this complication was 38%, a figure comparable to the 63% rate of periprocedural death or disability in a more recent study [70]. In the CLARITY study in 2010, including 782 patients, the intraprocedural rupture rate was 4.3% [78]. Aneurysm rupture was more frequent in MCA aneurysms and in patients younger than 65 years. There was no death related to rupture, and the morbidity was very low (0.6%), suggesting that management of aneurysm bleeding during endovascular treatment has been much improved in recent years. Rupture of aneurysm usually occurs when the patient is fully anticoagulated, needing to be prepared for managing the complication in order to

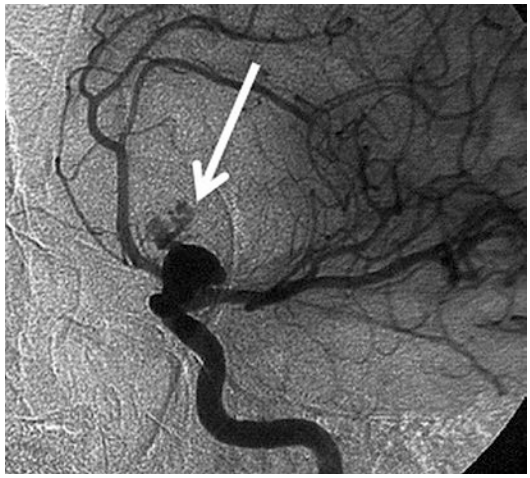

Fig. 8.4 Intraoperative rupture of an aneurysm just before coil embolization. The extravasation of contrast media outside the aneurysm (arrow) allows the diagnosis of aneurysm rupture

Table 8.3 Management of intracranial bleeding due to aneurysm rupture during coil embolization

Stop bleeding	Control intracranial hypertension	Brain protection
Inform the neuroradiologist Call for help Antagonize heparin (protamine) Occlude the aneurysm as fast as possible or inflate a balloon in the artery *Do not infuse antihypertensive agent* Give thiopental (decreases blood pressure and ICP)	*During procedure* Mannitol 1 g/kg Hyperventilation ($PaCO_2$ 26–30 mm Hg) Stop inhaled anesthetic agents (or shift to propofol) Give thiopental Allow mild hypothermia *Post procedure* Ventricular drainage	Ventilate with 100% O_2 Mild hypothermia Thiopental Ventricular drainage

stop bleeding as soon as possible. In an anesthetized patient, the signs of SAH due to aneurysm rupture are those due to intracranial hypertension. The early signs of rupture are severe hypertension and bradycardia (Fig. 8.2). This should not be interpreted as light anesthetic depth. Communication with the neuroradiologist is essential because injection of contrast media is necessary to confirm the diagnosis and take appropriate therapeutic measures (Fig. 8.4). The management of aneurysm bleeding is summarized in Table 8.3. Heparin should be immediately reversed with protamine. Antihypertensive agents compromise cerebral perfusion and should not be given. During severe hypertension, thiopental is the only possible agent to lower blood pressure because it is frequently associated with a parallel decrease in intracranial pressure and may afford cerebral protection. A treatment for raised intracranial pressure is indicated. Increasing the inspired oxygen fraction improves brain oxygen content. It is relatively innocuous and may afford some cerebral protection. After the procedure has been completed, a CT scan is needed to assess the extent of intracranial bleeding and discuss the indication of ventricular drainage. The neurosurgical team should be informed of the complication, and the anesthesia team should be prepared to go to the operating room if needed.

8.6.5 Cerebral Artery Thrombosis

8.6.5.1 Risk of Thrombosis

The most frequent severe complications of INR are the thrombotic complications. The risk of thrombosis is related to vessel wall damage, thrombogenicity of contrast material, guidewires, microcatheters, vascular coils, and stents. In a review on 1547 patients, the immediate and delayed thromboembolic risk after coil embolization of aneurysm was 8.2% [79]. The risk is high in the first 48 h, and then it decreases rapidly. In the CLARITY study, the incidence of thromboembolic events was 12.5% [78]. A higher rate was observed in smokers, in aneurysms larger than 10 mm or with a large neck. Thromboembolic events lead to permanent neurologic deficit or death in 3.8% of patients. The risk of thrombosis is particularly high with stents, needing treatment with an antiplatelet agent before the procedure, which is rarely possible after SAH.

8.6.5.2 Prevention of Cerebral Artery Thrombosis

Considering the risk of thrombosis, intravenous heparin is mandatory during the procedure. After a baseline activated clotting time (ACT) is obtained, 50–70 units/kg is given to obtain an ACT of 2–3 times the baseline value. ACT should

be checked every hour to maintain adequate anticoagulation. The injection of acetylsalicylic acid has been associated with a lower rate of thromboembolic events [80]. Nevertheless, it may increase the risk of bleeding if a neurosurgical procedure is needed (ventricular drainage).

8.6.5.3 Treatment of Cerebral Artery Thrombosis

This complication should be recognized and treated as soon as possible. The first step is to promote oxygen transport to the ischemic brain which can be achieved by increasing the blood pressure in order to recruit collateral arteries and by increasing the inspired oxygen fraction to 100% in order to increase the diffusion of oxygen to the ischemic penumbra. The second step is to recanalize the vessel. The activated coagulation time is checked, and additional heparin is given if the ACT is less than 250 s. Infusion of thrombolytics in situ (rt-PA, maximum dose 0.9 mg/kg) has been used with an approximately 50% recanalization rate [81]. Fragmentation of the clot mechanically improves the efficiency of thrombolysis. Glycoprotein IIb/IIIa receptor antagonists (abciximab, eptifibatide, tirofiban) have been associated with a higher recanalization rate than thrombolytics, a lower perioperative morbidity, and a better long-term outcome [82]. The incidence of bleeding was low in the reported case series. Thus, they can be used as first-line agents in case of vessel thrombosis. Mechanical thrombectomy is a logical option, but the experience is very limited in this indication.

8.7 Emergence and Recovery After Anesthesia

Early clinical assessment is essential after surgery or coil embolization. After an uneventful procedure, grade 1 or 2 patients should be allowed to awaken as soon as possible. Moderate hypertension (systolic blood pressure < 180 mm Hg) is usually not aggressively treated. Higher blood pressure levels may cause cerebral hemorrhage or swelling and should be treated with low-dose labetalol (5–10 mg), nicardipine (0.5–1 mg), or urapidil (10–20 mg) as needed. Any new neurologic deficit in the immediate postoperative period should raise the possibility of clip or coil complication and lead to emergency CT angiography. Grade 3 or 4 patients usually need postoperative ventilation, but neurologic examination is possible after stopping anesthesia to rule out any new focal neurologic deficit. Grade 5 patients are sedated and ventilated in the postoperative period. TCD is a convenient monitoring to assess the patency of arteries of the circle of Willis.

The main risk in the postoperative period is cerebral ischemia related to vasospasm. A systolic blood pressure above 120 mm Hg is a safe objective to maintain adequate brain blood flow.

In the postoperative period, the patients are usually monitored in an intensive care unit, to detect medical or surgical complications. A brain CT scan 24–48 h after the aneurysm securing procedure is important to detect any ischemia related to the procedure.

8.8 Conclusion

Anesthesia for patients with SAH requires a clear understanding of the cerebral consequences of aneurysm rupture. Hemodynamic management needs to balance the risks of cerebral ischemia due to impaired CBF and the risk of rebleeding. Several medical complications, including heart failure and neurogenic pulmonary edema, are challenging to perform emergency anesthesia for a major surgical or endovascular procedure. The objectives of anesthesia are both to make the aneurysm securing procedure as safe as possible and at the same time maintain brain homeostasis in order to prevent cerebral ischemia.

Key Points

- The main complication after aneurysmal subarachnoid haemorrhage (SAH) is cerebral ischemia.
- Cerebral ischemia may occur early after SAH, due to the cerebral bleeding, during the treatment of the aneurysm (surgery or interventional neuroradiology), and after 5 to 15 days after SAH (delayed cerebral ischemia).
- Cardiac and pulmonary complications are frequent after severe SAH, needing appropriate monitoring in the ICU.
- In patients with severe SAH, cardiac output monitoring has been demonstrated to improve outcome.
- The management of intracranial hypertension is a hallmark of anaesthesia for the aneurysm securing procedure.
- Delayed cerebral ischemia may be related to cerebral vasospasm and other pathophysiological processes.
- Close clinical and transcranial Doppler monitoring is needed to detect cerebral vasospasm and initiate emergency treatments to avoid the development of cerebral ischemia.

References

1. Stevens RD, Naval NS, Mirski MA, Citerio G, Andrews PJ. Intensive care of aneurysmal subarachnoid hemorrhage: an international survey. Intensive Care Med. 2009;35(9):1556–66.
2. Velly LJ, Bilotta F, Fabregas N, Soehle M, Bruder NJ, Nathanson MH. Anaesthetic and ICU management of aneurysmal subarachnoid haemorrhage: a survey of European practice. Eur J Anaesthesiol. 2015;32(3):168–76.
3. Boogaarts HD, van Amerongen MJ, de Vries J, Westert GP, Verbeek AL, Grotenhuis JA, et al. Caseload as a factor for outcome in aneurysmal subarachnoid hemorrhage: a systematic review and meta-analysis. J Neurosurg. 2014;120(3):605–11.
4. Pandey AS, Gemmete JJ, Wilson TJ, Chaudhary N, Thompson BG, Morgenstern LB, et al. High subarachnoid hemorrhage patient volume associated with lower mortality and better outcomes. Neurosurgery. 2015;77(3):462–70.
5. Rush B, Romano K, Ashkanani M, McDermid RC, Celi LA. Impact of hospital case-volume on subarachnoid hemorrhage outcomes: a nationwide analysis adjusting for hemorrhage severity. J Crit Care. 2017;37:240–3.
6. 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(7):635–42.
7. Mukhtar TK, Molyneux AJ, Hall N, Yeates DR, Goldacre R, Sneade M, et al. The falling rates of hospital admission, case fatality, and population-based mortality for subarachnoid hemorrhage in England, 1999-2010. J Neurosurg. 2016;125(3):698–704.
8. Mackey J, Khoury JC, Alwell K, Moomaw CJ, Kissela BM, Flaherty ML, et al. Stable incidence but declining case-fatality rates of subarachnoid hemorrhage in a population. Neurology. 2016;87(21):2192–7.
9. Vergouwen MD, Jong-Tjien-Fa AV, Algra A, Rinkel GJ. Time trends in causes of death after aneurysmal subarachnoid hemorrhage: a hospital-based study. Neurology. 2016;86(1):59–63.
10. Rosengart AJ, Schultheiss KE, Tolentino J, Macdonald RL. Prognostic factors for outcome in patients with aneurysmal subarachnoid hemorrhage. Stroke. 2007;38(8):2315–21.
11. Macdonald RL, Higashida RT, Keller E, Mayer SA, Molyneux A, Raabe A, et al. Clazosentan, an endothelin receptor antagonist, in patients with aneurysmal subarachnoid haemorrhage undergoing surgical clipping: a randomised, double-blind, placebo-controlled phase 3 trial (CONSCIOUS-2). Lancet Neurol. 2011;10(7):618–25.
12. Macdonald RL. Delayed neurological deterioration after subarachnoid haemorrhage. Nat Rev Neurol. 2014;10(1):44–58.
13. Claassen J, Bernardini GL, Kreiter K, Bates J, Du YE, Copeland D, et al. Effect of cisternal and ventricular blood on risk of delayed cerebral ischemia after subarachnoid hemorrhage: the fisher scale revisited. Stroke. 2001;32(9):2012–20.
14. Lee VH, Ouyang B, John S, Conners JJ, Garg R, Bleck TP, et al. Risk stratification for the in-hospital mortality in subarachnoid hemorrhage: the HAIR score. Neurocrit Care. 2014;21(1):14–9.

15. Degos V, Apfel CC, Sanchez P, Colonne C, Renuit I, Clarencon F, et al. An admission bioclinical score to predict 1-year outcomes in patients undergoing aneurysm coiling. Stroke. 2012;43(5):1253–9.
16. Suwatcharangkoon S, Meyers E, Falo C, Schmidt JM, Agarwal S, Claassen J, et al. Loss of consciousness at onset of subarachnoid hemorrhage as an important marker of early brain injury. JAMA Neurol. 2016;73(1):28–35.
17. Hallevi H, Dar NS, Barreto AD, Morales MM, Martin-Schild S, Abraham AT, et al. The IVH score: a novel tool for estimating intraventricular hemorrhage volume: clinical and research implications. Crit Care Med. 2009;37(3):969–74, e1.
18. Hijdra A, Brouwers PJ, Vermeulen M, van Gijn J. Grading the amount of blood on computed tomograms after subarachnoid hemorrhage. Stroke. 1990;21(8):1156–61.
19. Varsos GV, Richards HK, Kasprowicz M, Reinhard M, Smielewski P, Brady KM, et al. Cessation of diastolic cerebral blood flow velocity: the role of critical closing pressure. Neurocrit Care. 2014;20(1):40–8.
20. Budohoski KP, Czosnyka M, Kirkpatrick PJ, Reinhard M, Varsos GV, Kasprowicz M, et al. Bilateral failure of cerebral autoregulation is related to unfavorable outcome after subarachnoid hemorrhage. Neurocrit Care. 2015;22(1):65–73.
21. Cropp GJ, Manning GW. Electrocardiographic changes simulating myocardial ischemia and infarction associated with spontaneous intracranial hemorrhage. Circulation. 1960;22:25–38.
22. Wartenberg KE, Schmidt JM, Claassen J, Temes RE, Frontera JA, Ostapkovich N, et al. Impact of medical complications on outcome after subarachnoid hemorrhage. Crit Care Med. 2006;34(3):617–23.
23. Bruder N, Rabinstein A. Cardiovascular and pulmonary complications of aneurysmal subarachnoid hemorrhage. Neurocrit Care. 2011;15(2):257–69.
24. Katayama Y, Haraoka J, Hirabayashi H, Kawamata T, Kawamoto K, Kitahara T, et al. A randomized controlled trial of hydrocortisone against hyponatremia in patients with aneurysmal subarachnoid hemorrhage. Stroke. 2007;38(8):2373–5.
25. Kruyt ND, Biessels GJ, DeVries JH, Luitse MJ, Vermeulen M, Rinkel GJ, et al. Hyperglycemia in aneurysmal subarachnoid hemorrhage: a potentially modifiable risk factor for poor outcome. J Cereb Blood Flow Metab. 2010;30(9):1577–87.
26. Bilotta F, Spinelli A, Giovannini F, Doronzio A, Delfini R, Rosa G. The effect of intensive insulin therapy on infection rate, vasospasm, neurologic outcome, and mortality in neurointensive care unit after intracranial aneurysm clipping in patients with acute subarachnoid hemorrhage: a randomized prospective pilot trial. J Neurosurg Anesthesiol. 2007;19(3):156–60.
27. Latorre JG, Chou SH, Nogueira RG, Singhal AB, Carter BS, Ogilvy CS, et al. Effective glycemic control with aggressive hyperglycemia management is associated with improved outcome in aneurysmal subarachnoid hemorrhage. Stroke. 2009;40(5):1644–52.
28. Patet C, Quintard H, Zerlauth JB, Maibach T, Carteron L, Suys T, et al. Bedside cerebral microdialysis monitoring of delayed cerebral hypoperfusion in comatose patients with poor grade aneurysmal subarachnoid haemorrhage. J Neurol Neurosurg Psychiatry. 2017;88(4):332–8.
29. Helbok R, Schmidt JM, Kurtz P, Hanafy KA, Fernandez L, Stuart RM, et al. Systemic glucose and brain energy metabolism after subarachnoid hemorrhage. Neurocrit Care. 2010;12(3):317–23.
30. Galea JP, Dulhanty L, Patel HC. Predictors of outcome in aneurysmal subarachnoid hemorrhage patients: observations from a multicenter data set. Stroke. 2017;48(11):2958–63.
31. Ohkuma H, Ogane K, Tanaka M, Suzuki S. Assessment of cerebral microcirculatory changes during cerebral vasospasm by analyzing cerebral circulation time on DSA images. Acta Neurochir Suppl. 2001;77:127–30.
32. van Donkelaar CE, Bakker NA, Veeger NJ, Uyttenboogaart M, Metzemaekers JD, Luijckx GJ, et al. Predictive factors for rebleeding after aneurysmal subarachnoid hemorrhage: rebleeding aneurysmal subarachnoid hemorrhage study. Stroke. 2015;46(8):2100–6.
33. Park J, Woo H, Kang DH, Kim YS, Kim MY, Shin IH, et al. Formal protocol for emergency treatment of ruptured intracranial aneurysms to reduce in-hospital rebleeding and improve clinical outcomes. J Neurosurg. 2015;122(2):383–91.
34. de Oliveira Manoel AL, Mansur A, Silva GS, Germans MR, Jaja BN, Kouzmina E, et al. Functional outcome after poor-grade subarachnoid hemorrhage: a single-center study and systematic literature review. Neurocrit Care. 2016;25(3):338–50.
35. Inamasu J, Nakae S, Ohmi T, Kogame H, Kawazoe Y, Kumai T, et al. The outcomes of early aneurysm repair in World Federation of Neurosurgical Societies grade V subarachnoid haemorrhage patients with emphasis on those presenting with a Glasgow coma scale score of 3. J Clin Neurosci. 2016;33:142–7.
36. Chang HS, Hongo K, Nakagawa H. Adverse effects of limited hypotensive anesthesia on the outcome of patients with subarachnoid hemorrhage. J Neurosurg. 2000;92(6):971–5.
37. Hitchcock ER, Tsementzis SA, Dow AA. Short- and long-term prognosis of patients with a subarachnoid haemorrhage in relation to intra-operative period of hypotension. Acta Neurochir. 1984;70(3–4):235–42.
38. Mutoh T, Kazumata K, Ishikawa T, Terasaka S. Performance of bedside transpulmonary thermodilution monitoring for goal-directed hemodynamic management after subarachnoid hemorrhage. Stroke. 2009;40(7):2368–74.
39. Mutoh T, Kazumata K, Terasaka S, Taki Y, Suzuki A, Ishikawa T. Early intensive versus minimally invasive approach to postoperative hemodynamic management after subarachnoid hemorrhage. Stroke. 2014;45(5):1280–4.
40. Matta BF, Lam AM, Mayberg TS, Shapira Y, Winn HR. A critique of the intraoperative use of jugular

venous bulb catheters during neurosurgical procedures. Anesth Analg. 1994;79(4):745–50.
41. Clavier N, Schurando P, Raggueneau JL, Payen DM. Continuous jugular bulb venous oxygen saturation validation and variations during intracranial aneurysm surgery. J Crit Care. 1997;12(3):112–9.
42. Ter Minassian A, Poirier N, Pierrot M, Menei P, Granry JC, Ursino M, et al. Correlation between cerebral oxygen saturation measured by near-infrared spectroscopy and jugular oxygen saturation in patients with severe closed head injury. Anesthesiology. 1999;91(4):985–90.
43. Rozet I, Tontisirin N, Muangman S, Vavilala MS, Souter MJ, Lee LA, et al. Effect of equiosmolar solutions of mannitol versus hypertonic saline on intraoperative brain relaxation and electrolyte balance. Anesthesiology. 2007;107(5):697–704.
44. Gelb AW, Craen RA, Rao GS, Reddy KR, Megyesi J, Mohanty B, et al. Does hyperventilation improve operating condition during supratentorial craniotomy? A multicenter randomized crossover trial. Anesth Analg. 2008;106(2):585–94.
45. Matta BF, Mayberg TS, Lam AM. Direct cerebrovasodilatory effects of halothane, isoflurane, and desflurane during propofol-induced isoelectric electroencephalogram in humans. Anesthesiology. 1995;83(5):980–5.
46. Matta BF, Heath KJ, Tipping K, Summors AC. Direct cerebral vasodilatory effects of sevoflurane and isoflurane. Anesthesiology. 1999;91(3):677–80.
47. Pasternak JJ, McGregor DG, Lanier WL, Schroeder DR, Rusy DA, Hindman B, et al. Effect of nitrous oxide use on long-term neurologic and neuropsychological outcome in patients who received temporary proximal artery occlusion during cerebral aneurysm clipping surgery. Anesthesiology. 2009;110(3):563–73.
48. Maurtua MA, Deogaonkar A, Bakri MH, Mascha E, Na J, Foss J, et al. Dosing of remifentanil to prevent movement during craniotomy in the absence of neuromuscular blockade. J Neurosurg Anesthesiol. 2008;20(4):221–5.
49. Futier E, Constantin JM, Paugam-Burtz C, Pascal J, Eurin M, Neuschwander A, et al. A trial of intraoperative low-tidal-volume ventilation in abdominal surgery. N Engl J Med. 2013;369(5):428–37.
50. Serpa Neto A, Hemmes SN, Barbas CS, Beiderlinden M, Biehl M, Binnekade JM, et al. Protective versus conventional ventilation for surgery: a systematic review and individual patient data meta-analysis. Anesthesiology. 2015;123(1):66–78.
51. Hemmes SN, Gama de Abreu M, Pelosi P, Schultz MJ. High versus low positive end-expiratory pressure during general anaesthesia for open abdominal surgery (PROVHILO trial): a multicentre randomised controlled trial. Lancet. 2014;384(9942):495–503.
52. Ferrando C, Soro M, Unzueta C, Suarez-Sipmann F, Canet J, Librero J, et al. Individualised perioperative open-lung approach versus standard protective ventilation in abdominal surgery (iPROVE): a randomised controlled trial. Lancet Respir Med. 2018;6(3):193–203.
53. Neto AS, Hemmes SN, Barbas CS, Beiderlinden M, Fernandez-Bustamante A, Futier E, et al. Association between driving pressure and development of postoperative pulmonary complications in patients undergoing mechanical ventilation for general anaesthesia: a meta-analysis of individual patient data. Lancet Respir Med. 2016;4(4):272–80.
54. Boone MD, Jinadasa SP, Mueller A, Shaefi S, Kasper EM, Hanafy KA, et al. The effect of positive end-expiratory pressure on intracranial pressure and cerebral hemodynamics. Neurocrit Care. 2017;26(2):174–81.
55. Muench E, Bauhuf C, Roth H, Horn P, Phillips M, Marquetant N, et al. Effects of positive end-expiratory pressure on regional cerebral blood flow, intracranial pressure, and brain tissue oxygenation. Crit Care Med. 2005;33(10):2367–72.
56. Tankisi A, Rasmussen M, Juul N, Cold GE. The effects of 10 degrees reverse Trendelenburg position on subdural intracranial pressure and cerebral perfusion pressure in patients subjected to craniotomy for cerebral aneurysm. J Neurosurg Anesthesiol. 2006;18(1):11–7.
57. Lee JM, Bahk JH, Lim YJ, Lee J, Lim L. The EC90 of remifentanil for blunting cardiovascular responses to head fixation for neurosurgery under total intravenous anesthesia with propofol and remifentanil based on bispectral index monitoring: estimation with the biased coin up-and-down sequential method. BMC Anesthesiol. 2017;17(1):136.
58. Bayer-Berger MM, Ravussin P, Fankhauser H, Freeman J. Effect of three pretreatment techniques on hemodynamic and CSFP responses to skull-pin head-holder application during thiopentone/isoflurane or propofol anesthesia. J Neurosurg Anesthesiol. 1989;1(3):227–32.
59. Malinova V, Schatlo B, Voit M, Suntheim P, Rohde V, Mielke D. The impact of temporary clipping during aneurysm surgery on the incidence of delayed cerebral ischemia after aneurysmal subarachnoid hemorrhage. J Neurosurg. 2017;15:1–7.
60. Lavine SD, Masri LS, Levy ML, Giannotta SL. Temporary occlusion of the middle cerebral artery in intracranial aneurysm surgery: time limitation and advantage of brain protection. J Neurosurg. 1997;87(6):817–24.
61. Ogilvy CS, Carter BS, Kaplan S, Rich C, Crowell RM. Temporary vessel occlusion for aneurysm surgery: risk factors for stroke in patients protected by induced hypothermia and hypertension and intravenous mannitol administration. J Neurosurg. 1996;84(5):785–91.
62. Kett-White R, Hutchinson PJ, Al-Rawi PG, Czosnyka M, Gupta AK, Pickard JD, et al. Cerebral oxygen and microdialysis monitoring during aneurysm surgery: effects of blood pressure, cerebrospinal fluid drainage, and temporary clipping on infarction. J Neurosurg. 2002;96(6):1013–9.

63. Todd MM, Hindman BJ, Clarke WR, Torner JC. Mild intraoperative hypothermia during surgery for intracranial aneurysm. N Engl J Med. 2005; 352(2):135–45.
64. Hindman BJ, Bayman EO, Pfisterer WK, Torner JC, Todd MM. No association between intraoperative hypothermia or supplemental protective drug and neurologic outcomes in patients undergoing temporary clipping during cerebral aneurysm surgery: findings from the intraoperative hypothermia for aneurysm surgery trial. Anesthesiology. 2010; 112(1):86–101.
65. Stendel R, Pietila T, Al Hassan AA, Schilling A, Brock M. Intraoperative microvascular Doppler ultrasonography in cerebral aneurysm surgery. J Neurol Neurosurg Psychiatry. 2000;68(1):29–35.
66. Nishiyama Y, Kinouchi H, Senbokuya N, Kato T, Kanemaru K, Yoshioka H, et al. Endoscopic indocyanine green video angiography in aneurysm surgery: an innovative method for intraoperative assessment of blood flow in vasculature hidden from microscopic view. J Neurosurg. 2012;117(2):302–8.
67. Sharma M, Ambekar S, Ahmed O, Nixon M, Sharma A, Nanda A, et al. The utility and limitations of intraoperative near-infrared indocyanine green videoangiography in aneurysm surgery. World Neurosurg. 2014;82(5):e607–13.
68. Al-Mousa A, Bose G, Hunt K, Toma AK. Adenosine-assisted neurovascular surgery: initial case series and review of literature. Neurosurg Rev. 2017:1–8. https://doi.org/10.1007/s10143-017-0883-3
69. 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(1):37–47.
70. Elijovich L, Higashida RT, Lawton MT, Duckwiler G, Giannotta S, Johnston SC. Predictors and outcomes of intraprocedural rupture in patients treated for ruptured intracranial aneurysms: the CARAT study. Stroke. 2008;39(5):1501–6.
71. Leipzig TJ, Morgan J, Horner TG, Payner T, Redelman K, Johnson CS. Analysis of intraoperative rupture in the surgical treatment of 1694 saccular aneurysms. Neurosurgery. 2005;56(3):455–68.
72. Batjer H, Samson D. Intraoperative aneurysmal rupture: incidence, outcome, and suggestions for surgical management. Neurosurgery. 1986;18(6):701–7.
73. Molyneux A, Kerr R, Stratton I, Sandercock P, Clarke M, Shrimpton J, et al. International subarachnoid aneurysm trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial. Lancet. 2002;360(9342):1267–74.
74. Doerfler A, Wanke I, Egelhof T, Dietrich U, Asgari S, Stolke D, et al. Aneurysmal rupture during embolization with Guglielmi detachable coils: causes, management, and outcome. AJNR Am J Neuroradiol. 2001;22(10):1825–32.
75. Murayama Y, Nien YL, Duckwiler G, Gobin YP, Jahan R, Frazee J, et al. Guglielmi detachable coil embolization of cerebral aneurysms: 11 years' experience. J Neurosurg. 2003;98(5):959–66.
76. Vanninen R, Koivisto T, Saari T, Hernesniemi J, Vapalahti M. Ruptured intracranial aneurysms: acute endovascular treatment with electrolytically detachable coils--a prospective randomized study. Radiology. 1999;211(2):325–36.
77. Cloft HJ, Kallmes DF. Cerebral aneurysm perforations complicating therapy with Guglielmi detachable coils: a meta-analysis. AJNR Am J Neuroradiol. 2002;23(10):1706–9.
78. Pierot L, Cognard C, Anxionnat R, Ricolfi F. Ruptured intracranial aneurysms: factors affecting the rate and outcome of endovascular treatment complications in a series of 782 patients (CLARITY study). Radiology. 2010;256(3):916–23.
79. Qureshi AI, Luft AR, Sharma M, Guterman LR, Hopkins LN. Prevention and treatment of thromboembolic and ischemic complications associated with endovascular procedures: part II--clinical aspects and recommendations. Neurosurgery. 2000;46(6):1360–75.
80. Ries T, Buhk JH, Kucinski T, Goebell E, Grzyska U, Zeumer H, et al. Intravenous administration of acetylsalicylic acid during endovascular treatment of cerebral aneurysms reduces the rate of thromboembolic events. Stroke. 2006;37(7):1816–21.
81. Hahnel S, Schellinger PD, Gutschalk A, Geletneky K, Hartmann M, Knauth M, et al. Local intra-arterial fibrinolysis of thromboemboli occurring during neuroendovascular procedures with recombinant tissue plasminogen activator. Stroke. 2003;34(7):1723–8.
82. Brinjikji W, Morales-Valero SF, Murad MH, Cloft HJ, Kallmes DF. Rescue treatment of thromboembolic complications during endovascular treatment of cerebral aneurysms: a meta-analysis. AJNR Am J Neuroradiol. 2015;36(1):121–5.