SCIENCE, MEDICINE, AND THE ANESTHESIOLOGIST
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Key Papers from the Most Recent Literature Relevant to Anesthesiologists

Association of a liberal fasting policy of clear fluids before surgery with fasting duration and patient well-being and safety. JAMA Surg 2023 Jan 4 [Epub ahead of print]. PMID: 36598762

The impact of guidelines liberalizing fluid intake in adults prior to surgery has not been well studied. This single-center, prospective, quality-improvement study (tertiary center, The Netherlands, January 2016 to July 2021) studied effects of implementation of a liberal clear fluid policy on fasting duration, well-being, and safety for elective adult surgeries. The primary outcome was change in fasting duration. Secondary outcomes included patient well-being (preoperative thirst), postoperative nausea and vomiting, and administration of antiemetics. The safety outcome was the incidence of regurgitation and aspiration pneumonia. Of 76,451 patients analyzed (mean ± SD age, 56 ± 17 yr; 48% female), 78% followed the older standard policy *versus* 22% using the newer liberal policy. Time series analysis demonstrated an estimated fasting duration difference of 3:07 h (interquartile range, 1:36 to 7:22; $P < 0.001$) after implementation to a median fasting duration of 1:20 h (0:48 to 2:24 h). Thirst feelings were less (37% *vs.* 46%; $P < 0.001$). Incidence of postoperative nausea and vomiting was less (9.4 *vs.* 10.6%, $P < 0.001$), as was antiemetic administration (9.5 *vs.* 11.0%, $P < 0.001$). The incidence of regurgitation (18 of 10,000 patients [95% CI, 14 to 21] *vs.* 24 [95% CI, 17 to 32]) and of aspiration (1.7 [95% CI, 0.6 to 2.7] *vs.* 2.4 [95% CI, 0.5 to 4.7]), respectively, was not different. *(Article Selection: Martin J. London, M.D. Image: Adobe Stock.)*

Take home message: In this single-center quality-improvement project, a liberal preoperative fasting policy was associated with clinically relevant differences in fasting duration and patient well-being. There was no difference in aspiration and pneumonia.

Racial and ethnic disparities in access to minimally invasive mitral valve surgery. JAMA Netw Open 2022; 5:e2247968. PMID: 36542380.

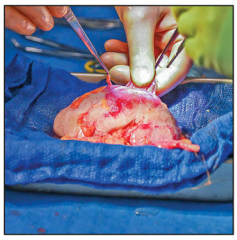
Minimally invasive mitral valve surgery is more complex than the standard open chest approach. Prior studies document racial and ethnic disparities in access to invasive cardiovascular interventions and minimally invasive surgical approaches in noncardiac surgery. This cross-sectional study using data from the Society of Thoracic Surgeons Database evaluated such disparities between 103,753 patients undergoing mitral valve surgery. Of the total sample (mean ± SD age, 62 ± 13 yr; female, 46.2%), 85.5% were non-Hispanic White, 10.0% non-Hispanic Black, and 4.2% Hispanic individuals; the minimally invasive approach was used in 29.3%, 21.2%, and 31.0% of patients, respectively. Non-Hispanic Blacks were less likely to receive minimally invasive surgery (odds ratio, 0.65; 95% CI, 0.58 to 0.73; $P < 0.001$) in contrast to Hispanics (odds ratio, 1.08; 95% CI, 0.67 to 1.75; $P = 0.74$) compared with non-Hispanic White patients. Non-Hispanic Black patients were more likely to be covered by Medicaid (odds ratio, 2.21; 95% CI, 1.64 to 2.98; $P < 0.001$) and have a low-volume surgeon (odds ratio, 4.45; 95% CI, 4.01 to 4.93; $P < 0.001$) than non-Hispanic White patients. After risk adjustment, non-Hispanic Black individuals remained less likely to undergo minimally invasive surgery (adjusted odds ratio, 0.88; 95% CI, 0.78 to 0.99; $P = 0.04$) and had greater risk for major complications or death (adjusted odds ratio, 1.25; 95% CI, 1.16 to 1.35; $P < 0.001$) compared with non-Hispanic White individuals. *(Article Selection: Martin J. London, M.D. Image: Adobe Stock.)*

Take home message: This large cross-sectional cohort study found that non-Hispanic Black patients were less likely to receive a minimally invasive approach for mitral surgery and were at higher risk for complications and death compared with Hispanic and non-Hispanic White patients.

Comparison of postoperative outcomes of laparoscopic vs open inguinal hernia repair. JAMA Surg 2023; 158:172–80. PMID: 36542394.

Laparoscopic repair of inguinal hernias requires general anesthesia. Prior studies suggest that outcomes of open inguinal hernia repairs are improved with local rather than general anesthesia, but none have compared laparoscopic repair with open repair using local anesthesia. This retrospective cohort study using the Veterans Affairs Surgical Quality Improvement Program (VASQIP) database evaluated unilateral first-time inguinal hernia repairs between three groups: (1) open repair with local anesthesia (n = 22,333), (2) open repair with general anesthesia (n = 75,104), and (3) laparoscopic repair with general anesthesia (n = 9,636). The primary outcome was postoperative morbidity using predefined VASQIP outcomes; duration of surgery was a secondary outcome. Laparoscopic repair was associated with a nonsignificant 0.15% (95% CI, −0.39 to 0.09; $P = 0.22$) difference in postoperative complications compared with open repair with general anesthesia. There were no significant differences in complications between laparoscopic and open repair with local anesthesia (−0.05%; 95% CI, −0.34 to 0.28; $P = 0.70$). Duration of surgery was similar for the laparoscopic and open general anesthesia groups (4.3 min longer; 95% CI, 0.45 to 8.57; $P = 0.048$), but operative times were significantly longer for laparoscopic compared with open repair with local anesthesia (10.4 min longer; 95% CI, 5.80 to 15.05; $P < 0.001$). *(Article Selection: BobbieJean Sweitzer, M.D. Image: Adobe Stock.)*

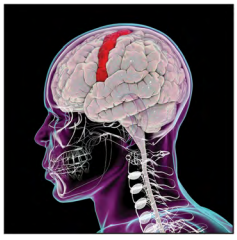
Take home message: This retrospective analysis of the Veterans Affairs Surgical Quality Improvement Program database demonstrated no differences in the incidence of postoperative complications between open *versus* laparoscopic inguinal hernia repairs or those done with general *versus* local anesthesia, although surgical duration was longer with the laparoscopic approach.



Association of pretransplant coronary heart disease testing with early kidney transplant outcomes. JAMA Intern Med 2023; 183:134–41. PMID: 36595271.

The use of routine testing for coronary heart disease is common prior to first-time kidney transplantation even in low-risk adults (age younger than 60 yr, absence of diabetes or known coronary heart disease) despite a lack of evidence supporting it. This retrospective cohort study (January 2000 to December 2014) in the U.S. Renal Data System evaluated the association of pretransplant testing (stress testing, nuclear imaging, computed tomography, or coronary angiography) in these low-risk patients with rates of death and myocardial infarction (composite outcome) within 30 days after transplantation. An instrumental variable analysis, (*e.g.*, program-level coronary heart disease testing rate in the year of the transplant), was used, stratified by four temporal epochs. The instrumental variable ranged from 0 (no low-risk patients tested) to 1 (all such patients tested). A total of 79,334 adults (female 38%; 21% Black, mean ± SD age 56 ± 14 yr) were analyzed. The primary outcome occurred in 5.3% of patients (2.6% death, 2.9% myocardial infarction). The testing rate was 56% in patients in the most test-intensive transplant programs and 24% in patients at the least test-intensive transplant program. Testing was not associated with a change in the rate of primary outcome (rate difference, 1.9%; 95% CI, 0 to 3.5%). Results were similar across epochs, except for 2000 to 2003, when testing was associated with a higher event rate (rate difference, 6.8%; 95% CI, 1.8 to 12.0%). *(Article Selection: Martin J. London, M.D. Image: J. P. Rathmell.)*

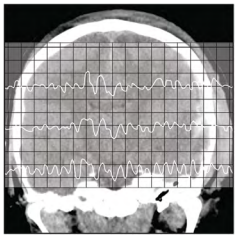
Take home message: In this large, retrospective, observational analysis of U.S centers, pretransplant testing for coronary heart disease in low-risk patients undergoing first-time kidney transplantation was not associated with a difference in early mortality or myocardial infarction, calling into question this practice.



Layer-specific pain relief pathways originating from primary motor cortex. Science 2022; 378:1336–43. PMID: 36548429.

Therapies based on the stimulation of the primary motor cortex M1, an area known to modulate pain, present alternatives to drug treatments for chronic pain. However, the circuits linking M1 and the pain matrix are unknown. This study used behavioral and molecular approaches to modulate M1 microcircuitry in a preclinical model of neuropathic nociception in mice, demonstrating that M1 stimulation alleviated mechanical and cold nociception hypersensitivity in this model and reduced the negative emotional component evaluated with the conditioned place preference paradigm. No effect was observed on the nociceptive threshold in uninjured animals nor on motor behaviors. Specific M1 subpopulations of neurons controlling the inhibitory or excitatory effects of M1 were isolated. To evaluate mechanisms, circuits modulating the different dimensions of pain after M1 activation were identified. Thus, *via* synaptic tracing, M1 layer 5 was directly connected to the zona incerta and to the periaqueductal gray. These pathways were involved in nerve injury–induced mechanical and cold allodynia. A second pathway connecting M1 layer 6 and the nucleus accumbens reward circuit *via* the mediodorsal thalamus was shown to be specifically involved in emotional pain. *(Article Selection: Cyril Rivat, Ph.D. Image: Adobe Stock.)*

Take home message: The M1 cortex controls sensorial and emotional dimensions of chronic pain *via* the engagement of distinct microcircuitries with no impact on normal nociception in the absence of injury findings with potential to eventually improve neurostimulation therapies of chronic pain.



Selective and replicable neuroimaging-based indicators of pain discriminability. Cell Rep Med 2022; 3:100846. PMID: 36473465.

The mechanisms by which the brain encodes the ability to discriminate between different intensities of painful stimuli are unexplored. Understanding these processes might enable the development of an objective measure of pain intensity. This would be useful to assess nonverbal individuals, and guide diagnostic screening and treatment for chronic pain patients who typically exhibit impaired pain discriminability. Reanalysis of two neuroimaging (functional magnetic resonance imaging, n = 399) and three electroencephalography (EEG) (n = 366) datasets was done. Participants received repeated pain (laser), touch, auditory, and visual stimuli, at high and low intensities, and the resultant perceptual pain ratings and evoked neural responses were collected. For the EEG, the difference in amplitude of laser-evoked potentials (N1, N2, P2 amplitudes) could distinguish between low- and high-intensity pain ($r = 0.446$, $P < 0.0001$); but this was not true for other sensory modalities and absolute pain sensitivity. For the functional magnetic resonance imaging group, there were within-subject increased brain activations in the thalamus, primary and secondary sensory cortices, insula, and anterior cingulate cortex (corrected $P < 0.05$) between low- and high-intensity stimulations. *(Article Selection: Jamie Sleigh, M.D. Image: J. P. Rathmell.)*

Take home message: EEG responses and functional magnetic resonance imaging regions associated with pain processing also encode different intensities of pain, a finding that could provide a foundation for more objective pain assessment.

 DOI: 10.1097/ALN.0000000000004532

Protective down-regulated states in the human brain: A possible lesson from COVID-19. Proc Natl Acad Sci U S A 2022; 119:e2120221119. PMID: 36343241.

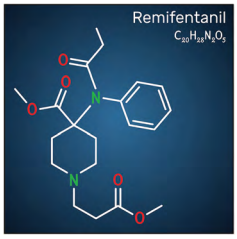
Some COVID-19 patients requiring prolonged mechanical ventilation require extended periods to recover from unconsciousness, despite a lack of structural brain injury. A common electroencephalogram (EEG) signature in these patients is burst suppression, which is also seen after cardiac arrest coma with target hypothermia. This study presents a conceptual framework of the brain state of slowly recovering COVID-19 patients building on the Ching model of burst suppression, a biophysical model suggesting that burst suppression reflects a cellular strategy of neuroprotection when metabolic substrates are limited. It further proposes that the trace alternant EEG pattern seen in sleeping term neonates has similarities to burst suppression and of note, in the painted turtle, the most anoxia-resistant organism known, tolerating months of hypoxia at low temperatures with neuronal recovery. This anoxia is accompanied by an 80-fold increase in endogenous γ-aminobutyric acid (GABA) levels and a 20-fold increase in GABA sensitivity. It is proposed in humans that a protective down-regulated state of neuronal activity is induced by hypoxia, augmented by GABAergic sedatives, further augmented by hypothermia. GABAergic hypnotics likely play a crucial role in unmasking this evolutionarily conserved neuronal state by suppressing excitatory neural activity. *(Article Selection: Charles Emala, M.D. Image: Adobe Stock.)*

Take home message: Hypoxia, combined with GABA-mediated sedation, may initiate a previously uncharacterized protective down-regulated state in the human brain in sedated COVID-19 patients and post–cardiac arrest patients treated with hypothermia. A better mechanistic understanding of this effect might identify pharmacologic targets to enhance recovery of consciousness in prolonged anoxic states in the absence of structural brain injury.

Effects of race and ethnicity on perinatal outcomes in high-income and upper-middle-income countries: An individual participant data meta-analysis of 2,198,655 pregnancies. Lancet 2022; 400:2049–62. PMID: 36502843.

Studies of disparities in pregnancy outcomes related to race and ethnicity are restricted to studies conducted within specific countries and health systems. This meta-analysis used data from the International Prediction of Pregnancy Complications Network of studies (94 studies, 53 countries, 4,539,640 pregnancies) to evaluate differences between high-income and upper-middle-income countries and geographic regions. Studies reporting perinatal outcomes (neonatal death, stillbirth, preterm birth, and small-for-gestational-age babies) in at least two racial or ethnic groups (White, Black, south Asian, Hispanic, or other) were considered. The primary outcomes were neonatal mortality and stillbirth. Secondary outcomes were preterm birth and a small-for-gestational-age baby. A total of 51 studies (20 high-income and upper-middle-income countries, 2,198,655 pregnancies) were analyzed. The primary outcomes were twice as common in Black women (mortality odds ratio, 2.0 [95% CI, 1.44 to 2.78]; stillbirth, 2.16 [1.46 to 3.19]); mortality was three times more common in Hispanic women (odds ratio, 3.34 [95% CI, 2.77 to 4.02]) relative to White women. Of the secondary outcomes, Black women were at increased risk of preterm birth (1.65, 1.46 to 1.88) and being small for gestational age (1.39, 1.13 to 1.72) and south Asian women were at increased risk of preterm birth (odds ratio, 1.26 [95% CI, 1.07 to 1.48]) and being small for gestational age (1.61 [1.32 to 1.95]). There was no effect on outcomes by geographic region. *(Article Selection: Martin J. London, M.D. Image: Adobe Stock.)*

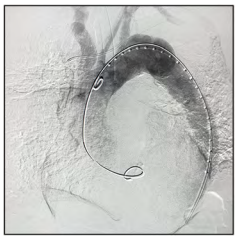
Take home message: Meta-analysis of 51 studies of more than 2 million pregnancies demonstrates that Black, Hispanic, and south Asian women have significantly higher risk of adverse neonatal outcomes relative to White women.



Effect of remifentanil vs neuromuscular blockers during rapid sequence intubation on successful intubation without major complications among patients at risk of aspiration: A randomized clinical trial. JAMA 2023; 329:28–38. PMID: 36594947.

Rapid-sequence intubation is commonly used in patients at elevated risk for gastric aspiration. Although rapid-onset neuromuscular blockade is usually used along with hypnotic agents, recent survey studies have reported their avoidance in a substantial percent of patients, given concerns over their potential adverse effects. This multicenter (15 French hospitals), open-label noninferiority trial of 1,150 such patients randomized the use of a hypnotic agent accompanied by neuromuscular blockade (1 mg/kg of succinylcholine or rocuronium; n = 575) *versus* a hypnotic accompanied by remifentanil (3 to 4 μg/kg; n = 575). The primary outcome was successful tracheal intubation on the first attempt without major complications (pulmonary aspiration, desaturation, hemodynamic instability, sustained arrhythmia, cardiac arrest, or anaphylaxis). A noninferiority margin of 7.0% was used. Of the randomized patients (mean age, 51 yr; 50% female), 98% completed the trial. Of these, the difference in primary outcome (66.1% remifentanil *vs.* 71.6% neuromuscular blocker) did not meet the criteria for noninferiority (adjusted between-group difference, –6.1%; 95% CI, –11.6 to –0.5%; $P = 0.37$ for noninferiority). There were more episodes of hemodynamic instability in the remifentanil group (3.3% *vs.* 0.5%), adjusted difference, 2.8%; 95% CI (1.2% to 4.4%). *(Article Selection: Martin J. London, M.D. Image: Adobe Stock.)*

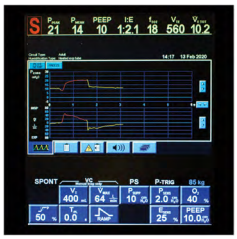
Take home message: In a large multicenter trial of two techniques for rapid-sequence intubation in patients at elevated risk of aspiration, the adjunctive use of remifentanil instead of a neuromuscular blocking agent did not meet the prespecified noninferiority margin for first-attempt tracheal intubation and was associated with more hemodynamic instability.



Zone 1 endovascular balloon occlusion of the aorta vs resuscitative thoracotomy for patient resuscitation after severe hemorrhagic shock. JAMA Surg 2023; 158:140–50. PMID: 36542395.

Aortic occlusion is performed in patients with severe traumatic hemorrhagic shock as a lifesaving treatment. However, it is unclear whether resuscitative thoracotomy or endovascular balloon occlusion of the aorta in zone 1 is the superior procedure. This multicenter observational, comparative effectiveness study was prospectively performed using the Aortic Occlusion for Resuscitation in Trauma and Acute Care Surgery (AORTA) registry of adult trauma patients (October 2013 to September 2021) comparing outcomes accomplished either by thoracotomy or *via* the endovascular route. The primary outcome was in-hospital survival; secondary outcomes were ventilation-free days, intensive care unit–free days, Glasgow Coma Scale, and Glasgow Outcome Score on discharge. Of 991 adult patients with a median age of 32 yr (interquartile range, 25 to 48 yr), the majority were male (82%). Thirty one percent of patients had endovascular aortic occlusion, 69% *via* thoracotomy. Fifty-six propensity-scored matched pairs were identified. A significant lower mortality was found for the endovascular route (79% *vs.* 93%, $P = 0.03$; Cox proportional hazards model). A multivariate analysis for the overall study sample confirmed better survival in this group (relative risk, 1.25; 95% CI, 1.15 to 1.36, $P < 0.001$). Secondary outcomes were comparable between the two propensity-scored matched groups. *(Article Selection: Beatrice Beck-Schimmer, M.D. Image: Adobe Stock.)*

Take home message: In this observational comparative effectiveness study, resuscitative endovascular balloon occlusion of the aorta in zone 1 is associated with a better survival than resuscitative thoracotomy in patients with severe traumatic hemorrhagic shock.



Spontaneous-breathing trials with pressure-support ventilation or a T-piece. N Engl J Med 2022; 387:1843–54. PMID: 36286317.

It remains unclear whether the use of either pressure-support ventilation or a T-piece is superior for spontaneous breathing trials prior to extubation, particularly in patients at high risk of extubation failure (age older than 65 yr or underlying chronic cardiac or respiratory disease). This multicenter trial (31 French intensive care units) randomly assigned such patients to either pressure-support (8 cm of water, no positive end-expiratory pressure, FIO_2 40% or lower) or a T-piece (flow rate up to 6 l/min approximating 40% FIO_2) for approximately 1 h after meeting standardized criteria for weaning. Subjects were extubated 1 h after returning to initial ventilator settings. The primary outcome was the number of ventilator-free days at day 28 after the initial spontaneous-breathing trial. Secondary outcomes included measures of time to extubation and reintubation. Of the 969 patients analyzed (49% pressure support, 51% T-piece group), there was no difference in the primary outcome between groups (pressure support median, 27 days [interquartile range, 24 to 27 days] *vs.* T-piece, 27 days (23 to 27 days; difference, 0 days; 95% CI, –0.5 to 1; $P = 0.31$). Of the secondary outcomes, higher percentages of pressure support subjects were extubated by either 24 h or 7 days, although there were no differences in the percentage of patients requiring reintubation. *(Article Selection: Martin J. London, M.D. Image: J. P. Rathmell.)*

Take home message: In a large, multicenter, randomized trial, no differences were noted in the number of ventilator-free days in high-risk patients undergoing weaning using either pressure-support ventilation or a T-piece.

Optimal timing of perioperative chemoprophylaxis in patients with high thromboembolic risk undergoing major abdominal surgery: A multicenter cohort study. Ann Surg 2022 Sep 5 [Epub ahead of print]. PMID: 36512695.

The incidence of postoperative bleeding and venous thromboembolism (VTE) is increased in patients undergoing major abdominal surgery. However, the optimal timing of perioperative antithromboembolic chemoprophylaxis is debated. It has been recently demonstrated that bleeding is more common when chemoprophylaxis is given before skin closure rather than postoperatively and that benefits are limited to patients at high risk of VTE. This retrospective analysis of five multicenter observational cohort studies powered for both VTE and bleeding outcomes investigated the effects of chemoprophylaxis administered before skin closure *versus* postoperatively in high-risk patients (Caprini score 5 or higher). Daily low-molecular-weight heparin or unfractionated heparin (twice daily) were evaluated. The primary endpoint was VTE (radiologically proven and symptomatic VTE) within 30 days after surgery. Secondary endpoints included rates of overall, major, and minor postoperative bleeding; hemostatic reintervention; and blood transfusion. Chemoprophylaxis was initiated before skin closure in 32% and postoperatively in 68% of subjects (Caprini score of 6 in both groups). Postoperative chemoprophylaxis did not increase the incidence of clinical VTE (odds ratio, 1.11; 95% CI, 0.60 to 2.15; $P = 0.73$) and lowered bleeding risk (odds ratio, 0.49; 95% CI, 0.37 to 0.66; $P < 0.001$), while early chemoprophylaxis was independently associated with postoperative bleeding (odds ratio, 1.71; 95% CI, 1.25 to 2.34; $P < 0.001$). *(Article Selection: Michael Zaugg, M.D., M.B.A. Image: J. P. Rathmell.)*

Take home message: For patients at high risk of VTE undergoing major abdominal surgery, the use of postoperative antithromboembolic chemoprophylaxis is associated with reduced bleeding without increasing the risk of VTE in contrast to administration prior to skin closure.