Year in Review: Synopsis of Selected Articles in Neuroanesthesia and Neurocritical Care from 2022

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Abstract

This review is a synopsis of selected articles from neuroscience, neuroanesthesia, and neurocritical care from the year 2022 (January–November 2022). The journals reviewed include anesthesia journals, critical care medicine journals, neurosurgical journals as well as high-impact medical journals such as the *Lancet*, *Journal of American Medical Association* (JAMA), *New England Journal of Medicine* (NEJM), and *Stroke*. The summary of important articles will serve to update the knowledge of neuroanesthesiologists and other perioperative physicians who provide care to neurosurgical and neurocritical cases.

Keywords
► neurocritical care
► neuroanesthesia
► stroke
► traumatic brain injury

Awake Craniotomy versus General Anesthesia in Brain Cancer Progression

High-grade gliomas (World Health Organization [WHO] grade III and IV) are associated with poor prognosis owing to rapid progression and recurrence. Previous studies in non-neurological malignancies have explored the association between the type of anesthesia and outcomes.[1,2] However, there is minimal literature on the type of anesthesia and brain cancer progression. In a multicenter retrospective study by Chowdhury et al, they compared the effect of awake craniotomy (AC) versus general anesthesia (GA) on progression-free survival (PFS) and overall survival (OS) in patients with high-grade gliomas undergoing surgical resection.[3] A total of 891 patients across five centers were included. The two groups were similar with respect to age, sex, location of the tumor, and preoperative Karnofsky Performance Status. However, the GA group had more patients with grade IV tumors and larger tumor size compared to the AC group. Regarding the outcomes, the median PFS in the AC group was 0.54 (95% confidence interval [CI]: 0.45–0.65) years compared with 0.53 years (95% CI: 0.48–0.60) in the GA group; hazard ratio (HR) 1.05; $p = 0.553$. The OS was greater in the AC group compared to GA [median survival of 1.7 (95% CI: 1.30–2.32) versus 1.25 (95% CI: 1.15–1.37) years; HR: 0.76; $p < 0.009$]. However, multivariable analyses did not show a significant difference for PFS or OS after controlling for other variables of interest. The median length of hospital stay was significantly shorter in the AC group (2 [interquartile range, IQR: 3] vs. 5 [IQR: 5] days in the GA [$p < 0.001$]). Though this study suffered from inherent limitations of retrospective study, this is the first large series study on this topic and future prospective randomized controlled trials (RCTs) are needed to study the effect of the different anesthetic techniques in glioma progression.

Asleep-Awake-Asleep Technique and Monitored Anesthesia Care for Awake Craniotomy

AC is often indicated for the resection of pathology close to eloquent areas of the brain. Two commonly used anesthesia

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techniques are asleep-awake-asleep (SAS) and monitored anesthesia care (MAC). However, there is very limited evidence comparing these two commonly used anesthesia techniques in terms of safety and efficacy. Natalini et al conducted a systematic review and meta-analysis to compare SAS and MAC techniques during AC.[4] The main outcome measures of their study included the incidences of AC failure, perioperative nausea and vomiting, intraoperative seizures, intraoperative respiratory adverse events, and the hospital length of stay (LOS). Eighteen studies were included (4 RCTs, 4 prospective observational studies, 5 retrospective studies, and 5 case series). Among the 11 studies that adopted MAC, dexmedetomidine was the first-line sedative, either alone or in combination with propofol or remifentanil. On the other hand, propofol/remifentanil combination was the most frequently used regimen during the SAS technique. There was moderate and substantial heterogeneity in the MAC and SAS groups (I^2 was 49 and 81%, respectively). The pooled proportions of AC failure in the MAC and SAS subgroups were 1 (95% CI: 0–3) and 5% (95% CI: 1–10), respectively. They concluded that MAC was associated with a lower AC failure rate, shorter procedure time, and a (not statistically significant) trend toward reduced LOS and incidence of nausea and vomiting compared with SAS. The main limitations of the study were a high risk of bias due to the inclusion of retrospective studies and a single large study that influenced the result of higher AC failure. However, further RCTs are recommended to directly compare the two techniques.

Enhanced Recovery after Elective Craniotomy

Enhanced recovery after surgery (ERAS) protocols have proven benefits in outcomes in various surgical subspecialties.[5,6] However, the literature about its implementation and benefits in neurosurgical patients is sparse. Wang et al conducted an RCT to evaluate the clinical effectiveness and safety of ERAS protocols compared to the usual care in patients undergoing elective craniotomy for a single intracranial lesion.[7] A total of 151 patients were randomized into ERAS (76 patients) and control (75 patients) groups. Their self-formulated ERAS protocol was based on existing literature and it was compliant with the ERAS society reporting guidelines. Patient demographics and surgical characteristics were comparable between the groups. The main findings of the study include the reduced LOS in the hospital (3 vs. 4 days, [95% CI: 1–2], $p < 0.0001$), lower hospitalization costs (5880 USD vs. 6266 USD, [95% CI: 234.8–633.6], $p < 0.0001$), and early ambulation (75.0 vs. 30.7%, odds ratio [OR]: 7.5, [95% CI: 3.6–15.8], $p < 0.0001$). They recommend the evaluation of the ERAS protocol in larger multicenter studies.

Erector Spinae Plane Block in Lumbar Spine Surgery

Postoperative pain management after lumbar spine surgery can be challenging and inadequate pain management can predispose patients to develop chronic postsurgical pain. Multimodal analgesia regimens have been proposed and more recently, the use of regional anesthesia techniques especially erector spinae plane block (ESPB) has been popular.[8,9] Oh et al published a systematic review and meta-analysis of the RCTs comparing the efficacy of ESPB with either no block or sham block.[10] They included 12 studies and a total of 665 patients with 330 of them in the ESPB group and 335 in the control group. ESPB significantly reduced opioid (intravenous morphine milligram equivalents) consumption in the first 24 hours after surgery (mean difference = – 14.55; 95% CI: –21.03 to –8.07; $p < 0.0001$; I^2 99%) compared to the control group. However, this difference was not seen at 48 hours. In addition, the ESPB group had less rescue analgesia, a longer time to need rescue analgesia, less postoperative nausea and vomiting, shorter LOS, and higher overall satisfaction scores compared to the control group. Heterogeneity was the major limitation of the study due to wide variation in block techniques with different timings, positions, approaches, vertebral levels, and variations in local anesthetics in type, concentration, and volumes.

Pain Management after Transsphenoidal Pituitary Surgery

Transsphenoidal resection of pituitary adenomas (PAs) is a minimally invasive neurosurgical procedure and postoperative pain in this subset of patients is not well studied. There are contrary beliefs about the severity of pain ranging from modest to severe.[11] Nevertheless, opioids are the most used analgesics in this patient population and in general nonsteroidal anti-inflammatory drugs (NSAIDs) are avoided in neurosurgical patients. Guo et al conducted a randomized, single-center, noninferiority trial to compare the efficacy and safety of NSAIDs with tramadol following transsphenoidal surgery for PAs.[12] A total of 202 patients were assigned to either the NSAIDs group ($n = 101$) or the tramadol group ($n = 101$). The patients in the NSAIDs group were treated with intravenous parecoxib sodium (40 mg) and oral loxoprofen sodium (60 mg). The tramadol group was treated with intramuscular tramadol hydrochloride (100 mg) and oral tramadol hydrochloride (100 mg). Both groups were similar in demographics, clinical characteristics, and tumor imaging features. Intention-to-treat analysis was used to analyze the patient data. The mean visual analog scale scores for the first 24, 48, and 72 hours were significantly lower in the NSAIDs group. Nausea was observed in 39.6 and 61.4% of the NSAIDs group and tramadol group respectively. Importantly, 4.0% in the NSAIDs group and 15.8% in the tramadol group received rescue analgesics. In addition, none of the patients had sellar hematomas based on magnetic resonance imaging done on the second postoperative day. The study concluded that the NSAIDs were a better choice, though exploring the better subtype of NSAIDs was suggested by the researchers.

Risk Factors for Postoperative Diabetes Insipidus in Transsphenoidal Surgery

Diabetes insipidus (DI) is one of the complications after transsphenoidal pituitary surgery that could be transient or permanent. There is a wide variation in the clinical and biochemical definition of DI resulting in a wide range of reported incidences ranging from 2 to 54%. Nevertheless, its occurrence is associated with increased morbidity, hospital readmissions, and mortality. Hence, it is plausible to find predictors of DI for better patient care and outcomes.[13] Joshi et al published a retrospective study to identify the perioperative risk factors that may predispose to DI after pituitary surgery.[14] They included 2,529 patients of which postoperative DI was observed in 10.7% of patients (6.2% had transient DI and 4.5% had permanent DI). The DI occurrence was highest in patients with craniopharyngiomas (46.3%) followed by pituitary apoplexy (14.3%) and Rathke's cleft cysts (14.3%). They found that younger age, intraoperative cerebrospinal fluid encounter, and postoperative hyponatremia increased the risk of DI. Postoperative hyponatremia is believed to be due to intraoperative pituitary damage, causing subsequent vasopressin release and osmotic dysregulation in the body, similar to syndrome of inappropriate antidiuretic hormone secretion (SIADH). Increasing tumor diameter increased the risk of DI in patients with functional PAs but not in nonfunctional PAs.

Risk Factors for Venous Air Embolism in the Semi-Sitting Position

The semi-sitting position in neurosurgery has many advantages including better anatomical orientation, less brain swelling with decreased need for mechanical retraction, and better operative field with less bleeding. However, the risk of venous air embolism (VAE) in this position is high. The reported incidence and the risk factors for VAE vary in the literature and often from a small number of patient cohorts. In a retrospective study, Al-Afif et al looked at the incidence and the risk factors for VAE in 740 patients who underwent surgery in the semi-sitting position.[15] The incidence of VAE in their cohort was 16.1% (119/740 patients). VAE was apparent on transthoracic doppler echocardiography or transesophageal echocardiography in all cases. Decrease in end-tidal carbon dioxide (EtCO2) and blood pressure (BP) and a reduction in both parameters were seen in 19, 15, and 19% of the patients, respectively. Occurrence of VAE was most common during tumor resection (67%) followed by craniotomy (24%) and wound closure (9%). The VAE was managed well in all the cases, except for one where the surgery had to be aborted. Management strategies for VAE included flushing of the surgical site with 0.9% normal saline, gentle compression of the jugular veins by the anesthesiologist, Trendelenburg positioning, aspiration from the central line (if present), and rapid treatment of hypotension by intravenous fluids and/or vasopressors. Only two patients had VAE-related systemic or cerebral consequences (cerebral infarctions with transient or permanent neurological deficits). No significant differences were noted between patients with and without VAE regarding age, height, weight, body mass index, preoperative hemoglobin concentration, a history of chronic cardiovascular disorders, surgical approach, and type of tumor. The study could not identify any perioperative risk factors for the occurrence of VAE. Therefore, the authors suggest that the semi-sitting position is safe and its advantages outweigh the benefits due to the lower incidence of VAE and lower complications secondary to VAE.

Management of Hyperglycemia in Patients with Intracranial Pathology

A. Intracranial Hemorrhage

Current guidelines on optimal blood sugar management in patients with intracerebral hemorrhage (ICH) remain unclear as there is still debate on the optimal glucose targets for this patient population. Guidelines from the American Heart Association/American Stroke Association state that serum glucose should be monitored and both hypoglycemia and hyperglycemia should be avoided; however, no definite cuff-offs are provided.[16] Qureshi et al retrospectively evaluated the effect of persistent hyperglycemia on outcomes in 1000 patients with ICH (within 4.5 hours of symptom onset).[17] The patients investigated were part of the ATACH-2 trial (Antihypertensive Treatment of Acute Cerebral Hemorrhage II) in which patients with hyperglycemia (>185 mg/dL and possibly > 140 mg/dL) were treated with insulin. Multivariate analysis, adjusted for variables (Glasgow Coma Scale (GCS) score, hematoma volume, presence or absence of intraventricular hemorrhage, hyperlipidemia, cigarette smoking, and hypertension) showed that persistent hyperglycemia, either moderate (140 -180mg/dL) (OR: 1.8 [95% CI: 1.1–2.8]) or severe (> 180mg/dL) (OR: 1.8 [95% CI: 1.2–2.7]), was associated with increased risk of death or disability in nondiabetic patients with ICH. However, this association was not seen in diabetic patients ($p = 0.996$).

Similarly, Eagles et al performed a retrospective post-hoc analysis of data sets of patients with subarachnoid hemorrhage (SAH) from the CONSCIOUS I Trial (Clazosentan to overcome neurological ischemia and infarction occurring after SAH).[18] Three hundred ninety-nine patients with SAH were compared in this matched analysis and propensity scores were used on covariates and outcomes of interest. It showed that maintaining blood glucose (BG) levels below 9.2 mmol/L (<165 mg/dL) in SAH patients was associated with a decreased risk for unfavorable outcomes (defined as a modified Rankin Scale [mRS] grade > 2). However, there was no statistically significant decrease in the risk of death.

B. Acute Ischemic Stroke

Hyperglycemia during thrombolysis for acute ischemic stroke (AIS) has been associated with worse functional outcomes and hemorrhagic complications.[19] However, whether hyperglycemia during an AIS worsens functional outcomes or is purely a marker of insulin resistance or stress remains unclear. Previous research from 2019 did not show a significant difference in functional outcomes at 90 days between the standard versus intensive glycemia treatment groups.[20] Recently, Torbey et al performed a subgroup analysis of the SHINE (Stroke Hyperglycemia Insulin Network Effort) study.[21] In this study, authors did a subgroup analysis of patients with ischemic stroke randomized to standard (target BG 80–179 mg/dL) versus intensive (target BG 80–130 mg/dL) BG control for 72 hours. Subgroup analysis was based on various glycemic parameters: acute BG level, absence versus presence of diagnosed and undiagnosed diabetes, hemoglobin A1c (HbA1c), glycemic gap (baseline BG—expected average daily BG), stress hyperglycemia ratio (baseline BG concentration/HbA1c), and BG variability. Their primary outcome was a 90-day functional outcome, based on the 90-day mRS, adjusted for stroke severity. Their study found no significant difference in the 90-day functional outcomes with different glycemic parameters.

Mechanical thrombectomy (MT) in patients with AIS, due to a large artery occlusion, is becoming the standard of care in patients who can be treated within 24 hours of the time last known to be well. However, complications such as malignant cerebral edema (MCE) and ICH can occur and are associated with poor neurological outcomes. Cannarsa et al retrospectively analyzed 500 patients who underwent MT for anterior cerebral circulation large vessel occlusions.[22] They found that elevated initial stress glucose ratios (iSGR = initial blood glucose/estimated average glucose) significantly increased (OR: 14.26, [95% CI: 3.82–53.26], $p < 0.001$) the risk of MCE and ICH was an independent predictor of poor functional outcome. However, whether stress hyperglycemia represents a modifiable risk factor remains uncertain and further investigations are needed.

C. Elective Brain Surgery

Optimal target values for BG after elective brain surgery also remain unclear. Postoperative infection after brain surgery is a serious complication with complex pathophysiology and hyperglycemia can be a factor that contributes to both infectious and noninfectious complications.[23,24] Kulikov et al did a prospective single-center observational cohort study with 514 patients.[25] Severe intraoperative hyperglycemia ([BG] ≥180 mg/dL) was found to be associated with a higher risk of infections within the first postoperative week in patients undergoing elective brain neurosurgical procedures (OR: 3.71, [95% CI: 1.24–11.09], $p = .018$). Preoperative levels of HbA1c showed a reliable marker of risk for both severe hyperglycemia and postoperative infection in these patients. However, until now it is not known if more precise monitoring and tighter control of perioperative hyperglycemia have an impact on the clinical outcome.

Revascularization in Carotid Artery Stenosis

Carotid artery stenting (CAS) or carotid endarterectomy (CEA) is well-established treatment options for patients with symptomatic carotid artery stenosis.[26] Whether CAS or CEA is a better revascularization choice for asymptomatic carotid stenosis patients remains undetermined. Wang et al conducted a systematic review on this topic (7,230 patients) and found that CAS has comparable perioperative and long-term composite outcomes compared with CEA in patients with asymptomatic carotid artery stenosis.[27] However, CAS may have a higher risk of any stroke and nondisabling stroke in the perioperative period.

On a similar subject, the choice of anesthesia technique (local anesthesia [LA] versus [GA]) for CEA is debatable. Rerkasem et al conducted a Cochrane review (16 RCTs) on the topic of LA versus GA for CEA.[28] The review showed that there were no differences between LA and GA in the 30-day incidence of stroke (OR: 0.91, [95% CI: 0.66–1.26]; $p = 0.58$; low-quality evidence) and death (OR: 0.61, [95% CI: 0.35–1.06]; $p = 0.08$; low-quality evidence).

Association of End-Tidal Carbon Dioxide and Blood Pressure with Perioperative Stroke

Perioperative stroke leads to increased morbidity, mortality, and prolonged hospital stay.[29] Although preexisting risk factors for perioperative stroke are well known, it is important to find modifiable intraoperative risk factors for the prevention of perioperative stroke.[30] In the pursuit of finding intraoperative risk factors, Vlisides et al conducted a multicenter, retrospective, observational case–control study to find the relationship between changes in intraoperative $EtCO_2$, hypotension and perioperative ischemic stroke (within 30 days after surgery) in adult patients scheduled for noncardiac, nonintracranial, and nonmajor vascular surgeries.[31] One of the physiologic basis of their study was that reduced cerebral blood flow (due to hypotension) and carbon dioxide dysregulation can lead to watershed infarction by hypoperfusion or impaired clearance of microemboli.[32] In this study, they included 122 patients with stroke and 496 matched (1:4) controls. Regression modelling was used to find the relationship between stroke and physiologic variables. The strongest association was noted for mean arterial pressure (MAP) less than 55 mm Hg and $EtCO_2$ 30 mm Hg or less and 45 mm Hg or greater. However, no interaction effect was observed between MAP and $EtCO_2$ in relation to stroke. It was observed that 58% of the strokes occurred within the first 3 postoperative days and it was most common in the middle cerebral artery territory. Fifteen percent of stroke patients died in the hospital, and less than 30% of patients could be discharged home in the 30-day period. The study concluded that intraoperative hypotension and both hypo- and hypercarbia were independently associated with postoperative ischemic stroke.

Effect of Anesthesia on Outcome after Endovascular Treatment for Acute Ischemic Stroke

Endovascular treatment of AIS of large vessel occlusion has now become the standard of care and it has been shown to reduce post-stroke disabilities. Albeit, there is still a lot of controversy around the optimal type of anesthesia for patients undergoing endovascular treatment.[33] Wagner et al conducted a retrospective matched comparison study of 1284 patients (GA: $n = 851$, non-GA: $n = 433$) from eight stroke centers (Swiss Stroke Registry).[33] They showed a worse functional outcome (3-month mRS with an estimated coefficient of 3.40 [1.76–5.04]), and dependency or death (OR: 1.49 [1.07–2.07]) after endovascular treatment of anterior circulation stroke with GA compared to without GA and this finding was independent of known patient differences. However, data analysis showed that the reason for GA was not always known, as factors of agitation could also have played a role in the decision making and the GA group had patients who had an intraoperative conversion from conscious sedation (CS) to GA. Hence, it remains to be determined whether a change in anesthesia technique would change the clinical outcome and if a change in technique would be even feasible in some of these patients.

Maurice et al recently finished the General Anesthesia versus Sedation for Acute Stroke Treatment (GASS) trial in France.[34] Their study investigated GA versus CS, both with hemodynamic control during intraarterial treatment for stroke. Their single-blind randomized trial studied 351 patients and found that the functional outcomes 3 months after endovascular treatment for stroke were similar between GA and CS (relative risk: 0.91, [95% CI: 0.69–1.19], $p = 0.474$) and therefore, suggest that clinicians can use either approach. The incidence of technical failure of endovascular therapy in the CS group was found to be greater, while recanalization results were better in the GA group (144 of 169 [85%] vs. 131 of 174 [75%]; P= 0.021). Patients experienced more episodes of hyper- and hypotension in the GA group, but the cumulative duration of hypotension was found to be the same in both groups.

On a similar topic, Liang et al performed a RCT (CANVAS II trial—Choice of Anesthesia for Endovascular Treatment of Acute Ischemic Stroke) in 87 patients with acute posterior circulation stroke. They showed that CS is not better than GA for functional recovery (mRS at 90 days) after endovascular treatment of posterior circulation AIS (48.8 vs. 54.5%; risk ratio 0.89; [95% CI: 0.58–1.38]; adjusted OR: 0.91; [95% CI: 0.37–2.22]). In addition, the rate of successful reperfusion was higher with GA when compared to CS (95.3 vs. 77.3%; adjusted OR 5.86; [95% CI: 1.16–29.53]).[35,36]

Blood Pressure Management after Endovascular Treatment for Acute Ischemic Stroke

One of the big concerns in patients undergoing MT is BP management before and after revascularization. Anadani et al did a post-hoc analysis of the BP-TARGET multicenter trial (Blood Pressure Target in Acute Stroke to Reduce Hemorrhage After Endovascular Therapy) to assess the association between BP changes after revascularization and clinical outcome.[37] In the BP-TARGET trial, patients were randomized into intensive systolic blood pressure (SBP) treatment (SBP target 100–129 mm Hg to be achieved within 1 hour of randomization) or standard SBP treatment (SBP target 130–185 mm Hg) and they found that intensive SBP targets did not result in lower radiographic intraparenchymal hemorrhage rates at 24 to 36 hours compared to standard care BP targets.[38] In this post-hoc analysis, authors looked at the change of systolic blood pressure (ΔSBP) as end-of-procedure SBP minus mean SBP at different time intervals (15–60 minutes, 1–6 hours, and 6–24 hours post-procedure) and outcomes after successful MT. This study showed that ΔSBP had a linear relationship with poor outcomes and the risk of poor outcomes was higher with less reduction from the baseline SBP. Blood pressure management is complex after successful reperfusion, as findings reinforce the potential beneficial effect of rapidly lowering elevated SBP within the first few hours after reperfusion. Potential deleterious effect of significant alteration of BP after successful reperfusion is seen giving the U-shaped relationship with mortality.

Effect of Hyperoxia on Outcomes in Ventilated Patients with Aneurysmal Subarachnoid Hemorrhage

The early goals of management of a patient with aneurysmal subarachnoid hemorrhage (aSAH) include optimization of oxygenation and ventilation for favorable outcomes. While hypoxia aggravates brain injury, hyperoxia could be deleterious as well. Available evidence suggests that hyperoxia results in poor neurological outcomes, delayed cerebral ischemia (DCI), and mortality in patients with aSAH.[39] However, the optimal oxygenation parameters in this patient population are unknown, and various thresholds for hyperoxia have been proposed in studies on this topic. Grensemann et al conducted a single-center, retrospective, study with an aim to identify an optimum target range of arterial partial pressure of oxygen (PaO_2) in mechanically ventilated patients with aSAH.[40] They included 282 patients with aSAH who were mechanically ventilated for at least 72 hours. Their outcome measures were 30-day mortality, a favorable outcome (Glasgow Outcome Scale of 4 or 5), and DCI. To determine the optimal target range of PaO2, the integral values of PaO2 (> 80, 100, 120, and 150 mm Hg) and the time-weighted quartiles of PaO2 (62–78, 78–85, 85–93, and 93–228 mm Hg) were calculated from four hourly blood gas analyses. All these calculations were done on day 1 (hyperacute phase), up to day 3 (acute phase) and up to day 14 from admission. Patients with higher PaO_2 integrals had higher OR for 30-day mortality. The 30-day mortality rate was lowest (20%) between time-weighted PaO_2 values between 78 and 85 mm Hg, while it was 28, 23, and 32%, respectively, for the quartiles 62 to 78, 85 to 93, and 93 to 228 mm Hg. In addition, favorable outcomes at 3 months were highest (53%) for 78 to 85 mm Hg and 32, 39, and 32%, respectively, for 62 to 78, 85 to 93, and 93 to 228 mm Hg. No association was found between oxygenation parameters and DCI. Thus, the authors conclude that hyperoxia is associated with poorer outcomes in patients with aSAH. Additionally, they suggested 78 to 85 mm Hg as the optimal target range for time-weighted PaO_2. Further prospective studies were needed to confirm this finding.

Management of Traumatic Brain Injury

Traumatic brain injury (TBI) is a major cause of global death and disability. Significant research has been conducted on the effect of TBI on the brain; however, until recently extracranial organ dysfunction following TBI was not yet investigated. Krishnamoorthy et al published pilot data from the TRACK-TBI study and investigated the incidence of myocardial injury (MI) after TBI.[41] High-sensitivity troponin, a sensitive marker of myocardial injury, was used to determine the incidence of early MI. Their study showed that MI is common following TBI, seen in 20% of the studied population, with a probable dose-response association with TBI severity. In addition, the early timing of MI seemed to be associated with poor 6-month clinical outcomes after moderate to severe TBI. On a similar topic, circulatory shock can occur in patients with TBI. The risk factors and long-term functional neurological outcomes associated with circulatory shock in this patient population are not well understood. Toro et al conducted a retrospective analysis of the TRACK-TBI database and showed that race, GCS in the emergency department, computed tomography Rotterdam scores less than 3, and development of hypotension in the emergency department were associated with developing circulatory shock and showed to be associated with poor long-term functional outcome.[42]

In this same TRACK-TBI study population, Toro et al investigated the association of vasopressor choice with clinical and functional outcomes following moderate-to-severe TBI through a retrospective cohort study.[43] The study included 156 adult patients with moderate-to-severe TBI (defined as GCS score < 13) admitted to the intensive care unit (ICU) and who received intravenous vasopressors within 48 hours after ICU admission. Regression analysis with propensity score matching showed the patients received either phenylephrine or norepinephrine as first-line agents for BP support. The choice of vasopressor showed not to be associated with improved clinical or functional outcomes.

The main goals in the management of patients with severe TBI include reducing intracranial pressure (ICP), maintaining an adequate cerebral perfusion pressure, and improving oxygen delivery to the brain. Ischemia of the brain is considered a major cause of secondary brain injury. Rezoagli et al did a study on the association between arterial PaO2 and fraction of inspired oxygen (FiO2) levels within the first week of TBI and clinical outcomes. They performed a secondary analysis on two previously performed multicenter, prospective observational cohort studies from Europe and Australia; Collaborative European Neuro Trauma Effectiveness in Research in Traumatic Brain Injury (CENTER-TBI) study, and Australia–Europe Neuro Trauma Effectiveness Research in Traumatic Brain Injury (Oz ENTER-TBI) study.[44] In patients with TBI, exposure to high PaO2 or high FiO2 was shown to be independently associated with 6-month mortality in the CENTER-TBI cohort, and it showed that the severity of brain injury did not modulate this relationship. However, this finding was not validated in the Oz ENTER-TBI cohort due to the smaller sample size. Though this study does support the need for caution with liberal oxygen therapy in patients with TBI, one must remember that this association may not apply to patients where FiO2 and PaO2 are titrated to optimize brain tissue oxygen (PbtO2) levels.

On the topic of PbtO2 monitoring, a recent systematic review and meta-analysis looked at the use of brain tissue oxygen-guided management and outcomes in patients with TBI.[45] This study showed that combined PbtO2-guided management with standard ICP-based management was not significantly associated with increased favorable neurological outcomes but showed increased survival and reduced ICP. However, the level of evidence for this meta-analysis was low and more research needs to be conducted.

Management of Thrombolysis in Acute Ischemic Stroke

Intravenous thrombolysis with alteplase is the currently approved therapy for patients with AIS who present within 4.5 hours of symptom onset.[46] In recent years, there has been increased interest in tenecteplase, a modified version of alteplase, due to its ease of administration, lower cost, and better outcomes when compared to alteplase. A recent systematic review (6 RCTs) comparing alteplase and tenecteplase for thrombolysis in patients with AIS has shown that tenecteplase appeared to be a better thrombolytic agent for AIS when compared to alteplase.[46] In addition, Tsivgoulis et al conducted a propensity score-matched data set from 20 centers on this topic and came to the same conclusion.[47] In 2017, the Norwegian tenecteplase stroke trial (NOR-TEST) showed that 0.4 mg/kg tenecteplase had an efficacy and safety profile similar to that of a standard dose (0.9 mg/kg) of alteplase in AIS, albeit in a patient population with a high prevalence of minor stroke.[48] However, Kvistad et al conducted the NOR-TEST 2 trial, a phase 3, randomized, open-label, noninferiority trial in 11 hospitals with stroke units in Norway.[49] The trial was prematurely terminated because tenecteplase at a dose of 0.4 mg/kg yielded worse functional outcomes compared with alteplase. Currently, it remains the question if tenecteplase is better than alteplase. Future trials are needed to assess a lower dose of tenecteplase versus alteplase in patients with moderate or severe stroke.

Narrative Reviews of Interest

Several excellent review papers focused on topics of particular interest to neuroanesthesiologists were published over the last year. *Anaesthesia* published a special issue entitled perioperative and critical care management of the brain—current evidence.[50] It covered a wide spectrum of clinically important topics including anesthesia for MT, clinical application of point-of-care ultrasound, management of TBI, status epilepticus, and many other. There have been two excellent reviews on idiopathic intracranial hypertension (IIH). First, on the pathophysiology, diagnosis and treatment options and the second is a systematic review of cerebrospinal fluid shunting pathways as a treatment of IIH.[51,52] On a similar topic, Atchley et al have published an updated review on cerebrospinal fluid dynamics.[53] Ma and Bebawy published an excellent narrative review on the physiological mechanisms that underlie the burst-suppression pattern and the evidence for its clinical use in various perioperative settings.[54] Chowdhury et al published a continuing professional development module on anesthetic considerations and management of endovascular thrombectomy for patients with AIS.[55] There have been few focused reviews on BP and hemodynamic management in patients with acute brain injuries. The first was on the current evidence, knowledge gaps, and emerging concepts on BP management after SAH and ICH and the second was on BP management in the first 24 hours after ischemic stroke.[56,57] The final one was on optimal hemodynamic parameters for brain-injured patients in the clinical setting.[58] Other interesting reviews include opioid alternatives in spine surgery, the effects of anesthesia on glioma progression and cardiac-cerebral coupling.[59–61] Finally, there are the recent clinical practice guidelines from the Society for Neuroscience in Anesthesiology and Critical Care on Perioperative care of patients undergoing major complex spinal instrumentation surgery, and the guideline from the American Heart Association/American Stroke Association on the management of patients with spontaneous intracerebral hemorrhage.[62,63]

Conflict of Interest
None declared.

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