



Hi, this is Evan Kharasch, Editor-in-Chief of ANESTHESIOLOGY, with some highlights from the August 2021 issue, as selected by the journal editors.

In this month's podcast, we'll be exploring new information about combining epidural and general anesthesia. We'll take a closer look at computer-assisted hemodynamic management. We'll also discuss some details of risk factors associated with gastric aspiration that prompted malpractice claims. And we'll close this month by highlighting a clinical review of new discoveries regarding opioid-induced pruritus.

1) 20-02003

Let's begin this month with a look at how combined epidural and general anesthesia can reduce the incidence of delirium in older patients after major surgery compared to general anesthesia alone. Postoperative delirium remains a common problem in older patients who undergo major surgery, and it is associated with short-term and long-term complications. Epidural anesthesia is often used in patients undergoing major thoracic or abdominal surgeries, but its role in preventing delirium has not been well studied. In a prospective study led by Dr. Ya-Wei Li of Peking University First Hospital, Beijing, China, more than 1,800 adults ages 60 to 90 years were randomized to either general anesthesia alone, followed by intravenous opioids, or to general anesthesia combined with an epidural followed by postoperative epidural analgesia. The primary outcome was the incidence of delirium, which was assessed twice daily during the first week after surgery. Delirium was significantly less common in the epidural/general anesthesia combination group than in the general anesthesia-only group. It occurred in 1.8% of patients receiving general/epidural anesthesia compared with 5% of those receiving general anesthesia. However, there was a trade-off, as 49% of the patients in the epidural combination group developed intraoperative hypotension, compared to 33% of the general anesthesia-only group. An editorial accompanying this article notes that that epidural analgesia could help reduce delirium risk by reducing pain itself, but also by reducing opioid use, both of which can impair cognition. The reviewers add that epidural analgesia also may reduce inflammation, including the neuroinflammatory processes that can impact delirium. Check out the full article for free in this month's issue.

2) 20-02004

We continue to explore the potential of the combined general anesthesia/epidural approach with a study involving cancer surgery patients. This was led by Dr. Ya-Ting Du, also of the Peking University First Hospital, Beijing, China. Some preliminary research had previously suggested that combined epidural-general anesthesia may improve long-term survival in cancer patients after surgery, possibly by reducing use of postoperative anesthetics and opioids, and by controlling post-surgical inflammation. Dr. Du and colleagues conducted a prospective study of more than 1,700 adults aged 60 to 90 years who were randomized to combined epidural-general anesthesia with postoperative epidural analgesia, or to general anesthesia alone with postoperative intravenous analgesia. The patients underwent thoracic or abdominal surgeries. The primary outcome of overall survival was not significantly different between the groups; 42% of patients in the combination group died compared with 38% of patients in the general anesthesia-only group. Rates of cancer-specific survival and recurrence-free survival also were not different between the groups. According to the authors, these findings suggest that either protocol can be used according to patient and clinician preference. This article is available for free in this month's issue.

3) 20-02006

Next, we have a randomized, controlled trial of computer-assisted individualized hemodynamic management. Individualized hemodynamic management has the potential to reduce intraoperative hypotension and possibly associated perioperative complications. Recent innovations in computer-assisted technology have made the process of accurately titrating vasopressors and fluids easier for anesthesia providers. Dr. Alexandre Joosten, of the Université Libre de Bruxelles, Brussels, Belgium, and colleagues prospectively identified 38 patients who underwent abdominal or orthopedic surgery and randomized them to hemodynamic management by manual titration or with computer assistance for norepinephrine infusion and mini fluid challenges. Hypotension was defined as the percentage of intraoperative case time patients spent with a mean arterial pressure less than 90% of their baseline mean arterial pressure. For patients in the computer-assisted group, hypotension was 1.2%, compared to 22% in the manual titration group. The incidence of minor postoperative complications was not

different between the two groups. A related editorial highlights the need for larger studies to examine the impact on patient-centered outcomes. Also, it will be important to identify which patients would or would not benefit from the use of advanced technologies as part of considering costs. This article is available for free in this month's issue.

4) 21-00082

Our next study is a retrospective look at adverse events. It identifies outcomes, and, both patient risk factors and process of care risk factors associated with gastric aspiration claims in a malpractice database. Perioperative pulmonary aspiration of gastric contents remains a significant cause of severe morbidity and death, despite interventions and updated guidelines. Researchers led by Dr. Mark Warner of the Mayo Clinic, Rochester, Minnesota, reviewed almost 2,500 claims in the American Society of Anesthesiologists Closed Claims Project that were associated with an aspiration event between 2000 and 2014. They found that 5% of the claims regarding aspiration of gastric contents during the study period met inclusion criteria. This included 115 claims. Death directly related to pulmonary aspiration occurred in 57% of the 115 claims. Another 14% of the claims had documented permanent severe injury. In addition, the authors found that 61% of the patients who aspirated had either gastrointestinal obstruction or another type of acute intraabdominal process. Overall, 59% of the claims judged anesthetic management as substandard. However, in 93% of claims, the researchers found at least one risk factor for aspiration, and 77% had more than one risk factor. The most common risk factors were emergency procedures in 45% of cases, gastrointestinal obstructions in 36%, and other acute intraabdominal processes in 25%. In a related editorial, two authors explain how the study provides insights into the value of identifying risk factors to improve patient safety.

The article is available for free in this month's issue.

5) 20-02186

Next, we turn to an updated systematic review and meta-analysis of the effectiveness of systemic drugs to prevent chronic post-surgical pain. Managing and especially preventing chronic post-surgical pain remains a challenge. Research on the effectiveness of various methods, including perioperative administration of systemic drugs, is ongoing. Meg Carley and colleagues at Queen's University, Kingston, Ontario, Canada, conducted a retrospective review of 70 new studies published since their original review on this topic appeared in 2013. The current study also included 40 studies from that 2013 article. All included studies were double-blind, placebo-controlled, randomized control trials of patients aged 18 years and older who underwent planned surgeries. The primary outcome of the review was the percentage of patients reporting pain 3 months or more after surgery at the site of the procedure, or referred pain, or both. The main drugs included in the studies were ketamine, pregabalin, gabapentin, IV lidocaine, and non-steroidal antiinflammatory drugs. Overall, superiority of the drug over placebo was reported in none of 15 ketamine meta-analyses, 5 of 17 pregabalin meta-analyses, none of 4 gabapentin meta-analyses, caution in generalizing the results. The article is available for free in this month's issue. Check out the related editorial from David Clark, at Stanford University, for perspective about how improvements in study design might address some of the limitations of research in chronic pain management.

6) 20-02005

Our next study compares the pharmacokinetics of prolonged-release ketamine tablets to intravenous ketamine. Ketamine is widely used, but it does have known psychoactive side effects. Ketamine has multiple metabolites, and these may be pharmacologically active, and mediate some of the effects of ketamine. One metabolite of interest is 2,6-hydroxynorketamine, which is formed in the liver. Oral ketamine undergoes more metabolism than intravenous ketamine, and a prolonged-release oral tablet might be converted into even more 2,6-hydroxynorketamine. Researchers led by Dr. Mahmoud Hasan, of the University of Greifswald, Germany, hypothesized that an oral prolonged release tablet would increase exposure to 2,6-hydroxynorketamines more effectively than an IV infusion. The authors prospectively evaluated single oral ascending-doses of 10 mg, 20 mg, 40 mg, and 80 mg of ketamine and compared the oral doses to intravenous infusion of 5.0 mg. The study population included 15 healthy adults. Overall, the systemic exposure to the hydroxynorketamines was 10 to 11 times higher after individuals received a 40-mg tablet compared to a 5 mg IV infusion. The tablets were safe and well tolerated, with no reports of serious adverse events or serious adverse drug reactions. The results suggest that prolonged-release ketamine tablets might be a safe and effective option for patients with chronic neuropathic pain.

7) 21-00041

This month's clinical focus review revisits the impact of viscoelastic point-of-care tests on clinical decision-making. The two most common assays used during the perioperative period are thromboelastography-based (TEG) and rotational thromboelastometry-based (ROTEM), but they have their limitations. Such limitations include inadequate sensitivity and specificity to detect platelet inhibition. Dr. Gabor Erdoes of the University of Bern, Switzerland, and colleagues examined which patient care issues could be addressed using these assays. Despite the limitations of the assays, the authors concluded that, based on the latest literature, viscoelastic testing is more effective than standard laboratory testing, and that therapy guided by these assays may reduce the need for blood products in patients who experience perioperative bleeding. They also noted that the two assays were more effective than clinical judgment alone in reducing allogenic blood product exposure and postoperative bleeding. Although new diagnostic instruments and assays continue to arrive on the scene, the TEG and ROTEM assays retain their status as a foundation for clinical decision-making, the authors concluded.

8)21-00287

Our comprehensive review this month addresses opioid-induced pruritus and describes recent discoveries of mechanisms of action for this burdensome condition. The latest treatments spring from advances in

spinal cord circuitry and mast cell biology. This review was authored by Eileen Nguyen, and colleagues at the University of Pittsburgh School of Medicine. The authors explained that mast cells may contribute to pruritus by inducing histamine release, but a mast cell-dependent mechanism does not explain the prevalence and spread of neuraxial opioid-induced pruritus. Neuraxial opioid-induced pruritus occurs instead as a result of neuronal disinhibition in the spinal cord dorsal horn. The authors described emerging research suggesting that dysregulation of opioid-sensitive pathways, specifically those involving mu- and kappa-opioid receptor signaling, might cause pruritus. They concluded by emphasizing the need to pursue causes of opioid-induced pruritus to build a foundation for developing therapies that could manage pain without the itch.

Anesthesiology has two current calls for papers, both related to Annual Meeting sessions. The first topic is SARS-CoV2 and COVID-19: New Paradigms and Challenges for Anesthesiologists which will be presented at the Annual Journal Symposium. The second is the annual call for papers regarding initial results of Clinical Trials. For more information about either of these sessions, please visit the author center on the journal website.

As always, thank you for listening to this podcast and your support of ANESTHESIOLOGY. I hope you find the information presented helps to guide and improve your clinical practice. I look forward to sharing more important research with you next month.