NEUROSURGICAL PRACTICE

Current Management of Aneurysmal Subarachnoid Hemorrhage Guidelines from the Canadian Neurosurgical Society

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ABSTRACT: Published medical evidence pertaining to the management of aneurysmal subarachnoid hemorrhage (SAH) was critically reviewed in order to prepare practice guidelines for this condition. SAH should be considered as a possible cause of all sudden and/or unusual headaches, and every attempt should be made to recognize mild SAHs, as they are still frequently misdiagnosed. The first test for SAH is computed tomography (CT), followed by lumbar puncture when the CT is negative for intracranial bleeding (the case in only several per cent of patients within 24 hours of aneurysm bleeding). Urgent cerebral angiography is necessary to detect the underlying cerebral aneurysm. The advantage of rapid diagnosis of SAH followed by early aneurysm repair is minimizing the risk of catastrophic aneurysm rebleeding. Early surgery for aneurysm repair is often possible and is recommended, unless the aneurysm location or size renders it technically difficult to expose in clot-laden subarachnoid cisterns beneath an acutely swollen brain. Aneurysm ablation is optimally accomplished with open microsurgery and clipping of the aneurysm neck, although other options include proximal parent artery occlusion, "trapping" of the aneurysmal segment of the artery, and embolization of thrombogenic materials (e.g., platinum "microcoils") directly into the aneurysm dome using endovascular techniques. Neurological outcome following SAH is also optimized through the prevention of secondary SAH complications, and further management specific for ruptured cerebral aneurysms can include anticonvulsants, neuroprotectants, and various agents and techniques to prevent or reverse delayed-onset cerebral vasospasm. All patients with aneurysmal SAH should be treated with the calcium antagonist nimodipine, and in certain circumstances patients should receive anticonvulsants. Induced arterial hypertension, hypervolemia and in some instances percutaneous balloon angioplasty are recommended to reverse vasospasm causing symptomatic cerebral ischemia prior to cerebral infarction.

RÉSUMÉ: Traitement actuel de l'hémorragie sous-arachnoïdienne anévrismale Lignes de conduite de la Société Canadienne de Neurologie. Les données médicales publiées concernant le traitement de l'hémorragie sous-arachnoïdienne anévrismale (HSA) ont été revisées de façon critique afin de préparer des lignes de conduite pratiques pour le traitement de cette affection. L'HSA devrait être considérée comme une cause possible de toutes les céphalées subites et/ou inusitées et tous les efforts devraient être faits pour reconnaître les HSA légères parce qu'elles sont encore fréquemment mal diagnostiquées. Le premier test pour l'HSA est la tomodensitométrie (CT), suivie de la ponction lombaire quand le CT est négatif pour un saignement intracrânien (ce qui est le cas chez un faible pourcentage des patients dans les 24 heures d'un saignement provenant d'un anévrisme). L'angiographie cérébrale faite en urgence est nécessaire pour détecter l'anévrisme cérébral sous-jacent. L'avantage d'un diagnostic rapide de l'HSA suivi d'une réfection précoce est de minimiser le risque de resaignement catastrophique de l'anévrisme. La chirurgie précoce est souvent possible et est recommandée, à moins que le site de l'anévrisme ou sa taille le rende difficile d'accès dans les confluents sous-arachnoïdiens chargés de caillots, sous un cerveau oedématié de façon aiguë. L'exérèse de l'anévrisme est effectué idéalement par microchirurgie ouverte et ligature du collet de l'anévrisme, bien qu'il existe d'autres options comme l'occlusion proximale de l'artère qui nourrit l'anévrisme, le "trapping" du segment artériel anévrismal, l'embolisation d'une substance thrombogénique (microserpentins de platine par exemple) directement dans le dôme de l'anévrisme au moyen de techniques endovasculaires. L'issue neurologique suite à l'HSA est également optimisée par la prévention de complications secondaires de l'HSA et leur traitement spécifique inclut les anticonvulsivants, les neuroprotecteurs et d'autres agents et techniques pour prévenir ou faire régresser le vasospasme cérébral tardif. Tous les patients qui ont une HSA devraient être traités avec la nimodipine, un antagoniste du calcium, et dans certaines circonstances, les patients devraient recevoir des anticonvulsivants. L'hypertension artérielle induite, l'hypervolémie et dans certains cas l'angioplastie percutanée, sont recommandées pour maîtriser le vasospasme causant l'ischémie cérébrale symptomatique avant que ne survienne l'infarctus cérébral.

Can. J. Neurol. Sci. 1997; 24:161-170

Subarachnoid hemorrhage (SAH) from a ruptured cerebral aneurysm is a common and often devastating medical emergency. The annual incidence of SAH in North America is approximately 10 cases per 100,000 persons,[1] and it has been estimated that up

RECEIVED SEPTEMBER 24, 1996. ACCEPTED IN FINAL FORM DECEMBER 7, 1996.

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https://doi.org/10.1017/S0317167100021521 Published online by Cambridge University Press

to one-half of those suffering aneurysm rupture will either die or be seriously disabled as a result.[1-3] Although poor outcome is often primarily due to direct effects of the initial hemorrhage, timely and appropriate management of these patients will prevent secondary complications and additional neurological injury.

The following practice guidelines were prepared by Canadian Neurosurgical Society to update the Canadian neuroscience community on current management recommendations for aneurysmal SAH. The levels of evidence established by the Canadian Task Force on the Periodic Health Examinations were applied.[4] These recommendations are based upon a review of the pertinent literature to date, but since most studies in this area are nonrandomized trials or case series (levels II and III evidence, Table 1), all recommendations required consensus from a panel of experts. It should be emphasized that the following management recommendations have been formulated as guidelines only, to complement rather than replace clinical judgment, since individual patient and clinical circumstances sometimes require variation from the treatments strategies set forth below. Wherever appropriate, these guidelines were compared with similar guidelines, published in 1994, from a special writing group of the American Heart Association,[5,6] to ensure no serious discrepancies arose.

Table 1:

Canadian Task Force classification of study designs	
I	Evidence obtained from at least one properly designed randomized controlled trial.
II-1	Evidence obtained from well-designed controlled trials without randomization.
II-2	Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group.
II-3	Evidence obtained from comparisons between times or places with or without intervention; dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category.
III	Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of an expert panel.

Categories for strength of each recommendation	
Category	**Definition**
A	Good evidence to support a recommendation for use
B	Moderate evidence to support a recommendation for use
C	Poor evidence to support a recommendation against use
D	Moderate evidence to support a recommendation against use
E	Good evidence to support a recommendation against use

Clinical grading and diagnosis of SAH

The characteristic symptoms of SAH are sudden, worst-ever headache, emesis, and the development of a painful, stiff neck (meningismus) over several hours. Generally speaking, the smaller the SAH, the fewer the symptoms and signs. A SAH causing sudden headache that then steadily abates without an alteration in consciousness usually corresponds to mild bleeding. In reference to the more severe *rebleeding* from an aneurysm that often follows if the patient remains untreated, mild hemorrhages are sometimes referred to as a "warning" or "sentinel" leaks.

The variable severity of aneurysm bleeding, and the corresponding range of conditions SAH patients present in, is expressed in SAH grading scales derived from a system originated by Botterell and Lougheed at The Toronto General Hospital in the 1950s.[7] In current and commonly used SAH scales such as the modified Botterell and Lougheed scale,[8] and the Hunt and Hess scale[9] grade I represents mild to moderate headache; grade II, severe headache but alert; grade III, drowsy with otherwise minimal neurological deficit; grade IV, comatose; and grade V, moribund with brainstem dysfunction (Table 2). The grading scale devised by the World Federation of Neurological Surgeons is often used in multicentre trials of subarachnoid hemorrhage[10] (Table 2). Additional scoring using the Glasgow Coma Scale is helpful in assessing grades IV and V patients. Any specific focal or lateralizing neurological deficits are also noted.

Table 2: Subarachnoid Hemorrhage Grading Scales

Botterell-Lougheed	
Grade I:	(minimal bleed) alert, no neurological deficit
Grade II:	(mild bleed) alert, minimal neurological deficit such as third nerve palsy, stiff neck.
Grade III:	(moderate bleed) drowsy or confused, stiff neck, with or without neurological deficit.
Grade IV:	(moderate or severe bleed) semi-coma, with or without neurological deficit.
Grade V:	(severe bleed) coma and decerebrate movements.

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

World Federation of Neurological Surgeons		
MFNS Grade	**GCS* Score**	**Motor Deficit**
I	15	absent
II	14-13	absent
III	14-13	present
IV	12-7	present or absent
V	6-3	present or absent

*Glasgow Coma Score

Misdiagnosis of SAH continues to be a significant problem, often with serious consequences. Roughly 25% of patients admitted to neurosurgical units with SAH have suffered a prior hemorrhage that was not recognized when the patient first sought medical attention.[11] Because repeat and more severe hemorrhaging commonly occurs in this group, these patients have a poorer overall prognosis[12,13] than those without a history of prior bleeding. Therefore neurosurgeons must continue to emphasize to emergency and primary care physicians that *SAH must be considered when a headache is sudden in onset, unusual to the patient in terms of its severity and nature, and painful enough to bring it to medical attention.* The spontaneous development of a third cranial nerve palsy (with pupillary involvement) may indicate acute expansion or rupture of usually a carotid artery aneurysm adjacent to the oculomotor nerve.

https://doi.org/10.1017/S0317167100021521 Published online by Cambridge University Press

The investigation of choice to diagnose SAH is unenhanced (noncontrast) computed tomography (CT) of the head[14] (Table 3) (category A recommendation). When performed within a day of aneurysm rupture, CT reveals high-density (white) blood clot in basal subarachnoid cisterns in roughly 95% of patients.[15,16] Patients presenting with a depressed level of consciousness due to a significant SAH uniformly have CT scans positive for blood. As SAH is a medical emergency, it is recommended that patients with suspected acute SAH presenting at a facility without a CT scanner be referred to the nearest institution with a scanner, and preferably also with neurosurgical coverage, as soon as possible[17] (category A). In addition to detecting the presence of SAH, CT scanning also provides an estimate of the origin and extent of the hemorrhage, and it allows recognition of associated intracerebral hemorrhage (ICH), intraventricular hemorrhage (IVH), and hydrocephalus. Rarely, aneurysm rupture will result in the formation of an acute subdural hemorrhage (approximately 2% of patients), due to dissection of blood through the arachnoid membrane into the subdural space.[18] Hence, in the setting of the spontaneous appearance of a subdural hematoma and the coincident presence of subarachnoid blood on CT scan, an underlying ruptured aneurysm should be suspected.

Table 3:

Diagnosis of Subarachnoid Hemorrhage	
Investigation	**Comment/Recommendation category**
computed tomography (CT)	investigation of choice, positive in over 95% of patients within 24 hours of rupture (cat. A)
lumbar puncture	all patients with suspected SAH and CTs negative for hemorrhage (cat. A)
cerebral angiography	as soon as can be performed (cat. B) CT-angiography in emergency situations when available (cat. B)

While CT scanning is strongly recommended first in all patients with suspected SAH, those presenting with acute but mild (grade I) SAH, and those patients investigated several days after SAH may have a normal CT scan. In all cases where SAH is suspected but the CT scan is interpreted as normal by a trained observer, a lumbar puncture should be performed (category A recommendation).

Physicians undertaking a lumbar puncture to diagnose SAH should be aware that this procedure has been reported to precipitate aneurysm rebleeding, although this occurrence is rare.[19] It is also recommended that they be familiar not only with the technique of lumbar puncture, but also with the methods used to distinguish a pre-existing "true" SAH from a traumatic SAH resulting from the lumbar puncture itself.[14] A constant level of thousands of red blood cells per mm^3 of cerebrospinal fluid (CSF) in sequential tubes of collected CSF is suggestive of true SAH, particularly when the CSF supernatant remains xanthochromic after centrifugation. Centrifugation causes sedimentation of intact cellular elements from the CSF, so that yellow pigmentation of the resultant CSF is due to free hemoglobin in solution. This indicates the presence of red blood cells in the CSF for at least several hours prior to the lumbar puncture by which time spontaneous erythrocyte lysis occurred. Clear CSF following centrifugation indicates that only intact erthrocytes were staining the CSF confirming a traumatic tap.

Spectrophotometry is superior to the naked eye in detecting CSF xanthochromia,[20] but this investigation is not available in all hospital emergency laboratories. It should be emphasized that no type of CSF analysis is fail-safe in making the distinction between true and traumatic SAH, and that if any doubt remains in the clinician's mind, a neurosurgical consultation is recommended. In some such instances, direct imaging of the cerebral arteries is the only certain way to exclude a cerebral aneurysm. On the other hand, if both the CT and CSF analysis are normal within several days of suspected aneurysm rupture, then SAH can be confidently ruled out, and cerebral artery imaging is not indicated[14] (category D).

At the present time selective, catheter cerebral angiography remains the current standard for diagnosing cerebral aneurysms causing SAH. Although there are no data in the literature that address this issue directly, cerebral angiography is recommended as soon as it can be safely performed in all patients with spontaneous SAH who are not moribund (category B recommendation). Those patients with unilateral uncal herniation due to a parenchymal hematoma and where the herniation syndrome has been stopped or temporarily reversed by medical treatment to lower intracranial pressure (hyperventilation and mannitol administration) should, whenever possible, undergo immediate angiography (category B recommendation). Most neuroradiologists and neurosurgeons prefer to defer angiography until the following morning if a SAH patient presents in the late evening or night and is neurologically stable. If the patient is in a stable medical and neurological condition, it is considered by many safer to wait until complete, experienced and fresh angiography and surgical teams are available in the morning (category C recommendation).

A promising new diagnostic technique is computed tomographic angiography (CTA).[21-23] A helical CT scanner is used to scan the patient's head following the rapid, power injection of a contrast bolus, and the axial images obtained are then reconstructed to provide three-dimensional vascular anatomical information. The technique is relatively less invasive than catheter angiography, fast, and can provide a multitangential view of the arteries and aneurysm complex, including its relationship to adjacent bony structures. Adjacent cisternal blood does not interfere with the images, although as with conventional angiography only the part of aneurysms filling with contrast agent will be opacified and demonstrated. While this technique is still under development, it appears likely that its sensitivity and specificity compared to the gold-standard catheter angiography will be sufficient to replace the latter at least in emergency situations.

Immediate treatment measures

All aneurysm patients must be protected from acute rebleeding, which is most common in the minutes and hours following initial aneurysm rupture (4.1% in the first 24 hours of the Cooperative Aneurysm Study).[24] Acute arterial hypertension in response to a painful and frightening SAH plays a role in early rebleeding, and it is recommended that patients with suspected SAH be treated with adequate analgesia prior to investigations (category A). It is also recommended that in patients in "good" condition (grades I-III) without evidence of raised intracranial

https://doi.org/10.1017/S0317167100021521 Published online by Cambridge University Press

pressure (ICP) either clinically or on CT, persistent hypertension be lowered pharmacologically with intravenous labetolol or hydralazine (Table 4) (category A). Sublingual or oral antihypertensives are less reliable alternatives, and are not first choice in this setting (category D).

Table 4:

Pharmacological Management of SAH	
Agent(s)	**Comment/Recommendation category**
antihypertensives	intravenous agents (i.e., labetolol, hydralazine) for acute hypertension following SAH unresponsive to analgesia in awake patients (unprotected aneurysm) (cat. A)
anticonvulsants	patients with documented seizure, cortical hemorrhage or infarction, or in coma (cat. B)
antifibrinolytic agents	not recommended (cat. E)
corticosteroids	no evidence to support their use
nimodipine	recommended for all patients until time of discharge (patients in good condition with no evidence of vasospasm) or for 21 days from SAH (cat. A)

Grade IV (semi-comatose) SAH patients have a more than doubled acute rebleeding rate and a higher incidence of severe arterial hypertension. Rebleeding within 24 hours of admission has also been found to correlate with rebleeding prior to admission, high systolic blood pressure, intracerebral or intraventricular hematoma, and those who undergo angiography within 6 hours of the last SAH.[25] These patients frequently have elevated ICP, so that excessive lowering of blood pressure may result in inadequate cerebral perfusion pressure (CPP) and cerebral infarction. In semicomatose or comatose SAH patients, pharmacological lowering of arterial hypertension is not recommended until neurosurgical consultation is obtained and the CPP is monitored (category D). These patients usually require intubation during or following the initial assessment, and prior to angiography. Early ventriculostomy enables treatment of raised ICP, which is sometimes accompanied by clinical improvement, and allows calculation of the CPP for more appropriate blood pressure control.[26]

It is recommended that Grade V (moribund) SAH patients who are either elderly (i.e., > 70 years old), or have obvious vital, deep brain destruction on CT scan receive only compassionate care, or that they are provided only temporary cardiorespiratory support if brain death is imminent and organ donation is being considered (category C). Younger patients who have failing brainstem function in the absence of clear vital brain destruction on CT often undergo ventricular drainage, and further aneurysm treatment is undertaken if their clinical condition improves, for example as demonstrated by the recovery of a localizing motor response. Intractably elevated ICP or poor angiographic filling of the cerebral vasculature on angiography are generally regarded as contraindications to surgery[26] (category B recommendation, grade III evidence). The early management of poor-grade patients with SAH is problematic, however. A recent series of grades IV and V patients treated uniformly with early surgery and aggressive postoperative measures was retrospectively reviewed to determine management results and what factors predicted outcome.[27] As has been the case in previous studies it was found that older age, poorer neurological status, greater amounts of intracranial bleeding and hypodense changes in cerebral parenchyma correlated significantly with worse outcome. However a multivariate analysis of these factors used in a preoperative model of outcome prediction applied to this same patient population correctly predicted favourable outcome (capable of independent life and all self-care) in only approximately 70% of patients. Thus, 30% of patients who went on to make a satisfactory recovery could not be accurately identified using standard poor-prognosis criteria, including age and Glasgow Coma Score (level II-2 evidence). While surgical results in poor-grade patients, compared to those in good-grade patients are unavoidably much poorer, it is possible that the best overall management results for poor-grade patients will be obtained following aggressive surgery and treatment. On the basis of currently available data, it is difficult to offer definitive recommendations regarding the care of poor-grade SAH patients.

Patients whose brainstem dysfunction is due to uncal herniation from a spontaneous, large cortical or subcortical blood clot that by its location is felt likely to be aneurysmal in origin should be treated urgently with intubation, hyperventilation and intravenous mannitol administration (1 g/kg). If herniation can be temporarily reversed with these measures, an angiogram is recommended prior to craniotomy, although under these circumstances an aneurysm can sometimes be identified prior to surgery by rapid sequence axial CT scanning following a bolus intravenous administration of contrast agent,[28] or CTA which was discussed previously.[21-23]

In the initial management phase of SAH, pharmacological treatment is directed at pain, blood pressure and ICP control, as discussed above. There is no proven role for corticosteroids in the treatment of SAH.

Aneurysm repair

Timing of surgery:

The timing of aneurysm surgery has been the subject of considerable neurosurgical debate over the years.[29] Following rebleeding there is an immediate mortality in roughly one-third of good grade patients and one-half of poor grade patients.[30] The advantages of early surgery and aneurysm obliteration, in addition to eliminating the risk of rebleeding, include the possibility of removing subarachnoid blood and thereby reducing the risk of vasospasm,[31,32] as well as allowing more aggressive treatment of symptomatic vasospasm with induced hypertension. Early surgery also avoids to some extent the complications of inactivity forced upon patients awaiting delayed surgery and may contribute to a shorter hospitalization. The disadvantage of early surgery is the possibility of a more swollen brain that, together with clot-laden subarachnoid cisterns, makes exposure of the aneurysm more difficult and the risk of intraoperative complications greater, although this latter point has recently been disputed in a single-institution, retrospective cohort study.[33] As well, there is a concern that early surgery might, by preventing fatal rehemorrhages, preserve the life of patients destined to remain in poor neurological condition, thereby decreasing mortality at the expense of increased morbidity.

https://doi.org/10.1017/S0317167100021521 Published online by Cambridge University Press

The International Cooperative Study on Timing of Aneurysm Surgery was a prospective, nonrandomized study that examined the outcome of 3521 patients with acutely ruptured aneurysms that were treated with surgical clipping at various time intervals following primary hemorrhage, according to the philosophy and preference of the treating surgeon (grade II-2 evidence).[34,35] As expected, it was found that early surgery conferred significant protection from rebleeding, but there was no significant difference in overall outcome related to timing of surgery. The group of patients who had surgery planned for days 7 through 10 had the least favourable outcome and the highest mortality rate, although this trend was not significant. Following publication of this report, an analysis of just those patients treated in North American centres revealed that early-surgery patients in this subgroup had significantly improved rates of good recovery as compared with the delayed-surgery patients.[36]

A single prospective, randomized study on the timing of operation for ruptured supratentorial aneurysms examined 216 grades I-III patients (grade I evidence).[37] Operation within 3 days of SAH was associated with a trend toward better overall results, and deaths due to rebleeding did not occur in the early group. As in the Cooperative Study, operation during an "intermediate" period, 4-7 days after SAH, was associated with more unfavourable outcomes, and this difference was significant when this group was compared to the early surgery group.

A rigid policy of early versus late aneurysm surgery cannot be defended at this time. In general, it is recommended that patients with acute SAH undergo aneurysm repair as early as possible following rupture, especially if their clinical condition is clearly compatible with a satisfactory neurological outcome (clinical grades I-III and selected grade IV patients) (category B recommendation, grade II-1 evidence). One small randomized trial indicated that early clot evacuation and aneurysm clipping for patients with intracerebral hemorrhages may be particularly valuable in improving outcome[38] (grade II-1 evidence). Emergent surgery for grade V patients with peripheral clots causing uncal herniation is sometimes warranted, as discussed previously[28,39] (category B recommendation, grade III evidence).

It appears that the timing of aneurysm surgery alone is not a strong determinant of outcome following aneurysm rupture, and some circumstances might call for a more delayed intervention. It is recommended that patients harboring ruptured aneurysms that by virtue of their size, morphological complexity, or anatomical location, are considered difficult to access surgically, especially in the acute stage of SAH when the brain is intolerant of prolonged or severe retraction, should be treated by delayed operation or endovascular techniques (next section) (category B recommendation, grade III evidence). The decision that early surgery is excessively dangerous in any individual patient rests with the treating surgeon. It is recommended that surgery during the "vasospastic interval", days 4-10 following SAH, be undertaken with caution, owing to the possibility of aggravating latent cerebral ischemia (category B, grade II-2 evidence). Surgery during this interval is especially precarious in the presence of significant cerebral vasospasm determined either by angiography or by cerebral blood flow studies.

Endovascular aneurysm treatment:

Currently, endovascular aneurysm occlusion is most often undertaken with thrombogenic "microcoils" deposited into the aneurysm dome through an arterial catheter.[40-49] Performed in the neuroradiology suite, general anaesthesia is sometimes required to obtain a motionless patient, necessary for accurate and safe catheter and coil placement. The Guglielmi detachable coil (GDC) (Target Therapeutics, Freemont, CA, USA) system, the only one currently approved for use in Canada, uses delicate platinum wires of several different calibers and variable lengths (when straightened) that form different sized coils. These soft coils easily straighten to fit through a microcatheter and then reform their helical shape once advanced past the tip of the microcatheter into the aneurysm dome. They are detached from their stainless steel delivery wire atraumatically with an electrolytic current (1 to 2 mA) passed through the guidewire which erodes a noninsulated solder connection between the delivery wire and coil. The number of coils required to completely occlude an aneurysm depends on the aneurysm size.

Endovascular treatment of aneurysms with GDC coils requires a specially trained interventional neuroradiologist or neurosurgeon. A combined analysis of selected series provided by the manufacturer (and reporting the best results in the literature) suggests that in expert hands the complication rates for the two major risks of the procedure, hemorrhage and arterial occlusion, to be approximately 6% and 2%, respectively. Failure to completely occlude the aneurysm is a more common problem, and is usually a result of a wide aneurysm neck (greater than approximately 4 mm in diameter) associated with a larger aneurysm, that prevents packing of the dome with coils. Dense coil packing, necessary for complete aneurysm obliteration, is not possible when a wide aneurysm orifice permits coil herniation into the parent artery. Among the various reported series of patients that have undergone GDC coiling, the percentage of incomplete occlusions depends on the number of patients with large aneurysms that were treated. For example, in a recently reported series of 33 basilar tip aneurysms where 17 were greater than 10 mm in diameter, only 7 (21%) could be completely occluded by an experienced team of neurointerventionalists.[50] In contrast, it has been reported that over 80% of small or "small-necked" aneurysms can be completely occluded with GDC coils in certain centres[51-53] (level II-2 evidence). An aneurysm remnant following GDC treatment has a continued risk of bleeding as well as a recognized propensity to enlarge, owing to progressive compaction of the intraaneurysmal coils with pulsatile blood flow (the "water-hammer" effect). Bridging the entire neck area with a dense meshwork of coils appears to be a determining factor in preventing early aneurysm regrowth, although long-term follow-up of even completely occluded aneurysms is not yet available. It is quite possible that partial coil obliteration of the aneurysm dome reduces the rebleeding risk among those patients presenting with SAH, and some anecdotal evidence would suggest this (level III evidence).[50] This may then provide an opportunity for a more delayed intervention, including aneurysm neck-clipping. However, repair of aneurysms partly occluded with coils may be impeded by the presence of the non-compressible aneurysm coils and associated thrombus.[54] Alternatively, a distal bypass conduit can be constructed followed by parent vessel occlusion.

The technique of aneurysm occlusion with GDC coils has opened up new opportunities in aneurysm treatment. In North America their use until now has been primarily in patients with

https://doi.org/10.1017/S0317167100021521 Published online by Cambridge University Press

aneurysms that are considered dangerous to clip, or in patients who either are considered unfit for surgery or refuse surgery. At present it is recommended that these continue to be the indications for this technique in those centres where it is available (category B, level III evidence). The use of this technique in broad-necked aneurysms where it is not possible to achieve a complete occlusion is controversial. It is unlikely that the results of this procedure in general practice will, at least initially, match the very good results reported from centres with already a broad experience with the technique. Unless future randomized trials demonstrate that the morbidity and mortality associated with endovascular occlusion are less than those associated with microsurgical clipping, and that aneurysm occlusion with coil embolization results in long-term cure over many years, surgical repair will remain the recommended first treatment choice for intracranial aneurysms (Table 5).

Table 5:

Surgical Methods of Aneurysm Repair

Method	Comment/Recommendation category
clipping of aneurysm neck	treatment of choice (cat. A)
proximal parent artery ligation	sometimes indicated, effective (cat. A)
aneurysm "trapping"	sometimes indicated, effective (cat. A)
aneurysm "wrapping or "coating"	not recommended as sole treatment (cat. D)

Proximal artery occlusion, antifibrinolytics, and aneurysm wrapping or coating:

In selected patients with sufficient collateral flow, or in those patients where collateral flow has been provided with a surgically created bypass graft,[55] occlusion of the parent artery proximal to a very large or giant aneurysm is an acceptable method of aneurysm treatment[46,47,56] (level III evidence). Carotid ligation in the neck alone is not recommended, as the rebleeding rate may not be significantly lowered with this form of treatment[57] (category D, level III evidence). Endovascular detachable balloon,[58] or more recently GDC occlusion[49] and sacrifice of the immediately proximal parent artery is simpler and probably more efficacious than an open surgical occlusion in many instances. It is recommended that this form of treatment be followed by repeat angiography to ensure complete aneurysm thrombosis. Any continued aneurysm filling signals a persistent risk of rebleeding, and in such cases aneurysm trapping is recommended (category A, level III evidence).

The administration of antifibrinolytic agents, such as epsilon aminocaproic acid, to retard subarachnoid clot lysis and prevent aneurysm rebleeding until delayed surgery is undertaken, is not recommended. Nonrandomized and randomized trials have shown that while these agents reduce the rebleeding rate of acutely ruptured aneurysms, this benefit is offset by an increased rate of cerebral infarction, so that overall outcome is not improved[49-57] (category E recommendation, level I evidence). Similarly, coating or wrapping an aneurysm sac with a material to strengthen its wall or induce a strengthening fibrotic reaction does not completely protect from rebleeding and is not recommended for definitive aneurysm repair[59,60] (category D, level III evidence).

Perioperative care of SAH patients

Patient monitoring and the aneurysm team:

It is recommended that all pre- and postoperative patients with impaired LOC be treated in an intensive care unit (ICU) or close-monitoring unit.[61] While neurosurgeons play a central role in the management of SAH, "aneurysm teams" are being created in many centres to collaborate on individual patient treatment. Such teams are typically made up of neurosurgeons, neurologists, interventional neuroradiologists, intensive care physicians, and critical care nurses.

Delayed surgery and the SAH "routine":

Patients in whom definitive aneurysm clipping is being delayed should be managed in a quiet environment, with adequate analgesia and sedation, a bowel routine to reduce straining, and normotension with normo- to slight hypervolemia. Drug treatment during this period is the same as in the postoperative period described below.

Monitoring and fluids:

All SAH patients should be monitored with an indwelling arterial line initially, and a central venous line should be considered in any patient where volume status is a special concern, such as those patients with large volume SAHs at high risk of developing vasospasm. Pulmonary artery catheters are reserved for patients with cardiopulmonary instability or severe symptomatic vasospasm. Patients should receive isotonic fluids in sufficient amounts to maintain mild hypervolemia, and packed red blood cell infusions are given as necessary to avoid anemia[62] (category B evidence, level III evidence). Hypovolemia and hypotonic intravenous fluids, which can aggravate cerebral ischemia and swelling, are carefully avoided.[63] During the acute phase of their illness patients should have complete blood counts, serum electrolytes, and arterial blood gases or oxygen saturation levels measured at least once daily.

Pharmacological management of SAH:

Risk factors that have been identified for seizures following aneurysm rupture include an MCA aneurysm location, parenchymal hemorrhage or infarction, a history of hypertension, persistent neurological deficit, and a young age[64-68] (level II-2 evidence). Anticonvulsants are recommended at least for the short-term for any patient with a documented seizure in the acute phase of SAH, which was recorded in as many as one-quarter of patients in one series (Table 4).[69] Seizures must be distinguished clinically from episodes of rebleeding, which they can closely resemble. Although prophylactic anticonvulsants have not been proven effective following SAH in a randomized trial, they should be considered in patients with significant cortical damage or in coma (category B). Phenytoin is the recommended parenteral anticonvulsant under these circumstances, given as a 15 mg/kg loading dose followed by 3 to 5 mg/kg/day in divided doses. If anticonvulsants are prescribed to aneurysm patients, then therapeutic serum levels of the drug should be ensured.

Corticosteroids have no clearly proven role following SAH, and are not recommended for routine use at this time (category D).

Six randomized controlled trials[70-75] have shown that the calcium antagonist nimodipine has a modest but significant

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beneficial impact on clinical outcome following aneurysmal SAH, although its mechanism of action is uncertain. Two meta-analyses have also indicated drug efficacy.[76,77] The dosage of nimodipine is 60 mg every 4 hours either orally or via a nasogastric tube. It is recommended for all SAH patients until either the time of discharge from hospital (with the patient in good condition and with no evidence of vasospasm) or for twenty-one days for patients hospitalized for this entire period of time with persistent neurological impairment (category A recommendation, level I evidence). It should be given with caution to patients with congestive heart failure or hepatic insufficiency due to the risk of aggravating these conditions.

Vasospasm:

Cerebral vasospasm is delayed-onset arterial narrowing following SAH, occurring usually between the fourth and fourteenth day following aneurysm rupture, but peaking in incidence and severity between the seventh and eleventh day. Cerebral ischemia due to vasospasm can lead to brain infarction, permanent disability and death. Vasospasm is an arterial response to subarachnoid blood clots, and patients at greatest risk for severe vasospasm are those with thick persistent clots evident on CT scan.[78]

There is evidence that the intraoperative, intracisternal administration of the fibrinolytic agent recombinant tissue plasminogen activator (rt-PA) promotes clearance of subarachnoid clot, and significantly reduces severe angiographic vasospasm[79,80] (level I evidence). However, this treatment can induce severe aneurysm rebleeding if the aneurysm has been incompletely repaired prior to treatment,[80] and it has not been proven to significantly improve outcome following SAH in a large series of patients.

When available, SAH patients can undergo daily transcranial Doppler (TCD) monitoring before and throughout the vasospastic interval. An increase in mean blood flow velocities over 150 cm/sec as measured by TCD is suggestive of significant vasospasm[81-84] (level III evidence). Patients who exhibit early symptoms of cerebral ischemia and/or have a worrisome elevation of TCD velocities during the vasospastic interval should receive increased intravenous fluid administration, including colloid infusions, to achieve hypervolemia (category B recommendation, level III evidence). At this time the synthetic volume-expander hetastarch is not recommended for SAH patients, since it has been shown to induce coagulopathy through an unknown mechanism.[85]

Patients who develop symptomatic vasospasm should also be treated with hypervolemia and induced hypertension in an attempt to improve cerebral blood flow through the vasospastic arteries. Although recommended, the use of "triple-H therapy" (hypervolemia, hemodilution and hypertension) has never been confirmed efficacious in either a randomized or nonrandomized trial, and it is not known what component of the therapy, hypertension, hypervolemia, or hemodilution, is the most important in reversing cerebral ischemia.[86-88] Significant hemodilution risks lowering oxygen delivery, and therefore it is recommended that the hematocrit be monitored and maintained above 35%.[89,90] Inotropes such as dopamine or dobutamine are used, and if the neurological deficit is profound, fails to improve, or worsens despite initial treatment, and additional hemodynamic treatment is necessary, then a pulmonary artery catheter is indicated (category B recommendation). In order to maximize cerebral blood flow, a pulmonary capillary wedge pressure in the range of 14 to 16 mm Hg should be sought,[91] as is a systolic blood pressure of 180 to 200 mm Hg using various combinations of dopamine, dobutamine, norepinephrine and occasionally phenylephrine. When triple-H therapy is instituted, and especially when a pulmonary artery catheter has been inserted, very close patient monitoring is required to avoid complications such as pulmonary edema, heart failure and infarction, pulmonary artery rupture, pneumothorax, and catheter-related sepsis.[92,93]

If these hemodynamic parameters are not easily met, or if they do not result in reversal of the ischemic neurological deficit within approximately 30 minutes, it is recommended to proceed directly to endovascular treatment, providing this therapy is available at the treating institution (category A recommendation, level II-3 evidence). This treatment consists of cerebral transluminal balloon angioplasty, sometimes combined with intraarterial papaverine infusions.[94-97] Intra-arterial therapy is also preferred over extreme hypertensive therapy in any patient possessing additional unruptured and unclipped aneurysms. Transluminal balloon angioplasty is successful in improving ischemic deficits in about three-quarters of patients.[94-97] This treatment is not recommended for patients whose ruptured aneurysms have not been repaired (due to the risk of aneurysm rebleeding), and those with infarction evident on CT scan (due to the risk of hemorrhage into the new infarct).

Summary statement: treatment of vasospasm

To date, there is no treatment which has been proven in controlled trials to improve outcome following SAH through a prevention or reversal of vasospastic arterial narrowing alone (Table 6), although case-series would suggest that both triple-H therapy and balloon angioplasty are capable of reversing ischemia and preventing infarction in individual case situations. More recent large aneurysm series demonstrating a trend towards less vasospasm-related morbidity and mortality compared to historical controls provides anecdotal evidence that these modern therapies are having a favourable impact on overall outcome.[26,98-101]

Table 6:

Quality of evidence supporting various therapies for cerebral vasospasm

Treatment	Prevents/reverses angiographic vasospasm	Prevents/reverses clinical vasospasm	Improves Overall Outcome
cisternal fibrinolysis (rt-PA)	grade I	no evidence	no evidence
"Triple-H" therapy (see text)	no evidence	grade III	no evidence
Transluminal balloon angioplasty	grade II	grade III	no evidence

Intraventricular hemorrhage and hydrocephalus:

In general, it is recommended that any ventricular drain inserted before or at the time of surgery be left postoperatively as long as drainage is required to maintain normal ICPs. Acute hydrocephalus is seen in 15-30% of patients.[102-108] If external drainage is required beyond 7 to 10 days, then either replacing

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the catheter with a ventriculoperitoneal shunt or another external catheter on the opposite side is recommended because of the potential risk of infection[109] (category B, level III evidence).

There is uncontrolled evidence that severe intraventricular hemorrhage causing persistent ventricular enlargement and contributing to elevated ICPs in the postoperative phase can be rapidly lysed with small doses of fibrinolytic agent rt-PA administered through the ventricular catheter[110-112] (level III evidence). This treatment consists of 4 mg of rt-PA administered directly into the lateral ventricles is followed by alternate-hourly or continuous CSF drainage against low resistance (approximately 2 cm pressure). CT scans and rt-PA injections are repeated daily until the CSF pathways are opened, which generally occurs within one to three days. In addition to facilitating ICP management, intraventricular fibrinolytic treatment maintains ventricular catheter patency, a benefit, but the efficacy of this treatment in improving patient outcome has not been tested in a randomized trial.

Other postSAH complications:

Cardiac, pulmonary and infectious complications frequently occur in patients recovering from SAH. Serum sodium imbalance is relatively common, and most often takes the form of mild to moderate hyponatremia. Hyponatremia following aneurysmal SAH is usually due to a salt-wasting syndrome rather than the syndrome of inappropriate antidiuretic hormone secretion (SIADH).[113-115] Whereas fluid restriction is the treatment for SIADH, this is inappropriate for salt wasting, since hypovolemia can aggravate vasospastic cerebral ischemia. If the hyponatremia is mild, it should be simply followed, and isotonic fluid administration continued. However, if the serum sodium falls < 125 mEq/L and becomes symptomatic, it is recommended that hypertonic saline solutions (i.e., 3, 5, or 7%) be administered to maintain normovolemia.

Diabetes insipidus can also occur following SAH and aneurysm surgery, and is recognized by high urine output (> 300 ml/hour) prior to actual hypernatremia. Fluid balance is carefully followed and the diuresis, if severe or maintained, should be controlled with subcutaneous DDAVP injections.

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