THIS MONTH IN ANESTHESIOLOGY

154 Ketamine and Magnesium for Refractory Neuropathic Pain: A Randomized, Double-blind, Crossover Trial

Ketamine is an antagonist of the *N*-methyl-D-aspartate (NMDA) receptor, a pharmacologic target in central sensitization and neuropathic pain. Magnesium sulfate is a physiologic blocker of the NMDA receptor. The hypotheses that intravenously administered ketamine would produce analgesic benefits compared to placebo for 5 weeks postinfusion and that coadministration of magnesium with ketamine would have an additive effect were tested in a randomized, placebo-controlled, crossover, double-blind study of 20 ketamine-naïve patients with neuropathic pain. Each patient received one infusion every 35 days. Placebo, ketamine (0.5 mg/kg) plus placebo, or ketamine (0.5 mg/kg) plus magnesium (3,000 mg) was administered intravenously over 30 min in a random order. Average daily pain intensity was assessed on a 0 to 10 numeric pain rating scale once a day for 35 days after placebo or drug administration. The primary endpoint, the area under the curve of the pain intensity score *versus* time relationship for 35 days, did not differ among the treatments. *See the accompanying Editorial on* **page 13.** *(Summary: M. J. Avram. Image: S. M. Jarret/J. P. Rathmell.)*

31 Individualized Fluid Management Using the Pleth Variability Index: A Randomized Clinical Trial

The aim of intraoperative fluid management should be to minimize fluids while maintaining euvolemia. Perioperative goal-directed hemodynamic management has been shown to reduce postoperative complications in high-risk patients having major surgery. The pleth variability index is used to assess fluid responsiveness using plethysmographic variations induced by mechanical ventilation and thus achieve euvolemia during surgery. The hypothesis that pleth variability index–guided fluid management reduces hospital length of stay was tested in randomized, nonblinded, clinical trial conducted in 438 intermediate-risk patients undergoing hip or knee arthroplasty under general anesthesia. Patients in the intervention group first received fluids according to their pleth variability index values, followed by vasopressors according to a hemodynamic algorithm, and patients in the control group received either fluid loading or vasopressors at the discretion of the anesthesiologist to maintain their mean arterial pressure above 65 mmHg. The mean (± SD) hospital length of stay was 6 ± 3 days for both the pleth variability index group and the control group (adjusted difference, 0.0 day; 95% CI, –0.6 to 0.5 day). *See the accompanying Editorial on* **page 5.** *(Summary: M. J. Avram. Image: J. P. Rathmell.)*

41 Incidence and Classification of Nonroutine Events during Anesthesia Care

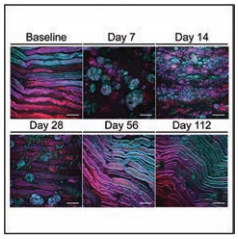
A nonroutine event is any aspect of the clinical care of a patient that is perceived by clinicians or trained observers to be a deviation from optimal care for that patient in that clinical situation. The authors video recorded 511 anesthesia cases in a prospective observational study, captured data about the provider, patient, and case, measured clinician workload, and used the nonroutine event survey tool to identify cases containing nonroutine events. Domain experts then reviewed the videos and accompanying data to understand the epidemiology of these events. They reported 173 nonroutine events in 111 of 511 cases (22%). Among the nonroutine event–containing cases, 39 (35%) had more than one event, 23 (21%) had two events, and 16 (14%) had three or more events. Most (69%) nonroutine events were rated as having patient impact while 13% were rated as involving patient injury. Cases with nonroutine events had from 1 to 12 contributory factors with a median of 4 (interquartile range, 2.5 to 6.0). *See the accompanying Editorial on* **page 8.** *(Summary: M. J. Avram. Image: J. P. Rathmell.)*

78 Accuracy and Feasibility of Clinically Applied Frailty Instruments before Surgery: A Systematic Review and Meta-analysis

Many guidelines recommend that frailty be assessed routinely before surgery because it plays an important role in predicting adverse outcomes in older surgical patients. The abilities of well-studied frailty instruments to predict postoperative mortality were assessed and compared in a systematic review and meta-analysis of 70 studies that prospectively assessed frailty status in preoperative clinical practice. Available data about the feasibility of these instruments were also synthesized. Frailty was defined using 35 different instruments, the most prevalent of which were the Fried Phenotype, the Clinical Frailty Scale, and physical measures of frailty. Thirty-two studies reported outcome data for in-hospital or 30-day mortality. Frailty based on the Fried Phenotype was associated with mortality (odds ratio, 3.95; 95% CI, 2.00 to 7.81) as were the Clinical Frailty Scale (odds ratio, 4.89; 95% CI, 1.83 to 13.05) and physical measures of frailty (odds ratio, 3.21; 95% CI, 2.37 to 4.36). Thirty-two studies reported aspects of feasibility. Although all available data supported the feasibility of the Clinical Frailty Scale, most did not support that of the Fried Phenotype. *(Summary: M. J. Avram. Image: ©gettyimages.)*

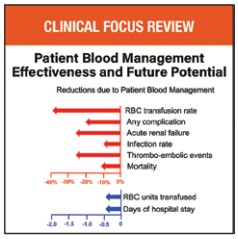
53 Subcutaneous Nitroglycerin for Radial Arterial Catheterization in Pediatric Patients: A Randomized Controlled Trial

Cannulation of the radial artery is difficult in small pediatric patients because of the small vessel size. In adults, nitroglycerin facilitates radial artery cannulation by increasing the internal diameter, shortening the procedure time, improving the success rate, and decreasing the incidence of radial arterial occlusion after cardiac catheterization. The hypothesis that subcutaneous injection of nitroglycerin would dilate the radial artery and increase the first attempt cannulation success rate was tested in a double-blinded, randomized controlled trial of 113 patients less than 2 yr old scheduled for elective surgery under general anesthesia requiring invasive arterial blood pressure monitoring or frequent blood sampling. The first attempt success rate of radial artery cannulation was 91.2% (52 of 57) in the nitroglycerin group and 66.1% (37 of 56) in the control (normal saline) group (odds ratio, 5.3; 95% CI, 1.8 to 15.6; absolute risk reduction, –25.2%; 95% CI, –39.6 to –10.7%). *(Summary: M. J. Avram. Image: J. P. Rathmell.)*



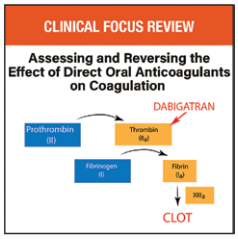
185 Neural Selective Cryoneurolysis with Ice Slurry Injection in a Rat Model

Most prolonged postoperative pain includes a neuropathic component caused by damage to peripheral nerves. Cryoneurolysis uses direct cooling to reversibly inhibit peripheral nerve function for weeks to months, but the extremely cold temperature used is destructive to any tissue. The hypothesis that injection of a moderately cold biocompatible ice slurry consisting of sterile ice particles suspended in normal saline and glycerol around the rat sciatic nerve will change the nociceptive response from baseline through neural selective cryoneurolysis was tested in 62 adult male Sprague-Dawley rats. There was a decrease in mechanical pain response to a 15 g von Frey hair applied to the lateral plantar aspect of the ipsilateral hind paw 8 days after injection of ice slurry that lasted through day 60, with a median (interquartile range) peak reduction of 68% (60 to 94%) compared to baseline at day 22. Half-recovery occurred at 9 to 10 weeks. Thermosensitivity testing of the plantar hind paw to noxious radiant heat did not show significant changes. *(Summary: M. J. Avram. Image: From original article.)*



212 Patient Blood Management: Effectiveness and Future Potential (Clinical Focus Review)

Preoperative anemia is common in patients scheduled for major surgery; surgical bleeding contributes to anemia; and transfusion of allogeneic blood products, which are a limited resource, is associated with increased morbidity and mortality and increased costs. The concept of Patient Blood Management was introduced in 2008 to decrease the transfusion of allogeneic blood products and improve patient outcomes. The present Clinical Focus Review discusses the three pillars of Patient Blood Management: correction of anemia; reduction of perioperative erythrocyte loss; and tolerance of anemia. It begins with the need to correct preoperative anemia and management of patients receiving preoperative anticoagulation or dual platelet inhibition. The intraoperative and postoperative periods are then considered, including use of surgical techniques that reduce blood loss as well as individualized goal-directed coagulation algorithms and restrictive transfusion thresholds, which remain important in the postoperative period, and the need to identify and quickly control postoperative bleeding. The review concludes with an extensive discussion of strategies for implementing Patient Blood Management. *(Summary: M. J. Avram. Image: From original article.)*



223 Assessing and Reversing the Effect of Direct Oral Anticoagulants on Coagulation (Clinical Focus Review)

The direct thrombin inhibitor dabigatran and the factor Xa inhibitors apixaban, rivaroxaban, and edoxaban have been approved for treatment of venous thromboembolism and prevention of stroke in nonvalvular atrial fibrillation. Direct oral anticoagulants have predictable pharmacokinetics and wide therapeutic windows, but clinically relevant threshold concentrations are uncertain. Although routine coagulation tests have limited utility for detection of high or low direct oral anticoagulant concentrations, the anti-Xa assay can be used to exclude the presence of factor Xa inhibitors and specific assays are in development. Until specific assays are available, the timing of last ingestion may help guide clinical decisions regarding timing of procedures and need for reversal. The specific reversal agents for dabigatran and anti-Xa inhibitors are the humanized monoclonal antibody idarucizumab and the factor Xa decoy molecule andexanet alfa, respectively. When managing patients taking direct oral anticoagulants who need urgent or emergency surgery, priority should be given to managing life-threatening bleeding in the setting of direct oral anticoagulant coagulopathy followed by evaluation of the need for surgery. *(Summary: M. J. Avram. Image: J. P. Rathmell.)*

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