

Key Papers from the Most Recent Literature Relevant to Anesthesiologists



Assessment of perioperative outcomes among surgeons who operated the night before. *JAMA Intern Med* 2022; 182:720–8. PMID: 35604661.

The extent to which operating overnight is associated with worse patient outcomes when the attending surgeon continues to operate the subsequent day has not been fully assessed. This retrospective cross-sectional analysis evaluated this association using data from the Multicenter Perioperative Outcomes Group, a large multicenter registry of surgical cases. The sample consisted of 498,234 procedures performed during the day by 1,131 surgeons from 20 U.S. institutions, of which 13,098 procedures (3%) involved an attending surgeon who had operated the previous night. In addition to adjusting for observable factors such as type of surgery and patient comorbidities, the study also compared outcomes within a given surgeon's set of cases to minimize confounding. After adjusting for these factors, the incidence of major in-hospital death or major complication was 5.89% (95% CI, 5.41 to 6.43%) for procedures where the attending surgeon operated overnight compared to 5.87% (95% CI, 5.85 to 5.89%) where the same surgeon did not, a clinically and statistically insignificant difference ($P = 0.93$). (Article Selection: Eric Sun, M.D., Ph.D. Image: J. P. Rathmell.)

Take home message: In a large retrospective cross-sectional analysis, operating overnight was not associated with worse patient outcomes when the surgeon continued to operate the next day.



The effects of dexmedetomidine on perioperative neurocognitive outcomes after cardiac surgery: A systematic review and meta-analysis of randomized controlled trials. *Ann Surg* 2022; 275:864–71. PMID: 35543164.

Neurocognitive disorders such as delirium and dementia affect approximately 25% of cardiac surgery patients up to three years after surgery. Dexmedetomidine is a common sedative which appears to reduce intensive care unit delirium after noncardiac surgery, but its effect in cardiac surgery patients is unclear. This study systematically analyzed clinical trials of adult cardiac surgery patients randomized to dexmedetomidine versus placebo. Included trials reported a primary outcome of postoperative cognitive function at least one week and up to three months after surgery. The primary outcome was delayed neurocognitive recovery ascertained at ≥ 1 week after surgery, defined as new cognitive decline of at least one standard deviation compared to a normative sample, a decline by at least the minimal clinically important difference of the assessment utilized, or transition from normal to impaired function as defined by the cognitive test per the Nomenclature Consensus Working Group guidelines. Nine trials were qualitatively reviewed and seven ($n = 807$; 402 received dexmedetomidine and 405 placebo) were included. Patients who received dexmedetomidine had less delayed neurocognitive recovery compared to placebo (odds ratio, 0.39; 95% CI, 0.25 to 0.61; $P < 0.0001$; $I^2 = 2\%$). However, there were no differences in the incidence of delirium or hemodynamic instability (secondary outcomes). (Article selection: Meghan Prin, M.D., M.S. Image: J. P. Rathmell.)

Take home message: This meta-analysis suggests that perioperative dexmedetomidine is associated with a lower risk of delayed neurocognitive recovery after cardiac surgery in adults without impact on the incidence of delirium or hemodynamic instability.



Accuracy difference of noninvasive blood pressure measurements by sex and height. *JAMA Netw Open* 2022; 5:e2215513. PMID: 35671057.

Female sex is generally associated with higher risk of cardiovascular events than male sex at similar blood pressures. Potential confounding effects of accuracy of brachial cuff blood pressure measurements or differences in central aortic blood pressure have not been studied. This study included 500 participants (29% female, 71% male, 94% white, mean age 66 yr) without aortic stenosis or atrial fibrillation undergoing nonurgent coronary angiography at a tertiary care hospital in whom simultaneous measurements of invasive aortic blood pressure and noninvasive brachial and central blood pressure were obtained. Despite similar brachial cuff systolic blood pressure (mean [SD], 124 [187] mm Hg in women vs. 124 [16] mm Hg in men; $P = 0.97$), invasive aortic systolic blood pressure was higher in women (131 [22] vs. 125 [20] mm Hg; $P < .001$). Noninvasive brachial measurement was relatively accurate compared with invasive aortic systolic blood pressure in men, but not in women (mean [SD] difference, -0.3 [11.7] mm Hg vs. -6.5 [12.1] mm Hg). Noninvasive central systolic blood pressure was more accurate in women than in men (0.6 [15.3] mm Hg vs. 8.3 [14.2] mm Hg). Mediation analysis suggested that the association of sex with accuracy was predominantly related to height (55% mediation). (Article Selection: Martin J. London, M.D. Image: J. P. Rathmell.)

Take home message: In a cross-sectional invasive study, women had higher aortic systolic blood pressure than men with similar brachial cuff measurement. This association is primarily mediated by a shorter stature potentially leading to unrecognized undertreatment of hypertension in women.

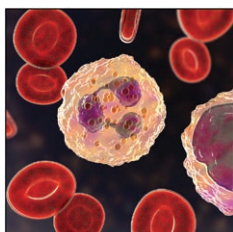


A conceptual framework for consciousness. *Proc Natl Acad Sci U S A* 2022; 119:e2116933119. PMID: 35486693.

The scientific study of consciousness seems to be intractable because it does not have a coherent framework in which to pose sensible questions. Human consciousness is often defined as being subjectively aware of oneself as an agent in the world. The unknown mechanism by which the brain produces subjective experience (the mind) has been termed the “hard problem”—because it seems to lie outside the domains of measurement and logic. From a “self-model” perspective, the brain constructs a set of information (model) that is the proximal cause of belief in a conscious experience. The resultant, scientifically approachable question becomes: How does the brain make this model? The Attention Schema Theory pro-

poses that the brain has properties of selective attention—modulated by bodily awareness, prediction, emotion, and memory. It has been correlated with cortical networks in the temporoparietal junction, precuneus, and prefrontal cortex. The evolutionary basis for different types of consciousness among a huge range of animals is that the ability to construct models of self strongly facilitates social interactions, with resultant survival benefit. (*Article Selection: Jamie Sleigh, M.D. Image: J. P. Rathmell.*)

Take home message: “Mechanisms of anesthesia” can thus specifically be restated as the mechanisms by which anesthesia prevents the brain making self-models.



Acute inflammatory response via neutrophil activation protects against the development of chronic pain. *Sci Transl Med* 2022; 14:eabj9954. PMID: 35544595.

Emerging evidence suggests that interactions between the nervous and immune systems are involved in the transition from acute to chronic pain. A genomewide transcriptomics analysis was obtained from blood cells collected from 98 patients with lower back pain, at the time of acute pain and 3 months later. Participants were divided into a group with resolved pain and a group with persistent pain according to their pain scores. Patients with resolved pain showed at the time of acute pain upregulation of genes related to cell activation and neutrophil leukocyte-induced inflammatory response and degranulation, such as S100A8, S100A9, the calcium-binding “alarmins,” which subsequently resolved 3 months later. This finding could be replicated in another musculoskeletal pain condition (temporomandibular disorder), emphasizing the importance of acute upregulation of the inflammatory response as a protective measure against the development of chronic pain. In a mouse model of inflammatory paw injury, early administration of diclofenac or dexamethasone reduced nociception but prolonged its recovery as did leukocyte depletion. Injection of neutrophils or S100A8/S100A9 directly into the paw prevented the development of chronic nociception in dexamethasone-treated mice. Using the UK Biobank project database on back pain, NSAID use was associated with greater risk of developing chronic back pain by 1.76-fold. (*Article Selection: Michael Zaugg, M.D., M.B.A. Image: Adobe Stock.*)

Take home message: Treatment of inflammation at the onset of acute lower back pain may be detrimental because it fosters transitioning to chronic back pain.



Management of hypertension in patients with ventricular assist devices: A scientific statement from the American Heart Association. *Circ Heart Fail* 2022; 15:e000074. PMID: 35430896.

Effective blood pressure control is imperative in patients supported with continuous-flow left ventricular assist devices. High systemic vascular resistance can lead to decreased left ventricular assist device flow, increased stasis, and thromboembolic complications. Hypertension can also worsen symptoms of heart failure by decreasing unloading of the left ventricle. Due to the diminished to absent pulsatile pressure, reliable measurement of blood pressure is challenging during continuous-flow left ventricular assist device support. While routine automated devices can be used, it is recommended to measure

the blood pressure at least twice and to average the blood pressure values obtained. Doppler ultrasound with sphygmomanometer is recommended in patients with no palpable pulse. International societies have recommended to target a mean arterial blood pressure < 80 mm Hg in the absence of pulsatility and blood pressure < 130/85 mm Hg with pulsatility. The guidelines recommend using heart failure medications to treat hypertension as patients were likely receiving most of these medications before implantation. In the acute phase post-implant, parenteral vasodilators such as sodium nitroprusside or nitroglycerin or alternatively hydralazine or nicardipine are recommended. (*Article Selection: David Faraoni, M.D., Ph.D. Image: Adobe Stock.*)

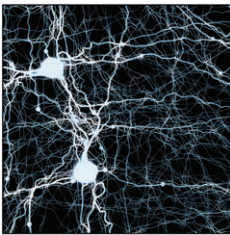
Take home message: Accurate blood pressure measurement and treatment of hypertension are key elements to improve outcome in patients treated with continuous-flow left ventricular assist devices.



Sex differences in treatment of adult intensive care patients: A systematic review and meta-analysis. *Crit Care Med* 2022; 50:913–23. PMID: 35148525.

Previous studies suggest that women have higher adjusted intensive care unit (ICU) mortality than men, but how or whether sex affects ICU treatment choices is unclear. This study systematically extracted and meta-analyzed observational studies of adult ICU patients from MEDLINE and EMBASE that focused on how ICU treatments (mechanical ventilation, renal replacement therapy, and length of ICU stay) are associated with sex. Data were pooled using random-effects models. Among 545,538 patients in 21 studies, the overall proportion of women was 43%. Although the duration of mechanical ventilation was not associated with sex, females were less likely than men to receive mechanical ventilation (six studies, $n = 100,700$; pooled adjusted odds ratio, 0.89; 95% CI, 0.84 to 0.94; $P = 70\%$). Women were also less likely to receive renal replacement therapy (five studies, $n = 94,818$; pooled adjusted odds ratio, 0.81; 95% CI, 0.73 to 0.89; $P = 57\%$). These disparities persisted after excluding studies with high risk of bias. Women spent less time in the ICU in both unadjusted and adjusted analyses (three studies, $n = 40,494$; pooled mean difference, -0.50 days; 95% CI, -0.86 to -0.14 ; $P = 94\%$), but there was no difference in the overall length of hospitalization. (Article Selection: Meghan Prin, M.D., M.S. Image: Adobe Stock.)

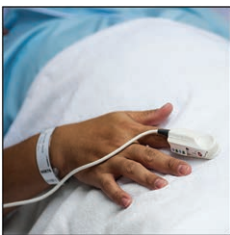
Take home message: This meta-analysis suggests that women spend less time in the ICU and are less likely to receive mechanical ventilation or renal replacement therapy compared with men, even when adjusting for illness severity.



Neuropathic pain caused by miswiring and abnormal end organ targeting. *Nature* 2022; 606:137–45. PMID: 35614217.

It is well known that nerve injury may lead to neuropathic pain, but not whether nerve injury directly causes neuropathic pain or indirectly serves as a trigger for central neuroplasticity. If nerve regeneration is blocked and neighboring undamaged nerve fibers invade denervated territory, it is unknown whether normal, pain-free sensation will be preserved, or neuropathic pain will develop. Using multiphoton excitation fluorescence imaging, the study visualized degeneration, regeneration, collateral sprouting, and end-organ connectivity of tactile fibers and nociceptors in skin before and for 10 to 12 months after spared nerve injury (ligation and transection of the tibial and common peroneal nerve leaving the sural branch intact) in mice, along with behavioral assessments. Three to seven days later, the denervated tibial nerve territory was insensate to noxious and non-noxious stimuli. Around 8 weeks, responsiveness to noxious stimuli occurred, followed by responsiveness to non-noxious stimuli at 16 weeks. Histologically, this was accompanied by reinnervation in the same preinjury pattern by sural nociceptors, but not $A\beta$ tactile fibers, which was attributed to scaffolding guidance by small blood vessels. Lowered nociceptive thresholds were attributed to aberrant terminal connectivity, *e.g.*, nociceptors terminating in the dermis rather than epidermis, and remodeling of Meissner corpuscles that link light touch to nociceptor activation (allodynia). Genetic ablation of nociceptors eradicated signs of neuropathic nociception. (Article Selection: Steven Cohen, M.D. Image: Adobe Stock.)

Take home message: These findings suggest a novel mechanism for neuropathic nociception driven by structural plasticity, abnormal terminal connectivity, and malfunction of nociceptors during reinnervation.



Racial and ethnic discrepancy in pulse oximetry and delayed identification of treatment eligibility among patients with COVID-19. *JAMA Intern Med* 2022; 182:730–8. PMID: 35639368.

Pulse oximetry (SpO_2) is expected to be an accurate reflection of arterial blood oxygen saturation (SaO_2) and plays a critical role in clinical decisions regarding recognition and treatment of COVID-19. This study evaluated whether race and ethnicity affected the frequency and magnitude of inaccurate reflection of SaO_2 by SpO_2 . A total of 7,126 patients at five sites in an integrated U.S. hospital system were characterized by race and were analyzed for occult hypoxemia (SaO_2 of $<88\%$ with an SpO_2 reading of 92 to 96% within 10 min of each other). Occult hypoxemia occurred in 30% of Asians, 29% of Blacks, and 30% of non-Black Hispanics compared to 17% of non-Hispanic Whites; SpO_2 overestimated SaO_2 by approximately 2%, 1%, and 1%, respectively. In a subset of patients, an estimate was made of the proportion of patients who may have a delay in the initiation of therapy due to occult hypoxemia or fail to have their occult hypoxemia ever detected. Black and non-Black Hispanic patients had a higher risk of having a delay in the detection of eligibility for treatment (hazard ratio, 0.71; 95% CI, 0.63 to 0.80 and 0.77; 95% CI, 0.66 to 0.89 respectively), although Black patients were the only group where a documented delay in treatment recognition occurred (median delay 1 h). (Article Selection: Charles Emala, M.D., M.S. Image: Adobe Stock.)

Take home message: In patients presenting with COVID-19, the accuracy of SpO_2 as a reflection of SaO_2 is differentially affected by race and ethnicity with occult hypoxemia occurring with greater frequencies in Asian, Black, and non-Black Hispanic compared to White patients, potentially leading to delay in the initiation of appropriate therapies.



Educational strategies to promote clinical diagnostic reasoning. *N Engl J Med* 2006; 355:2217–25; republished at: https://cloud.info-nejm.org/healer/bowen?cid=DM1062817_JW_SOI&bid=988035334 (accessed June 5, 2022). PMID: 17124019.

Teaching methods evolve. This seminal educational publication focused on teaching clinical diagnostic reasoning. Development of learners' reasoning and diagnostic acumen is a fundamental goal of clinical teaching. The ability to blend existing knowledge, prior experience, and acquired data is an essential ingredient the learner must master to form a diagnostic hypothesis. "Pattern recognition," gained through experience, abets the learner's ability to grasp diagnostic gestalt. The

revised publication features educational strategies using case "clues" to reach a diagnosis. The teaching recommendations are intuitive, *i.e.*, role model diagnostic skill, employ open-ended questions to assess what the learner thinks, provide cognitive feedback, and stress the value of reading to conceptualize rather than memorize diagnoses. These recommendations require teachers to accompany learners to the patient's bedside. Key updates include the following: (1) promote awareness of interdependence of patients, families, and healthcare practitioners; (2) caution regarding unconscious bias; (3) directly observe learner's patient care and offer formative feedback; (4) employ simulation and problem-based learning scenarios; (5) formulate illness scripts (risk factors, pathophysiology, clinical findings) based on Bayesian principles; (6) add management scripts based on conceptual knowledge to extend illness scripts; and (7) appreciate problems related to transitions in healthcare that interrupt the ability to learn. (Article Selection: Alan Jay Schwartz, M.D., M.S.Ed. Image: Adobe Stock.)

Take home message: In a seminal updated educational strategy review for medical education, the emphasis is on the importance of observation of learners with patients, provision of formative feedback, and application of Bayesian probability to facilitate correct diagnoses.



Theories of consciousness. *Nat Rev Neurosci* 2022; 23:439–52. PMID: 35505255.

Recent years have seen an explosion of new theories about consciousness. Theories are essential to properly understand and manipulate any phenomenon. Four conceptual approaches to consciousness are higher-order theories, global workspace theories, predictive processing theories, and integrated information theory. Higher-order theories suggest that the contents of consciousness arise because anterior cortical regions are able to redescribe the representation from lower-order networks. Global workspace theories propose that conscious mental states arise from widespread ignition of functional connectivity across fronto-parietal association areas. Integrated information theory proposes that consciousness

arises from how much extra information is generated from the whole system, as compared with that obtained from the sum of its parts. It implies some form of pan-psychism and predicts that consciousness depends mainly on posterior cortical regions. Predictive processing theories suggest that the primary function of the brain is to compare the errors between internally generated models and sensory data. To evaluate these theories, one needs to have more precise testable predictions, to be more comprehensive and include other conscious creatures, and to have trustworthy measures of consciousness. (Article Selection: Jamie Sleight, M.D. Image: Adobe Stock.)

Take home message: The specificity of anesthetic manipulation of consciousness will play an important role in testing which of these theories of consciousness is best.



Effect of intraoperative urinary catheter use on postoperative urinary retention after laparoscopic inguinal hernia repair: A randomized clinical trial. *JAMA Surg* 2022; e222205. PMID: 35704302.

Urinary retention is a common complication after elective laparoscopic inguinal hernia repair. Whether prophylactic intraoperative catheter placement is superior to a routine postoperative observation is unknown. This is a two-arm, single-blinded, randomized clinical trial (six U.S. hospitals) of 491 patients (median age 61 yr, 95% male) comparing placement of a urinary catheter after induction of general anesthesia (with removal at the end of procedure) ($n = 241$) *versus* no intraoperative urinary catheter placement ($n = 250$). The primary outcome was postoperative urinary retention (failure to void requiring straight cath-

eterization, placement of an indwelling catheter, or return to emergency room within 30 days for retention). A total of 44 patients (9%) developed postoperative urinary retention. There was no difference in primary outcome between groups (10% vs. 9%, $P = 0.79$). Retention was most common on the day of surgery (61%) and treated with an indwelling catheter with discharge on the same day (68%). No intraoperative bladder injuries were detected. One patient in the catheter group had postoperative urethral trauma leading to a suprapubic catheter placement. (Article Selection: Martin J. London, M.D. Image: J. P. Rathmell.)

Take home message: Placement of an intraoperative urinary catheter with removal at the end of surgery did not lessen the risk of postoperative urinary retention after laparoscopic inguinal hernia repair.