ANESTHESIOLOGY



992 Multimodal Analgesic Regimen for Spine Surgery: A Randomized Placebo-controlled Trial

Multimodal analgesic regimens are an essential component of Enhanced Recovery After Surgery programs, potentially reducing postoperative complications and improving recovery. The hypothesis that patients given multimodal analgesia consisting of oral gabapentin and acetaminophen with intravenous lidocaine and ketamine infusions have superior Quality of Recovery scores 3 days after multilevel spine surgery was tested in a randomized, double-blinded, placebo-controlled trial of 299 patients at high risk for postoperative pain. The mean (\pm SD) Quality of Recovery scores 3 days after surgery were 109 (\pm 25) in the multimodal analgesia pathway group *versus* 109 (\pm 23) in the placebo group; the estimated difference in means was 0 (95% CI, -6 to 6).

The median (interquartile range) 48-h intravenous morphine equivalent opioid dose was 72 (48 to 113) mg in the analgesic pathway group *versus* 75 (50 to 152) mg in the placebo group. The mean (\pm SD) 48-h time-weighted average pain scores were 4.8 (\pm 1.8) in the analgesic pathway group *versus* 5.2 (\pm 1.9) in the placebo group. (*Summary: M. J. Avram. Image: A Johnson, Vivo Visuals.*)



1114 Usefulness of Parasternal Intercostal Muscle Ultrasound during Weaning from Mechanical Ventilation

The thickening fraction of the diaphragm measured by ultrasound can be used as a surrogate of diaphragm function and is a reliable predictor of spontaneous breathing trial outcome during weaning from mechanical ventilation. The present study sought to determine whether the thickening fraction of the parasternal intercostal muscle alone or the addition of the thickening fraction of the parasternal intercostal muscle to the thickening fraction of the diaphragm would improve the prediction of the trial outcome. The median (interquartile range) parasternal thickening was higher in the 22 patients that failed the spontaneous breathing trial, 18% (10 to 33%), than it was in the 32 patients who did not, 7% (4 to 10%), while the diaphragm thickening was lower in

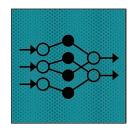
the patients who failed the trial, 17% (13 to 21%) *versus* 34% (29 to 38%). The outcome of the spontaneous breathing trial was predicted reasonably well by parasternal thickening (area under the receiver operating characteristic curve [95% CI] 0.88 [0.76 to 0.95]), but neither it nor the combination of the two indices (0.92 [0.81 to 0.98]) performed better than diaphragm thickening (0.88 [0.77 to 0.95]). *See the accompanying Editorial on page 947. (Summary: M. J. Avram. Image: A Johnson, Vivo Visuals.)*



981 Hydromorphone Unit Dose Affects Intraoperative Dosing: An Observational Study

Hydromorphone was historically dispensed to anesthesia providers at an American academic medical center in 2-mg vials but became exclusively available in 1-mg vials in July 2017 due to a change in pharmaceutical supplier. In a retrospective cohort study including more than 15,000 patients, an interrupted time series analysis was used to test the hypothesis that the change in the unit dose of hydromorphone from 2 mg to 1 mg led to a decrease in the quantity of hydromorphone administered to patients in the intraoperative period. The change in the hydromorphone unit dose from 2 mg to 1 mg was associated with a 49% relative decrease in the probability of receiving a hydromorphone dose more than 1 mg (risk ratio, 0.51; 95%Cl, 0.40 to 0.66). The authors

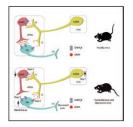
speculate that with a decrease in the unit dose, a provider may decrease the amount of hydromorphone they would normally administer to that dose so they would not have to return a portion of an additional vial. See the accompanying Editorial on page 942. (Summary: M. J. Avram. Image: J. P. Rathmell/The Noun Project.)



968 Machine Learning Prediction of Postoperative Emergency Department Hospital Readmission

This study tested the hypothesis that machine learning methods are capable of producing hospital-specific models able to predict a patient's risk for 30-day postoperative readmission *via* the emergency department with excellent discrimination. Three different types of models that differ from classical logistic regression in their ability to scale to large numbers of features without overfitting were considered: regularized logistic regression and two tree ensemble models, the random forest and gradient boosted trees. The complete data set for this retrospective, machine learning project consisted of 34,532 patients admitted from April 2013 to December 2016, 1,942 (5.6%) of whom were readmitted *via* the emergency department. Using only surgical and demographic

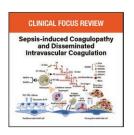
data led to moderate discrimination for prediction (areas under the receiver operating characteristic curve of 0.73 to 0.76). Adding laboratory data improved discrimination (areas under the receiver operating characteristic curve values of 0.85 to 0.87). Medication, team, and current procedural terminology data did not improve discrimination. The discrimination of the predictions calculated 36 h after surgery nearly matched those from time of discharge. See the accompanying Editorial on page 939. (Summary: M. J. Avram. Image: J. P. Rathmell/The Noun Project.)



1175 A Central Amygdala-Ventrolateral Periaqueductal Gray Matter Pathway for Pain in a Mouse Model of Depression-like Behavior

Numerous brain regions are involved in the central mechanisms of depression, most of which are part of the descending pain modulatory system that contributes to pain processing. The hypothesis that the central amygdala—periaqueductal gray circuitry is involved in the pathologic causes of pain in depression states was tested in a chronic restraint stress model in mice that is used to simultaneously induce psychological and physiological stress and can induce both depressive-like behaviors and increased nociception. Retrograde tracing strategies were used to dissect the pathway from the central nucleus of the amygdala to the ventrolateral periaqueductal gray, and optogenetic and chemogenetic experiments were conducted to manipulate the activity

of this pathway to explore its roles in nociception. Increased activity of the central amygdala-ventrolateral periaqueductal gray pathway was observed in mice manifesting pain symptoms under depression conditions. Further activation of this pathway reversed rather than intensified the pain symptoms, suggesting the increased activity of this circuitry is likely a compensatory effect attempting to counteract the pain symptoms caused by chronic stress. (Summary: M. J. Avram. Image: From original article.)



1238 Sepsis-induced Coagulopathy and Disseminated Intravascular Coagulation (Clinical Focus Review)

Sepsis is a common cause of vascular injury and thrombocytopenia that can progress to disseminated intravascular coagulation, which is synonymous with sepsis-induced coagulopathy, an important and common complication in patients with sepsis. Development of thrombocytopenia is often the clue to recognize coagulopathy in sepsis-induced coagulopathy, which is often not diagnosed early or correctly. Criteria for diagnosing sepsis-induced coagulopathy include thrombocytopenia, prolonged prothrombin time, and organ dysfunction as assessed by the Sequential Organ Failure Assessment (SOFA) score. Although disseminated intravascular coagulation is a laboratory-based diagnosis representing the decompensated status of coagulopathy, coagulopathy

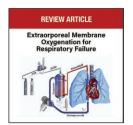
can also arise from other causes. In addition, other conditions in critically ill patients, such as thrombotic thrombocytopenic purpura and hemolytic uremic syndrome, can occur in patients with sepsis and should be differentiated for therapy. Until new therapies are developed, a multimodal approach is needed that includes timely antibiotic therapy of the underlying infection, cardiopulmonary resuscitation, and appropriate management of the underlying coagulopathy if bleeding or thrombotic sequelae have occurred. (Summary: M. J. Avram. Image: From original article.)



1246 Ventilatory Mechanics in the Patient with Obesity (Clinical Focus Review)

Although obesity in the adult is classically defined as a body mass index of more than $30 \, \text{kg/m}^2$, the detrimental effects of obesity are due to not only the absolute amount of excessive adipose tissue but also its distribution. The central obesity subtype, in which the adipose tissue accumulates around visceral organs (particularly in the abdominal cavity), has been linked to a higher cardiovascular risk than the gynoid subtype, in which fat accumulates around the hips and the proximal extremities. In obesity, the cephalic displacement of the diaphragm by abdominal fat affects the lung volumes, producing a restrictive pattern, the hallmark of which is the reduction in the functional residual capacity and in the expiratory reserve volume. This Clinical Focus Review discusses how abdominal fat influences airway management and the mechanics of respiration during spontaneous breathing, the

peri-induction period, artificial ventilation without lung injury and with it, and during weaning from mechanical ventilation. (Summary: M. J. Avram. Image: From original article.)



1257 Extracorporeal Membrane Oxygenation for Respiratory Failure (Review Article)

The term *extracorporeal membrane oxygenation* refers to procedures that support the lungs, the heart, or both. Lung support is mostly performed with veno-venous access, which is the focus of this Review Article. After an overview of extracorporeal membrane oxygenation development, the technical requirements of the extracorporeal membrane oxygenation circuit, blood pump, and membrane oxygenators are reviewed. The physiology of oxygenation and carbon dioxide removal are then considered as are the need for anticoagulation and effects of extracorporeal membrane oxygenation on drug pharmacokinetics. Acute, sustained, and refractory

hypoxia represents the most common indication for high flow veno-venous extracorporeal membrane oxygenation, which is also used as a bridge to lung transplant. Low flow veno-venous extracorporeal membrane oxygenation has been used to remove carbon dioxide in patients with respiratory failure to allow reduction of aggressive mechanical ventilation and its resulting lung injury and as an option for several stages in the course of exacerbated chronic obstructive pulmonary disease. Ethical considerations raised by the use of extracorporeal membrane oxygenation in respiratory failure are reviewed before concluding with developments that may make extracorporeal membrane oxygenation safer and more effective. (Summary: M. J. Avram. Image: From original article.)