

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

Perioperative Medicine

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

Submaximal cardiopulmonary exercise testing predicts complications and hospital length of stay in patients undergoing major elective surgery. *Ann Surg* 2010; 251:535–41

Current preoperative risk stratification methods for non-cardiac surgery may not be sensitive enough to accurately predict postoperative complications. Furthermore, these techniques may be subjective. In contrast, cardiopulmonary exercise testing, a noninvasive, objective test, determines cardiorespiratory reserve, including the anaerobic threshold (AT), which may be a better indicator of mortality.

A prospective, single-center cohort study compared an objective, noninvasive technique of measuring cardiorespiratory reserve with a standard questionnaire-based assessment of functional capacity as preoperative assessments of patient risk for postoperative complications. Consecutive patients (N = 171) with low subjective functional capacity (metabolic equivalent score < 7) being assessed for major surgery underwent cardiopulmonary exercise testing and completed a Veterans Activity Score Index questionnaire. Complication rates were assessed on postoperative day 7.

Patients who had more than one complication had a lower AT compared to those with 0 or one complication (9.1 vs. 11.9; $P = 0.001$). AT demonstrated high predictive sensitivity, specificity, and accuracy (88%, 79%, and area under the curve = 0.85, respectively) using an optimum AT of 10.1 ml/kg/min. Independent predictors of complications included not only AT but also Veterans Activity Score Index and emergency surgical reintervention. No major adverse events during cardiopulmonary exercise testing were reported.

Interpretation

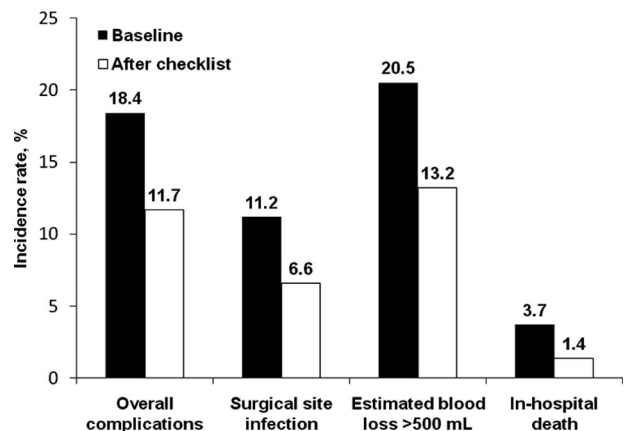
Predicting postoperative complications can often be difficult. These authors found that cardiopulmonary exercise testing had superior predictive value for postoperative complications compared to a subjective assessment of activity. These data suggest that moderate- and high-risk patients might benefit from preoperative exercise testing to determine complication risk.

Effect of a 19-item surgical safety checklist during urgent operations in a global patient population. *Ann Surg* 2010; 251:976–80

Implementation of the World Health Organization 19-item Surgical Safety Checklist was associated with significant reductions in complications and deaths. However, use of a checklist during urgent intervention may delay workflow and, consequently, the delivery of therapeutic care.

Therefore, to assess the impact of implementation of the World Health Organization checklist, a prospective study was conducted at eight hospitals worldwide, pre- and postintervention. Clinical process and outcome data for 1,750 consecutively enrolled patients aged 16 yr or older undergoing urgent noncardiac surgery were collected before (n = 842) and after (n = 908) the introduction of the World Health Organization Surgical Safety Checklist.

Complication rate, death rates, and estimated blood loss all significantly decreased after the checklist was introduced. Importantly, adherence to six measured safety steps improved from 18.6% to 50.7% ($P < 0.0001$).



Interpretation

Emerging data suggest that using simple checklists immediately before surgery can decrease complications. These authors found that using a 19-point checklist at several hospitals worldwide substantially lowered complication and death rates for urgent surgeries. The checklist included simple questions, such as presence of allergies, surgical site, and whether airway management would be difficult. All hospitals should consider using these checklists for urgent operations.

The role of reputation in U.S. News & World Report's rankings of the top 50 American hospitals. *Ann Intern Med* 2010; 152:521–5

The *U.S. News & World Report's* annual rankings of the top 50 American hospitals in 12 specialties are often used as marketing tools and as examples of models for health care reform. However, such rankings are based on a combination of subjective and objective measures of quality. In addition, the role of reputation alone in determining the relative standings has not been quantified.

A cross-sectional study was conducted to quantify the role of reputation in determining relative standings for the top 50 hospitals in the 2009 edition of *U.S. News & World Report's* rankings in each of 12 specialties. Subjective reputation was assessed using survey responses from 250 randomly selected board-certified physicians. Subjective and objective components of the *Report's* rankings were used to calculate a specialty-specific index of hospital quality (*i.e.*, *U.S. News* score).

Only 4% of hospitals had reputation scores greater than 30. On average, rankings based on reputation score alone agreed with *U.S. News & World Report's* overall rankings (100%, 97%, 91%, and 89% of the time for the top hospital, top five hospitals, top 10 hospitals, and top 20 hospitals, respectively). This trend was consistent in all 12 specialties. Other components of the *U.S. News* score, such as risk-adjusted mortality ratio, patient safety index, and nurse-to-patient ratio, were similar across the top 50 hospitals.

Interpretation

The current push for “pay for performance” highlights the demand for objective information about hospital quality. Some news organizations provide rankings of hospitals, but these rankings might be based more on subjective reputations and less on objective data.

Trends, major medical complications, and charges associated with surgery for lumbar spinal stenosis in older adults. *JAMA* 2010; 303:1259–65

Despite the increase in spinal surgery in recent years, there are no clear consensus guidelines for choosing one specific procedure over another. As the benefit-risk profile is different with each procedure, it is important to understand which procedures are being used as well as the rate of associated complications. Furthermore, comorbidities, which are common in older patients, may increase risk of complications and may also be considered when selecting a surgical procedure.

A retrospective analysis of the Medicare database was conducted to examine trends in use patterns of stenosis operations, associated complications, and resource use with surgical complexity. Operations for Medicare recipients undergoing sur-

gery for lumbar stenosis ($n = 32,152$ in the first 11 months of 2007) were grouped by decompression alone, simple fusion (*e.g.*, one or two disk levels, single surgical approach), or complex fusion (*e.g.*, more than two disk levels, combined anterior and posterior approach).

Overall, surgical rates and simple fusions declined slightly from 2002–7 while the rate of complex fusion procedures increased by 15-fold. Life-threatening complications increased with increasing age, surgical invasiveness, and comorbidities. After adjustment for age, comorbidities, previous spine surgery, and other features, the odds ratio of life-threatening complications for complex fusion compared with decompression alone was 2.95 (95% CI, 2.50–3.49). Also rehospitalization within 30 days occurred for 13.0% having a complex fusion *versus* 7.8% of patients undergoing decompression (adjusted odds ratio, 1.94; 95% CI, 1.74–2.17).

Interpretation

In this retrospective analysis of Medicare claims between 2002 and 2007, the authors demonstrated that, for patients aged 65 yr or older, the rate of spinal stenosis surgery has stayed relatively constant. However, rates of complex surgery have substantially risen. Patients undergoing complex surgery are at a higher risk for life-threatening complications compared with patients undergoing decompression alone. Therefore, additional factors such as age and comorbidities should be considered when selecting an invasive spinal surgery.

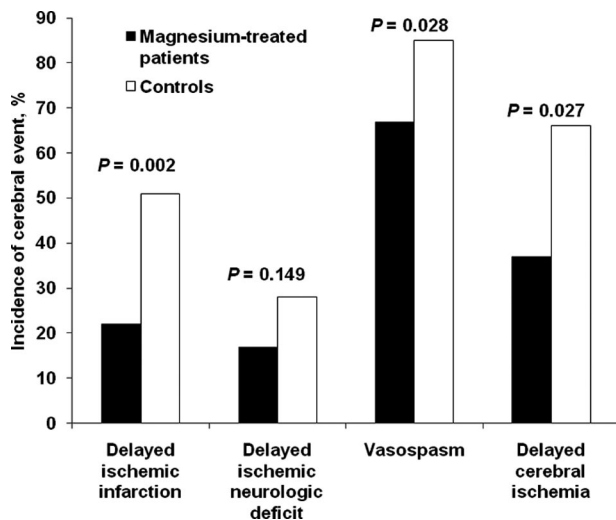
Critical Care Medicine

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

Prophylactic intravenous magnesium sulfate for treatment of aneurysmal subarachnoid hemorrhage: A randomized, placebo-controlled, clinical study. *Crit Care Med* 2010; 38:1284–90

Aneurysmal subarachnoid hemorrhage has a mortality rate up to 50%, mostly because of delayed cerebral ischemia and cerebral vasospasm. Magnesium therapy has demonstrated neuroprotective effects in animal models of ischemic brain injury.

A prospective, randomized, placebo-controlled study was conducted to examine the effects of maintenance of increased serum magnesium concentrations by intravenous administration of magnesium sulfate on the occurrence of cerebral ischemic events after aneurysmal subarachnoid hemorrhage. Patients admitted to a neurosurgical intensive care unit ($N = 110$) were randomized to receive intravenous magnesium sulfate (16 mmol bolus, then continuous infusion of 8 mmol/hr) or to serve as controls. Delayed ischemic infarction was assessed by analyzing serial computed tomography scans.



Fewer patients with signs of vasospasm had delayed cerebral infarction compared to patients without vasospasm (28% and 58% in the magnesium and control groups, respectively). No serious adverse events occurred.

Interpretation

This study demonstrates the efficacy and safety of continuous magnesium infusion. Target plasma concentrations of 2.0–2.5 mM decreased the incidence of delayed ischemic infarction. This treatment offers a promising therapeutic option for subarachnoid hemorrhage.

Early versus late tracheotomy for prevention of pneumonia in mechanically ventilated adult ICU patients: A randomized controlled trial. JAMA 2010; 303:1483–9

Although tracheotomy is widespread in patients requiring prolonged ventilation, there is considerable variability regarding the optimal timing for such interventions. Timing of tracheotomy can affect time to weaning from mechanical ventilation, incidence of adverse events (including ventilator-associated pneumonia), and overall health care resources.

This multicenter, randomized controlled study was conducted to compare the effectiveness of early (*i.e.*, after 6–8 days of laryngeal intubation) and late (*i.e.*, after 13–15 days of laryngeal intubation) tracheotomy. Patients (N = 600) who had worsening of respiratory conditions, unchanged or worse sequential organ failure assessment score, and no pneumonia 48 h after inclusion were randomized to early or late tracheotomy groups.

The majority of tracheotomies were performed using percutaneous techniques. Similar rates of ventilator-associated pneumonia were observed in patients in the early and late tracheotomy groups (14% *vs.* 21%; $P = 0.07$). Secondary endpoints at 28 days were also similar including ventilator-

free days (11 *vs.* 6 days), percentage of patients successfully weaned (77% *vs.* 68%), intensive care discharge (48% *vs.* 39%), and survival (74% *vs.* 68%) in the early and late tracheotomy groups.

Interpretation

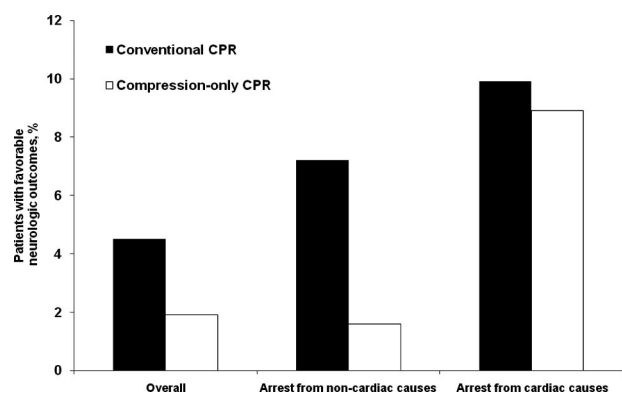
This study demonstrates that tracheotomy performed before day 8 in mechanically ventilated intensive care patients offers no advantage over tracheotomy performed after day 15. There was no difference in nosocomial pneumonia and long-term outcomes. Therefore, tracheotomy should not be performed before day 15 in these patients.

Conventional and chest compression–only cardiopulmonary resuscitation by bystanders for children who have out-of-hospital cardiac arrest: A prospective, nationwide, population-based cohort study. Lancet 2010; 375:1347–54

In adults, survival rates after sudden cardiac arrests are similar after conventional cardiopulmonary resuscitation (CPR) with rescue breathing as with chest compression–only CPR. However, in children, most cardiac arrests have respiratory causes. Therefore, it is believed that conventional CPR is better than compression alone.

A prospective, nationwide, population-based, observational study was conducted in Japan to assess the effect of conventional CPR *versus* chest compression–only CPR on neurologic outcomes after out-of-hospital cardiac arrests in children. Data were collected from 5,170 children (≤ 17 yr) over the 2-yr study period.

The majority of arrests had noncardiac causes (71%). The remaining 29% were cardiac arrests. Fifty-two percent were not able to receive CPR. Of those that received CPR, 30% had conventional CPR and 17% had compression-only CPR. Overall, 1-month survival was 9.2% and favorable neurologic 1-month survival was 3.2%. Those children with no CPR had the least favorable outcomes. Conventional CPR was beneficial in children with noncardiac arrest.



Interpretation

This important study strongly supports that conventional CPR, including rescue breathing, should remain the standard treatment for children who have out-of-hospital cardiac arrest from presumably noncardiac causes. It also emphasizes that chest compression—even that provided by bystanders—is far better than no attempt at resuscitation.

Activated protein C and hospital mortality on septic shock: A propensity matched analysis. *Crit Care Med* 2010; 38:1101–7

The global impact of sepsis is growing and current treatments require additional study. Two large clinical trials of human recombinant-activated protein C (APC) in severe sepsis had conflicting results.

To further assess the safety and efficacy of APC in clinical practice, a retrospective cohort study of patients in 404 hospitals was undertaken over a 2-yr period. Patients with sepsis who were admitted to intensive care and administered antibiotics and vasopressors within 2 days of admission and those who did (n = 1,576) or did not (n = 1,576 matched controls) receive APC were included.

Characteristic	APC-treated (n = 1,576)	Total (N = 33,749)
Age, yr	61	67
White, %	70	63
Mechanical ventilation, %	77	48
≥Two vasopressors, %	68	41
Pulmonary artery catheterization, %	9	4
In-hospital mortality, %	40.7	38.1

ACP = human recombinant-activated protein C.

Because of the allocation discrepancies, several subanalyses were performed. A multivariate model was used that accounted for all patient and hospital characteristics and therapies. Patients who received APC had a 17% relative risk reduction for in-hospital mortality. In a second analysis using a matched cohort by treatment and hospital covariates, there was an absolute mortality difference of 5.9%. Adverse events included gastrointestinal bleeding (6.8%), major transfusion requirement (0.3%), and hemorrhagic stroke (0.25%).

Interpretation

In this retrospective study, propensity-matched analyses indicated that treatment with APC during the first 2 days of hospitalization was associated with reduced inpatient mortality among patients with septic shock. Further prospective investigation is needed to determine whether early treatment with APC actually improves outcomes in patients with septic shock.

Pain Medicine

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

Intravenous immunoglobulin treatment of the complex regional pain syndrome: A randomized trial. *Ann Intern Med* 2010; 152:152–8

Complex regional pain syndrome (CRPS) usually occurs posttraumatically in a limb and may or may not involve injury to major nerves. Although patients may experience improvement within 6 months, many patients experience long-term pain and reduced quality of life because of a lack of response to therapy. On the basis of preliminary data, sustained CRPS may involve the immune system.

This randomized, double-blind, placebo-controlled crossover trial evaluated the pain-reducing efficacy of intravenous immunoglobulin (IVIG) in patients with longstanding CRPS. Eligible patients with pain intensity rated higher than 4 on an 11-point (0–10) numerical rating scale and had refractory CRPS for 6–30 months received IVIG, 0.5 g/kg, and normal saline in separate treatments, divided by a wash-out period of at least 28 days.

Of all eligible patients (N = 13), 12 completed the trial. Most (n = 10) were women with type 1 CRPS (n = 12) and mean baseline pain scores of 7.9. The average pain intensity rating was 1.55 lower after IVIG treatment than after saline (95% CI, 1.29–1.82; *P* < 0.001). In three patients, pain intensity after IVIG was less than after saline by 50% or more. No serious adverse reactions were reported.

Interpretation

In this very small trial, pain relief after IVIG was greater compared with saline in patients who had CRPS for more than 6 months. Although there is the potential that effects were the result of chance, this study indicates that additional evaluation of IVIG in CRPS patients is warranted in larger studies to confirm these results and maximize dosing regimens.

Heat generates oxidized linoleic acid metabolites that activate TRPV1 and produce pain in rodents. *J Clin Invest* 2010; 120:1617–26

The transient receptor potential vanilloid 1 (TRPV1) channel is highly expressed in nociceptors and can be activated by endogenous lipids and exogenous substances (e.g., capsaicin). In the periphery, TRPV1 is also a detector of noxious heat including heat-induced hyperalgesia and thermoregulation. However, the precise mechanism(s) mediating the thermal sensitivity of TRPV1 is unknown.

The heat-evoked generation of endogenous TRPV1 ligands was evaluated in this *in vivo* animal study. Rat skin biopsies were exposed to noxious heat and release of the oxidized linoleic acid

metabolites 9- and 13-hydroxyoctadecadienoic acid were measured as well as activation of TRPV1.

9- and 13-Hydroxyoctadecadienoic acid and their metabolites 9- and 13-oxooctadecadienoic acid were released in a temperature-dependent manner similar to that for activation of TRPV1. Electrophysiologic studies confirmed that these agonists were TRPV1 agonists. Additional studies demonstrated that these substances substantially decreased the heat sensitivity of TRPV1 in rats and mice and produced nociception.

Interpretation

This study demonstrated that oxidized lipid metabolites derived from linoleic acid are released during heat generation and activate the pain-transducing receptor, TRPV1. These lipid metabolites may be released by other tissue injuries such as burns, trauma, and surgery. These results may provide the basis for discovery of new analgesic treatments for acute postinjury states.

Plasma disc decompression compared with fluoroscopy-guided transforaminal epidural steroid injections for symptomatic contained lumbar disc herniation: A prospective, randomized, controlled trial. *J Neurosurg Spine* 2010; 12:357–71

Lumbar disc herniation affects millions of Americans annually. Associated radiculopathy may be resolved within 6 months for 90% of cases. However, for patients with radiculopathy, with or without back pain, who do not respond to conservative care, epidural steroid injection therapy or medical management are considerations.

This multicenter randomized controlled clinical study was conducted to compare the effectiveness of a new treatment, plasma disc decompression (PDD) using the Coblation SpineWand device (a percutaneous, minimally invasive interventional procedure), with standard care using fluoroscopy-guided transforaminal epidural steroid injection.

Adult patients (N = 90) with sciatica (visual analog scale score \geq 50) associated with a single-level lumbar–contained disc herniation, refractory to initial conservative care (and after failure to respond to one epidural steroid injection), were enrolled. Participants were randomized to receive either PDD (46 patients) or transforaminal epidural steroid injection (44 patients, up to two injections) and observed for 2 yr.

Baseline characteristics were similar between groups, except for leg pain duration, which was significantly greater in the injection group.

Leg pain scores were significantly reduced in the PDD group, which also showed improved Oswestry Disability Index scores. During the 2-yr follow-up period, more patients in the PDD group compared with the injection group did not have a secondary procedure (25 *vs.* 11; log-rank $P = 0.02$). Adverse events were similar between study groups.

Interpretation

This study evaluated a highly selected group of patients, those with small disc protrusions caused by contained herniations and with symptoms of persistent leg pain. This specific patient population benefited from the PDD procedure.

Caution is recommended because randomization was unequal, though analysis attempted to compensate for this. Improved outcome was noted at 6 months but many patients were lost to follow-up at 2 yr. The treatment effect is modest but clinically meaningful. Larger studies should be undertaken to further define long-term benefits.