SCIENCE, MEDICINE, AND THE ANESTHESIOLOGIST

Key Papers from the Most Recent Literature Relevant to Anesthesiologists

ANESTHESIOLOGY



Deborah J. Culley, M.D., Editor



Open-label placebo treatment in chronic low back pain: A randomized controlled trial. Pain 2016; 157:2766–72.

Placebos are commonly used in clinical trials including those involving pain relief therapeutics. Recently, it has been suggested that clinical improvements can be seen even in patients that are aware they are being treated with a placebo. In this study by Carvalho *et al.*, the investigators evaluated whether administration of open-label placebo pain relief pills (two pills twice per day) added benefit to baseline treatment regimens for back pain in 97 patients randomly assigned between (1) placebo and (2) unchanged treatment regimens with a 3-month follow-up. Patients receiving open-label placebo reported approximately 30% more pain relief (primary outcome) and 30% lower disability scores when compared with patients maintaining their treatment as usual. While the mechanism and durability of these pla-

cebo responses remain unclear, the results suggest that placebo responses can occur and may be beneficial even when patients have knowledge that they are receiving a placebo. Limitations of this trial include the exclusive use of subjective outcomes and the self-selected nature of the study participants. (Summary: David Clark and Deborah J. Culley. Image: J. P. Rathmell.)

Take home message: Beneficial placebo responses can occur in patients with knowledge that they are being randomized to the administration of a placebo in the setting of pain management.



Five-year outcomes after off-pump or on-pump coronary-artery bypass grafting. N Engl J Med 2016; 375:2359–68.

The authors of this study have previously reported no differences in 30-day or 1-yr composite outcomes among 4,752 patients who underwent coronary-artery bypass grafting after randomization to bypass with or without the use of a cardiopulmonary bypass pump. In this study, the authors report the 5-yr individual (death, stroke, myocardial infarction, renal failure, and repeat coronary revascularization) and composite outcomes, hospital costs, and quality-of-life measures in the same 4,752 patients from 19 countries. The authors found no differences in death (P = 0.30), myocardial infarction (P = 0.41), stroke (P = 0.32), renal failure (P = 0.60), coronary revascularization (P = 0.29), or composite outcomes (P = 0.72) between patients randomized to coronary-artery bypass grafting with cardiopulmonary bypass and those ran-

domized to "off-pump" techniques. Similarly, there were no differences in hospital costs (mean, \$96; 95% CI, –\$607 to \$799) or quality of life (*P* = 0.57) 5 yr after the procedure. (Summary: Deborah J. Culley. Image: J. P. Rathmell.)

Take home message: In this large prospective international study involving 4,752 patients, there were no differences in outcomes at 5 yr between patients randomized to coronary-artery bypass with the use of cardiopulmonary bypass pump and those randomized to off-pump (beating heart) coronary-artery bypass.



Migraine and risk of perioperative ischemic stroke and hospital readmission: Hospital based registry study. BMJ 2017; 356:i6635.

Perioperative stroke is a cause of significant morbidity and mortality. Accordingly, it is important to identify patients at risk for the development of perioperative stroke. This study investigated whether preoperative migraine with and without aura, as detected by International Classification of Diseases, Ninth Revision codes, was associated with 30-day ischemic stroke (primary outcome measure based upon International Classification of Diseases, Ninth Revision codes) and hospital readnission within 30 days of discharge from the hospital between 2007 and 2014. Among the 124,558 patients that were included in this study, 8% had a history of migraines with the majority of them (87%) being without aura. The 30-day stroke rate among all patients was 0.7%. On multivariate analysis, the incidence of ischemic stroke within 30 days of a surgical

procedure was significantly higher in patients with history of migraine with and without aura when compared to patients without history of migraine (P < 0.001). This risk was greatest in patients with history of migraines with aura. History of migraines was also associated with hospital readmission within 30 days of discharge (P < 0.001). (Summary: Deborah J. Culley. Image: J. P. Rathmell.)

Take home message: A history of migraine headaches with and without aura has been associated with an increased risk of perioperative stroke.



Epidemiology of acute kidney injury in critically ill children and young adults. N Engl J Med 2017; 376:11–20.

Acute kidney injury is associated with significant morbidity and mortality in the perioperative and intensive case unit setting. This prospective international observational study investigated the epidemiology of acute kidney injury in critically ill patients under the age of 25 yr with an anticipated intensive case unit stay of more than 2 days. Among the 4,683 patients enrolled in the study, there was a high incidence of acute kidney injury (27%). More surprisingly, 12% of the patients enrolled in this study developed severe kidney injury identified by a twofold increase in creatinine or less than 0.5 ml • kg⁻¹ • h⁻¹ of urinary output for more than 12 h. Severe acute kidney injury was associated with a higher 28-day mortality rate (11%) when compared to patients without severe acute kidney injury (3%; P < 0.001). The most interesting finding of this study is that plasma creatinine

levels alone failed to identify acute kidney injury in 67% of the patients with low urine output. (Summary: Deborah J. Culley. Image: J. P. Rathmell.)

Take home message: Patients under the age of 25 yr in the intensive care setting have a high prevalence of severe acute kidney injury that is associated with a high 28-day mortality rate but may not be initially detected by measuring creatinine alone.

Anesthesiology, V 126 • No 4 April 2017

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Effect of delirium and other major complications on outcomes after elective surgery in older adults. JAMA Surg 2015; 150:1134–40.

Postoperative delirium is common in older surgical patients and a strong predictor for other adverse outcomes. The authors of this article hypothesized that delirium and other major complications would be associated with adverse outcomes. The authors enrolled 566 elderly surgical patients into the study and demonstrated that delirium was the most common adverse postoperative complication in this elderly patient population and occurred in 24% of the patients. All other adverse outcomes occurred cumulatively in 8% of the patients. Delirium alone (relative risk [RR], 2.8; 95% CI, 1.9–4.0), other complications alone (RR, 1.9; 95% CI, 1.4–2.7), and the combination of delirium and other complications (RR, 3.4; 95% CI, 2.3–4.8) were associated with a longer hospital length of stay. Interestingly, complications other

than delirium were not independently associated with discharge to place other than home or a higher 30-day readmission rate. Delirium alone and delirium in combination with another complication was associated with a higher discharge to place other than home and a higher 30-day readmission rate. (Summary: Deborah J. Culley. Image: J. P. Rathmell.)

Take home message: Delirium alone and in combination with other perioperative complications is associated with a longer hospital length of stay, discharge to place other than home, and a higher 30-day readmission rate.



A "resident-as-teacher" curriculum using a flipped classroom approach: Can a model designed for efficiency also be effective? Acad Med 2016 Dec 27. [Epub ahead of print].

According to the Accreditation Council for Graduate Medical Education, one of the responsibilities of resident training includes the development of residents to teach. The authors of this article report an effective and efficient train-the-teacher technique that utilizes a flipped classroom and preworkshop readings followed by four 1-h workshops on adult learning theory, orienting a learner, teaching a skill, and giving feedback. Based upon an objective structured teaching examination performed before and after the training exercise, the 29 second-year resident participants had improvements in their ability to teach a skill (P < 0.001), provide feedback (P = 0.005), and orient a learner (P < 0.001) after this intensive educational experience. In addition, they had more positive attitudes about their teaching abilities

after completing the training curriculum (P < 0.001). This report provides preliminary evidence that a novel yet practical approach on how to teach residents to teach may efficiently and effectively educate residents to become teachers even if they are not choosing an academic career. (Summary: Cathleen L. Peterson-Layne and Deborah J. Culley. Image: $@Adobe\ Stock$.)

Take home message: Formal training in teaching may increase a resident's confidence in his or her ability to teach and allow him or her to become a better teacher.



Perioperative major adverse cardiovascular and cerebrovascular events associated with noncardiac surgery. JAMA Cardiol 2016 Dec 28. [Epub ahead of print].

In the setting of noncardiac surgery, myocardial infarction and stroke are associated with significant perioperative morbidity and mortality. This study used the National Inpatient Sample database from 2004 to 2013 to evaluate trends in perioperative in-hospital death, myocardial infarction, and stroke in 10,581,621 hospitalizations for noncardiac surgery in patients of age 45 yr and older. The authors noted an overall decrease in perioperative death (P < 0.001; odds ratio [OR], 0.79; 95% CI, 0.77–0.81) and myocardial infarction (P < 0.001; OR, 0.87; 95% CI, 0.84–0.89) between 2004 and 2013 but an increase in the incidence of perioperative ischemic stroke (P < 0.001; OR, 1.79; 95% CI, 1.73–1.86). While there are a number of limitations to this study including the reporting bias intrinsic to database studies, these data sug-

gest that perioperative ischemic stroke may be becoming a more prominent cause of perioperative morbidity in patients of age 45 yr and older undergoing noncardiac surgical procedures. (Summary: Deborah J. Culley. Image: J. P. Rathmell.)

Take home message: During the past 10 yr, the incidence of perioperative death and myocardial infarction has decreased, while the incidence of perioperative ischemic stroke has increased in patients of age 45 yr and older undergoing noncardiac surgery.



Tranexamic acid in patients undergoing coronary-artery surgery. N Engl J Med 2017; 376:136–48.

In patients undergoing cardiac surgery, tranexamic acid has been shown to decrease blood loss, although there is concern that its use may increase the risk of perioperative thrombotic events. This prospective, international study was designed to determine whether the use of tranexamic acid in the setting of cardiac surgery was associated with perioperative thrombotic events (stroke, myocardial infarction, renal failure, pulmonary embolism, and bowel infarction) or death within 30 days of the surgical procedure in 2,311 patients that were randomized to receive tranexamic acid when compared to 2,320 control patients. Interestingly, the administration of tranexamic acid was not associated with an increased risk of perioperative thrombotic events or death within the first 30 days of surgery (relative risk, 0.92; 95% CI, 0.81–1.05) but was associated

with a decrease in the number of blood products used during the incident hospitalization (*P* < 0.001). This study suggests that the administration of tranexamic acid in patients undergoing cardiac surgery is not associated with an increased 30-day risk of thrombotic events or mortality. (Summary: Deborah J. Culley. Image: J. P. Rathmell.)

Take home message: Tranexamic acid administration in patients undergoing coronary-artery surgery does not increase the risk of thrombotic events or death in the first 30 days after surgery.

Anesthesiology, V 126 • No 4 April 2017