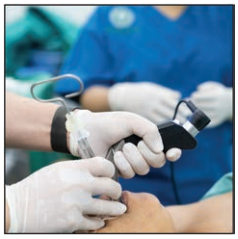
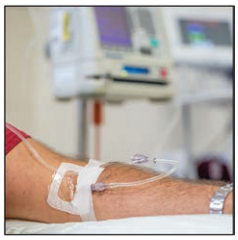
SCIENCE, MEDICINE, AND THE ANESTHESIOLOGIST
ANESTHESIOLOGY®
Martin J. London, M.D., Editor
Key Papers from the Most Recent Literature Relevant to Anesthesiologists



Video versus direct laryngoscopy for tracheal intubation of critically ill adults. N Engl J Med 2023; 389:418–29. PMID: 37326325.

Tracheal intubation of critically ill adults is predominantly performed using direct laryngoscopy with a reported first-attempt failure rate between 20% and 30%, increasing risks of life-threatening complications. The effectiveness of video laryngoscopy in this setting is controversial. This pragmatic, multicenter, randomized trial, conducted at 17 U.S. emergency rooms or intensive care units in 2022, randomly assigned adult patients to intubation with either direct or video laryngoscopy. The primary outcome was successful intubation on the first attempt. Secondary outcome included severe complications (hypoxemia, hypotension, vasopressor use, cardiac arrest, or death). The type of equipment used was not mandated, although all intubations employed either a stylet or bougie and were confirmed by expiratory carbon dioxide. The trial was stopped for efficacy at a prespecified interim analysis, prior to recruitment of an intended 2,000 patients. Of the total 1,417 patients enrolled, 705 received video laryngoscopy and first-attempt success was 85%, while 712 had direct laryngoscopy with 71% first-attempt success (absolute risk difference, 14%; $P < 0.001$ by unadjusted chi square test). Secondary outcomes were similar between groups (21% *vs.* 21%; absolute risk difference, 0.5 percentage points; 95% CI, −3.9 to 4.9). Safety outcomes were similar. *(Article Selection: William G. Tharp, M.D., Ph.D. Image: Adobe Stock.)*

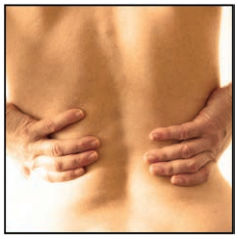
Take home message: In a large, multicenter, randomized trial, video laryngoscopy led to higher first-attempt intubation success rates over direct laryngoscopy in critically ill adult patients intubated in an emergency room or intensive care unit.



Balanced crystalloid solution versus saline in deceased donor kidney transplantation (BEST-Fluids): A pragmatic, double-blind, randomised, controlled trial. Lancet 2023; 402:105–17. PMID: 37343576.

As a result of ischemia-reperfusion injury, 30 to 50% of renal transplant patients receiving kidneys from a deceased donor are at risk for delayed graft function, defined as the requirement for dialysis within the first week after transplantation. Of particular importance is its association with long-term adverse patient outcomes and increased health-care costs. Concerns have been raised regarding the potential harm of using 0.9% sodium chloride *versus* balanced low-chloride crystalloid solution (Plasma-Lyte 148) perioperatively, although prior single-center studies showed no differences. The BEST-Fluids was a pragmatic, registry-embedded, multicenter, double-blind, randomized controlled trial (16 centers in Australia and New Zealand; 2018 to 2020) designed to better test this comparison. Adult or child recipients (excluding those less than 20 kg or receiving multiple organs) were randomly assigned (1:1) to intravenous balanced crystalloid solution (Plasma-Lyte 148) or saline during surgery and up until 48 h after transplantation. The primary outcome was delayed graft function. Of 807 subjects analyzed (404 balanced and 403 saline), the primary outcome was significantly lower in the balanced group (30% *vs.* 40%; adjusted relative risk, 0.74 [95% CI, 0.66 to 0.84; $P < 0.0001$]; adjusted risk difference, 10.1% [95% CI, 3.5 to 16.6]). Serious adverse events were similar in both groups. *(Article Selection: Martin J. London, M.D. Image: Adobe Stock.)*

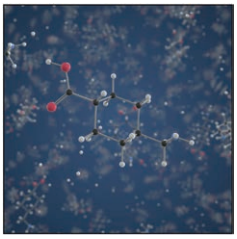
Take home message: In a large multicenter, randomized trial, the use of balanced crystalloid solution was associated with significantly lower risk of delayed graft function in patients receiving a deceased donor kidney transplant.



Opioid analgesia for acute low back pain and neck pain (the OPAL trial): A randomised placebo-controlled trial. Lancet 2023; 402:304–12. PMID: 37392748.

The use of opioids for spinal pain is controversial, but guidelines recommend consideration for debilitating acute back pain in some circumstances. This multicenter placebo-controlled study at 157 Australian sites randomized 347 patients who reported no low back or neck pain in the past month with a new spinal pain episode less than 12 weeks in duration to guideline-based care consisting of education and nonopioid analgesics alone, or with opioids. Opioid therapy ranged from 5 to 10 mg oxycodone two times daily mixed with naloxone, or placebo. The study included individuals with radicular and nonradicular pain who were not receiving more than 15 oral morphine equivalents per day for longer than 5 days. At the primary endpoint 6 weeks after therapy, no significant difference in pain severity was observed; average pain score (2.78 [standard error, 0.20] in the opioid group *vs.* 2.25 [0.19] in the placebo group; adjusted mean difference, 0.53; 95% CI, −0.00 to 1.07; $P = 0.051$) between groups. There were also no differences in pain at other points through 1 yr or for secondary outcomes except that the placebo group experienced less disability at 6 weeks and better mental health at weeks 6 and 12. There were no overall differences in adverse events except that the opioid group experienced greater opioid-related side effects. *(Article Selection: Steven Cohen, M.D. Image: J. P. Rathmell.)*

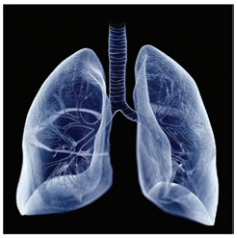
Take home message: In this randomized controlled trial, opioids provided no benefit for acute nonspecific back or neck pain, with a change in prescribing habits recommended.



Prehospital tranexamic acid for severe trauma. N Engl J Med 2023; 389:127–36. PMID: 37314244.

The effectiveness of prehospital administration of the antifibrinolytic agent tranexamic acid in patients with major trauma has been called into question following initial promising results in two highly publicized randomized controlled trials (CRASH-2 and 3). This double-blind, placebo-controlled, multinational, multicenter pragmatic trial (15 emergency medical services, 21 hospitals in Australia, New Zealand, and Germany) randomized 1,310 major trauma patients to either tranexamic acid (1 g slow bolus before hospital admission followed by 1-g infusion over 8 h in the hospital) or a placebo. The primary outcome was survival with a favorable functional outcome at 6 months, assessed using the Glasgow Outcome Scale–Extended; 1 to 8 scale with at least a 5 considered a favorable outcome. Secondary outcomes included all-cause mortality within 28 days and 6 months after injury. Of the 1,131 patients analyzed, no difference was noted in the primary outcome between groups (54% *vs.* 54%; risk ratio, 1.00; 95% CI, 0.90 to 1.12; $P = 0.95$). Differences in secondary outcome survival were negligible: 28 days: 17% *versus* 22%; risk ratio, 0.79; 95% CI, 0.63 to 0.99; 6 months: 19% *versus* 23%; risk ratio, 0.83; 95% CI, 0.67 to 1.03. No differences in serious adverse events including occlusive events were noted. *(Article Selection: Martin J. London, M.D. Image: Adobe Stock.)*

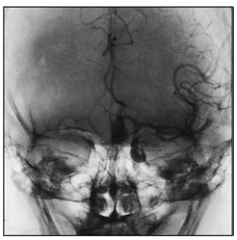
Take home message: This multicenter randomized trial in nations with advanced trauma systems did not demonstrate a benefit of tranexamic acid in improving functional outcomes at 6 months after injury in patients with major trauma.



Mild hypercapnia or normocapnia after out-of-hospital cardiac arrest. N Engl J Med 2023; 389:45–57. PMID: 37318140.

International guidelines recommend normocapnia in resuscitated adult patients in coma after out-of-hospital cardiac arrest, but evidence from randomized studies is lacking. Based on observational and small clinical studies suggesting a possible benefit of mild hypercapnia (increasing cerebral blood flow), this multicenter randomized clinical trial tested this unproven hypothesis. The primary outcome was a favorable neurologic outcome, defined as Glasgow Outcome Scale–Extended score of 5 to 8 at 6 months (score of 1: death, 5 to 6: moderate disability, 7 to 8: good recovery). Secondary outcomes included death and poor functional outcome at 6 months. A total of 1,700 patients (21% female; mean age, 61 yr) from 63 intensive care units in 17 countries were allocated to either mild targeted hypercapnia ($Paco_2$ 50 to 55 mmHg) or targeted normocapnia ($Paco_2$ 35 to 45 mmHg) for 24 h right after randomization. There was no difference in the primary outcome at 6 months: 44% *versus* 45% patients in the mild hypercapnia and normocapnia arm, respectively, had a favorable neurologic outcome (adjusted relative risk with mild hypercapnia 0.98 [95% CI, 0.87 to 1.11]; $P = 0.76$). Secondary outcomes were also comparable. *(Article Selection: Beatrice Beck-Schimmer, M.D. Image: Adobe Stock.)*

Take home message: This multicenter randomized clinical trial found that early intervention with a targeted mild hypercapnia in resuscitated patients after out-of-hospital cardiac arrest did not improve neurologic outcome at 6 months.



Effectiveness of lumbar cerebrospinal fluid drain among patients with aneurysmal subarachnoid hemorrhage: A randomized clinical trial. JAMA Neurol 2023; 80:833–42. PMID: 37330974.

Subarachnoid hemorrhage is often associated with cerebral vasospasm leading to ischemia or infarction. Retrospective analyses have suggested that cerebrospinal fluid drainage *via* a lumbar drain may be associated with an improved outcome. The EARLYDRAIN trial was a multicenter, pragmatic, randomized, open-label trial conducted at 19 sites in Germany, Switzerland, and Canada, analyzing 287 patients (2011 to 2016) receiving either standard care of the additional use of a lumbar drain within 48 h of either aneurysm clipping or coiling. The primary outcome was significantly improved in the in the lumbar drain group (33% *vs.* 45%; risk ratio, 0.73; 95% CI, 0.52 to 0.98; absolute risk difference, −0.12; 95% CI, −0.23 to −0.01; $P = 0.04$). Patients treated with a lumbar drain had fewer secondary cerebral infarctions at discharge (41 patients [29%] *vs.* 57 patients [40%]; risk ratio, 0.71; 95% CI, 0.49 to 0.99; absolute risk difference, −0.11; 95% CI, −0.22 to 0; $P = 0.04$). *(Article Selection: Martin J. London, M.D. Image: J. P. Rathmell.)*

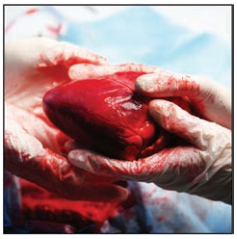
Take home message: In this multicenter randomized trial, the use of a lumbar drain as an additional intervention in patients with subarachnoid hemorrhage after aneurysm occlusion improved clinical neurologic outcomes at 6 months.

 DOI: 10.1097/ALN.0000000000004772

High-dose dual-antibiotic loaded cement for hip hemiarthroplasty in the UK (WHiTE 8): A randomised controlled trial. Lancet 2023; 402:196–202. PMID: 37354913.

It is unclear whether addition of a second antibiotic in the bone cement decreases the incidence of deep surgical-site infections after hemiarthroplasty operations. This multicenter controlled blinded trial at 26 United Kingdom hospitals randomized patients having cemented hip arthroplasties for intracapsular displaced hip fractures to either standard care: cement loaded with a single antibiotic (gentamicin) or cement loaded with high-dose dual antibiotics (gentamicin and clindamycin). The primary outcome was the incidence of deep surgical-site infection within 90 days of the operation. Secondary outcomes included mortality, antibiotic use, complications, health-related quality of life, mobility, and residential status, which were assessed at 120 days postoperatively. Deep surgical infection was found in 38 of 2,183 patients (2%) in the standard care group, and in 27 of 2,214 (1%) in the high-dose dual-antibiotic group (adjusted odds ratio, 1.43; 95% CI, 0.87 to 2.35; $P = 0.16$). There were also no differences in secondary outcomes between the groups. *(Article Selection: Jamie Sleigh, M.D. Image: J. P. Rathmell.)*

Take home message: In this randomized trial, the use of high doses of two antibiotics in cement relative to a single antibiotic did not reduce the incidence of postoperative deep surgical infections in hemiarthroplasty patients.



Transplantation outcomes with donor hearts after circulatory death. N Engl J Med 2023; 388:2121–31. PMID: 37285526.

Given the severe shortage of donor hearts suitable for transplantation, using organs from donors after circulatory death (DCD) has emerged as an alternative to the traditional process after brain death owing primarily to the widespread use of extracorporeal machine perfusion. In this randomized noninferiority trial at 15 U.S. centers, adult candidates for heart transplantation were assigned in a 3:1 ratio (with allowance for the receipt of either type of donor heart to protect a recipient's chance of transplantation without delay) to receive a DCD heart or a heart after brain death. The primary outcome was risk-adjusted survival at 6 months. Safety was assessed by occurrence of adverse events at 30 days after transplantation. In a total of 166 as-treated transplanted recipients (80 with DCD hearts and 86 with hearts donated after brain death), risk-adjusted 6-month survival was 94% (95% CI, 88 to 99%) among DCD recipients as compared with 90% (95% CI, 84 to 97%) among recipients of hearts donated after brain death (least-squares mean difference, –4 percentage points; 90% CI, –11 to 3; $P < 0.001$ for noninferiority). Primary graft dysfunction within the first 30 days after transplantation occurred in 22% of DCD hearts and in 10% of hearts donated after brain death. *(Article Selection: Michael Zaugg, M.D., M.B.A. Image: Adobe Stock.)*

Take home message: In this randomized trial, survival at 6 months after transplantation with a DCD heart was not inferior to standard-care transplantation.

Relationship between clinic and ambulatory blood pressure and mortality: An observational cohort study in 59 124 patients. Lancet 2023; 401:2041–50. PMID: 37156250.

Ambulatory blood pressure provides a comprehensive assessment of blood pressure over the course of a 24-h period and has been reported to predict health outcomes better than clinic or home pressure. This observational cohort study analyzed age, sex, all blood pressure measurements, and body mass index for patients from 223 primary care centers in the Spanish National Health System using the Spanish Ambulatory Blood Pressure Registry (2004 to 2014) with follow-up until death or the end of 2019. Over a median follow-up of 9.7 yr, 7,174 (12%) of 5,9124 patients died. All-cause death (hazard ratio, 1.41 per 1-SD increment [95% CI, 1.36 to 1.47]) was more strongly associated with 24-h systolic blood pressure (SBP) than clinic SBP (1.18 [1.13 to 1.3]). Night-time SBP was approximately 6 times more informative about risk of either all-cause or cardiovascular death. Elevated all-cause mortality and elevated cardiovascular mortality were observed for ambulatory-only hypertension (hazard ratio, 1.24 [95% CI, 1.12 to 1.37]) and hypertension in both the ambulatory and clinic settings (1.24 [1.5 to 1.32]) but were not observed for white-coat hypertension relative to normal blood pressure. *(Article Selection: BobbieJean Sweitzer, M.D. Image: Getty Images.)*

Take home message: In this large observational cohort analysis, night-time ambulatory blood pressure was more predictive of all-cause and cardiovascular deaths compared to that measured in a clinic setting.