

Patterns in neurosurgical adverse events: open cerebrovascular neurosurgery

JUDITH M. WONG, M.D., M.P.H.,¹⁻³ JOHN E. ZIEWACZ, M.D., M.P.H.,⁴ ALLEN L. HO, B.A.,⁵ JAYKAR R. PANCHMATIA, M.P.H., M.B.B.CHIR., M.R.C.S.,⁶ ALBERT H. KIM, M.D., PH.D.,⁷ ANGELA M. BADER, M.D., M.P.H.,^{1,2,8} B. GREGORY THOMPSON, M.D.,⁴ ROSE DU, M.D., PH.D.,³ AND ATUL A. GAWANDE, M.D., M.P.H.^{1,2,9}

¹Department of Health Policy and Management, Harvard School of Public Health; ²Center for Surgery and Public Health and Departments of ³Neurosurgery, ⁸Anesthesiology, Perioperative and Pain Medicine, and ⁹Surgery, Brigham and Women's Hospital; and ⁵Harvard Medical School, Boston, Massachusetts;

⁴Department of Neurosurgery, University of Michigan Health Systems, Ann Arbor, Michigan; ⁶Department of Orthopaedics and Trauma, Heatherwood and Wexham Park Hospitals, London, United Kingdom; and

⁷Department of Neurosurgery, Barnes-Jewish Hospital, Saint Louis, Missouri

Object. As part of a project to devise evidence-based safety interventions for specialty surgery, we sought to review current evidence concerning the frequency of adverse events in open cerebrovascular neurosurgery and the state of knowledge regarding methods for their reduction. This review represents part of a series of papers written to consolidate information about these events and preventive measures as part of an ongoing effort to ascertain the utility of devising system-wide policies and safety tools to improve neurosurgical practice.

Methods. The authors performed a PubMed search using search terms “cerebral aneurysm”, “cerebral arteriovenous malformation”, “intracerebral hemorrhage”, “intracranial hemorrhage”, “subarachnoid hemorrhage”, and “complications” or “adverse events.” Only papers that specifically discussed the relevant complication rates were included. Papers were chosen to be included to maximize the range of rates of occurrence for the reported adverse events.

Results. The review revealed hemorrhage-related hyperglycemia (incidence rates ranging from 27% to 71%) and cerebral salt-wasting syndromes (34%–57%) to be the most common perioperative adverse events related to subarachnoid hemorrhage (SAH). Next in terms of frequency was new cerebral infarction associated with SAH, with a rate estimated at 40%. Many techniques are advocated for use during surgery to minimize risk of this development, including intraoperative neurophysiological monitoring, but are not universally used due to surgeon preference and variable availability of appropriate staffing and equipment. The comparative effectiveness of using or omitting monitoring technologies has not been evaluated.

The incidence of perioperative seizure related to vascular neurosurgery is unknown, but reported seizure rates from observational studies range from 4% to 42%. There are no standard guidelines for the use of seizure prophylaxis in these patients, and there remains a need for prospective studies to support such guidelines.

Intraoperative rupture occurs at a rate of 7% to 35% and depends on aneurysm location and morphology, history of rupture, surgical technique, and surgeon experience. Preventive strategies include temporary vascular clipping.

Technical adverse events directly involving application of the aneurysm clip include incomplete aneurysm obliteration and parent vessel occlusion. The rates of these events range from 5% to 18% for incomplete obliteration and 3% to 12% for major vessel occlusion. Intraoperative angiography is widely used to confirm clip placement; adjuncts include indocyanine green video angiography and microvascular Doppler ultrasonography. Use of these technologies varies by institution.

Discussion. A significant proportion of these complications may be avoidable through development and testing of standardized protocols to incorporate monitoring technologies and specific technical practices, teamwork and communication, and concentrated volume and specialization. Collaborative monitoring and evaluation of such protocols are likely necessary for the advancement of open cerebrovascular neurosurgical quality.

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KEY WORDS • surgical safety • adverse events • perioperative care

PROGRESS in the science of improving surgical safety has been notable in recent years. Methods for evaluating outcomes have been developed and de-

Abbreviations used in this paper: ICG = indocyanine green; MEP = motor evoked potential; SAH = subarachnoid hemorrhage; SSEP = somatosensory evoked potential.

ployed,^{15,27,28,41,70,76,114} and the resulting data have been used to investigate patterns of errors and complications. From these findings, solutions have been designed and tested with sometimes striking improvements, whether based on simple process tools like checklists^{15,16,34,113} or technological changes.^{29,86,110} Neurosurgery is a high-risk surgical specialty and is beginning to pursue systematic,

nationwide approaches to measuring and improving outcomes and developing evidence-based guidelines for a variety of neurosurgical disorders. As part of a project funded by the US Agency for Healthcare Research and Quality to devise evidence-based checklists and protocols for specialty surgery, we sought to review current evidence in neurosurgery concerning the frequency of adverse events in practice, their patterns, and the state of knowledge about how to improve them. We hypothesized that this consolidation of existing data, even if commonly known to neurosurgeons, will not only highlight the need for system-wide policies and safety tools to improve neurosurgical practice but will inform future efforts to develop and implement these tools and policies. This document reviews such evidence for open cerebrovascular neurosurgery.

Much of the data describe adverse events related to surgery and perioperative care for patients with ruptured aneurysms and SAH, as these patients are the most severely ill. However, many of the same precautions are taken for elective procedures for the treatment of these and other vascular entities even though these procedures are performed under substantially more controlled conditions.

Scope of the Problem

Approximately 2% of the general population has intracranial aneurysms, based on autopsy and angiographic studies.¹⁵ Many of these aneurysms have a low risk of hemorrhage;¹⁵ however, approximately 30,000 people suffer catastrophic aneurysmal SAH in the US each year, with an incidence of 2–23 per 100,000 person-years.^{9,38,53} The indications for treatment of unruptured aneurysms remain controversial but depend on aneurysm size, location, and morphology; age of the patient; family and personal history of aneurysm rupture; and experience and availability of microvascular neurosurgeons and neurointerventionalists.^{47,115} According to data from the National Inpatient Sample, 62,820 aneurysms were treated with open surgical clipping between 2002 and 2007 (<http://hcupnet.ahrq.gov/Hcupnet.jsp>).

The perioperative morbidity and mortality rates for aneurysm surgery vary depending on a variety of patient and aneurysm characteristics. According to 2 meta-analyses, for patients with unruptured aneurysms the morbidity rate ranges from 4% to 11% and the mortality rate from 1% to 3%.^{44,80} For patients with ruptured aneurysms, perioperative outcome is inexorably linked to hemorrhage severity, making assessment of such complication rates difficult.⁹ Regardless, the most common adverse events that occur following, but not necessarily as the result of, open cerebrovascular surgery are hemorrhage-related hyperglycemia, cerebral salt-wasting syndrome, new cerebral infarction, perioperative seizure, intraoperative rupture, incomplete aneurysm obliteration, major vessel occlusion, failure to secure the rupture site, and other medical adverse events (Table 1). Many of these events are related to the severity of intracranial hemorrhage and are not a direct result of surgery. Some, such as incomplete aneurysm obliteration, may represent an intentional strategy to

prevent adverse consequences such as cerebral infarction. We nonetheless present them here to remain as comprehensive as possible when designing targeted safety tools.

Methods

We performed a PubMed search of the English literature using the search terms “cerebral aneurysm,” “cerebral arteriovenous malformation,” “intracerebral hemorrhage,” “intracranial hemorrhage,” “subarachnoid hemorrhage,” AND “complications” or “adverse events.” This series of papers reflects our efforts to encompass all of neurosurgery broadly; thus we describe here the most commonly occurring events in cerebrovascular surgery. We have chosen the surgical treatment of SAH and aneurysms, the conditions most commonly treated by vascular neurosurgeons, to represent the field and to focus the review. Only papers that specifically discussed the relevant complication rates were included. Papers were selected to maximize the range of rates of occurrence for the reported adverse events rather than to include all possible studies. We did not impose any threshold of minimum patients or publication year; however, we attempted to choose series that were representative of the most common complications.

Hemorrhage-Related Hyperglycemia

Patients with SAH are at increased risk of perioperative hyperglycemia, with an incidence of 27% to 71%.^{5,60} Recent data link serum glucose levels to neurological outcome. Several observational studies suggest an association between elevated intraoperative and/or perioperative glucose levels and subsequent cognitive impairment and decreased gross neurological function following surgery for ruptured aneurysm(s).^{49,50,60,75} A small, prospective randomized pilot study found lower infection rates with aggressive compared with standard glycemic control but was not sufficiently powered to detect any difference in mortality or functional outcome.¹¹ Another observational study found an association between inpatient hyperglycemia and increased risk for vasospasm.⁵ Although close monitoring of perioperative serum glucose is currently recommended in other fields,¹⁰⁸ emerging data suggest that tight glucose control may actually be harmful to the injured brain.¹⁰⁵ There is no prospective, randomized trial to evaluate tight glycemic control with outcomes in neurosurgery; thus no standard guidelines are currently recommended.

Cerebral Salt-Wasting Syndrome

Hyponatremia is the most frequently occurring electrolyte abnormality in clinical medicine,¹² and it is particularly common among neurosurgical patients, with an estimated prevalence of 34% to 57% in patients with SAH.^{33,98} This patient population in particular experiences increased morbidity in the setting of hyponatremia.⁸⁴ Data from one retrospective study of patients with SAH suggest an association between hyponatremia and increased risk for cerebral infarction compared with normonatremic patients.³³ A more recent observational study

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TABLE 1: Frequency of adverse events reported in cerebrovascular surgery*

AE w/ Authors & Year	Sample Size (no. of cases)	Aneurysm Rupture Status	Frequency (%)
hemorrhage-related hyperglycemia			
Badjatia et al., 2005	352	ruptured	71
McGirt et al., 2007	97	ruptured	27
cerebral salt-wasting syndrome			
Sherlock et al., 2006	316	ruptured	57
Hasan et al., 1990	208	ruptured	34
new cerebral infarction			
Rabinstein et al., 2004	143	ruptured	40
Umredkar et al., 2010	174	ruptured	39
perioperative seizure			
Shaw & Foy, 1991	252	ruptured	42
Rhoney et al., 2000	95	ruptured	4
intraoperative rupture			
Sandalcioglu et al., 2004	169	ruptured	35
Schramm & Cedzich, 1993	222	ruptured	27
Batjer & Samson, 1986	307	mixed	19
Elijovich et al., 2008	711	ruptured	19
Fridriksson et al., 2002	355	mixed	18
Leipzig et al., 2005	1694	mixed	7
incomplete aneurysm obliteration†			
Molyneux et al., 2002	1012	ruptured	18
Kivisaari et al., 2004	808	mixed	12
Johnston et al., 2008	706	ruptured	8
Macdonald et al., 1993	78	mixed	8
McLaughlin & Bojanowski, 2004	143	ruptured	5
major vessel occlusion			
Macdonald et al., 1993	78	mixed	12
Kivisaari et al., 2004	808	mixed	5
Fridriksson et al., 2002	355	mixed	3
failure to secure rupture site			
Molyneux et al., 2002	1012	ruptured	6
Macdonald et al., 1993	78	mixed	4
Kivisaari et al., 2004	808	mixed	3
McLaughlin & Bojanowski, 2004	143	ruptured	1
other medical adverse events			
Fridriksson et al., 2002	355	mixed	17
Molyneux et al., 2002	1012	ruptured	2

* AE = Adverse Event.

† Includes both intentional and unintentional cases.

failed to corroborate these data, however.⁷⁸ Aggressive intravenous fluid and/or mineralocorticoid repletion reduces the incidence of hyponatremia and hypovolemia,^{65,100} but no controlled trials exist to correlate this correction with decreased risk for cerebral ischemia.

New Cerebral Infarction

Cerebral infarction associated with SAH is well-documented, with a reported incidence of approximately 40%.^{81,107} This rate is no better than reports from 25 years ago in the original Cooperative Aneurysm Study.¹ Occur-

rence of early infarct varies with clinical and radiographical grade and nuances of surgical technique, whereas late infarct is related mostly to vasospasm.¹⁰⁷ Patients with cerebral infarction after SAH are much less likely to make a good recovery than those without.^{81,82,107}

There are many causes of new infarction after SAH. Many result directly from the initial hemorrhage or subsequent ICP elevation.^{17,94,99} These are largely unavoidable. Many late infarcts result from vasospasm. Prevention of these spasm-related infarcts includes intensive critical-care management with goal-directed hyperten-

sion, hypervolemia, and hemodilution as described in the literature.^{42,67,90,109} Vasospasm treatment and stroke prevention also include angiographic intervention at many institutions.^{10,43,83}

The proportion of new infarcts that can be attributed directly to surgery is unknown, but it is likely a small fraction. Many techniques are employed during surgery to minimize the risk of this development. Intraoperative neurophysiological monitoring for cerebral aneurysm surgery classically consists of some combination of MEPs and SSEPs.³⁰ Other intraoperative measures such as Doppler ultrasonography, electroencephalography when possible, and electrocorticography have also been employed with some benefit.^{18,71} Such monitoring is primarily used to detect early and potentially reversible ischemic or mechanical damage, with the intent of altering surgical strategy to minimize iatrogenic neurological deficit.^{22,36,63} Monitoring of SSEPs is particularly useful during temporary vessel occlusion (discussed in a subsequent section), as alterations in SSEP are reversible and associated with good neurological outcome when promptly corrected.⁹⁶ Randomized trials of this technique do not exist and may not be warranted given the plethora of supporting data. The existing studies have led monitoring to be widely recommended as a technique to prevent postoperative infarction. However, it is not universally used due to variable availability of appropriate staffing and equipment as well as to surgeon preference.

Perioperative Seizure

The incidence of perioperative seizure related to vascular neurosurgery is unknown, but reported values from observational studies range from 4% to 42% in patients undergoing craniotomy for aneurysm.^{56,87,97} This incidence is thought to be declining with the maturation of microsurgical techniques.⁷ The use of perioperative seizure prophylaxis is common but variable. To date, no randomized trials have evaluated use or duration of seizure prophylaxis following craniotomy for aneurysm. Existing data suggest reduction in immediate postoperative seizure rate but are conflicting regarding longer-term seizure reduction and functional outcome.⁸⁹ The reason for this observation remains unclear but is supported in other studies of prophylactic seizure therapy for non-aneurysmal intracranial hemorrhage.^{62,68,89} There are no standard guidelines for the use of seizure prophylaxis in this patient population, and there remains a need for strong prospective and randomized studies to support such guidelines.

Intraoperative Rupture

Intraoperative rupture (IOR) is an unexpected and potentially catastrophic complication of aneurysm surgery.¹³ Its incidence ranges from 7% to 35% in observational series and depends on aneurysm location and morphology, history of rupture, surgical technique, and surgeon experience.^{8,21,26,52,93,95} Whether its occurrence portends worse prognosis remains unclear. Some limited retrospective data suggest no association between IOR and outcome,⁹³ while other data suggest a negative effect. One retrospective study of 307 consecutive aneurysm procedures found

a significant association between IOR and poor outcome.⁸ The multiinstitutional CARAT study demonstrated a 19% risk of IOR, with perioperative death or disability in the IOR group almost double that of the group without IOR.²¹ Other authors suggest that rapid IOR control, reflecting the team's level of preparation, is more important than its incidence in determining outcome.⁹⁵

The use of temporary vascular clipping may help to prevent intraoperative rupture by facilitating dissection around the aneurysm and parent vessel reconstruction.¹⁰⁴ It remains unknown how long a major vessel may be safely occluded before irreversible ischemia results. Data from retrospective studies suggest a maximum of 20 minutes for temporary clipping depending on the artery involved, with patients over 60 years of age or those with more severe Hunt and Hess grades even more susceptible to ischemic changes.^{72,92} In a prospective, uncontrolled study of a series of 126 cases in which temporary clipping was performed, occlusion time greater than 20 minutes was corroborated as an independent predictor of postoperative infarct, even with induced hypothermia and hypertension, and intravenous mannitol administration during temporary clipping.⁷³ Some authors advocate brief occlusion times followed by reperfusion;⁹ however, this practice is debated given that multiple occlusion-reperfusion cycles may actually worsen ischemic injury.¹⁰⁴

Induced hypothermia and barbiturate neuroprotection may prevent or mitigate ischemic events during aneurysm surgery, particularly during temporary clipping.⁵⁹ While animal studies suggest both long- and short-term benefit,^{88,111,112,118} prospective randomized trials in humans have failed to show convincing data.^{35,106}

No prospective, randomized studies exist to compare surgery with temporary occlusion, without temporary occlusion, and with multiple shorter episodes of occlusion followed by intermittent reperfusion. Use of temporary clipping varies by aneurysm morphology, vascular anatomy, and surgeon preference and is not recommended in formal guidelines, but it is considered by most to be an important adjunct to open cerebrovascular neurosurgery.

Similar to intraoperative monitoring, the use of temporary clipping is not conducive to guidelines or the design of safety tools. However, targeted safety interventions should include preparation for such interventions long before the start of the procedure. Practices such as intraoperative monitoring and temporary clipping require timely and coordinated efforts from all members of the surgical team, including the surgeon, anesthesiologist, and nursing staff. Preparation therefore requires extensive planning, which should occur before the procedure rather than during an emergent situation such as early rupture before proximal control has been obtained.

Incomplete Aneurysm Obliteration, Major Vessel Occlusion

Technical adverse events directly involving application of the aneurysm clip include incomplete aneurysm obliteration and parent vessel occlusion. While many of these events are intentional and unavoidable due to the vascular anatomy, some are unintentional and/or unexpected. These occurrences depend largely on aneurysm morphology, surrounding vessel anatomy, rupture sta-

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tus, and surgical experience, and the rates range from 5% to 18% for incomplete obliteration and from 3% to 12% for major vessel occlusion, according to observational studies using postoperative angiography.^{39,45,54,61,64} The incomplete obliteration incidence of 18% reported in ISAT is likely an overestimate, given that only half of the surgically treated patients underwent postoperative angiography and the majority of these angiographic studies were performed between 2–12 months after surgery.⁶⁴ Similarly, in the study by McLaughlin and Bojanowski,⁶¹ postoperative imaging was not performed in all cases. Fridriksson et al.²⁶ report the lowest rate of vessel occlusion, but their analysis was performed in the setting of intraoperative complications, and the mode of detection was not specified.

Intraoperative angiography is widely used to confirm parent vessel and branch patency as well as aneurysm obliteration during the procedure, and the results often alter the surgical course.^{3,46,58,69,77} Intraoperative angiography is particularly useful in the setting of complex anatomy and/or giant aneurysm.^{23,74} Adjunctive modalities include ICG video angiography and microvascular Doppler ultrasonography;^{2,6,14,24,40,57,79,101} benefit has been shown for both in small uncontrolled series but has not yet been confirmed in large randomized trials. The technology of CT angiography is improving, and this modality may also be used in the postoperative setting, particularly with aneurysms in the anterior circulation, though conventional angiography remains the gold standard.^{19,55,119}

Avoidance of aneurysm clip misplacement, which results in incomplete aneurysm obliteration and/or parent vessel occlusion, has improved with the development of microsurgical technique, optimization of patient positioning, and formalized fellowship training. There is some evidence supporting the value of specialization and increased surgical case volume for reducing complications in carotid endarterectomy,^{31,32} and this is likely to hold true for other open cerebrovascular procedures as well.

Since Kurze's initial use in the 1950s, the operating microscope has revolutionized neurosurgery and has become the standard of care for open cerebrovascular procedures.^{20,48} Microscope-related errors include use of the improper microscope, improper microscope balance, and delays due to the absence or delayed delivery of related equipment (such as drape) (B.G. Thompson, personal communication, 2010). Such errors can result in technical failure, increased infection risk due to prolonged procedure time, or inability to complete the procedure.

Patient positioning is critical for the surgeon, who requires the most favorable access to the vascular lesion,³⁷ and the anesthesiologist, who must maintain cerebral venous outflow as well as prevent compressive peripheral neuropathy.⁹¹ These considerations are of particular importance in cerebrovascular neurosurgery because of the extended length of these procedures.⁴ Complications related to positioning and/or securing of the patient's head are rare but potentially catastrophic and completely avoidable. Such occurrences include structural failure of the Mayfield headrest,¹⁰³ CSF rhinorrhea,⁶⁶ or epidural hematoma from laceration of the middle meningeal artery by the pins.⁵¹

Failure to Secure Rupture Site

Unlike incomplete aneurysm obliteration in general, failure to secure the rupture site of a ruptured aneurysm can lead to early rerupture and subsequent mortality; it therefore must be promptly remedied. Incidence of early rerupture in the 1st year after treatment is approximately 2% according to the CARAT investigators, with half of reruptures occurring within 3 days after treatment.³⁹ Failure to secure the rupture site is rarely reported in the literature; however, it may be inferred from the rate of retreatment immediately following surgical clipping. The 6% "incomplete occlusion" rate reported in the ISAT study represents a select subgroup since less than half of patients underwent postoperative angiography, and the majority of the angiograms were performed between 2 and 12 months postoperatively.⁶⁴ The CARAT study made no mention of a retreatment rate, although the investigators noted that the rerupture rate in aneurysms that were less than 70% occluded was similar to that of untreated ruptured aneurysms in prior studies.³⁹ Kivisaari et al.⁴⁵ noted neck remnants in 9% of aneurysms in their series and fundus remnants in 3%, but only mentioned retreatment in the case of major vessel occlusion. Macdonald and colleagues⁵⁴ reported a 4% incidence of completely unclipped aneurysms discovered on postoperative angiography; all were successfully obliterated on repeat surgery. Of the incompletely obliterated aneurysms found in the study by McLaughlin and Bojanowski,⁶¹ two were intentionally left incompletely obliterated at surgery and were subsequently obliterated endovascularly. The incidence of this adverse event has declined with more widespread use of intraoperative angiography (with or without ICG). Preventive techniques include those for avoidance of a misplaced aneurysm clip discussed in the previous section.

Other Medical Adverse Events

Other medical adverse events such as myocardial infarction, thromboembolism, septicemia, meningitis, or respiratory disease may also complicate open cerebrovascular procedures in the perioperative period. Given the severity of the disease, there are few reports of these rates directly related to surgery. For two of the studies on our review, other medical adverse events were reported to occur in 2%–17% of cases.^{26,64} This wide range is likely due to incomplete reporting and different definitions of perioperative complications.

It is unknown what proportion of these events could have been prevented. Good quality perioperative care including preoperative medical optimization,²⁵ infection control,^{102,117} and judicious use of mechanical and pharmacological thromboprophylaxis⁸⁵ may be of benefit. Adherence to these practices is likely inconsistent.

Conclusions

Open cerebrovascular neurosurgery is a high-risk procedural specialty. A significant proportion of these complications may be avoidable using practices to encourage standardized protocols, improved teamwork and communication, increased use of beneficial technologies,

and concentrated experiences and specializations. These ideas, including centralization of care, are discussed in more detail in the summary paper of this series.¹¹⁶ Coordinated efforts aimed at large-scale monitoring of neurosurgical complications and consistent quality improvement within these highlighted realms may significantly improve patient outcomes.

Disclosure

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Address correspondence to: Atul A. Gawande, M.D., M.P.H., Department of Surgery, Brigham and Women's Hospital, 75 Francis Street, Boston, Massachusetts 02115. email: agawande@partners.org.