Purpose of review
In the last decade, there has been a rapid development in new endovascular treatment options for cerebral aneurysms. These techniques have their own inherent risk and can be challenging for the attending anesthetist.

Recent findings
The recent developments of stent-assisted aneurysm coiling, flow-diverting stents and gel embolization, have implications for the attending anesthesiologist and the patient. These developments allow embolization of more complex aneurysms, but require anticoagulation with its inherent risks.

Summary
The different endovascular techniques relevant to the anesthetist, the anesthetic options and complications that can occur during endovascular treatment of these patients will be discussed. This article can be a guidance to the anesthesiologist attending endovascular procedures for cerebral aneurysms.

Keywords
anesthesia, cerebral aneurysm, coil embolization, endovascular treatment

INTRODUCTION
The worldwide prevalence of cerebral aneurysms in the adult population is estimated to be between 0.65 and 3.2% [1••] and is increasing because of improved screening and imaging techniques. [2–4]. The annual rupture rate of these aneurysms is estimated at 0.5–0.95% [5,6•,7], with an associated mortality of 24–67% [6•,5] and morbidity among survivors ranging from 40 to 44% [5,6•,8••].

Prevention of rupture or rerupture from the aneurysm is mandatory and can be achieved by either neurosurgical clipping or endovascular treatment [8••,9].

Despite criticism to the International Subarachnoid Aneurysm Trail, endovascular treatment is firmly established in the management of cerebral aneurysms and resulted in the development of various new techniques [1••,10,11,12••].

These new developments are very appealing and less invasive than surgery, but the associated risks are in the range of surgery and complications remain problematic [13•,14].

The anesthetic management of these procedures implies understanding the goals of the therapeutic intervention, the risks and anticipation of potential problems associated with these techniques, often performed in remote areas [2,11].

ENDOVASCULAR TECHNIQUES
Endovascular treatment of a cerebral aneurysm can be achieved either by parent artery occlusion or by obliteration of the aneurysmal sac [11]. In the coiling method, small platinum coils are placed in the aneurysm to initiate a clotting response [15]. The remaining volume is occluded by the forming clot. Instead of relying on the body’s clotting response, a liquid to solid gelling polymer system has been developed [15].

Balloon-assisted coiling uses a temporary balloon to provide support in wide-necked aneurysms to prevent coil prolapse in the parent artery [1••]. Stent-assisted coiling can be achieved by the so-called jailing or meshing techniques [10]. Both techniques expanded the range of aneurysms amendable to vascular treatment. Bodily et al. [16] reviewed studies involving stent-assisted coiling in acutely
ruptured aneurysms and reported a success rate of 93% with a mortality of 13%, hemorrhagic complications and thromboembolic events in 6%.

Flow-diverting stents are developed to disrupt the flow into the aneurysm and to allow a progressive obliteration of the aneurysmal sac. The results in unruptured wide-necked and large aneurysms are promising [17,18], but there is no immediate aneurysm occlusion and patients are on dual antiplatelet therapy for several months. For this reason, this treatment should not be considered in acutely ruptured cerebral aneurysms [10].

ANESTHETIC CONSIDERATIONS

Anesthesiologists are confronted with several challenges during endovascular procedures for cerebral aneurysms.

Remote location

Neuroradiology procedures are performed in the radiology suite in a remote area where the anesthesiologist is confronted with a limited working space, difficult access to patient and a lack of equipment for appropriate monitoring and delivery of anesthesia [2,4,19*,20]. Yamakawa et al. [4] reviewed 602 patients treated in a hybrid operating suite and could not conclude whether this type of operating room improved outcomes.

Ionizing radiation

Interventional neuroradiology procedures use high-speed digital subtraction angiography and fluoroscopic technology, digital subtraction angiography delivering considerably more radiation than fluoroscopy [2,11,21].

Radiation can come from the radiograph tube, leakage or scattering [2,11,12**]. Anesthesiologists should wear a lead apron, thyroid shields and radiation exposure badges to detect cumulative radiation exposure [11,12**,22*,23].

Patients presenting for cerebral aneurysm treatment

A patient may present for elective treatment of the aneurysm, or may have suffered a subarachnoid hemorrhage. Subarachnoid hemorrhage can present as a grade I, [World Federation of Neurological Surgeons subarachnoid hemorrhage (SAH) grading scale, Table 1] [24], to grade V. Preoperative assessment of these patients requires a full neurologic assessment to determine the level of consciousness and the presence of focal neurologic or cranial nerve deficits, and an evaluation of the cardiovascular reserve as SAH is accompanied by catecholamine release, causing left ventricular dysfunction and/or dysrhythmias [2,20,21,25]. Information of the baseline blood pressure is also essential as blood pressure manipulation is often required during these procedures [11,12**]. Airway assessment, presence of aspiration pneumonia or impending neurologic pulmonary edema should also be evaluated [20,21,25].

Evaluation of coagulation screen, renal function and electrolytes is required, as patients will receive anticoagulation and contrast during the procedure [2,20,21,25,26].

MONITORING

Standard American Society of Anesthesiologist monitoring is required for all patients regardless of the anesthetic technique used [21]. Blood pressure manipulation during the procedure requires invasive continuous blood pressure monitoring, preferably inserted before induction of anesthesia [2,21,25]. Central line insertion can be decided on

<table>
<thead>
<tr>
<th>WFNS Grade</th>
<th>Glasgow Outcome Score</th>
<th>Motor Deficit</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>15</td>
<td>Absent</td>
</tr>
<tr>
<td>II</td>
<td>13–14</td>
<td>Absent</td>
</tr>
<tr>
<td>III</td>
<td>13–14</td>
<td>Present</td>
</tr>
<tr>
<td>IV</td>
<td>7–12</td>
<td>Present or absent</td>
</tr>
<tr>
<td>V</td>
<td>3–6</td>
<td>Present or absent</td>
</tr>
</tbody>
</table>

Reproduced with permission from [24].
patient presentation and procedure characteristics [2,21,25], continuous infusions of drugs and/or monitoring of central venous pressure to facilitate fluid management. A low threshold for central line insertion is indicated, as postprocedure insertion of central lines carries an increased risk for hemorrhagic complications because of the anticoagulated state of the patient [25]. Patients on intravenous sedation should have airway monitoring by capnography; loss of capnography is often the first sign of oversedation or airway obstruction [12**].

ANESTHETIC TECHNIQUES

Anesthetic goals for these procedures are patient immobility, physiological stability with manipulation of systemic blood pressure, managing anticoagulation, and anticipation and treatment of procedural complications [2,11,21,22*].

Sedation

Sedation is most often used for interim follow-up angiography, with conversion to general anesthesia if further treatment is required. Which sedation regime is used, depends on the experience of practitioners [11]. Sedation with propofol is widely used [27*].

Dexmedetomedine gives patient tranquility, without respiratory depression [2]; however, the effects on cerebral perfusion are not clear and hypotension in the postoperative period has been reported [11]. In SAH patients, autoregulation may be impaired, rendering them critically dependent on adequate collateral perfusion pressure. Therefore, regimens that may result in blood pressure decreases should only be used with great caution [11].

Sedation allows an easy and frequent neurological assessment of the patient and avoidance of hemodynamic changes associated with intubation and emergence. Disadvantages are an unprotected airway with the risk of aspiration and potential for hypoxemia and hypercapnia. Sudden patient movements and delays in managing a neurological emergency may also occur [2,12**]. In a recently published study on sedation for low-grade ruptured and nonruptured cerebral aneurysms, 25.4% of sedations was aborted or associated with technical problems. [12**]. Other studies suggest that the treatment of ruptured intracranial aneurysms under conscious sedation is well tolerated and feasible in low-grade SAH patients [23].

General anesthesia

General anesthesia during endovascular treatment of ruptured cerebral aneurysms can be beneficial in selected patients [8**,10] and it is generally established for long, complex procedures [8**,28].

Patient immobility, improved imaging quality, increased procedural safety and efficiency, if complications occur, are the main advantages of general anesthesia [1**,12**].

Fluctuations in hemodynamics caused by induction of anesthesia and emergence, and inability to continuously assess neurologic status are reported as major drawbacks [2,12**].

The choice of anesthesia should be guided by cardiovascular and cerebrovascular considerations, as there is no clear superiority of one modern anesthetic to another in terms of pharmacologic protection against neuronal injury [11,12**,26].

Sevoflurane, desflurane and propofol have been used for general anesthesia with minimal hemodynamic changes and smooth and rapid emergence.

A recent study, which compared the speed of recovery after the maintenance of anesthesia for neuroradiology with sevoflurane or propofol, found that sevoflurane was associated with more rapid recovery; however, depth of anesthesia was not controlled [29]. Higher concentrations of desflurane cause increased cerebral blood flow and loss of autoregulation [2], making sevoflurane the volatile agent of choice [2,21]. Nitrous oxide should be avoided because of the possibility of air emboli in the cerebral circulation [2,11,21,26].

The combination of propofol and remifentanil target-controlled infusion is often used and gives cardiovascular stable anesthetic with rapid emergence [2,21]. Continuous use of neuromuscular-blocking drugs is rarely required for angiographic procedures as there is minimal surgical stimulation [26].

Laryngeal mask airway has the advantage of airway control with a less hemodynamic stress and a smooth emergence from anesthesia, but only for selected patients, there is no evidence for routine use [2]. Relative normocapnia or modest hypocapnia should be maintained unless intracranial pressure is a concern [11].

Blood pressure management

There are no guidelines on the optimum blood pressure during the procedure [1**], although there is a consensus that surges in blood pressure, certainly at induction of anesthesia, should be prevented [2,10,21].

Hypotension should be avoided, as mentioned earlier, whereas hypertension has been associated with rebleeding [30]. The current guidelines suggest that blood pressure should be monitored and controlled to balance the risks of aneurysmal rerupture...
and cerebral hypoperfusion [10]. A decrease in blood pressure to less than 160 mmHg is suggested to avoid rebleeding [2,8∗∗,10,21].

The antihypertensive options for blood pressure control are nicardipine and labetolol [10]. Labetolol exerts minimal effects on the cerebral circulation and intracranial pressure. Vasodilators, such as hydralazine, glyceryl trinitrate and sodium nitroprusside, may worsen cerebral perfusion and ischemia [2,21].

Higher blood pressures are indicated once the aneurysm is secured [10] or if thromboembolic events or vasospasm occur [11]. The extent of blood pressure increase depends on the patient’s condition and nature of the disease. Phenylephrine, metaraminol or norepinephrine with close monitoring of the ST-segment on ECG to detect ischemia are often used [11].

**Fluid management**

Avoidance of hypovolemia and maintenance of normovolemia with cristalloids and/or colloids is advised in SAH patients to prevent delayed cerebral ischemia. Fluid management can be guided by central venous pressure or pulmonary wedge pressure [8∗∗,11].

Fluid administration by the interventionalist can be considerable and become problematic, if unnoticed [11]. Large volumes of hypotonic fluids or intravascular volume contraction are not recommended [8∗∗].

**Emergence**

Emergence from anesthesia should be smooth and fast with blood pressure returning to normal or up to 160 mmHg. In case of an unsecured or incompletely secured aneurysm, lower blood pressures are indicated [1∗∗,25].

**Anticoagulation**

Heparin (70 UI/kg) is administered after baseline activated clotting time (ACT) is obtained, to prolong ACT two to three times during the procedure, [2,11,21,22∗,26] by a heparin infusion (1000 IU/h) or intermittent bolus [2,22∗,31∗∗], with ACT monitoring at least hourly [2]. The first heparin dose can be given after femoral artery cannulation [25] or after first coil deployment [10]. In case of antithrombin III deficiency, fresh frozen plasma can be given [11].

Heparin-induced thrombopenia is a rare disease, requiring the use of direct thrombin inhibitors (lepirudine, bivalirudine and argatroban), which can be titrated by ACT [11].

Antiplatelet agents (clopidogrel, thienopyridines and glycoprotein IIb-IIIa receptor antagonists) are controversial in the acute setting, although there is an increased use in prevention and treatment of thromboembolism [12∗∗]. Abciximab has a long duration and potent effect but increases the likelihood of bleeding [11,12∗∗]. Clopidogrel is commonly used for procedures that require placements of devices, primarily in patients with non-ruptured aneurysms [11].

These patients receive dual antiplatelet preloading during 3–7 days before endovascular treatment or receive a high-loading dose during the procedure [18].

Thirty percent of patients are resistant to conventional dose of clopidogrel [18,32], requiring a reloading dose of the same agent or an alternative agent such as plasugrel or ticagrelor [14∗,18].

Reversibility to antiplatelet agents is average to poor, necessitating the use of concentrated platelets if hemorrhage complications occur [33].

**PROCEDURAL COMPLICATIONS**

Despite improved technologies and material, there is no measurable impact on the reduction of iatrogenic complications, probably due to the treatment of more complex aneurysms [14∗,15,31∗∗,32–34].

Successful management of complications depends on a correct diagnosis and prompt action by the anesthesiologist and the interventionalist [11].

**Hemorrhagic complications**

Intraprocedural aneurysm rupture or perforation can occur at any moment: spontaneous, during induction of anesthesia or inadequate depth of anesthesia or inadequate titration of vasoactive drugs; by microcatheter manipulation, contrast injection or coil deployment [25].

The incidence varies from 1.4 to 6.1% for ruptured and from 1.3 to 2.6% for unruptured aneurysms [34], with mortality ranging from 0 to 40% [4] and morbidity ranging from 17 to 50% [10,35].

Cardiovascular instability (hypertension and bradycardia) or contrast extravasation on radiograph may indicate intraprocedural rupture [21,25]. Reversal of anticoagulation is not clear and should always be discussed with the interventionalist [10]. Some authors recommend [2,11,21,25] immediate reversal by protamine sulphate (1 mg for each 100 international units of heparin given); others suggest that this is rarely needed [26].

Lowering the systemic arterial pressure by deepening anesthesia or antihypertensive treatment and packing the aneurysm is essential in the treatment...
of intraprocedural rupture [2,25,26,34]. If aneurysm packing fails, urgent craniotomy and clipping of the aneurysm is indicated with external ventricular drain placement, if indicated [2,25,34].

Occlusion

Occlusion can be caused by vasospasm, parent artery occlusion by material or thrombus, hypercoagulability in SAH patients, prolapse of coil loops and platelet adherence on the coil mass [10].

According to a meta-analysis, thromboembolism occurs in 8% (7% Atena study to 12.5% Clarity study) [13] of all interventions for intracranial aneurysms [36]. Most thromboembolic events cause silent infarctions (51%) and are only symptomatic in 5% [10].

Treatment starts with correct diagnosis, followed by blood pressure augmentation to increase collateral perfusion 33–40% above baseline [11].

Thrombectomy can be done either by the intraarterial administration of tissue plasminogen activator (recanalization rates 40–50%) and/or intravenous glycoprotein IIb-IIIa receptor inhibitors (bolus at 0.25 mg/kg). Also, the latter drugs can be given intrarterial in small doses up to 10 mg [29,37–39], followed by an intravenous infusion. There are reports on stent-assisted thrombus retrieval [40].

Vasospasm

Symptomatic vasospasm presents in 30–70% [1**,41] of SAH patients leading to a delayed ischemic neurologic deficit, but can also occur during endovascular treatment [11,41,42,43**].

Neuroradiology treatment options are pharmacological intraarterial dilation for distal arteries and balloon angioplasty for proximal large arteries [11,43**]. Balloon angioplasty is radiologically effective in 98–100% and clinically in 70–80%, if performed within 2 h of symptoms [2,21,43**].

Intraarterial infusions of nimodipine [42] or nicardipine may be given during the procedure by the radiologist and have been reported to improve perfusion with no increase in major periprocedural morbidity [26,43**]. Nimodipine has minimal systemic complications but can cause hypotension, diarrhea, rash and bradycardia, whereas nicardipine can increase intracranial pressure [43**].

Intraarterial papaverine is not often used anymore because of systemic hypotension and elevation of intracranial pressure [43**]. Intravenous use of verapamil is reported with hypotension and bradycardia, although this is not reported with intraarterial use [43**].

Other pharmacologic agents, such as amrinone, L-Arg and colforsindaropate hydrochloride, have been tested for their effect on vasospasm, but none have shown significant differences [44].

A mean arterial pressure of 30–50% above baseline is recommended in an attempt to improve cerebral perfusion in the ischemic brain region [11,12**]. If the aneurysm is not secured, those targets may be tampered.

Allergies

Acute reactions to iodinated contrast usually present within 20 min of exposure. Allergic reaction to protamine is also reported and should be treated according to the standard guidelines [19*].

Contrast-induced nephropathy

An increase in creatinine of 25% within 3 days to exposure to contrast is highly suggestive of contrast-induced nephropathy [19*].

N-acetylcysteine, 600–1200 mg twice daily [45] and isotonic bicarbonate infusion are both reported to reduce the incidence of contrast-induced nephropathy [3].

POSTOPERATIVE CARE

After endovascular treatment, patients are transferred to a monitored unit for close hemodynamic follow-up and frequent neurologic assessment [2,11].

CONCLUSION

Endovascular treatment for cerebral aneurysm is an expanding field in which the anesthetist has to be aware of the possible risks and complications. Understanding the procedure, the anticoagulation management and the comorbidities of the patients can contribute to a better outcome. Good communication with the interventionalist before, during and after procedure is vital, in this not only challenging environment but also challenging patient population.

Acknowledgements

None.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

* of special interest
** of outstanding interest

