

ANESTHESIOLOGY



Deborah J. Culley, M.D., Editor

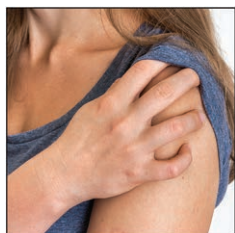


Causal analysis of World Health Organization's Surgical Safety Checklist implementation quality and impact on care processes and patient outcomes: Secondary analysis from a large stepped wedge cluster randomized controlled trial in Norway. *Ann Surg* 2017 Nov 6 [Epub ahead of print].

The implementation of the World Health Organization's Surgical Safety Checklist may result in improved patient outcomes and a reduction in morbidity and mortality of surgical patients. In the primary analysis of their randomized clinical trial, published in 2015, the authors showed that implementation of the surgical safety checklist resulted in a significant reduction in the rate of complications from 19.9 to 11.5% (absolute risk reduction 8.4%). In this secondary analysis, the authors aimed to determine how precisely implementing a surgical safety checklist may improve care processes and patient outcomes.

Comparing 2,304 intervention procedures to 1,398 controls, implementation of the surgical safety checklist was associated with an increase in the use of forced air warming from 35.3 to 42.4% (odds ratio, 1.25; 95% CI, 1.07 to 1.45; $P < 0.001$), an increase in preincision antibiotic administration from 54.5 to 63.1% (odds ratio, 1.25; 95% CI, 1.07 to 1.48; $P < 0.001$), a reduction in surgical infections from 7.4 to 3.6% ($P < 0.001$), and a reduction in blood transfusion costs by 40%. (Summary: Peter Nagele. Image: Reprinted from WHO Surgical Safety Checklist, 2009, <http://www.who.int/patientsafety/topics/safe-surgery/checklist/en/>.)

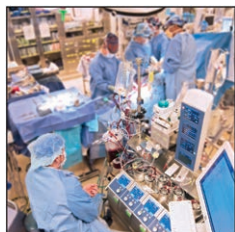
Take home message: Implementation of a surgical safety checklist improves operating room care processes and patient outcomes.



Arthroscopic subacromial decompression for subacromial shoulder pain (CSAW): A multicentre, pragmatic, parallel group, placebo-controlled, three-group, randomised surgical trial. *Lancet* 2017 Nov 20 [Epub ahead of print].

Shoulder pain is a common complaint brought to primary and specialty providers. A range of treatment options exist, but the use of surgical subacromial decompression has expanded rapidly over the past two decades. Data regarding the utility of this arthroscopic procedure are sparse and conflicting. This study was designed as a randomized, partially blinded trial comparing arthroscopic decompression, diagnostic arthroscopy, and no treatment. A total of 303 patients were randomized to the three groups with the Oxford Shoulder Score (OSS), an instrument that measures both pain and function, delivered at 6 months as the primary outcome. The OSS at 6 months postsurgery did not differ between the surgical groups. A small statistically significant but clinically irrelevant improvement in the OSS was noted over no treatment with decompression (2.8 points; 95% CI, 0.5 to 5.2; $P = 0.2$) and arthroscopy (4.2 points; 95% CI, 1.8 to 6.6; $P = 0.001$). The authors suggest that these data should be shared with patients when discussing options for the treatment of their shoulder pain. (Summary: J. David Clark. Image: ©ThinkStock.)

Take home message: Surgery may not increase the likelihood of clinically relevant improvements in pain and function in patients with preoperative shoulder pain.



Restrictive or liberal red-cell transfusion for cardiac surgery. *N Engl J Med* 2017; 377:2133–44.

The optimal hemoglobin (Hgb) level for transfusion of allogeneic red cells in patients undergoing cardiac surgery with cardiopulmonary bypass is controversial. This study reports on a multicenter, open-label, noninferiority trial randomizing patients to one of two Hgb triggers: restrictive (less than 7.5 g/dl) versus liberal (less than 9.5 g/dl in the intensive care unit or 8.5 g/dl in a nonintensive care unit). The primary composite outcome was all-cause mortality, myocardial infarction, stroke, or new onset renal failure with dialysis. In the per-protocol analysis, 4,860 patients were studied at 73 sites in 19 countries with a mean age of 72 yr and mean EUROSCORE of 7.8. The primary outcome occurred in 11.4% of the restrictive versus 12.5% of liberal patients (absolute risk difference, -1.11; 95% CI, -2.93 to 0.72; $P < 0.001$ for noninferiority). Mortality was 3.0% in the restrictive versus 3.6% in the liberal group (P value nonsignificant). Patients in the restrictive group were less likely to receive a transfusion when compared to the liberal group (odds ratio, 0.41; 95% CI, 0.37 to 0.47; $P < 0.001$) with a median of two units transfused versus three units, respectively (odds ratio, 0.85; 95% CI, 0.82 to 0.88; rate ratio). (Summary: Martin J. London. Image: J. P. Rathmell.)

Take home message: A restrictive transfusion trigger of 7.5 g/dl in patients at elevated risk for perioperative mortality undergoing cardiac surgery with cardiopulmonary bypass is noninferior to a liberal trigger of 9.5 g/dl.



Optimizing surgical quality datasets to care for older adults: Lessons from the American College of Surgeons NSQIP Geriatric Surgery Pilot. *J Am Coll Surg* 2017; 225:702–12.e1.

The majority of current databases are used to gather information about the average patient to make associations between outcomes and patient and/or surgical variables. Rarely is information on geriatric factors such as cognition, decision-making, function, and mobility included in these analyses. This study used the National Surgical Quality Improvement Program database involving 36,399 older patients from 31 hospitals as a part of the Geriatric Surgery Pilot designed to evaluate whether geriatric-specific risk factors contribute to 30-day outcomes in terms of morbidity and mortality. After risk adjustment, geriatric factors including surrogate consent (odds ratio, 1.5; 95% CI, 1.3 to 1.8) and use of a mobility aid (odds ratio, 1.3; 95% CI, 1.1 to 1.4) increased the risk of morbidity and/or mortality in patients undergoing general or vascular surgical procedures. Geriatric-specific adverse outcomes that were identified in this study included delirium (12%), functional decline (43%), new mobility aid (30%), and pressure ulcers (2%). (Summary: Deborah J. Culley. Image: ©ThinkStock.)

Take home message: Geriatric factors such as the need for surrogate consent and use of a mobility aid may be associated with adverse outcomes in older surgical patients.



Effect of treatment delay on the effectiveness and safety of antifibrinolytics in acute severe haemorrhage: A meta-analysis of individual patient-level data from 40 138 bleed-ing patients. *Lancet* 2018; 391:125–32.

There is strong evidence that the use of antifibrinolytics, such as tranexamic acid, is associated with reduced mortality in patients suffering from life-threatening hemorrhage. It is unclear whether delaying the administration of antifibrinolytics reduces the effectiveness. This study describes an individual patient data-level meta-analysis of all large clinical trials that investigated the use of tranexamic acid in the setting of major hemorrhage. More than 40,138 patients were included in the analysis with observed death in 3,558. Most bleeding deaths (63%) occurred within 12h of onset although deaths from postpartum hemorrhage peaked 2 to 3h after childbirth. Compared to placebo, the use of tranexamic acid significantly increased overall survival from bleeding (odds ratio, 1.20; 95% CI, 1.08 to 1.33; $P = 0.001$). Immediate treatment improved survival by more delayed treatment (odds ratio, 1.72; 95% CI, 1.42 to 2.10; $P < 0.0001$), with the beneficial effects of tranexamic acid decreasing by 10% for every 15 min delay in treatment. After 3h, there was no benefit of tranexamic acid. No increase in vascular occlusive events with tranexamic acid was observed. (Summary: Peter Nagele. Image: J. P. Rathmell.)

Take home message: To maximize the beneficial effects of tranexamic acid in severe hemorrhage, the drug should be given without delay.



Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. *N Engl J Med* 2018; 378:11–21.

Previous studies demonstrate a benefit of endovascular thrombectomy in patients presenting within 6h of stroke symptoms. It is unknown if patients known to be well 6 to 24h before presentation and who have a mismatch in the severity of clinical symptoms relative to infarct volume on imaging can benefit from this therapy. This industry-sponsored international study randomized 206 such patients presenting with ischemic stroke to thrombectomy plus standard care or standard care alone. Coprimary outcomes were the mean score for disability and the rate of functional independence using the modified Rankin scale at 90 days. The trial was stopped at the first interim analysis as it met the predictive probability of superiority for thrombectomy. The mean disability score at 90 days was 5.5 in the thrombectomy group versus 3.4 in the standard care group (adjusted difference by Bayesian analysis 2.0 points, posterior probability of superiority > 0.999); the rate of functional independence at 90 days was 49% in the thrombectomy group versus 13% in the standard care group (adjusted difference 33 points, posterior probability of superiority > 0.999). (Summary: Martin J. London. Image: T. Leslie-Mazwi, Massachusetts General Hospital.)

Take home message: Among patients presenting with acute ischemic stroke known to be well 6 to 24h earlier and with a mismatch between the severity of their clinical deficit and the volume of infarct on imaging, thrombectomy resulted in improved disability outcome ratings at 90 days compared to standard care.



Fremanezumab for the preventive treatment of chronic migraine. *N Engl J Med* 2017; 377:2113–22.

Migraine headache is a common and sometimes refractory neurologic disorder affecting approximately 15% of the population. The calcitonin gene-related peptide (CGRP) signaling system has recently been targeted to control acute, episodic (fewer than 15 headaches per month) and chronic (15 or more headaches per month) episodic migraine. This study randomized patients with chronic migraines to receive 625mg fremanezumab, an anti-CGRP receptor antibody, intramuscular at baseline followed by placebo intramuscular at weeks 4 and 8; 675mg fremanezumab intramuscular at baseline followed by 675mg of fremanezumab intramuscular at weeks 4 and 8; or placebo intramuscular at baseline, 4 and 8 weeks in 1,130 patients. Patients in the placebo group had an average reduction in the number of headache-free days per month by 2.5 ± 0.3 days, whereas in those taking fremanezumab quarterly there was a 4.3 ± 0.3 day reduction in migraine days ($P < 0.001$), and in those taking fremanezumab monthly there was a 4.6 ± 0.3 day reduction in migraine days ($P < 0.001$). (Summary: J. David Clark. Image: ©ThinkStock.)

Take home message: Fremanezumab, an anti-CGRP receptor antibody, may increase the number of migraine-free days.

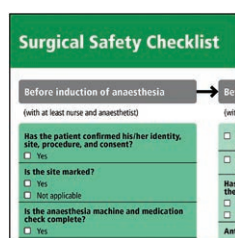


Outcomes after angiography with sodium bicarbonate and acetylcysteine. *N Engl J Med* 2017 Nov 12 [Epub ahead of print].

The impact of prophylactic intravenous sodium bicarbonate and oral acetylcysteine on acute kidney injury (AKI) and related adverse outcomes after angiography is controversial. The authors performed a randomized study involving 5,177 patients at elevated risk for renal complications undergoing elective angiography. Subjects received either 1.26% sodium bicarbonate or 0.9% sodium chloride for 1 to 12h before, during, and for 2 to 12h postangiography and 1,200mg oral acetylcysteine or placebo 1h before, 1h after, and for 4 days after angiography. The primary endpoint was a composite of death, need for dialysis, or a 50% persistent increase in serum creatinine after angiography. The trial was stopped before its projected 7,680 target on the basis of an absence of between-group differences in study endpoints.

The primary outcome occurred in 4.4% of the sodium bicarbonate *versus* 4.7% of the sodium chloride group (odds ratio, 0.93; 95% CI, 0.72 to 1.22; $P = 0.62$) and in 4.6% of the acetylcysteine *versus* 4.5% of the placebo group (odds ratio, 1.02; 95% CI, 0.78 to 1.33; $P = 0.88$). Contrast-associated AKI occurred in 8.3 to 9.5% of patients with no significant difference between treatment groups. (Summary: Martin J. London. Image: J. P. Rathmell.)

Take home message: In patients at elevated risk for renal complications undergoing elective angiography, there was no benefit of intravenous sodium bicarbonate or acetylcysteine over 0.9% sodium for the prevention of death, need for dialysis, acute kidney injury, or persistent decline in renal function.

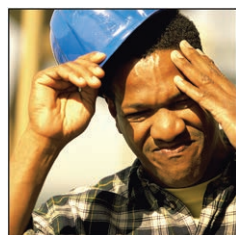


Mortality trends after a voluntary checklist-based surgical safety collaborative. *Ann Surg* 2017; 266:923–9.

Population-based evidence for the efficacy of team-based safety checklists is absent in the literature. This article utilized all-payer discharge claims from 2008 to 2013 and linked them to state vital statistics to identify changes in risk-adjusted 30-day mortality among 14 hospitals using propensity score analysis. There were 22,514 and 18,112 patients in checklist-completing hospitals in 2010 and 2013, respectively. These were compared to patients admitted to all other participating hospitals in South Carolina and involved 38,876 and 30,218 patients in 2010 and 2013, respectively. The 30-day mortality between patients where the checklists were completed was reduced from 3.4% in 2010 to 2.8% in 2013 ($P < 0.001$). However, in the comparison hospitals there was no difference between the 2010 and 2013 30-day mortality rates ($P = 0.33$). The authors report a 0.74% (95% CI, 0.27 to 1.22%; $P = 0.002$) difference in mortality rates

between the two cohorts. (Summary: Deborah J. Culley. Image: Reprinted from WHO Surgical Safety Checklist, 2009, <http://www.who.int/patientsafety/topics/safe-surgery/checklist/en/>.)

Take home message: Use of a surgical safety checklist may reduce 30-day mortality among surgical patients.



A controlled trial of erenumab for episodic migraine. *N Engl J Med* 2017; 377:2123–32.

This study used a prospective, randomized, placebo-controlled study design involving 955 patients to compare whether 70 or 140mg per month of intramuscular erenumab, an anti-calcitonin gene-related peptide (CGRP) receptor antibody, was superior to placebo in reducing the number of episodic headaches experienced per month. After 6 months of treatment, patients randomized to placebo had a 1.8 day decrease in their number of migraine days per month, whereas those randomized to 70 and 140mg erenumab had a 3.2 and 3.7 day decrease in their number of migraine-free days per month, respectively. When compared to placebo, 70mg per day erenumab decreased the number of migraine days per month by –1.4 days (95% CI, –1.9 to –0.9; $P < 0.001$), whereas 140mg erenumab decreased the number of migraine-free days per month by –1.9 (95% CI, –2.3 to –1.4; $P < 0.001$). (Summary: J. David Clark. Image: ©ThinkStock.)

Take home message: Once monthly intramuscular administration of erenumab, an anti-CGRP receptor antibody, may lead to a significant reduction in migraine days.



Inhaled xenon attenuates myocardial damage in comatose survivors of out-of-hospital cardiac arrest: The Xe-Hypotheca trial. *J Am Coll Cardiol* 2017; 70:2652–60.

Survival after cardiac arrest is markedly influenced by the extent of brain damage. The authors of this study have previously shown that 24 h of xenon inhalation combined with hypothermia attenuates brain white matter damage compared to hypothermia alone. In this prespecified secondary analysis, the authors investigated if xenon combined with hypothermia also influenced the extent of myocardial injury, as measured by cardiac troponin elevation, compared to hypothermia alone. Cardiac troponin T concentrations were measured at hospital admission, and at 24, 48, and 72 h postcardiac arrest. The authors compared 54 patients in each group and observed that patients who received xenon combined with hypothermia had a significantly reduced myocardial injury as evidenced by lower cardiac troponin levels (mean difference, -0.66 ; 95% CI, -1.16 to -0.16) 72 h after out-of-hospital cardiac arrest compared to patients

who received hypothermia alone. The effect of xenon on the extent of myocardial injury did not differ between patients with or without percutaneous coronary intervention or in those with a diagnosis of ST-elevation myocardial infarction. (Summary: Peter Nagele. Image: J. P. Rathmell.)

Take home message: Xenon combined with hypothermia appears to attenuate not only brain white matter damage after cardiac arrest, but also myocardial injury.



Association between wait time and 30-day mortality in adults undergoing hip fracture surgery. *JAMA* 2017; 318:1994–2003.

Wait times before hip fracture repair vary significantly, with longer wait times being associated with an increased mortality rate. This population-based retrospective cohort study involving 42,230 patients from Canada attempted to identify the inflection point at which the wait time between hospital arrival and surgery was associated with an increase in postoperative mortality (primary outcome measure). To address this issue they used a risk-adjusted restricted cubic splines model to determine the probability of mortality and other complications according to wait time. Comparing propensity-score matched patients who received early surgery to those who received surgery more than 24 h after hospital arrival, the authors identified a lower absolute risk (0.79; 95% CI, 0.23 to 1.35) of 30-day mortality in the early surgery group, which remained significant at 90 and 365 days after surgery. Secondary outcomes including pulmonary

embolism, pneumonia, and myocardial infarction were also increased in the patients that had surgery more than 24 h after arrival to the hospital despite no difference in negative tracer outcomes. (Summary: Deborah J. Culley. Image: ©ThinkStock.)

Take home message: Delayed surgery in patients with hip fracture has been associated with increased mortality and postoperative complications when compared to patients operated on within 24 h of arrival to the hospital.