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Year in Review: Synopsis of Selected Articles in Neuroanesthesia and Neurocritical Care from 2020

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Abstract

This review is a synopsis of selected articles from neuroscience, neuroanesthesia, and neurocritical care from the year 2020 (January–December 2020). 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

In the last year, several excellent articles focused on topics of particular interest to the neuroanesthesiologist were published. This review is a synopsis of selected articles from neuroscience, neuroanesthesia, and neurocritical care from the year 2020. 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.

Anesthesia and Brain Cancer Outcomes[1]

Studies have shown that use of inhalational anesthetics is associated with poor long-term outcomes following cancer surgeries when compared with total intravenous anesthesia (TIVA).[2] However, there are limited data in brain cancer population. Dong et al have conducted a retrospective study on the impact of anesthesia on the long-term survival of patients with high-grade glioma (HGG).[1] They looked at the progression-free survival (PFS) and overall survival (OS) in 294 patients who underwent craniotomy for tumor resection under general anesthesia, maintained with either propofol (154 patients) or sevoflurane (140 patients). The baseline demographics and the patient characteristics were comparable between the groups. The univariate and multivariate Cox proportional hazard analysis revealed that there were no differences in PFS or OS between the groups. However, in the subgroup analysis of patients with Karnofsky Performance Score (KPS) of <80, anesthesia maintained with sevoflurane increased the risk of death compared with propofol (hazard ratio, 1.66), with no difference in PFS. This difference was not seen in patients with KPS score of >80. Authors proposed that the difference in outcome might be due to better ICP control and cerebral hemodynamics with TIVA than the inhalational group. This study does suffer from major limitations related to its retrospective nature. Hence there is a need for a large, randomized control trial to study the interactions of the anesthetics to tumor progression and survival following HGG resection.

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Scalp Block and Postoperative Pain[3]

Preoperative scalp blocks are routinely indicated during awake craniotomy and occasionally during craniotomy under general anesthesia. However, the usefulness of postoperative scalp block during craniotomy under general anesthesia has not been studied. Rigamonti et al have conducted a randomized controlled trial (RCT) investigating the use of scalp block (0.5% bupivacaine with 1 in 200,000 epinephrine) performed at the end of surgery in reducing the postoperative pain and improving the clinical outcomes in patients who underwent supratentorial craniotomy under general anesthesia.[3] Eighty-nine patients (n = 44 in block group and n = 45 in control group) were enrolled in this study. The primary outcome was assessment of postoperative visual analog scale (VAS) score for pain at 24 hours. Secondary outcome measures included 48-hour VAS score; 24-hour hydromorphone consumption; incidence of nausea and vomiting; time to discharge from recovery room and the hospital; long-term pain scores on days 5, 30, and 60; and finally overall patient satisfaction. The mean VAS score at 24 hours was not different between the treatment and the control groups. There were no statistically significant differences between the groups in the secondary outcomes. However, the plot of VAS scores over time showed a nonlinear trend over time that differed between the two groups. A higher VAS score was observed in the control group in the first 12 hours, and after 12 hours the VAS score was higher in the treatment group. Hence, overall opioid consumption at 24 hours was similar between the groups. This observation was consistent with the duration of scalp block leading to an increase in pain and opioid consumption in the study group after 12 hours. Therefore, there was an underutilization of opioids in the first 12 hours with the rebound pain once the block was resolved. Though this study failed to show a benefit in postoperative analgesia with scalp block, this study does provide important information on the duration of scalp blocks. Future studies should focus on how to prolong the duration of the scalp blocks to use them for postoperative analgesia.

Daytime versus Night-time Emergent Neurosurgical Procedures and Outcomes[4]

Multiple factors play a role in the outcome of neurosurgical procedures. This study investigated the role of diurnal variation on the outcome of emergent neurosurgical procedures.[4] The patient cohort consisted of two groups, "daytime" (7:00 a.m. to 6:59 p.m.) group (n = 199) and "night-time" (7:00 p.m. to 6:59 a.m.) group (n = 105). Primary outcome of the study was the neurological outcome at discharge (Glasgow Outcome Scale [GOS]) that was dichotomized into "favorable" (GOS 4 or 5—moderate disability or good recovery) and "unfavorable" (GOS 1–3—death, persistent vegetative state, or severe disability) outcomes. Secondary outcomes were the effect of perioperative variables on neurological outcome, length of hospital stay, and perioperative anesthetic and surgical complications. Patient demographics and baseline variables were comparable between the groups. A higher proportion of patients in the night-time surgery group had a lower median baseline Glasgow Coma Scale (GCS) and a larger midline shift on admission compared with the daytime surgery group. Majority of the night-time group patients had craniotomy for evacuation of hematoma and also had wide fluctuations in mean arterial pressure (MAP) intraoperatively (40.1 vs. 36.3 mm Hg, p = 0.0434). There was no significant difference in GOS on discharge or at 1 month after discharge. Similarly, there was no significant difference in the rate of intraoperative complications between the two groups. However, the night-time group had a longer length of stay in the hospital (15.3 days vs. 13.7 days, p = 0.0013). The logistic regression model showed that the baseline GCS score, procedure type, surgery acuity, and intraoperative complications were associated with unfavorable outcomes. Among these variables, intraoperative complications and surgical acuity were stronger predictors (odds ratio of 4.8 and 3.4, respectively) of unfavorable outcomes. The authors conclude that night-time emergent surgery is not associated with unfavorable outcome compared with daytime surgeries. However, given the limitations of retrospective study, a possible association between the timing of surgery and the outcome cannot be ruled out. Further well-designed prospective trials are needed to confirm their findings.

Frailty and Outcomes after Brain Tumor Surgery[5]

Frailty has been shown to be associated with multiple complications after surgery.[6,7] This study investigated the association between frailty and outcomes after elective craniotomy for the resection of brain tumors.[5] Frailty assessment was based on a 5-factor modified frailty index (mFI-5) and classified as nonfrail (mFI-5 = 0), low frailty (mFI = 0.2), or medium to high frailty (mFI > 0.2). Patient demographics, comorbidities, and operative factors were compared between nonfrail, low, and medium to high frailty groups. Primary outcome was major complications within 30 days and secondary outcome was discharge destination other than home, 30-day readmission, and 30-day mortality. Multivariate logistical regression was performed to establish the relationship between frailty and individual outcomes. Of the total 20,333 patients analyzed, 30.7% of patients were low frailty and 10.6% were medium to high frailty patients. Multivariate logistic regression adjusting for the demographics, comorbidities, and operative factors has shown a significant association between complications among the low to medium frailty and high frailty groups (aOR 1.41, 95% confidence interval [CI]: 1.23–1.60, p < 0.001 and aOR 1.61, 95% CI: 1.35–1.92, p < 0.00, respectively). In addition, there is an increased risk of discharge destination other than home (aOR 1.32, 95% CI: 1.20–1.46, p < 0.001 and aOR 1.80, 95% CI: 1.58–2.05, respectively), 30-day readmission (aOR 1.29, 95% CI: 1.15–1.44, p < 0.001 and aOR 1.39, 95% CI: 1.19–1.62, p < 0.001, respectively), and 30-day mortality (aOR 1.87, 95% CI: 1.41–2.47, p < 0.00 and aOR 2.42, 95% CI: 1.74–3.38, p < 0.001, respectively) between two frailty groups. While tumor type was not associated with major complications it did influence the secondary outcomes. Metastatic tumors had increased risk of 30-day readmission (aOR 1.47) and 30-day mortality (aOR 2.61). Intrinsic tumors had increased risk of discharge destination other than home (aOR 1.29),

30-day readmission (aOR 1.28), and 30-day mortality (aOR 1.81). These results show that frailty determined preoperatively by the mFI-5 is associated with increasing odds of major postoperative complications and outcomes warranting increased attention to preoperative indicators of frailty in patients for intracranial tumor surgeries.

Safety of Nonsteroidal Anti-inflammatory Drugs after Pediatric Craniotomy for Tumor[8]

Postoperative pain can be a limitation in the recovery of patients after craniotomy. Recently, opioid-sparing techniques have been of great interest, especially in children, as opioid-related complications are a major concern in this group of patients. The use of nonsteroidal anti-inflammatory drugs (NSAIDs) is a well-recognized adjunct to opioid-sparing anesthesia and an important part of multimodal analgesia. However, there is a significant concern of postoperative hemorrhage with the use of NSAIDs after craniotomy due to their antiplatelet effects. Nesvick et al performed this retrospective study to determine the relative risk of hemorrhagic-related outcomes in pediatric surgical patients (age <18 years) who underwent craniotomy for excision of intracranial and skull tumors.[8] They performed a retrospective analysis of a prospectively collected database of patients between January 2009 and June 2019 with the criteria mentioned above who received NSAIDs on postoperative day zero (POD0). Two hundred and seventy-six patients were identified, with 308 craniotomies performed. One hundred and fifty-four (50%) were given an NSAID on POD0. Most common NSAID used was ketorolac (49.0%) (0.5 mg/kg/dose every 6–8 hours up to 15 mg per dose, unless the patient was an adolescent, in which case a one-time dose of 30 mg was allowed). Primary outcome was the return to the operating room for a hemorrhage-related complication and the secondary outcome was the presence of "more than minimal" hemorrhage (as defined by Richardson et al[9]) on routine postoperative imaging within 7 days. From the cohort, six patients (1.9%) returned to the operating room for hemorrhage-related complications and three patients received NSAIDs. Of the 268 (87%) patients who had post-op imaging within 7 days, 17 (6.3%) had more-than minimal hemorrhage on imaging. Among these patients, 9 received NSAIDs and 8 did not (OR 1.08). Overall, there was no significant difference in the rate of return to the operating room or the rates of more than minimal hemorrhage between patients who received NSAIDs on POD0 and those who did not. Though this retrospective study found no evidence that same day NSAIDs are associated with an increased risk of postoperative hemorrhage, the results should be interpreted with a caution. Sample size in this study is quite small, especially when looking for low-incidence events, such as postoperative intracerebral hemorrhage.

Intracranial Pressure—Normal Values and Treatment Threshold[10]

The magnitude and duration of elevated intracranial pressure (ICP) determines the outcome after traumatic brain injury (TBI). However, the threshold at which the ICP causes the detrimental effects that warrants treatment, and whether a common threshold that should be used for all patients remains unclear. Hawryluk et al have conducted a prospective observational study on 523 patients who had ICP monitoring.[10] A total of 4,090,964 1-minute ICP measurements were recorded for the included patients during the entire intensive care unit (ICU) stay. Majority (72.1%, *n* = 377) of the patients had TBI. The mean ICP values and 79 different ICP thresholds from 1 to 80 mm Hg in 1 mm Hg increments were analyzed. The mean ICP value from day 1 to day 30 was 9 mm Hg in patients with TBI and 8 mm of Hg in all other patients. Thus, ICP value of 8 to 9 mm Hg could possibly reflect normal values. While ICP values > 20 mm Hg were associated with mortality, ICP < 20 mm Hg was associated with variable outcomes (vegetative, moderate, or severe disability) in surviving patients. Plotting across different ICP thresholds for the five physiological variables (heart rate, S_pO_2, $P_{bt}O_2$, ICP, and mean arterial pressure [MAP]) demonstrated changes in these physiological variables occurred at ICPs greater than 19 mm Hg and 24 mm Hg. Elastic net regression identified an ICP threshold of 19 mm Hg as most robustly associated with mortality outcome when considering all neurocritical care patients, patients with TBI, and patients with TBI who underwent craniectomy.

Second-Line Antiepileptic Drugs in Status Epilepticus[11]

Benzodiazepines are commonly used in the first line of management for status epilepticus. With no consensus on optimal second line therapy, this multicenter, double-blind, response-adaptive, RCT compared the effectiveness and safety of fosphenytoin, levetiracetam, and valproate in three age groups (<18 years, 18–65 years, and >65 years).[9] Patients 2 years of age or older with persistent generalized convulsive seizures lasting more than 5 minutes to not more than 30 minutes after the last dose of benzodiazepine (minimal adequate cumulative dose of benzodiazepine) were included in this study. Response adaptive randomization for every 100 patients was used to allocate them to a particular treatment group that was most effective after the first 300 patients. The study medications were given over 10 minutes as an intravenous infusion based on patient's weight. The primary outcome was absence of clinically apparent seizures, with improving GCS at 60 minutes after the start of study drug administration without the use of any other medication. The primary safety outcome comprised life-threatening hypotension or arrhythmia. Secondary safety outcome was the need for endotracheal intubation within 60 minutes of the start of study drug infusion, seizure recurrence between 60 minutes to 12 hours, acute respiratory depression, and mortality. The four hundred and sixty-two patients enrolled for this study included 225 children, 186 adults, and 51 older adults. There was no difference in primary outcome or the efficacy between the different drugs within each age group. The primary safety outcome was also rare between the drugs in all age groups. However, the only secondary safety outcome encountered was a higher incidence of endotracheal intubation with children in the fosphenytoin group (33% in fosphenytoin group, 8% in levetiracetam group, and 11% in valproate group; Fisher's exact

test $p = 0.0001$). The effectiveness of stopping a seizure was ~50% for each of the study medications across all the age groups. Thus, this study concludes that in patients with established benzodiazepine-resistant status epilepticus high doses of fosphenytoin, levetiracetam, or valproate are effective as second line of treatment across all age groups.

Tranexamic Acid in Chronic Subdural Hemorrhage Recurrence[12]

Chronic subdural hemorrhage (CSDH) is a common condition encountered in neurosurgical practice around the world. Symptomatic patients undergo hematoma evacuation and up to 38.7% of patients may require repeat surgery for recurrence. This study evaluated the role of tranexamic acid (TXA) in reducing postoperative recurrence of CSDH.[12] Patients were randomized into two groups—standard neurosurgical treatment only (observation arm) and standard neurosurgical treatment with TXA (TXA arm). The patients in TXA arm received 500 mg of TXA postoperatively twice daily for 21 days. Computed tomography (CT) brain scans were performed on postoperative day 1, postoperative week 6, 12 and 24 or as clinically indicated. Primary outcome was the reduction in incidence of recurrence of CSDH within 6 months. Secondary outcome was volumetric differences at baseline and 6, 12, and 24 weeks. Ninety patients were studied (49 in observation arm and 41 in TXA arm). The observation arm had five recurrences at a median of 2.3 weeks while the TXA arm had two recurrences at the 6th week follow-up. Univariate logistical regression analysis showed no statistical differences between the two arms in the primary outcome (OR 0.51, 95% CI 0.11–2.47, $p = 0.40$). Patients in TXA arm had a greater reduction in CSDH volume at 6 weeks (36%) compared with the observation arm (23.3%, $p = 0.66$); however it was not sustained further at 12 and 24 weeks. The difference in hematoma volume at 6, 12, and 24 weeks was not statistically significant between the two arms. Prior use of antiplatelet drugs or anticoagulants or history of cardiac disease did not have significant impact on the primary or secondary outcomes with the TXA arm. Of the 4 patients who had serious adverse events in the TXA arm, only one was possibly related to TXA (asymptomatic 5 × 4 mm thalamic infarct). With the widespread use of TXA in many conditions, this study is the first randomized trial on the use of TXA in reducing recurrence in CSDH. Though this study did not show a significant reduction in the incidence of recurrence of CSDH with TXA, larger trials with different dose regimes and in specific subset of patients who might benefit from the usage of TXA are needed.

Use of Tranexamic Acid during Pediatric Craniosynostosis Surgery[13]

Craniofacial procedures in children are associated with major blood loss and often requiring massive blood transfusions. Use of antifibrinolytic agents like TXA is a common practice to reduce intraoperative blood loss. A previous study has shown that loading dose of 50 mg/kg followed by a maintenance dose of 5 mg/kg/hour significantly reduced the blood loss and the blood transfusions.[14] In contrast, another study on pharmacokinetic modeling based on simulated dose–response curves showed that a loading dose of 10 mg/kg followed by a maintenance of 5 mg/kg/hr maintained the plasma concentration of TXA above the accepted therapeutic concentration of 16 µg/mL.[15] Goobie et al have conducted a randomized controlled noninferiority trial comparing two different loading doses of TXA (low dose—10 mg/kg and high dose—50 mg/kg) followed by a maintenance dose of 5 mg/kg/hour in children undergoing craniosynostosis reconstruction surgery. The primary outcome measure was intraoperative blood loss and the secondary outcomes were blood product transfusion, biological markers of fibrinolysis and inflammation, and plasma TXA concentrations. The low-dose group was considered noninferior to the high-dose group if the 95% confidence interval (CI) for the mean difference in blood loss (high-dose TXA minus low-dose TXA) was above the noninferiority margin of 20 mL/kg. For the packed red blood cell transfusion (PRBC), the noninferiority margin was set at 10 mL/kg. Sixty-six children (34 in low-dose group and 32 in high-dose group) with comparable characteristics were enrolled in the study. Perioperative care was standardized. With regards to mean intraoperative blood loss, this study showed that low-dose TXA *was not less effective* compared to high-dose TXA (39.4 [4.4] vs. 40.3 [6.2] mL/kg [95% CI:–14.2, 15.9]; within the 20 mL/kg noninferiority margin). Similarly, low dose TXA was *not less effective* than the higher dose TXA regarding mean PRBC transfusion (21.3 [1.6] vs. 23.6 [1.5] mL/kg [95% CI:–2.1, 6.7]; within the 10 mL/kg noninferiority margin). There were no differences in transfusion of other blood products or the postoperative hemoglobin concentration between the groups. Similarly, there were no quantitative differences in the concentration of markers of fibrinolysis or inflammation between the two groups. Both groups had no adverse events and had a comparable length of hospital stay. This randomized controlled noninferiority trial concludes that low (10 mg/kg) loading dose of TXA is not inferior to high (50 mg/kg) loading dose of TXA in reducing blood loss and transfusion requirements in pediatric craniosynostosis surgery when used as part of multimodal patient blood management interventions. However, the absence of a placebo group meant that the markers of fibrinolysis and inflammation could not be compared between treatment and nontreatment groups to arrive at a decisive conclusion on the biological effects of TXA.

Effect of Ephedrine and Phenylephrine on Cerebral Hemodynamics[16]

Phenylephrine and ephedrine are frequently used perioperatively to treat hypotension. Studies using near infrared spectroscopy (NIRS) show that phenylephrine reduces regional cerebral oxygen saturation ($CMRO_2$) in spite of an increase in MAP.[17] Koch et al conducted a randomized study to quantify the effects of phenylephrine and ephedrine on cerebral blood flow (CBF) and oxygen consumption in patients with brain tumors using positron emission tomography (PET). They studied 24 patients with brain tumors. They compared the changes in CBF, and $CMRO_2$ from the baseline between ephedrine and phenylephrine in both ipsilateral peritumoral areas

and the contralateral hemisphere. All patients had standardized anesthesia induction and maintenance by TIVA titrated to achieve a bispectral index (BIS) of 40 to 60. Ventilation was adjusted to maintain a $PaCO_2$ of 35 to 45 mm Hg. After baseline PET studies, the study medications were administered with a dedicated infusion line to achieve a MAP of 60 mm Hg or 20% relative to the pretreatment MAP. PET studies were repeated once the desired MAP was reached and remained stable for 5 minutes. The oxygen extraction fraction was calculated from the CBF and the $CMRO_2$. Regional cerebral oxygen saturation was measured with NIRS. Baseline $PaCO_2$, PaO_2, MAP, heart rate, regional cerebral oxygen saturation, and BIS were similar between both groups. Infusion of phenylephrine and ephedrine were associated with a statistically insignificant 21% and 25% reduction in oxygen extraction fraction in the peritumoral areas and 16% and 19% reduction in contralateral areas of interest. This reduction was associated with an increase in CBF without corresponding changes in $CMRO_2$. Hence, this study showed that concerns regarding the effect of phenylephrine in reducing the regional cerebral oxygen saturation with NIRS might not be justifiable as the changes in regional oxygen saturation might not effectively reflect changes in $CMRO_2$.

Arteriovenous Malformations and Postoperative Hemodynamic Management[18]

One of the main concerns following surgical resection of cerebral arteriovenous malformations (AVM) is the postoperative complication of intracranial hemorrhage and/or cerebral edema. Despite the controversy surrounding the pathophysiology of postoperative hyperemic complications and the lack of high-level evidence, most neurosurgical teams and the literature recommend strict control of BP and maintaining BP below preoperative baseline BP after the surgery. However, we do not know the ideal postoperative BP target, as well as the relationship between failure of maintaining postoperative BP targets and the occurrence of postoperative hyperemic complications. This retrospective study reviewed the postoperative hemodynamic management in patients after surgical resection of cerebral arteriovenous malformations and the incidence of postoperative intracranial hemorrhage and/or cerebral edema.[18] They further assessed the factors that determine the postoperative BP targets, and explored the relationship between failure of maintaining postoperative BP targets and the occurrence of postoperative hyperemic complications. Two hundred and seven patients who underwent elective surgical resection of cerebral AVM were included. The median (IQR) of postoperative maximal systolic BP target was 110 (100–120) mm Hg but the range was 90 to 150 mm Hg. The preoperative baseline SBP was the main factor to determine the postoperative SBP target. Failed hemodynamic control was consistently found in half of the patients during the first 72 hour postoperatively. The incidence of postoperative intracranial hemorrhage and/or cerebral edema was 4.4% (9/207 patients). All patients who had hyperemic complications had a preceding event of failed BP control. However, there was no relationship between postoperative control of BP and the incidence of hyperemic complications. Thus, the overall role of BP control especially the target BP values should be tailored to individual patients' clinical condition. Further studies are required to develop a more effective strategy to implement strict BP control in the postoperative period.

Impact of Goal-Directed Therapy on Delayed Ischemia after Aneurysmal Subarachnoid Hemorrhage[19]

Delayed cerebral ischemia (DCI) is a devastating clinical syndrome common after aneurysmal subarachnoid hemorrhage (SAH). Although there are some risk predictors for this complication there are no significant treatments to prevent its occurrence other than hemodynamic therapy. This single-center randomized controlled prospective study was conducted to test the theory that goal-directed hemodynamic therapy (GDHT) would reduce DCI after SAH.[19] One hundred and eight patients with similar characteristics (55% coiling, 45% clipping) were randomized to two groups—GDHT group and the control group. Both the groups had similar ICU care. The GDHT group had advanced monitoring including transpulmonary thermodilution to guide fluid therapy. This was initiated as soon as possible and continued for up to 14 days or when patients were discharged from the ICU. MAP, cardiac index (CI), global end diastolic index, and extravascular lung water index were used to guide hemodynamic management. The primary outcome was the occurrence of DCI. Several secondary outcomes were also analyzed. Lastly, functional outcome at 3 months after discharge was measured using GOS. Incidence of DCI was 13% of patients in the GDHT group compared with 32% in the control group. This was consistent after adjusting for several cofounders. However, there was no difference in the occurrence of vasospasm in either group. In addition, this study showed that here were more patients with low disability (GOS = 5) in the GDHT group (66%) compared with the control group (44%). However, there was no difference in mortality between the groups. This study does suggest that the future is toward a more personalized approach with goal-directed parameters for preventing DCI. It is important to note that this study was different from previously published data where volume expanders such as hydroxyethyl starch were used.

Protective Effects of Obstructive Sleep Apnea on Outcomes after Subarachnoid Hemorrhage[20]

Obstructive sleep apnea (OSA), which is defined by apneas and hypopneas due to obstructed upper airways during sleep, is the quintessential disease for chronic intermittent hypoxia and hypercapnia. Evidence from recent literature has identified that hypercapnia could potentially provide protection against ischemic events, like stroke. Westermaier et al showed the use of hypercapnia to increase cerebral blood flow (CBF) and potentially elevating the brain tissue oxygen.[21] Therefore, Kaculini et al ventured to evaluate of the impact of an OSA diagnosis on the treatment outcomes in patients with SAH.[20] The National Inpatient Sample (NIS), a large national database on inpatient stays in the United States, was used to collect data between 2011 and 2015. Outcomes were measured through the NIS–SAH Outcome Measure

(a binary tool with strong correlation to the modified Rankin score [mRS]). A total of 49,265 patients met the inclusion criteria and 95% of them had a diagnosis of SAH. Two thousand four hundred and eight of these patients also had a diagnosis of OSA. However, the NIS database does not have details of disease severity. Patients with OSA also had other significant medical comorbidities. The study results showed that there was an increased chance that OSA patients went for embolization of their ruptured aneurysm (OR 1.37) than clipping (OR 0.73). Surprisingly, patients with OSA were less likely to suffer vasospasm (OR 0.52) and had a lower in hospital mortality rate compared with those not diagnosed with OSA (p = 0.003). In addition, it was less likely for a patient with OSA to experience a stroke after SAH (OR 0.5, $p < 0.001$). There was a trend to a shorter hospital stay for patients with OSA; however, it was not statistically significant. The fact that the rates for the two most crucial predictors of a poor outcome in SAH (vasospasm and stroke) were found to be lower in patients who also had OSA deserves some thought, especially since these patients present with other severe comorbidities. The theory goes back to animal studies which show that OSA is associated with less severe injury after an ischemic event, as a result of ischemic preconditioning, a nonlethal reduction in blood flow–releasing factors that increase tolerance to subsequent events of a similar nature. This phenomenon would lead to increased collateral flow or angiogenesis. In the patient with OSA the physiological advantage of hypercapnia resulting in dilation of cerebral blood vessels may lead to improved neurological outcomes and prevention of further infarction. Another theory proposed relates to the disruption of cerebral autoregulation in OSA. This would result in a pressure passive cerebral circulation in a population of patients with comorbid hypertension and therefore may see higher pressures in the brain at baseline, providing a protective effect in this very specific circumstance. Although there are some limitations to the data collected, OSA having a protective effect in SAH is an interesting finding and future work to identify relation to severity and testing of $PaCO_2$ levels to establish this relationship will be fascinating.

Intravenous Alteplase for Stroke with Unknown Time of Onset Guided by Advanced Imaging[22]

Intravenous alteplase is the standard of care for patients with AIS who present within 3 to 4.5 hours from the time of onset of symptoms. Unfortunately, timing is unknown in 20 to 25% of patients, mostly due to patients waking up from sleep with symptoms. There have been several individual trials to look at thrombolysis in the late or unknown time window. Thomalla et al endeavored to establish whether IV alteplase is safe and effective in patients with a stroke of unknown timing when salvageable tissue is identified with imaging biomarkers (DWI-FLAIR mismatch or CT/magnetic resonance imaging [MRI] penumbral imaging). They used individual patient data from four eligible trials (WAKE-UP, EXTEND, THAWS, and ECASS-4). Their primary outcome was defined as favorable, which was 0 to 1 on the mRS at 90 days post stroke, and secondary outcome were functional improvements over the entire mRS at 90 days and independent outcome (defined by a 0–2 on the mRS at 90 days). Individual patient data of 843 patients were included for the metanalysis. Median time from last seen well to symptom recognition was 7 hours, with a median NIHSS of 7 as well. There was an absolute increase of 8% of patients with favorable outcome (number needed to treat [NNT] = 12) in the alteplase group. In addition, the treatment with alteplase showed significant trends toward better functional outcomes and higher functional independence. Safety endpoint data showed an increase in the death at 90 days in the alteplase group (6% vs. 3% in control) as well as increased incidence of symptomatic intracerebral hemorrhage (sICH). However, overall patients with severe disability or death (mRS 4–6) were lower in the alteplase group than the control (21% vs. 25%). This meta-analysis was able to show that IV alteplase is beneficial in patients within unknown time of onset (as selected by the imaging biomarkers). The necessity for advanced imaging (beyond noncontrast CT) may be a limitation for real world practice, although this study indicates that it should be the standard that we strive for.

Modeling Blood Pressure Management after Endovascular Thrombectomy[23]

The role of BP in post–endovascular thrombectomy (EVT) treatment is not well understood. Existing guidelines recommend that maintaining the BP < 180/105 mm Hg for 24 hours post thrombectomy to avoid reperfusion injury and hemorrhagic complications. However, this recommendation is based mainly on observational studies. Matusevicius et al designed this study to be an exploratory analysis on the potential associated between BP levels post EVT and correlation to clinical outcome. Primary outcome was defined as 0 to 2 on the mRS at 3 months and 3-month mortality, as well as sICH. They looked at 3,631 patients treated with EVT between Jan 2014 and Dec 2017, 2,920 of which had successful recanalization. Multivariable analysis of systolic blood pressure (SBP) occurred in 20 mm Hg intervals. Due to a paucity of patients with SBP > 180, SBP > 160 was used as the upper cutoff. Regardless of recanalization success there was a trend down of SBP and diastolic blood pressure (DBP) post procedure. Patients with successful recanalization and SBP between 100 and 119 mm Hg had the highest percentage of functional independence (63%). For those with unsuccessful recanalization, SBP between 120 and 139 mm Hg was associated with highest functional independence (31%). Thus, this study demonstrated a very complex relationship between SBP after EVT treatment and outcomes, which differ based on recanalization status. Specifically, it has highlighted that a linear model may not be the best way to describe the association, and that a quadratic multivariate logistic regression model may be better in successful recanalization patients. Overall, SBP higher than 160 mm Hg was associated with less favorable functional independent outcomes at 3 months (aOR 0.987) in patients with successful recanalization. If patients did not have a successful recanalization the higher SBP values were associated with more sICH (aOR 1.040) but not with functional independence (aOR 1.003).

As a continuous independent variable, the SBP > 160 mm Hg was associated with more sICH regardless of recanalization success. The complexity of the blood pressure relationship to outcomes post EVT is evident in this study, although some crucial models have been developed to use with future RCTs investigating SBP targets, which will be important for evolving guidelines.

Admission Blood Pressure and Clinical Outcomes after Successful Endovascular Stroke Treatment[24]

The acute phase of a stroke is often met with hypertension, a compensatory mechanism thought to increase blood flow to the ischemic area. In patients with large vessel occlusions, U-shaped curves highlighting the relationship between low and high blood pressure values and poor clinical outcomes have been described.[25] It is likely there is an individual blood pressure target that varies among patients and types of stroke. Currently, there is a lack of clarity on the effects of early blood pressure management on the clinical outcomes in patients with stroke. Berg et al looked into 3,180 patients between March 2014 and Nov 2017 from the multicenter randomized controlled trial of endovascular treatment for acute ischemic stroke in the Netherlands (MR CLEAN).[24] The median age of the patients was 71 years and 48% were male. Using the first available admission BP recordings in the emergency department and the mRS at 90 days as a primary outcome measure, they found a nonlinear association. The J-shaped relationship showed an inflection point at SPB 150 mm Hg and DBP 81 mm Hg. Increased SBP was associated with poorer functional outcomes. For every 10 mm Hg increase the aOR was 1.09, but for lower blood pressures there was no association (aOR = 1.00). These findings were also reflected in the DBP analysis. Secondary outcomes were successful reperfusion, sICH and 90-day mortality. For the secondary outcomes of mortality and NIHSS at 24 to 48 hours, J-shaped associations continued with an inflection point at SPB 150 mm Hg. Higher blood pressures associated with higher mortality, but lower blood pressures were not. The relationship between SBP and sICH or successful recanalization was both linear. There was a nonsignificant upward trend between increased BP and sICH, and the higher the BP the less successful the odds of reperfusion were. Further studies are needed to investigate whether these patients benefit from decrease in BP before EVT.

Narrative Reviews of Interest

In addition to clinical studies, following are some of the narrative reviews that are of interest to neuroanesthesiologists. Zeiler et al have done a narrative review focusing on the concept of cerebral autoregulation, proposed mechanisms of control and methods of continuous cerebrovascular reactivity monitoring used in moderate/severe traumatic brain injury.[26] Minhas et al have presented a multidisciplinary narrative review describing the key pathophysiological and clinical considerations on the perioperative care for patients with a prior diagnosis of stroke.[27] On the similar topic, Society for Neuroscience in Anesthesiology and Critical Care has recently updated the initial consensus statement from 2014 and have provided evidence-based recommendations regarding perioperative care of patients at high risk for stroke.[28] A large multidisciplinary, international panel have recently presented a consensus statement of recommendations on determination of brain death and death by neurological criteria (the World Brain Death project).[29] Other reviews of interest include an excellent narrative review on the perioperative management of aneurysmal subarachnoid hemorrhage by Sharma[30] and a narrative review on the anesthesia and critical care providers' roles in the management of both perioperative stroke and acute ischemic stroke with a focus on anesthetic management for mechanical thrombectomy.[31] There is a recent update on the Guidelines for the Management of Severe Traumatic Brain Injury. This update focuses on the recommendations on Decompressive Craniectomy incorporating evidence from the recent Trial of Decompressive Craniectomy for Traumatic Intracranial Hypertension (RESCUEicp) and the Decompressive Craniectomy in Patients with Severe Traumatic Brain Injury (DECRA) trials.[32]

Finally, 2020 was the year of the coronavirus disease 2019 (COVID-19) pandemic which continued to have a significant implication for the anesthesiologists. There have been many research articles, consensus statements, guidelines, protocols, and recommendations on the various aspects of COVID-19–related illness and its management. There are few excellent reviews on the neurological manifestations of COVID-19[33-35] and recommendations on the neuroanesthesia practice during the COVID-19 pandemic.[36,37]

Conflict of Interest

None declared.

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