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REVIEW

Contemporary management of aneurysmal subarachnoid haemorrhage. An update for the intensivist

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Abstract

Aneurysmal subarachnoid haemorrhage (aSAH) is a rare yet profoundly debilitating condition associated with high global case fatality and morbidity rates. The key determinants of functional outcome include early brain injury, rebleeding of the ruptured aneurysm and delayed cerebral ischaemia. The only effective way to reduce the risk of rebleeding is to secure the ruptured aneurysm quickly. Prompt diagnosis, transfer to specialized centers, and meticulous management in the intensive care unit (ICU) significantly improved the prognosis of aSAH. Recently, multimodality monitoring with specific interventions to correct pathophysiological imbalances has been proposed. Vigilance extends beyond intracranial concerns to encompass systemic respiratory and haemodynamic monitoring, as derangements in these systems can precipitate secondary brain damage. Challenges persist in treating aSAH patients, exacerbated by a paucity of robust clinical evidence, with many interventions showing no benefit when tested in rigorous clinical trials. Given the growing body of literature in this field and the issuance of contemporary guidelines, our objective is to furnish an updated review of essential principles of ICU management for this patient population. Our review will discuss the epidemiology, initial stabilization, treatment strategies, long-term prognostic factors, the identification and management of post-aSAH complications. We aim to offer practical clinical guidance to intensivists, grounded in current evidence and expert clinical experience, while adhering to a concise format.

Keywords: Subarachnoid haemorrhage, Vasospasm, Delayed cerebral ischaemia, Outcome, Intensive care, Aneurysm

Epidemiology and need for intensive care management

Aneurysmal subarachnoid haemorrhage (aSAH) is characterized by bleeding in the subarachnoid space from the rupture of an intracranial aneurysm (Fig. 1) [1]. aSAH accounts for only 2–5% of all strokes, and global incidence declined from 10.2 per 100,000 person-years in 1980 to 6.1 in 2010, with significant variabilities across regions, age, and sex [1]. The global decrease in aSAH incidence paralleled a global reduction in prevalence of hypertension and smoking [1]. The incidence of aSAH increases with age and is 1.3 times higher in women than in men [1, 2]. Although the prognosis of aSAH has improved over the last decades, 12% of patients die before reaching the hospital, and the 90-day case-fatality of patients hospitalized for aSAH is approximately 30% [3]. Survivors often suffer from functional and cognitive sequelae that decrease quality of life and hamper the ability to return to work. Since half of patients with aSAH are younger than 55 years, many are in their most productive working years. Hence, the economic burden is high due to the loss of productive years of life[4]. In the United Kingdom, total costs from aSAH are estimated to be £510 million ($645, €591) per year. On a community level, the

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loss of productive years of life after aSAH is similar in magnitude to that of ischaemic stroke.

Major determinants of poor functional outcome and case fatality are early brain injury, rebleeding of the ruptured aneurysm, and delayed cerebral ischaemia (DCI) [5, 6]. Rapid diagnosis, transfer to dedicated centres, management strategies to prevent rebleeding, and haemodynamic management to preserve organ perfusion in the early phase after aSAH can improve the chances of favourable outcomes [7]. Admission to high-volume centres, defined by the management of at least 35 patients per year, is also associated with better functional outcomes after aSAH [8].

Criteria for admission to the intensive care unit (ICU) are not well defined but determined by the need for specialized care to manage early and delayed intracranial and extracranial complications. Management in dedicated neuroICUs has been shown to improve patient outcomes [7]. The optimal duration of ICU management is not well defined. In studies comparing neurointensivist-managed ICUs, the median ICU stay was around 11–12 days, which parallels the time window to address aSAH-related complications [9]. However, these studies do not take into account disease severity. aSAH patients may necessitate critical care management for many weeks. In contrast, good-grade patients may require fewer days of monitoring in the ICU, although often even good-grade aSAH patients benefit from close neurologic observation by specially trained staff during the risk period for vasospasm and DCI.

Clinical presentation and severity scales

Although the clinical presentation of patients with aSAH may vary, the characteristic presenting symptom is a thunderclap headache, a sudden severe headache generally described as the "worst headache of life". Other symptoms include nausea, vomiting, confusion, disturbance in vision and language, focal neurological deficits and loss of consciousness [1].

Severity scales are based on neurological examinations and early computed tomography (CT) findings [10]. The most widely utilized clinical assessment scale to capture clinical severity in patients with aSAH is the World Federation of Neurosurgical Societies (WFNS) scale [10], (electronic supplementary material, ESM, Figure S1). The WFNS scale (full range 0–5) transforms the Glasgow Coma Scale (GCS) score into different levels (3–6, 7–12, 13–14 with/without motor deficit, and 15). Similarly, the Hunt and Hess Scale is a clinical grading system ranging from a score of 1 to 5, based on neurological symptoms and signs ranging from mild headache to a comatose state [11].

Imaging-based scales such as the Fisher scale [12] or modified Fisher scale [13, 14] quantify the extent of subarachnoid, intraventricular, and intraparenchymal haemorrhage and are associated with outcomes. The Subarachnoid haemorrhage Early Brain Oedema Score (SEBES) has been proposed to quantify global cerebral oedema [15], and seems to be associated with increased intracranial pressure and outcomes after aSAH [16].

Take-home message

The review highlights significant progress in managing aneurysmal subarachnoid hemorrhage (aSAH), underscoring the crucial role of timely diagnosis, transfer to specialized centers, and intensive care in improving prognosis.
It presents monitoring and intervention strategies in intensive care aimed at addressing both intracranial and systemic complications, despite persistent challenges due to the lack of robust evidence for many treatments. Future research focusing on closing knowledge gaps, particularly in early and late complications management, is deemed essential to enhance long-term outcomes for aSAH patients.

Early complications before aneurysm securing

Early brain injury, defined as a cascade of events that develop in the first hours after subarachnoid haemorrhage, is related to a variety of pathophysiological mechanisms, which include cerebral oedema from bleeding, microcirculatory alterations, oxidative and inflammatory cascade, and blood–brain-barrier breakdown, thus leading to neuronal damage [17].

Early management of patients includes intubation and mechanical ventilation in comatose patients to protect the airway and optimize ventilation, neuroimaging (non-contrast head CT, and if negative lumbar

(See figure on next page.)

Fig. 1 After the rupture of an intracranial aneurysm, a cascade of events ensues. Arterial blood under pressure enters the subarachnoid space, inducing swift mechanical effects, such as abrupt increases in intracranial pressure and related cerebral impact. This sets off intracranial repercussions in the form of early brain injury, accompanied by immediate systemic consequences, impacting cardiovascular and respiratory functions. The presence of blood in the subarachnoid space may contribute to cerebral vasospasm, delayed cerebral ischemia, hydrocephalus, and seizures. Systemically, there can be hyperglycaemia, an inflammatory response, electrolyte imbalances (primarily hypo/hypernatremia), and hormonal disturbances. *ICP* intracranial pressure, *CBF* cerebral blood flow, *NPO* neurogenic pulmonary oedema, *ECG* electrocardiography, *BBB* brain blood barrier, *DCI* delayed cerebral ischemia, *LV* left ventricle

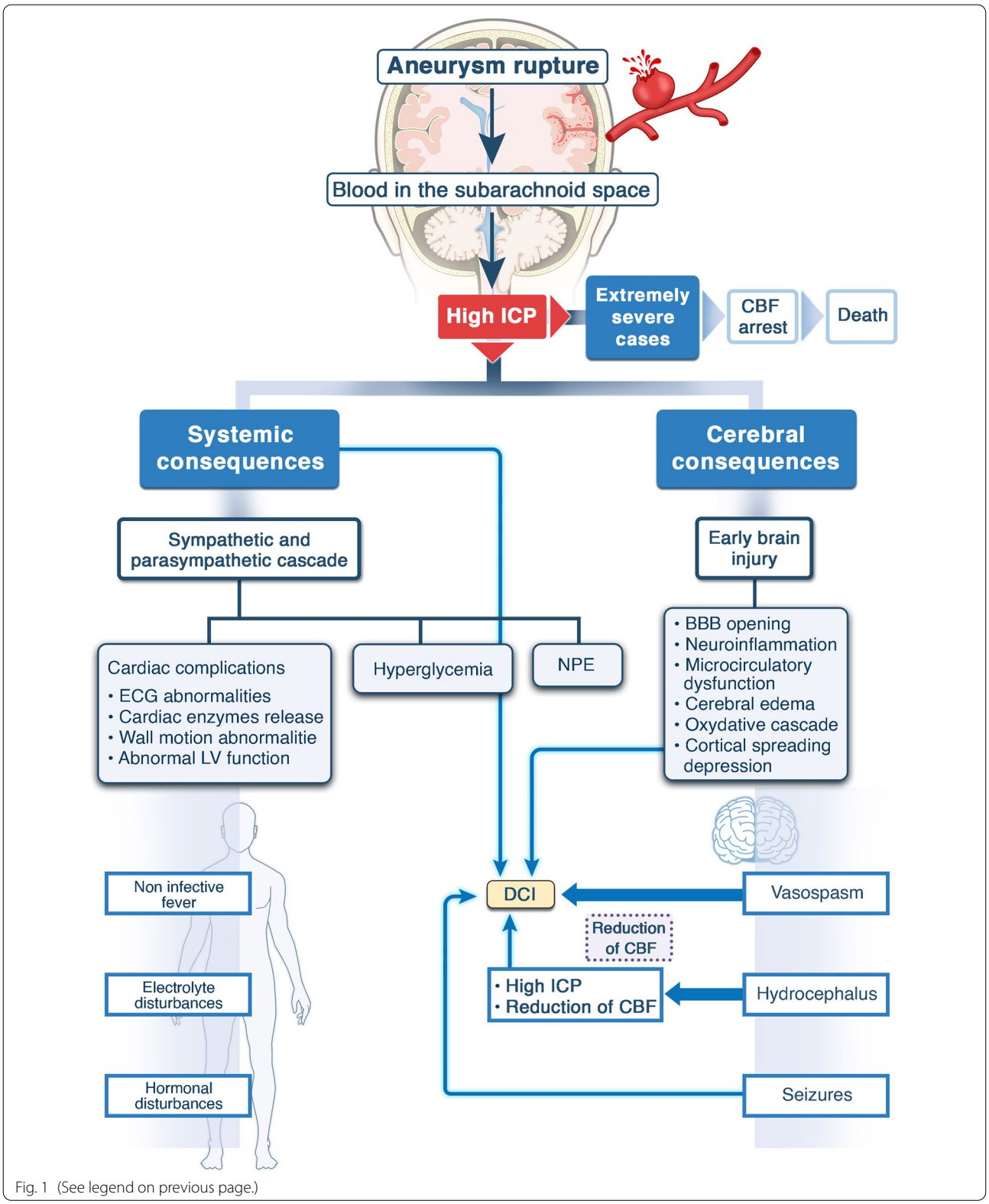

Fig. 1 (See legend on previous page.)

puncture, CT angiography, digital subtraction angiography) to establish the diagnosis and guide interventions (i.e. modality of aneurysm treatment, need for diversion of cerebrospinal fluid), treatment of haemodynamic instability, and reversal of coagulopathy [18]. At this stage, a multidisciplinary case discussion for further treatment planning (neurologist, neurosurgeon, interventional neuro-radiologist) is recommended.

Rebleeding

Rebleeding after acute rupture of an intracranial aneurysm markedly increases the risk of poor outcome [18]. It occurs in approximately 3–6% of patients within the first 24 h; the risk rapidly declines afterwards. The only effective way to reduce the risk of rebleeding is to secure the ruptured aneurysm quickly.

For this reason, guidelines recommend aneurysm repair by surgical or endovascular means as soon as feasible, preferably within 24 h. Nevertheless, logistical challenges render this goal difficult, and patients should be haemodynamically stable before aneurysm treatment can be safely pursued [19]. Interestingly, studies have found no benefit with repair within 24 h compared to 24–72 h [20].

The initial instability of the blood clot sealing the defect in the aneurysm is the target of antifibrinolytics. In several initial, randomized-controlled trials, tranexamic acid had been associated with reduced rebleeding [21], but longer-term use (weeks) was also associated with an increased risk of DCI. However, a recent large, adequately powered randomized controlled trial (RCT) that investigated ultra-early and short-term treatment with tranexamic acid found no difference in outcome, and antifibrinolytic use has since been widely abandoned [22].

Acute aSAH can be associated with a sympathetic response and rise in blood pressure, aggravating the risk of rebleeding. While intuitive, no high-quality data exist that treatment of hypertension reduces the risk of rebleeding [23]. Additionally, hypotension should also be avoided, as the lack of adequate perfusion of viable brain in the setting of elevated intracranial pressure may lead to acute cerebral ischaemia. The thresholds to lower systolic arterial blood pressure, commonly set at a goal of < 160 mmHg, for these risks are likely unique to each patient and ideally should be individualized in relation to

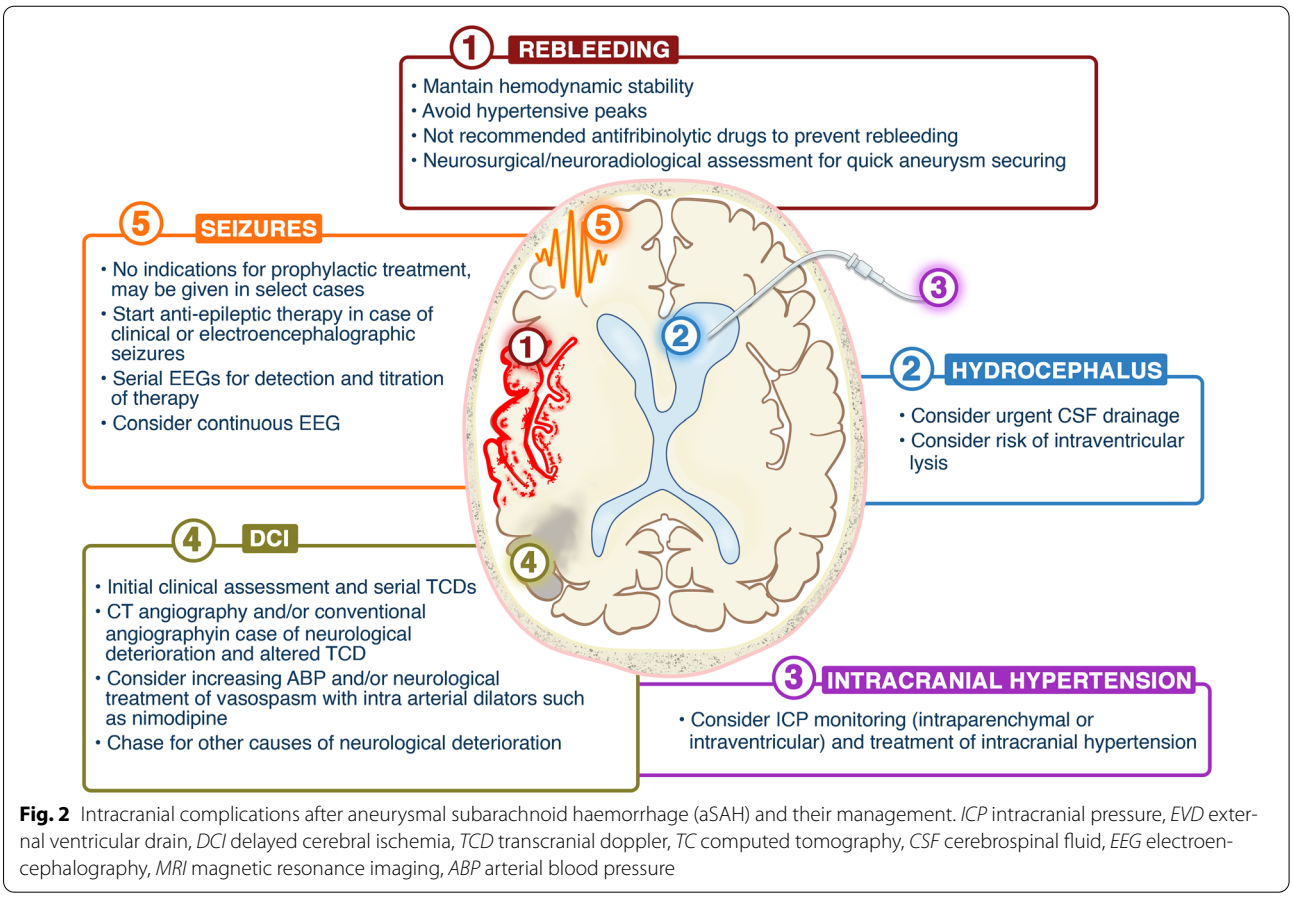

Fig. 2 Intracranial complications after aneurysmal subarachnoid haemorrhage (aSAH) and their management. *ICP* intracranial pressure, *EVD* external ventricular drain, *DCI* delayed cerebral ischemia, *TCD* transcranial doppler, *TC* computed tomography, *CSF* cerebrospinal fluid, *EEG* electroencephalography, *MRI* magnetic resonance imaging, *ABP* arterial blood pressure

the patient's status and baseline arterial blood pressure values.

Hydrocephalus

Hydrocephalus is a common acute or, less often, delayed complication after aSAH (Figs. 1, 2). Although it is more frequent in patients with intraventricular haemorrhage (especially when the third and fourth ventricles are filled with blood), it can develop in the absence of visible intraventricular extension of the bleeding on head CT [24]. Its mechanism can be obstructive (typically by clot impeding cerebrospinal fluid flow through the aqueduct), malabsorptive (from lack of cerebrospinal fluid absorption by the arachnoid granulations) [24], or both. Clinical presentation is characterized by a depressed level of alertness and, in severe cases, by downgaze deviation (from compression of the mesencephalic tectum by the dilated third ventricle), and a combination of bradycardia and hypertension.

Cerebrospinal fluid drainage by external ventricular drain (EVD), lumbar drain or lumbar puncture should be performed in patients with hydrocephalus to reduce intracranial pressure, thereby improving cerebral perfusion [25]. Ventriculostomy is the method of choice in aSAH patients with obstructive hydrocephalus and those with extensive intraventricular haemorrhage. Inserting an EVD before aneurysm occlusion can protect against abrupt ICP increases in case of rebleeding [26]. However, attention should be paid to excessive ventricular drainage before aneurysm obliteration which could prompt rerupture.

Treatment of the aneurysm (surgical clipping/endovascular treatment)

Timely repair of ruptured aneurysms reduces the risk of rebleeding and allows for more targeted and safer management of DCI [27]. Studies suggest that early aneurysm securement, i.e. within 24–72 h from onset of aSAH, yields better outcomes than delayed treatment after 7–10 days [28]. Complete obliteration of the aneurysm during initial treatment is vital to minimize rebleeding risk and risks associated with the need for retreatment. In cases where complete obliteration is not immediately feasible, securing the rupture site during the acute phase reduces the risk of early rebleeding. Retreatment within 1–3 months is then recommended to prevent future rebleeding [29].

The choice of the method to treat the ruptured aneurysm is complex and necessitates a careful balance between securing the aneurysm and the associated procedural risks [30]. This multidisciplinary decision-making process involves evaluating patient- and aneurysm-specific factors, including age, aneurysm characteristics (such as location, size, and configuration) and degree of intraparenchymal clot burden.

The two primary approaches for aneurysm treatment are open surgical techniques and endovascular methods. Each option presents distinct advantages and disadvantages. Coiling is generally preferred over open clipping if the aneurysm is amenable to such a technique, although differential considerations apply based on the setting. Good-grade aSAH patients from ruptured aneurysms of the anterior circulation are often equally suitable for both primary coiling and clipping; primary coiling is generally preferred to clipping as it is linked to improved 1-year functional outcomes [30, 31]. Similarly, some demographical subpopulations, such as older patients, may be preferably treated with coiling, whereas in case of longer life expectancy and better long-term protection from re-rupture, clipping should be taken into consideration [27]. In addition, most posterior circulation aneurysms benefit from endovascular coiling over surgical clipping [31]. Finally, aneurysm morphology (e.g. wide neck) may favour one procedure over another, and placing high-density stents (such as pipeline) over the necks of aneurysms unsuitable for clipping or coiling can be considered. However, the evidence supporting treatment recommendations is somewhat limited, particularly concerning the comparison of various, especially newer, endovascular techniques with each other and surgical methods, and in most cases, the choice is made according to clinical features but also local practice and expertise [30].

Management in the ICU

After aneurysm securement, the ICU management of aSAH involves close monitoring, optimization of systemic function and preventing and treating cranial and systemic complications. A comprehensive multidisciplinary team is fundamental to provide appropriate and aggressive treatment of these patients [32]. Minimizing or avoiding sedation seems to provide a shorter duration of mechanical ventilation and length of hospital stay and allows appropriate clinical neuromonitoring for early detection of neurodeterioration [33]. However, sedation may be required to manage intracranial hypertension, pain, agitation, status epilepticus or severe respiratory failure. The choice of sedative needs to be balanced with the patients' clinical conditions. Midazolam and propofol are most frequently adopted as first-line sedatives, but ketamine appears promising [33].

Intracranial complications

Delayed cerebral ischaemia

DCI occurs in about 30% of patients with aneurysmal aSAH, mostly between days 4–14 after ictus, and is the

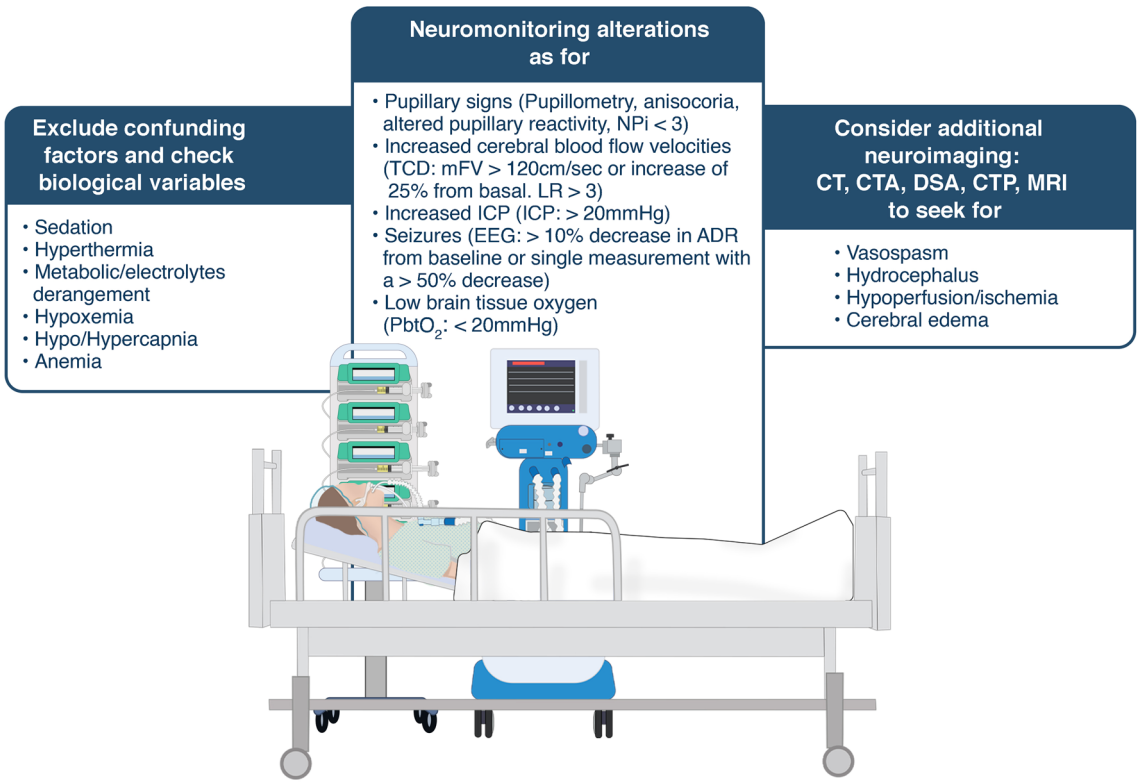

Fig. 3 Detection of causes of delayed cerebral ischemia (DCI). *CT* computed tomography, *CTA* CT angiography, *DSA* digital subtraction angiography, *CTP* perfusion computed tomography, *MRI* magnetic resonance imaging, *TCD* transcranial Doppler, *PbtO2* brain tissue oxygen, *ICP* intracranial pressure, *EEG* electroencephalography, *NPi* neurological pupillary index, *ADR* alpha/delta ratio, *LR* Lindegaard ratio

leading cause of functional disability in survivors [34, 35] (Figs. 2, 3). It is often associated with angiographic vasospasm, but documentation of vasospasm is not a sine-qua-non for the diagnosis of DCI [36]. Only half of patients with angiographic vasospasm develop ischaemic symptoms, and DCI may develop without angiographic vasospasm [34]. Recent work has suggested that other factors may contribute to DCI; it also occurs in cortical spreading depolarization [37], impaired autoregulation with reduced regional blood flow, intravascular volume contraction, and microthrombosis [38]. Vasospasm can affect small vessels escaping angiographic detection. Poor initial clinical (i.e. Hunt Hess or WFNS score) and radiographic (i.e. modified Fisher, Hijdra) grades [39] are established predictors of DCI. Other risk factors, variably associated, include female sex [40], smoking, hydrocephalus, hyperglycaemia, and diabetes [41].

Guideline-recommended strategies to reduce DCI risk include enteral administration of nimodipine and prevention of hypovolaemia and hypotension [42]. Nimodipine reduces infarction rates and improves functional outcomes despite not significantly preventing angiographic vasospasm [43]. Intravenous nimodipine more often leads to hypotension with compared to oral nimodipine, with significant drops in blood pressure in one-third of patients after the start of intravenous nimodipine as opposed to after every tenth oral intake [30] Hypotension may require dose adjustment, discontinuation, or vasopressor support increase [44]. Nimodipine can also be used as a potential intraarterial vasodilator [45], although robust data on eventual burden of DCI are lacking for such use.

A summary of measures aimed at DCI prevention and treatment is provided in Table 1, and Fig. 3.

As preventive measures are limited, detecting and treating DCI before it leads to cerebral infarction is important. Clinical monitoring through serial neurologic assessments is fundamental but misses DCI-related neurologic changes in one-fifth of patients [46]. Hence, imaging aimed at vasospasm detection and assessment of cerebral perfusion is commonly entertained. The gold standard for diagnosis of large-vessel vasospasm, digital subtraction angiography, enables endovascular treatment

Table 1 Prevention and management of delayed cerebral ischemia

Guideline recommendations American Heart Association [30], Neurocritical Care Society [122] & European Stroke Organization [123]	
DCI prevention	
Strong recommendation	Nimodipine (early initiation, enteral) [30, 122, 123]
Moderate recommendation	Maintenance of euvolemia [30, 122, 123]
Insufficient evidence	Calcium channel blockers (other than nicardipine), intravenous or intraventricular [122] or into surgical space [123]
Not recommended	Intravenous nicardipine [122, 123], endothelin receptor antagonist [122], statins [30, 122], magnesium sulphate [30, 122, 123], hypervolemia [122, 123], prophylactic hemodynamic augmentation [30]
Management of DCI	
Weak recommendations	Hemodynamic augmentation if symptomatic vasospasm present [30] Intraarterial vasodilator therapy for severe vasospasm [30] Cerebral angioplasty for severe vasospasm [30]
Insufficient evidence	Hemodynamic augmentation [122, 123]
Investigations on methods aimed at DCI prevention and management[a]	
Anti-inflammatory strategies	
Ongoing trials	CytoSorb: removal of IL-6 from CSF (NCT05259514)
	Deferoxamine (NCT04566991)
	Dexamethasone (NCT05132920)
	Etanercept (NCT01865630)
	Ibuprofen (pilot trial) [124]
	Sulforaphane: SAS trial [125]
No benefit	Clazosentan: REACT (phase 3 study of clazosentan for DCI) and CONSCIOUS 2/3 [126–129]
	Eculizumab: CLASH (phase 2a randomized clinical trial) [130]
Cerebral perfusion and oxygen delivery	
Preliminary data	Milrinone [131, 132]
Ongoing trials	OPTIMIL (milrinone to prevent DCI) (NCT04282629)
	Red blood cell transfusions: SAHaRA [131], TRAIN [134]
Removal of subarachnoid blood	
Preliminary data	Lumbar drain for CSF removal (EARLY-DRAIN) [74]
Ongoing trials	PILLAR: Cerebrospinal Fluid Filtration [135] SPLASH: Stereotactic cisternal lavage with urokinase and nimodipine [136]
Prevention and treatment of DCI	
Preliminary data	Cilostazol [137]
	Intrathecal nicardipine [138, 139]
	Nicardipine prolonged-release implants [140]
	Stellate ganglion blockade [141, 142]
	Tirofiban [143]
Ongoing trials	Cilostazol-nimodipine combined therapy [144]
	Heparin: ASTROH (NCT02501434)
	Nadroparin (NCT04507178)
	Nicardipine-prolonged release implants(NCT04269408)
	Stellate ganglion block: BLOCK-CVS [145]
	Tirofiban (NCT03691727)
No benefit	Intracisternal nimodipine microparticles (NEWTON-2) [146]

[a] Comprehensive listing of trials investigating magnesium and statins is deferred here as references are provided in current guidelines

DCI delayed cerebral ischemia, *CSF* cerebrospinal fluid, *IL-6* interleukin 6

if indicated. Computed tomography-angiography (CTA) reaches 82% and 97% sensitivity and specificity for angiographic vasospasm detection [47]. CT perfusion may allow recognition of impaired perfusion, which may occur independently of vasospasm [48].

Transcranial Doppler ultrasonography (TCD) is non-invasive and can be performed daily or even more often, but it lacks high sensitivity for vasospasm detection, reaching only 38% in a recent review [49]. In addition, agreement between CTA and TCD is limited [50].

Continuous electroencephalography (cEEG) with quantitative analysis can predict the development of DCI earlier than TCD. When combining cEEG and TCD, diagnostic accuracy to predict DCI increases [51]. Invasive DCI monitoring modalities include cerebral oxygenation, brain-tissue biochemistry, electrocorticography, and intracortical EEG (Fig. 3) [52]. If DCI is detected, physiological and biological factors such as sedation, hyperthermia, and arterial blood gases should be considered (Fig. 3).

No data are available to support the treatment of subclinical vasospasm detected by monitoring. Therefore, at the current stage of knowledge, these techniques mainly aim at identifying patients at higher risk of DCI and may guide stricter monitoring or lower thresholds to trigger further examination or more advanced management.

Treating DCI aims to improve perfusion and minimize or prevent infarction. Haemodynamic augmentation through induced hypertension is often used as a primary intervention in patients with DCI in the absence of cardiac failure and severe baseline hypertension. Induced hypertension may reduce the risk of DCI-related cerebral infarction and lead to better outcomes [52], but optimal target blood pressures remain unclear, and the only randomized controlled trial on this topic failed to support induced hypertension in this setting but likely was underpowered [53]. Haemodynamic augmentation appears safe in the presence of other small, unruptured and untreated aneurysms [54]. Vasopressor selection depends on cardiovascular status; norepinephrine and phenylephrine are commonly used. While cardiac output changes generally do not affect cerebral blood flow, they may do so in SAH patients. Accordingly, inotropic agents, such as milrinone (that also has cerebral vasodilatory properties), may be useful in patients with ventricular dysfunction.

Endovascular rescue therapy with either intraarterial infusion of vasodilators (i.e. verapamil, nicardipine or milrinone) and/or balloon angioplasty may be considered when haemodynamic augmentation fails or is contraindicated [55]. There is no evidence supporting these interventions from phase 3 RCTs, although a recent small phase 2 RCT [56] showed worse outcomes in patients treated with endovascular rescue therapy than those treated with hypertension induction. Retrospective data suggest improved outcomes in centres offering endovascular intervention for DCI compared to those that do not [56].

Seizures and status epilepticus

Seizures in aSAH may be encountered at the time of bleeding, during hospitalization, and months or years later (ESM, Table S1). Underlying mechanisms are debated and may include gliosis, neuroinflammation [57], and cerebral hyperaemia [58]. The SAFARI score may help identify those at risk for convulsive in-hospital seizures based on older age, pre-hospitalization seizures, ruptured anterior circulation aneurysms, and ventricular drainage [59]. Recent guidelines [30] state that cEEG is reasonable, primarily for aSAH patients with impaired consciousness or fluctuating examination, ruptured middle cerebral artery aneurysm, high-grade aSAH, intracranial haemorrhage, hydrocephalus, and cortical infarction. Periodic discharges not qualifying as seizures [60] are prevalent and of controversial significance. Long-term epilepsy appears less likely in patients who underwent coil embolization [27].

Electrographic seizures [61] and high-frequency periodic discharges (>2.5 Hz) [62] have been associated with increased metabolic demand that may be insufficiently compensated for by local increases in cerebral blood flow. In aSAH patients during and post-hospitalization [63], electrographic seizures have been associated with worse outcomes. Importantly, these associations do not imply causal effects and possibly relate to other secondary complications, such as late diagnosis of delayed cerebral ischaemia [64].

No adequately powered clinical trial has been conducted to guide seizure prophylaxis or treatment in aSAH patients. Recent guidelines [30] do not recommend the routine use of prophylactic antiseizure medication (ASM), although ASM may be reasonable in patients at high risk for seizures. Phenytoin as ASM should be avoided since it may induce harm. In an underpowered, prospective, single-centre, randomized, open-label trial, the benefit from prolonged levetiracetam prophylaxis was greatest for those with imaging evidence of early brain injury [65] and others have suggested a possible benefit against DCI with newer ASMs (levetiracetam and perampanel) [66]. All clinical or electrographic seizures that are diagnosed should be treated for at least 7 days and for those with delayed seizures or those with risk factors for seizures, more prolonged treatment should be considered. Management of periodic discharges or other ictal-interictal patterns is highly controversial, and the benefit of treatment has not been demonstrated [67].

ICP indications, management and cerebral oxygenation

The practice of intracranial pressure (ICP) monitoring in patients with aSAH remains a matter of debate due to the absence of high-level evidence tailored to this condition [68] (Fig. 2). While the Neurocritical Care Society suggests ICP monitoring for acute brain injuries at risk of elevated ICP based on clinical and imaging features, there are no distinct indications for aSAH patients [69]. However, in certain circumstances, ICP monitoring should be considered in aSAH, including GCS $\leq$ 8, neurological deterioration, acute hydrocephalus, cerebral oedema, intracranial mass lesions, and need for perioperative or drainage of cerbrospinal fluid (CSF) [30].

The gold standard method for ICP measurement is via a ventricular catheter connected to a pressure transducer [39–41]. This approach also allows for CSF drainage and recalibration. Of note, while potential benefits of fibrinolytic treatment of intraventricular haemorrhage have been demonstrated for primary intracranial haemorrhage, there are no data to support this for the aSAH population [70, 71].

Drainage practices after aneurysm treatment vary across centres and include open drainage by adjustment of the drainage system above the foramen of Monro or intermittent drainage based on ICP values [26]. Timing, triggers of weaning and how to discontinue ventricular drainage are subject to debate [26]. Reports suggest that direct clamping may be preferable to weaning before clamping [72], but the evidence is weak.

A lumbar drain is considered a less invasive alternative to EVD but may be precluded in case or obstructive hydrocephalus and contraindicated based on head CT findings [73]. In a recent trial, prophylactic lumbar drainage after aSAH reduced secondary infarctions and the rate of an unfavourable outcome at 6 months [74]. These findings support the use of lumbar drains after aSAH, but additional research is necessary to determine the value of lumbar drainage to improve outcomes after aSAH, especially because an earlier RCT found no effect of lumbar drainage on outcome at 6 months [75].

Patients receiving lumbar punctures need to be carefully monitored to confirm that they do not need additional CSF diversion.

Ventriculoperitoneal shunting is necessary in patients with persistent hydrocephalus. Risk factors for requiring ventriculoperitoneal shunting include intraventricular haemorrhage and higher radiological grade (such as modified Fisher), older age, higher clinical grade (Hunt and Hess or WFNS), more significant acute ventricular dilatation, rebleeding, posterior location of the ruptured aneurysm, and multiple clamp failures [76].

Alternative noninvasive methods for estimating ICP are being explored, including ultrasound assessment of optic nerve sheath diameter, although their reliability and use in aSAH patients is questionable [77].

The appropriate threshold for treating elevated ICP remains poorly understood. While the classic threshold is around 20–22 mmHg, poor outcomes have also been linked to lower values [78], suggesting a potential need to lower ICP targets. Recent studies indicate that a "dose" concept, considering both the magnitude and duration of exposure to high ICP, may better quantify the ICP burden and predict outcomes [79].

Elevated ICP in aSAH may arise primarily from hydrocephalus (30%), intracerebral haemorrhage (ICH), and early or delayed global cerebral oedema (GCO) (8–12%) [68, 80]. Less common causes include subdural hematoma, cerebral infarction, and extracranial factors. aSAH-related ICP elevation can occur acutely, subacutely, within a few days from bleeding, or delayed. Early GCO risk is linked to cerebral hypoperfusion, vasomotor paralysis, and blood volume increase [81]. Later, ICP may normalize due to reduced blood, improved CSF dynamics, and brain oedema reduction. Further risk of GCO arises from ischaemic injury, ion channel dysfunction, and cellular swelling.

The management of increased ICP in aSAH patients lacks specific guidelines, prompting the application of recommendations from traumatic brain injury (TBI) guidelines [76].

The SYNAPSE-ICU study [82] revealed that episodes of high ICP necessitating treatment were frequent in aSAH patients, especially those with parenchymal devices, and ICP monitoring and treatment were associated with improved outcomes [83].

When intracranial hypertension is caused by hydrocephalus, CSF removal is vital for controlling ICP, with current guidelines recommending CSF diversion for acute symptomatic hydrocephalus [84].

Hyperventilation, head elevation, and osmotherapy are commonly used to manage high ICP. The transient effect of hyperventilation makes it suitable for short-term ICP control but carries the risk of cerebral ischemia and should be avoided in patients at risk for DCI, while the choice of osmotherapy between mannitol and hypertonic saline remains debatable [84].

Hypothermia and high-dose barbiturates are reserved for refractory cases due to their risks and limited supporting evidence [84]. Decompressive craniectomy (DC) has shown efficacy in reducing ICP, but its impact on functional outcomes is questionable [84]. While evidence for the routine use of DC for managing elevated ICP in SAH is lacking, it remains a last resort option when medical management fails. Finally, cerebral monitoring with brain tissue oxygen tension ($PbtO_2$) can be taken into consideration—although evidence on $PbtO_2$ monitoring

mainly stems from traumatic brain-injured patients; reductions in brain oxygen tension have been associated with angiographic vasospasm or altered regional cerebral blood flow [85], and recent evidence supports its use for the detection of DCI in selected patients [85].

Extracranial complications

Cardiac complications

While the primary concern in the setting of aSAH is its direct effects on the brain through primary and secondary brain injury, the post-bleeding course can be complicated by an array of cardiac adverse events ranging from arrhythmias and myocardial dysfunction to myocardial infarction [86]. Cardiac complications increase the complexity of medical management and can worsen prognosis of patients with aSAH [87]. Therefore, prompt medical management of both the neurological and cardiac aspects of aSAH is crucial to improve outcomes and reduce the risk of further complications (Figs. 1, 4).

aSAH can disrupt the electrical sinus pacing or cause conduction abnormalities, leading to arrhythmias [88]. Encountered rhythm abnormalities include sinus arrhythmia, atrial fibrillation, ventricular tachycardia, or ventricular fibrillation. Prompt correction of electrolyte abnormalities is important, and use of antiarrhythmic medications may be required. Serial electrocardiograms (ECG), troponin sampling, and continuous monitoring of vital signs in an intensive care setting are recommended [89]. In addition, more advanced haemodynamic monitoring, including pulse index continuous cardiac output (PICCO), pulse dye densitometry, and pulmonary artery catheterization, can be considered to minimize cerebral and haemodynamic complications in specific cases [90].

aSAH can also result in wall motion abnormalities [91]. These changes are thought to result from the massive catecholamine release and sympathetic surge during ictus bleed and are typically not reflective of an anatomic territory of the coronary arteries. Decreased cardiac output and impaired ejection fraction may ensue, which could

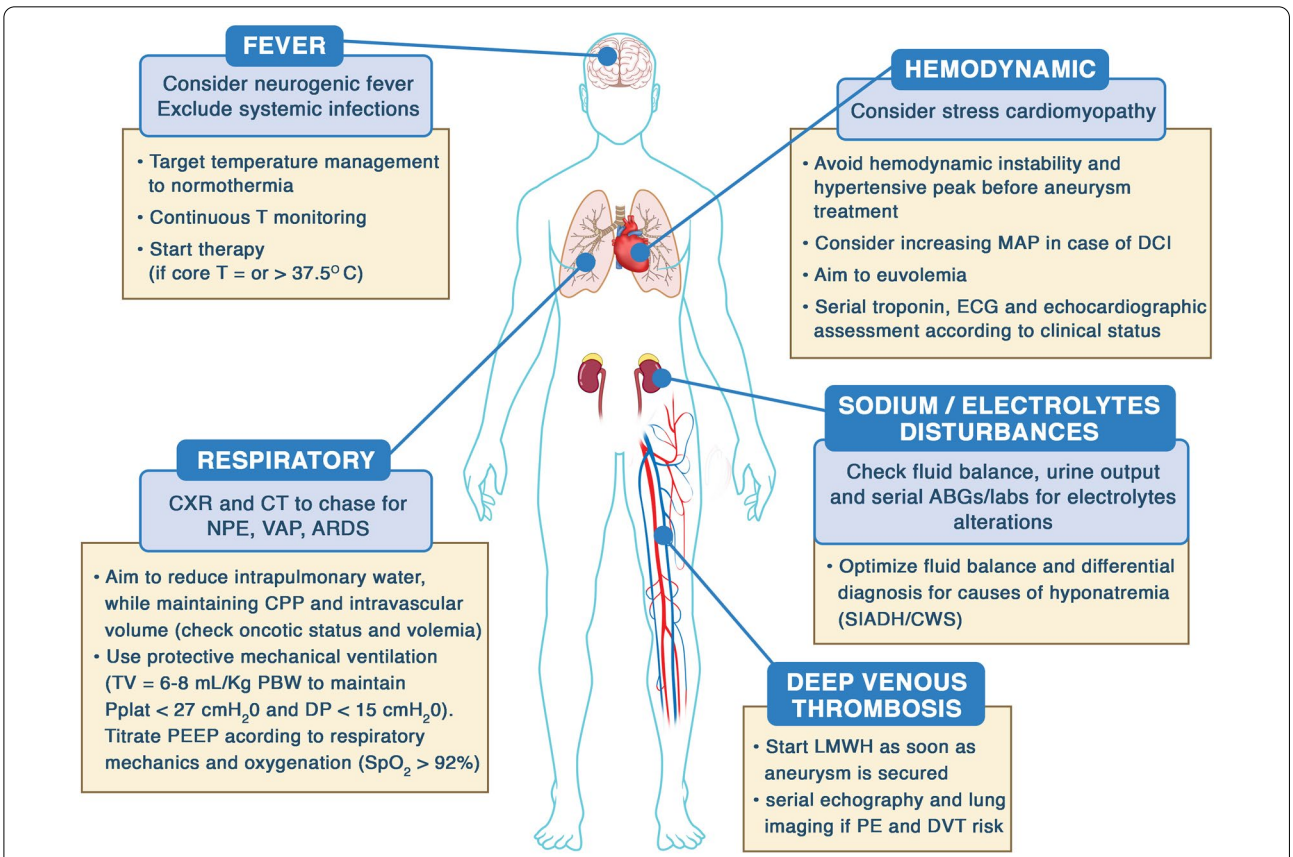

Fig. 4 Extracranial complications after aneurysmal subarachnoid haemorrhage. *T* temperature, *ABG* arterial blood gases, *MAP* mean arterial pressure, *ECG* electrocardiography, *PBW* predicted body weight, *DP* driving pressure, *Pplateau* Plateau pressure, *PEEP* positive end-expiratory pressure, *TV* tidal volume, *PPlat* plateau pressure, *SpO2* oxygen saturation, *NPO* neurogenic pulmonary oedema, *VAP* ventilator-associated pneumonia, *ARDS* acute respiratory distress syndrome, *PE* pulmonary embolism, *DVT* deep venous thrombosis, *SIADH* syndrome of inappropriate antidiuretic hormone, *CWS* cerebral salt-wasting, *CXR* chest X-ray, *CT* computed tomography, *LMWH* low molecular weight heparin

result in hypotension, fluid overload, and heart failure. In most cases, these changes are reversible and will resolve without sequelae.

In more severe cases, patients may present with profound neurogenic myocardial stunning, called Takotsubo cardiomyopathy [92]. This condition is characterized by biventricular apical hypo- or akinesia, leading to signs and symptoms mimicking a myocardial infarction, such as chest pain, shortness of breath, abnormal ECG with changes characterized by ST-segment elevation, and troponin elevation [93]. Echocardiography can assist in the differential diagnosis of myocardial infarction. The important distinction from ischaemic cardiac disease is that aSAH-related cardiac findings are non-ischaemic due to disturbance of the contraction bands in cardiac muscle and are fully reversible.

Infrequently, aSAH can trigger ischaemic myocardial infarction [94]. This complication can occur due to a combination of factors, including increased sympathetic activity, arterial spasm, and microvascular dysfunction in a susceptible individual, mostly in the setting of underlying coronary artery disease. The risk of myocardial infarction is highest within the first few days after aSAH. A multidisciplinary approach involving cardiology, neurosurgery, and neurointensivists for determination of the appropriateness of prompt initiation of management of acute coronary syndrome should be coordinated in a timely fashion.

Pulmonary complications

aSAH patients are at risk for pulmonary complications, which contribute to worse outcomes and mortality. Patients with a decrease in neurologic function also are at increased risk for aspiration pneumonia due to loss of control of swallowing [95]. Mechanical ventilation for airway protection can lead to ventilator-associated pneumonia. In a large prospective multicentre study of aSAH in the United States (US) and Canada from 1995 (50 hospitals), pneumonia occurred in 22% of aSAH cases [96] (Fig. 4).

Neurogenic pulmonary oedema (NPO), caused by increased interstitial and alveolar lung fluid, occurs as a consequence of central nervous system injury and, when most severe, can result in acute respiratory distress syndrome (ARDS) [97]. It is an early complication, occurring in up to 23% of cases, and is thought to be related to sympathetic activation due to the SAH [96]. Treatment of NPO is supportive, including mechanical ventilation with positive end-expiratory pressure (PEEP), and reduction of ICP. Euvolemia is central to the management of NPO and aSAH and must balance the slightly competing imperatives (avoidance of hypervolemia in NPO and avoidance of hypovolemia in aSAH).

Classic ARDS, characterized by hypoxemic respiratory failure associated with diffuse lung inflammation and increased alveolar-capillary permeability, generally occurs as a response to injury (such as pneumonia, sepsis, and aspiration) in post-aSAH patients [98]. The incidence of ARDS increases with aSAH severity, including cerebral oedema, cardiac arrest and cardiogenic shock. Unsurprisingly, ARDS is also associated with significantly worse outcomes [99]. It is encouraging that the incidence of ARDS after aSAH has decreased from 38% in 2008 to 4% in 2014 [100]. It is also noted to be of similarly low incidence (< 4%) in a large multicentre European cohort in 2021 [101]. Lung-protective ventilation strategies for ARDS (low tidal volume, titrated positive end-expiratory pressure, PEEP, limiting plateau pressure and driving pressure, cautious recruitment manoeuvres and permissive hypercapnia) started to become the standard of care around 2000 (Figs. 2, 3) [102]. The declining incidence of ARDS with evolving management of both aSAH and ARDS suggests that this is a preventable condition and should be a target for improving outcomes after aSAH [103].

Metabolic and fluid management

Metabolic and fluid management in aSAH patients is an essential aspect of neurointensive care, aiming to maintain an even fluid balance, prevent complications, and support optimal cerebral perfusion [104]. A key concept of haemodynamic management is the optimization of cardiovascular function to ensure sufficient cerebral perfusion pressure and oxygen delivery to the brain. Haemodynamic optimization is essentially achieved by avoiding hypovolemia, maintaining adequate blood pressure, and targeting optimal cardiac output by ensuring adequate preload (intravascular volume) and contractility based on the Starling curve principle. Goal-directed therapy is a reasonable approach to achieve the hemodynamic optimization goals. The specific targets may vary based on individual patient factors and institutional protocols; commonly used parameters include mean arterial pressure (MAP) goals with a target MAP > 65 to 70 mmHg and cardiac output (CO) or cardiac index (CI), to guide fluid administration, vasopressor dosing and inotropic support [105].

Invasive blood pressure monitoring with arterial catheterization is advisable for most cases. Noninvasive cardiac output monitoring, central venous catheterization, or—in select and severe cases—pulmonary artery catheterization may be utilized to closely monitor hemodynamic parameters, especially in patients requiring active intervention with fluids and vasopressors or inotropes. Accurate and frequent monitoring of fluid intake, urine

output, and clinical assessment of hydration status is crucial.

Assessing fluid responsiveness through dynamic indices (e.g. stroke volume variation, pulse pressure variation) or bedside echocardiography can help guide fluid administration, and these approaches are likely most reliable in determining the intravascular volume and guiding fluid administration.

Electrolyte imbalances, including hypokalaemia, hypomagnesemia and hypophosphatemia, are common in aSAH patients, primarily due to excess renal losses. They can significantly affect neurological and cardiac function [106]; monitoring and prompt correction of electrolyte abnormalities are important aspects of aSAH management to prevent arrhythmias or other cardiac abnormalities.

Hyponatremia has been attributed to the syndrome of inappropriate antidiuretic hormone (SIADH), excessive salt wasting, hypovolemia or a combination of both [107]. Determination of intravascular volume status along with urinary osmolarity and sodium excretion may be used to determine the cause of hyponatremia and guide the approach to its correction that may include free water optimization, avoiding fluid restriction, sodium supplementation (hypertonic saline or enteral replacement), or occasionally administration of mineralocorticoids, even if debatable [108].

Adequate nutrition is essential for recovery. Oral or enteral feeding is preferred over parenteral nutrition when possible. Hyperglycaemia is associated with worse outcomes [109]. Glucose levels should be closely monitored, and if elevated, appropriate insulin therapy may be initiated to maintain glycaemia in a typical range between 140 and 180 mg/dL [110].

It is important to note that individual patient characteristics, the severity of aSAH, and other co-existing conditions may influence the specific approach to metabolic and fluid management. Thus, these strategies should be tailored to each patient's unique circumstances, and close monitoring and collaboration with a multidisciplinary team are crucial for optimal management.

Fever is extremely common in patients after aSAH; early, i.e. within the first 3 days, fever is frequently neurogenic. Its occurrence (regardless of the cause, neurogenic, infective, or drug-related) is associated with worse outcomes. Recent recommendations suggest active fever treatment, continuous core temperature monitoring, and avoiding temperatures > 37.5° [111]. Other principles for the general management of these patients and their complications include deep venous thrombosis prophylaxis after aneurysm treatment to prevent thromboembolic events, and screening/ treatment for systemic infective complications.

Long-term outcomes of SAH patients

Long-term outcomes of aSAH have improved over the years, even in patients presenting with very severe illness [112]. A favourable functional outcome is achieved in a third of poor-grade aSAH patients [112]. Many factors have likely led to this improvement, including earlier timing of aneurysm treatment [113], and specialized neurocritical care management [114]. There is tremendous variability in aSAH care [115] and associated outcomes [116], and evidence-based and guideline-driven care [30] have the potential to improve population outcomes for aSAH. Long-term outcomes in aSAH trials and observational studies have been historically measured on scales of function such as modified Rankin Score (mRS) or Glasgow Outcome Scale or Extended (GOS/GOSE), and are dichotomized by researchers inconsistently into good or poor outcomes.

Importantly, functional outcome measures can have poor agreement with patients' self-assessed outcomes after aSAH [117]. The recorded outcome measures often miss important aspects, as reported by patients and families: cognitive, psychological, and social dependence [118]. Even if patients improve in physical function, most patients suffer from neurocognitive morbidity, which is a driver of the economic burden of aSAH [35]. Memory deficits and impairment in executive functions are most common and are closely related to impaired quality of life, which is reported in a third of survivors a year after ictus [35]. More than half of patients with good neurological outcomes a year after aSAH still had mild to moderate difficulties even 20 years out [119]. Unfortunately, these symptoms can be underrecognized and underdocumented, and current prognostic models are limited in their assessment [120]. The high prevalence of neurocognitive morbidity despite functional independence underscores the importance of measures of quality of life in outcomes assessments and as targets of prevention and intervention. Outcome tools for the prognosis after aSAH have been proposed, such as the SAHOT (subarachnoid haemorrhage outcome tool) for individual assessment of prognosis after aSAH [121], but these need to be better implemented and validated in clinical practice. Importantly, post-ICU clinical trajectory needs to be taken into consideration through rehabilitation programs, assessments and follow-up to minimize long-term symptoms such as anxiety, depression, and fatigue and ensure a better quality of life.

Conclusions and future perspectives

aSAH still has high mortality and morbidity, which significantly depend on the initial severity and the occurrence of early and late complications. Management of this entity in specialized centres with dedicated personnel may improve outcomes. A growing body of evidence is available regarding the ICU management of these patients, but still significant knowledge gaps and a lack of high-quality data remain. Future research and randomized controlled trials are warranted in order to understand better the management of early and late complications in this population, especially regarding DCI detection and treatment (in the ESM we present a list of the ongoing trials on aSAH). In particular, research should focus on the aim to address the gaps in the understanding of aSAH pathophysiology and strategies that could improve long term outcomes.

Supplementary Information
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Declarations

Conflicts of interest
CR received fees as a speaker from Masimo and Edwards Lifesciences, Nihon Kohden and BD, all outside the submitted work. GC reports grants and personal fees as a speakers' bureau member and advisory board member from Integra Neurosciences, NeurOptics, Biogen, Invex Ltd and Idorsia, all outside the submitted work. KMB has received honoraria from the American Academy of Neurology for speaking, editing and course directing and is an Associate Editor for Critical Care Medicine. JC is a minority shareholder at iCE Neurosystems.

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