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Aneurysmal subarachnoid haemorrhage and the anaesthetist

H.-J. Priebe*

Department of Anaesthesia, University Hospital, Hugstetter Str. 55, 79106 Freiburg, Germany
**E-mail: priebe@ana1.ukl.uni-freiburg.de*

The anaesthetist may be involved at various stages in the management of subarachnoid haemorrhage (SAH). Thus, familiarity with epidemiological, pathophysiological, diagnostic, and therapeutic issues is as important as detailed knowledge of the optimal intraoperative anaesthetic management. As the prognosis of SAH remains poor, prompt diagnosis and appropriate treatment are essential, because early treatment may improve outcome. It is, therefore, important to rule out SAH as soon as possible in all patients complaining of sudden onset of severe headache lasting for longer than an hour with no alternative explanation. The three main predictors of mortality and dependence are impaired level of consciousness on admission, advanced age, and a large volume of blood on initial cranial computed tomography. The major complications of SAH include re-bleeding, cerebral vasospasm leading to immediate and delayed cerebral ischaemia, hydrocephalus, cardiopulmonary dysfunction, and electrolyte disturbances. Prophylaxis and therapy of cerebral vasospasm include maintenance of cerebral perfusion pressure (CPP) and normovolaemia, administration of nimodipine, triple-H therapy, balloon angioplasty, and intra-arterial papaverine. Occlusion of the aneurysm after SAH is usually attempted surgically ('clipping') or endovascularly by detachable coils ('coiling'). The need for an adequate CPP (for the prevention of cerebral ischaemia and cerebral vasospasm) must be balanced against the need for a low transmural pressure gradient of the aneurysm (for the prevention of rupture of the aneurysm). Effective measures to prevent or attenuate increases in intracranial pressure, brain swelling, and cerebral vasospasm throughout all phases of anaesthesia are prerequisite for optimal outcome.

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Diagnosis and management of subarachnoid haemorrhage (SAH) can be challenging.[19 117] As the prognosis remains poor,[38] and early treatment may improve outcome,[21] prompt diagnosis and appropriate treatment of SAH are essential.[2 9 10] The anaesthetist may be involved in the management of SAH at various stages such as providing first medical care at an out-of-hospital location, transporting the patient with suspected SAH to a hospital, supporting the initial investigations for suspected SAH in the emergency ward, as anaesthetist providing care in the neuroradiology suite or operating theatre for diagnostic and therapeutic interventions, or as intensive care physician providing medical care in the perioperative period or in a non-operative setting. Thus, the anaesthetist needs to be familiar not only with aspects directly related to the intraoperative anaesthetic management, but also with epidemiological, pathophysiological, diagnostic, and therapeutic issues. Accordingly, the following review seeks to provide the knowledge required to administer adequate care at various stages in the management of SAH. As SAH is mostly caused by rupture of a cerebral aneurysm (see below), this review primarily addresses aneurysmal SAH.

Epidemiology and aetiology

The estimated incidence of SAH is 8–10 cases per 100 000 persons per year.[56 119] SAH occurs most frequently in individuals between the ages of 55 and 60 yr.[33] Ruptured intracranial aneurysms may account for 5–15% of strokes.[5] Approximately three quarters of spontaneous episodes of SAH are caused by ruptured cerebral aneurysms.[2] The cause for another 20% of those episodes is unknown, with roughly half of these being because of idiopathic or non-aneurysmal, perimesencephalic SAH. The rest of the episodes are caused by various rare disorders such as arterio-venous malformations of brain and spine, arterial dissections, vasculitis, and tumours.[2]

Most cerebral aneurysms are probably the result of a combination of a possibly genetically, haemodynamically, nicotine abuse- or alcohol abuse-induced structural defect (i.e. a decrease in the middle muscular layer, the tunica media of the arterial wall), and chronic haemodynamically-induced intravascular shear stress that can cause aneurysmal out-pouchings in the subarachnoid space at the base of the brain.[9 30 96] Aneurysms develop mostly at vascular bifurcations, because turbulent flow preferably develops at such sites. Only a few aneurysms may be caused by infections or trauma. With an increase in the size of the aneurysm, wall compliance will decrease and wall tension increase that, in turn, render the aneurysm increasingly susceptible to rupture. According to Laplace's law, aneurysmal wall tension changes proportionally to the fourth power of the aneurysm's radius that, in turn, changes proportionally to arterial pressure. In the absence of rupture, the aneurysm may grow in size to >2 cm in diameter (giant aneurysm).

The vast majority of aneurysms (80–90%) are located in the anterior (carotid) circulation, the anterior and posterior communicating, and the middle cerebral artery. The remaining 10–20% are located in the posterior (vertebro-basilar) circulation.

Pathophysiology

During rupture of the aneurysm, free communication exists between intra-arterial and subarachnoid spaces. The sudden increase in regional intracranial pressure (ICP) to a level equal to that of systemic arterial pressure is the cause of sudden onset of severe headache and (transient or permanent) loss of consciousness. The spread of blood through the subarachnoid space is the cause of headache, meningism, and subsequent development of hydrocephalus [as a consequence of either impaired reabsorption of cerebrospinal fluid (CSF) or formation of a blood clot in the ventricle].

After recurrent episodes of bleeding, blood clots and adhesions hinder the free spread of blood through the subarachnoid space, supporting the formation of intracerebral haematomas. The blood (by oxyhaemoglobin and its breakdown products) in the subarachnoid space is likely to contribute to the aetiology of cerebral vasospasm. The amount and location of blood seem to correlate with the incidence of cerebral vasospasm.

The expanding mass effect of the haemorrhage and the development of brain oedema and hydrocephalus contribute to increase in ICP. Soon after SAH, ICP may approach systemic blood pressure. This phase is of short duration (possibly only minutes) and thought to be the limiting factor in further leakage of blood from the aneurysm. With recurrent episodes of bleeding, ICP may increase further because of a mass effect of clots, cerebral oedema, or obstructive hydrocephalus. Intracerebral and intraventricular haematomas contribute to the increase in ICP in one-third of patients with SAH.[42]

Autoregulation of cerebral blood flow (CBF)

SAH is usually accompanied by a decrease in CBF and in cerebral metabolic rate (CMR). Frequently, cerebral autoregulation is impaired. The degree of impairment correlates with the neurological condition. The combination of a shift in the cerebral autoregulation curve to the right and cerebral vasospasm may cause delayed cerebral ischaemic deficits.[49] The shift in the cerebral autoregulation curve to the right would explain the reversal of newly developed neurological deficits after pharmacologically induced increase in blood pressure in patients with SAH. The frequent finding of impaired cerebral autoregulation during SAH and the documented association between low blood pressure and neurological deficits underline the importance of an adequate cerebral perfusion pressure (CPP) in the overall management of SAH, and is an argument against the liberal use of intraoperatively induced hypotension (see below).

Cerebrovascular CO_2 reactivity

The reactivity of the cerebral vasculature to changes in arterial carbon dioxide (CO_2) tension is usually preserved during SAH. CO_2 reactivity becomes impaired only in patients with poor neurological condition. Thus, in most cases of SAH, hyperventilation would remain an option to treat increased ICP and cerebral blood volume temporarily.

Natural history

The overall case fatality of all-cause SAH is as high as 50%.[38] Aneurysmal SAH carries a 30 day mortality rate of 45%.[33] An estimated one-third of survivors remain moderately to severely disabled.[38 41] Approximately 10% of patients with SAH die before, and many more are comatose or exhibit severe neurological deficits when receiving medical attention for the first time.[119] Almost all deaths after SAH are caused by re-bleeding and cerebral vasospasm, and occur within the first 3 weeks. Ruptured aneurysms tend to re-bleed in 2–4% of cases within the first 24 h, and in 15–20% within the first 2 weeks of the initial haemorrhage.[33] The three main predictors of mortality and dependence are impaired level of consciousness on admission, advanced age, and large volume of blood on initial cranial computed tomography (CT).[2]

Clinical presentation

SAH is usually accompanied by a combination of characteristic symptoms (i.e. sudden onset of severe headache, meningism, transient or persistent loss of consciousness, epileptic seizures, and focal neurological deficits).[56] Neurological injury varies between unconsciousness, depressed consciousness, focal neurological deficits, and isolated cranial nerve palsy from 'jet impact' injury. Progressive obtundation and

Table 1 Hunt and Hess[39] grading scale for SAH

Grade	Clinical description
I	Asymptomatic or minimal headache and slight nuchal rigidity
II	Moderate to severe headache, nuchal rigidity, no neurological deficit other than cranial nerve palsy
III	Drowsiness, confusion, or mild focal deficit
IV	Stupor, moderate to severe hemiparesis, and possibly early decerebrate rigidity and vegetative disturbances
V	Deep coma, decerebrate rigidity, and moribund appearance

non-reactive small pupils are characteristic, but non-specific findings of hydrocephalus are observed in only half of the cases.

Clinical grading scales such as the one of Hunt and Hess (Table 1)[39] or the World Federation of Neurological Surgeons (Table 2)[25] are used to standardize clinical assessment and to estimate the prognosis.[52] Knowledge and understanding of the grading scales are required for effective communication between physicians, assessment of the severity of the underlying pathophysiological abnormalities, and rational planning of the perioperative anaesthetic management.

In general, the higher the clinical grade, the more likely are cerebral vasospasm, elevated ICP, impaired cerebral autoregulation, impaired vascular CO_2 reactivity, cardiac arrhythmias and dysfunction,[20] hypovolaemia, and hyponatraemia.[24] Patients with Hess and Hunt grade I and II (Table 1) are likely to have normal ICP and preserved cerebrovascular reactivity; thus, they can be expected to respond to hyperventilation with cerebral vasoconstriction. In contrast, patients with Hess and Hunt grade III and IV are likely to have increased ICP and impaired cerebrovascular reactivity; hyperventilation is thus unlikely to result in reliable cerebral vasoconstriction. A low Glasgow Coma Scale score ($\leq$8) is usually associated with increased ICP.

Diagnosis

Although SAH is usually accompanied by a combination of characteristic symptoms, no single sign or symptom allows reliable establishment of the diagnosis of SAH.[2 56] It is, therefore, important to exclude SAH as soon as possible in all patients complaining of sudden onset of severe headache

Table 2 World Federation of Neurological Surgeons Grading Scale for aneurysmal SAH.[25] GCS, Glasgow Coma Scale. *Excludes cranial neuropathies, but includes dysphasia

Grade	GCS score	Motor deficit*
I	15	Absent
II	13 or 14	Absent
III	13 or 14	Present
IV	7–12	Present or absent
V	3–6	Present or absent

Table 3 Initial investigations for suspected SAH. R/o, rule out; CCT, cranial computerized tomography. Modified after Al-Shahi and colleagues[2]

Investigation	Comment
Full blood count	R/o anaemia and leucocytosis
Coagulation screen	R/o coagulopathy
Serum urea and electrolytes	Hyponatraemia, common after SAH
Serum glucose	Hyperglycaemia, associated with poor outcome
Serum magnesium	Hypomagnesaemia, common and associated with poor outcome after SAH
Chest X-ray	R/o pulmonary oedema and aspiration
12-lead ECG	ST-segment changes common after SH; R/o cardiac arrhythmias and ischaemia
Unenhanced CCT	As soon as possible (within 24 h) after onset of sudden severe headache
Lumbar puncture	If unenhanced CCT is normal in case of suspected SAH
CT angiography	If SAH confirmed by CCT or lumbar puncture

lasting for longer than an hour with no alternative explanation (Table 3).[2 56] Unenhanced (no use of contrast media) cranial CT is the initial diagnostic tool of choice in all cases of suspected SAH.[2 10] As the findings suggestive of SAH can be subtle, and as subarachnoid blood degrades quickly and is almost completely reabsorbed within 10 days of SAH, the CT needs to be carried out and interpreted by an experienced neuroradiologist as soon as possible after the onset of sudden severe headache, and immediately in the case of impaired consciousness.[2]

The amount of blood on unenhanced CT can be described by the Fisher four-point scale (Table 4).[31] It is possibly the best predictor of cerebral vasospasm and overall patient outcome. The location and distribution of blood on CT helps to identify the cause of SAH. However, as there are overlaps in the blood distribution pattern on CT, after the rupture of aneurysms in different locations of the brain and in idiopathic perimesencephalic SAH, and as even third-generation CT scanners miss approximately 2 and 7% of episodes of SAH within 12 and by 24 h, respectively, additional investigations are almost always required. Such investigations include lumbar puncture, multi-slice CT angiography, four-vessel catheter angiography, spinal catheter angiography, and magnetic resonance imaging.[2]

Lumbar puncture has been advocated in approximately 5% of patients with suspected SAH but normal CT.[2 33 114] Blood-containing CSF that does not clear during continued flow and xanthochromic CSF are highly suspicious of SAH.[27] However, the timing and conduct of lumbar puncture, the

Table 4 Fisher grading scale[31] of cranial computerized tomography (CCT)

Grade	Findings on CCT
1	No subarachnoid blood detected
2	Diffuse or vertical layers $\leq$1 mm
3	Localized clot and/or vertical layer $>$1 mm
4	Intracerebral or intraventricular clot with diffuse or no subarachnoid haemorrhage

processing of the CSF sample, and the interpretation of the CSF's macroscopic appearance and laboratory findings require considerable expertise.[19 110 115–117 122]

After having established the diagnosis of SAH, the next step is to determine whether a ruptured aneurysm is the cause of it. The three methods of choice for detecting and delineating the anatomy of intracranial aneurysms are (1) CT angiography after injection of contrast media, (2) magnetic resonance angiography, and (3) catheter angiography by direct intra-arterial catheterization, the latter being considered the benchmark technique.[10] The development of three-dimensional, rotational catheter angiography allows rotation of formatted images and, in turn, assessment of the aneurysm's relationship to other vessels.[3 104]

Major complications of SAH

The major complications of SAH include re-bleeding, cerebral vasospasm leading to immediate and delayed cerebral ischaemia, hydrocephalus, cardiopulmonary dysfunction, and electrolyte disturbances (Table 5).[33 58] Non-neurological complications of SAH (e.g. anaemia, hypertension, hypotension, hyperglycaemia, electrolyte disorders, cardiac insufficiency, and arrhythmias) develop in more than half of patients and adversely affect outcome.[118]

Cerebral vasospasm

Cerebral vasospasm usually develops 3–12 days after SAH, lasts on average 2 weeks, and affects 60–70% of patients with SAH. It frequently results in cerebral ischaemia, and is the major cause of morbidity and mortality after SAH.[6] Cerebral ischaemia may cause subtle (e.g. decrease in the level of arousal) and obvious neurological deficits (e.g. new hemiparesis) and death. Severe cerebral vasospasm may account for infarction and death in up to one-third of patients with SAH.

The diagnosis of cerebral vasospasm is made angiographically or clinically. Angiographic vasospasm is defined as a narrowing of the contrast medium column in major cerebral arteries. Clinical vasospasm is defined as the ischaemic consequences of cerebral vasospasm resulting in various degrees of neurological deficits. Interestingly, although the time course of clinical vasospasm parallels that of angiographic vasospasm, far more patients will develop angiographic vasospasm (up to 70%) than symptomatic vasospasm (20–30%).[35]

The exact cause of the intracranial vasospasm is not known. Theories of its aetiology include (1) SAH-induced changes in biochemically mediated contractions and relaxations of cerebral arterial smooth muscle cells; (2) direct vasoconstrictive activity of breakdown products of extravasated blood; (3) development of structural changes within the blood vessels; and (4) immune-mediated vasoconstriction.[35] A large blood burden (amount of subarachnoid blood or size of blood clots in the subarachnoid cisterns as diagnosed by CT; Table 4) is the only consistent predictor for the development of cerebral vasospasm after SAH.[35] The combination of increased ICP and hypovolaemia increases the likelihood for cerebral vasospasm. Cerebral vasospasm, in turn, may *per se* increase ICP. The associated reduction in CBF is accompanied by vasodilation of distal cerebral blood vessels. This response may cause an increase in cerebral blood volume followed by a possible (further) increase in ICP.

Table 5 Complications of aneurysmal SAH. Modified after Al-Shahi and colleagues.[2] ICP, intracranial pressure; CPP, cerebral perfusion pressure

Re-bleeding
On day 1: 15%
By 1 month: 40%
After 6 months: 3% per year
Cerebral ischaemia
Immediate onset (increased ICP resulting in decreased CPP)
Delayed onset (peaks 4–14 days after SAH)
Seizures
Hydrocephalus (in 15–20% of cases)
Cardiac dysfunction (reflected by echocardiographic abnormalities and by increases in serum concentration of cardiac troponin)
Hyponatraemia, hypomagnesaemia or both (because of salt wasting)

Cardiac dysfunction

SAH is frequently accompanied by marked systemic and pulmonary hypertension, cardiac arrhythmias, myocardial dysfunction and injury, and neurogenic pulmonary oedema. ECG abnormalities (e.g. QT_c prolongation, repolarization abnormalities) have been reported in 25–100% of cases,[40 101 123] along with an increase in serum concentration of cardiac troponin in 17–28% and of creatine kinase MB isoenzyme in 37%,[11 22 109 123] and left ventricular dysfunction in 8–30% of cases.[20 47 124] The most severe form of cardiac injury associated with SAH is the syndrome of neurogenic-stunned myocardium, which is characterized by reversible left ventricular systolic dysfunction, cardiogenic shock, and pulmonary oedema.[46 62]

The cardiac abnormalities are probably the result of excessive myocardial release of catecholamines from sympathetic nerve terminals triggered by the SAH, resulting in calcium overload and necrosis of myocytes.[93] High sympathetic tone and increased serum concentrations of catecholamines were observed in patients after SAH.[50]

In most cases, myocardial dysfunction seems to correlate more with the degree of neurological deficit than with the severity of ECG abnormalities. It is unclear whether electro- and echocardiographic and biochemical signs of myocardial injury associated with SAH require the same therapy and carry the same prognosis as those associated with primary myocardial injury. However, in the presence of symptomatic cardiac dysfunction, myocardial injury or both, the indication for triple-H therapy (see below) must be carefully considered, because the therapeutic goals of such therapy (increase in blood pressure and cardiac filling

pressures and reduction in haematocrit) are contrary to that of a primarily cardioprotective therapy (relatively low preload, afterload, and contractility).

As cardiac injury and dysfunction mostly resolve over time and do not seem to directly affect morbidity and mortality,[22] the ECG, functional and biochemical cardiac abnormalities associated with SAH are widely regarded as epiphenomena that primarily reflect the severity of intracranial injury and do not require adjustment of the overall management. However, peak cardiac troponin concentration was an independent predictor of hypotension requiring treatment with vasopressors, pulmonary oedema, left ventricular dysfunction, and delayed cerebral ischaemia from cerebral vasospasm; it was also associated with increased mortality or severe disability at discharge.[73]

If cardiovascular dysfunction should, in fact, directly affect outcome, it may be worthwhile to measure serum concentrations of cardiac troponin after SAH in patients with clinical, ECG, or echocardiographic evidence of cardiac dysfunction. In view of the adverse effect on outcome, therapy of cardiac insufficiency with inotropic drugs should be considered.[54 63 77] Individual patients with severe cardiovascular failure and cerebral vasospasm were reported even to benefit from temporary intra-aortic balloon pump counterpulsation.[89 102]

Electrolyte disturbances

SAH is frequently accompanied by hyponatraemia, hypokalaemia, hypocalcaemia, and hypomagnesaemia. Hyponatraemia develops in approximately 30% of cases as a result of either the cerebral salt wasting syndrome or the syndrome of inappropriate secretion of antidiuretic hormone (SIADH). The cerebral salt wasting syndrome is caused by the secretion of brain and atrial natriuretic hormone, which leads to a negative sodium balance, hyponatraemia, and intravascular volume depletion.[120]

The therapeutic options for the cerebral salt wasting syndrome are limited. Appropriate treatment consists of i.v. infusion of normal saline, rarely of hypertonic saline. Administration of fludrocortisone and hydrocortisone prevented or attenuated intravascular volume depletion and decreased the incidence of negative sodium balance.[36 68 121] SIADH is accompanied by retention of excess free water. Although fluid restriction would be the theoretical treatment of choice, salt-containing i.v. solutions are usually used during SAH to ensure a normal to high intravascular volume.

Prophylaxis and therapy of cerebral vasospasm

General measures in the prophylaxis of cerebral vasospasm include administration of nimodipine, mild sedation, positive fluid balance, and avoidance of hypotensive episodes and hyponatraemia. Antifibrinolytic drugs are no longer recommended, because even under nimodipine prophylaxis, complications related to vasospasm-induced thrombo-embolism occurred.[88] There is no evidence that antiplatelet therapy improves outcome.[112] Symptomatic treatment of cerebral vasospasm consists of triple-H therapy, balloon angioplasty, and intra-arterial papaverine.

Nimodipine

Nimodipine, a calcium channel blocker, improves outcome after SAH.[4] Nimodipine therapy (60 mg orally or by nasogastric tube every 4 h; maximal daily dose 360 mg) should thus be started in all patients at admission and continued for 21 days. Nimodipine administered as a continuous infusion is no more effective than when administered orally, but is associated with a higher incidence of hypotension ($1\ mg\ h^{-1}$ during the first 6 h; if blood pressure remains stable, increase to $1.5\ mg\ h^{-1}$ for another 6 h; if blood pressure continues to remain stable, increase to the maximal dose of $2\ mg\ h^{-1}$). Because of the risk of causing thrombophlebitis when administered peripherally, nimodipine must be administered through a central venous catheter. In addition, the infusion system must be protected from light. If an adequate (systolic blood pressure 130–150 mm Hg) and stable blood pressure cannot be maintained, blood pressure management takes priority over nimodipine administration. In general, nimodipine renders patients prone to hypotension, especially when hypovolaemic and during induction of anaesthesia. As nimodipine does not reliably relieve angiographically documented vasospasm, its beneficial effect may be based more on a general brain protective mechanism.

Triple-H therapy

Triple-H therapy (hypertension, hypervolaemia, and haemodilution) is usually started in patients with an increase in transcranial Doppler velocities (as a reflection of cerebral vasospasm), the development of neurological deficits, or both.[33 52 119] As the main cerebrovascular resistance during cerebral vasospasm is determined by blood vessels that lack effective autoregulation (i.e. the major branches of the circle of Willis and their proximal branches), CBF becomes pressure dependent.[75] An increase in perfusion pressure and a decrease in blood viscosity would increase CBF (Poiseuille's law), and thereby possibly reverse cerebral ischaemia.[97]

The therapeutic goal of triple-H therapy is to increase CBF, increase CPP, and improve the rheological blood characteristics. For this purpose, systolic arterial pressure is increased (by administration of i.v. fluid or cardiovasoactive drugs) to approximately 120–150 mm Hg in unclipped and 160–200 mm Hg in clipped aneurysms; central venous pressure is maintained at 8–12 mm Hg (or pulmonary artery wedge pressure at 15–18 mm Hg); and haematocrit is decreased to approximately 0.3–0.35. Most

neurosurgeons consider triple-H therapy contraindicated in patients with unclipped aneurysm.

Although triple-H therapy is regarded by some as the most effective treatment of cerebral vasospasm (because it reverses neurological symptoms associated with cerebral vasospasm in up to 70% of patients), its efficacy in reducing the incidence of delayed ischaemic neurological deficits and death after SAH remains unproven; it does not seem to reduce the incidence of delayed ischaemic neurological deficits, and it may actually increase mortality.[75 107] The potentially life-threatening complications of triple-H therapy (e.g. pulmonary oedema, myocardial ischaemia, respiratory insufficiency, hyponatraemia, and indwelling catheter-associated morbidity) may more than offset its possible benefits. If triple-H therapy is, nevertheless, considered for patients with cardiac dysfunction, myocardial injury, ischaemic changes on ECG, and respiratory impairment, it may be worthwhile confirming transcranial Doppler findings suggestive of cerebral vasospasm by catheter angiography, and closely monitoring volume status and cardiac function by pulmonary artery catheter, transoesophageal echocardiography, or both.

Balloon angioplasty

Urgent catheter angiography is indicated in patients with persistent new neurological deficit that is unresponsive to medical therapy. If segmental stenosis (reflecting vasospasm) of the distal carotid artery, the proximal M1 and A1 segments, or the vertebral and basilar artery is confirmed, and infarction in the area supplied by the spastic vessels is ruled out by CT, transluminal balloon angioplasty of the vasoconstricted vessel(s) is indicated, with or without concomitant intra-arterial administration of papaverine.[28 90] Usually, long-lasting clinical improvement occurs after balloon angioplasty, in comparison with intra-arterial papaverine administration (see below).[28 75] Complications of balloon angioplasty include dissection, rupture, and thrombosis of the cerebral artery with subsequent cerebral infarction or haemorrhage. If infarction is already present in the area supplied by the spastic vessel, reperfusion may result in cerebral oedema and haemorrhage.

Intra-arterial papaverine

When vasospasm affects more distal vessel segments, intra-arterial administration of papaverine may be more effective (maximally 300 mg per hemisphere).[78] As papaverine is relatively short acting, some patients require repeated treatments. When both methods are equally indicated, balloon angioplasty may be superior to intra-arterial administration of papaverine.[28] In addition, papaverine is neurotoxic and has been associated with seizures, coma, blindness, and irreversible brain injury.[99]

Although balloon angioplasty and intra-arterial administration of papaverine result in angiographically documented amelioration of the vasospasm in the majority of patients,[83 90] radiographic improvement does not always correlate with improvement in cerebral perfusion and clinical status,[29 79 90 111] and they are not necessarily of greater benefit than triple-H therapy.

Occlusion therapy of cerebral aneurysm

Occlusion of the aneurysm after SAH is usually attempted either surgically ('clipping') or endovascularly by detachable coils ('coiling'). The decision on whether occlusion of the aneurysm is indicated is based on patient age, World Federation of Neurological Surgeons grade (Table 2), co-morbidity, SAH onset time, and the anatomy of the aneurysm. The main rationale for early intervention is the prevention of re-bleeding and possibly a reduction in the incidence of cerebral vasospasm by the removal of blood from the subarachnoid space.

All ruptured aneurysms in patients with Hunt and Hess grades I–IV (Table 1) are generally treated within 72 h. Controversy exists as how to proceed in patients with grade V. On the basis of historically poor outcome with early treatment, and of the idea that cerebral oedema would clear, blood clots in the aneurysm organize, and the period of maximal cerebral vasospasm pass by, conservative treatment until clinical improvement had been recommended in the past. However, as cerebral oedema is less of an issue with modern anaesthetic and surgical techniques, even in the patients with severe brain injury, placement of a ventricular drain, and early clipping or coiling of the aneurysm seems to be of benefit.[52]

Procedural risks

Clipping

Clipping of an unruptured aneurysm has been associated with overall procedural morbidity and mortality rates of 4.0–10.9% and 1.0–3.0%, respectively.[44 82 100] Intraoperative leak and frank rupture of aneurysms occurred in approximately 6 and 13% of cases, respectively.

Coiling

Coiling of an aneurysm has been associated with overall procedural morbidity and mortality rates of 3.7–5.3% and 1.1–1.5%, respectively.[8 37] In general, minor morbidity is related to that of diagnostic catheter angiography, including reaction to contrast material, groin haematoma, infection, and pseudo-aneurysm.[32] Major morbidity includes arterial dissection, parent artery occlusion, thromboembolism, and rupture of the aneurysm.[71] The cited incidence of intraprocedural rupture and associated mortality rate vary between 1–2.7% and 0–40%, respectively.[14 71 108]

Limitations of coiling

Because of mostly morphological characteristics or location of the aneurysm, coiling is not indicated or possible in

approximately 5–15% of cases.[71 98] Especially in cases of large aneurysms or aneurysms with wider necks, occlusion of the aneurysm with coiling is likely to be less complete compared with clipping.[37 71 105] Detachable coils of different shape and quality that are biologically active or expand inside the aneurysm, and intracranial stents placed within the artery from which the aneurysm originates, have recently been introduced.[9 15 59 72] These technological advances are likely to reduce the problems associated with the inability to advance the catheter to the site of the aneurysm, and associated with only partial occlusion of the aneurysm and coil compaction over time, resulting in a higher risk of recurrence and re-bleeding of the aneurysm.

Clipping vs coiling

Minimally invasive percutaneous endovascular treatment of intracranial aneurysms (coiling) has proved to be a safe alternative to traditional neurosurgical clip ligation (clipping)[10] and may be associated with better outcome in selected patients at lower perioperative risk.[67 113] In the International Subarachnoid Aneurysm Trial (ISAT) comprising a total of 2143 patients with ruptured aneurysms, patients randomized to coiling experienced a 23.7% incidence of neurological dependency or death compared with a 30.6% incidence in patients randomized to clipping.[66] The findings were confirmed in a follow-up report.[67]

However, several aspects of this study need to be emphasized to place the findings into proper clinical perspective: (1) only 22.4% of the initially screened 9559 patients with ruptured aneurysm underwent randomization; (2) <10% of the patients were at high clinical risk; (3) approximately 95% of them had aneurysms in the anterior cerebral circulation with a size of <10 mm; (4) complete occlusion of the aneurysm was achieved more often in the surgically treated group compared with the endovascularly treated group (82 *vs* 66%); and (5) re-bleeding occurred more often in the endovascularly treated group compared with the surgically treated group (52 *vs* 41%).

Different professional societies and associations have responded differently to these clinically relevant limitations. The recommendations vary between having the patient with a ruptured cerebral aneurysm independently evaluated by a physician experienced in the coiling of aneurysms,[23] and performing surgical clipping if an experienced vascular neurosurgeon regards this as the treatment of choice.[34]

Perioperative anaesthetic management

Preoperative evaluation

As electrolyte and cardiac abnormalities are frequent during and after SAH, in the presence of preoperative ECG findings suggestive of electrolyte disturbances (e.g. prolonged QT-interval, abnormal T-wave, and arrhythmias) and myocardial injury (e.g. ST-segment elevation or depression, Q-waves, and arrhythmia), appropriate diagnostic and therapeutic measures should be considered. While diagnosis and correction of electrolyte derangements are usually straightforward, ECG findings consistent with myocardial injury can pose a considerable management dilemma. On the one hand, ECG abnormalities during SAH are mostly of neurogenic rather than cardiac origin, correlate with the severity of the neurological damage, and do not seem to be independent predictors of adverse perioperative outcome.[123] On the other hand, increases in the serum concentration of cardiac troponin during SAH reflect myocardial cell injury and are associated with poor outcome.[73]

Thus, in patients with high suspicion of cardiac damage (based on clinical presentation or ECG changes), serum concentrations of cardiac enzymes and biomarkers may be determined, and echocardiography performed. However, in most cases, urgent surgery is indicated and takes priority over additional preoperative cardiac testing. In such case, it may be safest to consider any cardiac symptoms and ECG abnormalities as reflecting true cardiac damage, and to adjust the perioperative anaesthetic management accordingly (i.e. choice of anaesthetic drugs and monitoring, immediate postoperative care).

Underlying cardiac impairment may influence the decision in favour of endovascular occlusion rather than surgical occlusion of the aneurysm. However, the type of aneurysm therapy does not necessarily affect the prevalence of cardiac dysfunction and myocardial injury.[65]

Premedication

As with all areas of anaesthetic practice, premedication needs to be individualized. No drug can be considered the drug of choice in all situations. The risk of an anxious patient becoming hypertensive (possibly causing the aneurysm to rupture) needs to be balanced against that of respiratory depression (causing an increase in Pa_{CO_2} followed by an increase in ICP). The decision for or against any premedication, the choices of the type (e.g. benzodiazepine, barbiturate, and opioid), and the dose of the premedication drug will depend on clinical grade, ICP level, respiratory status, co-morbidity, and chronic medication. Nimodipine administered for prophylaxis or treatment of cerebral vasospasm and any infusion of a vasoactive drug administered to maintain an adequate CPP need to be continued uninterrupted.

Monitoring

Standard monitoring

Standard monitoring usually includes 5-lead ECG, continuous intra-arterial pressure, pulse oximetry, capnography, urinary output, body temperature, and neuromuscular

block. Many neuroanaesthetists routinely insert a central venous catheter for guidance of intravascular volume, for the injection of potent cardiovascular drugs in the case of severe cardiovascular instability, and for the administration of mannitol (which may cause local inflammation when administered through a smaller peripheral vein). Elderly patients, clinically relevant co-morbidity (particularly cardio-respiratory), expected surgical difficulties or the sitting position may require additional cardiovascular and neurophysiological monitoring (pulmonary artery catheterization, transoesophageal echocardiography, precordial Doppler, and evoked potentials).

In critically ill patients (poor clinical grade and increased ICP), continuous intra-arterial pressure monitoring (and possibly central venous access) is preferably established before induction of anaesthesia for continuous calculation of CPP and transmural pressure gradient (TMPG) of the aneurysm during the critical period of induction of anaesthesia, and for the immediate availability of arterial blood sample for blood gas analysis. In patients with suspected or documented decreased intracranial compliance or increased ICP, the indication for cannulation of the internal jugular or subclavian veins for central venous access should be restrictive, because the required Trendelenburg position and head-turning during placement of the central venous catheter may critically increase ICP. In this situation, cannulation of the femoral or basilic vein (the latter for mostly short-term use of a central venous catheter) is a valid alternative.

ICP monitoring

In patients who have poor clinical grade or hydrocephalus and who require treatment, some type of ICP monitor, or a ventricular catheter that can be used for pressure measurements, are frequently in place. ICP monitoring is particularly helpful in the blood pressure management during induction of anaesthesia and in the postoperative management of patients who remain unconscious after surgery.

Neurophysiological monitoring

The benefit of neurophysiological monitoring during aneurysm clipping remains to be defined. Cortical somatosensory-evoked potential (SSEP) and brainstem auditory-evoked potential (BAEP) can be used to monitor cerebral function. SSEP monitoring has mostly been used during aneurysm surgery in the territory of both anterior and posterior cerebral circulation, whereas BAEP monitoring has been used during operations in the territory of the vertebral-basilar circulation. Detection of cerebral ischaemia by evoked potential monitoring may lead to adjustments in surgical technique (e.g. removal or replacement of a vascular clip) and haemodynamic management (e.g. increasing blood pressure to augment collateral perfusion during temporary or permanent vessel occlusion). Evoked potentials can be elicited even during maximal pharmacological suppression of the electroencephalogram by high-dose barbiturates.

Unfortunately, evoked potential monitoring lacks specificity, has high false-positive and false-negative predictive values, can be affected by the baseline anaesthetic, and it can be difficult to access the recording sites.[48] No controlled, randomized trial exists that documents improved outcome with intraoperative neurophysiological monitoring. These limitations make evoked potential monitoring unsuitable as a routine monitoring device. Nevertheless, evoked potential monitoring may be useful when transient or permanent occlusion of blood vessels is anticipated. In addition, combined SSEP and BAEP monitoring may reduce the rate of false-positive and false-negative predictive values.[60] When neurophysiological monitoring is used, total i.v. anaesthesia is probably the method of choice, because i.v. anaesthetics interfere less with recordings of evoked potentials than volatile anaesthetics.[87 95]

Jugular venous bulb monitoring

Cerebral venous oxygen saturation can be monitored by retrograde placement of a catheter in the jugular bulb. In the presence of stable CMR, it reflects the global balance between cerebral oxygen demand and supply. Analogous to mixed venous oxygen saturation in the assessment of the balance between systemic oxygen demand and supply, cerebral venous oxygen saturation is a global measure that does not necessarily reflect regional imbalances. Additional measurements of serum lactate concentration improve the quality of jugular venous bulb monitoring.

While jugular venous bulb monitoring is an established monitoring technique in neuro-intensive care, its intraoperative value remains to be determined. It may help, in the early recognition of the potential for cerebral ischaemia associated with hyperventilation,[61] in the intraoperative blood pressure management[69] and in the detection of hyperaemia and luxury perfusion.[13] As with neurophysiological monitoring, it may be of value during temporary occlusion of the artery feeding the aneurysm as a means of judging the adequacy of collateral perfusion. The potential but unproven benefits of such intraoperative monitoring on outcome must be carefully balanced against the risk of impaired cerebral venous drainage (associated with head-down and head-turning position during placement and with location of the catheter tip in the jugular bulb).

Brain relaxation

Optimal brain relaxation and reduction in brain bulk help surgical exposure, reduce the forces required for brain retraction, and facilitate clipping of the aneurysm. Both goals are usually achieved by providing an adequate CPP, avoiding episodes of hypotension and hypertension, administering the appropriate anaesthetic drugs at appropriate doses and concentrations, and maintaining normoventilation and adequate oxygenation. However, not

infrequently (especially in patients with poor clinical grades), pharmacological treatment of increased ICP (before opening of the dura) or brain swelling (during open dura) becomes necessary.

Mannitol

Mannitol is usually the drug of choice to decrease brain water content. The increase in plasma osmolality coupled with the impermeability of the intact blood–brain barrier to mannitol creates an osmotic pressure gradient across an intact blood–brain barrier that makes water move out of the cell. With increasing area of brain damage, the surface area of intact blood–brain barrier diminishes and mannitol becomes increasingly less effective. Under such circumstances, mannitol may actually follow its concentration gradient, explaining the occasionally observed rebound increase in ICP.

The peak effect of mannitol on ICP and brain bulk usually occurs approximately 30–45 min after the start of the infusion. The clinical effect is primarily judged by the response of the ICP, the brain bulk, or both (whatever parameter is monitored) rather than by that of the urine output. The early reduction in ICP in response to mannitol administration may be a reflection of a compensatory vasoconstriction in areas of brain with preserved autoregulation, in an attempt to return CBF to physiological values.

Mannitol administration is accompanied by characteristic, sequential haemodynamic responses. Initially, transient hypotension may develop during rapid infusion of mannitol.[16] Subsequently, mannitol increases cardiac output, cardiac filling pressures, and blood volume.[91] This effect is largest by the end of the infusion.[91] The accompanying increase in CBF and volume may transiently increase ICP.[85] A transient increase in ICP in response to administration of mannitol is less likely in patients with elevated ICP[86] and with slow infusion of a solution with a concentration of not higher than 20%. In patients at risk, temporary, mild hyperventilation may counteract the initial increase in ICP. Thirty minutes after the termination of the mannitol infusion, blood volume returns to baseline value, but cardiac output and filling pressures may decrease to below baseline values (probably because of peripheral pooling of blood).[91]

By nature of its mechanism of action, mannitol transiently decreases haematocrit and increases serum osmolality, and may cause hyponatraemia, hyperkalaemia, and metabolic acidosis as a result of dilution of bicarbonate. This is of particular concern in patients with renal insufficiency.[7]

The recommended dose of mannitol varies between 0.25 and 2 $g\,kg^{-1}$ body weight. Usually, a dose of 0.5–1.0 $g\,kg^{-1}$ is administered. Compared with slow (during approximately 20–30 min) and lower dose (0.5–1.0 $g\,kg^{-1}$) administration of mannitol, faster and higher dose (>1.0 $g\,kg^{-1}$) administration achieves a more rapid and larger decrease in ICP and brain swelling, and requires less frequently repeat administration, but is accompanied by a higher incidence of transient hypotension and electrolyte disorders and larger increases in intravascular and cerebral blood volumes. The decision regarding dose and speed of infusion should be based on the underlying clinical circumstances. When serum osmolality exceeds 330 mOsm $litre^{-1}$, additional mannitol is unlikely to affect ICP.

As mannitol (particularly when administered rapidly and at higher dosage) may cause an abrupt decrease in ICP (resulting in an increase in the TMPG of the aneurysm) and brain shrinkage (resulting in traction and possible tearing of the bridging veins), it should, at least theoretically, not be administered as long as the dura is closed. In clinical practice, however, the surgeon frequently requests its administration after final positioning of the patient. In such a case, the initial infusion rate should be slow (approximately 100–200 ml h^{-1}) and may be increased once the dura has been opened.

Frusemide

Frusemide is an alternative to mannitol. When administered either alone at high dose (1 mg kg^{-1}) or in combination with mannitol (0.25–1 g kg^{-1}) at lower dose (5–20 mg), it decreases ICP and brain water content.[17 94] The primary mechanism of action of frusemide in causing the decrease in ICP is unrelated to its diuretic effect, and remains unclear. Possible mechanisms include reduced CSF formation, and water and ion movement across the blood–brain barrier. The administration of frusemide before mannitol may blunt the mannitol-induced initial increase in ICP. In patients with cardiopulmonary and renal impairment, the risk of hypervolaemia and electrolyte derangements may be reduced when frusemide rather than mannitol is used. The prolonged diuresis after the administration of (particularly high dose) frusemide can potentiate the effect of mannitol by sustaining elevated serum osmolality. Consequently, the therapeutic effect of a combination of mannitol and frusemide on ICP and brain bulk was consistently larger and more prolonged than that of either drug alone.[94]

On the down side, it is the overall clinical impression that frusemide alone does not decrease ICP and brain bulk as reliably and effectively as mannitol. In addition, the combined therapy can be associated with large losses of free water and electrolytes. Thus, very close monitoring of intravascular volume, electrolytes, acid–base, and serum osmolality are required.

Drainage of CSF

The volume of the CSF in an adult is approximately 150 ml. Decreasing the volume of CSF using a lumbar subarachnoid or ventriculostomy catheter is an effective means of reducing brain bulk and may become necessary to achieve satisfactory brain relaxation.

During and after placement of the catheter, extreme care must be taken to avoid acute drainage of a large volume of CSF. Rapid and large volume CSF drainage may cause an abrupt decrease in ICP and brain 'sagging'. As a consequence, the TMPG of the aneurysm increases abruptly, traction on the bridging veins develops, and cardiovascular reflexes are activated. By these mechanisms, the aneurysm may re-bleed, and intracerebral haematoma and reflex hypertension, bradycardia, and asystole may develop. In patients with intracerebral haematoma, lumbar CSF drainage is contraindicated because of the risk of brainstem herniation.

Theoretically, as with mannitol and for the aforementioned reasons, CSF drainage should not be started before opening the dura. However, in clinical practice, neurosurgeons frequently drain CSF before opening of the dura to provide improved conditions at the time of dural incision. The amount of acutely drained CSF should not exceed 20–30 ml. The lumbar drain is usually kept open until the aneurysm is secured or until the start of closure of the dura. An excessive CSF drainage by third ventriculostomy and spinal catheter during aneurysm surgery may cause severe CSF hypovolaemia. The subsequent 'brain sag' may result in considerable postoperative clinical deterioration.[45]

Miscellaneous interventions

At times, brain swelling will not satisfactorily respond to the aforementioned interventions. Adequate ventilation and oxygenation, CPP and acid–base status, unobstructed cerebral venous return (check the patient's head position), and drainage of CSF (check patency of lumbar drain) have to be assured at all times. Hyperthermia has to be excluded. The feasibility of a head-up tilt should be discussed with the surgeon to optimize cerebral venous drainage. In critical situations, temporary, mild hyperventilation may be considered (e.g. aiming at 4.0–4.6 kPa of Pa_{CO_2} or 30–35 mm Hg before opening the dura and at 3.3–4.0 kPa of Pa_{CO_2} or 25–30 mm Hg during opening of the dura), by carefully balancing the beneficial effect of reduction in brain bulk against the risk of cerebral ischaemia.

If volatile anaesthetics and N_2O are being used, they should be discontinued and replaced by i.v. anaesthetic drugs. Some neuroanaesthetists administer a bolus dose of thiopentone (approximately 2–3 mg kg^{-1}) for its cerebrovasoconstrictive property. If this intervention improves brain relaxation, continuous infusion of thiopentone (approximately 4–5 mg kg^{-1} h^{-1}) might be useful. This may, however, necessitate pharmacological blood pressure support and delay awakening. Brain swelling refractory to any therapy may be caused by an intracerebral haematoma.

Conduct of anaesthesia

General principles

The principal goals of the anaesthetic management for aneurysm surgery include (1) control of the TMPG of the aneurysm, (2) preservation of adequate CPP and oxygen delivery, (3) avoidance of large and sudden swings in ICP, (4) providing conditions that allow optimal surgical exposure with least brain retraction, and (5) allowing rapid awakening of the patient.

It is important to realize that the intensity of non-surgical and surgical stimuli varies tremendously throughout the procedure. Laryngoscopy, tracheal intubation, positioning of the patient, placement of the pin head-holder, and raising of the bone flap are highly stimulating interventions. The resultant haemodynamic stimulation can cause a dangerous increase in the TMPG of the aneurysm with the associated risk of rupture of the aneurysm. In contrast, no stimulus exists at the time of induction of anaesthesia, and little or no stimulus exists once the dura is open.

Sufficient doses of hypnotics (thiopentone or propofol), opioids, non-depolarizing neuromuscular blocking agents (e.g. vecuronium, atracurium, and cisatracurium), and infiltration of the scalp with local anaesthetic at the sites of pin placement will suppress an inordinate blood pressure response to the various interventions. Although a continuously deep level of anaesthesia will reduce the incidence of hypertensive episodes, it will equally increase the incidence of episodes of hypotension and inadequately low CPP once the potent stimulus has vanished.

An alternative approach is to maintain a lesser depth of baseline anaesthesia and acutely control the changing intensities of stimulation by prophylactic administration of bolus doses of anaesthetic (e.g. propofol or thiopentone before placement of the pin head-holder) or cardiovascular depressant drugs (e.g. esmolol or labetalol before laryngoscopy and tracheal intubation) that abolish or blunt the hypertensive response to intense stimuli. This goal can be equally well achieved through the additional use of remifentanil, an ultra-short-acting opioid, either as bolus doses administered shortly before the expected potent stimulus or as continuous infusion adjusting the dosages to the respective degree of stimulation.

During the period of an open dura with lack of stimulation, one must resist the temptation of titrating the depth of anaesthesia solely on the basis of blood pressure. Such an approach may result in awareness and sudden movement of the patient while the surgeon may be in a critical phase of the operation. If hypotension is present during optimal depth of anaesthesia and hypovolaemia is excluded, vasoactive drugs should be administered to increase the blood pressure.

Choice of anaesthetic drug

A detailed description of the cerebral effects of anaesthetic drugs is well beyond the scope of this review. However, some general principles deserve a mention. Providing an adequate depth of anaesthesia and neuromuscular block, controlling the blood pressure in a manner that would avoid hypertensive episodes and ensure adequate CPP, and

striving for a physiological ICP and optimal brain relaxation are more important than the choice of a particular anaesthetic drug. Principally, any drug or drug combination in whatever dose and concentration that achieves these goals is acceptable.

The specific effects of individual anaesthetic drugs on cerebral vasomotor tone (and, in turn, on CBF and volume, and on ICP) and on CMR *per se* are mostly well defined (Table 6). However, the overall *in vivo* effect of the various anaesthetic drugs on each of these variables may be modified considerably by the underlying cerebral compliance and ICP, the interactions between the drug's effect on cerebral vasomotor tone and metabolic rate, the dose and concentration of anaesthetic drug (in particular, in the case of inhalation anaesthetics), the combination of drugs, the management of the Pa_{CO_2}, and the effect of the anaesthetic drug on CPP.

The anaesthetic drug-induced changes in CBF are the overall result of the drug's individual effects on cerebral vasomotor tone and CMR. A reduction in metabolic rate induces a metabolism-coupled cerebral vasoconstriction (and thus a decrease in CBF), which counteracts the direct vasodilatory effect of the drug. Cerebral vasomotor tone and metabolic rate can be affected to a different extent at different concentrations. Consequently, despite the direct cerebral vasodilatory effects of volatile anaesthetics, CBF may remain relatively unchanged at concentrations of up to 1 MAC because of the concomitant cerebral vasoconstriction-induced decrease in CBF triggered by the decrease in metabolic rate.

The cerebral effects of an anaesthetic drug may be considerably modified by the blood pressure response to its administration. When MAP decreases in the presence of preserved cerebral autoregulation, cerebral vessels dilate, resulting in an increase in cerebral blood volume and possibly an increase in ICP. By this mechanism, opioids may lead to a transient increase in ICP.[1 103] The administration of etomidate is associated with the least cardiovascular side-effects compared with other anaesthetic drugs. It may decrease ICP while preserving CPP. However, cerebral hypoxia was observed in some patients during aneurysm surgery, which worsened during temporal cerebral artery occlusion.[26] In addition, as etomidate can cause involuntary muscle and seizure activity, it should not be administered to patients with increased ICP and seizure activity.

In general, in patients with suspected or documented decreased intracranial compliance, increased ICP and cerebral injury, it is advisable to avoid all anaesthetic drugs with cerebro-vasodilatory potential (basically all volatile anaesthetics and N_2O) and rather use those with cerebro-vasoconstrictive and cerebro-depressant characteristics (basically all i.v. anaesthetics with the exception of ketamine; Table 6). If sensory-evoked potentials are to be recorded, a total i.v. anaesthetic may be the preferred technique.[87 95]

Table 6 Effects of anaesthetic drugs on cerebral blood flow (CBF), cerebral metabolic rate (CMR), and intracranial pressure (ICP). ↑ or ↓, mild decrease or increase; ↑↑ or ↓↓, moderate decrease or increase; ↑↑↑ or ↓↓↓, marked decrease or increase; Ø, no effect. The effects may vary considerably with underlying cerebral compliance and ICP, dose and concentration of anaesthetic drug, combination of drugs, Pa_{CO_2}, and CPP

Drug	CBF	$CMRO_2$	ICP
Volatile anaesthetics			
Isoflurane	↑/↑↑	↓↓↓	↑
Sevoflurane	↓/Ø	↓↓↓	Ø/↑
Desflurane	↑/↑↑	↓↓↓	Ø/↑
N_2O	↑/↑↑	↑/↑↑	↑/↑↑
I.v. anaesthetics			
Barbiturates	↓↓/↓↓↓	↓↓↓	↓↓/↓↓↓
Etomidate	↓↓/↓↓↓	↓↓↓	↓↓/↓↓↓
Propofol	↓↓/↓↓↓	↓↓↓	↓↓/↓↓↓
Benzodiazepines	↓/↓↓	↓/↓↓	Ø/↓
Opioids	Ø/↓	Ø/↓	Ø/↑

Management of CPP and TMPG of the aneurysm

The two variables that require considerable attention are CPP and TMPG of the aneurysm. CPP is calculated as the difference between mean arterial pressure (MAP) and ICP (CPP=MAP−ICP). The TMPG of the aneurysm is calculated as the difference between the pressure within the aneurysm (equal to MAP) and the pressure outside the aneurysm (equal to ICP) (TMPG=MAP−ICP). Thus, TMPG and CPP are governed by the same variables (MAP and ICP). The objectives are to maintain TMPG as low as possible to reduce the risk of aneurysm rupture, and CPP as high as needed to provide adequate cerebral oxygenation.

As changes in MAP and ICP will result in identical changes of TMPG and CPP, and as TMGP and CPP values are numerically identical, it will often come down to the choice between an optimal TMPG and an optimal CPP. The obvious clinical challenge is to maintain an adequate CPP while avoiding a high TMPG; in other words, the dilemma is one of balancing the risk of inadequate cerebral perfusion against that of rupture of the aneurysm. Ideally, CPP and TMPG of the aneurysm are maintained at preoperative baseline values throughout. This goal is rarely achievable.

Overall, it seems sensible to maintain blood pressure at preoperative levels until the aneurysm is secured. If treatment of the increased ICP becomes necessary before opening of the dura, such treatment should not be overly aggressive because an abrupt decrease in ICP causes an equally abrupt increase in the TMPG of the aneurysm. Opening of the dura in the presence of markedly elevated ICP may have the same detrimental effect.

Induction of anaesthesia

Besides the obvious goal of achieving an adequate depth of anaesthesia, the main goals during induction of anaesthesia are (1) prevention of rupture of the aneurysm, (2) preservation of cerebral oxygenation, and (3) prevention of

an increase in ICP. This requires a low TMPG of the aneurysm, adequate CPP, and unhindered gas exchange.

One practical approach is to aim for a moderate (approximately 20%) initial reduction in baseline blood pressure during induction of anaesthesia, administer drugs that abolish or blunt the hypertensive response to laryngoscopy and tracheal intubation (e.g. esmolol, labetalol, and i.v. lignocaine), and then proceed with tracheal intubation.

Another approach is to provide a deep level of anaesthesia (implied by the use of high doses of anaesthetic drugs, or verified by monitoring of depth of anaesthesia) while counteracting the anticipated decrease in blood pressure (and thus in CPP) by a continuous infusion of a vasopressor (e.g. phenylephrine or norepinephrine) from the beginning of induction of anaesthesia. The deep level of anaesthesia will reliably prevent the hypertensive response to laryngoscopy and tracheal intubation (reducing the risk of rupture of the aneurysm), whereas the continuous infusion of a vasopressor will ensure adequate CPP (reducing the risk of cerebral ischaemia).

Yet another approach is to try to balance the baseline risk of inadequate cerebral perfusion against that of rupture of the aneurysm, based on the patient's clinical grade. Usually, patients with clinical grades I and II have normal ICP and do not exhibit acute ischaemic deficits. These patients can be expected to tolerate a >20% transient decrease in CPP without becoming acutely ischaemic, thereby considerably decreasing the risk of rupture of the aneurysm.

In contrast, patients with poor clinical grades often have increased ICP, decreased CPP, and signs and symptoms of cerebral ischaemia. These patients are less likely to tolerate even transient episodes of hypotension, and the duration and the degree of hypotension must be kept to a minimum. At the same time, the increased ICP decreases the TMPG of the aneurysm and, thus, partially protects the aneurysm from rupture. In these patients, it might be justified to accept a slightly higher TMPG in exchange for reducing the higher risk of cerebral ischaemia.

Respiratory management

Usually, normoventilation is the goal. With the possible exception of N_2O, cerebrovascular reactivity to CO_2 is mostly preserved with all anaesthetic drugs. As prolonged hyperventilation may cause cerebral ischaemia,[70] transient and moderate hyperventilation should only be considered in patients with increased ICP. It should not be routinely used to counteract the cerebro-vasodilatory effects of volatile anaesthetics (including N_2O).

The benefits of increased, positive, end-expiratory pressure on respiratory function need to be carefully balanced against the risk of increased cerebral venous pressure and impaired cerebral venous drainage secondary to the PEEP-induced increase in central venous pressure. The resulting increase in cerebral blood volume is of particular concern in patients with decreased cerebral compliance and increased ICP. In such patients, PEEP should be used very restrictively.

Induced hypotension

A reduction in systemic arterial pressure decreases the TMPG of the aneurysm and thereby the wall stress of the aneurysm. This may facilitate preparation and clipping of the aneurysm, and help control bleeding should rupture of the aneurysm occur. However, induced systemic hypotension is no longer used routinely in clipping of aneurysms, because it may critically impair overall cerebral perfusion, especially in the presence of hypovolaemia, and has been associated with adverse outcome and a higher incidence of severe cerebral vasospasm.[12]

Local hypotension at the site of the aneurysm can be established by temporary clipping of the artery feeding the aneurysm. The duration of temporary occlusion should not exceed 15–20 min, because this is associated with a decrease in brain P_{O_2} and an increase in brain P_{CO_2},[43] and seems to be the critical threshold for the development of postoperative cerebral ischaemic events.[76 92] During such temporary clipping, blood pressure should be maintained at or even slightly above baseline values to ensure adequate collateral blood flow. Close communication with the neurosurgeon is important, because with the removal of the temporary clip, the unsecured aneurysm is exposed to a high shear stress.

Induced hypothermia

The randomized, prospective International Hypothermia Aneurysm Trial did not find a beneficial effect of induced mild (33°C) intraoperative hypothermia during aneurysm surgery.[106] In clinical practice, passive cooling usually leads to some degree of hypothermia. It is tolerated, as long as it does not interfere with immediate postoperative extubation and awakening. If clipping of a giant aneurysm (>2 cm in diameter) is planned (especially when located close to the brainstem), use of cardiopulmonary bypass, complete circulatory arrest, and profound hypothermia (<22°C) may be necessary.

Pharmacological brain protection

No controlled, randomized clinical trial exists to demonstrate a cerebro-protective effect of any anaesthetic drug during the surgery for clipping of aneurysms. Some neuroanaesthetists prophylactically administer barbiturate or propofol at critical phases (e.g. during difficult dissection of an aneurysm; before temporary clipping of blood vessels proximal and distal to the aneurysm), at doses that result in EEG burst suppression. If such an approach is taken, hypotension must be avoided.

Prophylaxis of cerebral vasospasm

Fluid management

In patients without preoperative symptoms of cerebral vasospasm and good clinical grades, normovolaemia should be maintained until the aneurysm is clipped. Careful volume loading and maintenance of a slightly higher than baseline MAP towards the end of surgery may help reduce the incidence of postoperative cerebral vasospasm.

In patients with symptomatic preoperative cerebral vasospasm, volume loading (and induction of moderate hypertension after the clipping of the aneurysm) should preferably be guided by invasive monitoring, transoesophageal echocardiographic monitoring or both. If hypertension had been induced before operation, MAP should be maintained intraoperatively at a comparable level. In these patients, intraoperatively induced hypotension is relatively contraindicated. If nevertheless requested by the surgeon, neurophysiological monitoring should be considered.

Patients undergoing surgery for clipping of the aneurysm within 72 h of SAH have lower circulating blood volumes than those undergoing clipping within 6 h of SAH.[74] Perioperative, normovolaemic fluid management may thus be appropriate in patients undergoing acute clipping of the aneurysm, and a relatively hypervolaemic fluid management in those undergoing surgery within 72 h of SAH.

Papaverine

Intracisternal installation of papaverine after clipping of the aneurysm and before closure of the dura is another attempt at preventing cerebral vasospasm.[18] However, it may cause mydriasis,[80] facial nerve palsy,[51] signs and symptoms resembling malignant hyperthermia,[64] and bradycardia and hypotension.[84] As cerebral vasospasm rarely occurs later than 12 days after SAH, the risk of postoperative cerebral vasospasm is relatively low in patients undergoing aneurysm surgery at or beyond 10–12 days after the initial rupture, and the aspect of prophylaxis of cerebral vasospasm does not require special attention.

Intraoperative aneurysm rupture

Intraoperative aneurysm rupture carries a high morbidity and mortality. It may occur at any time during the procedure, associated mostly with an abrupt increase in the TMPG of the aneurysm (as a consequence of either a sudden increase in blood pressure or an abrupt decrease in ICP) or with surgical manipulation. It is to be expected that rupture of an aneurysm with an open skull and dura carries a better prognosis than a rupture occurring during induction of anaesthesia.

The incidence of aneurysm rupture varies with size and location of the aneurysm, and with surgical experience. Frank intraoperative rupture occurred in approximately 11% of patients with previously ruptured aneurysm (compared with an incidence of 1.2% in previously unruptured aneurysms).[53] Haemorrhagic shock may develop in 8% of aneurysm ruptures.[42]

The choice of acute interventions will depend on the size of the leak/rupture, the completeness of the dissection of the aneurysm and thus the surgeon's direct access to it, and the feasibility of temporary occlusion of blood vessels proximally and distally to the aneurysm. The primary haemodynamic goal during rupture of an aneurysm is maintenance of normovolaemia. Temporary occlusion of cerebral arteries proximal and distal to the aneurysm is an effective means of gaining control over ruptured aneurysms.

The blood pressure management during rupture of an aneurysm is controversial. On the one hand, a transient decrease in MAP to 40–50 mm Hg decreases wall shear stress, reduces bleeding, and facilitates surgical orientation, exposure, and clipping. On the other hand, in the presence of clinically relevant blood loss, the combination of hypotension and hypovolaemia may result in profound cerebral ischaemia. Thus, temporary vessel occlusion is the preferred technique to gain control over a ruptured aneurysm—with the possible exception of when temporary occlusion is not possible.

Recovery

After surgery, patients should be responsive to verbal command as soon as possible to allow early neurological assessment and decisions regarding diagnostic (e.g. CT and angiography) and therapeutic (e.g. initiation of treatment for cerebral vasospasm) interventions. Various anaesthetic drug combinations at various dosages allow reasonably rapid and smooth awakening. If emergence from anaesthesia is unexpectedly delayed or a new neurological deficit is present upon awakening, CT or angiography may be used to rule out intracerebral haematoma or occlusion of a blood vessel. In some centres, radiological assessment is part of standard intraoperative practice.

Definition of what constitutes an 'adequate' blood pressure range during and immediately after emergence from anaesthesia is difficult and should be agreed upon between anaesthetist and neurosurgeon. A 20–30% increase in blood pressure above preoperative baseline values poses the risk of intracranial haemorrhage and oedema. Such a degree of hypertension should be prevented by the prophylactic administration of the appropriate type and dose of analgesic, anti-emetic, anti-shivering or anti-hypertensive drugs. In patients at increased risk of cerebral vasospasm, a 10–20% increase in blood pressure above preoperative baseline values may be of benefit.

Patients with preoperative Hunt and Hess grades III or IV (Table 1) or intraoperative complications should not be extubated immediately after operation. Critically ill patients frequently require intensive postoperative cardiopulmonary and general supportive care. Early tracheotomy

should be considered in stuporous or comatose patients with poor medium term prognosis. It can shorten the duration and decrease the depth of sedation, and it can hasten weaning from mechanical ventilation, allowing earlier neuro-rehabilitation.

Anaesthetic management for coiling

There is a considerable overlap in the overall anaesthetic management for endovascular (coiling) or surgical (clipping) treatment of a cerebral aneurysm. Obvious differences in management include the location where the intervention is performed (neuroradiology suite *vs* operating theatre), the likelihood of periprocedural blood loss (considerably higher during clipping), and the need for brain relaxation (frequently required during clipping).

In many centres, general anaesthesia is administered during coiling of cerebral aneurysms. In some centres, only sedation is provided to be able to monitor the patient's neurological function during the procedure.[81] If sedation alone is not an option, neurological function may be assessed by neurophysiological monitoring.[57]

Conclusion

An anaesthetist who is familiar with the aetiology, pathophysiology, and complications of SAH and who knows how to maintain overall homeostasis and adequate CPP effectively, and prevent or attenuate increases in ICP, brain swelling, and cerebral vasospasm throughout all phases of anaesthesia by whatever means, and a skilled surgeon who dissects and clips the aneurysm in an atraumatic but speedy manner are the most important determinants of maximal intraoperative brain protection, surgical success and, thus, ultimate overall outcome.

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