



Year in Review: Synopsis of Selected Articles in Neuroanesthesia and Neurocritical Care from 2021

Evan Shao¹ Nahemah Hasanaly¹ Lashmi Venkatraghavan¹

¹Department of Anesthesiology and Pain Medicine, University of Toronto, Toronto Western Hospital, Toronto, Ontario, Canada

Address for correspondence: Lashmi Venkatraghavan, MBBS, MD, DNB, FRCA, FRCPC, Department of Anesthesia, University of Toronto, 2McL-405, Toronto Western Hospital, 399, Bathurst Street, Toronto, Ontario M5T 2S8, Canada (e-mail: Lashmi.Venkatraghavan@uhn.ca).

J Neuroanaesthesiol Crit Care 2022;9:3–9.

Abstract

This review is a synopsis of selected articles from neuroscience, neuroanesthesia, and neurocritical care from 2021 (January–December 2021). The journals reviewed include anesthesia journals, critical care medicine journals, neurology, and neurosurgical journals as well as high-impact medical journals such as the *Lancet*, *Journal of American Medical Association*, *New England Journal of Medicine*, and *Stroke*. This summary of important articles will serve to update the knowledge of anesthesiologists and other perioperative physicians who provide care to neurosurgical and neurocritical care patients. In addition, some of the important narrative reviews that are of interest to neuroanesthesiologists are also listed.

Keywords

- ▶ brain tumor
- ▶ neuroanesthesia
- ▶ neurocritical care
- ▶ stroke

Introduction

Last year, several excellent articles focusing on topics of particular interest to neuroanesthesiologists were published. This review is a synopsis of selected articles from neuroscience, neuroanesthesia, and neurocritical care from 2021. The articles were selected on the basis of their clinical relevance and their implications for day-to-day clinical practice. The aim of this review is to provide a recent update to anesthesiologists and other perioperative physicians who provide care to neurosurgical and neurocritical care patients.

Ephedrine versus Phenylephrine on Cerebral Macro- and Microcirculation in Patients with Brain Tumors

Maintaining mean arterial pressure (MAP) to provide adequate cerebral perfusion is important in the perioperative anesthesia management of patients undergoing resection of brain tumors. However, MAP may not correlate well with homogenous microcirculatory blood flow in all situations.¹ Under certain circumstances, microcirculatory blood flow may be uneven and be impaired, leading to decreased local perfusion

despite maintaining adequate MAP. Erythrocyte transit time heterogeneity can reveal excessive shunting through regions of the brain. Two commonly used vasopressors to help with maintaining MAP are the pure α -adrenergic agonist phenylephrine and the α - and β -adrenergic agonist ephedrine. In a prospective, single-center, double-blinded, randomized controlled trial, Koch et al. compared two commonly used vasopressors (phenylephrine and ephedrine) on erythrocyte transit time heterogeneity in 24 patients with a brain tumor measuring at least 3 cm.² Patients were anesthetized and underwent magnetic resonance imaging (MRI) with ephedrine or phenylephrine infusion. Patients' depth of anesthesia, PCO_2 , and PO_2 were maintained throughout the procedure. Capillary transit times (CTT) in the ipsilateral and contralateral brain regions were measured. CTT in the contralateral side was increased with phenylephrine infusion (from 3.0 ± 0.5 to 3.2 ± 0.7 s), while it was decreased with ephedrine infusion (3.1 ± 0.8 to 2.7 ± 0.7 s) despite a similar increase in MAP. This was statistically significant. A similar effect was also seen in the peritumoral region, but this was not statistically significant. Furthermore, ephedrine was also shown to

DOI <https://doi.org/10.1055/s-0042-1744045>
ISSN 2348-0548.

© 2022. Indian Society of Neuroanaesthesiology and Critical Care. All rights reserved.

This is an open access article published by Thieme under the terms of the Creative Commons Attribution-NonDerivative-NonCommercial-License, permitting copying and reproduction so long as the original work is given appropriate credit. Contents may not be used for commercial purposes, or adapted, remixed, transformed or built upon. (<https://creativecommons.org/licenses/by-nc-nd/4.0/>).

Thieme Medical and Scientific Publishers Pvt. Ltd. A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

significantly increase both CPP and brain tissue oxygenation. This suggests that ephedrine is superior to phenylephrine at improving cerebral macro- and microcirculation. However, small sample size, heterogeneity in tumor pathology, and age-related changes in cerebral hemodynamics are some of the limitations.

Dexmedetomidine and Subthalamic Local Field Potentials in Parkinson's Disease

Deep brain stimulation (DBS) surgery involves inserting electrodes into the subthalamic nucleus (STN) and globus pallidus interna for the treatment of Parkinson's disease. Microelectrode recording and stimulation testing of an awake patient are two commonly used methods of target localization. Hence, monitored anesthesia care with/without conscious sedation is the most used anesthetic technique in these patients. Among the anesthetic agents used for sedation, dexmedetomidine is popular for its favorable pharmacological effect. However, the effect of dexmedetomidine on neuronal discharges from STN has not been studied systematically. In this prospective observational study, Martinez-Simon et al. have studied the effect of varying doses of dexmedetomidine on the neuronal activity from the subthalamic nuclei.³ Twelve patients who had STN DBS electrodes *in situ* (inserted 5 days prior) coming for the second stage of the procedure (internalization and insertion of pulse generator) were studied. The activity of the STN was measured under varying doses of dexmedetomidine using local field potentials from the inserted electrodes; these oscillations are considered a summation of the synchronized postsynaptic changes surrounding the electrodes. At higher doses of dexmedetomidine (0.5–0.6 µg/kg/h), the patient became sedated and showed a significant decrease in characteristic Parkinsonian activity in the STN. However, all patients were able to be awakened by external stimuli and had full recovery of STN by 1 minute (median) with a range from 0 to 9 minutes. The authors conclude that during STN-DBS insertions, dexmedetomidine infusions up to 0.6 µg/kg/h can be used safely without having significant changes in the STN activity. However, one should be cautious that this study was conducted in patients who already had STN electrodes *in situ*. This is different from intraoperative target localization using microelectrode recording. For further reading on the effect of different anesthetic agents on microelectrode recordings, please refer to a recent review on this topic by Bos et al.⁴

General Anesthesia versus Local Anesthesia for DBS Insertion for Parkinson Disease (GALAXY Trial)

DBS surgeries are typically performed with the patient awake or under light sedation due to the need for intraoperative clinical observation for optimal electrode placement. Improvements in MRI and neurophysiological microelectrode recordings have allowed DBS to be performed under general anesthesia (GA). Previous studies on the effects of GA versus local anesthesia (LA) for DBS placement on outcomes included small numbers of patients, involved a variety of anesthetic agents, and measured heterogeneous outcomes, and there were no randomized trials of this issue.⁵ Holewijn

et al. have conducted a single-center prospective randomized open-label blinded end-point clinical trial on 110 Parkinson patients undergoing DBS.⁶ The patients were randomized to GA or LA with no sedation. Their primary outcome was a composite score of cognitive, mood, and behavior adverse events at 6 months. They found no significant differences in the composite adverse score between GA (22%) and LA (29%) groups. Similarly, there was no difference between the two groups in terms of the off-medication Movement Disorders Society Unified Parkinson's Disease Rating Scale. However, GA was felt to be less burdensome by patients and had shorter procedural time. This is the first randomized controlled trial that showed that long-term outcomes with GA were comparable to LA in patients undergoing microelectrode recording-guided DBS insertion for Parkinson's disease.

Subcutaneous Sumatriptan for Postoperative Pain in Elective Cranial Surgery

Post-craniotomy headache is a common complication after supratentorial craniotomies, and this can be different from postsurgical pain. Although the mechanism of post-craniotomy headaches is not completely understood, several studies suggest activation of nociceptors on the dura mater, mediated by trigeminal afferents involving serotonin-based molecular mechanisms.⁷ Sumatriptan is a serotonin receptor agonist that is used to treat primary headaches through multiple mechanisms. In post-craniotomy headaches, sumatriptan may act directly on the meningeal blood vessels or via the inhibition of vasoactive peptides to cause vasoconstriction and attenuation of the nociceptive process.⁸ In this single-center, retrospective study on 60 patients who had a supratentorial or suboccipital craniotomy, Patel et al. compared the postoperative pain scores and opioid use amongst patients who received 6 mg of subcutaneous sumatriptan ($n = 15$) and those who did not ($n = 45$).⁹ Patients who received sumatriptan had significantly decreased average pain score at 1 hour compared with those who did not (1.3 vs. 3.9). These statistically significant differences between the groups remained constant for the first 24 hours in both adults (1.1 vs. 7.1) and pediatric patients (1.1 to 3.9). Though there was a trend toward lower opioid use (intravenous and oral) in the sumatriptan group, this was not statistically significant. There were no reported complications or side effects related to sumatriptan use. Though the sample size in this study is quite small, the authors have identified sumatriptan as a possible adjuvant to opioids and non-steroidal anti-inflammatory agents for postoperative pain after craniotomy. However, large multicenter randomized controlled studies are needed to further evaluate the safety and efficacy of sumatriptan in postoperative pain management after craniotomy.

Early versus Late Tracheostomy in Patients with Acute Traumatic Spinal Cord

Acute traumatic spinal cord injuries (SCI) often result in impairments in respiration that may lead to pulmonary dysfunction with secondary infections, prolonged mechanical ventilation, and even death.¹⁰ Optimal timing of tracheostomy

and whether an early tracheostomy can improve outcomes in patients with SCI is currently not known. Mubashir et al. have conducted a systematic review and meta-analysis to assess the optimal timing of tracheostomy in patients with SCI and evaluate the potential benefits of early versus late tracheostomy.¹⁰ Eight studies with 1,220 patients were included in the study, of which 441 had an early tracheostomy (within the first 7 days of injury or intubation) and 779 underwent late tracheostomy (≥ 8 days). Patients with cervical SCI were twice likely to undergo an early tracheostomy than those with thoracic SCI. Early tracheostomy reduced the mean length of stay in intensive care by 13 days (95% CI, -19.18 to -7.00; $p = 0.001$) and mean duration of mechanical ventilation by 18.3 days (95% CI, -23.33 to -12.28; $p = 0.001$). Although mortality rates were lower among patients in the early tracheostomy group compared with the late tracheostomy group, the results were not significant (odds ratio [OR] = 0.57; 95% CI, 0.32–1.01; $p = 0.054$) in these patients. There were no significant differences between the groups with regard to the risk of in-hospital mortality and pneumonia. In summary, this study showed that in patients with SCI, specifically cervical SCI, early tracheostomy may be beneficial in weaning patients off mechanical ventilation faster and in turn quicker ICU discharge. However, caution should be exercised in the interpretation of the results due to the low quality of included studies. There were only 8 studies, of which 2 were abstracts, and there was significant heterogeneity amongst the many variables and outcome measures.

Intraoperative Neurophysiologic Monitoring During Scoliosis Correction in Adolescents

Iatrogenic spinal cord injury and subsequent new neurologic deficits (NNDs) are the major risks in patients undergoing corrective surgery for idiopathic scoliosis. Various methods have been used to identify intraoperative spinal cord injury. While Stagnara wake-up test has been in use since the 1970s,¹¹ intraoperative neurophysiologic monitoring (IONM) techniques such as somatosensory evoked potential (SSEP), motor evoked potential (MEP) have largely replaced the Stagnara wake up test. Currently, there are limited published data on the utility of IONM in improving outcomes in adolescent patients with idiopathic scoliosis. Nassef et al. conducted a retrospective exploratory study to examine the incidence and severity of NNDs after idiopathic scoliosis surgery with a focus on IONM use.¹² In addition, they compared the incidence of NND before and after the implementation of IONM. They reviewed the charts of 547 patients aged 10–18 years old from two large tertiary pediatric centers; of these, 359 patients were monitored by IONM and 186 patients were monitored by wake-up test (Pre IONM). NND was defined as any sensory (mild) or motor (severe) deficit that was not present before the surgery. Both groups had similar demographic data and the overall incidence of NND was 4.9%. NND was significantly lower in the IONM group compared with the wake-up test group (3.3% vs. 8.1%, $p < 0.02$); however, the severity of NND was similar between the groups. The total operating time and estimated blood loss were significantly lower in the IONM group than in the wake-up test group. In

addition, combined anterior release and posterior instrumentation was more likely to develop NND than staged procedure. Further, 50% of patients with severe NND in the IONM group had partial recovery at 3 months. Although IONM is not a foolproof tool, data on neurologic complication in spinal surgery are difficult to interpret as there are confounding variables in spinal disease, monitoring modalities, and surgical techniques offered.

Inhalational versus Intravenous Anesthesia and Delayed Cerebral Ischemia after Subarachnoid Hemorrhage

Delayed cerebral ischemia (DCI), a known complication after aneurysmal subarachnoid hemorrhage (aSAH) is associated with significant morbidity and mortality. Despite many strategies to combat DCI that have been developed, none of them have shown to be effective in improving long-term functional outcomes. Previous preclinical and clinical studies have shown that inhalational anesthetics were associated with reduced incidence of angiographic vasospasm and DCI.¹³ Molecular mechanisms by which inhalational anesthetics provide this DCI protection include upregulation of hypoxia-inducible factor-1 α 7 and increased expression of endothelial nitric oxide synthase.¹⁴ Similar protective effect with intravenous anesthetics is not known. Athiraman et al. conducted a retrospective study of patients with aSAH who underwent aneurysm repair that received either intravenous anesthesia or inhalational anesthesia.¹⁵ The aneurysm repair was performed within 24 hours of admission in two large centers, where one center used intravenous anesthesia ($n = 206$) and the other used inhalational anesthesia ($n = 179$). The outcome measures were angiographic vasospasm ($>25\%$ of narrowing), DCI (decrease in GCS score >2 , neurological deficit after day 4), and neurological outcome (disposition at hospital discharge). Baseline characteristics were comparable between the two groups. The rates of angiographic vasospasms between inhalational and intravenous anesthesia groups were 32% vs. 52% (OR = 0.49, CI: 0.32–0.75, $p = 0.001$) and DCI were 21% vs. 40% (OR = 0.47, CI: 0.29–0.74, $p = 0.001$) after adjustment of imbalance between sites, SAH grade, type of treatment, and ASA status. There was no impact of anesthetic on the neurological outcome between the groups (78% vs. 72%, $p = 0.23$). Thus, this study suggests that inhalational anesthetics had significant protection against SAH-induced vasospasm and DCI. However, the authors acknowledge that being a non-randomized study, with modest sample size and the differences in the protocol between the groups could have caused a significant selection bias. Future prospective randomized controlled trials are needed to confirm the neuroprotective effect of inhalational agents.

Advanced Hemodynamic Monitoring in Patients with Subarachnoid Hemorrhage

Patients with aSAH often develop medical complications including cardiac, pulmonary, renal, hematological, and endocrine dysfunction. These complications can lead to a worsening of secondary brain injury because of hypotension, hypoxia, or hypovolemia. Hence, in addition to standard

hemodynamic monitoring (invasive arterial/central venous pressure measurements, fluid balance assessment), some patients may require advanced hemodynamic monitoring (continuous cardiac output monitoring). However, the utility of these advanced hemodynamic monitoring on clinical outcomes in patients with aSAH is not clear. Simonassi et al. conducted a systematic review and meta-analysis of the literature to determine whether standard compared with advanced hemodynamic monitoring can improve patient management and clinical outcomes after aSAH.¹⁶ This systematic review looked at the prevalence of dichotomous (DCI, pulmonary edema, neurological outcome [modified Rankin scale]) and continuous outcomes (fluid balance) between the groups. A total of 14 studies were selected for the qualitative synthesis and 3 randomized controlled trials for meta-analysis. The incidence of DCI was lower in the advanced compared with standard hemodynamic monitoring group (relative risk [RR] = 0.71, 95% CI = 0.52–0.99; $p = 0.044$). There were no differences in neurological outcome (RR = 0.83, 95% CI = 0.64–1.06; $p = 0.14$), pulmonary edema onset (RR = 0.44, 95% CI = 0.05–3.92; $p = 0.46$), or fluid intake (mean difference = -169 mL; 95% CI = -1463 to 1126 mL; $p = 0.8$) between the two groups. Overall, there was a very limited number of good-quality randomized controlled studies. Hence, this study has identified very low-quality evidence to support the use of advanced hemodynamic monitoring in aSAH patients. The authors have provided a flow chart to aid in decision-making for the use of advanced hemodynamical monitoring after aSAH. The decision to use advanced hemodynamic monitoring in aSAH patients should be based on an individualized approach, considering the patient characteristics, risks, and benefits of monitoring, and likely prognosis.

Recent Concussion and Postoperative Complications

A concussion is a form of mild traumatic brain injury (TBI) that is often accompanied by changes in cerebral hemodynamics, which manifest as a spectrum of neurological symptoms, lasting for days to months. During this period, this “vulnerable” brain may be exposed to anesthesia for trauma-related procedures. Physiological alterations during the perioperative period may contribute to secondary neurocognitive injury after a concussion. D’Souza et al. conducted an exploratory retrospective matched cohort study to describe postoperative outcomes in patients who recently sustained a concussion and underwent surgery that required anesthesia.¹⁷ A total of 60 patients with concussions were matched with 176 patients with no concussions (1:4 matching). There were no differences between the groups with regard to perioperative and postoperative physiological variables. Among the 12 outcome variables studied, 3 variables namely postanesthetic care unit pain score > 7, headache within 90 days of anesthesia exposure, and headache within 90 days of anesthesia in patients who had surgery within 30 days of concussion were significantly higher in the concussion group. However, subgroup analysis based on the period of time that elapsed between their concussion and surgical dates (0 to 30, 31 to 60, and 61 to 90 days) failed to show any difference between the groups. Overall, they reported a 3.3% incidence of newly

diagnosed post-concussive syndrome in patients who underwent anesthesia within 30 days of concussive head trauma. In summary, this retrospective exploratory study concluded that anesthesia and surgery after recent concussion were not associated with significant differences in intraoperative physiological variables or postoperative complications compared with patients without concussion after correction for multiple comparisons. Further, adequately powered studies will be required to identify periprocedural and peri-anesthetic risks in patients with concussions.

Intensive Care Management of Traumatic Brain Injury (TBI) (CENTER-TBI, OzENTER-TBI, and SYNAPSE-ICU Studies)

Several studies used data from a large observational cohort from large multicenter databases to better characterize TBI management in the ICU. These included an international prospective observational Study on Intracranial Pressure in Intensive Care Unit (SYNAPSE-ICU),¹⁸ the Collaborative European Neurotrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI) study,^{19,20} and the Australia-Europe Neurotrauma Effectiveness Research in Traumatic Brain Injury (OzENTER-TBI) study.²¹

Using data from SYNAPSE-ICU, Robba et al. observed 4,776 patients from 146 ICUs who were admitted for TBI or primary hemorrhagic stroke.¹⁸ They found 56% of the patients received intracranial pressure (ICP) monitoring and they tended to be younger and had a lower prevalence of co-morbidities. There was also significant variability in the indications for the use of ICP monitoring between centers. Patients who received ICP monitoring had improved 6-month mortality and better neurologic outcome with a hazard ratio of 0.35 and 0.38, respectively. Patients who had ICP monitoring also had higher therapeutic interventions, which was also associated with a reduction in mortality.

Looking at data from 196 patients from CENTER-TBI, Zeiler et al. analyzed whether using pressure reactivity index (PRx) to target individualized ICP targets will lead to better outcomes over current guidelines.¹⁹ PRx uses mathematical algorithms to calculate the individualized ICP targets by calculating the ability of a vessel to autoregulate using the correlation between ICP and mean arterial pressure (MAP).²² They found that patients with individualized ICP targets had better 6 to 12 months’ mortality outcomes. There was a trend toward higher favorable outcomes, but it did not reach statistical significance even when controlling for baseline admission characteristics.

Using data from CENTER-TBI, Citerio et al. performed a secondary analysis on 1,100 patients to observe how different centers managed PaCO₂ of TBI patients and its outcomes.²⁰ They found that the mean and minimum PaCO₂ were 38.9 and 35.2 mm Hg, respectively. Centers that had ICP measurements had lower daily minimum PaCO₂ at 34.5 versus 36.7 mm Hg. Similarly, patients with increased ICP also had lower daily minimum PaCO₂. There was no difference in 6-month mortality or unfavorable neurological outcomes when comparing patients who received hyperventilation (PaCO₂ < 30 mm Hg).

Combining data from CENTER-TBI and Oz ENTER-TBI, Wieggers et al. analyzed 2,125 patients on daily fluid balance for patients in ICU with TBI.²¹ They found that there was large variability in fluid management between centers; the mean daily fluid balance was found to range between -0.85 and 1.13 L. Patients with positive fluid balance were associated with higher ICU mortality and worse functional outcome with OR of 1.10 per 0.1 L and 1.04 per 0.1 L increase, respectively. Similarly, increased daily fluid input was found to be associated with higher ICU mortality and worse functional outcome with OR of 1.05 per 0.1 L and 1.04 per 0.1 L increase, respectively. Centers with overall increased fluid balance had increased mortality and worse functional outcome, but this was not seen in increased fluid intake.

Results from three large multicenter, prospective, observational studies reinforce the importance of previously known principles namely maintaining CPP, PaCO₂, and the patient's fluid status in the management of patients with TBI.

Hyperosmolar Therapy in TBI

Hyperosmolar therapy with mannitol and/or hypertonic saline (HS) is routinely used to treat raised ICP after acute brain injury. Both mannitol and hypertonic saline have been shown to be effective with no clinical superiority of one over the other. Previous clinical trials, systematic reviews, and meta-analyses looking at the clinical efficacy of mannitol and hypertonic saline are restricted to surrogate endpoints such as ICP reduction and have not detected significant differences in mortality or functional outcome. Schwimmbeck et al. conducted a systematic review and meta-analyses to identify the effect of hypertonic saline compared with mannitol on mortality, functional outcome (Glasgow Outcome Scale [GOS] ≥ 4 or extended GOS [GOS-E ≥ 5]), and cerebral physiologic variables (ICP, CPP, brain tissue oxygen partial pressure in patients with TBI).²³ A total of 12 randomized controlled trials with 464 patients were included in the analysis. This study results showed a non-significant trend toward lower mortality with HS but no significant differences in the functional outcome between HS and mannitol. However, in post hoc sensitivity analysis, there was a statistically significant reduction in mortality and improved functional outcome with HS. Regarding physiological variables, there was no difference in ICP at 30 to 60 minutes after treatment, but it was significantly lower in the HS group at 90 to 120 minutes (mean difference [MD] = -2.33 mm Hg, 95% CI: -3.17 to -1.5, $p < 0.00001$). CPP was significantly higher in the HS group at both 30 to 60 minutes (MD = 5.48 mm Hg, 95% CI: 4.84-6.12, $p < 0.00001$) and 90 to 120 minutes (MD = 9.08, 95% CI: 7.54-10.62, $p < 0.00001$). Similarly, treatment failure analysis showed the superiority of HS over mannitol. The authors acknowledge that despite their attempt to limit the heterogeneity by choosing the random effect model, it was difficult to elucidate the predefined subgroup analyses as the studies were heterogeneous and had qualitative deficiencies. Nevertheless, this meta-analysis demonstrated that HS is safe and well-tolerated in the treatment of elevated ICP and especially in the treatment of refractory intracranial hypertension.

Continuous Infusion of Hypertonic Saline and Neurological Outcome in Patients with TBI

TBI guidelines and protocols have been shown to improve patient outcomes.²⁴ Fluid therapy is an important component of the care bundle for patients with TBI. However, whether it modulates clinical outcomes remains unclear. Roquilly et al. conducted a multicentre randomized clinical trial to determine whether a continuous infusion of 20% normal saline solution in addition to standard care improved neurological outcome (GOS-E at 6 months) in patients with TBI.²⁴ Three hundred seventy adult patients with moderate-to-severe TBI were randomly assigned to receive a continuous infusion of 20% hypertonic saline solution plus standard care ($n = 185$) or standard care alone (controls; $n = 185$). The intervention (0.5-1 g/h of 20% NS) was initiated within 24 hours of injury and continued as long as patients were considered at risk of intracranial hypertension. In the standard care group, an isotonic crystalloid solution was used as the maintenance fluid and a bolus of mannitol or HS would be given along with specific therapies against intracranial hypertension advocated. Regarding the outcome measures, GOS-E score 6-8 (indicating upper moderate disability to good recovery) were similar between the groups (32.6% in the intervention group vs. 35.4% in the standard group). Of the 12 secondary outcomes, 10 were not significantly different. Hyponatremia (Na >160 mmol/L) and thromboembolic events were higher in the intervention group. The authors conclude that the treatment with continuous infusion of 20% hypertonic saline compared with standard care did not result in a significantly better neurological status at 6 months. However, confidence intervals for the findings were wide, and the study may have had limited power to detect a clinically important difference. Continuous infusion of HS was associated with a lower risk of intracranial hypertension during the first 2 days and a rebound of intracranial pressure was apparent from day 4 onward. Thus, the authors believed that discontinuation of infusion may be an important step to prevent secondary brain injury.

Intravenous versus Volatile Anesthetics for Mechanical Thrombectomy

The role of endovascular thrombectomy (EVT) in the treatment of acute ischemic stroke (AIS) in patients with large vessel occlusion is now well-established. However, the choice of anesthetic technique in these patients remains controversial. Recent randomized trials, systematic reviews, and meta-analyses indicate that GA is non-inferior to conscious sedation. However, it is not clear whether the choice of an anesthetic agent influences clinical outcomes in patients undergoing EVT under GA. Diprose et al. published a retrospective study comparing TIVA and volatile anesthesia for EVT under GA.²⁵ They reviewed the database of 313 consecutive patients. Overall, 59 and 254 patients were administered TIVA with propofol and volatile anesthetics, respectively. All patients were intubated, ventilation adjusted to aim end-tidal carbon dioxide values of 35-45 mmHg, systolic blood pressure (SBP) between 140 and 180 mm Hg, normothermia, and normoglycemia. The median of

minimum alveolar concentration (MAC) for a volatile agent was at 0.59 (0.50–0.68), while that of intravenous propofol at target-controlled infusion (TCI) was 2.7 $\mu\text{g/mL}$ (2.0–3.7). While both groups were quite similar demographically, multivariable logistic regression analysis showed that propofol anesthesia was associated with improved functional independence at 3 months (OR = 2.65; 95% CI: 1.14–6.22; $p = 0.03$) and a nonsignificant trend toward reduced 3-month mortality (OR = 0.37; 95% CI: 0.12–1.10; $p = 0.07$). Though this retrospective study had an imbalance in sample size between the groups, the authors did a good comparison using false discovery rate adjusted p -value to calculate the significant differences in the outcome. The findings of this study should be considered as hypothesis-generating for future prospective randomized controlled trials.

Intensive Blood Pressure Lowering after Successful Mechanical Thrombectomy (BP-TARGET Study)

Blood pressure management is an important consideration in the perioperative management of patients with acute ischemic stroke (AIS) undergoing endovascular thrombectomy (EVT). While maintaining high blood pressure is vital before thrombectomy, high SBP after thrombectomy is associated with an increased risk of intracerebral hemorrhage (ICH). The optimal blood pressure target after successful thrombectomy is not known. Mazighi et al. conducted a multicenter, randomized controlled trial to assess whether an intensive SBP target resulted in reduced rates of intraparenchymal hemorrhage compared with a standard SBP target.²⁶ Three hundred twenty-four patients with AIS that was successfully treated with EVT were randomly assigned (1:1) to either an intensive SBP target (100–129 mm Hg) or a standard care SBP target (130–185 mm Hg). In both groups, the target SBP had to be achieved within 1 hour after randomization and maintained for 24 hours with intravenous blood pressure-lowering treatments. The mean SBP in the intensive and standard groups were 128 and 138 mm Hg, respectively, and 66% and 29.5% of patients respectively achieved the target within the first hour after reperfusion. There was no statistically significant difference between the groups on the incidence of intraparenchymal hemorrhage (43% in the intensive group vs. 42% in the standard group). Similarly, there were no differences between the groups regarding the incidence of symptomatic intracranial hemorrhage or hypotensive events. Although this study showed no evidence that intensive lowering of SBP was superior to the standard SBP target, the difference of 10 mm Hg between these groups might be too low to be statistically significant. Hence, the variability of the SBP and the type of antihypertensives used need to be considered for future clinical trials.

Blood Pressure Trajectory Groups and Outcome after Mechanical Thrombectomy

As a follow-up to the previous study on the same topic, Petersen et al. conducted a multicenter retrospective study on 2,268 patients with AIS who underwent EVT and recorded their post-procedure blood pressure trends.²⁷ They used latent variable mixture modeling and identified five

distinct systolic blood pressure (SBP) trajectories over the first 72 hours after EVT: low, moderate, moderate-to-high, high-to-moderate, and high groups. They found that the SBP trajectories were independently associated with functional outcome at 90 days where patients with high-to-moderate and high trajectories had adjusted ORs of 2.2 and 3.5, respectively, for poor outcomes. Furthermore, the high-to-moderate trajectories group had an increased risk of symptomatic intracranial hemorrhage. This study provides an insight to identifying patients at risk of complications and hence targeted intervention can be initiated instead of a single target with a one-size fit all approach. More studies are needed to see if at-risk groups benefit from intensive blood pressure management.

Narrative Reviews of Interest

In addition to clinical studies, the following are some of the narrative reviews that are of interest to neuroanesthesiologists. Bernier et al. have recently published a review and a future study proposal on the use of milrinone in treating SAH-associated DCI.²⁸ Uribe et al. have provided an evidence-based review of general considerations, risk factors, and management of postoperative nausea and vomiting (PONV) after craniotomy.²⁹ Ma et al. have reviewed some basic concepts, indications, and controversies behind the use of albumin in brain-injured and neurosurgical patients.³⁰ Cerebral venous thrombosis is an unusual cerebrovascular disorder that is of current interest, in part because of rare cases associated with a certain strain of the coronavirus disease 2019 (COVID-19) vaccines. The characteristics of infarction caused by cerebral venous thrombosis differ from those of the usual forms of ischemic stroke caused by the occlusion of arterial vessels. Rooper et al. have recently published a brief review that describes the diagnosis of cerebral venous thrombosis, based on clinical and imaging features, and treatments.³¹ A review by Mendelson et al. summarizes current evidence regarding the diagnosis of AIS and TIA and early management methods to improve outcomes and prevent recurrent ischemic strokes.³² Vestibular Schwannomas are the most common cerebellopontine angle tumors. Carlson et al. have published a recent review on this topic discussing pathophysiology, clinical presentation, and its management.³³

Conflict of Interest

None declared.

References

- 1 Dubin A, Pozo MO, Casabella CA, et al. Increasing arterial blood pressure with norepinephrine does not improve microcirculatory blood flow: a prospective study. *Crit Care* 2009;13(3):R92
- 2 Koch KU, Mikkelsen IK, Espelund US, et al. Cerebral macro- and microcirculation during ephedrine versus phenylephrine treatment in anesthetized brain tumor patients: a randomized clinical trial using magnetic resonance imaging. *Anesthesiology* 2021;135(5):788–803
- 3 Martinez-Simon A, Valencia M, Cacho-Asenjo E, et al. Effects of dexmedetomidine on subthalamic local field potentials in Parkinson's disease. *Br J Anaesth* 2021;127(2):245–253

- 4 Bos MJ, Buhre W, Temel Y, Joosten EAJ, Absalom AR, Janssen MLF. Effect of anesthesia on microelectrode recordings during deep brain stimulation surgery: a narrative review. *J Neurosurg Anesthesiol* 2021;33(4):300–307
- 5 Liu Z, He S, Li L. General anesthesia versus local anesthesia for deep brain stimulation in Parkinson's disease: a meta-analysis. *Stereotact Funct Neurosurg* 2019;97(5-6):381–390
- 6 Holewijn RA, Verbaan D, van den Munckhof PM, et al. General anesthesia vs local anesthesia in microelectrode recording-guided deep-brain stimulation for parkinson disease: the GALAXY randomized clinical trial. *JAMA Neurol* 2021;78(10):1212–1219
- 7 Rocha-Filho PAS. Post-craniotomy headache: a clinical view with a focus on the persistent form. *Headache* 2015;55(5):733–738
- 8 Venkatraghavan L, Li L, Bailey T, Manninen PH, Tymianski M. Sumatriptan improves postoperative quality of recovery and reduces postcraniotomy headache after cranial nerve decompression. *Br J Anaesth* 2016;117(1):73–79
- 9 Patel KS, Laiwalla AN, DiCesare JAT, Garrett MC, Wang AC. Subcutaneous sumatriptan: association with decreases in postoperative pain and opioid use after elective cranial surgery. *J Neurosurg* 2020;134(2):1–9
- 10 Mubashir T, Arif AA, Ernest P, et al. Early versus late tracheostomy in patients with acute traumatic spinal cord injury: a systematic review and meta-analysis. *Anesth Analg* 2021;132(2):384–394.
- 11 Tamaki T, Kubota S. History of the development of intraoperative spinal cord monitoring. *Eur Spine J* 2007;16(Suppl 2): S140–S146
- 12 Nassef M, Splinter W, Lidster N, et al. Intraoperative neurophysiologic monitoring in idiopathic scoliosis surgery: a retrospective observational study of new neurologic deficits. *Can J Anaesth* 2021;68(4):477–484
- 13 Athiraman U, Dhar R, Jayaraman K, et al. Conditioning effect of inhalational anesthetics on delayed cerebral ischemia after aneurysmal subarachnoid hemorrhage. *Neurosurgery* 2021;88(2):394–401
- 14 Athiraman U, Jayaraman K, Liu M, Giri T, Yuan J, Zipfel GJ. Role of endothelial nitric oxide synthase in isoflurane conditioning-induced neurovascular protection in subarachnoid hemorrhage. *J Am Heart Assoc* 2020;9(20):e017477
- 15 Athiraman U, Lele AV, Karanikolas M, et al. Inhalational versus intravenous anesthetic conditioning for subarachnoid hemorrhage-induced delayed cerebral ischemia. *Stroke* 2021; Doi: 10.1161/STROKEAHA.121.035075
- 16 Simonassi F, Ball L, Badenes R, et al. Hemodynamic monitoring in patients with subarachnoid hemorrhage: a systematic review and meta-analysis. *J Neurosurg Anesthesiol* 2021;33(4): 285–292
- 17 D'Souza RS, Sexton MA, Schulte PJ, Pasternak JJ, Abcejo AS. Recent preoperative concussion and postoperative complications: A retrospective matched-cohort study. *J Neurosurg Anesthesiol* 2021;33(3):221–229
- 18 Robba C, Graziano F, Rebora P, et al; SYNAPSE-ICU Investigators. Intracranial pressure monitoring in patients with acute brain injury in the intensive care unit (SYNAPSE-ICU): An international, prospective observational cohort study. *Lancet Neurol* 2021; 20(7):548–558
- 19 Zeiler FA, Ercole A, Cabeleira M, et al; CENTER-TBI High Resolution ICU Sub-Study Participants and Investigators. Patient-specific ICP epidemiologic thresholds in adult traumatic brain injury: A CENTER-TBI validation study. *J Neurosurg Anesthesiol* 2021;33(1):28–38
- 20 Citerio G, Robba C, Rebora P, et al; Center-TBI participants and investigators. Management of arterial partial pressure of carbon dioxide in the first week after traumatic brain injury: results from the CENTER-TBI study. *Intensive Care Med* 2021;47(9):961–973
- 21 Wiegers EJA, Lingsma HF, Huijben JA, et al; CENTER-TBI; OzENTER-TBI Collaboration Groups. Fluid balance and outcome in critically ill patients with traumatic brain injury (CENTER-TBI and OzENTER-TBI): a prospective, multicentre, comparative effectiveness study. *Lancet Neurol* 2021;20(8):627–638
- 22 Steiner LA, Czosnyka M, Piechnik SK, et al. Continuous monitoring of cerebrovascular pressure reactivity allows determination of optimal cerebral perfusion pressure in patients with traumatic brain injury. *Crit Care Med* 2002;30(4):733–738
- 23 Schwimbeck F, Voellger B, Chappell D, Eberhart L. Hypertonic saline versus mannitol for traumatic brain injury: a systematic review and meta-analysis with trial sequential analysis. *J Neurosurg Anesthesiol* 2021;33(1):10–20
- 24 Roquilly A, Moyer JD, Huet O, et al; Atlanrea Study Group and the Société Française d'Anesthésie Réanimation (SFAR) Research Network, et al; Effect of continuous infusion of hypertonic saline vs standard care on 6-month neurological outcomes in patients with traumatic brain injury: the COBI randomized clinical trial. *JAMA* 2021;325(20):2056–2066
- 25 Diprose WK, Wang MT, Campbell D, et al. Intravenous propofol versus volatile anesthetics for stroke endovascular thrombectomy. *J Neurosurg Anesthesiol* 2021;33(1):39–43
- 26 Mazighi M, Richard S, Lapergue B, et al; BP-TARGET investigators. Safety and efficacy of intensive blood pressure lowering after successful endovascular therapy in acute ischaemic stroke (BP-TARGET): a multicentre, open-label, randomised controlled trial. *Lancet Neurol* 2021;20(4):265–274
- 27 Petersen NH, Kodali S, Meng C, et al. Blood pressure trajectory groups and outcome after endovascular thrombectomy: a multicenter study. *Stroke* 2021; Doi:10.1161/STROKEAHA.121.034408
- 28 Bernier TD, Schontz MJ, Izzy S, et al. Treatment of subarachnoid hemorrhage-associated delayed cerebral ischemia with milrinone: a review and proposal. *J Neurosurg Anesthesiol* 2021;33(3):195–202
- 29 Uribe AA, Stoicea N, Echeverria-Villalobos M, et al. Postoperative nausea and vomiting after craniotomy: an evidence-based review of general considerations, risk factors, and management. *J Neurosurg Anesthesiol* 2021;33(3):212–220
- 30 Ma HK, Bebawy JF. Albumin use in brain-injured and neurosurgical patients: concepts, indications, and controversies. *J Neurosurg Anesthesiol* 2021;33(4):293–299
- 31 Ropper AH, Klein JP. Cerebral venous thrombosis. *N Engl J Med* 2021;385(1):59–64
- 32 Mendelson SJ, Prabhakaran S. Diagnosis and management of transient ischemic attack and acute ischemic stroke: a review. *JAMA* 2021;325(11):1088–1098
- 33 Carlson ML, Link MJ. Vestibular Schwannomas. *N Engl J Med* 2021;384(14):1335–1348