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

Perioperative Medicine

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

Effect of blood products transfusion on the development of postinjury multiple organ failure. *Arch Surg* 2010; 145:973–7

In critically injured patients, coagulopathy can have serious adverse effects. There are few evidence-based guidelines for administering blood products to these patients. Furthermore, the risk of multiple organ failure (MOF) increases with administration of packed red blood cells. A review of a prospectively collected database was performed to determine if transfusion of fresh frozen plasma and platelets is independently associated with MOF in critically injured patients.

Data was obtained from a level I trauma center's surgical intensive care unit. Twelve years of prospectively collected data on admissions of critically injured patients were reviewed. MOF was established based on evaluation of four organ systems (*i.e.*, pulmonary, hepatic, renal, cardiac) as evaluated daily. Each organ was graded on a four-point scale (0–3). MOF was defined as a total score of 4 or higher 48 h postinjury.

Of 1,440 critically injured patients analyzed, the mean injury severity score was 29.3. Overall, 24% of patients developed MOF and 8.2% died. Before adjustments, older age, higher injury severity score, and more units transfused of fresh frozen plasma and platelets were all significantly associated with MOF ($P < 0.001$). The frequency of comorbid conditions was similar among patients who developed MOF and those who did not. A significant ($P < 0.001$) interaction between transfused units of fresh frozen plasma and packed red blood cells and MOF was detected by multivariate logistic regression analysis. Transfused fresh frozen plasma was also independently associated with MOF, regardless of the number of units of packed red blood cells transfused.

Interpretation

MOF is an unfortunate and common complication in critically injured patients. These data suggest that early transfusion of fresh frozen plasma is associated with increased occurrence of MOF, especially among patients who received less than six units of packed red blood cells. Further work is needed to determine how fresh frozen plasma might cause MOF, and whether stricter administration guidelines will decrease the occurrence of MOF.

Normothermia to prevent surgical site infections after gastrointestinal surgery: Holy grail or false idol? *Ann Surg* 2010; 252:696–704

A major cause of postoperative morbidity and a significant burden to the healthcare system is surgical site infection (SSI). As part of the Surgical Care Improvement Project, participating hospitals are required to report the percentage of patients who had immediate postoperative normothermia (first postoperative body temperature of 36°C or higher) and received active warming. It is unclear, however, whether normothermia is associated with reduced SSI.

Using a nested, matched, case-control study design, the potential association of perioperative normothermia and SSI after gastrointestinal surgery was explored. Data were collected from the American College of Surgeons National Surgical Quality Improvement Program database from patients who did (n = 146) *versus* did not (n = 323) develop superficial or deep incisional SSI after gastrointestinal surgery.

Compared with controls, patients who experienced an SSI were more likely to have a history of alcohol use or diabetes, higher ASA (American Society of Anesthesiologists) Physical Status Classification System category, and to have undergone an emergent procedure. There was no difference between cases and controls in terms of antibiotic prophylaxis. There was no difference between study groups for median first postoperative temperature or rate of perioperative normothermia (91.5 *vs.* 86.1%; $P = 0.11$). Variables that increased SSI risk included diabetes, small-bowel surgery, and surgical complexity.

Interpretation

In the authors' analyses of patients who underwent gastrointestinal surgery between 2006 and 2009, risk factors for SSI included diabetes, increasing surgical complexity, small-bowel surgery, and nonlaparoscopic surgery. No independent association between SSI and normothermia was found. In this study, no evidence for using patient body temperature as a pay-for-reporting process measure was shown.

Evaluating the risks of clinical research. *JAMA* 2010; 304:1472–9

Clinical investigators, funding sources, and institutional review board members often are forced to rely on intuition to determine potential risk to research subjects—despite well-established processes and frameworks for assessing such risk. The process, therefore, introduces several limitations and inherent biases. Therefore, a systematic evaluation process is required to ensure appropriate risk assessments and to protect potential research subjects from harm.

The authors propose a four-step process for the systematic evaluation of research risks, the goal of which is to independently compare the risks of research interventions with those of a comparator activity. These steps are as follows: (1) iden-

tification of potential harm of intervention, (2) categorization of the magnitude of each harm, (3) quantification of the likelihood of harm, and (4) comparison of the likelihood of harm in the interventional arm with the likelihood of harms of the same magnitude in the comparator arm. Comparative estimates of the likelihood of risk used were epicutaneous allergy testing and percutaneous liver biopsy. Comparison of these procedures to the proposed research intervention demonstrated the potential benefit of using the systematic evaluation of research risks approach to estimate risk. Because empirical data are used as comparators, the accuracy of risk estimates may be increased and bias reduced because familiar comparator activities are used. Systematic evaluation of research risks also increases consistency in evaluation across research studies and/or interventions because the comparator activity is consistent and delineates a threshold for acceptable risks.

Interpretation

Although clinical investigators must have their research approved by institutional review boards and funding organizations, patient risk often remains indeterminate. The authors developed a systematic evaluation of research risks that involves a four-step process. It is hoped that this process will further protect research subjects. Further testing of the process is needed.

Variation in use of blood transfusion in coronary artery bypass graft surgery. *JAMA* 2010; 304:1568–75

Transfusion of red blood cells (RBC) for patients who have cardiac surgery has been associated with increased morbidity and mortality. To date, there has not been an evaluation of the transfusion recommendations published by the Societies of Thoracic Surgeons and Cardiovascular Anesthesiologists.

To assess the use of RBC, fresh frozen plasma, and platelet transfusions in patients undergoing coronary artery bypass graft surgery with cardiopulmonary bypass, a review of the Society of Thoracic Surgeons Adult Cardiac Surgery Database was performed.

Of 102,470 cases analyzed, 56% of patients received perioperative packed RBC transfusions; 19%, fresh frozen plasma; and 25%, platelets. Patients who received RBC transfusion were generally women, older, and had exhibited traditional risk factors for morbidity and mortality compared with patients who did not receive RBC. Blood product usage was dramatically variable across hospitals, 7.8 to 92.8% for RBC; 0 to 97.5%, fresh frozen plasma; and 0.4 to 90.4%, platelets. Using hierarchical modeling to estimate distribution of transfusion rates, it was found that hospitals in the 99th percentile were 4.6 times more likely to use RBC and 24.3 times more likely to use platelets compared with hospitals in the first percentile. Hospitals with the largest coronary artery bypass graft surgery volume had the lowest usage of perioperative RBC ($P < 0.001$). A significant association was also found between academic hospital status and perioperative RBC usage ($P = 0.03$). Geographical/regional differences also contributed to the variation. Using adjusted and unadjusted analyses, no association was identified between hospital-specific RBC transfusion rates and all-cause mortality.

Interpretation

The authors measured blood product usage for coronary artery bypass graft surgery in the United States in 2008 using the Society of Thoracic Surgeons Adult Cardiac Surgery Database. Although the perioperative transfusion rate was 56%, there was enormous variability in blood product usage. Evidence-based information for future recommendations was difficult to discern.

Transfusion requirements after cardiac surgery: The TRACS randomized controlled trial. *JAMA* 2010; 304:1559–67

Blood transfusion as a quality indicator in cardiac surgery. *JAMA* 2010; 304:1610–1

Perioperative erythrocyte transfusion rates are high among cardiac surgery patients in part because anemia is an independent risk factor for morbidity and mortality. Yet transfusions may be associated with adverse outcomes. Furthermore, there is high variability in the types of blood products used and a deficit of data regarding appropriate thresholds for transfusion.

A prospective, randomized, controlled clinical trial was conducted to evaluate if a restrictive (24% hematocrit) perioperative strategy for erythrocyte transfusion is as safe as a liberal strategy (at least 30% hematocrit) among patients undergoing elective cardiac surgery. The Transfusion Requirements After Cardiac Surgery (TRACS) study enrolled consecutive patients undergoing coronary artery bypass graft surgery, cardiac valve replacement or repair, or both.

Baseline characteristics were well balanced between the liberal (n = 253) and restrictive (n = 249) strategy groups. In the liberal group, hemoglobin concentrations were significantly higher immediately after surgery and within the first week of intensive care unit admission. Significantly more patients in the liberal group received blood transfusion compared with the restrictive group (78 *vs.* 74%; $P < 0.001$). No differences were observed between groups in the use of fresh frozen plasma, platelets, or cryoprecipitate. There was no significant difference between groups in the composite endpoint of all-cause 30-day mortality, cardiogenic shock, acute respiratory distress syndrome, or acute renal injury (10 *vs.* 11%, respectively). Patients who received erythrocyte transfusion were generally older women and had longer lengths of intensive care unit and hospital stay. Mortality rates increased with increasing amounts of erythrocyte units transfused.

Interpretation

In this randomized trial, 30-day mortality was not different between patients undergoing elective cardiac surgery with cardiopulmonary bypass and liberal (at least 30%) *versus* restrictive (24%) perioperative hematocrit strategy. However, the number of transfused red blood cell units was associated with an increase in clinical complications and 30-day mortality. The accompanying editorial discusses the optimal balance of providing the best risk-benefit and cost-effective outcomes of transfusion therapy for patients.

Association between implementation of a medical team training program and surgical mortality. *JAMA* 2010; 304:1693–700

Improving teamwork to reduce surgical mortality. *JAMA* 2010; 304:1721–2

Many studies have evaluated the implementation of teamwork and effective communication strategies to improve surgical safety. However, these studies rarely include a control group. Therefore, the Veterans Health Administration implemented a national team training program and evaluated the effect of this change on patient outcomes.

This large analysis of 180,000 procedures in 108 Veterans Health Administration facilities aimed to test if facilities where the program was implemented had reduced surgical mortality rates when compared with their own baseline and with facilities that had not yet received the training. They also tested whether the degree of implementation had an effect on surgical mortality rates. The crew resources management theory of aviation was adapted for the healthcare setting and clinicians were trained to work as a team. This process included challenging each other when risks were identified, completing checklists, debriefing, and implementing new communication strategies. Learning sessions included lectures, group interactions, and videos with quarterly follow-up. Data were assessed as a retrospective health services cohort study using a contemporaneous control group and 2 yr of surgical mortality data.

Although observed mortality decreased significantly within the trained facilities (18%; $P = 0.01$), it also decreased in nontrained facilities (7%; $P = 0.59$). Using propensity-matched controls, there was an almost 50% greater decrease in annual mortality at trained *versus* nontrained facilities ($P = 0.01$). Mortality rates continued to decline with increasing quarterly follow-up by 0.5 per 1,000 procedure deaths ($P = 0.001$).

Interpretation

The authors implemented a program of teamwork training that included checklist-guided briefings and debriefings as well as more effective communication models during care transitions. In their analyses of more than 180,000 procedures in 108 Veterans Health Administration facilities, surgical mortality was significantly reduced with training. An accompanying editorial outlines important implications of the study, including the requirement of teamwork competency for hiring and training.

Critical Care Medicine

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

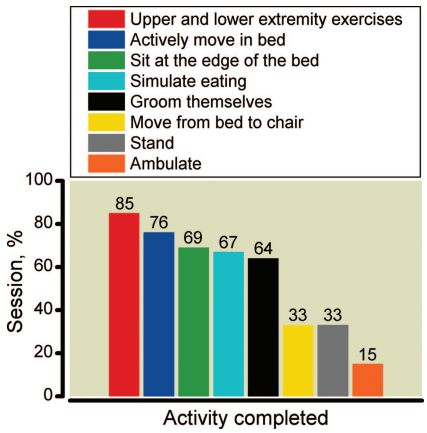
Feasibility of physical and occupational therapy beginning from initiation of mechanical ventilation. *Crit Care Med* 2010; 38:2089–94

What is stopping us from early mobility in the intensive care unit? *Crit Care Med* 2010; 38: 2254–5

Physical therapy and occupational therapy (PT/OT) is sometimes used in intensive care units (ICUs) for critically ill patients. However, relatively few studies have examined protocols for this patient population. Recent studies have begun investigating the potential for early mobilization to improve long-term outcomes for these patients.

The authors provide further details on protocols and the feasibility for providing early PT/OT to mechanically ventilated patients. Patients received daily assessment for PT/OT contraindications. Those who had no contraindications received sedative interruption and early PT/OT. A successful PT/OT day included the ability to respond to 3 of 4 commands (*e.g.*, squeezing a hand on request). Early mobilization intervention was initiated in delirious and nondelirious patients.

Forty-nine patients underwent PT/OT for 87% of eligible days on study. Sessions lasted 26–28 min on average. Sedation was stopped for the majority (83%) of sessions. Agitation after sedative interruption that required stopping PT/OT and resedation occurred in less than 10% of sessions. Adverse events occurred in 16% of all sessions with heart rate increase being the most common (more than 20%).



Interpretation

PT/OT reduces morbidity and mortality in mechanically ventilated ICU patients. The authors present practical procedures for PT/OT in ICU patients. The procedures were feasible in a majority of ICU patients who had once daily interruption of sedation. Therapy was achievable even in the presence of *a priori* significant barriers such as mechanical ventilation, adult respiratory distress syndrome, vasopressor therapy, intermittent hemodialysis, or delirium. These data represent a potential cornerstone of ICU care that should be encouraged.

Restoring arterial pressure with norepinephrine improves muscle tissue oxygenation assessed by near-infrared spectroscopy in severely hypotensive septic patients. *Intensive Care Med* 2010; 36:1882–9

Impairment of macro- and microcirculation processes can contribute to septic shock. Although norepinephrine has proven beneficial among patients with septic shock and severe hypotension, its effects on microcirculation are unknown.

Using a prospective observational design, the authors sought to determine whether restoration of adequate mean arterial pressure for patients with septic shock after norepinephrine administration affects muscle tissue oxygen saturation and its changes during a vascular occlusion test using a near-infrared spectroscopy. Recently admitted (within 6 h) intensive care unit patients who had mean arterial pressure lower than 65 mmHg (n = 28) were included in the study along with healthy volunteers (n = 17).

Mean patient age was 59 yr. Most patients (65%) were male. For the majority (75%) of patients, community-acquired pneumonia was the source of sepsis. Among septic patients, norepinephrine produced significant ($P < 0.05$) increases in systolic, diastolic, and mean arterial pressures as well as cardiac index, global end-diastolic volume index, and central venous oxygen saturation. Muscle tissue oxygen saturation was within range of healthy volunteers in 18 of 28 patients. Among patients with sepsis, norepinephrine produced a significant ($P < 0.05$) increase in multiple near-infrared spectroscopy variables, including muscle tissue oxygen saturation, the muscle tissue oxygen saturation recovery slope, and cardiac index.

Interpretation

In this study, norepinephrine improved muscle tissue oxygenation while restoring mean arterial pressure above 65 mmHg in severely hypotensive patients with septic shock. Recruitment of the microvasculature during blood pressure elevation may be one mechanism for this improvement in microcirculation. This study emphasizes the significant benefit of norepinephrine therapy in severely hypotensive septic patients.

Out-of-hospital hypertonic resuscitation following severe traumatic brain injury: A randomized controlled trial. *JAMA* 2010; 304: 1455–64

To reduce the potential for secondary brain damage after traumatic brain injury, intravenous fluid resuscitation is often started in the out-of-hospital setting to help reduce intracranial pressure. Although animal studies and small clinical trials have suggested a role for hypertonic fluid among patients with severe traumatic brain injury and hypovolemic shock, its effects in patients without hypovolemic shock is not known.

This double-blind, three-group, randomized controlled trial compared the effects of intravenous administration of saline *versus* hypertonic saline as the initial resuscitation fluid administered to patients with severe traumatic brain injury in the out-of-hospital setting. Patients received 250 ml saline, 7.5% (hypertonic saline); 7.5% saline/6% dextran 70 (hypertonic saline/dextran); or saline, 0.9% (normal saline).

The futility boundary was crossed at a planned interim analysis of data from 1,073 patients. Crude differences between groups ranged from −0.017 to −0.041 and the study was terminated early. There were no significant differences in baseline characteristics, injury severity scores, or out-of-hospital care provided in treatment groups. There were no significant changes between groups in intracranial pressure, 6-month neurologic outcomes, or 28-day mortality.

Interpretation

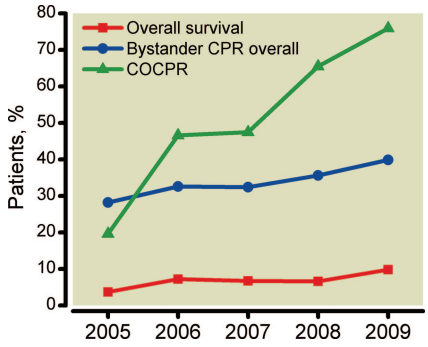
Hypertonic saline may be useful for patients with combined hypovolemic shock and traumatic brain injury. For patients with severe brain injury without hypovolemic shock, out-of-hospital resuscitation with either hypertonic saline or hypertonic saline/dextran compared with normal saline did not show superiority for 6-month neurologic outcomes or mortality. There is no compelling evidence for hypertonic saline use in patients with severe trauma brain injury in the out-of-hospital setting.

Chest compression-only CPR by lay rescuers and survival from out-of-hospital cardiac arrest. *JAMA* 2010; 304:1447–54

Despite its known benefits, bystander cardiopulmonary resuscitation (CPR) is performed in less than 30% of out-of-hospital cardiac arrests. Compression-only CPR (COCPR) and other minimally interrupted cardiac resuscitation methods have been introduced recently in an attempt to improve patient outcomes.

This prospective, observational cohort analysis investigated the survival of patients with out-of-hospital cardiac arrest who received COCPR compared with conventional CPR. Data were collected from patients in Arizona during 5 yr.

Of 4,415 cases, the overall survival was 7.1%. By 2009, the majority of cases where CPR was used involved COCPR (76%). The rate of bystander CPR (conventional or COCPR), the proportion of patients receiving COCPR, and overall survival rates increased significantly during the study period ($P < 0.001$). After controlling for multiple variables, COCPR was associated with improved odds of survival compared with no CPR (odds ratio [OR] = 1.59) and conventional CPR (OR = 1.60). Survival for noncardiac etiologies was similar regardless of the type of CPR administered.



Interpretation

A growing body of evidence suggests that COCPR may improve survival among patients who have out-of-hospital cardiac arrest with early rescue from bystanders. This prospective cohort study indicates that improved survival occurs using this simplified strategy of early COCPR, instead of conventional CPR, among patients with out-of-hospital cardiac arrest. These data support COCPR as the new reference technique for early resuscitation during out-of-hospital cardiac arrest.

Pain Medicine

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

Post-surgical inflammatory neuropathy. *Brain* 2010; 133:2866–80

Most peripheral nerve damage that occurs after a surgical procedure is attributed to mechanical forces occurring during the procedure. The authors present a case series of patients who developed difficult-to-explain postsurgical neuropathies.

Patients who had peripheral neuropathy within 30 days of surgery without documented nerve trauma were included in the case series (N = 33). Patients had undergone a variety of surgical interventions. Axonal damage was demonstrated *via* electrophysiology and magnetic resonance imaging. Results showed abnormally increased T_2 nerve signals in all 22 patients imaged. Twenty-one of 23 patients had abnormal nerve biopsies. Fifteen were diagnostic or suggestive of microvasculitis. Nineteen of 21 patients biopsied had evidence of ischemic nerve injury. Patients were treated with immunotherapy: methylprednisolone, oral steroids, or immunoglobulin. Of the 17 patients treated with immunotherapy, 13 had significant improvement in the Neuropathy Impairment Score ($P < 0.001$) at a median follow-up of 10.5 months.

Patient Characteristics (n=21)	No.
Median age, yr	65
Women	11
Type 2 diabetes mellitus	7
Previous surgeries without complications	17
Median days to onset	2
Pain	18
Prickling	11
Lancinating	10
Burning	9
Aching	7
Cramping	5
Allodynia	5
Median, NIS	38
Neuropathy type	—
Focal (one limb or nerve)	6
Multifocal	11
Diffuse (all limbs)	4

NIS, Neuropathy Impairment Score

Interpretation

Perioperative neuropathy is an adverse event among patients undergoing surgery. A variety of factors have been implicated in perioperative neuropathy. In this case series, a novel mechanism is proposed, that is, perioperative inflammatory neuropathy. The authors suggest that immunotherapy may provide benefit to these patients because an ischemic inflammatory response during surgery may contribute to neuropathy in patients undergoing surgery.

Radiofrequency treatment relieves chronic knee osteoarthritis pain: A double-blind randomized controlled trial. Pain 2010 doi: 10.1016/j.pain.2010.09.029

Current pharmacologic therapies for chronic knee osteoarthritis pain are not adequate. Many patients experience limited pain relief and serious adverse effects from existing treatments. Previous studies have shown some potential for radiofrequency neurotomy in neck and back pain.

This randomized, double-blind, sham lesion–controlled study was conducted to investigate whether radiofrequency neurotomy applied to the genicular nerves is effective in relieving chronic (at least 3 months) osteoarthritic knee joint pain. Patients aged 50–80 yr who did not respond favorably to previous treatments received either percutaneous radiofrequency genicular neurotomy (n = 17) or the same procedure

without effective neurotomy (n = 18). Knee pain at 12 weeks was assessed *via* visual analog scale.

Most patients were women (88 and 83% in the radiofrequency and control groups, respectively). Mean patient age was approximately 66 yr. Compared with baseline, patients' visual analog scale knee pain scores were significantly lower in the radiofrequency group at all postprocedure time points ($P < 0.001$). The radiofrequency group demonstrated superiority compared with the control group in reduced subjective knee pain over baseline, Oxford Knee Scores, and patient satisfaction at 4 and 12 weeks ($P < 0.001$). Fifty-nine percent of patients in the radiofrequency group achieved at least a 50% reduction in knee pain, compared with none in the control group.

Interpretation

Knee replacement is currently the definitive treatment for osteoarthritis of the knee joint. In this randomized study of patients with osteoarthritis pain at 12 weeks, more than half of the patients in the RF group reported greater than 50% pain relief, whereas no patients in the control group had greater than 50% pain relief. These data suggest that further studies using larger groups of patients and long-term follow-up are warranted.