

## ANESTHESIOLOGY



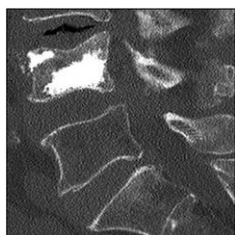
Jean Mantz, M.D., Ph.D., Editor

**Tranexamic acid in patients undergoing coronary-artery surgery. N Engl J Med 2016 Oct 23. [Epub ahead of print.]**

The risk-benefit balance of using tranexamic acid in cardiac surgical patients remains unclear. While tranexamic acid reduces the risk of bleeding among patients undergoing cardiac surgery, there are concerns that it may have prothrombotic and proconvulsant effects. In a trial with a 2-by-2 factorial design, patients scheduled to undergo coronary-artery surgery and at risk for perioperative complications were randomly allocated to receive aspirin or placebo and tranexamic acid or placebo. The results of the tranexamic acid comparison are reported here. The primary outcome was a composite of death and thrombotic complications (nonfatal myocardial infarction, stroke, pulmonary embolism, renal failure, or bowel infarction) within 30 days after surgery.

Four thousand six hundred thirty-one patients underwent surgery and had available outcome data. A primary outcome event occurred in 386 patients (16.7%) in the tranexamic acid group and in 420 patients (18.1%) in the placebo group (relative risk, 0.92; 95% CI, 0.81 to 1.05;  $P = 0.22$ ). Major intraoperative bleeding and transfusion rates during hospitalization were significantly lower in the tranexamic acid group, while the incidence of seizures was greater in the tranexamic group. (Summary: J. Mantz. Image: J. P. Rathmell.)

**Take home message:** Among patients undergoing coronary-artery surgery, tranexamic acid was associated with a lower risk of bleeding and a higher risk of seizures than placebo, without a higher risk of death or thrombotic complications within 30 days after surgery.

**Safety and efficacy of vertebroplasty for acute painful osteoporotic fractures (VAPOUR): A multicentre, randomised, double-blind, placebo-controlled trial. Lancet 2016; 388:1408–16.**

Vertebroplasty is a common, minimally invasive technique aimed at reducing pain by stabilizing acute vertebral fractures associated with osteoporosis. The effectiveness of vertebroplasty for acute osteoporotic spinal fractures was evaluated in this multicenter, randomized, double-blind, placebo-controlled trial including 120 patients in four hospitals in Australia. Vertebroplasty was done with the adequate vertebral fill technique and compared with a sham, simulated vertebroplasty. The primary outcome was the proportion of patients with Numeric Rating Scale (NRS) pain below 4/10 at 14 days postintervention. Twenty-four (44%) patients in the vertebroplasty group and 12 (21%) in the control group had an NRS pain score below 4/10 at 14 days (between-group difference, 23 percentage points; 95% CI, 6 to 39;  $P = 0.011$ ). Three patients in each group died from causes judged unrelated to the procedure. There were two serious adverse events in each group, related to the procedure (vertebroplasty group) and the fracture (control group). (Summary: J. Mantz. Image: R. V. Chandra, Monash University.)

**Take home message:** Vertebroplasty is superior to placebo intervention for pain reduction in patients with acute osteoporotic spinal fractures of less than 6 weeks in duration; this small study adds more uncertainty to the vast and growing literature on this controversial treatment.

**Association of anesthesia and surgery during childhood with long-term academic performance. JAMA Pediatr 2016 Nov 7. [Epub ahead of print.]**

This study examines the impact of anesthesia in childhood on academic performance, adding uncertainty to the findings reported in numerous negative trials on this topic. This large cohort study included 33,514 patients exposed to anesthesia and surgery before the age of four and 159,619 unexposed children in whom long-term academic and cognitive performance indexed by school grades at age 16 yr and IQ test scores at military conscription was evaluated and the association of cognitive decline with exposure was measured. The analysis included adjustment to the main confounders. Exposure before age 4 yr was associated with a mean difference of 0.41% (95% CI, 0.12 to 0.70) lower school grades and 0.97% (95% CI, 0.15 to 1.78) lower IQ test scores. (Selection: E. Kharasch. Summary: J. Mantz. Image: S. Suresh, Northwestern University.)

**Take home message:** In this cohort study, long-term cognitive performance was minimally affected by exposure to anesthesia and surgery before the age of four.

**Effect of hydrocortisone on development of shock among patients with severe sepsis: The HYPRESS randomized clinical trial. JAMA 2016; 316:1775–85.**

The potential benefit of corticosteroids in the treatment of septic shock remains controversial more than 20 yr after the effectiveness of this treatment was first examined. In this randomized clinical trial, patients with severe sepsis were randomly allocated 1:1 to receive either a continuous infusion of 200mg hydrocortisone for 5 days followed by dose tapering until day 11 ( $n = 190$ ) or to placebo ( $n = 190$ ). The primary outcome was development of septic shock within 14 days. Septic shock occurred in 36 of 170 patients (21.2%) in the hydrocortisone group and 39 of 170 patients (22.9%) in the placebo group (difference, -1.8%; 95% CI, -10.7 to 7.2;  $P = 0.70$ ). No significant difference between groups was observed for secondary outcomes.

(Summary: J. Mantz. Image: J. P. Rathmell.)

**Take home message:** The results from this trial do not support the use of corticosteroids in patients with severe sepsis, adding another negative trial to a growing list reporting no benefit to their use.



### Effect of conservative vs. conventional oxygen therapy on mortality among patients in an intensive care unit: The Oxygen-ICU randomized clinical trial. JAMA 2016; 316:1583–9.

Despite the common practice of administering supplemental oxygen to critically ill patients, the optimal target for  $P_{aO_2}$  has not been defined. Profound hypoxia is clearly deleterious, but hyperoxia may also cause harm through lung injury and other causes. To address this issue, the authors randomized adults admitted to the intensive care unit who were expected to stay at least 72h to a targeted oxygenation group ( $P_{aO_2}$  between 70 and 100 mmHg) or a standard practice group allowing  $P_{aO_2}$  values up to 150 mmHg. The study was stopped after enrollment of 434 of a targeted 660 patients due to the results of an interim analysis.

Analysis of this dataset revealed a lower intensive care unit mortality (primary outcome: absolute risk reduction, 0.086; 95% CI, 0.017 to 0.150;  $P = 0.01$ ) and improved secondary outcomes in terms of shock, liver failure, and bacteremia among the more conservatively treated patients. (Summary: D. Clark. Image: J. P. Rathmell.)

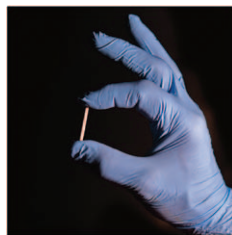
**Take home message:** While not conclusive, these results suggest that supplementing oxygen to the point of moderate hyperoxia may not be entirely benign in critically ill patients.



### Association between tracheal intubation during pediatric in-hospital cardiac arrest and survival. JAMA 2016; 316:1786–97.

Tracheal intubation is common during pediatric in-hospital cardiac arrest although the relationship between intubation during cardiac arrest and outcomes is unknown. This observational study of data from U.S. hospitals in the Get With The Guidelines-Resuscitation registry included pediatric patients (less than 18 yr) with in-hospital cardiac arrest between January 2000 and December 2014. The primary outcome was survival to hospital discharge. Secondary outcomes included return of spontaneous circulation and neurologic outcome. Of the 2,294 included patients, 1,555 (68%) were intubated during the cardiac arrest. In the propensity score-matched cohort ( $n = 2,270$ ), survival was lower in those intubated compared with those not intubated (411/1,135 [36%] vs. 460/1,135 [41%]; risk ratio, 0.89 [95% CI, 0.81 to 0.99];  $P = 0.03$ ). No difference was observed in secondary outcomes between intubated and nonintubated patients. (Summary: J. Mantz. Image: J. P. Rathmell.)

**Take home message:** Among pediatric patients with in-hospital cardiac arrest, tracheal intubation during cardiac arrest compared with no intubation was associated with decreased survival to hospital discharge.



### Buprenorphine implants (Probuphine) for opioid dependence. JAMA 2016; 316:1820–1.

The Food and Drug Administration has approved subdermal implants of the partial opioid agonist buprenorphine (Probuphine—Titan) for maintenance treatment of opioid dependence in patients stabilized on low to moderate doses of transmucosal buprenorphine. Probuphine was designed to provide continuous low levels of buprenorphine for 6 months and to safeguard against illicit use of the drug. This paper briefly reviews the pharmacology and therapeutic uses of Probuphine. Probuphine may provide more consistent dosing for opioid-dependent patients stabilized on low to moderate doses of transmucosal buprenorphine. The implants also provide an additional safeguard against illicit use of buprenorphine, but they are much more expensive than oral transmucosal buprenorphine, which is similarly effective. (Summary: J. Mantz. Image: J. P. Rathmell.)

**Take home message:** This paper summarizes the pharmacological and therapeutic characteristics of recently Food and Drug Administration-approved buprenorphine implants for opioid dependence.



### Improving learner handovers in medical education. Acad Med 2016 Nov 1. [Epub ahead of print.]

A handover in clinical medicine is a potentially vulnerable period that may result in patient harm. The same appears to be true in medical education. Specifically, communication failures between medical school and residencies may represent a missed opportunity to identify clinical or professional deficiencies in trainees that may have an impact on the trainee, the patient, and the program that accepts them. This paper identifies a significant issue in medical education. It suggests that the absence of agreed-upon outcomes and assessments and lack of standardized ways to communicate learner deficiencies may explain these poor learner handovers. The authors propose a handover process that mirrors a clinical handover called the CLASS model. This model would involve a comprehensive system that includes standardized assessments and interventions by medical school deans, program directors, and possibly coaches. This process would be carried from medical school to residency and then from residency to fellowship. It is the hope that, like patient care handovers, augmented learner handovers will ultimately improve training and patient care. (Summary: F. Cladis. Image: J. P. Rathmell.)

**Take home message:** The authors propose using a learner handover process to improve the current learner handover situation.