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REVIEW ARTICLES

EDITOR'S CHOICE

Neurological complications of surgery and anaesthesia

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Editor's key points

- In this narrative review, the authors describe the potentially devastating neurological complications that may arise around the time of anaesthesia.
- They review recent advances in the field, and provide guidance on the prevention of adverse outcomes.

Summary. Injury to the central and peripheral nervous systems is often permanent. As such, adverse neurological outcomes of surgery and anaesthesia can be devastating for patients and their families. In this article, we review the incidence, risk factors, outcomes, prevention, and treatment of a number of important neurological complications in the perioperative period.

Keywords: anaesthesia; delirium; neurological complications; neurological outcomes; postoperative cognitive dysfunction; postoperative visual loss; spinal cord ischaemia; stroke; surgery

Neurological injury during the course of surgery can be devastating to patients and their families. Importantly, there is neither a temporary nor sustainable alternative to native neurological function as there is with other organs such as the kidney (dialysis machine, transplant), heart (ventricular assist device, transplant), liver (transplant), lungs (extracorporeal membrane oxygenation, transplant), or skeletal system (artificial joints). Despite the importance of the central and peripheral nervous systems, it could be argued that the field of anaesthesiology has *systematically* ignored neural function in the perioperative period. This provocative assertion is meant to highlight the fact that there is no standard monitor for the brain or other neural structures during surgery and anaesthesia, while standard monitors for the cardiovascular and respiratory systems have been used routinely for decades. This gap in clinical care is even more striking considering the fact that the brain and spinal cord are the primary therapeutic targets for both anaesthetics and analgesics. In other words, we have traditionally focused the least on what is arguably the field's most important physiological system, comprised organs that are the most difficult to heal or replace if injured.

In this article, we provide a concise review of five neurological complications of surgery and anaesthesia. Given the extensive literature and significant number of possible neurological outcomes, we have chosen to focus on adverse events that are common (delirium), controversial [postoperative cognitive decline (POCD)], and potentially catastrophic [stroke, spinal cord ischaemia, and postoperative visual loss (POVL)]. The objective of this review is to familiarize practicing anaesthetists with the incidence, risk factors, outcomes, prevention, and management of important neurological complications in order to heighten attention and improve care in the perioperative period.

Delirium

Delirium is an acute and fluctuating neurological disorder that reflects a change from baseline cognition and is characterized by the cardinal features of inattention and disorganized thinking (Table 1).[1 2] Delirium is arguably one of the most important postoperative complications because (i) it is common, affecting up to 70% of patients older than 60 undergoing major inpatient surgeries and (ii) it is associated with adverse outcomes, including mortality, persistent cognitive decline, and prolonged intensive care and hospital length of stay.[3–8] Delirium or agitation upon emergence from general anaesthesia occurs frequently, especially in children,[9] but will not be discussed in this section. Instead, we will focus on postoperative delirium because of its significance as a complication associated with increased morbidity and mortality.

In many patients, postoperative delirium is a marker of brain vulnerability and its occurrence suggests the possibility of underlying neurological disease, such as early or preclinical dementia.[6 10 11] Despite its high incidence and serious implications, delirium is frequently undiagnosed because it presents with a hypoactive rather than hyperactive phenotype (Fig. 1).[12 13] Furthermore, without targeted questioning, patients may appear normal or perhaps slightly lethargic. In order to promote diagnosis of delirium, reliable and user-friendly diagnostic algorithms have been developed. The Confusion Assessment Method and the Confusion Assessment Method for the Intensive Care Unit

Table 1 Diagnostic criteria for delirium (from the Diagnostic and Statistical Manual of Mental Disorders-5, pp. 599–600)

(A) There is a *disturbance in attention*, manifesting as a decreased ability to focus, shift, direct, and sustain attention. Patients may be either agitated (hyperactive) or lethargic (hypoactive)
(B) It *develops over a short period* of time, typically hours to days, and tends to fluctuate in its severity, and is often worse in the evening and night
(C) There is a *cognitive change*. This typically manifests as memory problems, disorientation, or hallucinations
(D) Delirium should *not* be diagnosed *in the context of coma*, but acute-onset low arousal states are compatible with delirium with severe inattention
(E) It is associated *with an acute insult*, such as a medical illness or a major surgery, which leads to neurophysiological perturbation

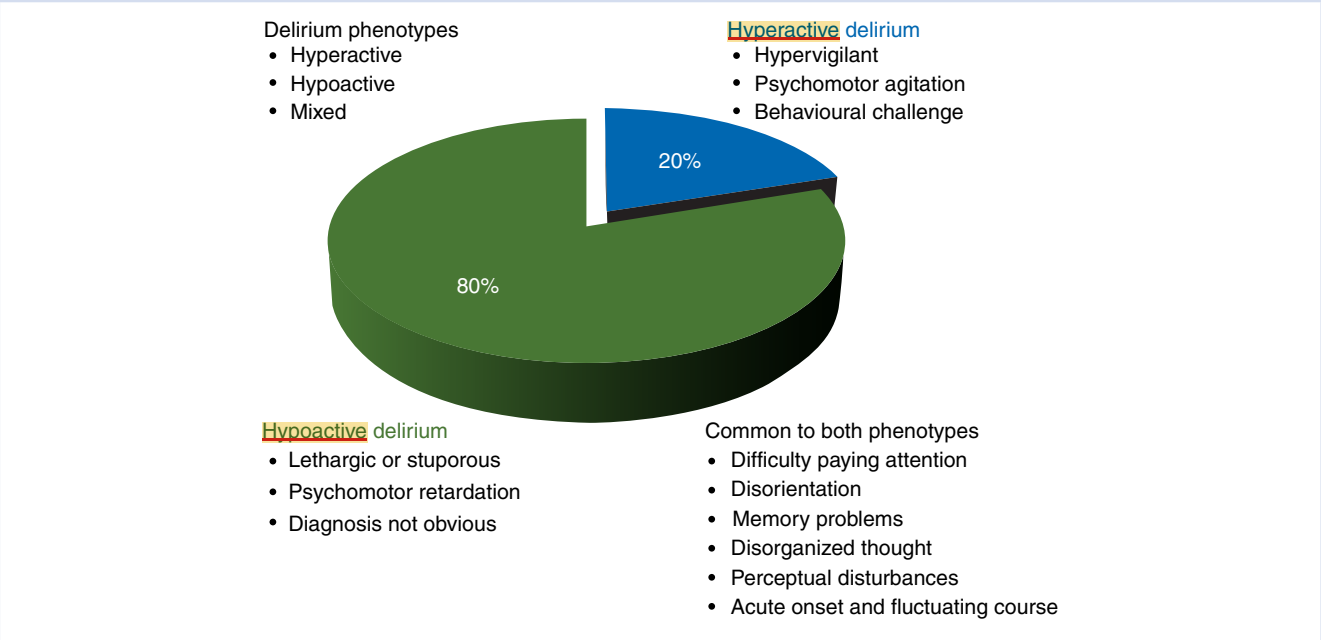

Fig 1 Signs and subtypes of postoperative delirium.

(for patients unable to speak) are the approaches that have been most widely adopted.[14–17]

Anaesthetists have historically not focused on delirium because it typically manifests when patients are no longer under their direct care. Delirium causes distress to patients and their families, and is a frustrating problem for clinicians as no treatments have been available to decrease its incidence or mitigate its duration. One of the reasons that delirium is difficult to prevent or treat is that several pathological pathways have been implicated, including neurotransmitter imbalance, neuroinflammation, endothelial dysfunction, impaired oxidative metabolism, and altered availability of large neutral amino acids.[10 18 19] With such complexity, no single intervention is likely to be a panacea. Nonetheless, there are important risk factors for delirium that should be prevented or alleviated. These include pain, acute medical conditions, sleep disturbance, sensory impairment, social isolation, daylight deprivation, infections, withdrawal syndromes, dehydration, blood loss, blood transfusion, electrolyte abnormalities, acid–base abnormalities, hypoxaemia, temperature derangements, seizures, and endocrine dysfunction.[11 20–22] Certain drugs commonly used in the perioperative period—such as atropine, antihistamines, corticosteroids, benzodiazepines, propofol, and opioids—can precipitate delirium and should be minimized in vulnerable patients.[23 24]

Given that postoperative delirium is so common, any approach that prevented it or lessened its consequences would have major clinical impact. Evidence has recently emerged from randomized controlled trials that guiding both total i.v. anaesthesia and volatile-based general anaesthetic administration with a processed EEG might decrease incident postoperative delirium.[25–27] A theoretical mechanism by which this could occur is that a processed EEG prevents relatively excessive anaesthetic administration to vulnerable patients. However, if slightly deeper anaesthesia in vulnerable surgical patients were to increase the risk of postoperative delirium, we would expect regional anaesthesia to be associated with a considerably lower incidence of postoperative delirium than general anaesthesia. A meta-analysis of small trials that randomized surgical patients to regional (albeit with light sedation) or general anaesthesia surprisingly found no increased risk for delirium with general anaesthesia (odds ratio, 0.88; 95% confidence interval, 0.51–1.51).[28] This apparent paradox warrants further exploration through a large, pragmatic clinical trial.

Various perioperative pharmacological agents have been investigated for the prevention of delirium and some success has been noted with low-dose haloperidol, subanaesthetic dose ketamine, and perioperative dexmedetomidine.[29–31] Of these interventions, dexmedetomidine for postoperative or intensive care unit sedation has been most rigorously investigated, and might be superior to benzodiazepines and morphine in terms of the genesis or duration of delirium.[31–35] Dexmedetomidine has not been found to be superior to propofol in relation to incidence or duration of delirium, and might be associated with increased haemodynamic side-effects.[36] Pending definitive research, switching to dexmedetomidine or propofol from alternative analgesic or sedative agents cannot currently be recommended to prevent delirium specifically or to improve outcomes generally.

After operation or in the critical care setting, the discomfort caused by limb restraints, bladder catheters, tracheal tubes, invasive lines, surgical drains, and enteral tubes increase agitation, and these should be discontinued when possible.[37] Antipsychotic medications such as haloperidol, risperidone, olanzapine, and quetiapine are frequently administered after operation to delirious patients to treat agitation, but their impact on outcome is unknown.[38–40] It is worth emphasizing the challenge confronting clinicians that both pain and many analgesic medications—not to mention the acute withdrawal of sedative and analgesic medications—can precipitate delirium.[41] As such, non-sedating analgesics and regional anaesthetic techniques should be considered in patients at risk for delirium. However, when pain is severe, opioid medications have been reported both to alleviate pain and to decrease delirium.[42]

The National Institute of Health and Care Excellence in the UK has highlighted clinical pathways covering risk, prevention, diagnosis, and management for patients at risk of delirium, although the focus on and evidence regarding surgical patients is limited (pathways.nice.org.uk/pathways/delirium).

Postoperative cognitive decline

POCD is a major concern for elderly surgical patients and their families. In 1955, Bedford[43] warned in the *Lancet* that people older than 50 yr should avoid surgery if possible in view of the high risk of cognitive decline. In recent years, influential studies have reinforced the perception that up to 50% of elderly patients undergoing both cardiac and non-cardiac surgery experience persistent POCD.[44 45] POCD is a controversial diagnosis and is not described in the Diagnostic and Statistical Manual of Mental Disorders. Furthermore, there is no International Classification of Disease Code for POCD. Conceptually, POCD is a subtle and frequently transient cognitive decline that is often only detectable with appropriate neuropsychological tests and a comparison with preoperative cognition.[46]

Seminal studies have found that older patients undergoing major surgery experience POCD lasting for weeks to months, with ~10% of those older than 60 having POCD at 3 months after operation.[7 47–49] This early POCD has major negative impact on patients and their families, could delay return to work, has been associated with increased mortality,[49 50] and has been linked with premature departure from the workforce.[50] However, it is unclear whether early POCD frequently reflects patient frailty, and when studies have followed patients long term, their cognitive trajectories have been similar to age- and disease-matched controls.[51–54] In support of the underlying frailty or vulnerability hypothesis, the same incidence of cognitive decline has been detected at 3 months after major surgery with general anaesthesia as after coronary angioplasty with no surgery or general anaesthesia.[48] A recent multicentre trial in the Netherlands has the potential to challenge conceptions regarding POCD after cardiac surgery.[55] This study randomized 280 patients to percutaneous coronary intervention (i.e. no surgery or general anaesthesia) or to off-pump coronary artery bypass grafting and rigorously assessed cognition through a battery of nine neuropsychological tests. The study found that at 7.5 yr follow-up, the surgical group had similarly improved cognitive performance compared with the non-surgical cohort.[55]

As meaningful cognitive decline occurs with ageing, even from the age of 45 yr,[56] it is unsurprising that studies without appropriate age- and disease-matched controls have found cognitive decline in older patients with various morbidities during the intermediate- to long-term period after surgery. Many studies in this area have had major limitations including lack of appropriately matched non-surgical controls, absence of data on preoperative cognitive trajectories, suboptimal statistical approaches, and failure to contextualize cognitive outcomes considering the success of surgery and the general postoperative course.[57] For example, consider an older patient who has significant vascular disease, who is already declining cognitively before surgery, who has complicated surgery with hypotension and substantial blood component transfusion, who has a difficult postoperative recovery on the intensive care unit with delirium, subclinical stroke, wound infection, and renal dysfunction, and who has chronic pain from his surgical incisions. It would not be surprising if this hypothetical patient were to experience persistent POCD.

Pain, inflammation, and acute illness carry a cognitive burden;[58–60] it is therefore to be expected that patients will experience cognitive impairment in the early postoperative period, analogous to sickness behaviour. However, when patients recover from the insult of surgery, they might revert to their predicted cognitive paths, based on their preoperative trajectories. Those who have improvement of their general health compared with the preoperative baseline might even experience relative cognitive improvement. This could occur when surgery results in decreased pain (e.g. from angina pectoris), decreased inflammation (e.g. from arthritis), increased cerebral blood flow, and enhanced ability to function in daily life. Although the notion that cognition could improve and decline after surgery is controversial, it is consistent with discoveries that the brain retains plasticity throughout life and preliminary research showing increased brain volumes or cognitive performance after successful surgeries, such as back surgery, joint surgery, carotid surgery, cardiac surgery, and ventricular assist device surgery.[61–64]

From the anaesthetist's perspective, whether or not general anaesthesia contributes to POCD remains uncertain and highly relevant. A recent meta-analysis aggregating 26 randomized trials that compared general and regional anaesthesia—albeit with light sedation—did not find that general anaesthesia was independently associated with POCD.[65] If general anaesthesia does contribute to persistent POCD, it is likely that the contribution is small. It has become clear that postoperative cognition should not be assessed in a vacuum and cannot be dissociated from the general outcome of surgery. Given that even early POCD is associated with intermediate-term mortality and worse long-term quality of life,[49 50] efforts should be focused on general and cognitive perioperative rehabilitation in order to minimize persistent POCD, to return cognition to the preoperative trajectory, and where possible to promote relative cognitive improvement.

Stroke

Perioperative stroke is defined as a cerebral infarction of ischaemic or haemorrhagic origin that occurs during or after surgery, with the postoperative time period sometimes defined as up to 30 days. Cardiac surgery and carotid endarterectomy are associated with the highest risk for perioperative stroke, with an incidence of ~4–5%. Bucerius and colleagues[66] studied 16 184 consecutive patients presenting for cardiac surgery and identified a perioperative stroke incidence of 4.8%; double-valve surgery was associated with a risk of ~10%. The multicentre GALA trial studied 3526 patients presenting for carotid surgery with general anaesthesia or local anaesthesia with sedation.[67] The risk of stroke was ~4% in each group suggesting that, at least for carotid endarterectomy, general anaesthesia is not a risk factor for perioperative stroke. The incidence of stroke in the non-cardiac, non-vascular, and non-neurological surgical population is significantly lower. Mashour and colleagues[68] used the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database to study >500 000 patients undergoing a wide variety of such surgeries and identified a 0.1% incidence of perioperative stroke, with ~2% incidence when five or more risk factors were present. Sharifpour and colleagues[69] used the NSQIP database to examine ~38 000 patients undergoing non-carotid vascular surgery and found an incidence of 0.6%. It is important to note that these data reflect the incidences of *overt* stroke, that is, stroke with a clinically obvious neurological deficit. Recent preliminary data derived from non-cardiac surgery in patients with cardiovascular risk factors (NeuroVISION trial) suggest that the incidence of *covert* stroke (i.e. without obvious deficit) is 10%, as identified by magnetic resonance imaging in the postoperative period.[70] If confirmed by the larger trial, this striking finding could have major implications for the study and prevention of perioperative stroke after non-cardiac surgery.

Perioperative strokes have varying aetiologies across different patient populations and surgical procedures, but are primarily ischaemic as opposed to haemorrhagic. Strokes after cardiac surgery are most likely to be embolic,[71] whereas strokes occurring in the non-cardiac surgery population are of both embolic and thrombotic origin.[72] Preoperative risk factors for stroke in surgical patients are similar to those for stroke in non-operative settings (Fig. 2). One of the most consistent risk factors for perioperative stroke in cardiac and non-cardiac surgery is a history of cerebrovascular disease, as evidenced by past stroke or transient ischaemic attack.[66 68 69 74–76] History of atrial fibrillation or new-onset atrial fibrillation is another consistent risk factor for perioperative stroke.[75 76] Intraoperative risk factors have not been studied extensively, but there has been a recent increase in focus on arterial pressure management. In one study of cardiac surgery patients, 20% of patients had impaired cerebral autoregulation during cardiopulmonary bypass, which would make them dependent on higher-than-normal mean arterial pressure for adequate cerebral blood flow.[77] Patients who had compromised cerebral autoregulation in this study had a higher incidence of perioperative stroke (12.8%) compared with those who did not (2.7%). Intraoperative hypotension has been associated with perioperative stroke in the non-cardiac surgical population, but the effect size is minimal and the clinical significance is not yet clear.[76 78]

Surgical patients with perioperative stroke have a higher mortality than propensity-matched surgical patients without stroke.[68] Importantly, stroke-associated mortality in the setting of surgery is higher than stroke-associated mortality in the community.[72] Given the increases in mortality and permanent disability, prevention of perioperative stroke is of paramount importance. A current controversy regarding perioperative stroke risk and prevention relates to the role of β-blockers in non-cardiac surgical patients. The PeriOperative Ischemic Evaluation (POISE) trial randomized 8351 patients undergoing non-cardiac surgery to either perioperative metoprolol or placebo.[79] Although adverse cardiac complications were reduced in the metoprolol arm of the trial, the incidence of stroke and mortality increased significantly. However, it was unclear from the POISE trial whether this effect was specific to metoprolol or simply high doses of β-blockers in drug-naïve surgical patients. Recent studies from Mashour and colleagues[76] and Ashes and colleagues[80] have found that the routine use of perioperative metoprolol is associated with stroke after non-cardiac surgery. Importantly, the incidence of perioperative stroke attributable to metoprolol was higher than in a matched cohort taking β-blockers with higher selectivity for the β-1 adrenergic receptor. Given the significant percentage of surgical patients taking metoprolol, future investigation of alternative β-blockers in the perioperative period may have significant implications for the prevention of stroke.

If a stroke is identified in the postoperative setting, it is imperative to consult immediately with a stroke neurologist, arrange for neuroimaging (non-contrast head computed tomography and possibly magnetic resonance imaging), and avoid physiological perturbations that can exacerbate neural injury (e.g. hypotension, hypoxia, hyperthermia, and hyperglycaemia). It is important to remember that surgeries (other than intracranial or spinal procedures) are not an absolute contraindication to therapy with tissue plasminogen activator

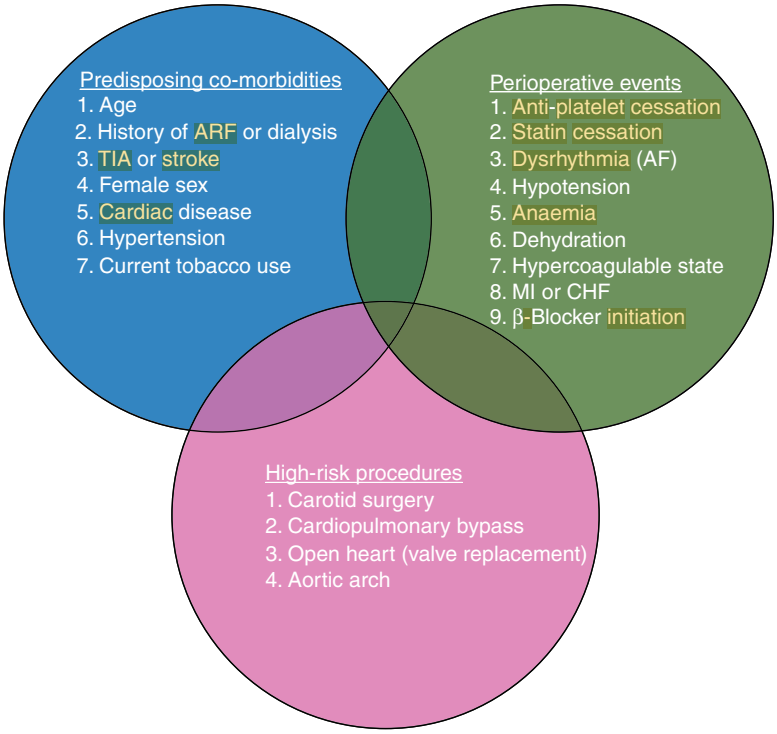

Fig 2 Risk factors for perioperative stroke. Modified with permission from Moore and colleagues, pp. 31–9, in *Neurologic Outcomes of Surgery and Anesthesia*, Oxford University Press.[73] AF, atrial fibrillation; ARF, acute renal failure; CHF, congestive heart failure; MI, myocardial infarction; TIA, transient ischemic attack.

(given i.v. or intra-arterially) or mechanical thrombolysis, both of which may be options for the postoperative patient.

Spinal cord ischaemia

Spinal cord ischaemia (SCI) is a potentially devastating complication associated with the surgical repair of thoracoabdominal aneurysms and dissections. The reported incidence of SCI is varied, likely because patient cohorts are heterogeneous with regard to aneurysm type, preventive modalities, and surgical technique. Historically, rates of SCI have been reported between 5% and 40%,[81–84] while more contemporary reports of incidence are generally $\leq$10%.[85–87]

Immediate-onset SCI (present on emergence from anaesthesia) may be caused by interruption of the blood supply to the spinal cord at any point of the operation; a spinal cord infarction may be several hours old at the time of initial recognition. Native blood supply to the anterior spinal cord is from both the single anterior spinal artery and from multiple segmental radicular (intercostal) tributaries. Collateral artery ligation during surgical dissection, aortic cross-clamp application, and collateral artery coverage by an endovascular stent can all cause immediate SCI by interrupting blood flow through the intercostal arteries. Delayed-onset SCI may be because of postoperative collateral thrombosis or a decrease in spinal cord perfusion pressure [hypotension, increased cerebrospinal fluid (CSF) pressure of ischaemia–reperfusion, or both].

The most widely accepted risk factor for SCI is the location and extent of the aortic aneurysm itself. Svensson and colleagues[84] and Conrad and colleagues[88] correlated the incidence of SCI and the location of the aneurysm, demonstrating a decreasing incidence from Crawford types I and II (both high thoracic origin) to type III (mid-thoracic origin) to type IV (distal thoracic origin) aneurysms. Other risk factors include cross-clamp time (more important when distal reperfusion techniques are not utilized), emergency operations, aortic rupture or dissection, and possibly intraoperative hypotension. Identification and reimplantation of non-selected segmental intercostal arteries does not clearly reduce SCI risk but may be of benefit when extensive aortic replacement is necessary. Thoracic endovascular aneurysm repair may have a lower incidence of SCI, which is likely attributable to fewer risk factors associated with the procedure. This is despite the fact that multiple segmental arteries are covered in the course of the operation, again pointing to a varied set of SCI risk factors for any particular patient. A history of infrarenal abdominal aortic aneurysm repair or internal iliac artery obstructions (decreased contributions to collateral flow) may increase SCI risk in patients undergoing endovascular repair.

Outcome after SCI is exceptionally poor. Postoperative mortality rate in patients with SCI is as high as 50%,[89] which is 10

times higher than the mortality rate in patients without spinal cord injury. Five year mortality has been reported to be 75% with SCI and 49% without.[88] The clinical presentation of the cord injury has also been correlated with functional outcome. At 2 yr follow-up, the rate of ambulation (alone or with assist devices) was 100% when the motor strength at initial injury was >50% of baseline. Only 73% of patients were ambulatory at 2 yr when strength at presentation was <50%, and no patients were ambulatory at the 2 yr time point when flaccid paralysis was the presenting symptom.

The protection provided to the spinal cord by CSF drainage has been demonstrated in case reports and case series for both open and endovascular repairs of thoracoabdominal aneurysms. In the largest prospective randomized controlled trial, it was demonstrated that CSF drainage was associated with a decreased incidence of SCI: 2.6% with CSF drainage *vs* 13% in controls.[89] A spinal drain allows the spinal cord perfusion pressure (which equals mean arterial pressure minus CSF pressure in the subarachnoid space) to be optimized by manipulating CSF volume during the perioperative period. Spinal fluid drainage and appropriate haemodynamic management are likely the most important factors in preventing spinal cord injury; CSF drainage is the only therapy that carries the highest level of endorsement (Class I; 'should be performed') from a multidisciplinary task force on the perioperative management of thoracoabdominal aortic aneurysms.[90] However, it should be noted that two large, systematic reviews were not able to reach definitive conclusions regarding CSF drainage and both recommended further study.[91 92] Ultimately, the risks of spinal drain placement must be balanced against the risk of SCI for each particular patient. Risks of placement include infection, haematoma, spinal cord or nerve root injury, meningitis, retained drain fragments, and intracranial haemorrhage.[93]

Delayed SCI resulting in partial or complete paraplegia has been reported even several weeks after surgery, but it most commonly presents in the first several postoperative days. Hypotension is the most common cause and reflects the pressure-dependent nature of collateral flow. When delayed-onset paraplegia does present, immediate treatment (e.g. supporting mean arterial pressure and draining CSF) is critical. Placement or replacement of a spinal drain has been successfully used to rescue patients with delayed-onset paraplegia in the postoperative period.

Postoperative visual loss

POVL is a rare but devastating neurological complication of elective surgery and can be caused by central retinal artery occlusion, cortical blindness, and ischaemic optic neuropathy (ION). Using the Nationwide Inpatient Sample database in the USA, Shen and colleagues[94] identified the overall incidence of POVL to be 0.02%, with cardiac surgery (0.09%) and posterior spine surgery (0.03%) associated with the highest risk. Patil and colleagues[95] used the same database with different inclusion criteria and found a 0.09% incidence of POVL for spine surgery, with 0.02% attributable to ION. Stevens and colleagues[96] reported an even higher incidence of POVL after spine surgery at three institutions, with 0.2% for all aetiologies and 0.1% for ION. Discrepancies in the incidence likely relate to the database used and also inclusion criteria. Collectively, the data suggest that cardiac surgery and posterior spine surgery are the highest risk categories for POVL and ION, although the complication is by no means limited to these surgeries.

The cause of POVL is diverse and can involve embolic phenomena (linked to central retinal arterial occlusion and cortical blindness), cerebral hypoperfusion (linked to cortical blindness), or an intraocular 'compartment syndrome' in which there is insufficient perfusion of the optic nerve (potentially linked to ION). Risk factors associated with anterior ION in cardiac surgery include prolonged cardiopulmonary bypass, anaemia, excessive perioperative weight gain, and use of epinephrine and amrinone.[97] A case–control study of cardiopulmonary bypass found the following factors associated with ION: clinically significant and severe peripheral vascular disease, preoperative angiogram within 48 h of surgery (presumed to be a marker of disease severity or surgical urgency), and postoperative anaemia.[98] ION after posterior spine surgery has more recently been investigated with a multicentre case–control study involving events reported to the ASA Postoperative Visual Loss Registry.[99] There were 93 cases of POVL after spine surgery reported to the registry; 83 were associated with ION. Blood loss of ≥1 litre or anaesthetic duration ≥6 h was present in 96% of the cases. The Postoperative Visual Loss Study Group compared 80 of the ION registry cases with 315 matched patients undergoing spine surgery at 17 institutions who did not suffer from ION.[100] Independent predictors of ION included male sex, obesity, Wilson frame use, anaesthetic duration, blood loss, and percentage of colloid used for non-blood fluid resuscitation (protective). Notably, neither anaemia nor haemodynamic variables were predictors; a single-centre case–control study was also unable to find haemodynamic differences associated with ION.[101] See Figure 3 for a risk assessment profile based on independent predictors identified by the Postoperative Visual Loss Study Group.

Given the rarity, the outcomes of POVL are difficult to assess. In the POVL registry, ~40% of patients with ION had some improvement in vision, but such improvements were noted to be of unclear clinical significance.[99] Given the significant potential for permanent blindness, prevention of this complication is critical. In 2012, the ASA published a practice advisory for POVL associated with spine surgery.[102] The recommendations for prevention and treatment of POVL in spine surgery patients were recently summarized by Ramaiah and Lee[103] (Table 2). These recommendations were formulated before the major study by the Postoperative Visual Loss Study Group.

The rarity of POVL makes the prospective study of preventive strategies extremely difficult. However, increased intraocular pressure is a more tractable variable of relevance to POVL pathophysiology that has been the subject of recent randomized trials. Farag and colleagues[104] conducted a factorial, randomized trial assessing the effect of topical brominidine *vs* albumin (and topical placebo) *vs* crystalloid (and topical placebo) on intraocular pressure during prone spine surgery. As has been shown before,[105] prone

Sex	Obesity	Wilson frame	Anaesthesia (h)	EBL (litre)	Colloid (%)*	Absolute risk of ION per 10 000 procedures† (based on 0.017% overall rate)	Absolute risk of ION per 10 000 procedures† (based on 0.1% overall rate)	Relative risk‡
Female	**No**	**No**	**5**	**1**	**10**	0.08	0.45	1.00§
Female	**Yes**	No	5	1	10	0.22	1.27	2.83
Female	No	**Yes**	5	1	10	0.33	1.93	4.30
Female	No	No	**7.5**	1	10	0.17	1.01	2.26
Female	No	No	**10**	1	10	0.39	2.30	5.12
Female	No	No	5	**2**	10	0.10	0.60	1.34
Female	No	No	5	**3**	10	0.14	0.80	1.78
Female	No	No	5	1	**0**	0.17	1.00	2.24
Female	**Yes**	**Yes**	**10**	**3**	**0**	18.98	111.67	249.27
Male	No	No	5	1	10	0.19	1.14	2.53
Male	**Yes**	No	5	1	10	0.55	3.21	7.17
Male	No	**Yes**	5	1	10	0.83	4.89	10.91
Male	No	No	**7.5**	1	10	0.44	2.57	5.74
Male	No	No	**10**	1	10	0.99	5.82	12.98
Male	No	No	5	**2**	10	0.26	1.52	3.39
Male	No	No	5	**3**	10	0.34	2.03	4.52
Male	No	No	5	1	**0**	0.43	2.54	5.67
Male	**Yes**	**Yes**	**10**	**3**	**0**	48.11	283.00	631.73

Fig 3 Risk prediction for ION after posterior spine surgery. Reproduced from Postoperative Visual Loss Study Group[100] with permission. *Colloid as % of total non-blood replacement, where total non-blood replacement (crystalloid + albumin + hetastarch).' Range of low and high absolute risks of ION based on the literature from multicentre studies or national databases. †Relative risk of ION compared with the lowest risk set of patient variables in this table: first row (bold, no shading), reference value = 1. ‡Reference category for relative risk: female, non-obese, non-Wilson frame, 5 h anaesthesia duration, 1% EBL, and 10% colloid of non-blood replacement administered, first row (bold, no shading). EBL, estimated blood loss; ION, ischaemic optic neuropathy.

Table 2 Summary of recommendations to prevent POVL

- Consider informing high-risk patients that there is a small, unpredictable risk of POVL
- Continually monitor the arterial pressure and consider use of central venous pressure monitoring in high-risk patients
- Colloids should be used along with crystalloids to maintain intravascular volume in patients who have substantial blood loss
- Haemoglobin or haematocrit should be monitored periodically during surgery in patients who experience substantial blood loss
- Position the head at or above the level of heart. The head should be maintained in a neutral, forward position when possible
- Avoid direct pressure on the globe
- Consider staging spine procedures in high-risk patients
- Patients at high risk should have their vision assessed after recovery from anaesthesia
- If there is concern for POVL, an urgent ophthalmological consultation should be obtained
- Additional management may include optimizing haemoglobin/haematocrit values, haemodynamic status, and arterial oxygenation
- Consider magnetic resonance imaging to rule out intracranial causes of POVL

positioning increased intraocular pressure; brominidine, but not albumin, significantly reduced the time-weighted average of intraocular pressure measurements in this study. Another randomized controlled trial recently found that reverse Trendelenburg positioning during prone spine surgery significantly reduced intraocular pressure compared with neutral positioning.[106] The impact of these interventions on the outcome of POVL is unclear, especially since increased intraocular pressure is a common event during prone surgery. Focused study of intraocular pressure in patients at very high risk for POVL may reveal insight that can lead to positive changes in clinical care.

Conclusion

It is important to recognize the surgical patients that are at highest risk for neurological complications and mitigate risk in the perioperative period based on current guidelines and clinical judgement. Although this recommendation may appear trite, the traditional focus of anaesthesiology on cardiopulmonary monitoring and cardiac risk modification—in conjunction with the many unknowns of perioperative neuroscience—has created conditions that may lead to insufficient vigilance regarding neurological status and neural injury in the perioperative period. The neurological complications reviewed in this

article are not comprehensive and more general topics of relevance such as anaesthetic neurotoxicity, neuroprotection, neural monitoring, and neuronal biomarkers of injury have not been discussed.[73] Perioperative neuroscience represents the cutting edge of outcomes research, with a number of exciting and controversial lines of investigation that will hopefully impact clinical practice and improve patient lives.

Authors' contributions

G.A.M., D.T.W., and M.S.A. wrote the manuscript.

Declaration of interest

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