



Hi, this is Evan Kharasch, Editor-in-Chief of ANESTHESIOLOGY with some highlights from the January 2022 issue, as selected by the journal editors. In this month's podcast, we'll look at the potential use of tranexamic acid to reduce early mortality in trauma patients. We'll explore new information about hypotension and acute kidney injury in infants and children. We'll discuss the impact of pain on postoperative mobility and the potential impact of opioid use. We'll present a two-part clinical review on the important topic of perioperative pulmonary atelectasis. And we will close, with mention of the updated ASA practice

guidelines for the management of the difficult airway, and a special article on the opioid crisis and opioid stewardship.

Let's begin this month with a randomized trial that investigates carbon dioxide changes at different flow rates of 100% oxygen in elective surgery patients. Previous studies of high-flow, humidified heated oxygen using nasal cannulas have shown that it can eliminate carbon dioxide, but studies in children dispute this finding. The ability of high flow nasal oxygen to eliminate carbon dioxide remains controversial. Dr. Thomas Riva of the University of Bern, Switzerland and his team randomized 125 adult surgery patients to five groups of 25 patients each. They received minimum flow, low flow, medium flow, and high flow 100% oxygen, between 0.25 and 70 L/min, with continuous jaw-thrust and laryngoscopy, during a 15-minute apnea period. There were also controls who did not receive nasal oxygen. The primary outcome was the rate of increase in partial pressure of carbon dioxide during this period. The study showed no significant difference in carbon dioxide increases at any of the various low or high flow nasal oxygen rates. The authors concluded that high-flow nasal oxygen had no additional ventilatory effect. This differed from previous studies, but this study stands out as a prospective, randomized trial rather than a historical review. In an accompanying editorial, Drs. Allan Simpao and Martin London noted that the study supports guidelines from the European Society of Intensive Care Medicine recommending high-flow nasal cannula in patients with hypoxemic respiratory failure, but not for patients during intubation. However, they concluded that the findings from the current study can be useful to anesthesiologists in deciding when to use high-flow nasal cannula therapy, such as in the operating room. This article is available for free in this month's issue.

We next take a look at a secondary analysis from a prospective study of late adverse outcomes in trauma patients. Both hyper- and hypofibrinolysis are associated with adverse clinical events after traumatic injury. Trauma patients often receive tranexamic acid to inhibit hyperfibrinolysis, but its impact has not been well studied in the emergency setting. Dr. Andrea Rosetto of Queen Mary University, London, and colleagues reviewed data on 731 patients who were treated at a trauma center in the United Kingdom. A total of 299 received tranexamic acid, and 432 did not. The authors assessed data on clot lysis using rotational thromboelastometry (ROTEM). Overall, tranexamic acid had a significant impact on early fibrinolytic transition patterns, but not on late mortality. Among patients who survived to 24 hours, 28% of those treated with tranexamic acid transitioned to low-maximum lysis from normal-maximum admission lysis, compared to only 12% of untreated patients. Early mortality was 14% in tranexamic acid-treated patients, compared to 29% in untreated patients. The authors found no significant difference in late mortality associated with tranexamic acid across any transition patterns. However, they suggested that the early transition patterns could provide unique data to predict clinical outcomes. An editorial by Drs. Paul Myles and Robert Medcalf accompanies this article. The editorial emphasizes the challenges of evaluating functional fibrinolysis in real time in the clinical setting. It added that the data do not suggest a causal effect on trauma outcomes. However, they agreed with the study authors that tranexamic acid may be useful to reduce early mortality, notably in patients with ongoing evidence of bleeding. And they agreed that tranexamic acid should be used in major trauma. Check out the full article for free in this month's issue.

Our next clinical study focuses on our younger patients. We know that intraoperative hypotension is common in infants and young children, but published reference information lacks harm thresholds for intraoperative blood pressure in this population. Hypotension during noncardiac surgery has been associated with acute kidney injury in adults, and hypotension is common after cardiac surgery in children. But less is known about the relationship between hypotension and kidney injury in noncardiac surgery

pediatric patients. Dr. Nadav Schacham, of the Cleveland Clinic, Ohio, and colleagues explored the relationship between intraoperative hypotension and acute kidney injury in infants and children following noncardiac surgery. This retrospective analysis included approximately 4,000 children up to 18 years old whose serum creatinine concentrations were assessed before and after surgery. The overall incidence of acute kidney injury was 11%. The incidence was 17% in children younger than 6 years, but the authors wrote that this finding may be due to the challenges of blood sampling in young children. The authors defined absolute hypotension as the lowest intraoperative mean arterial pressure sustained for at least 5 minutes. They defined relative hypotension as the largest mean arterial pressure reduction sustained for at least 5 minutes. They found no association between intraoperative hypotension and postoperative kidney injury. The results contrasted with findings in adult patients. The authors concluded that short periods of hypotension should not be the primary concern in preventing intraoperative renal injury in children. An editorial by Dr. Andrew Davidson accompanies this article. Dr. Davidson wrote that although the rate of 11% kidney injury might seem high, approximately three-quarters of the children had a Grade 1 kidney injury. He added that it is premature to discount hypotension as an issue for renal function in children. But it is important to remember, as he put it, that 'kiddie kidneys are not little adult kidneys.' You can access this article for free in this month's issue.

Now, let's turn to the topic of pain and postoperative mobility. Early mobilization is an essential part of recovery after surgery, but concerns persist that using opioids for pain relief might reduce patients' mobility. Dr. Eva Rivas of the Cleveland Clinic, Ohio, led colleagues in a post hoc analysis of two randomized trials including more than 600 patients who underwent abdominal surgery. The authors tested the hypothesis that postoperative pain and opioid consumption were inversely related to mobility. In this study, mobility was defined as the fraction of monitored time sitting up or standing. Patients with average pain scores of 3 or lower had 1.9 mobile hours per day, while those with scores of 6 or greater had only 1.2 mobile hours per day. Increases in pain scores were significantly associated with decreases in mobilization. Opioid consumption varied widely, but there was no association between postoperative opioid use and patients' daily mobility. The authors noted that overall mobilization time was low, and that all postoperative complications occurred in patients in the lowest quartiles of mobilization times. The authors did not find an association between pain and mobilization, but they suggested that improving postoperative analgesia might increase mobilization. Check out this article for free in this month's issue.

We move next to the hot topic of central airway occlusion, and the care of patients with an anterior mediastinal mass. We know that central airway collapse and cardiovascular collapse are serious risks for patients with large, mediastinal masses who undergo general anesthesia. Current recommendations are to maintain spontaneous breathing and avoid neuromuscular blockade in these patients. However this lacks direct evidence, despite being presented as safer than positive pressure ventilation and paralysis. In a prospective, observational study, a team led by Dr. Philip Hartigan of Beth Israel Deaconess Medical Center, took a unique approach to comparing the impact of different anesthetic interventions. The team used real-time video recordings to evaluate the effects of general anesthesia, positive pressure ventilation, and neuromuscular blockade on airway patency. Their population of 17 adults had large, mediastinal masses and underwent awake intubation. Changes in airway anterior-posterior diameter relative to baseline were assessed by 7 bronchoscopists in side-by-side blinded and scrambled comparisons. Changes greater than 50% were considered clinically significant. The authors found no significant changes from baseline in the mean airway patency scores after general anesthesia. However, the mean airway patency scores increased significantly after adding positive pressure ventilation and neuromuscular blockade. In their article, the authors included links to video images from patients, which they said provide direct visual evidence of the effects of general anesthesia, positive pressure ventilation, and neuromuscular blockade on airway patency. They concluded that their findings challenge the prevailing recommendations against positive pressure ventilation and neuromuscular blockade in patients with mediastinal masses, but they acknowledged the challenge of separating the effect of neuromuscular blockade from the preceding positive pressure ventilation phase. The authors also emphasized that the findings do not prove the safety of nonstaged inductions for patients with mediastinal masses. This article is available for free in this month's issue.

Our next clinical study examines diaphragm thickening fraction and transdiaphragmatic pressure. Transdiaphragmatic pressure is often used as a surrogate for diaphragm function, but we see ultrasound being used more commonly to measure changes in diaphragm function based on diaphragm thickening fraction. However, the relationship between these methods is unclear. To explore this relationship, researchers led by Thomas Poulard of the Neuromuscular Physiology and Evaluation Laboratory, Paris, France, evaluated data from 14 healthy subjects and 25 mechanically ventilated patients from two previous studies. The changes in both transdiaphragmatic pressure and diaphragm pressure-time index were moderately correlated to diaphragm thickening fraction. In mechanically ventilated patients, the authors found a weak correlation between transdiaphragmatic pressure and diaphragm thickening fraction. They found no correlation between diaphragm pressure-time index and diaphragm thickening fraction. A total of 8 of 14 healthy subjects and 2 of 25 ventilated patients had a significant correlation in changes between transdiaphragmatic pressure changes and diaphragm thickening fraction. According to the authors, the findings showed that diaphragm thickening fraction was a poor reflector of transdiaphragmatic pressure, and should be used with caution, if at all, as a surrogate.

Our clinical review this month is a two-part exploration of perioperative pulmonary atelectasis. We know that pulmonary atelectasis is an ongoing challenge in the perioperative setting. This is driven by the imbalance of physical forces at work in the lungs under anesthesia. In Part I of our review, lead author Dr. Congli Zeng of Massachusetts General Hospital, Boston, and colleagues discussed the biology and mechanisms of atelectasis, and how insight into the physiology might guide anesthesiologists in practice. The authors begin by reviewing the principles of bronchiolar and alveolar expansion. They explained the three main stresses that act on bronchiolar and alveolar walls. These are fluid pressure, tethering stress, and surface tension. They emphasized that lung elastic recoil is the main physiological mechanism of passive exhalation. We know that mechanisms of atelectasis in the perioperative period may be prompted by general anesthesia, mechanical ventilation, and surgical interventions. These mechanisms produce biophysical factors that promote collapse of lung tissue. Three interrelated collapsing factors—increased pleural pressure, low alveolar pressure, and surfactant impairment—contribute to airway and alveolar closure. In a section on the pathophysiologic effects of pulmonary atelectasis, the authors explain relationships between atelectasis and various inflammatory responses. They note that the biologic response associated with atelectasis could make lung injury worse. The authors concluded by stating that the presumed impact of intraoperative pulmonary atelectasis on outcomes including acute lung injury and pneumonia requires further study. They also proposed that future management of atelectasis might involve cellular and molecular level strategies through use of perioperative medications. The article includes detailed figures that illustrated these complex processes.

Part 2 of our Clinical Review this month tackles the clinical implications of perioperative pulmonary atelectasis. Lead author Dr. David Lagier of Massachusetts General Hospital, Boston, presents risk factors, diagnostic approaches, and management strategies. The authors explored clinical risk factors in three categories: patient-related, anesthesia-related, and surgery-related. Patient-related factors included obesity, age, diaphragmatic dysfunction, intra-abdominal hypertension, and pulmonary conditions, including smoking. Anesthesia-related risk factors included the use of general anesthesia drugs, regional anesthesia, and blood transfusion. Surgery-related risk factors included body position, pneumoperitoneum, cardiac surgery, one-lung ventilation, surgery duration, and minimally invasive procedures. The authors emphasized that an accurate diagnosis of atelectasis should be made directly, using imaging methods of computed tomography, ultrasound, MRI, or chest radiography. They

also summarized indirect physiologic assessment techniques including blood oxygenation and electrical impedance tomography. Finally, the authors reviewed strategies for therapeutic management of perioperative atelectasis during the pre-, intra- and postoperative periods. Preoperatively, a recent meta-analysis supported the value of preoperative inspiratory muscle training prior to surgery, but the study size was small and more research is needed. During the intraoperative period, tidal volume remains a key intervention, but current data suggest that the protective effects may lie not in tidal volume itself, but in the resulting limited lung strain. Postoperatively, noninvasive ventilatory support, analgesia, and oxygen therapy are options to prevent pulmonary atelectasis, according to the authors. Evidence is weaker for the postoperative use of oxygen therapy and mucolytics, they said. The authors concluded that we need a better understanding and more information to explore risk stratification for severe pulmonary atelectasis. They also urged further exploration of the use of titrated physiology-based strategies and the extension of lung recruitment. This article includes a useful algorithm for the intraoperative management of pulmonary atelectasis. If you want to delve deeper, you'll also find a table summarizing randomized clinical trials on alveolar expansion strategies during general anesthesia.

In addition to these original research articles and reviews, there are 2 special articles in the January issue.

One special article is the updated American Society of Anesthesiologists practice guidelines for the management of the difficult airway. These guidelines were developed by an international task force of anesthesiologists representing several anesthesiology, airway and other medical associations. They replace the previously published guidelines and provide new evidence obtained from recent scientific literature along with findings from new surveys of expert consultants, ASA members and 10 participating organizations. The guidelines update equipment for standard and advanced difficult airway management, recommend supplemental oxygen administration before initiating and throughout difficult airway management and other noninvasive and invasive alternatives. These Practice Guidelines are available for free.

The other special article is on opioid use. We are all acutely aware of the opioid crisis in the US, and the rapidly escalating number of fatal opioid overdoses. Opioid prescribing in the US has decreased 38% in the past decade, but opioid deaths have increased 300%. This opioid paradox is poorly recognized. Current approaches to opioid management are not working, and new approaches are needed. The Special Article reviews the outcomes and shortcomings of recent US opioid policies and strategies that focus primarily or exclusively on reducing or eliminating opioid prescribing. It introduces concepts of a prescription opioid ecosystem and opioid pool, and discusses how the pool can be influenced by supply-side, demand-side, and opioid returns factors. It illuminates pressing policy needs for an opioid ecosystem that enables proper opioid stewardship, identifies associated responsibilities, and emphasizes the necessity of making opioid returns as easy and common as opioid prescribing, in order to minimize the size of the opioid pool available for potential diversion, misuse, overdose, and death. Approaches are applicable to opioid prescribing in general, and to opioid prescribing after surgery.

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As always, thank you for listening to this podcast and thank you for 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.