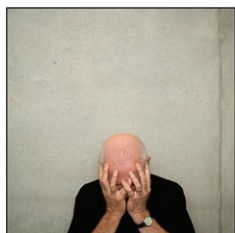


ANESTHESIOLOGY



Deborah J. Culley, M.D., Editor



Pre-existing psychological depression confers increased risk of adverse cardiovascular outcomes following cardiac surgery: A systematic review and meta-analysis. J Thorac Cardiovasc Surg 2017; 154: 1578–86.

Observational studies and meta-analyses have suggested an increased mortality in depressed patients with stable coronary artery disease and after myocardial infarction, but the impact of depression on perioperative and long-term outcomes after coronary artery bypass grafting is unclear. This manuscript describes a meta-analysis of 10 selected observational studies with good methodologic quality from 1,388 publications on the topic and reports the results from 152,491 patients from the United States, Australia, and Sweden. The authors identified a prevalence of depression of 13.6% before coronary artery bypass surgery. Nine studies reported on outcomes greater than 6 months after surgery. Among these studies, the hazard ratio for long-term mortality was 1.42 (95% CI, 1.26 to 1.60; $P < 0.001$) in depressed patients. Six studies reported on composite endpoints of cardiac mortality, morbidity, and hospital readmission with a hazard ratio of 1.57 (95% CI, 1.39 to 1.77; $P < 0.001$). Although different questionnaires were used to assess depression and several studies used administrative database coding (International Classification of Diseases, ninth or tenth revision) for most outcomes, sensitivity analyses revealed similar findings. (Summary: Martin J. London. Image: ©ThinkStock.)

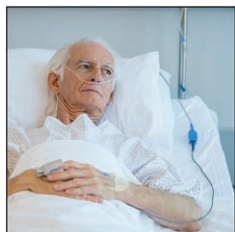
Take home message: Preoperative depression is associated with adverse long-term mortality and cardiac morbidity after cardiopulmonary bypass surgery. Greater efforts at preoperative screening and potential interventions may be indicated.



Results of a flipped classroom teaching approach in anesthesiology residents. J Grad Med Educ 2017; 9:485–90.

Identification of “best” teaching technique continues to elude educators. The flipped classroom is a technique that is proposed to eclipse traditional lectures. The suggested benefit of the flipped classroom is that it actively engages the learner through preclassroom homework coupled with didactic sessions involving interactive discussion and problem solving. This manuscript studied the flipped classroom approach in anesthesiology resident education. A total of 155 anesthesiology residents learned anesthetic pharmacology in either a lecture or flipped classroom setting. Educational outcome was assessed using a benchmark pretest, a knowledge acquisition posttest, and a 4-month knowledge retention test. While initial knowledge acquisition was not augmented by the flipped classroom approach, the 4-month posteducation test demonstrated enhanced retention. The authors speculate that the engaged flipped classroom learners may have had more “...triggers during clinical learning...over the ensuing 4 months...” that explained the improved knowledge retention. A secondary outcome assessment revealed a strong preference for the flipped classroom active learning style compared to more traditional lectures. (Summary: Alan J. Schwartz. Image: ©ThinkStock.)

Take home message: Learning in a flipped classroom setting augments knowledge retention and is preferred by anesthesiology residents when compared to traditional lectures.



Cognitive impairment and overall survival in frail surgical patients. J Am Coll Surg 2017; 225:590–600.e1.

Frailty and cognitive impairment have been independently associated with adverse surgical outcomes. This study investigated whether the addition of a clock-drawing task to a 4-point frail scale added predictive value for long-term postoperative outcomes. This study evaluated 330 surgical patients 18 yr of age and older scheduled for a major surgical procedure for up to 4 yr. Overall mortality was 12% for robust patients with no cognitive impairment or frailty, 13% for those with only cognitive impairment, 25% in those with physical frailty, and 42% in those with physical frailty and cognitive impairment ($P < 0.001$). On multivariate analysis, those patients with physical frailty and cognitive impairment had a 3.92 higher risk of death (95% CI, 1.66 to 9.26) compared with the robust patients ($P = 0.002$). This study suggests that the combination of frailty and cognitive impairment is a strong predictor of 1-, 2-, and 3-yr mortality. (Summary: Deborah J. Culley. Image: ©ThinkStock.)

Take home message: Physical frailty and cognitive impairment are predictors of postoperative mortality.



Hats off: A study of different operating room headgear assessed by environmental quality indicators. *J Am Coll Surg* 2017; 225:573–81.

Regulatory agencies often insist that disposable bouffant head coverings be used in the operating room to decrease the risk of airborne contamination. Few studies have been designed to identify the most efficacious type of head coverings for this purpose. This study compared disposable bouffant covers, disposable skull caps, and newly laundered cloth skull caps in a 1-h mock surgical procedure where each hat was utilized by each member of the seven-member team at least four times. Disposable bouffant caps were noted to have greater penetration of particulate matter ($101.9 \pm 1.1\%$) compared with disposable skull cap crowns ($94.6 \pm 1.8\%$, $P < 0.05$) and disposable skull cap sides ($92.0 \pm 0.6\%$, $P < 0.05$), and microbial shed was greater with bouffant hats when compared to disposable skull caps or newly laundered cloth skull caps ($P < 0.05$). The authors note multiple limitations to their study including a lack of randomization and the use of a mock surgical procedure; they also suggest that disposable bouffant head coverings are not superior to disposable skull caps or newly laundered cloth skull caps in preventing airborne contamination. (Summary: Deborah J. Culley. Image: Brigham and Women's Hospital.)

Take home message: The use of a disposable bouffant head covering may not decrease particulate matter penetration or microbial shed when compared to disposable or newly laundered skull caps.



Association of prehospital blood product transfusion during medical evacuation of combat casualties in Afghanistan with acute and 30-day survival. *JAMA* 2017; 318:1581–91.

Massive hemorrhage is the leading cause of death in trauma. Historically, trauma patients in shock received either fluid resuscitation with crystalloid or colloid solutions in the field or during transport, but recent data suggest that prehospital blood transfusion may positively influence survival. From 2012 on, U.S. military medical evacuation units in Afghanistan had the ability to transfuse blood during transport for combat casualties. In this retrospective cohort study, investigators from the U.S. Joint Trauma System found that combat casualties who received blood transfusions had a markedly lower risk of early (within 24h) or delayed (within 30 days) death compared to patients who did not receive blood.

Patients were matched by several relevant variables, including mechanism of injury, prehospital shock, severity of limb amputation, head injury, and torso hemorrhage, to ensure a valid comparison between the two groups. The findings from this study suggest that early blood transfusion for combat casualties in shock will lower mortality. It will be important to determine whether the same is true for civilian trauma patients. (Summary: Peter Nagele. Image: J. P. Rathmell.)

Take home message: Prehospital blood transfusion may influence survival in the setting of trauma.



Evaluation of military use of tranexamic acid and associated thromboembolic events. *JAMA Surg* 2017 Oct 25 [Epub ahead of print].

Since the publication of the Clinical Randomization of an Antifibrinolytic in Significant Hemorrhage 2 (CRASH-2) trial, tranexamic acid has been included in clinical practice guidelines for trauma patients, both in the military and civilian setting. Tranexamic acid should only be administered to patients requiring massive transfusion within 3h of the injury, as it may increase the risk of thromboembolism. In this retrospective cohort study, the appropriate use of tranexamic acid in 455 U.S. military casualties was studied. The authors found that overuse (tranexamic acid administered in a setting without massive transfusion) occurred in 18 of 282 patients (6.4%) and underuse (massive transfusion, but no tranexamic acid administered) in 46 of 173 patients (26.6%), and delayed administration (longer than 3h) was found in 6 of 145 patients (4.3%). Patients who received tranexamic acid had an increased risk of thromboembolism compared to patients who did not receive tranexamic acid (odds ratio, 2.80; 95% CI, 1.20 to 6.49; $P = 0.02$). (Summary: Peter Nagele. Image: J. P. Rathmell.)

Take home message: Patients who receive tranexamic acid may be at increased risk of thromboembolism.



Daytime variation of perioperative myocardial injury in cardiac surgery and its prevention by Rev-Erba antagonism: A single-centre propensity-matched cohort study and a randomised study. *Lancet* 2017 Oct 26 [Epub ahead of print].

Studies in circadian gene knockout and mutant mice suggest a biorhythm in tolerance to myocardial ischemia-reperfusion, although the evidence in human ST-segment myocardial infarction is conflicting. This study evaluated the role of circadian variation in patients undergoing on-pump aortic valve replacement surgery on major adverse cardiovascular events and the potential molecular mechanisms involved in these changes. The authors report on both observational and randomized cohorts of patients with aortic stenosis and preserved ejection fraction at a single center and compared the impact of surgery in the morning or afternoon on major adverse cardiovascular events. To identify the signaling pathways involved in these changes, the authors evaluated myocardial samples using *ex vivo* hypoxia-reoxygenation models and transcriptomic analyses. In a cohort analysis of 596 patients, there was a reduced hazard ratio of 0.5 (95% CI, 0.32 to 0.77; $P = 0.002$) in the afternoon surgery group 500 days after surgery. In the randomized cohort of 88 patients, troponin T release was significantly lower in the afternoon group when compared to the morning group (odds ratio 0.79; 95% CI, 0.68 to 0.93; $P = 0.005$). Analysis of human myocardium revealed circadian variation in the expression of the nuclear receptor Rev-Erba. A murine myocardial hypoxia-reoxygenation model demonstrated that gene deletion and antagonism of this receptor might reduce myocardial injury. (Summary: Martin J. London. Image: J. P. Rathmell.)

Take home message: Cardiac surgery in the afternoon may reduce myocardial injury perhaps due to circadian changes in the expression of the nuclear receptor Rev-Erba gene.

Key Papers from the Most Recent Literature Relevant to Anesthesiologists


Percutaneous coronary intervention in stable angina (ORBITA): A double-blind, randomised controlled trial. Lancet 2017 Nov 1 [Epub ahead of print].

The efficacy of percutaneous coronary interventions in reducing angina and improving exercise tolerance and quality of life remains controversial, and the impact of the placebo effect in this setting has not been investigated. This study reports on the first multicenter, blinded, placebo-controlled trial involving 200 patients with stable angina and severe single-vessel stenosis (70% or more) receiving guideline-directed optimal medical therapy and/or percutaneous coronary intervention in an intent-to-treat manner. The primary outcome was the difference in exercise time between groups at 6 weeks postprocedure. A battery of secondary outcomes assessed other exercise parameters, angina symptoms, and quality-of-life parameters. In the intervention group, 69% of lesions treated involved the left anterior descending artery and the mean area stenosis was 84.4%. All stents were drug eluting. In the placebo group, sensory isolation with

earphones and sedation with intravenous opiates and benzodiazepines for amnesia and analgesia were used during coronary angiography. The authors found no significant difference in exercise time between the groups (percutaneous coronary intervention exercise time minus placebo exercise time = 16.6 s; 95% CI, -8.9 to 42.0; $P = 0.200$). (Summary: Martin J. London. Image: J. P. Rathmell.)

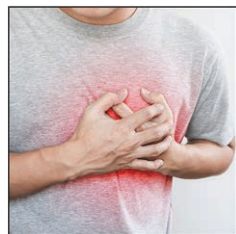
Take home message: In guideline-treated patients with single-vessel coronary artery disease, the placebo effect may play a substantial role in the clinical improvements noted after percutaneous coronary intervention.


Effectiveness of injectable extended-release naltrexone vs daily buprenorphine-naloxone for opioid dependence: A randomized clinical noninferiority trial. JAMA Psychiatry 2017; 74:1197–1205.

Medication-assisted treatment involving either an opioid agonist (methadone, buprenorphine) or antagonist (naltrexone) is the standard for the treatment of opioid use disorder. Opioid agonist therapy is common but associated with dependence and long-term side effects. Until recently, naltrexone therapy was limited by the need for daily administration and poor compliance. This study describes an open-label randomized trial involving 159 opioid users in five urban addiction clinics in Norway between November 1, 2012, and December 23, 2015. The goal of the study was to determine whether a 4-week extended-release naltrexone preparation was as effective as daily sublingual buprenorphine-naloxone in reducing the use of heroin and other illicit substances. Extended-release naltrexone was noninferior to buprenorphine-naloxone

in terms of retention in the 12-week study (69.3 ± 25.9 and 63.7 ± 29.9 days, respectively; $P = 0.33$) and was as effective as buprenorphine-naloxone in reducing heroin use (mean difference -3.6; 95% CI, -6.0 to -1.2; $P = 0.003$) when administered once every 4 weeks. These results demonstrate that opioid antagonist therapy using extended-release medications may be as effective as more traditional opioid agonists in the treatment of opioid use disorder and may help opioid users avoid long-term dependence on these drugs. (Summary: David J. Clark. Image: J. P. Rathmell.)

Take home message: Opioid antagonist therapy using extended-release naltrexone may be as effective as opioid agonists in the treatment of opioid use disorder.


Stable high-sensitivity cardiac troponin T levels and outcomes in patients with chest pain. J Am Coll Cardiol 2017; 70:2226–36.

High-sensitivity cardiac troponin assays have had a major impact on emergency department triage of patients presenting with chest pain. However, this sensitivity is associated with decreased specificity among patients presenting without classical signs of myocardial infarction. This study describes an observational cohort study involving 19,460 patients presenting to the Karolinska University emergency department 2012 and 2014 with chest pain that had at least two high-sensitivity cardiac troponin assays performed. Hospital and national databases were used to obtain risk, medication, and long-term outcome data including mortality. Patients were stratified into five groups by ascending high-sensitivity cardiac troponin T values above the 5 ng/l lower limit. Statistical models evaluated associations of these groups with all-cause, cardiovascular, and noncardiovascular mortality along with myocardial infarction and

hospitalization for heart failure. The mean overall follow-up was 3.3 yr, and 6.9% of the patients died. There were graded associations between all detectable high-sensitivity cardiac troponin T levels and mortality. Deaths from cancer (35%), cardiovascular disease (34%), and lung disease (5.8%) were most common. (Summary: Martin J. London. Image: ©ThinkStock.)

Take home message: Patients presenting to an emergency department with chest pain and any detectable level of high-sensitivity cardiac troponin may be at increased risk of mortality.



Immediate interruption of sedation compared with usual sedation care in critically ill postoperative patients (SOS-Ventilation): A randomised, parallel-group clinical trial. *Lancet Respir Med* 2017; 5:795–805.

Excessive sedation and prolonged mechanical ventilation in intensive care unit (ICU) patients have been associated with worse patient outcomes, but sparse data are available for postoperative patients admitted to an ICU. In this small randomized, controlled trial (the SOS-Ventilation study), 137 patients in three ICUs in France were randomized to either immediate interruption of sedation (intervention) or usual sedation (control). Time to successful extubation (primary outcome) was a median of 8 h in the intervention group (interquartile range, 4 to 36 h) *versus* 50 h (interquartile range, 29 to 93 h) in the control group, a nearly fivefold difference. Other clinical outcomes, including ventilator-free days and hospital length of stay, were also significantly better among patients who received immediate interruption of sedation.

Results from this small trial suggest that the immediate interruption of sedation in critically ill postoperative patients may improve outcomes. (Summary: Peter Nagele. Image: J. P. Rathmell.)

Take home message: Immediate interruption of sedation in critically ill patients admitted to an intensive care unit after surgery may improve outcomes.



Online surgeon ratings and outcomes in hernia surgery: An Americas Hernia Society Quality Collaborative analysis. *J Am Coll Surg* 2017; 225:582–9.

Some consumers view online physician ratings as a measure of physician quality. This study compared associations between online surgeon ratings and hernia-specific quality matrices. Seventy surgeons with at least ten patients entered into the Americas Hernia Society Quality Collaborative database and who had both a HealthGrades.com and Vitals.com rating were included in analysis. Surgeon ratings on HealthGrades.com correlated with physician ratings on Vitals.com ($P < 0.001$). Interestingly, these ratings did not correlate with physician risk-adjusted Americas Hernia Society Quality Collaborative database surgeon rankings for five prospectively determined outcomes ($P = 0.37$ for HealthGrades.com; $P = 0.18$ for Vitals.com). These data suggest that online surgeon ratings by patients may not correlate with the quality of surgical outcomes. (Summary: Deborah J. Culley. Image: J. P. Rathmell.)

Take home message: Online surgeon ratings may not correlate with the quality of a surgeon's procedural outcomes.