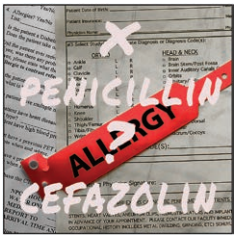
SCIENCE, MEDICINE, AND THE ANESTHESIOLOGIST

ANESTHESIOLOGY

Martin J. London, M.D., Editor

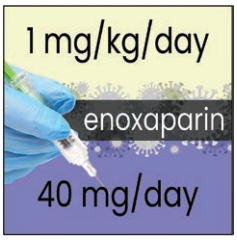
Key Papers from the Most Recent Literature Relevant to Anesthesiologists



Assessment of the frequency of dual allergy to penicillins and cefazolin: A systematic review and meta-analysis. JAMA Surg 2021; 156:e210021. PMID: 33729459.

Cefazolin is the preferred antibiotic for surgical prophylaxis with lower rates of surgical site infections than alternate agents but may be withheld in patients reporting a penicillin allergy history. The incidence of dual antibiotic allergy has not been systematically evaluated. This systematic review evaluated studies of patients who had allergies to penicillin and were tested for tolerability to cefazolin or that included patients who had allergies to cefazolin and were tested for tolerability to penicillin. Seventy-seven studies (6,147 subjects) met the eligibility criteria. Cefazolin allergy was identified in 44 subjects with a history of penicillin allergy, resulting in a dual allergy frequency of 0.7% (95% credible interval, 0.1 to 1.7%). The frequency was lower for subjects with unconfirmed (0.6% [95% credible interval, 0.1 to 1.3%]) than for those with confirmed penicillin allergy (3.0% [95% credible interval, 0.01 to 17.0%]). Thirteen studies evaluated surgical patients (n = 3,884), 0.7% (95% credible interval, 0 to 3.3%) with confirmed allergy to cefazolin. Penicillin allergy was confirmed in 16 participants with a history of cefazolin allergy, resulting in a frequency of 3.7% (95% credible interval, 0.03 to 13.3%). The frequency of penicillin allergy was 4.4% (95% credible interval, 0 to 23.0%) for the eight studies that exclusively assessed surgical patients allergic to cefazolin. *(Article Selection: Martin J. London, M.D. Image: M. Lane-Fall/Adobe Stock.)*

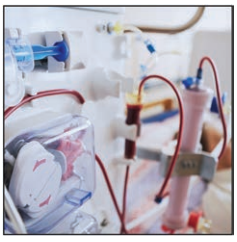
Take home message: Most surgical patients with a penicillin allergy history, with the exception of those with confirmed allergy, may safely receive cefazolin.



Effect of intermediate-dose vs standard-dose prophylactic anticoagulation on thrombotic events, extracorporeal membrane oxygenation treatment, or mortality among patients with COVID-19 admitted to the intensive care unit: The INSPIRATION randomized clinical trial. JAMA 2021; 325:1620–30. PMID: 33734299.

Critically ill patients with COVID-19 are at high risk of thrombotic complications. Evidence regarding the optimal anticoagulation strategy remains sparse. This multicenter randomized two-by-two factorial trial from 10 academic institutions in Iran compared intermediate (enoxaparin 1 mg/kg daily) *versus* standard (enoxaparin 40 mg daily) anticoagulation dosing in 562 COVID-19 patients requiring intensive care unit care. The primary endpoint was a composite of arterial and venous thrombosis, treatment with extracorporeal membrane oxygenation, or mortality within 30 days of admission. Prespecified safety outcomes included major bleeding according to the Bleeding Academic Research Consortium and severe thrombocytopenia (less than 20,000/μl). The primary outcome occurred in 46% of patients in the intermediate-dose group and 44% of patients in the standard-dose prophylaxis group (absolute risk difference, 1.5% [95% CI, –6.6 to 9.8%]; odds ratio, 1.06 [95% CI, 0.76 to 1.48]; $P = 0.70$). Seven patients (2.5%) in the intermediate-dose group and four patients (1.4%) in the standard-dose prophylaxis group experienced major bleeding (P for noninferiority > 0.99). Severe thrombocytopenia occurred only in patients assigned to the intermediate-dose group (6 *vs.* 0; $P = 0.01$). *(Article Selection: David Faraoni, M.D., Ph.D. Image: M. Lane-Fall/Adobe Stock.)*

Take home message: Among COVID-19 critically ill patients, standard anticoagulation with 40 mg enoxaparin daily was found to have a comparable therapeutic effect and safety profile compared to 1 mg/kg enoxaparin daily.



Comparison of two delayed strategies for renal replacement therapy initiation for severe acute kidney injury (AKIKI 2): A multicentre, open-label, randomised, controlled trial. Lancet 2021; 397:1293–300. PMID: 33812488.

Previous studies have shown that delaying renal replacement therapy in critically ill patients with severe acute kidney injury (oliguria for more than 72 h or a blood urea nitrogen concentration higher than 112 mg/dl) is safe relative to earlier intervention. This multicenter, prospective, open-label, randomized trial done in 39 French intensive care units compared this approach to a more delayed strategy (noticeable hyperkalemia or metabolic acidosis or pulmonary edema or blood urea nitrogen concentration higher than 140 mg/dl). The primary outcome was the number of days alive and free of renal replacement therapy between randomization and day 28. A total of 278 patients underwent randomization (2018 to 2019); 137 to the delayed strategy and 141 to the more delayed strategy. The median number of renal replacement therapy–free days was 12 days (interquartile range, 0 to 25) *versus* 10 days (interquartile range, 0 to 24), respectively ($P = 0.93$). The hazard ratio for death at 60 days was 1.65 (95% CI, 1.09 to 2.50; $P = 0.018$) with the more delayed strategy. The number of complications potentially related to acute kidney injury or renal replacement therapy did not differ between groups. *(Article Selection: Martin J. London, M.D. Image: Adobe Stock.)*

Take home message: For patients with severe acute kidney injury with oliguria for more than 72 h or blood urea nitrogen concentration higher than 112 mg/dl and no severe complication that would mandate immediate renal replacement therapy, postponing of renal replacement therapy for a further period of time did not confer additional benefit and was associated with adverse outcome.

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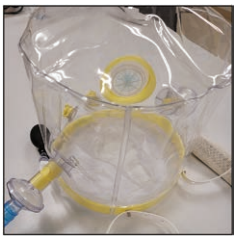
Postdischarge virtual visits for low-risk surgeries: A randomized noninferiority clinical trial. JAMA Surg 2021; 156:221–8. PMID: 33439221.

Live virtual postdischarge visits after surgery have become common during the COVID-19 pandemic given the necessity of social distancing measures and travel restrictions. It is unclear if virtual visits are inferior to in-person visits. This randomized, active controlled noninferiority trial compared video-based follow-up visits to in-person visits after minimally invasive appendectomy or cholecystectomy at two southeastern U.S. hospitals. The primary outcome was the percentage of patients with a postdischarge hospital encounter at 30 days, including emergency department visits, observation, or inpatient admission. A total of 432 patients were randomized; 289 patients to virtual and 143 patients to in-person follow-up visits; 53 crossed over from virtual to in-person visits. Virtual visits were noninferior to in-person visits, with hospital encounter percentages of 12.8% and 13.3%, respectively (difference of 0.5%, with one-sided 95% CI: $-\infty$ to 5.2%). The median patient postoperative visit (48 *vs.* 20 min), travel (13 *vs.* 0 min), and total commitment (66 *vs.* 14 min) time were all significantly longer for in-person visits compared with virtual visits. *(Article Selection: Beatrice Beck-Schimmer, M.D. Image: Adobe Stock.)*

Take home message: Video-based virtual follow-up visits after appendectomy or cholecystectomy did not result in greater use of care by patients after surgery compared to in-person visits and saved time for the patients overall.



Effect of helmet noninvasive ventilation vs high-flow nasal oxygen on days free of respiratory support in patients with COVID-19 and moderate to severe hypoxemic respiratory failure: The HENIVOT randomized clinical trial. JAMA 2021; 325:1731–43. PMID: 33764378.

Treatment of hypoxemic respiratory failure secondary to COVID-19 infection with possible avoidance of endotracheal intubation is a global priority. This randomized controlled trial of 110 patients (median age 65 yr, 19% female) admitted to four Italian intensive care units (October to December 2020) compared treatment with helmet noninvasive ventilation (n = 54; positive end-expiratory pressure, 10 to 12 cm H_2O; pressure support, 10 to 12 cm H_2O) for at least 48 h followed by high-flow nasal oxygen, to high-flow nasal oxygen alone (n = 55; 60 l/min). There was no difference in the primary outcome: days free from respiratory support within 28 days of enrollment were 20 days (interquartile range, 0 to 25) in the helmet group and 18 days (interquartile range, 0 to 22) in the high-flow nasal oxygen group (95% CI, –2 to 6; $P = 0.26$. There were also no significant differences for any of the secondary outcomes: except for the frequency of endotracheal intubation (30% helmet *vs.* 51% high-flow [95% CI, –38 to –3%]; $P = 0.03$) and days free from invasive mechanical ventilation (28 days [interquartile range, 13 to 28] *vs.* 25 days [interquartile range, 4 to 28]; $P = 0.04$). *(Article Selection: Meghan Prin, M.D., M.S. Image: M. Lane-Fall.)*

Take home message: In this small randomized trial, helmet noninvasive ventilation did not reduce the number of days free from respiratory support among patients with hypoxemic respiratory failure secondary to COVID-19 infection compared to high-flow nasal oxygen alone, but reduced the rate of endotracheal intubation.

Prevalence and nature of sexist and racial/ethnic microaggressions against surgeons and anesthesiologists. JAMA Surg 2021; 156:e210265. PMID: 33760000.

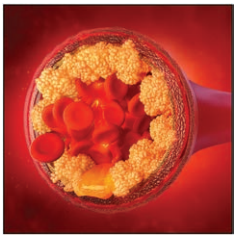
Workplace mistreatment related to sexism and racism can manifest either as macroaggressions (overt sexism or racism) or microaggressions (subtle insulting discriminatory comments) and may result in physician burnout. The prevalence data on these phenomena were assessed using a cross-sectional survey in a large U.S. health maintenance organization. The Maslach Burnout Inventory, the Racial Microaggression Scale, and the Sexist Microaggression Experience and Stress Scales were used to assess the primary outcome of prevalence and nature of sexist and racial/ethnic microaggressions. Secondary outcomes were frequency and severity of microaggressions, prevalence of physician burnout, and associations between microaggressions and physician burnout. Data from 588 respondents (44% female, 62% racial/ethnic minority) were analyzed. Ninety-four percent of females experienced sexist microaggressions while 81% of racial/ethnic respondents experienced racial/ethnic microaggressions. The prevalence of physician burnout was 47% and higher among female physicians (odds ratio, 1.60 [95% CI, 1.03 to 2.47]; $P = 0.04$) and racial/ethnic–minority physicians (odds ratio, 2.08 [95% CI, 1.31 to 3.30]; $P = 0.002$). Female physicians who experienced sexist microaggressions (racial/ethnic–minority female physicians: odds ratio, 1.84 [95% CI, 1.04 to 3.25], $P = 0.04$; white female physicians: odds ratio, 1.99 [95% CI, 1.07 to 3.69], $P = 0.03$) were more likely to experience burnout. Racial/ethnic–minority female physicians who had the compound experience of sexist and racial/ethnic microaggressions (odds ratio, 2.05 [95% CI, 1.14 to 3.69], $P = 0.02$) were more likely to experience burnout. *(Article Selection: Martin J. London, M.D. Image: Adobe Stock.)*

Take home message: In a large U.S. health maintenance organization the prevalence of sexist and racial/ethnic microaggressions against female and racial/ethnic–minority surgeons and anesthesiologists was high and associated with physician burnout.

Effect of low-intensity vs high-intensity home-based walking exercise on walk distance in patients with peripheral artery disease: The LITE randomized clinical trial. JAMA 2021; 325:1266–76. PMID: 33821898.

Guidelines for patients with lower extremity peripheral artery disease recommend a periodic high-intensity walking regimen to improve overall walking ability. The role of a lower intensity regimen performed without inducing ischemic pain is uncertain. This clinical trial randomized 305 patients with peripheral artery disease (mean age, 69 ± 10 yr, 48% women) to low-intensity walking exercise (n = 116), high-intensity walking exercise (n = 124), or a nonexercise control group (n = 65) for 12 months. Subjects were asked to walk five times per week for up to 50 min per session. The primary outcome was mean change in 6-min walk distance at 12 months. Two hundred fifty patients completed 12-month follow-up. The 6-min walk distance changed from 332 m at baseline to 328 m at 12-month follow-up in the low-intensity exercise group (within-group mean change, −6 m [95% CI, −22 to 9 m]; $P = 0.34$) and from 338 m to 371 m in the high-intensity exercise group (within-group mean change, 34 m [95% CI, 20 to 49 m]; $P < 0.001$); mean change for the between-group comparison was −41 m (97.5% CI, −62 to −20 m; $P < 0.001$). There was no significant difference between the low-intensity and nonexercise control group (between-group mean change, 9 m [97.5% CI, −17 to 34 m]; $P = 0.44$). Adverse events were not different between groups. *(Article Selection: Martin J. London, M.D. Image: Adobe Stock.)*

Take home message: Low-intensity home-based exercise in patients with peripheral artery disease was significantly less effective than a high-intensity regimen and was not significantly different from the nonexercise control for improving 6-min walk distance.



Identification of vulnerable plaques and patients by intracoronary near-infrared spectroscopy and ultrasound (PROSPECT II): A prospective natural history study. Lancet 2021; 397:985–95. PMID: 33714389.

Near-infrared spectroscopy and intravascular ultrasound facilitate imaging of nonobstructive plaques implicated in coronary-related events. This multicenter, prospective, natural history study evaluated patients with recent myocardial infarction at 14 Scandinavian hospitals. After treatment of flow-limiting lesions, all vessels were evaluated with near-infrared spectroscopy and intravascular ultrasound for plaque burden of nonculprit lesions and lipid content. The primary outcome was major adverse cardiac events (cardiac death, myocardial infarction, unstable angina, or progressive angina) from nonculprit lesions during follow-up. Between 2014 and 2017, 3,629 nonculprit lesions were identified in 898 patients (median follow-up, 4 yr). Adverse events within 4 yr occurred in 13% of patients, with 8% arising from 78 untreated nonculprit lesions. Highly lipidic lesions (24%, present in 59% of patients) were an independent predictor of nonculprit lesion-related major adverse cardiac events (adjusted odds ratio, 2.27 [95% CI, 1.25 to 4.13]). Large plaque burden (22% of lesions) was also an independent predictor. Lesions with both large plaque burden and lipid-rich cores had a 4-yr nonculprit lesion-related major adverse cardiac event rate of 7% (95% CI, 4 to 10). Patients in whom one or more such lesions were identified had a 4-yr nonculprit lesion-related major adverse cardiac event rate of 13% (95% CI, 9.4 to 17.6). In lesions with only one of the two high-risk features, the major adverse cardiac event rate was only 1.3 to 2.2%. *(Article Selection: Martin J. London, M.D. Image: Adobe Stock.)*

Take home message: Evaluation of nonobstructive coronary lesions around the time of myocardial infarction using near-infrared spectroscopy and intravascular ultrasound to identify high lipid content and large plaque burden facilitates prediction of future adverse cardiac events with a high negative predictive value.

Filtering facepiece respirator (N95 respirator) reprocessing: A systematic review. JAMA 2021; 325:1296–317. PMID: 33656543.

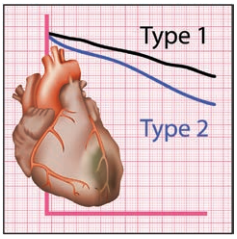
The transmission of the SARS-CoV-2 virus can be prevented efficiently using face masks, in particular N95 masks, which provide a high degree of microparticle filtration. Shortages during the COVID-19 pandemic necessitated their reprocessing by a variety of methods. However, it remains unclear which of these are optimal. This systematic review evaluated the effect and feasibility of different N95 mask reprocessing strategies. PubMed and EMBASE databases were searched for articles on five types of reprocessing methods yielding 42 studies of 65 mask types: ultraviolet irradiation (27), vaporized hydrogen peroxide (19), moist-heat incubation (9), microwave-generated steam (10), and ethylene oxide (7). SARS-CoV-2 was specifically evaluated in five studies. Of the reprocessing methods evaluated, ultraviolet irradiation, moist-heat incubation, and microwave-generated steam processing effectively removed pathogens, preserved the filtration capability of the masks, and were time efficient with readily available equipment, with ultraviolet irradiation the most feasible logistically. Vaporized hydrogen peroxide was found to be a more expensive method with longer decontamination times, and ethylene oxide could leave toxic residues while being a more complicated method. *(Article Selection: Beatrice Beck-Schimmer, M.D. Image: M. Lane-Fall/Adobe Stock.)*

Take home message: N95 masks can efficiently be sterilized and reprocessed using ultraviolet irradiation, moist-heat incubation, microwave-generated steam, and vaporized hydrogen peroxide, but more studies evaluating decontamination specifically of SARS-CoV-2 are needed.

Effect of ventral vs dorsal spinal surgery on patient-reported physical functioning in patients with cervical spondylotic myelopathy: A randomized clinical trial. JAMA 2021; 325:942–51. PMID: 33687463.

The optimal surgical approach for treatment of cervical spondylotic myelopathy is uncertain. This randomized, prospective trial compared a ventral approach (anterior cervical disk removal and instrumented fusion; 63 patients) *versus* dorsal approach (laminectomy with instrumented fusion or open-door laminoplasty at surgeon's discretion; 100 patients). Patients aged 45 to 80 yr with multilevel disease were enrolled at 15 North American hospitals. The primary outcome was change in the Short Form 36 physical component summary (SF-36) score (range, 0 [worst] to 100 [best]; minimum clinically important difference = 5) at 1 yr after surgery. Secondary outcomes were change in modified Japanese Orthopaedic Association scale score, complications, work status, sagittal vertical axis, health resource utilization, and changes in the Neck Disability Index and the EuroQol 5 Dimensions score. There was no significant difference in SF-36 mean improvement between ventral (6 points) and dorsal surgery (6 points; estimated mean difference, 0.3 [95% CI, −2.6 to 3.1]; $P = 0.86$). Six of the secondary outcomes showed no significant difference. Complications occurred in 48% of the ventral and 24% of the dorsal surgery groups (difference, 24% [95% CI, 9 to 38%]; $P = .002$) and included dysphagia (41% *vs.* 0%), neurological deficits (2% *vs.* 9%), reoperations (6% *vs.* 4%), and 30-day readmissions (0% *vs.* 7%). *(Article Selection: Beatrice Beck-Schimmer, M.D. Image: Adobe Stock.)*

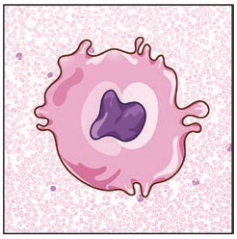
Take home message: A ventral surgical approach, compared to a dorsal approach, to treat cervical spondylotic myelopathy did not significantly improve patient-reported outcomes at 1 yr after surgery.



Patient characteristics and clinical outcomes of type 1 versus type 2 myocardial infarction. J Am Coll Cardiol 2021; 77:848–57. PMID: 33602466.

Myocardial infarction (MI) is now classified into five pathophysiological subtypes by the Universal Definition of MI task force. Type 1 MI is caused by a coronary thrombus. Type 2 MI is caused by a mismatch in myocardial oxygen supply-and-demand in the absence of coronary thrombosis. These subtypes may have specific clinical phenotypes and different clinical outcomes suggested by small single-center analyses. Using the U.S. National Readmissions Database, the authors compared characteristics and outcomes of type 2 (n = 37,765; 17%) *versus* type 1 (n = 216,657; 83%) myocardial infarction patients. Patients with type 2 were: older (71 *vs.* 69 yr; $P < 0.001$), more likely to be female (47% *vs.* 40%; $P < 0.001$), have heart failure (28% *vs.* 11%; $P < 0.001$), kidney disease (36% *vs.* 26%; $P < 0.001$), or atrial fibrillation (31% *vs.* 21%; $P < 0.001$); but had lower rates of coronary angiography (11% *vs.* 57%; $P < 0.001$), percutaneous coronary intervention (2% *vs.* 39%; $P < 0.001$), and coronary artery bypass grafting (0.4% *vs.* 7.8%; $P < 0.001$); and a lower risk of in-hospital mortality (adjusted odds ratio, 0.57 [95% CI, 0.54 to 0.60]). *(Article Selection: Jamie W. Sleigh, M.D. Image: M. Lane-Fall/Adobe Stock.)*

Take home message: The first national analysis of type 2 myocardial infarction, with the largest cohort size to date, confirms previous smaller analyses suggesting a specific cardiovascular phenotype and that in contrast to type 1 myocardial infarction management strategies remain very heterogeneous.



Primordial GATA6 macrophages function as extravascular platelets in sterile injury. Science 2021; 371:eabe0595. PMID: 33674464.

The pathogenesis of intraperitoneal adhesions, which are associated with significant clinical morbidity, is not well understood. Using inverted multiphoton intravital microscopy with highly sensitive detectors in a murine model (peritoneal pouch models with transmethothelial laser injury), this investigation found that fluorescence-labeled GATA6+ (a transcription factor) macrophages are abundantly present in the peritoneal fluid and passively transverse the peritoneal cavity in a respiration-dependent pattern, as they are recruited to sites of mesothelial injuries. Macrophage aggregation occurs rapidly within minutes similar to intravascular platelet aggregation and can be inhibited by EDTA and activated by adenosine triphosphate (ATP). Taking advantage of a targeted array of genetically modified mouse strains expressing fluorescence-labeled reporter proteins and knockout mouse models for specific cell adhesion proteins, the evolutionary conserved scavenger receptors MSR1 and MARCO, which recognize acetylated low-density lipoprotein but also bind a broad spectrum of polyanionic ligands with their positively charged cysteine-rich domains, were identified as major factors in macrophage super-aggregate formations (the precursor of peritoneal adhesions). Experiments with polyanionic molecules suggest that scavenger receptors of different macrophages bind to the same negatively charged polyanion bridging two adjacent macrophages. *(Article Selection: Michael Zaugg, M.D., M.B.A. Image: M. Lane-Fall/Adobe Stock.)*

Take home message: Inhibition of macrophage aggregation using scavenger receptor antagonists may be an attractive target to explore to prevent adhesions in the peritoneal cavity after surgery.