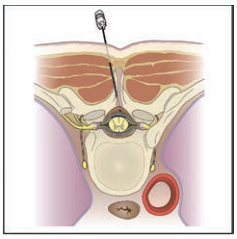
THIS MONTH IN ANESTHESIOLOGY

218 Delirium in Older Patients after Combined Epidural–General Anesthesia or General Anesthesia for Major Surgery: A Randomized Trial

Postoperative delirium is associated with worse perioperative and long-term outcomes. The causes and potential mechanisms leading to delirium after major surgery may include severe pain, high-dose opioids, and surgery-related stress and inflammation, which can be mitigated by epidural analgesia. The hypothesis that delirium during the first 7 postoperative days is less common in patients given combined epidural–general anesthesia with postoperative epidural analgesia than in those given general anesthesia followed by intravenous opioids was tested in a randomized controlled trial of 1,720 older patients having major thoracic and abdominal surgery. The incidence of postoperative delirium within 7 days was 1.8% (15 of 857 patients) in the epidural–general anesthesia group and 5.0% (43 of 863 patients) in the general anesthesia group (relative risk, 0.35 [95% CI, 0.20 to 0.63]). Patients randomized to epidural–general anesthesia were more likely to have intraoperative hypotension (relative risk, 1.47 [95% CI, 1.31 to 1.65]) and consumed less perioperative morphine equivalents (mean difference, –32 [95% CI, –41 to –23] mg). *See the accompanying Editorial on* ***page 197.*** *(Summary: M. J. Avram. Image: A. Johnson, Vivo Visuals.)*

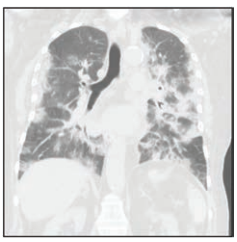


233 Long-term Survival after Combined Epidural–General Anesthesia or General Anesthesia Alone: Follow-up of a Randomized Trial

Epidural analgesia combined with general anesthesia reduces consumption of anesthetics and opioids and blunts the surgical stress response and inflammation, thus preserving cellular immune function. A previous trial compared postoperative analgesia in elderly patients having major noncardiac surgery randomized to combined epidural–general anesthesia or general anesthesia. The hypothesis that epidural anesthesia and analgesia may improve long-term survival after cancer surgery was tested in a preplanned long-term follow-up of 1,712 patients from that trial, 1,574 (92%) of whom had surgery for cancer, by determining the 5-yr overall and cancer recurrence-free survival. Among 853 patients assigned to combined epidural–general anesthesia, 355 (42%) deaths were reported, compared to 326 (38%) among 859 patients assigned to general anesthesia alone, for an adjusted hazard ratio of 1.07 (95% CI, 0.92 to 1.24). Recurrence-free survival was 47% for patients who had combined epidural–general anesthesia and 45% for those who had general anesthesia alone, for an adjusted hazard ratio of 0.97 (95% CI, 0.84 to 1.12). *(Summary: M. J. Avram. Image: G. Nelson/J. P. Rathmell.)*

258 Computer-assisted Individualized Hemodynamic Management Reduces Intraoperative Hypotension in Intermediate- and High-risk Surgery: A Randomized Controlled Trial

Optimizing blood flow and pressure during noncardiac surgery by repeated measurement of both variables and use of established protocols for vasopressor and fluid administration has been associated with decreased postoperative complications. The hypothesis that patients managed using closed-loop vasopressor and decision-support–guided fluid therapy (computer-assisted group) would experience less intraoperative hypotension than patients in whom vasopressor and fluid administration were controlled manually was tested in a randomized controlled study of 38 patients undergoing intermediate- to high-risk abdominal or orthopedic surgery. The median (IQR) percentage of intraoperative case time a patient had hypotension (defined as mean arterial pressure less than 90% of baseline value) was 1.2% (0.4 to 2.0%) in the computer-assisted group and 21.5% (14.5 to 31.8%) in the manually adjusted goal-directed therapy group (difference, –21.1% [95% CI, –15.9 to –27.6%]). The mean ± SD stroke volume index during the last 30 min of the case was higher in the computer-assisted group (42.1 ± 10.0 ml/m^2) than in the manually adjusted group (31.7 ± 8.4 ml/m^2). *See the accompanying Editorial on* ***page 203****. (Summary: M. J. Avram. Image: STRATUS Center for Medical Simulation, Brigham and Women's Hospital.)*

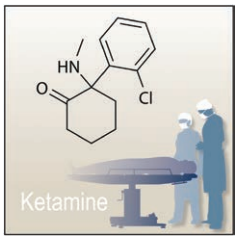


284 Pulmonary Aspiration of Gastric Contents: A Closed Claims Analysis

The present study reviewed malpractice claims in the Anesthesia Closed Claims Project database involving perioperative pulmonary aspiration of gastric contents that occurred between 2000 and 2014 to identify outcomes and patient and process of care risk factors associated with the claims. Aspiration of gastric contents accounted for 115 of the 2,492 (5%) claims in that time. Sixty-six (57%) of the patients who aspirated died as a result of their aspiration event and another 16 (14%) had a permanent severe injury. At least one risk factor for aspiration was identified in 107 (93%) of the claims, the most common of which were emergency procedures (52) and gastrointestinal obstruction (41) or some other acute intra-abdominal process (29). Eighty-eight (77%) of the patients had more than one risk factor present. Aspiration occurred during induction of general anesthesia in 55 (60%) of the 92 claims involving general anesthesia. Anesthesia care was assessed as substandard in 62 (59%) of the 105 claims in which an assessment was made. *See the accompanying Editorial on* ***page 209****. (Summary: M. J. Avram. Image: J. P. Rathmell.)*

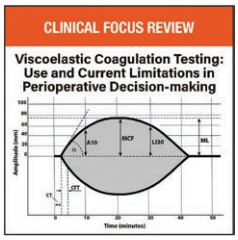
304 Pharmacotherapy for the Prevention of Chronic Pain after Surgery in Adults: An Updated Systematic Review and Meta-analysis

Chronic postsurgical pain can severely affect patients' health and quality of life. This update of a systematic review published in 2013 synthesized available evidence from double-blind, randomized, placebo-controlled trials of the effectiveness and safety of drugs administered systemically to prevent development of chronic postsurgical pain in adults undergoing elective surgeries. The primary outcome was the proportion of participants reporting any pain at the anatomical site of the procedure or pain referred to the surgical site, or both, 3 months or more after the surgery. One hundred ten studies were included in the qualitative analysis: 70 new studies and 40 that had been identified previously. Fifty-nine studies were included in meta-analyses. Subgroup analyses were conducted according to dose/duration of treatment, surgical procedure, and timing of outcome measurements. Superiority over placebo was demonstrated in none of 15 ketamine meta-analyses, 5 of 17 pregabalin meta-analyses, none of 4 gabapentin meta-analyses, 2 of 8 intravenous lidocaine meta-analyses, and 1 of 7 nonsteroidal anti-inflammatory drug meta-analyses. Data on treatment-related adverse effects resulting in study drop-outs were provided infrequently. *See the accompanying Editorial on* ***page 215****. (Summary: M. J. Avram. Image: J. P. Rathmell.)*



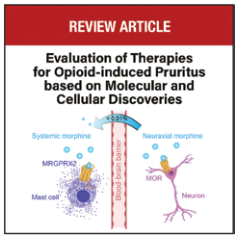
326 Chiral Pharmacokinetics and Metabolite Profile of Prolonged-release Ketamine Tablets in Healthy Human Subjects

Ketamine produces anesthesia and analgesia with psychoactive side effects. It has a high hepatic extraction ratio. Norketamine, its primary metabolite, is oxidized to 2R,6R- and 2S,6S-hydroxynorketamine, which may have analgesic and antidepressant activity without adverse psychoactive effects. Systemic exposure (*i.e.*, area under the serum drug concentration *vs.* time curve) to the 2,6-hydroxynorketamines is three times more than to ketamine after intravenous infusion and five times more than to ketamine after drinking a ketamine solution because of the extensive first pass metabolism of orally administered ketamine. The hypothesis that systemic exposure to the 2,6-hydroxynorketamines can be increased by administration of a prolonged-release ketamine dosage form was tested in a controlled, five-period, ascending-dose pharmacokinetic study in 15 healthy volunteers. The mean ± SD oral bioavailability of S- and R-ketamine were 15% ± 8% and 19% ± 10%, respectively. The systemic exposure to the hydroxynorketamine stereoisomers after oral administration of 40 mg of prolonged-release ketamine was 10 to 11 times greater than after administration of a comparable intravenous dose (5 mg). *(Summary: M. J. Avram. Image: A. Johnson, Vivo Visuals.)*



342 Viscoelastic Coagulation Testing: Use and Current Limitations in Perioperative Decision-making (Clinical Focus Review)

Rapid diagnosis and therapy of coagulopathy plays an important role in the care of the severely bleeding patient in major trauma, postpartum hemorrhage, and major surgery. The two viscoelastic point-of-care coagulation assays designed to help answer basic questions regarding treatment of perioperative coagulopathy that are used most often are the kaolin thromboelastography (TEG) and functional fibrinogen TEG assays and the tissue factor–activated rotational thromboelastometry (ROTEM) and fibrinogen ROTEM assays. This Clinical Focus Review re-evaluates randomized controlled trials, systematic reviews, meta-analyses, and society recommendations and guidelines on viscoelastic point-of-care tests and their effect on clinical decision-making. The focus of the review is on which fundamental questions affecting routine patient care in the perioperative period could be answered by TEG and ROTEM assays and which could not. The review concludes that while the basic assays of TEG and ROTEM remain the foundation for most clinical decisions, further improvement and clinical validation of these assays are needed. *(Summary: M. J. Avram. Image: J. P. Rathmell.)*



350 Evaluation of Therapies for Peripheral and Neuraxial Opioid-induced Pruritus based on Molecular and Cellular Discoveries (Review Article)

Although pruritus is occasionally observed with parenteral opioid use, it is a very common side effect of neuraxial opioids. Systemic opioids activate mast cells to drive itch through histamine release, whereas neuraxial opioids act on central nervous system pathways to cause itch through a mechanism of neuronal disinhibition. Because opioid-induced pruritus is dose dependent, unwanted side effects can be controlled by tightly titrating the dose needed to optimize analgesia. Nonetheless, pruritus persists as a side effect for some patients despite efforts to reduce the opioid dose administered. The most effective treatments for opioid-induced pruritus have included pharmacologic agents that antagonize the μ-opioid receptor, such as naloxone and naltrexone, which have the disadvantage that they can reverse analgesia. The mixed opioid receptor agonist butorphanol and the selective κ-opioid receptor agonist nalfurafine may have therapeutic advantages over selective μ antagonists due to their agonism of the κ-opioid receptor and their ability to modulate spinal itch circuits directly. The effectiveness, side effects, and status of other treatment options for opioid-induced pruritus are also discussed. *(Summary: M. J. Avram. Image: From original article.)*

DOI: 10.1097/ALN.0000000000003888