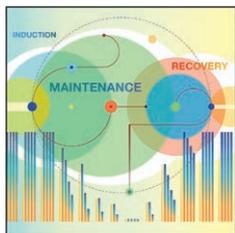


# THIS MONTH IN ANESTHESIOLOGY



## 901 Quantitative Neuromuscular Monitoring in Clinical Practice: A Professional Practice Change Initiative

Quantitative (train-of-four ratio) monitoring is the gold standard for assessing recovery from neuromuscular block. Residual neuromuscular block, defined as a train-of-four ratio of less than 0.9, is commonly observed in patients given nondepolarizing neuromuscular blocking drugs perioperatively. Inadequate reversal of residual neuromuscular block is associated with postoperative morbidity and mortality. Despite guidelines from several professional societies advocating quantitative neuromuscular monitoring for neuromuscular blocking drug management, it is infrequently used. A departmental professional practice change initiative was initiated with the goal of documenting a train-of-four ratio greater than or equal to 0.9 for all patients given a nondepolarizing neuromuscular blocking drug. This retrospective assessment of implementation of train-of-four ratio greater than or equal to 0.9 documentation before extubation found it improved from 2 (1%) of 172 cases in November 2016, which was preimplementation, to 250 (93%) of 269 cases in December 2020, which was postimplementation. Attaining this endpoint required not only placing a quantitative monitor in each anesthetizing location but also ongoing educational efforts and follow-up. See the accompanying Editorial on [page 875](#). (Summary: M. J. Avram. Image: A. Johnson, Vivo Visuals Studio.)



## 927 Intraoperative Hypotension and Acute Kidney Injury, Stroke, and Mortality during and outside Cardiopulmonary Bypass: A Retrospective Observational Cohort Study

Intraoperative hypotension is associated with major adverse postoperative events in patients having noncardiac surgery. The hypothesis that intraoperative hypotension duration throughout cardiac surgery or when separated into hypotension during and outside cardiopulmonary bypass (CPB) may be associated with major adverse postoperative events was tested in a retrospective study. The composite primary outcome of postoperative acute kidney injury, stroke, and mortality occurred in 256 (5%) of 4,984 patients. The mean  $\pm$  SD duration of mean arterial pressure (MAP) less than 65 mmHg was  $143 \pm 75$  min in patients with the composite primary outcome and  $104 \pm 48$  min in those without it. The area under the curve—MAP less than 65 mmHg, a measure of the severity of intraoperative hypotension, was  $1,528 \pm 1,134$  mmHg  $\cdot$  min in patients with the composite outcome and  $1,070 \pm 656$  mmHg  $\cdot$  min in the others. When compared with more than 80% hypotension duration occurring during CPB, less than 60% of hypotension occurring during CPB was associated with the primary composite outcome (odds ratio, 1.67; 95% CI, 1.10 to 2.60). (Summary: M. J. Avram. Image: J. P. Rathmell.)



## 916 Amiodarone with or without N-Acetylcysteine for the Prevention of Atrial Fibrillation after Thoracic Surgery: A Double-blind, Randomized Trial

Transient atrial fibrillation after noncardiac thoracic or general surgery may be a sentinel event that can be used to identify patients at risk of developing subsequent atrial fibrillation. More than 15% of patients at high risk of postoperative atrial fibrillation will experience it after thoracic surgery when the multichannel antiarrhythmic drug amiodarone is used for prevention. The hypothesis that the addition of *N*-acetylcysteine, an antioxidant anti-inflammatory agent, to amiodarone would reduce the incidence of postoperative atrial fibrillation compared with amiodarone alone was tested in a randomized, double-blind, placebo-controlled trial of 154 patients at high risk of postoperative atrial fibrillation scheduled to undergo major thoracic surgery. Interim analysis found the primary outcome, new-onset sustained atrial fibrillation for more than 30 s detected by telemetry (first 72 h) or symptomatic atrial fibrillation requiring intervention and confirmed by electrocardiography within 7 days of surgery, occurred in 15 (19%) of 78 patients in the *N*-acetylcysteine group and 13 (17%) of 76 patients in the placebo group. The trial was terminated due to futility. See the accompanying Editorial on [page 877](#). (Summary: M. J. Avram. Image: J. P. Rathmell.)



## 970 Basal Infusion versus Automated Boluses and a Delayed Start Timer for “Continuous” Sciatic Nerve Blocks after Ambulatory Foot and Ankle Surgery: A Randomized Clinical Trial

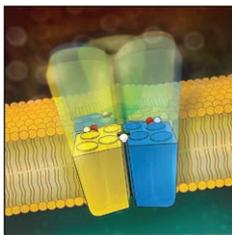
Analgesia after foot and ankle surgery is often provided by a popliteal–sciatic nerve block produced by a continuous basal local anesthetic infusion and patient-controlled bolus doses. The hypotheses that, compared to a continuous basal ropivacaine infusion initiated before discharge after foot and ankle surgery, perineural ropivacaine administered with automated boluses at a lower dose and a 5-h delay after discharge would provide at least noninferior analgesia while both techniques are functioning and result in a longer duration of administration were tested in a randomized controlled trial of 70 patients. The day after surgery, the median [interquartile range] pain score of participants receiving automated boluses was 0.0 [0.0 to 3.0] while that of the continuous infusion group was 3.0 [1.8 to 4.8]. The odds of worse average pain on day 1 with continuous basal infusion, adjusting for body mass index, was 3.1 (95% CI, 1.2 to 7.8). Local anesthetic reservoir exhaustion occurred after a median [interquartile range] of 119 h [109 to 125 h] in patients with automated boluses and 74 h [57 to 80 h] in the continuous infusion group. See the accompanying Editorial on [page 883](#). (Summary: M. J. Avram. Image: J. P. Rathmell/A. Johnson, Vivo Visuals Studio.)



## 940 Referral Indications for Malignant Hyperthermia Susceptibility Diagnostics in Patients without Adverse Anesthetic Events in the Era of Next-generation Sequencing

Most cases of malignant hyperthermia susceptibility are associated with variants in the gene encoding the skeletal muscle ryanodine receptor 1, *RYR1*. Next-generation sequencing has resulted in a rapid increase in the identification of both the number of patients with an *RYR1* variant and the number of newly identified *RYR1* variants. The hypothesis that there is an increased referral to malignant hyperthermia units of patients without a personal or family history of adverse anesthetic events suspected to be malignant hyperthermia was tested in a retrospective multicenter cohort study. The proportion of patients referred without a personal or

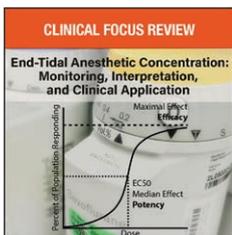
family history of adverse anesthetic events suspected to be malignant hyperthermia increased from 28% (61 of 215) between 2010 and 2014 to 44% (133 of 305) between 2015 and 2019. Patients with a personal or family history of adverse anesthetic events suspected to be malignant hyperthermia were more frequently diagnosed as malignant hyperthermia susceptible (133 of 220; 60%) than those without (47 of 120; 39%). (Summary: M. J. Avram. Image: J. P. Rathmell.)



## 954 Midazolam at Low Nanomolar Concentrations Affects Long-term Potentiation and Synaptic Transmission Predominantly via the $\alpha_1$ - $\gamma$ -Aminobutyric Acid Type A Receptor Subunit in Mice

Midazolam at low nanomolar concentrations causes moderate sedation and anterograde amnesia in humans. Consistent with its amnesic properties, midazolam blocks hippocampal long-term potentiation, a cellular correlate for learning and memory. The sedative properties of benzodiazepines are mediated by  $\alpha_1$ -containing  $\gamma$ -aminobutyric acid type A ( $GABA_A$ ) receptors expressed in forebrain glutamatergic neurons. The aims of this study were to identify the  $GABA_A$  receptor subtypes targeted by midazolam responsible for affecting long-term potentiation and synaptic inhibition in neocortical neurons. Mouse lines carrying knock-in

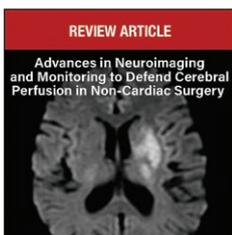
mutations in the  $\alpha$ -subunit of the  $GABA_A$  receptor, which cause a dramatic decrease in benzodiazepine binding, were used to determine the effect of midazolam on hippocampal neurons in electrophysiologic studies of acutely prepared brain slices. Midazolam at 10 nM completely blocked long-term potentiation. It was effective in blocking long-term potentiation in slices derived from  $\alpha_{2/3/5}$ -triple-knock-in mice and it failed to block long-term potentiation in slices derived from  $\alpha_1$ -single-knock-in mice, leading to the conclusion that midazolam blocked hippocampal long-term potentiation predominantly via  $\alpha_1$ - $GABA_A$  receptors. See the accompanying Editorial on [page 880](#). (Summary: M. J. Avram. Image: A. Johnson, Vivo Visuals Studio.)



## 985 End-tidal Anesthetic Concentration: Monitoring, Interpretation, and Clinical Application (Clinical Focus Review)

This Clinical Focus Review begins by describing the development of the concept of minimal alveolar concentration (MAC), the volatile anesthetic steady-state end-tidal partial pressure that results in a 50% probability of subject immobility after application of a noxious stimulus, and the semantic issues that have plagued the term. The current understanding of general anesthesia is then presented as a drug-induced reversible state of unconsciousness while providing immobility with blunting of excessive autonomic responses to noxious stimuli. This is followed by a discussion of the relationships between the steady-state fraction of MAC and each of these clinical effects and the effects of opioids on these relationships. Hysteresis, the delay between changes in the fraction of end-tidal

anesthetic concentration and changes in the partial pressure of anesthetic in the brain during non-steady-state conditions, and hysteresis-corrected fraction of MAC are then considered. The review concludes with a presentation of a pragmatic approach to achieving the anesthetic state based on the MAC and the fraction of MAC concepts and a discussion of the future of MAC. See the accompanying Editorial on [page 885](#). (Summary: M. J. Avram. Image: J. P. Rathmell.)



## 1015 Advances in Neuroimaging and Monitoring to Defend Cerebral Perfusion in Noncardiac Surgery (Review Article)

The brain is susceptible to perioperative injury from hypoperfusion and oxygen supply-demand mismatch. This review focuses on emerging techniques that have the capacity to perform multisite measurement/imaging of biomarkers of neurologic injury, potentially enabling early detection of organ hypoperfusion and avoidance of tissue oxygen supply-demand mismatch: optical, ultrasonographic, and magnetic resonance techniques. Optical techniques, such as near-infrared spectroscopy, are able to measure a range of properties of superficial cortical tissue continuously and noninvasively, thereby measuring surrogates of cerebral blood flow, cerebral oxygenation, and cellular oxygenation and/or metabolism. Transcranial Doppler ultrasound is a well-

established technique for evaluating cerebral perfusion intraoperatively. Magnetic resonance imaging can be used to diagnose perioperative stroke in the early stages and, due to its exquisite spatial resolution, is excellent for assessing regional blood flow in the brain. Although novel neuroimaging modalities may revolutionize perioperative care, few studies have assessed application of these methods in the perioperative setting. (Summary: M. J. Avram. Image: J. P. Rathmell.)