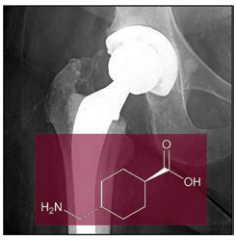
THIS MONTH IN ANESTHESIOLOGY

31 Levels of Evidence Supporting the North American and European Perioperative Care Guidelines for Anesthesiologists between 2010 and 2020: A Systematic Review

Anesthesiologists rely on published clinical practice guidelines on the perioperative management of patients to guide decision-making because they are based on the best available evidence and serve as the framework for best practices in perioperative care. The hypothesis that most clinical practice guideline recommendations are supported by low level of evidence was tested in a systematic review of anesthesiology evidence-based clinical practice guidelines published by major North American and European societies and anesthesiology subspecialty societies between 2010 and 2020. Sixty guidelines with 2,280 recommendations were reviewed. The evidence in individual guidelines was mapped to that used by standard classification systems: level A includes evidence from multiple randomized controlled trials or meta-analyses; level B represents evidence from one randomized controlled trial or observational studies; and level C is limited to evidence from case reports and expert opinion. Level A supported 16% of recommendations, level B supported 33%, and level C supported 51%. Nineteen percent of the 1,506 strong recommendations were supported by level A, 31% by level B, and 50% by level C. *See the accompanying Editorial on* **page 9.** *(Summary: M. J. Avram. Photo: J. P. Rathmell. Illustration: A. Johnson, Vivo Visuals.)*

95 Percutaneous Peripheral Nerve Stimulation (Neuromodulation) for Postoperative Pain: A Randomized, Sham-controlled Pilot Study

Percutaneous peripheral nerve stimulation is an analgesic alternative that may improve postoperative analgesia while reducing opioid requirements without risk of adverse systemic side effects. A multicenter, randomized, controlled pilot study was conducted in 65 patients undergoing ambulatory orthopedic surgery with a planned single-injection peripheral nerve block for postoperative analgesia to estimate dual primary outcome of analgesia and opioid-sparing effect of percutaneous peripheral nerve stimulation within the first postoperative week. The median (interquartile range) opioid consumption (in oral morphine equivalents) during the first seven postoperative days was 5 (0 to 30) mg in participants receiving active stimulation and 48 (25 to 90) mg in patients given sham; the estimated ratio of geometric means (97.5% CI) was 0.2 (0.1 to 0.6). The mean ± SD of the average daily pain scores measured on the 0 to 10 Numeric Rating Scale within the first seven postoperative days was 1.1 ± 1.1 in patients receiving active stimulation and 3.1 ± 1.7 in those given sham; the difference in means (95% CI) was –1.8 (–2.6 to –0.9). *(Summary: M. J. Avram. Image: B. Ilfeld.)*



57 Safety of Tranexamic Acid in Hip and Knee Arthroplasty in High-risk Patients

The hypothesis that tranexamic acid use would not be associated with an increased risk of complications in high-risk patients was tested in a retrospective cohort study using national claims data on lower extremity joint replacements performed between 2013 and 2016. The exposure of interest was use of tranexamic acid in patients with pre-existing comorbidities for which concerns exist of associated increased risks with tranexamic acid use. Three groups of high-risk patients were identified on the basis of histories of venous thromboembolism, myocardial infarction, seizures, or ischemic stroke/transient ischemic attacks (group I, n = 27,890), renal disease (group II, n = 44,608), and atrial fibrillation (group III, n = 45,952). The coprimary outcomes were blood transfusion and a complication composite of new onset venous thromboembolism, myocardial infarction, seizures, or ischemic stroke/transient ischemic attacks. In adjusted analyses tranexamic acid use was associated with decreased odds of blood transfusion in high-risk groups I (odds ratio, 0.31), II (odds ratio, 0.32), and III (odds ratio, 0.32). No increased odds of composite complications were observed in high-risk groups I (odds ratio, 0.89), II (odds ratio, 0.98), and III (odds ratio, 0.93). *See the accompanying Editorial on* **page 12.** *(Summary: M. J. Avram. Image: J. P. Rathmell.)*

83 Automated Nerve Monitoring in Shoulder Arthroplasty: A Prospective Randomized Controlled Study

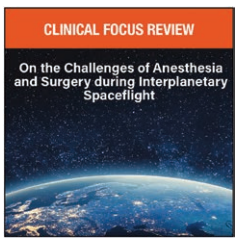
Perioperative evoked potential monitoring is used to quantify the functional integrity of the peripheral nerves and spinal pathways and to detect and mitigate neurological injury. The hypothesis that use of automated nerve monitoring can minimize intraoperative nerve injury during shoulder arthroplasty surgery, and thereby improve clinical outcomes, was tested in a prospective, blinded, randomized controlled trial of 200 adult patients between 2018 and 2019. The median (interquartile range) cumulative duration of abnormal nerve alerts, a measure of the extent of intraoperative nerve insult, was 1 (0 to 18) min in the nerve monitored group and 5 (0 to 26) min in the control group; the Hodges-Lehman difference (95% CI) was 0 (0 to 1) min. Secondary outcomes assessed at 2, 6, and 12 weeks after surgery included neurological deficit of the operative arm, functional outcome of the operative arm, and quality of life, which did not differ between groups. Ancillary analysis found a progressive improvement of clinical outcomes in both groups over the course of the study. *(Summary: M. J. Avram. Image: J. P. Rathmell.)*

69 Midazolam and Ketamine Produce Distinct Neural Changes in Memory, Pain, and Fear Networks during Pain

Anesthetic drugs are used to modulate memory formation and pain perception during what would otherwise be intolerably painful experiences. The hypothesis that midazolam would cause a greater reduction in recollection than ketamine was tested in a randomized single-blind within-subject crossover study of 26 healthy adults. The experimental model used an experience that could be characterized as unpleasant, painful, or anxiety-provoking, using repeated, unpredictable painful stimulation and a task that allowed later quantification of successful memory encoding. Targeted effect site concentrations were 10 ng/ml midazolam and 200 ng/ml ketamine. Pain scores from the encoding trial segments performed during drug infusion were reduced by ketamine but not by midazolam. Recollection performance under midazolam was reduced compared to saline and ketamine. Recollection under ketamine did not differ from that during saline. Aggregate performance for familiarity did not differ among saline, midazolam, and ketamine. In the secondary analysis, painful stimulation during light sedation with midazolam was associated with increased brain functional connectivity while functional connectivity decreased during sedation with ketamine. *(Summary: M. J. Avram. Image: J. P. Rathmell.)*

136 Sevoflurane Exerts Protective Effects in Murine Peritonitis-induced Sepsis *via* Hypoxia-inducible Factor 1α/Adenosine A2B Receptor Signaling

Neutrophils are the first cells of the innate immune system to be recruited to the site of infection in the early stage of sepsis, during which they clear pathogen and can impair organ function if their infiltration is excessive. The anti-inflammatory effects of the adenosine A2B receptor are crucial in acute inflammation, influencing neutrophil migration and microvascular permeability. Hypoxia-inducible factor 1α is a transcription factor of the adenosine A2B receptor. The hypothesis that sevoflurane controls neutrophil infiltration by stabilization of hypoxia-inducible factor 1α and elevated adenosine A2B receptor expression was tested in wild-type and adenosine A2B receptor knockout mice in the acute phase of zymosan- or polymicrobial-induced peritonitis. In wild-type animals sevoflurane reduced the detected neutrophils and induced expression of hypoxia-inducible factor 1α and adenosine A2B receptor in the lung, liver, and intestine but had no effect on neutrophil influx into the organs of the adenosine A2B receptor knockout animals. Capillary leakage was lower in wild-type mice after inhalation of sevoflurane, which did not affect microvascular permeability in the adenosine A2B receptor knockout animals. *See the accompanying Editorial on* **page 15.** *(Summary: M. J. Avram. Image: J. P. Rathmell.)*



155 On the Challenges of Anesthesia and Surgery during Interplanetary Spaceflight (Clinical Focus Review)

The most significant risks for space exploration missions are likely to be trauma, hemorrhagic shock, and infections. This Clinical Focus Review considers key challenges for a crew on the surface of Mars or the moon facing a severe surgical emergency, such as a major trauma, reviewing issues related to medical evacuation, telemedicine, delivery of anesthesia and surgery, and behavioral health and performance. It highlights the physiologic, logistic, medical, and environmental factors that could affect management of a serious medical emergency in a deep space settlement. It also considers technologies and futuristic concepts that could be useful in both the setting of a space mission and the practice of anesthesia on Earth. The review concludes that both the risk to health and the probability of severe medical events may be mitigated by careful planning and provision of necessary skills and equipment, with special consideration of in-mission uncertainties, personnel training, and on-site synthesis of equipment to address the heterogeneity of potential medical/surgical emergencies. *(Summary: M. J. Avram. Image: Adobe Stock.)*

164 Obstetric Anesthesia and Heart Disease: Practical Clinical Considerations (Review Article)

Cardiovascular disease is responsible for one quarter of maternal deaths in the United States. Many anesthesiologists optimize hemodynamics in heart disease daily but it unlikely to be routine for those who work regularly in labor and delivery units. This review answers practical questions related to the safe management of pregnant women with heart disease for the obstetric anesthesiologist and the general anesthesiologist who regularly practices obstetric anesthesiology on the basis of a nonsystematic literature review and national and international guidelines. It recommends anesthesiologists risk-stratify pregnant patients based on cardiac disease etiology and severity to determine the appropriate type of hospital and location within the hospital for delivery and anesthetic management. Because the physiology of pregnancy and the peripartum period can affect anesthetic management, it reviews hemodynamic changes to facilitate prediction of which cardiac lesions may result in peripartum hemodynamic compromise and guide intrapartum hemodynamic monitoring and anesthetic management. The anesthesiologist is cautioned to anticipate obstetric and cardiac emergencies including emergency cesarean delivery, postpartum hemorrhage, and peripartum arrhythmias. *(Summary: M. J. Avram. Image: J. P. Rathmell/Adobe Stock.)*

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