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

Perioperative Medicine

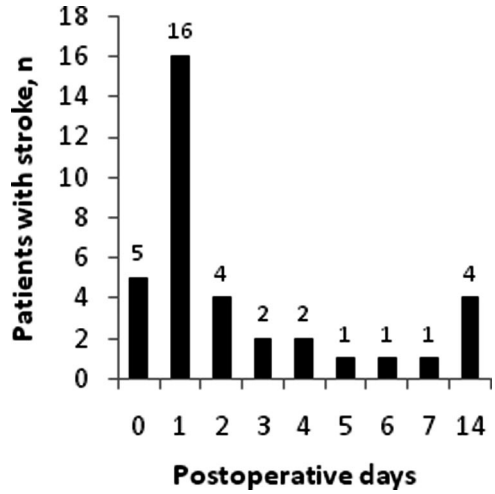
J. Lance Lichtor, M.D., and Joseph F. Antognini, M.D., Editors

Perioperative stroke after total joint arthroplasty: Prevalence, predictors, and outcome. J Bone Joint Surg Am 2010; 92:2095–101

Joint arthroplasty is becoming a more common procedure and is currently offered to older patients, who are at greater risk of stroke. Therefore, although the rate of stroke after general surgery is low (0.2%), the overall risk of stroke after joint arthroplasty is increasing and may result in increased mortality.

Using a case-controlled retrospective study from a prospective database, this study analyzed the incidence of perioperative stroke at a single institution among patients undergoing total joint arthroplasty during an 8-yr study period. Discharge abstracts and daily complication forms were used to identify patients diagnosed with cerebrovascular accident or stroke. Patients who had a stroke after hospital discharge were also included through evaluation of electronic medical records.

Of 18,745 patients who underwent primary or revision total knee or total hip arthroplasty, 36 patients (0.2%) had a stroke during hospital stay or within 30 days of surgery. The mean age of patients having a stroke was 68.2 yr. The majority (94%) were ischemic and two were hemorrhagic. The rate of mortality at 1 yr was 25%, with four patients dying during hospital stay. A history of coronary artery disease, cerebrovascular disease, atherosclerotic disease, or noncoronary cardiac disease were significantly associated with stroke. Independent predictors of stroke included history of noncoronary cardiac disease (odds ratio = 4.13), urgent *versus* elective surgery (odds ratio = 5.89), general anesthesia (odds ratio = 3.54), and intraoperative arrhythmia or changes in mean heart rate during surgery (odds ratio = 1.06). Stroke occurred most often on postoperative day 1.



Interpretation

In an analysis of perioperative stroke at a single institution for patients undergoing total joint arthroplasty, the authors found the incidence to be 0.2–0.4% in patients aged 75 yr or older. As expected, patients who suffered a stroke had a greater incidence of in-hospital mortality, discharge to a medical or chronic care facility *versus* home, and a longer hospital length of stay.

Risk assessment for respiratory complications in paediatric anaesthesia: A prospective cohort study. Lancet 2010; 376:773–83

Perioperative respiratory complications in children. Lancet 2010; 376:745–6

Perioperative respiratory adverse events are a major cause of morbidity and mortality in pediatric patients receiving anesthesia. With increasing rates of pediatric asthma and a rising incidence of upper respiratory tract infections, the rates and risk of perioperative respiratory adverse events have also increased. To help reduce the rate of this complication, introduction of an appropriate risk-assessment questionnaire would be helpful.

Using a large cohort (N = 9,297) prospective study of children undergoing general anesthesia for surgical or medical interventions at a single institution, family medical history and perioperative respiratory adverse event data were collected. A modified form of the International Study of Asthma and Allergies in Childhood questionnaire was used by anesthetists on the day of surgery. Information about passive or active smoking was also included.

Mean patient age was 6.21 yr, 60% were boys, and most (65%) were undergoing elective procedures. Baseline respiratory factors were low in the majority of patients: 66% had never had an upper respiratory tract infection, 85% had not had a wheezing attack within 12 months, 69% did not have a family history of asthma, and 76% did not have a family history of rhinitis. Overall, 15% of patients had perioperative respiratory adverse events, including oxygen desaturation (10%), coughing (7%), laryngospasm (4%), airway obstruction (4%), bronchospasm (2%), and stridor (1%). The rate of adverse events was higher among patients who had urgent *versus* elective procedures (17 *vs.* 14%; $P = 0.001$).

Factors	Risk of Adverse Events
Upper respiratory tract infection, < 2 wk	Increased
Family history of asthma, atopy, or smoking	Increased
Intravenous *vs.* inhalational induction	Decreased
Inhalational *vs.* intravenous maintenance	Decreased
Pediatric specialist	Decreased
Face mask anesthetic *vs.* tracheal intubation	Decreased

Interpretation

In a large, prospective study of children who underwent general anesthesia, increased occurrence of perioperative respiratory symptoms and events were found among those with the following characteristics: eczema, family history of asthma, upper respiratory infection within 2 weeks of the procedure, rhinitis, exposure to tobacco smoke, and induction with propofol rather than sevoflurane. Laryngospasm frequency decreased with increasing age. An accompanying editorial notes that this large study adds significantly to our understanding of perioperative respiratory adverse events in a cross-section of children undergoing surgery.

Acute glucose elevation is highly predictive of infection and outcome in critically injured trauma patients. Ann Surg 2010; 252:597–602

Maintenance of glucose concentrations is a highly regulated process that may be altered or impaired as a result of traumatic injury. Hyperglycemia has been associated with increased intensive care and hospital length of stay, infection, and mortality.

To evaluate a computational and graded algorithmic model to predict infection and outcomes among critically injured trauma patients, a large, prospective study was conducted with intensive care unit patients. After glucose stabilization (48 h with no significant change), daily monitoring for acute glucose elevation was conducted.

The majority of patients were men (77%) admitted for blunt injury (85%). Of the 2,200 patients observed, only 1,236 achieved glucose normalization and stabilization and were included in the study. Twenty-six percent of patients experienced infections within the first 2 weeks of hospitalization. When stratified by acute glucose elevation classification class I–IV, the most common infections were bloodstream and catheter-related (33%), respiratory (28%), intraabdominal (16%), or genitourinary (16%). The algorithm demonstrated specificity and sensitivity with positive predictive value for infection in the acute glucose elevation class IV group. Mortality was highest in the class III and IV groups ($P < 0.001$). The number of ventilator days, intensive care unit length of stay, and hospital length of stay were also significantly greater among patients with class III and IV acute glucose elevation ($P < 0.001$).

Interpretation

Hyperglycemia can have adverse effects on trauma patients during the postoperative period. These data show that hyperglycemia was associated with increased incidence of infection, need for ventilation, and mortality in trauma patients. Therefore, glucose elevation should be monitored to help predict and improve patient outcomes.

Endovascular repair of blunt traumatic thoracic aortic injuries: Seven-year single-center experience. Arch Surg 2010; 145:679–83

The second most common cause of death as a result of blunt trauma is blunt thoracic aortic injury. The mortality rate for these patients using standard-of-care open repair of blunt thoracic aortic injury is 5–28%. Endovascular stent grafts may provide a faster way to treat injury and improve mortality.

In a retrospective analysis of 24 consecutive patients, the efficacy of thoracic endovascular aortic repair was assessed during a 7-yr study period. Imaging (chest roentgenogram and computed tomography scan) was used to identify the extent of injury and measure proximal and distal neck length and aortic diameter. Patients underwent follow-up imaging studies at 1, 7, 12, and 24 months, and then every 2–3 yr after aortic repair.

Of 24 patients, 71% were men with a mean age of 41 yr. The majority of these patients had been injured in motor vehicle crashes. Mean injury severity score was 43. In 75% of patients, thoracic endovascular aortic repair was performed within 24 h of injury. Based on angiography and computed tomography results at the time of intervention, thoracic endovascular aortic repair was successful in all patients. One patient died of multisystem organ failure as a result of other associated injuries. Overall 30-day mortality was 4%. Access site complications occurred in two patients (8%) and one patient required a second intervention because of a collapsed device. One death was reported from unrelated causes after a mean follow-up time of 21 months. To date, there have been no additional device failures or complications.

Interpretation

Thoracic aorta injury after blunt trauma carries high rates of mortality. Open repair is the usual manner in which these injuries are treated. However, this small study showed that endovascular repair is a potential alternative that is effective and does not increase complications. Future larger, prospective trials are warranted.

Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med 2010; 363: 1597–607

At least 30% of patients with severe symptomatic aortic stenosis do not undergo surgery because of high surgical risk. However, among untreated patients, the rate of death is 50% within the first 2 yr of symptoms. Transcatheter aortic-valve implantation (TAVI) is a new procedure that may benefit patients at high surgical risk.

The PARTNER (Placement of AoRTic TraNscathetER Valves) Trial is a multicenter study that compared TAVI with standard therapy in patients with severe aortic stenosis. Trial investigators noted patients who were not suitable candidates for surgery. Patients had an aortic-valve area of less than 0.8 cm^2, a mean aortic valve gradient of at least 40

mmHg, a peak aortic jet velocity of at least 4.0 m/s, and class II–IV symptoms on the New York Heart Association functional classification system. Patients deemed to be not good candidates for surgery were randomly assigned to TAVI or standard therapy.

Overall, 358 patients at 21 sites were randomly assigned to TAVI (n = 179) or standard therapy (n = 179). Thirty-day mortality rates were 5.0% and 2.8% ($P = 0.41$) whereas 1-yr mortality was 30.7% and 50.7% ($P < 0.001$), respectively. The rate of death as a result of cardiovascular causes was also lower at 1 yr in the TAVI group (20.5 *vs.* 44.6%; $P < 0.001$). However, more patients in the TAVI group experienced major strokes (5.0 *vs.* 1.1%; $P = 0.06$) at both 30-day and 1-yr follow-up. Similarly, the frequency of major vascular complications and bleeding were also higher in the TAVI group.

Interpretation

Aortic stenosis is one of the most serious valvular diseases, but operative repair can be dangerous in critically ill patients. In this study, transcatheter aortic valve implantation was used to treat severe aortic stenosis in patients with coexisting disease. Although TAVI patients had lower mortality and better cardiac function than standard-care patients, their incidence of stroke was higher.

Critical Care Medicine

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

Acute lung injury is an independent risk factor for brain hypoxia after severe traumatic brain injury. Neurosurgery 2010; 67:338–44

Critically ill patients with traumatic brain injury are at higher risk for pulmonary complications and poor outcomes. Despite the high frequency of these events, relatively little is known regarding the relationship between brain tissue oxygen tension ($PbtO_2$) and lung function. A large cohort study was conducted to analyze the association between brain tissue and systemic oxygenation.

A retrospective study of a prospective observational database of patients with traumatic brain injury admitted to a level I trauma center was conducted. All patients were intubated and mechanically ventilated and were monitored for $PbtO_2$ and intracranial pressure.

Of 78 patients, the majority (78%) were men. Median Acute Physiology and Chronic Health Evaluation II score was 20, and 55% had a favorable outcome at 30 days. $PbtO_2$ was less than 20 mmHg in 23% of patients with an unfavorable outcome, compared with only 8% of patients with a favorable outcome ($P < 0.001$). Lower PaO_2/FIO_2 ratios were also significantly associated with reduced $PbtO_2$ values. Overall, there was a linear correlation among $PbtO_2$ and PaO_2/FIO_2 ($P < 0.01$), PaO_2 ($P < 0.01$), and SaO_2 ($P < 0.03$). Acute lung injury was observed in 60% of patients, and of these 85% had compromised $PbtO_2$ values compared with 54% of patients without acute lung injury. A PaO_2/FIO_2 ratio lower than 300 was an independent risk factor for compromised $PbtO_2$ in patients with traumatic brain injury (odds ratio = 2.13).

Interpretation

This retrospective observational study suggests that $PbtO_2$ strongly correlates with systemic oxygenation in patients with severe, nonpenetrating brain injury. Patients with severe brain injury who also had acute lung injury had decreased brain tissue oxygenation. These results support the use of lung-protective strategies aimed at improving oxygenation to limit secondary hypoxic insults to the brain.

Constipation in long-term ventilated patients: Associated factors and impact on intensive care unit outcomes. Crit Care Med 2010; 38:1933–8

Constipation is a common gastrointestinal complication of mechanical ventilation. Despite the known associations of constipation with prolonged intensive care unit (ICU) length of stay and increased mortality, constipation has not been widely studied in patients.

Using a prospective observational design, this study aimed to characterize the causes of constipation in patients in the ICU receiving mechanical ventilation for more than 6 days. Patients admitted to the ICU during the 41-month study period were observed for stool passage. Management of constipation was not protocolized.

Of 609 patients admitted to the ICU and included in the study, approximately half (42%) had "early" (less than 6 days) passage of stools and 58% had "late" (6 days or more) passage of stools. Baseline characteristics and time to enteral feeding were not significantly different between these two study groups. Length of ICU stay (15 *vs.* 17 days), duration of mechanical ventilation (11 *vs.* 14 days), central venous catheter use (10 *vs.* 12 days), and mortality rates (47 *vs.* 107%) were significantly different in the early *versus* late passage of stool groups. Overall, the median time until the first passage of stools was 6 days. A PaO_2/FIO_2 ratio lower than 150 mmHg (hazard ratio = 1.40) and systolic blood pressure of 70–89 mmHg (hazard ratio = 1.48) or less than 69 mmHg (hazard ratio = 1.29) were associated with delayed defecation.

Interpretation

This paper highlights a frequent and potentially harmful adverse event in ICU patients, constipation. Whether constipation is a surrogate marker of severity of illness or a predictor of poor outcome cannot be established from this study. However, an association between constipation lasting

more than 6 days and worsened ICU outcome, including mortality, is suggested.

Intensive care-acquired hypernatremia after major cardiothoracic surgery is associated with increased mortality. Intensive Care Med 2010; 36:1718–23

Surgical patients receiving large volumes of infusions for fluid management are at risk for serum sodium imbalances. Although often studied in medical intensive care units (ICU), hypernatremia in surgical ICU patients has not been studied as widely.

To identify the incidence of hypernatremia (serum sodium concentration higher than 145 mM) after major cardiac surgery and to determine whether its development is associated with adverse outcomes, a retrospective analysis of a prospectively collected database was performed. During the 8-yr study period, data were collected from 2,314 patients scheduled for any of the following procedures: cardiac surgery with cardiopulmonary bypass, coronary artery bypass grafting with or without cardiopulmonary bypass, thoracic aortic surgery with cardiopulmonary bypass, heart or lung transplant surgery, scheduled insertion of a cardiac assist device, operation on the descending aorta, or thromboendarterectomy of the pulmonary arteries. Only patients without hypernatremia or hyponatremia at ICU admission were included.

The average age of ICU patients was 62 yr, most (64%) were male, and had undergone either coronary artery (30%) or valve (26%) surgery. Ten percent of patients acquired hypernatremia during ICU stay, with the first incident occurring on day 4 of ICU stay. Patients who died in the ICU (n = 200) had higher Simplified Acute Physiology Score II and euroSCORE totals, lower body mass indexes, longer surgery duration, higher preoperative sodium concentrations and ICU-acquired hypernatremia, and higher postoperative lactate concentration.

	ICU-acquired Hypernatremia	
Variable	Yes (n = 221)	No (n = 2,093)
Intensive care unit	—	—
Mortality, %	19	8*
Stay, d	17	3*
Preoperative risk	6	6*
Illness severity	34	26*

Preoperative risk was evaluated via euroSCORE whereas illness severity was evaluated by Simplified Acute Physiology Score II.
* $P < 0.001$.
ICU = intensive care unit.

Interpretation

In this retrospective, large cohort study, hypernatremia was present in 10% of patients and was identified as a predictor of mortality at 28 days. Although this study has limitations, it suggests that treatments aimed at maintaining serum sodium concentrations below 145 mM should be considered in surgical ICU patients.

Neuromuscular blockers in early acute respiratory distress syndrome. N Engl J Med 2010; 363:1107–16

Acute respiratory distress syndrome occurs in critically ill patients and may be fatal in as many as 60% of patients. Although current guidelines recommend the use of neuromuscular blocking agents in mechanically ventilated patients, further investigation of outcomes (including mortality) are needed.

A multicenter, randomized, placebo-controlled, double-blind trial was conducted to assess the effects of a shorter period of treatment with cisatracurium besylate (a neuromuscular blocking agent) early in the course of severe acute respiratory distress syndrome. At 20 intensive care units in France, patients with endotracheal mechanical ventilation for acute hypoxemic respiratory failure received an intravenous infusion of either cisatracurium besylate (15 mg bolus, then 37.5 mg continuous infusion for 48 h) or placebo.

Compared with the placebo group—and after adjustments for PaO_2/FIO_2 ratio, Simplified Acute Physiology Score II, and plateau pressure—the hazard ratio for death at 90 days was 0.68 in the cisatracurium group ($P = 0.04$). In patients with PaO_2/FIO_2 ratios lower than 120, 90-day mortality was lower in the cisatracurium *versus* placebo group (30.8 *vs.* 44.6%; $P = 0.04$). Likewise, 28-day mortality was lower in the cisatracurium *versus* placebo group (23.7 *vs.* 33.3%; $P = 0.05$) as were the number of ventilator-free days (53.1 *vs.* 44.6 days; $P = 0.03$).

Interpretation

In this prospective, randomized, double-blind, multicenter, placebo-controlled trial, early administration of cisatracurium for 48 h after severe acute respiratory distress syndrome improved survival at 90 days and decreased ventilator time without increasing muscular weakness. This study should encourage the use of muscle relaxants in intensive care unit patients at the early stage of severe acute respiratory distress syndrome.

Pain Medicine

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

Tanezumab for the treatment of pain from osteoarthritis of the knee. N Engl J Med 2010; 363:1521–31

There is a need for improved therapies with a better side-effect profiles for patients with osteoarthritis of the knee. Tanezumab, a humanized immunoglobulin G2 monoclonal

antibody directed against nerve growth factor (NGF), has shown potential in phase I clinical trials.

This randomized, placebo-controlled, proof-of-concept study assessed the safety, side-effect profile, and efficacy of repeated doses of tanezumab in patients with advanced osteoarthritis of the knee. Adult patients with radiographically confirmed osteoarthritis were randomized to receive placebo or tanezumab (10, 25, 50, 100, or 200 μg/kg) intravenously on days 1 and 56 if they were (1) willing to take nonopiate pain medications, or (2) had unsatisfactory pain response to opiates. The primary study endpoints were the average change from baseline in pain while walking and the patient's global assessment of response to therapy.

Patients (N = 444) were aged 57–60 yr and had similar baseline pain characteristics across all six study groups. All doses of tanezumab were associated with an improvement in pain response. Mean pain reduction from baseline ranged from 31.0 to 45.2 points in the tanezumab groups, compared with 15.5 points in the placebo group ($P < 0.001$). Increase in patient global assessment of response to therapy also favored the tanezumab groups (16.3–23.7 *vs.* 9.2 points, respectively; $P \leq 0.001$). Improvements were seen as early as 1 week after initiation of therapy. Reductions in overall knee pain were also observed (43–62 *vs.* 23%, respectively; $P < 0.001$). Headache (8.9%), upper respiratory infection (7.3%), and paresthesia (6.5%) were the most common adverse events in the tanezumab groups. The highest dose of tanezumab (200 μg/kg) was associated with the most adverse events.

Interpretation

Antitumor necrosis factor therapy has produced remarkable benefits in several disease states. This is the first clinical study of anti-NGF therapy in patients. Anti-NGF showed remarkable efficacy against osteoarthritis pain. In general, adverse events were small. The article also notes the recent findings of osteonecrosis in some patients treated with anti-NGF therapy. Although it is possible anti-NGF therapy may have beneficial effects in other clinical pain conditions, concerns regarding adverse events are noted.

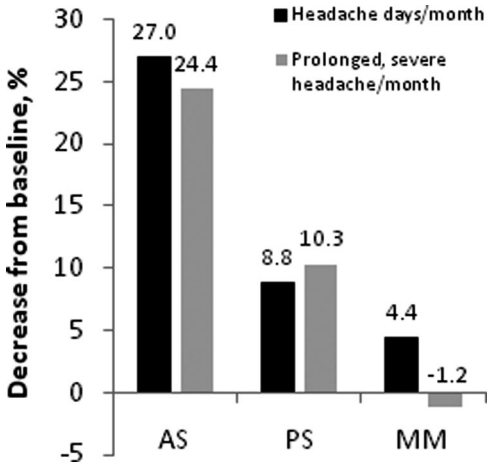
Occipital nerve stimulation for the treatment of intractable chronic migraine headache: ONSTIM feasibility study. Cephalalgia 2010 doi: 10.1177/0333102410381142

Occipital nerve stimulation for chronic migraine—interpreting the ONSTIM feasibility trial. Cephalalgia 2010 doi: 10.1177/0333102410383591

Chronic migraine is a disabling disorder. For many patients, migraine pain remains refractory to standard treatments, despite recent progress. Subcutaneous occipital nerve stimulation has demonstrated efficacy in patients with headache disorders, including chronic migraines.

A prospective, multicenter, randomized, blinded, placebo-controlled feasibility study was conducted to assess preliminary safety and efficacy for occipital nerve stimulation treatment of patients with chronic migraines. Patients were randomly assigned (2:1:1) to receive adjustable stimulation (n = 28), preset stimulation (n = 16), or medical management (n = 17). Patients in the adjustable stimulation group were instructed to keep the stimulator "on" and adjust it as necessary to minimize pain. The preset stimulation group was a control group who received preset stimulation rather than adjustable stimulation. Outcomes were assessed 3 months after implantation.

Patients were aged 41–50 yr, with a migraine history of at least 18 yr, and an average chronic migraine headache history of 10 yr. Compared with baseline, all three groups demonstrated reductions in the number of headache days per month (1–9 days) and duration of prolonged severe headaches per month (1–5 days). Overall, pain intensity was also reduced for the adjustable stimulation (1.5 days), preset stimulation (0.5 days), and medical management (0.6 days) groups. Of the 51 patients who had successful implant procedures, 56 adverse effects were observed in 36 patients. There were three serious adverse effects that required hospitalization. Lead migration occurred in 24% of patients.



Interpretation

Occipital nerve stimulation, like spinal cord stimulation, has been used to manage chronic headache. This preliminary study demonstrated efficacy of occipital nerve stimulation for chronic migraine headache. An accompanying editorial noted the difficulties in clinical trials and proper controls in these populations and suggests that, based on the positive results from this trial, further studies are needed.

Attentional and emotional mechanisms related to pain as predictors of chronic postoperative pain: A comparison with other psychological and physiological predictors. Pain 2010; 151:722–31

Many surgical patients experience chronic postoperative pain. Postoperative pain can be influenced by psychological factors, such as attentional bias for pain-related information. However, this factor has only been studied with acute postoperative pain.

A prospective study was conducted to determine whether attentional and emotional mechanisms of pain processing predict long-term postoperative pain in patients undergoing chest malformation corrective surgeries. Men with congenital malformations of the thorax and without a history of chronic pain conditions, major surgery, or psychological disorders were included (N = 84). Outcomes were assessed at baseline and at 3 and 6 months after surgery.

Twenty-five percent of patients had postoperative pain at 3 months and 14% at 6 months. High pain-related disability was found in 54% of patients at 3 months and 13% at 6 months. Positive words, assessed in the dot-probe task (d = 0.5074 and 0.6475, respectively), and morning cortisol concentration (d = 0.6615 and 0.5074, respectively) were potent predictors of pain intensity. Multivariate analysis confirmed that attentional preference for positive words (6 months; $P = 0.031$), temporal summation of heat pain (3 months; $P = 0.025$), and heat pain thresholds (3 months; $P = 0.028$) were significant predictors for pain intensity after surgery. The Pain Vigilance and Awareness Questionnaire was also found to be a predictor for pain-related disability at 3 and 6 months (d = 0.7131 and 0.5237, respectively).

Interpretation

Chronic pain after surgery is receiving greater attention. In this prospective study of young men undergoing pectus repair, a variable in the Pain Vigilance and Awareness Questionnaire predicted those with persistent pain. Other factors measured before surgery that predicted chronic pain were an attentional bias towards positive stimuli, and low pressure and high cold pain thresholds.