



Hi, this is Evan Kharasch, Editor-in-Chief of ANESTHESIOLOGY, with some highlights from the October 2020 issue, as selected by the journal editors.

I'll begin this month with a clinical study examining how different factors may independently impair lung mechanics during robotic laparoscopic surgery. These factors include body habitus, pneumoperitoneum, and Trendelenburg positioning. Dr. William Tharp of the University of Vermont, Burlington, Vermont, and colleagues there and at Midwestern University, Glendale, Arizona, conducted the study. They tested the

hypothesis that increasing body mass index is associated with more mechanical strain and alveolar collapse. They also tested the hypothesis that these impairments are exacerbated by pneumoperitoneum and by Trendelenburg position. This was a cross-sectional study that measured respiratory flow, airway pressures, and esophageal pressures in 91 surgical patients. Using esophageal manometry, the authors partitioned respiratory mechanical properties into lung and chest wall components. They also calculated the optimal positive end-expiratory pressure (PEEP) settings needed to achieve positive end-expiratory transpulmonary pressures. Increasing body mass index was associated with higher airway plateau and driving pressures, elevated esophageal pressures, and augmented lung elastance. These differences were exacerbated by pneumoperitoneum and by Trendelenburg positioning with pneumoperitoneum. Higher body mass index was also associated with more negative end-expiratory transpulmonary pressures and larger transpulmonary driving pressures. The authors concluded that increasing body mass index induces significant alterations in lung mechanics during robotic laparoscopic surgery, and, there is a wide range in the degree of impairment. Obese subjects were at higher risk for impaired gas exchange, atelectrauma, and intensified mechanical strain. Furthermore, these risks persisted despite the use of common lung protective ventilation strategies. In addition, optimizing PEEP settings may need individualization based on body mass index and surgical conditions.

Our clinical next study examined the effects of different anesthetic agents on cancer prognosis. Dr. Kanako Makito of the University of Tokyo and colleagues there and at the Tokyo Medical and Dental University conducted this nationwide retrospective cohort study. They compared overall and recurrence-free survival in patients given volatile-anesthetic based anesthesia or total intravenous anesthesia for digestive tract cancer surgery. The authors used a national database to select patients who had elective surgery for gastrointestinal cancers during an 8-year period. They divided patients into a volatile anesthesia group and a propofol-based total intravenous anesthesia group. The authors tested the hypothesis that total intravenous anesthesia would be associated with greater overall and recurrence-free survival than volatile anesthesia. The authors identified 196,000 patients who had cancer surgery. They found no significant difference between the two anesthetic groups in overall survival, and no significant difference in recurrence-free survival, regardless of surgery type. Makito et al. concluded that overall and recurrence-free survival were similar between volatile and total intravenous anesthesia in patients having digestive tract surgery. Therefore, selection of the anesthetic approach for these patients should be based on other factors besides effects on cancer recurrence.

Our next clinical study explored connected consciousness and information flow between regions of the cerebral cortex. Dr. Rebecca Pullon of the University of Auckland, Auckland, New Zealand, and colleagues there and at the University of Oxford conducted the study. They tested the hypothesis that loss of wakefulness caused by propofol anesthesia would be associated with loss of information flow. They tested an additional hypothesis, that this loss could be estimated by the effective connectivity in the scalp electroencephalogram (EEG) signal. The authors applied Granger causality analysis, a method to analyze whether one variable predict another variable, to multichannel EEG recordings. Data were recorded from 16 healthy adult volunteers undergoing induction and emergence from anesthesia with step-dose intravenous propofol. Participants also conducted auditory and motor tasks during wakefulness. The authors estimated functional connectivity using EEG coherence. Pullon and collaborators found that propofol-induced unresponsiveness coincided with a marked global decrease in EEG information flow. They concluded that this decrease is greatest from the lateral frontal and prefrontal brain regions in a posterior and medial direction.

They also concluded that information flow is an important indicator of wakefulness.

Next we have an examination of the cost-effectiveness of obstructive sleep apnea screening in surgical patients. Dr. Ashwin Sankar of the University of Toronto and colleagues there and elsewhere conducted the study. Their objective was to evaluate the cost-effectiveness of preoperative obstructive sleep apnea screening, both for the perioperative period, and for patients' remaining lifespans. The authors examined several screening modalities, including polysomnography, the STOP-Bang questionnaire, and portable monitors. Patients with a positive STOP-bang screening test received postoperative treatment modifications and expedited definitive testing. The authors concluded that the cost-effectiveness of preoperative obstructive sleep apnea screening differed depending on the time horizon. In the perioperative time horizon, no screening was favored, because the added effectiveness of any screening strategy was cost prohibitive. However, over a lifetime horizon, the favored strategy was to administer the STOP-Bang questionnaire and confirm a positive preoperative screening result using polysomnography. It was more cost-effective than either STOP-Bang + portable monitor or STOP-Bang alone. This may represent a cost-effective application of preoperative assessment for long-term health benefit.

Our next clinical study explored the effect of spinal anesthesia on early ambulation following total hip arthroplasty. Dr. Eric Schwenk of Thomas Jefferson University in Philadelphia and colleagues there and elsewhere in Philadelphia conducted the study. They tested the hypothesis that the intermediate-acting local anesthetic mepivacaine could enable earlier ambulation than hyperbaric or isobaric bupivacaine. They performed a randomized controlled trial of American Society of Anesthesiologists Physical Status I to III patients who were undergoing primary total hip arthroplasty. The 154 patients were randomized to 52mg of mepivacaine, 11mg of hyperbaric bupivacaine, or 12mg of isobaric bupivacaine for spinal anesthesia. The primary outcome was the ability to ambulate between 3 and 3.5 h post-operatively. In the mepivacaine group 70% of patients met this endpoint. In contrast, only 38% of patients in the hyperbaric bupivacaine group and 18% of patients in the isobaric bupivacaine group walked at 3 hours. Additionally, return of motor function occurred earlier with mepivacaine. Patients receiving a mepivacaine spinal also ambulated earlier and were more likely to be discharged the same day, compared with patients in either of the two bupivacaine groups. Schwenk et al. concluded that mepivacaine could be beneficial for outpatient total hip arthroplasty candidates if spinal anesthesia is preferred.

Our next study explored a new thermodilution technique during veno-arterial extracorporeal membrane oxygenation therapy, or ECMO. Thermodilution is a well-established method for measuring cardiac output but thermodilution during ECMO may overestimate cardiac output because of indicator loss into the ECMO circuit. Dr. Kaspar Bachmann and colleagues at the University of Bern in Switzerland conducted the study. Their hypothesis was that injectate volume is divided into the ECMO circuit and the lung circuit, depending on the different flows. They performed veno-arterial extracorporeal membrane oxygenation on 16 healthy pigs. They placed a precision flow probe for blood flow assessment on the pulmonary artery. They also had thermistors in the ECMO circuit and pulmonary artery to record temperature changes after injectate. The distribution of injection volumes passing each circuit was assessed, and this enabled calculation of pulmonary blood flow and right ventricular function. ECMO flows were varied from 1 to 4 L/min. The calculated pulmonary blood flows correlated well with flows measured by the flow probe. Right ventricular ejection fraction increased as ECMO flows decreased, with a marked increase in measured stroke volume. The authors concluded that this adapted thermodilution approach allows reliable assessment of both cardiac output and right ventricular behavior during ECMO.

We feature two Clinical Focus Reviews this month, both addressing hemodynamic measurements. The first is a technological assessment and objective evaluation of minimally invasive and noninvasive cardiac output monitoring systems. Dr. Bernd Saugel of University Medical Center Hamburg-Eppendorf, Hamburg, Germany, and colleagues elsewhere wrote this article. Maintaining adequate cardiac output is a mainstay of hemodynamic management in perioperative and intensive care medicine. In addition to the reference standard of invasive indicator dilution methods,

numerous minimally invasive and noninvasive methods for estimating cardiac output have been developed in recent years. These include noninvasive pulse wave analysis, pulse wave transit time, and thoracic electrical bioimpedance and bioreactance. Anesthesiologists must understand these systems and their limitations to select the appropriate method for each patient and clinical setting. Saugel et al. describe minimally invasive and noninvasive cardiac output monitoring technologies available in clinical practice. They also discuss how to evaluate these systems objectively. This review includes a discussion of how to assess a new monitoring method against a reference method in a method comparison study.

Our second Clinical Focus Review discusses the use of dynamic variables to guide perioperative fluid management. Dr. Azriel Perel of Tel Aviv University, Tel Aviv, Israel is the author. He notes that the general principles of perioperative fluid management may not help determine individual patient needs at any specific moment. A better assessment tool may be the patient's own fluid responsiveness status. This is the degree by which a modification of preload affects the stroke volume. Fluid responsiveness is best determined by measuring the change in cardiac output following administration of a fluid challenge. However, using a fluid challenge to determine fluid responsiveness has shortcomings. In contrast, preload is affected by mechanical ventilation, and hence, variations in the arterial pressure and plethysmographic waveforms during mechanical ventilation may reflect fluid responsiveness. They may help identify occult hypovolemia and prevent unnecessary fluid administration. Protocols that use stroke volume variation  $>12\%$  or plethysmographic variability index  $>13\%$  with mechanical ventilation, as triggers for fluid administration, result in less fluid being administered and in better outcome compared with standard care. This important value of dynamic variables stems from their ability to identify nonresponders and to prevent administration of ineffective fluid challenges.

Finally, I want to share my excitement that ANESTHESIOLOGY 2020, the annual meeting of the American Society of Anesthesiologists, will proceed, despite the challenges faced by our specialty, medicine, and society at large, during this tumultuous year. The annual meeting will be

held online from October 2–October 5 and will include all of the usual ANESTHESIOLOGY Journal features that make this meeting such a special event.

This year ANESTHESIOLOGY will host the 29th Annual Journal Symposium with Hemodynamics as our topic. There will be invited plenary lectures and selected research presentations. Additionally, ANESTHESIOLOGY will sponsor two Best Abstract Sessions, one in basic science and another in clinical science. A panel of our editors and ASA appointees will then choose one abstract in each category to receive the Best Abstract award for basic and clinical science at the meeting. We will also hold the annual Celebration of Research. The Annual Meeting and this event is a time to acknowledge our valued colleagues. Please join me in congratulating Robert D. Sanders, B.Sc., M.B.B.S., Ph.D., F.R.C.A., who has been chosen to receive the 2020 James E. Cottrell, M.D., Presidential Scholar Award. He was recently appointed as Nuffield Chair of Anaesthetics at the University of Sydney, Australia, and was formerly on faculty at the University of Wisconsin. His many research efforts focus on the relation between connectedness and consciousness, perioperative delirium in older patients, and how novel treatments such as xenon can impact recovery from central nervous system injury and anesthesia. Finally, I wish to recognize my colleague Ru-Rong Ji, Ph.D., recipient of the 2020 ASA Excellence in Research Award. He is Distinguished Professor of Anesthesiology, Professor of Neurobiology and of Cell Biology, and Co-Director of the Center for Translational Pain Medicine at Duke University. Dr. Ji's entire research career has focused on the molecular basis of pain, with more than 200 peer-reviewed publications to date. His work has been published in every major neuroscience journal, including *Nature*, *Science*, *Proceedings of the National Academy of Sciences*, the *Journal of Neuroscience*, the *British Journal of Anesthesia*, *Anesthesiology*, and others, and while also serving as an associate editor for six journals, including ANESTHESIOLOGY. He has served on numerous NIH Review Panels and has also received the prestigious NIH Transformative Award.

I hope you will look forward to and can attend the Annual Meeting, and will find these articles and others in this month's ANESTHESIOLOGY.