Published in final edited form as:

Curr Opin Anaesthesiol. 2020 October ; 33(5): 661–667. doi:10.1097/ACO.0000000000000905.

Interventions to Improve Perioperative Neurologic Outcomes

Matthew S. Vandiver, MD, PhD¹, Susana Vacas, MD, PhD^{1,*}

¹Department of Anesthesiology and Perioperative Medicine, University of California Los Angeles

Abstract

Purpose of the review: Few outcomes in surgery are as important to patients as that of their neurologic status. The purpose of this review is to discuss and categorize the most common perioperative neurologic complications. We will also discuss strategies to help prevent and mitigate these complications for our patients.

Recent findings: There are several strategies the anesthesiologist can undertake to prevent or treat conditions such as: Perioperative Neurocognitive Disorders (PNCD), Spinal Cord Ischemia (SCI), perioperative stroke, and PostOperative Visual Loss (POVL).

Summary:

A thorough understanding of threats to patients' neurologic well-being is essential to excellent clinical practice.

Keywords

Perioperative Neurocognitive Disorders; Spinal Cord Ischemia; perioperative stroke; postoperative visual loss; patient outcomes

Introduction

Each year, increasing numbers of adults are undergoing surgery, with the goal of treating acute conditions, improving function, and increasing duration and quality of life. Deleterious and even disastrous neurologic changes are a common and well-established occurrence after anesthesia and surgery. These adverse consequences are not only a significant burden to patients' quality of life but are also a financial burden on our healthcare system.

Significant resources have been invested into the identification of the primary threats to patients' neurologic outcomes. An increasingly strong culture of patient safety has focused efforts on prevention and treatment of these threats. Despite advances in anesthetic agents, monitors, and techniques, patients continue to encounter life-altering neurologic changes post anesthesia.

*Corresponding author: Susana Vacas, MD, PhD, 757 Westwood Plaza, Suite 3325, Los Angeles, CA, 90095, Phone: 3102678686, svacas@mednet.ucla.edu.

Conflicts of Interest: The authors declare no competing interests.

In this article we review five of the most common neurologic complications after surgery and anesthesia. We articulate the associated risk factors and currently available strategies and technological advancements for the prevention and management of **perioperative neurologic outcomes**.

Perioperative Neurocognitive Disorders

Perioperative Neurocognitive Disorders, or PNCD, is an overarching term for cognitive impairment identified or exacerbated in the perioperative period.(1–5) This includes any form of acute postoperative event, including postoperative delirium (POD) and delayed cognitive recovery, or in the longer term, newly diagnosed neurocognitive deficit, or further decline in cognition diagnosed up to 12 months after surgery.(1–5) POD is characterized by inattention, disorganized thinking, and altered level of consciousness with acute onset and fluctuating course.(6, 7) Further, long-term changes are symptomatically subtle, more complicated to detect, and have a later onset and prolonged time course. It is estimated that long-term cognitive changes occurs in more than 10% of non-cardiac surgical patients(8) over 60 years old,(9) and POD has been reported to occur in up to 70% of selected patient populations, depending on existing comorbidities and type of surgery(10).

POD leads to longer hospital and ICU stay, increased days of mechanical ventilation, and a 31% increase in hospital costs.(11) Even after discharge, patients who develop delirium are at an increased risk of institutionalization and death. Some studies suggest that POD is linked to long-term cognitive decline,(12) including a eight-fold increased risk for dementia.(13–15) It is estimated that the costs associated with delirium can reach \$150 billion per year in the US alone, and a staggering \$60,000 in personal health care costs during the first year after discharge.³ The postoperative restoration of functional independence, including cognition, constitutes a major challenge for the health care system.(16)

While there are numerous risk factors, surgery-induced inflammation is a major component in the development of PNCD.(17–19) Its etiology seems multifactorial and anesthetic management is one of the culprits. (17, 20) Basic and clinical studies have yet to identify effective strategies to completely halt the development of brain changes after surgery. In 2018, the American Society of Anesthesiologists published the Best Practices for Postoperative Brain Health.(21) Several Societies and Organizations have also published their specific guidelines.(22) However, these guidelines are very general, diffuse, and not readily applicable to individual patients.

Prevention Strategies:

Specific intraoperative anesthetic or physiologic variables are associated with increased risk for PNCD.(23, 24) Among precipitating factors, medications, depth of anesthesia,(25) hypothermia, and hypotension(26) or blood pressure fluctuation(27) may play a role in the incidence of PNCD. According to the Best Practices for Postoperative Brain Health(21), “anesthesiologists should monitor age-adjusted end-tidal MAC fraction, strive to optimize cerebral perfusion, and perform EEG-based anesthetic management.”

Some studies suggest that the use of specific **medications** may alter the risk of these disorders, particularly in patients over 65 years of age (see Table 1).(21)

Many sedatives induce a “pharmacologically-induced sleep”, with several important differences to natural sleep. While natural sleep normally cycles through a predictable series of phases, general anesthesia can precipitate changes in the electroencephalogram (EEG) not seen during physiologic sleep.(28) Although general anesthetics target the brain, the use of processed **EEG** devices is a controversial area, not commonly used in clinical anesthetic practice, though it has shown some promise in preventing the development of PNCD.(29) Still, no single EEG pattern can characterize the anesthetized state.(30)

Significantly reduced regional cerebral blood flow is observed in the vasculature for multiple brain regions in subjects undergoing surgery.(31) By failing to provide adequate cerebral blood flow to affected areas, (by intermittent changes of the hemodynamic parameters during anesthesia), the potential for even further neuroinflammation and brain tissue damage exists. Several studies have demonstrated that intraoperative hypotension or fluctuations of blood pressure(27) should be avoided. Of note, there is no consensus regarding the definition of hypotension and the optimal range for intraoperative blood pressure.(32) Also, the combination of hypotension depth and the cumulative time spent with low values might be associated with worse outcomes.(32–34) **Optimal intraoperative management** of patients may not only have an important role in reducing the incidence of PNCD, it may also lead to an improvement in general outcomes following major surgery.(23, 24, 35)

Spinal Cord Ischemia

Spinal cord ischemia (SCI) is one of the most dreaded complications associated with the repair of thoracoabdominal aortic (TAA) dissection/aneurysms. There is significant variability in the reported incidence of SCI secondary to patient factors, surgical techniques, and preventative measures employed. The historical incidence of SCI has been documented as high as 40%, but recent data suggests that it is <10%, perhaps given the advancements in patient care over the past several decades.(36–38)

Our understanding of the pathophysiology of SCI in TAA surgery is incomplete at this time. The anatomy of spinal cord blood supply is complex and often variable for different patients, even sometimes described as “Russian roulette” for the vascular surgeon.(39) The main blood supply is via one anterior spinal artery and two posterior spinal arteries, which arise from the vertebral arteries and are joined by collateral vessels from the aorta.(40)

SCI may be broken down into two categories: immediate-onset (following emergence from anesthesia) and delayed-onset SCI, which occurs sometime during the post-operative period. The pathogenesis of immediate-onset SCI is secondary to the interruption of the blood supply to the spinal cord during surgery, either coverage with a stent during thoracic endovascular aortic repair (TEVAR), debranching during surgical dissection, or during clamping of the aorta. The mechanisms of delayed-onset SCI includes postoperative thrombosis, a decrease in spinal cord perfusion pressure or ischemia-reperfusion injury.(41)

Risk factors for SCI include patient and surgery-specific features. The biggest risk factor for SCI is the size and location of the aortic aneurysm. Studies show a correlation between the incidence of SCI and the location of the TAA (Crawford types I and II versus type III and IV).(42) Other risk factors include emergency surgery, rupture or dissection of the aneurysm, aortic clamp time, the involvement of the left subclavian artery, and prior aortic surgery. Patient risk factors include age >70 years, renal insufficiency, chronic obstructive pulmonary disease, and perioperative hypotension.(43)

SCI carries significant post-operative mortality, with some reports as high as 50%.(44) Patients with SCI also carry severe morbidity with <75% of patients ambulatory at 2yrs in the event their presentation included a reduction of >50% of their baseline strength, and 0% if their presentation was consistent with flaccid paralysis. This leads to a severe reduction in functional status and increases the five-year mortality to nearly 75%.(42)

Prevention Strategies:

The American College of Cardiology/American Heart Association (ACC/AHA) recommends that **cerebral spinal fluid (CSF) drainage** be performed in the open repair of TAA and strongly considered for patients undergoing TEVAR.(45, 46) Several studies show a significant reduction in the incidence of paraparesis or paraplegia in those receiving CSF drainage for open repair.(44) However, this level of evidence is not available for TEVAR at this time.(47) CSF drain placement carries risks including infection, meningitis, spinal hematoma, nerve root injury, and ICH, which must be balanced with the risk for SCI. (48) (49)

The fundamental principles of adequate perfusion and oxygenation to the spinal cord guide much of the **anesthetic management** for both open TAA repair and TEVAR. The point at which ischemia occurs is unknown, however, ensuring adequate cardiac output and hemoglobin levels is essential for spinal cord oxygen delivery. Maintaining spinal cord perfusion pressure, by increasing MAP (>80mmHg) and decreasing CSF pressure (<10mmHg), is also recommended, although exact targets are not well defined. (46) Vasopressors may be used to increase the MAP, even if it must be balanced with increasing pressor requirement to the detriment of micro-capillary blood flow.(50)

Hypothermia is a possible means to reduce SCI and reportedly shown to be reasonably effective. This effect is already known in the case of circulatory arrest and cooling for procedures performed on the aortic arch and applied both in the case of cooling to mild hypothermia 32–34°C or profound hypothermia in the range of 15–18°C.(36) During TAA repair, without complete circulatory arrest or cardiopulmonary bypass, mild-moderate hypothermia is often used given the difficulty and risks of placing invasive cooling devices necessary to accomplish more profound hypothermia.(51) Systemic cooling techniques are not frequently utilized in TEVAR given a theoretical risk of interfering with the expansion and diameter of stent grafts during deployment.(52) However, local cooling in open TAA repair has also been described (using iced saline in the intrathecal space or double lumen epidural cooling catheters).(53)

Multiple clinical trials examining **novel pharmacological treatments** have been investigated for the prevention of SCI, but without definitive evidence for any particular agents. Naloxone was shown to be neuroprotective in cell models, yet it did not demonstrate a benefit in human studies.(54) One of the most well-known classes of pharmacologic agents, corticosteroids, has been studied in SCI. Methylprednisolone has been administered prior to aortic cross-clamp placement, in order to decrease the risk of SCI in animal studies, but similar to other agents, has yet to be confirmed by any large-scale clinical trials. (55) Lastly, more recent novel agents have been investigated in lab and animal models, including hydrogen sulfide,(56) MLN4924,(57) and inhibitors of microRNA 204,(58) with mixed results.(59)

Stroke

Perioperative stroke is defined as a brain infarction of ischemic or hemorrhagic etiology that occurs during surgery, or within 30 days after surgery, by the Society for Neuroscience in Anesthesiology and Critical Care (SNACC) Consensus Statement.(60) Cardiac and carotid surgery continue to carry the highest risk of perioperative stroke (in the 4–5% range), as shown in large trials.(61, 62) For non-carotid vascular surgery, the incidence was found to be 0.6%.(63) The risk of stroke in the general population undergoing non-cardiac, non-vascular surgery is significantly lower, with a reported incidence of 0.1% and 2% when multiple risk factors are present.(64) The incidence of covert stroke, in patients with risk factors undergoing non-cardiac surgery, suggests that 10% of patients have MRI findings consistent with stroke.(65) These striking findings suggest that the incidence and prevalence of perioperative stroke is far greater than previously thought, thus the need for identification and prevention strategies is all the more important.

The risk factors present in the perioperative setting are comparable to those of the general population at large. Evidence of cerebrovascular disease is the greatest single risk factor, and includes prior stroke or history of transient ischemic attack.(65) Other strong risk factors include age, cardiac disease, history of atrial fibrillation,(66) history of renal failure/dialysis, hypertension, tobacco use, and female sex.(63) As already described, high-risk procedures such as, carotid surgery, cardiac surgery with cardiopulmonary bypass, aortic arch procedures, any procedure requiring circulatory arrest all carry vastly higher incidences of stroke beyond the general perioperative population. Perioperative risk factors include patients that must stop their antiplatelet/anticoagulant medications, severe anemia, hypercoagulable states, and beta blocker initiation. Recently, there is a greater focus on intraoperative management of these patients as intraoperative hypotension or loss of cerebro-autoregulation carry a higher risk of perioperative stroke.(61)

Perioperative stroke carries a eight-fold increase in perioperative mortality and an absolute increase of mortality of 21%(67, 68) when compared to similar populations that do not experience a stroke event, as well as the general population that experiences a stroke outside of the perioperative setting.

If a perioperative stroke is suspected, rapid consultation with a stroke neurologist and neuroimaging is warranted. Former AHA/ASA guidelines suggest that surgery within two

weeks of symptom onset of acute ischemic stroke was a relative contraindication to IV thrombolysis. A careful discussion of the bleeding risks of IV thrombolysis vs expected deficits related to the stroke is essential. Mechanical thrombolysis has become more widely available, and can be quite effective, with lower risk of surgical-site bleeding. This has led to more recent provisions in the 2018 AHA/ASA guidelines for performance of endovascular thrombectomy as late as 24 hours since last known well time.(69)

Prevention Strategies:

Given the irreversibility of much of the perioperative stroke pathology, prevention is likely the most important area to tackle. **Modification of patient risk factors** prior to surgery is vital. For example, SNACC recommends that elective surgery be deferred for 6 months following a stroke, given the associated risk increase.(70)

Pharmacologic preventative agents have been recommended including statin therapy, anti-platelet agents, and anticoagulation in the perioperative period. Significant controversy emerged after the POISE-1 trial, as it showed a higher incidence of stroke and mortality with beta blocker therapy, and thus recommendations are only to continue beta blocker therapy for patients and not to institute new beta blockers in the absence of strong indications for them.(62) Other neuroprotective preventive strategies, including thiopentone, volatile anesthetics, magnesium, and hypothermia have been proposed but without significant evidence to be routinely recommended.(71)

Carotid disease investigation and treatment may also be undertaken but given that carotid surgery also carries increased stroke risk, this approach must be considered against the risk of general elective surgical perioperative stroke.

Perioperative **blood pressure control** is of utmost importance. In recent years, there has been a trend to maintain intraoperative MAP higher than 65 mmHg to avoid adverse outcomes.(32) During general surgery, MAP values which decreased more than 30% from baseline blood pressure were associated with increased postoperative ischemic stroke.(33) In patients undergoing cardiopulmonary bypass, MAP values are an important therapeutic hemodynamic target that has the potential to reduce the incidence of stroke.(72)

Perioperative control of **glycemic values** are also important cornerstones of stroke prevention.(73) While extremely tight glycemic control is not recommended, severe levels of hyper and hypo-glycemia have both been shown to worsen stroke outcomes.(74) Thus, glucose control in the 140–180mg/dL range is recommended for perioperative glycemic control.(73)

Postoperative Visual loss

Postoperative visual loss (POVL) is a potentially disabling complication of surgery. Ischemic optic neuropathy (ION), cortical blindness/stroke, and central retinal artery occlusion are all mechanisms by which POVL can occur. While the overall incidence is relatively low, specific surgical procedures carry higher risk profiles for POVL, with cardiac surgery and posterior spine surgery being the highest incidence surgeries, and the overall

incidence of POVL to be between ~0.02%–0.2% and 0.1% for ION, depending on the database and group reporting.(75, 76)

While the mechanisms of POVL described are varied, the likely culprits are embolic (CRAO and cortical blindness), cerebral hypoperfusion (cortical blindness), or increased intraocular pressure leading to ION. ION is associated with multiple risk factors, including type of surgery: cardiac surgery with prolonged cardiopulmonary bypass, anemia,(77) obesity, and use of epinephrine, and amrinone.(78) Other apparent risk factors include significant blood loss (>1L) or prolonged anesthetic time (>6hr).(79) Independent patient risk factors of ION include obesity, male sex, Wilson frame use, and percentage of colloid used for resuscitation (protective against ION likely secondary to reduced total fluid volume administered).(80)

The POVL registry puts the percentage of patients with some form of clinical improvement at ~40%. However, given the relative rarity of POVL, true outcomes are difficult to assess, as are any preventative measures, as a large RCT would be virtually impossible to execute with such a low incidence. Given that the mechanisms of POVL are relatively well understood, one might consider measures that reduce the likelihood of cerebral hypoperfusion, embolic phenomenon, and especially increased IOP. A recent RCT showed that reverse trendelenburg position significantly reduced IOP versus supine positioning.

Prevention Strategies:

Given the paucity of RCT, or even case control studies on prevention of POVL, it is reasonable to identify high-risk patients and to take measures known or suspected to be protective against POVL. Anesthetic management of cardiac and prone spine surgeries already incorporate many of these: keeping **hemoglobin** concentration at a reasonable level >7, **reverse trendelenburg** in posterior spine surgery, careful **positioning** to eliminate any direct pressure on the globe, colloid usage, close **monitoring of arterial pressure**, as well as **CVP** in especially high-risk patients. Additionally, it has been proposed that thorough discussion with high-risk patients during informed consent is an important step to take prior to surgery.(42) If POVL occurs, ophthalmological consultation is recommended, as is investigation with MRI to rule out any intracranial pathology leading to POVL that may be reversible. Rapid treatment of hypotension, severe anemia, or reversible embolic phenomenon may allow for more complete POVL recovery and should be implemented immediately upon discovery of POVL.

Conclusion:

The perioperative period involves immense physiologic stress and change, one where acute surgical factors (i.e., blood loss, laparoscopic insufflation, steep positioning, etc.) interact with underlying patient pathophysiology, and can sometimes lead to poor neurologic outcomes.(81, 82) Thus, further understanding perioperative neurologic complications and pathophysiology are necessary to elucidate the involved risks. For example, the exact mechanisms of PNCD remain poorly understood.(83)·(84) PNCD is thought to result from a complex interaction between patient's baseline vulnerability and comorbidities, the physiological stress and inflammation associated with surgery and anesthesia, and environmental factors associated with hospitalization.(9, 17) Optimal intraoperative

management of patients may not only have an important role in reducing the incidence of PNCD, it may also lead to an improvement in general outcomes following major surgery. (24) Advancements in anesthetic planning and optimization have resulted in the ability to decrease the risk of SCI and POVL in high risk surgeries, and offer the opportunity to further improve neurologic outcomes. Anesthetic optimization interventions are amenable to widespread use, and thus, will not only have a measurable impact, but also an enormously helpful effect on overall perioperative morbidity and mortality in surgical patients.

These improvements are well within our technological and medical grasp, but require a large-scale commitment to funding, conducting, and broadcasting well-designed studies that are focused on understanding the underlying clinical features of each complication with patient-specific clinical interventions and protocols in mind. Implementing these possible best practices and prevention will have a profoundly positive impact on our health care system.

Acknowledgements:

Supported by the National Institute of General Medical Sciences, grant No. K23GM132795 (to Dr. Vacas) and Department of Anesthesiology and Perioperative Medicine Research Seed Grant, University of California Los Angeles (to Dr. Vandiver).

References

1. Evered L, Silbert B, Knopman DS, Scott DA, DeKosky ST, Rasmussen LS, et al. Recommendations for the Nomenclature of Cognitive Change Associated with Anaesthesia and Surgery-2018. *Journal of Alzheimer's disease* : JAD. 2018;66(1):1–10.
2. Evered L, Silbert B, Knopman DS, Scott DA, DeKosky ST, Rasmussen LS, et al. Recommendations for the nomenclature of cognitive change associated with anaesthesia and surgery-2018. *British journal of anaesthesia*. 2018;121(5):1005–12. [PubMed: 30336844]
3. Evered L, Silbert B, Knopman DS, Scott DA, DeKosky ST, Rasmussen LS, et al. Recommendations for the Nomenclature of Cognitive Change Associated With Anaesthesia and Surgery-2018. *Anesthesia Analgesia*. 2018;127(5):1189–95. [PubMed: 30325748]
4. Evered L, Silbert B, Knopman DS, Scott DA, DeKosky ST, Rasmussen LS, et al. Recommendations for the nomenclature of cognitive change associated with anaesthesia and surgery-2018. *Acta Anaesthesiol Scand*. 2018;62(10):1473–80. [PubMed: 30325016]
5. Evered L, Silbert B, Knopman DS, Scott DA, DeKosky ST, Rasmussen LS, et al. Recommendations for the nomenclature of cognitive change associated with anaesthesia and surgery-2018. *Can J Anaesth*. 2018;65(11):1248–57. [PubMed: 30324338]
6. Sachs-Ericsson N, Blazer DG. The new DSM-5 diagnosis of mild neurocognitive disorder and its relation to research in mild cognitive impairment. *Aging & mental health*. 2015;19:2–12. [PubMed: 24914889]
7. Association AP. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition: DSM-5. 2013.
8. Abildstrom H, Rasmussen LS, Rentowl P, Hanning CD, Rasmussen H, Kristensen PA, et al. Cognitive dysfunction 1–2 years after non-cardiac surgery in the elderly. ISPOCD group. International Study of Post-Operative Cognitive Dysfunction. *Acta Anaesthesiol Scand*. 2000;44(10):1246–51. [PubMed: 11065205]
9. Moller JT, Cluitmans P, Rasmussen LS, Houx P, Rasmussen H, Canet J, et al. Long-term postoperative cognitive dysfunction in the elderly ISPOCD1 study. ISPOCD investigators. International Study of Post-Operative Cognitive Dysfunction. *Lancet*. 1998;351(9106):857–61. [PubMed: 9525362]

10. Leslie DL, Marcantonio ER, Zhang Y, Leo-Summers L, Inouye SK. One-year health care costs associated with delirium in the elderly population. *Archives of internal medicine*. 2008;168(1):27–32. [PubMed: 18195192]
11. Milbrandt EB, Deppen S, Harrison PL, Shintani AK, Speroff T, Stiles RA, et al. Costs associated with delirium in mechanically ventilated patients. *Crit Care Med*. 2004;32:955–62. [PubMed: 15071384]
12. Gambús PL, Trocóniz IF, Feng X, Gimenez-Milá M, Mellado R, Degos V, et al. Relation between acute and long-term cognitive decline after surgery: Influence of metabolic syndrome. *Brain, Behavior, and Immunity*. 2015;50.
13. Davis DH, Muniz Terrera G, Keage H, Rahkonen T, Oinas M, Matthews FE, et al. Delirium is a strong risk factor for dementia in the oldest-old: a population-based cohort study. *Brain : a journal of neurology*. 2012;135(Pt 9):2809–16. [PubMed: 22879644]
14. Aranake-Chrisinger A, Avidan MS. Postoperative delirium portends descent to dementia. *British journal of anaesthesia*. 2017;119(2):285–8. [PubMed: 28854545]
15. Sprung J, Roberts RO, Weingarten TN, Nunes Cavalcante A, Knopman DS, Petersen RC, et al. Postoperative delirium in elderly patients is associated with subsequent cognitive impairment. *British journal of anaesthesia*. 2017;119(2):316–23. [PubMed: 28854531]
16. Terrando N, Brzezinski M, Degos V, Eriksson LI, Kramer JH, Leung JM, et al. Perioperative cognitive decline in the aging population. *Mayo Clin Proc*. 2011;86.
17. Vacas S, Degos V, Feng X, Maze M. The neuroinflammatory response of postoperative cognitive decline. *British medical bulletin*. 2013;106:161–78. [PubMed: 23558082]
18. Vacas S, Degos V, Maze M. Fragmented Sleep Enhances Postoperative Neuroinflammation but Not Cognitive Dysfunction. *Anesthesia and analgesia*. 2017;124(1):270–6. [PubMed: 27755058]
19. Vacas S, Maze M. Initiating Mechanisms of Surgery-induced Memory Decline: The Role of HMGB1. *Journal of Clinical & Cellular Immunology*. 2016;07(6).
20. Mahanna-Gabrielli E, Schenning KJ, Eriksson LI, Browndyke JN, Wright CB, Culley DJ, et al. State of the clinical science of perioperative brain health: report from the American Society of Anesthesiologists Brain Health Initiative Summit 2018. *British journal of anaesthesia*. 2019;123(4):464–78. [PubMed: 31439308]
21. Berger M, Schenning KJ, Brown CHt, Deiner SG, Whittington RA, Eckenhoff RG, et al. Best Practices for Postoperative Brain Health: Recommendations From the Fifth International Perioperative Neurotoxicity Working Group. *Anesthesia and analgesia*. 2018;127(6):1406–13. [PubMed: 30303868]
22. Aldecoa C, Bettelli G, Bilotta F, Sanders RD, Audisio R, Borozdina A, et al. European Society of Anaesthesiology evidence-based and consensus-based guideline on postoperative delirium. *European journal of anaesthesiology*. 2017;34(4):192–214. [PubMed: 28187050]
23. Vacas S, Cannesson M. Noninvasive Monitoring and Potential for Patient Outcome. *Journal of cardiothoracic and vascular anesthesia*. 2019;33 Suppl 1(Suppl 1):S76–s83. [PubMed: 31279357]
24. Joosten A, Rinehart J, Bardaji A, Van der Linden P, Jame V, Van Obbergh L, et al. Anesthetic Management Using Multiple Closed-loop Systems and Delayed Neurocognitive Recovery: A Randomized Controlled Trial. *Anesthesiology*. 2020;132(2):253–66. [PubMed: 31939839]
25. Ballard C, Jones E, Gauge N, Aarsland D, Nilsen OB, Saxby BK, et al. Optimised anaesthesia to reduce post operative cognitive decline (POCD) in older patients undergoing elective surgery, a randomised controlled trial. *PloS one*. 2012;7(6):e37410.
26. Sessler DI, Sigl JC, Kelley SD, Chamoun NG, Manberg PJ, Saager L, et al. Hospital stay and mortality are increased in patients having a ‘Triple Low’ of low blood pressure, low bispectral index, and low minimum alveolar concentration of volatile anesthesia. *Anesthesiology*. 2012;116.
27. Hirsch J, DePalma G, Tsai TT, Sands LP, Leung JM. Impact of intraoperative hypotension and blood pressure fluctuations on early postoperative delirium after non-cardiac surgery. *British journal of anaesthesia*. 2015;115(3):418–26. [PubMed: 25616677]
28. Vacas S, Maze M. Can sedation fulfill the physiological role of sleep? *Handbook on Burnout and Sleep Deprivation: Risk Factors, Management Strategies and Impact on Performance and Behavior*. 2015.

29. Vacas S, McInrue E, Gropper MA, Maze M, Zak R, Lim E, et al. The Feasibility and Utility of Continuous Sleep Monitoring in Critically Ill Patients Using a Portable Electroencephalography Monitor. *Anesthesia and analgesia*. 2016;123(1):206–12. [PubMed: 27159066]
30. Sleigh JW, Scheib CM, Sanders RD. General anaesthesia and electroencephalographic spindles. *Trends in Anaesthesia and Critical Care*. 2011;1(5):263–9.
31. Yadav SK, Kumar R, Macey PM, Richardson HL, Wang DJ, Woo MA, et al. Regional cerebral blood flow alterations in obstructive sleep apnea. *Neuroscience letters*. 2013;555:159–64. [PubMed: 24076138]
32. Walsh M, Devereaux PJ, Garg AX, Kurz A, Turan A, Rodseth RN, et al. Relationship between intraoperative mean arterial pressure and clinical outcomes after noncardiac surgery: toward an empirical definition of hypotension. *Anesthesiology*. 2013;119(3):507–15. [PubMed: 23835589]
33. Bijker JB, Persoon S, Peelen LM, Moons KG, Kalkman CJ, Kappelle LJ, et al. Intraoperative hypotension and perioperative ischemic stroke after general surgery: a nested case-control study. *Anesthesiology*. 2012;116(3):658–64. [PubMed: 22277949]
34. Colak Z, Borojevic M, Bogovic A, Ivancan V, Biocina B, Majeric-Kogler V. Influence of intraoperative cerebral oximetry monitoring on neurocognitive function after coronary artery bypass surgery: a randomized, prospective study. *Eur J Cardiothorac Surg*. 2015;47(3):447–54. [PubMed: 24810757]
35. Yamada T, Vacas S, Gricourt Y, Cannesson M. Improving Perioperative Outcomes Through Minimally Invasive and Non-invasive Hemodynamic Monitoring Techniques. *Frontiers in Medicine*. 2018;5(144).
36. Okita Y. Fighting spinal cord complication during surgery for thoracoabdominal aortic disease. *Gen Thorac Cardiovasc Surg*. 2011;59(2):79–90. [PubMed: 21308433]
37. Coselli JS, Bozinovski J, LeMaire SA. Open surgical repair of 2286 thoracoabdominal aortic aneurysms. *Ann Thorac Surg*. 2007;83(2):S862–4; discussion S90–2. [PubMed: 17257942]
38. Crawford ES, Crawford JL, Safi HJ, Coselli JS, Hess KR, Brooks B, et al. Thoracoabdominal aortic aneurysms: preoperative and intraoperative factors determining immediate and long-term results of operations in 605 patients. *J Vasc Surg*. 1986;3(3):389–404. [PubMed: 3951025]
39. Doppman JL. Paraplegia after surgery for thoracoabdominal aneurysms: Russian roulette for the vascular surgeon. *Radiology*. 1993;189(1):27–8. [PubMed: 8372203]
40. Melissano G, Bertoglio L, Rinaldi E, Leopardi M, Chiesa R. An anatomical review of spinal cord blood supply. *J Cardiovasc Surg (Torino)*. 2015;56(5):699–706.
41. Awad H, Ramadan ME, El Sayed HF, Tolpin DA, Tili E, Collard CD. Spinal cord injury after thoracic endovascular aortic aneurysm repair. *Can J Anaesth*. 2017;64(12):1218–35. [PubMed: 29019146]
42. Conrad MF, Ye JY, Chung TK, Davison JK, Cambria RP. Spinal cord complications after thoracic aortic surgery: long-term survival and functional status varies with deficit severity. *J Vasc Surg*. 2008;48(1):47–53. [PubMed: 18486422]
43. Scali ST, Wang SK, Feezor RJ, Huber TS, Martin TD, Klodell CT, et al. Preoperative prediction of spinal cord ischemia after thoracic endovascular aortic repair. *J Vasc Surg*. 2014;60(6):1481–90 e1. [PubMed: 25282701]
44. Coselli JS, LeMaire SA, Koksoy C, Schmittling ZC, Curling PE. Cerebrospinal fluid drainage reduces paraplegia after thoracoabdominal aortic aneurysm repair: results of a randomized clinical trial. *J Vasc Surg*. 2002;35(4):631–9. [PubMed: 11932655]
45. Hiratzka LF, Bakris GL, Beckman JA, Bersin RM, Carr VF, Casey DE Jr., et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease: executive summary. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. *Catheter Cardiovasc Interv*. 2010;76(2):E43–86. [PubMed: 20687249]
46. Etz CD, Weigang E, Hartert M, Lonn L, Mestres CA, Di Bartolomeo R, et al. Contemporary spinal cord protection during thoracic and thoracoabdominal aortic surgery and endovascular aortic

repair: a position paper of the vascular domain of the European Association for Cardio-Thoracic Surgery. *Eur J Cardiothorac Surg*. 2015;47(6):943–57. [PubMed: 25991554]

47. Wong CS, Healy D, Canning C, Coffey JC, Boyle JR, Walsh SR. A systematic review of spinal cord injury and cerebrospinal fluid drainage after thoracic aortic endografting. *J Vasc Surg*. 2012;56(5):1438–47. [PubMed: 22884456]
48. Hanna JM, Andersen ND, Aziz H, Shah AA, McCann RL, Hughes GC. Results with selective preoperative lumbar drain placement for thoracic endovascular aortic repair. *Ann Thorac Surg*. 2013;95(6):1968–74; discussion 74–5. [PubMed: 23635449]
49. Estrera AL, Sheinbaum R, Miller CC, Azizzadeh A, Walkes JC, Lee TY, et al. Cerebrospinal fluid drainage during thoracic aortic repair: safety and current management. *Ann Thorac Surg*. 2009;88(1):9–15; discussion [PubMed: 19559180]
50. Arora L, Hosn MA. Spinal cord perfusion protection for thoraco-abdominal aortic aneurysm surgery. *Curr Opin Anaesthesiol*. 2019;32(1):72–9. [PubMed: 30507678]
51. Kouchoukos NT, Masetti P, Rokkas CK, Murphy SF, Blackstone EH. Safety and efficacy of hypothermic cardiopulmonary bypass and circulatory arrest for operations on the descending thoracic and thoracoabdominal aorta. *Ann Thorac Surg*. 2001;72(3):699–707; discussion –8. [PubMed: 11565644]
52. Robich MP, Hagberg R, Schermerhorn ML, Pomposelli FB, Nilson MC, Gendron ML, et al. Hypothermia severely effects performance of nitinol-based endovascular grafts in vitro. *Ann Thorac Surg*. 2012;93(4):1223–7. [PubMed: 22385821]
53. Shimizu H, Mori A, Yoshitake A, Yamada T, Morisaki H, Okano H, et al. Thoracic and thoracoabdominal aortic repair under regional spinal cord hypothermia. *Eur J Cardiothorac Surg*. 2014;46(1):40–3. [PubMed: 24335470]
54. Kuniyara T, Matsuzaki K, Shiiya N, Saijo Y, Yasuda K. Naloxone lowers cerebrospinal fluid levels of excitatory amino acids after thoracoabdominal aortic surgery. *J Vasc Surg*. 2004;40(4):681–90. [PubMed: 15472595]
55. Kirshner DL, Kirshner RL, Heggeness LM, DeWeese JA. Spinal cord ischemia: an evaluation of pharmacologic agents in minimizing paraplegia after aortic occlusion. *J Vasc Surg*. 1989;9(2):305–8. [PubMed: 2918625]
56. Kakinohana M, Marutani E, Tokuda K, Kida K, Kosugi S, Kasamatsu S, et al. Breathing hydrogen sulfide prevents delayed paraplegia in mice. *Free Radic Biol Med*. 2019;131:243–50. [PubMed: 30529602]
57. Yu S, Xie L, Liu Z, Li C, Liang Y. MLN4924 Exerts a Neuroprotective Effect against Oxidative Stress via Sirt1 in Spinal Cord Ischemia-Reperfusion Injury. *Oxid Med Cell Longev*. 2019;2019:7283639.
58. Yan L, Shi E, Jiang X, Shi J, Gao S, Liu H. Inhibition of MicroRNA-204 Conducts Neuroprotection Against Spinal Cord Ischemia. *Ann Thorac Surg*. 2019;107(1):76–83. [PubMed: 30278168]
59. Bredthauer A, Lehle K, Scheuerle A, Schelzig H, McCook O, Radermacher P, et al. Intravenous hydrogen sulfide does not induce neuroprotection after aortic balloon occlusion-induced spinal cord ischemia/reperfusion injury in a human-like porcine model of ubiquitous arteriosclerosis. *Intensive Care Med Exp*. 2018;6(1):44. [PubMed: 30357563]
60. Mashour GA, Moore LE, Lele AV, Robicsek SA, Gelb AW. Perioperative care of patients at high risk for stroke during or after non-cardiac, non-neurologic surgery: consensus statement from the Society for Neuroscience in Anesthesiology and Critical Care*. *J Neurosurg Anesthesiol*. 2014;26(4):273–85. [PubMed: 24978064]
61. Bucerius J, Gummert JF, Borger MA, Walther T, Doll N, Onnasch JF, et al. Stroke after cardiac surgery: a risk factor analysis of 16,184 consecutive adult patients. *Ann Thorac Surg*. 2003;75(2):472–8. [PubMed: 12607656]
62. Group PS, Devereaux PJ, Yang H, Yusuf S, Guyatt G, Leslie K, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. *Lancet*. 2008;371(9627):1839–47. [PubMed: 18479744]

63. Sharifpour M, Moore LE, Shanks AM, Didier TJ, Kheterpal S, Mashour GA. Incidence, predictors, and outcomes of perioperative stroke in noncarotid major vascular surgery. *Anesth Analg*. 2013;116(2):424–34. [PubMed: 23115255]
64. Mashour GA, Shanks AM, Kheterpal S. Perioperative stroke and associated mortality after noncardiac, nonneurologic surgery. *Anesthesiology*. 2011;114(6):1289–96. [PubMed: 21478735]
65. Mrkobrada M, Hill MD, Chan MT, Sigamani A, Cowan D, Kurz A, et al. Covert stroke after non-cardiac surgery: a prospective cohort study. *Br J Anaesth*. 2016;117(2):191–7. [PubMed: 27440630]
66. Bateman BT, Schumacher HC, Wang S, Shaefi S, Berman MF. Perioperative acute ischemic stroke in noncardiac and nonvascular surgery: incidence, risk factors, and outcomes. *Anesthesiology*. 2009;110(2):231–8. [PubMed: 19194149]
67. Mashour GA, Woodrum DT, Avidan MS. Neurological complications of surgery and anaesthesia. *Br J Anaesth*. 2015;114(2):194–203. [PubMed: 25204699]
68. Neuro VI. Perioperative covert stroke in patients undergoing non-cardiac surgery (NeuroVISION): a prospective cohort study. *Lancet*. 2019;394(10203):1022–9. [PubMed: 31422895]
69. Leslie-Mazwi T, Chandra RV, Fraser JF, Hoh B, Baxter BW, Albuquerque FC, et al. AHA/ASA 2018 AIS guidelines: impact and opportunity for endovascular stroke care. *J Neurointerv Surg*. 2018;10(9):813–7. [PubMed: 29807886]
70. Talke PO, Sharma D, Heyer EJ, Bergese SD, Blackham KA, Stevens RD. Society for Neuroscience in Anesthesiology and Critical Care Expert consensus statement: anesthetic management of endovascular treatment for acute ischemic stroke*: endorsed by the Society of NeuroInterventional Surgery and the Neurocritical Care Society. *J Neurosurg Anesthesiol*. 2014;26(2):95–108. [PubMed: 24594652]
71. Anastasian ZH. Anaesthetic management of the patient with acute ischaemic stroke. *Br J Anaesth*. 2014;113 Suppl 2:ii9–16. [PubMed: 25498583]
72. Sun LY, Chung AM, Farkouh ME, van Diepen S, Weinberger J, Bourke M, et al. Defining an Intraoperative Hypotension Threshold in Association with Stroke in Cardiac Surgery. *Anesthesiology*. 2018;129(3):440–7. [PubMed: 29889106]
73. Moghissi ES, Korytkowski MT, DiNardo M, Einhorn D, Hellman R, Hirsch IB, et al. American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. *Diabetes Care*. 2009;32(6):1119–31. [PubMed: 19429873]
74. McGirt MJ, Woodworth GF, Brooke BS, Coon AL, Jain S, Buck D, et al. Hyperglycemia independently increases the risk of perioperative stroke, myocardial infarction, and death after carotid endarterectomy. *Neurosurgery*. 2006;58(6):1066–73; discussion –73. [PubMed: 16723885]
75. Warner ME, Warner MA, Garrity JA, MacKenzie RA, Warner DO. The frequency of perioperative vision loss. *Anesth Analg*. 2001;93(6):1417–21, table of contents. [PubMed: 11726416]
76. Chang SH, Miller NR. The incidence of vision loss due to perioperative ischemic optic neuropathy associated with spine surgery: the Johns Hopkins Hospital Experience. *Spine (Phila Pa 1976)*. 2005;30(11):1299–302. [PubMed: 15928556]
77. Brown RH, Schauble JF, Miller NR. Anemia and hypotension as contributors to perioperative loss of vision. *Anesthesiology*. 1994;80(1):222–6. [PubMed: 8291715]
78. Shen Y, Drum M, Roth S. The prevalence of perioperative visual loss in the United States: a 10-year study from 1996 to 2005 of spinal, orthopedic, cardiac, and general surgery. *Anesth Analg*. 2009;109(5):1534–45. [PubMed: 19713263]
79. Dunker S, Hsu HY, Sebag J, Sadun AA. Perioperative risk factors for posterior ischemic optic neuropathy. *J Am Coll Surg*. 2002;194(6):705–10. [PubMed: 12081060]
80. Miller R. Miller's Anesthesia, 2-Volume Set: Elsevier Health Sciences; 2015. Available from: <https://www.r2library.com/Resource/Title/0702052833>.
81. Lonjaret L, Lairez O, Minville V, Geeraerts T. Optimal perioperative management of arterial blood pressure. *Integr Blood Press Control*. 2014;7:49–59. [PubMed: 25278775]
82. Monk TG, Saini V, Weldon BC, Sigl JC. Anesthetic management and one-year mortality after noncardiac surgery. *Anesth Analg*. 2005;100(1):4–10. [PubMed: 15616043]

83. Forsberg A, Cervenka S, Jonsson Fagerlund M, Rasmussen LS, Zetterberg H, Erlandsson Harris H, et al. The immune response of the human brain to abdominal surgery. *Ann Neurol*. 2017;81(4):572–82. [PubMed: 28253549]
84. Steinmetz J, Christensen KB, Lund T, Lohse N, Rasmussen LS. Long-term consequences of postoperative cognitive dysfunction. *Anesthesiology*. 2009;110(3):548–55. [PubMed: 19225398]

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Bullet points

- Perioperative Neurocognitive Disorders, is an overarching term for cognitive impairment identified or exacerbated in the perioperative period and several strategies can be adopted to prevent it.
- Cerebral spinal fluid (CSF) drainage, anesthetic management and hypothermia might have a role in decrease the incidence of spinal cord ischemia.
- Given the irreversibility of much of the perioperative stroke pathology, prevention is likely the most important area to tackle.
- It is crucial to identify high-risk patients and to take measures known or suspected to be protective against POVL.

Table 1.

Medications to be used with caution in patients over 65 years old

First-generation antihistamines
Phenothiazine-type antiemetics
Antispasmodics/anticholinergics
Antipsychotics
Benzodiazepines
Corticosteroids
H ₂ -receptor antagonists
Metoclopramide
Meperidine
Skeletal muscle relaxants