with adrenal insufficiency (86 *vs.* 48%; odds ratio, 6.7; $P < 0.0001$). No serious adverse events occurred with either study drug. No difference in 28-day mortality rates between groups was noted.

#### *Interpretation*

A single-bolus dose of etomidate was not associated with significant increases in morbidity or mortality compared with ketamine in patients admitted to intensive care unit, although use in patients with sepsis was inconclusive. Pending future studies, ketamine should be considered a valuable alternative for intubation in critically ill patients, particularly in septic patients. Etomidate should be used cautiously in critically ill patients with septic shock.

*Suggested by: Samir Jaber, M.D., Ph.D.*

### Intensive *versus* conventional glucose control in critically ill patients. N Engl J Med 2009; 360:1283–97

A large body of recent work supports the association of increased blood glucose levels in hospitalized patients with adverse clinical outcome. However, whether tight glycemic control improves mortality in intensive care unit (ICU) patients remains controversial. Several lines of evidence suggest that this strategy has favorable impact in specific patient subpopulations, including cardiac surgical patients, medical, or pediatric ICU patients. The aim of this prospective, randomized, nonblinded study was to examine the effect of tight *versus* conventional glycemic control on outcome in patients admitted to the ICU.

The primary end point was the mortality rate of any cause within 90 days after randomization. Target blood glucose level was 81–108 mg/dl (<180 mg/dl) in the intensive (conventional, respectively) glucose control group. Secondary outcome measures were survival time during the first 90 days, cause-specific death, duration of mechanical ventilation, renal-replacement therapy, and duration of stay in the ICU and hospital.

The two groups of patients (intensive control, $n = 3{,}054$; conventional control, $n = 3{,}050$) had similar baseline characteristics. The two treatment groups exhibited detectable glycemic separation (29 mg/dl). In contrast to recent previous trials, the 90-day mortality rate was increased in the intensive *versus* conventional glycemic control group (27.5 *vs.* 24.9%, $P = 0.02$). Overall, the distribution of proximal causes of deaths were similar in the two groups ($P = 0.12$). However, the rate of deaths from cardiovascular causes was higher in the intensive treatment group in comparison with the conventional treatment group (41.6 *vs.* 35.8%, $P = 0.02$). Noteworthy, the number of episodes of severe hypoglycemia (blood glucose level <40 mg/dl) was higher in the intensive glucose control group than in the conventional glucose control group (6.8 *vs.* 0.5%, $P < 0.001$). The median duration of ICU or hospital stay and days of mechanical ventilation or renal-replacement therapy was similar between the two groups. No difference in mortality was observed between medical and surgical ICU patients.

#### *Interpretation*

These data are in sharp contrast with recent studies, suggesting the beneficial impact of tight glycemic control in ICU patients. Study differences include multicenter *versus* single-center trials, differences between populations receiving parenteral *versus* enteral nutrition, disparities in steroid treatment, the blood glucose levels in the conventional control groups, and difficulties in achieving the targeted blood glucose in the tight control group. This study suggests that tight glycemic control does not offer additional benefit in ICU, mechanically ventilated, patients.

*Suggested by: Jean Mantz, M.D., Ph.D.*

## Perioperative Medicine

*J. Lance Lichtor, M.D., and Joseph F. Antognini, M.D., Editors*

### Incidence and sedation-related complications with propofol use during advanced endoscopic procedures. Clin Gastroenterol Hepatol July 14, 2009 (Epub ahead of print). doi: 10.1016/j.cgh.2009.07.008

Propofol is a popular sedative for endoscopic procedures because of its rapid onset of action and short duration of effect. The safe use of gastroenterologist-administered propofol is supported for advanced endoscopic procedures (*e.g.*, endoscopic retrograde cholangiopancreatography and endoscopic ultrasound). However, there are limited data on the administration of propofol by nurses and their ability to perform possible airway interventions required if patient rescue is necessary.

This single-institution prospective study evaluated the frequency of sedation-related complications associated with propofol use by three certified registered nurse anesthetists, under the direction of one anesthesiologist, in patients undergoing advanced endoscopic procedures including endoscopic retrograde cholangiopancreatography, endoscopic ultrasound, single-balloon or spiral overtube-assisted small-bowel enteroscopy, and enteral stenting. Sedation-related complications that were assessed included airway modifications (*e.g.*, chin lifts, modified face mask ventilation, and nasal airway), hypoxemia ($Sa_{O_2}$ <90%), hypotension requiring vasopressors, and early procedure termination.

Of 799 patients enrolled, endoscopic ultrasound and endoscopic retrograde cholangiopancreatography were the most common procedures performed (52.9 *vs.* 42.1%), and 61% of patients had an American Society of Anesthesiologists class of 3 or higher. The majority of patients showed no response to intubation (87.2%). Hypoxemia, hypotension, and premature termination occurred in 12.8%, 0.5%, and 0.6% of patients, respectively. No patients required bag-



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mask ventilation or tracheal intubation. One hundred fifty-four airway modifications were performed in 14.4% of patients, including chin lift (12.1%), modified face mask ventilation (3.6%), and nasal airway (3.5%). Male patients, patients with a higher body mass index, or patients with an American Society of Anesthesiologists class 3 or higher were most likely to need one or more airway modifications.

***Interpretation***

Propofol is useful for sedation for procedures such as endoscopy. In this study, where experienced certified registered nurse anesthetists performed sedation for advanced endoscopic procedures, 12.1% of patients needed a chin left and 12.8% experienced hypoxemia. Consistent with other studies, male sex, body mass index, and American Society of Anesthesiologists class 3 or higher were independent predictors of airway modifications. It is not clear if the findings would be similar if individuals not as experienced as certified registered nurse anesthetists administered sedation.

*Suggested by: Mark Warner, M.D.*

## Perioperative safety in the longitudinal assessment of bariatric surgery. N Engl J Med 2009; 361:445–54

Improved overall health, including remission of diabetes, improved cardiovascular disease, and reduced risk of death, has been demonstrated in patients who underwent bariatric surgery. However, safety concerns have increased with increasing frequencies of bariatric surgeries performed. The Longitudinal Assessment of Bariatric Surgery consortium conducts a prospective, multicenter, observational cohort study (Longitudinal Assessment of Bariatric Surgery-1) in consecutive patients undergoing bariatric surgery.

This study reports the incidence of and factors associated with 30-day safety outcomes in adult patients ($N = 4{,}776$) enrolled in Longitudinal Assessment of Bariatric Surgery-1 who underwent an initial bariatric surgical procedure. Roux-en-Y gastric bypass was the most common procedure performed in 3,412 patients, 87.2% of which were laparoscopic. Most patients (82.1%) had at least one coexisting condition (*e.g.*, hypertension, 55.1%; obstructive sleep apnea, 48.9%; diabetes, 33.2%; and asthma, 23.1%). Patients undergoing open Roux-en-Y gastric bypass generally had higher body mass index and more coexisting conditions ($P < 0.001$) compared with laparoscopic techniques.

Within 30 days of surgery, 0.3% of patients died, and the composite end point of death, deep vein thrombosis (DVT), reintervention, or failure to be discharged by 30 days occurred in 4.1% of patients. Death and the composite end point occurred most frequently in patients who underwent open Roux-en-Y gastric bypass. Abdominal reoperation and endoscopic intervention (2.6% and 1.1%, respectively) were the most common components of the composite end point. The risk of the composite end point was lowest among patients who did not have a history of DVT, venous thromboembolism, obstructive sleep apnea, and who were in the middle range of body mass index. Patients who underwent gastric bypass had a higher risk of adverse events regardless of preexisting characteristics (*e.g.*, high body mass index or DVT) compared with patients who underwent adjustable banding. Only 13.5% of procedures and 12.2% of events occurred in patients who had a body mass index less than 40 $kg/m^2$.

***Interpretation***

Bariatric surgery is an effective and safe procedure. Adverse events that included death, DVT, venous thromboembolism, reintervention, or failure to be discharged by 30 days after surgery were low. Risk increased for those with a history of DVT, pulmonary embolus, obstructive sleep apnea, or impaired functional status. Patients undergoing gastric bypass experienced more adverse events compared with those who underwent adjustable banding.

*Suggested by: J. Lance Lichtor, M.D.*

## Timing of antimicrobial prophylaxis and the risk of surgical site infections. Ann Surg 2009; 250:10–16

Antimicrobial prophylaxis (AMP) can reduce the risk of surgical site infections (SSIs). Recent guidelines suggest that the administration of perioperative antibiotics should occur within 1 h (parenteral AMP) or within 2 h (vancomycin or fluoroquinolones) before incision. To further explore the relationship among timing, duration, and intraoperative redosing of surgical AMP and the risk of SSI, a prospective, randomized, multicenter study was conducted. This was an ancillary study to the multisite Trial to Reduce Antimicrobial Prophylaxis Errors study.

Patients ($N = 4{,}472$) from 29 hospitals undergoing cardiac, hip/knee arthroplasty, or hysterectomy were randomly selected. Most hospitals (79.3%) were teaching hospitals, and the majority (55.2%) had fewer than 250 beds. The majority of patients (76%) received cephalosporins alone or other antibiotics, whereas 13%, 4.9%, and 5.3% of patients received cephalosporins plus vancomycin, vancomycin only, or fluoroquinolones, respectively. One hundred thirteen infections were detected in 109 patients. The majority of infections (69%) were diagnosed after initial hospital discharge. The association between timing and risk of SSI was statistically significant ($P = 0.04$). There was also a statistically significant risk ($P = 0.02$) associated with administration of AMP after incision. When AMP was administered within 30 min before incision, the incidence was 1.6% compared with 2.4% between 31 and 60 min (odds ratio = 1.74; 95% confidence interval = 0.98–3.08). Intraoperative AMP redosing was administered in 21% of 690 surgeries lasting longer than 4 h. Risk of SSI was lower in redosing cases only if the preoperative dose was administered in the recommended time frame. Increased risk was also associated with



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the lack of postoperative AMP; however, this analysis was confounded by procedure type and hospital.

### Interpretation

Antibiotic prophylaxis is most effective when administered less than or equal to 30 min before surgical incision, although the risk only slightly increases when administered 31–120 min before incision. The risk substantially increases when antibiotics are administered after incision. This study reinforces antibiotic timing guidelines. Because elective surgeries have a low risk of SSI, this study may not be adequately powered to address specific details of nonelective surgeries, timing of antibiotic administration, and SSI.

*Suggested by: Hervé Dupont, M.D., Ph.D.*

## Pain Medicine

*Timothy J. Brennan, Ph.D., M.D., Editor*

### A randomized trial of vertebroplasty for painful osteoporotic vertebral fractures. N Engl J Med 2009; 361:557–68

Osteoporotic vertebral fractures are a common cause of pain and disability occurring in 1.4 million people worldwide and are associated with increased mortality and direct care expenditures as high as 18 billion US dollars. Observational studies suggest an immediate and sustained reduction in pain after vertebroplasty, the percutaneous injection of cement (polymethylmethacrylate) into the affected vertebral body. Despite the paucity of randomized, controlled trials evaluating the true safety and efficacy of vertebroplasty, the number of vertebroplasty procedures doubled in the past 6 yr.

This blinded, randomized, parallel-group, multicenter, placebo-controlled trial analyzed the short-term efficacy of vertebroplasty for alleviating pain and improving physical function in patients with painful osteoporotic vertebral fractures. Patients with back pain of less than 12 months' duration and one or two recent fractures (≥grade 1) were randomly assigned to undergo either vertebroplasty or a sham procedure. Gentle tapping guided the needle through the pedicle into the anterior two thirds of the fractured vertebral body, and images were recorded to ensure the correct position before polymethylmethacrylate was injected. Patients in the sham group underwent the same procedures, except the vertebral body was gently tapped, and polymethylmethacrylatewas prepared.

Although significant mean reductions in overall pain occurred in the 71 patients enrolled who completed the 6-month follow-up, reductions were similar in the vertebroplasty and sham groups at 3 months (2.6 ± 2.9 and 1.9 ± 3.3, respectively). There were no significant between-group differences in any other health-related outcome scores except for one of three measurements at 1 week, which favored the sham group. Results were consistent irrespective of the duration of symptoms, sex, treatment center, or presence or absence of previous vertebral fractures. Although use of opioids decreased over time, there were no between-group differences.

### Interpretation

Both vertebroplasty and placebo were equally efficacious for pain relief in patients with painful vertebral compression fractures. The significant analgesic effect of placebo may warrant investigating the effectiveness of bupivacaine infiltration of the pedicles for pain relief of fractured vertebrae.

*Suggested by: Salim Hayek, M.D., Ph.D.*

### A randomized trial of vertebroplasty for osteoporotic spinal fractures. N Engl J Med 2009; 361:569-79

The Investigational Vertebroplasty Safety and Efficacy Trial (INVEST), a global, multicenter, randomized, controlled trial, evaluated the efficacy of polymethylmethacrylate (PMMA) infusion in vertebroplasty for patients with painful osteoporotic compression fractures compared with a simulated procedure in the absence of PMMA. Patients (>50 yr of age) with new fractures (<1-yr old) between vertebral levels T4 and L5, with inadequate pain relief with standard medical therapy, and a current rating for pain intensity of more than or equal to 3 were enrolled. All procedures were performed by experienced practitioners having performed a mean of approximately 250 procedures. PMMA was infused under constant lateral fluoroscopy into the vertebral body until PMMA reached to the posterior aspect of the vertebral body or entered an extraosseous space. During the control intervention, vertebral and physical cues were given, and the methacrylate monomer was opened to simulate mixing of PMMA.

The primary outcomes at 1 month did not differ significantly between the two study groups (vertebroplasty, $n = 68$; control, $n = 63$). The mean Roland-Morris Disability Questionnaire scores were 12.0 ± 6.3 and 13.0 ± 6.4, and the mean pain-intensity ratings were 3.9 ± 2.9 and 4.6 ± 3.0 in the vertebroplasty and control groups, respectively. Both groups had substantial improvement in back-related disability and pain immediately (3 days) after the procedure that was maintained at 1 month, with similar improvement in both groups. Pain measures, quality of life, or proportion of patients with clinically meaningful improvement in physical disability were similar between the two groups. Crossover to the alternative treatment did not demonstrate any additional benefit.

### Interpretation

This trial showed no significant benefit of vertebroplasty compared with the sham procedure during the 6-month follow-up period. Larger trials may identify subgroups of patients that benefit from vertebroplasty. In this trial, duration



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