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Induced Hypothermia: No Benefit After Head Trauma

ABSTRACT & COMMENTARY

This large, prospective, randomized, multi-institutional study was terminated early after interim analysis failed to demonstrate any significant improvement in survival or functional level in the group subjected to hypothermia. A total of 392 adult patients with severe closed head injury (Glascow Coma Scale score < 8, but > 3) were randomized to be managed with hypothermia (a body temperature of 33°C for 48 hours), initiated within 6 hours following injury, or normothermia. Hypothermia was continued for 48 hours and rewarming was allowed on the third day. Patients were excluded if they had another life-threatening organ injury, were hypoxemic or in persistent shock following initial resuscitation, were pregnant, or had any severe, preexisting organ disfunction. Patients presenting with hypothermia at entry that were randomized to the normothermia treatment arm were allowed to warm spontaneously, not actively rewarmed. The primary outcome measure was functional status at 6 months.

Surface cooling was used to achieve the desired body temperature. Patients were randomized on average 4 hours after injury, and achieved target temperature within 8.4 (± 3.0) hours following injury. Intracranial pressure (ICP) was measured in all patients, and elevations treated. Patients with ICP greater than 20 mm Hg were treated sequentially with vecuronium, ventricular drainage of CSF, hyperventilation (keeping the $PaCO_2$ > 30 mm Hg), mannitol (keeping the osmolality about 315), and barbiturate coma. Cerebral perfusion pressure was maintained at more than 70 mm Hg, using vasopressors if necessary. Hydration was kept normal, as judged by renal function and urinary output, and all patients received enteral or parenteral nutrition beginning within 48 hours in the normothermic group and 72 hours in the hypothermia group. All patients received sedation with morphine (5-10 mg/h) and seizure prophylaxis with phenytoin. Vecuronium was used to prevent shivering in the hypothermia group, and also in the control group, if needed, to facilitate mechanical ventilation.

The two groups of patients were well matched for age (31 years), severity of neurologic injury, trauma score (28), and incidence of prehospital hypoxemia and hypotension. Hypothermia patients required more vasopressors for more hours, less vecuronium, more fluids, and

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INSIDE

experienced more days with complications compared to the normothermia patients. During the initial 3 days, the hypothermic group experienced a slightly lower mean arterial blood pressure (92 vs 95 mm Hg), had fewer patients with an ICP greater than 30 mm Hg, and had fewer patients requiring aggressive ICP treatment. On rewarming, these differences between the groups were reversed (probably due to hyperperfusion from rewarming in the treatment group).

Functional status was not different in the 2 patient groups when evaluated by blinded investigators at 6 months: 28% of the hypothermic patients and 27% of the normothermic patients were dead, and 57% of both groups were either severely disabled or dead. (Clifton GL, et al. *N Engl J Med.* 2001;344:556-563.)

COMMENT BY CHARLES G. DURBIN, Jr, MD, FCCM

The role of hypothermia in brain protection is not clear. This negative study follows several smaller trials which suggested better functional outcome from closed head injury at 3 and 6 months following injury when patients were treated with mild hypothermia for 48 hours following injury.[1] This study was performed in a prospective, randomized fashion and the data were analyzed in an "intent to treat" fashion. Other treatment measures related to brain injury were standardized and applied according to protocols.

What is clear from this study is that mild hypothermia results in a lowering of blood pressure and ICP in brain injured patients. This is consistent with previous clinical work. It resulted in the need to use vasopressors in more patients and to administer larger volumes of fluids. There was less use of mannitol and muscle relaxants in the hypothermic patients. It is possible that these interventions, potentially adversely affecting outcome, balanced out any benefits and resulted in no difference between the two groups.

This paper raises several important issues. When the hypothermic patients were rewarmed on the third treatment day, a significant percentage of them experienced dramatically elevated ICPs, requiring aggressive treatment. It's possible that continued hypothermia or more gradual warming may have benefited these unstable patients, and a longer period of hypothermia, or a patient-response directed arm of treatment, should be tested.

There were some patients in this study who presented with initial body temperatures less than 35°C. Among these patients, those who were randomized to the normothermic group were allowed to warm spontaneously. In previous studies, such patients were actively rewarmed; this may have been detrimental and contributed to a worse outcome in the normothermia group. In this study, patients initially randomized to the hypothermic group tended to experience a better outcome than those hypothermic patients treated in the normothermic group: 61% of the former had a poor outcome compared to 78% of those treated to normothermia ($P < .09$.) The effect of maintaining hypothermia in initially hypothermic patients merits study.

There are many questions remaining about the use of hypothermia in brain injured patients. This well-designed and executed study suggests that hypothermia induced to 33°C within 6 hours of injury and continued for 48-72 hours is unlikely to have a dramatic improvement in neurologic functional outcome. More studies of other protocols and in different subgroups of patients are necessary to fully identify any benefit or lack of benefit of this therapy. Hypothermia use was associated with a lower incidence and less severe elevations in ICP, but required more aggressive cardiovascular support to maintain cerebral perfusion pressure. ❖

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Unintended Adverse Effects of Lung-Protective Ventilation

ABSTRACT & COMMENTARY

Synopsis: *Low-tidal-volume ventilation, as part of a lung-protective strategy for managing patients with ARDS, has recently been shown to decrease mortality. However, using lower tidal volumes may increase the risk of lung collapse, particularly when applied in other clinical settings.*

Source: Kallet RH, et al. *Respir Care.* 2001;46(1): 49-52.

Kallet and associates report the case of a 35-year-old man with the acute respiratory distress syndrome (ARDS) complicating hemorrhagic pancreatitis and abdominal compartment syndrome. This patient was managed with the currently recommended lung-protective mechanical ventilation strategy that incorporates the use of small tidal volumes and attempts to keep end-inspiratory plateau pressure below 35 cm H_2O in order to prevent ventilator-induced lung injury. While receiving tidal volumes of 4.5 mL/kg and 20 cm H_2O of positive end-expiratory pressure (PEEP), the patient abruptly desaturated while being turned, and a chest radiograph revealed total right lung collapse. Large amounts of tenacious secretions were removed by fiberoptic bronchoscopy, but hypoxemia recurred and repeat chest x-ray showed partial reinflation of the right lower lobe but new left upper lobe collapse. The tidal volume was increased to 7 mL/kg, and PEEP was increased to 30 cm H_2O for 2 breaths every 3 minutes. Although these intermittent PEEP breaths increased end-inspiratory plateau pressure from 38 to 50 cm H_2O, oxygenation improved and the lung remained fully inflated for the next 10 days. The patient eventually succumbed to multiple organ failure, but lung collapse did not recur.

COMMENT BY DAVID J. PIERSON, MD, FACP, FCCP

Within the last several months, a large randomized controlled trial of lung-protective, low-tidal-volume ventilation vs. traditional management in ARDS was published showing convincingly that using the new strategy reduced mortality.[1] This landmark paper confirmed the results of several case series and smaller randomized trials over the previous decade, and marked the first time that any specific approach to mechanical ventilation made a real difference in ultimate patient outcomes in ARDS. Appropriately, ICU clinicians everywhere are adopting the lung-protective ventilatory approach, or at least moving in that direction. However, as we use tidal volumes only about half as large as those we have used for more than 20 years, several related phenomena are becoming apparent.

First, because patients with ARDS have respiratory distress, and because low tidal volumes fall even shorter than larger ones in satisfying the air hunger of such patients, more sedation is often required, along with greater temptation to use muscle relaxants to achieve patient-ventilator synchrony. Patient distress and the need for more sedation are further augmented by the hypercapnia that often develops during lung-protective ventilation. It remains to be seen whether using higher doses of opioids, benzodiazepines, and other agents (including paralytic agents) to make patients appear more confortable also prolongs weaning and delays extubation once their ARDS has improved. In my experience, however, we are spending a lot more time and energy at the bedside dealing with sedation and patient-ventilator synchrony than we did before adoption of the new strategy.

Another downside of low-tidal-volume ventilation is the potential for lung collapse. Our traditional use of 10-12 mL/kg tidal volumes evolved from the demonstration nearly 40 years ago that anesthetized persons with normal lungs developed widespread atelectasis and impaired arterial oxygenation when ventilated with small tidal volumes and without intermittent sigh breaths.[2] Now that low-tidal-volume ventilation is in vogue for patients with ARDS, there seems to be a tendency for clinicians to use smaller tidal volumes in other patients as well—which is a definite mistake. Using tidal volumes of 7 or 8 mL/kg in someone without intrinsic lung disease, who is ventilated after cardiac surgery or a drug overdose and does not have diffuse acute lung injury, amounts to an invitation for the development of lobar collapse—or at least to greater impairment of oxygenation—which may delay weaning and invite other complications.

Patients with ARDS need small tidal volumes to avoid ventilator-induced parenchymal lung damage. Individuals with obstructive lung disease such as advanced chronic obstructive pulmonary disease or acute asthma should also receive small tidal volumes, in order to prevent further hyperinflation, hemodynamic compromise, and barotrauma. However, all other patients should still be ventilated with tidal volumes of 10-12 mL/kg.

In the report summarized above, Kallet et al fall somewhat short of demonstrating that the patient's lung col-

lapse was due solely to low-tidal-volume ventilation. Atelectasis did not develop until more than a week into the patient's course, despite the use of low tidal volumes for several days before the event. Although usual clinical criteria for ventilator-associated pneumonia were absent at the time of the event, lung collapse was associated with an increase in secretions, suggesting the possibility of lower respiratory infection. The atelectasis went away when several things were done, including institution of ventilation with larger tidal volumes, and did not recur.

Whatever the mechanisms for atelectasis and its correction in this specific case, I think the point is well taken that current ventilator management for patients with ARDS probably increases the likelihood of lung collapse, particularly in the presence of copious or especially viscous airway secretions. This is not a reason to go back to larger tidal volumes in managing ARDS, but should increase our awareness of the potential complication of lung-protective ventilation addressed by Kallet et al in this report. ❖

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Improved Aerosol Delivery with Heliox During Mechanical Ventilation

ABSTRACT & COMMENTARY

Synopsis: *At appropriate flow rates and concentrations, heliox in the ventilator circuit may improve aerosol delivery in mechanically ventilated patients with severe airway obstruction.*

Source: Goode ML, et al. *Am J Respir Crit Care Med.* 2001;163:109-114.

In mechanically ventilated patients with airway obstruction, heliox (helium-O_2) gas mixtures reduce airway resistance and improve ventilation. However, the influence of heliox on aerosol delivery is unknown. Accordingly, Goode and associates determined the effect of various heliox mixtures on albuterol delivery from metered-dose inhalers (MDIs) and jet nebulizers in an in vitro model of mechanical ventilation. Albuterol delivery from a MDI was increased when the ventilator circuit contained 80% helium and 20% oxygen (heliox 80/20) vs. O_2: 46.7 ± 3.3 vs. 30.2 ± 1.3 (SE)% of the nominal dose ($P < .001$). The difference was mainly due to decreased drug deposition in the spacer chamber, which was a mean of 39.2% and 55.2%, respectively ($P < .001$). Nebulizer efficiency at a flow of 6 L/min was 5 times lower with heliox 80/20 than O_2, and the amount of nebulized drug was correlated with gas density ($r = .94$, $P < .0001$). When the nebulizer was operated with O_2, greater albuterol delivery was achieved when the ventilator circuit contained heliox rather than O_2.

COMMENT BY DEAN R. HESS, PhD, RRT

A gas mixture of helium and oxygen has a lower density than air. As such, heliox can decrease the resistive work of breathing. In ambulatory patients with asthma, some investigators have reported that inhalation of heliox decreased dyspnea and pulsus paradoxus and improved pulmonary gas exchange. However, others have reported no benefit of heliox in this patient population. In spontaneously breathing patients with severe chronic obstructive pulmonary disease (COPD), inhalation of heliox has been reported to reduce $PaCO_2$ and auto-PEEP. In mechanically ventilated patients with severe asthma, inhalation of heliox has been reported to decrease airway resistance and improve $PaCO_2$. Beneficial effects of heliox combined with noninvasive ventilation have recently been reported in patients with acute exacerbations of COPD. Although breathing heliox improves aerosol delivery into the lungs of stable asthmatics, this has not been shown to be of benefit when used in the treatment of patients with acute bronchospasm. Compared with air, data reported from my laboratory demonstrated that operating a nebulizer with heliox decreased both the fraction of the nominal dose at the mouthpiece of the nebulizer and the aerosol's respirable mass. When a nebulizer is used with heliox, the flow used to power the nebulizer must be 12-15 L/min (compared to 6-8 L/min with air or O_2) to provide an appropriate nebulizer output.

In-line nebulizers and MDIs are used for bronchodilator therapy in mechanically ventilated patients. Generally, the efficiency of these devices in delivering aerosols to the lower respiratory tract is less in mechanically ventilated patients than in ambulatory patients. Methods for enhancing aerosol delivery in such patients could improve clinical benefit and reduce costs. The influence of heliox on aerosol delivery during adult mechanical ventilation has not been previously reported. The results of this lung model study suggest that a heliox mixture can substantially enhance or reduce the efficiency of bronchodilator

delivery during mechanical ventilation, depending on specific circumstances. Delivery of albuterol from a MDI to the lower respiratory tract was enhanced when the ventilator circuit contained heliox mixtures as opposed to air or O_2. On the other hand, when a nebulizer was operated with heliox instead of O_2, albuterol delivery was reduced. The greatest delivery of aerosol to the lower respiratory tract was achieved by operating the nebulizer with O_2 and entraining the aerosol into a ventilator circuit containing heliox.

This was a lung model study. As such, it does not answer the more important question. That is, does the increased aerosol delivery with heliox enhance bronchodilation in mechanically ventilated patients? The answer to this question is unclear at the present time. Although some studies have reported benefit with the use of heliox for acute asthma, others have been equivocal. Although aerosol delivery into the lungs is improved with heliox in stable asthmatics, a benefit is yet to be reported in patients with acute bronchospasm.

With the available evidence, I would not recommend heliox therapy during mechanical ventilation for the sole purpose of improving aerosol delivery. On occasion, however, in my practice I use heliox during mechanical ventilation for patients with acute severe asthma. The data from this study are encouraging in that they suggest that aerosol therapy can be delivered effectively during heliox with mechanical ventilation. At the least, this study suggests that heliox will improve aerosol delivery to the distal endotracheal tube. It is also comforting to know that the nebulizer can be operated with oxygen during heliox therapy with mechanical ventilation, as continuous beta agonist therapy is also frequently part of the care for these patients. Using heliox to power the nebulizer is problematic in that it affects nebulizer performance and increases the amount of heliox that is needed.

Finally, it is important to appreciate that respiratory care equipment is designed to operate with air or oxygen. When a gas of different density, viscosity, and thermal conductivity (ie, heliox) is delivered with this equipment, the results can be unpredictable and potentially dangerous. For example, some ventilators will not function correctly if powered by heliox instead of air or oxygen. As data from my laboratory and this study report, the function of nebulizers is affected if they are powered by heliox. Before using any type of respiratory care equipment with heliox, the safety of this combination must be adequately tested in the laboratory. To the extent that it does just that, this paper provides a service to the clinician. ❖

Special Feature

Atrial Fibrillation Following Coronary Artery Bypass Grafting

By Leslie A. Hoffman, RN, PhD and Marilyn Hravnak, RN, PhD, CRNP

About 400,000 adults undergo coronary artery bypass grafting (CABG) each year. Atrial fibrillation (AFib) is the most common complication following CABG, with an incidence ranging from 5-40%, and most commonly occurs on the second to fourth postoperative day. Although post-CABG AFib is not associated with a significant increase in mortality, it has been noted to result in increased morbidity related to post-operative stroke, hemodynamic compromise, ventricular dysrhythmias, and iatrogenic complications associated with treatment. Most commonly, post-CABG AFib lengthens hospitalization. Attempts to reduce the incidence of post-CABG AFib involve several strategies: 1) attempting to identify patients most at risk for development of this complication; 2) strategies for prophylaxis; and 3) strategies for management.

Predictors For Post-CABG Atrial Fibrillation

A variety of research studies have been conducted in an attempt to determine those patients most at risk for the development of post-CABG AFib, including several large multicenter trials. Older age is consistently the only preoperative risk factor predictive of this complication, with a 24% increase in prevalence for each 5-year incremental increase in age beyond 65 years.[1] Gender has been implicated (increased prevalence in males), but inconsistently. A variety of pre-existing co-morbid medical conditions have also been implicated, such as chronic obstructive pulmonary disease (COPD), chronic renal insufficiency, and congestive heart failure. However, the relationship between pre-existing medical conditions and the development of post-CABG AFib has been inconsistent across studies, and in predictive models developed from the findings of these studies. Another potential risk factor, *P* wave duration on the preoperative surface EKG, is not associated with prediction, but the predictive sensitivity and specificity of this risk factor appears to be somewhat heightened when signal-averaged *P* wave duration data are used. There is some evidence that right coronary artery disease presents an increased risk for development of post-CABG AFib.

Perioperative and postoperative factors have also been examined for their predictive abilities. Prosthetic valve implantation is associated with increased risk, although it is unknown whether the etiology is the procedure itself, pre-existing atrial impairment, or the combination. Characteristics associated with cardiopulmonary bypass (CPB), such as pulmonary vein venting, bicaval cannulation, and extended cross clamp time have been implicated, and the effects of various types of cardioplegia solution have also been examined. However, the prevalence of post-CABG AFib has not consistently differed between patients who have off-pump CABG (OPCABG) or minimally invasive direct vision coronary artery bypass (MIDCABG) vs. patients who undergo standard CABG with CPB. Tamis and associates reported an AFib prevalence of 26% for MIDCABG (n = 42) and 33% for CABG with CPB (n = 33), a difference that was not significant.[2] Similar findings were reported by Cohn and associates (AFib prevalence of 26% in MIDCABG and 34% in CABG with CPB; *P* = NS).[3]

AFib prevalence rates also seem to be similar when comparisons are made between CABG done without CPB (MIDCABG 25% vs OPCABG 29%).[4] Although study findings appear to demonstrate a trend toward a lower prevalence of AFib following off-pump procedures, other characteristics may have produced these trends. Typically, patients who underwent CABG with CPB had more than 3 vessels bypassed, whereas patients who underwent off-pump procedures had less than 2 vessels bypassed.

We compared the incidence of AFib in a matched set of patients who underwent CABG with CPB to patients who underwent MIDCABG (without CPB). Subjects were similar in age and gender (*P* = NS) and number of vessels bypassed (CABG 1 vessel n = 18; 2 vessels n = 80) and MIDCABG (1 vessel n = 90; 2 vessels n = 4). AFib prevalence rates were almost identical (CABG with CPB 24.5% vs MIDCABG 23.4%, *P* = .860), suggesting number of vessels bypassed may be the more important determinant.[5] Although postoperative characteristics have not been studied extensively, there is some evidence that postoperative fluid overload predisposes patients to this complication, even in noncardiac surgery cases.

To date, no studies have identified a strong prediction model for post-CABG AFib. Almassi and associates reported a model that found age to be the strongest predictor for AFib, followed by vein venting, COPD, use of digoxin, and heart rate less than 80 bpm.[6] Aranki and associates also reported a model with age as the strongest predictor, followed by male gender, hypertension, intra-aortic balloon pump, postoperative pneumonia, prolonged mechanical ventilation, and ICU readmission.[7] Neither study related a cumulative percentage of prediction for the model. Age was also found to be the best predictor of AFib in studies where signal averaged ECG data were used in the model.[8,9] When Frost and associates performed regression analysis on a variety of variables in a study using *P*-wave duration and morphology on signal-averaged ECG, they noted that only increased age (> 60 years) and increased body weight (> 80 kg) were independent predictors of AFib, for a cumulative positive prediction of 37%.[8] Fuller and associates reported a model based on age, gender, and beta-blockade that had a median predictive probability of 34% for subjects who had postoperative AFib, and 28% for those who did not.[10]

DeJong and Morton identified age and right coronary artery stenosis as correctly predicting AFib in 26.9% of AFib cases, although the sample size was small (only 52 subjects with AFib).[11] We comprehensively examined pre, peri, and postoperative characteristics that might predict AFib in 730 patients undergoing CABG in a single medical center.[12] Exclusion criteria were prior history of AFib (both active and inactive); prior or current heart, lung or heart-lung transplant; prior or current ventricular assist device; prior or current heart valve replacement or repair; any other surgical procedure during current admission; perioperative or postoperative myocardial infarction; and death in the operating room (OR) or within 12 hours of surgery. Prior CABG was not an exclusion criterion. The model correctly predicted AFib in 24% of subjects. Age provided the greatest percentage of prediction (15.3%), with body surface area adding an additional 8.1%, and entry of the location and number of bypasses adding only 1.2%. The goal of developing a sensitive and specific prediction model that would permit prospective identification of subjects likely to develop this complication remains elusive.

Post-CABG Prophylaxis Against Atrial Fibrillation

A variety of medications, electrolytes, and hormones have been examined for their efficacy in preventing post-CABG AFib. Postoperative administration of a beta blocker appears to be the most widely used strategy, with numerous individual studies and two meta-analyses supporting efficacy of this approach.[13,14] Neither digoxin, oral verapamil, nor intravenous procainamide have been shown to be consistently beneficial in preventing this complication. Magnesium administration had been shown to have some benefit and, although the effects have not been dramatic, is used because of its favorable cost-benefit ratio and low side-effect profile. Ott and associates reported a study (n = 553) applying a multi- drug prophylactic regimen using triiodothyronine and thyroxine, magnesium, metoprolol, digoxin, steroids, and aggressive

diuresis, resulting in AFib prevalence of 10.3%.[15] Amiodarone and ilbutilide have shown some promise of efficacy, but outcomes of using these drugs have yet to be evaluated in large randomized, controlled trials. Lack of an adequate prediction model prevents prophylactic strategies that carry a higher risk of side effects from being broadly targeted to all patients. Therefore, the search continues for mediations with low toxicity and high efficacy that can be applied comprehensively to CABG patients.

Management

The management of post-CABG AFib is centered upon 3 goals, which are sought in a stepwise fashion: 1) rate control conversion to sinus rhythm; 2) maintenance of sinus rhythm; 3) and if conversion cannot be achieved, anticoagulation presents an additional goal. Strategies described in the literature to achieve each of these goals are listed (*see Table*).

Table

Management of Atrial Fibrillation after CABG

Rate Control

- Intravenous (IV) diltiazem
- IV esmolol
- IV amiodarone
- Digoxin

Pharmacologic Conversion

- Procainamide
- Ibutilide
- Amiodarone
- Sotolol

Maintenance of Sinus Rhythm

- Discharge on antiarrhythmic therapy for 4-6 weeks

A variety of studies have demonstrated that most pharmacologic treatment regimens resulted in conversion to sinus rhythm within 24 hours: Hjelms and associates: procainamide converted 87% of patients in 40 minutes;[16] Mooss and associates: 67% of diltiazem group and 13% of esmolol group converted within 6 hours, and 67% of diltiazem group and 80% of esmolol group converted within 24 hours.[17] If pharmacological conversion is not achieved, electrical cardioversion is typically attempted within 48 hours of the onset of AFib. If electrical conversion is successful, patients are generally discharged on an antiarrhythmic agent for 6 weeks. If electrical cardioversion is unsuccessful, the patient may be discharged on a rate control agent and warfarin, and electrical cardioversion reapplied in 6 weeks. In many cases, however, spontaneous conversion is achieved prior to that time.

Resource Utilization

Although morbidity and mortality related to post-CABG AFib is low, this complication results in increased utilization of resources while treatment is applied, evaluated, and adjusted. Post-CABG AFib has been shown to increase the overall postoperative length of stay for these patients by 1-3 days, representing an additional $1500-7500 per patient for bed charges alone. Most studies have only examined bed charges. In studies that have more comprehensively evaluated costs, it has been noted that these additional days are also accompanied by consumption of additional resources from most hospital cost centers such as the pharmacy, laboratories, and respiratory care.[12,18] Thus, the economic ramifications of post-CABG AFib are substantial.

Summary

Post-CABG AFib occurs frequently, and the search for a strong prediction model continues to be elusive. Prophylactic strategies have shown some success at diminishing the frequency, but not obliterating the development, of this complication. Treatment modalities are generally successful, but the need to use these therapies increases length of stay. Targeted preventive therapies that are widely accepted by providers and tolerated by patients have yet to be identified. Given inability to identify a strong predictive model, a more productive strategy may be to focus attention on testing protocols with the goal of identifying treatment that leads to the most rapid conversion to normal sinus rhythm, has acceptable efficacy, and is cost-effective. (*Dr. Hravnak is Assistant Professor of Nursing and Director of the Acute Care Nurse Practitioner Program, University of Pittsburgh School of Nursing, Pittsburgh, Pa.)* ❖

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CME/CE Questions

1. **Hypothermia to 33°C for 48 hours following closed head injury:**
   a. results in better survival.
   b. results in less disability at 6 months.
   c. is difficult to achieve.
   d. does not worsen functional outcome at 6 months.
   e. results in uncontrolled hypotension in many patients.

2. **Which of the following patients should receive low-tidal-volume, lung-protective ventilation?**
   a. A 58-year-old woman ventilated after cardiac surgery
   b. A 22-year-old man ventilated after a sedative overdose
   c. A 40-year-old woman with ARDS complicating acute pancreatitis
   d. All of the above
   e. None of the above

3. **When heliox (rather than air or oxygen) is used to power a nebulizer delivering albuterol, the flow to the nebulizer is:**
   a. increased to provide an adequate output.
   b. decreased to provide an adequate output.
   c. the same flow that would be used for air or oxygen.
   d. irrelevant because nebulizers should never be used with heliox.

4. **The factor most consistently predictive of post-CABG AFIB is:**
   a. older age.
   b. use of cardiopulmonary bypass.
   c. signal-averaged *P* wave duration.
   d. right coronary artery disease.
   e. None of the above

5. **Patients who underwent MIDCABG had prevalence rates for AFIB that were:**
   a. significantly lower than standard CABG.
   b. not significantly different than standard CABG.
   c. significantly lower when postoperative fluid balance was negative.
   d. significantly lower than off-pump CABG.

CE/CME Objectives

After reading each issue of *Critical Care Alert*, readers will be able to do the following:

- Identify the particular clinical, legal, or scientific issues related to critical care.
- Describe how those issues affect nurses, health care workers, hospitals, or the health care industry in general.
- Cite solutions to the problems associated with those issues.

In Future Issues:

Protocol Weaning in 'Unweanable' Patients

CRITICAL CARE Plus

EXPANDING YOUR FOCUS IN INTENSIVE CARE

Benchmark ICUs Demonstrate Better Care, More Profit

Superiority Demonstrated in All Sizes, Kinds of Hospitals

By Julie Crawshaw

If all intensive care units (icus) adhered to the practice benchmarks of the best icus, more than 30,000 lives and $1.5 billion would be saved annually in the United States, according to a study released early this year.

The Solucient Leadership Institute, which provides health care and benchmark information, says its study—"100 Top Hospitals: Intensive Care Unit Benchmarks for Success"—is the first of its kind encompassing hospitals across the country. Solucient's executive director, Jean Chenoweth, says that ICUs have not pursued cost-cutting measures as aggressively as other departments because the wide range of potentially fatal illnesses ICUs handle makes it difficult to measure quality of care. (*For lists of the top teaching and community ICUs arranged by Medicare ID number, see Tables 1 and 2.*)

Overall, the benchmark hospitals paid higher wages but employed fewer staff than peer hospitals. And despite the biggest drop in profits since 1993—and financial stress brought on by the Balanced Budget Act of 1997—the 100 benchmark hospitals showed more profits, treated more difficult cases, and achieved better overall outcomes than did their peers. They also had a median total profit margin of 8.71% and a median cash flow margin of 16.44%, vs. 1.88% and 9.69%, respectively, for peer hospitals.

Sixty-three percent of this year's benchmark hospitals have made the Top 100 list more than once. More than half of those have performed at benchmark levels for at least four years. Boston's Brigham & Women's Hospital is the only facility selected as a benchmark hospital in each of the eight years since the study began. Thirty-seven hospitals in the South made the list. Only 15 in the Northeast did, but that region had the highest percentage increase in top hospitals. Study results indicate that competition, managed care, and regulation caused variability in the levels of hospital performance.

Hospitals in All Categories Show Superiority

"The research shows that regardless of whether we are comparing teaching hospitals, teaching hospitals with residencies in intensive care, or community hospitals, some institutions in all three categories exhibit superior intensive care management, resulting in much better outcomes and significantly lower costs," Chenoweth says.

Researchers used seven equally-weighted measures in assessing hospital performance:

- risk-adjusted mortality index
- risk-adjusted complications index
- severity-adjusted average length of stay
- expense per adjusted discharge
- profitability
- proportion of outpatient revenue
- productivity (total asset turnover ratio)

They included mortality factors separate from ICU care in their performance measurements and studied three different kinds of patient populations in 1200 hospitals:

- Patients with one or more of 10 medical diagnoses, such as stroke, that frequently require ICU care
- postoperative patients following surgeries that call for ICU care;
- life support patients who require a mechanical ventilator for four or more days.

Solucient calculated that by performing at the benchmark level, ICUs would lower mortality rates more than 20% for postsurgical patients, 15% for medical patients, and complication rates for postsurgical patients by 19%.

Researchers noted that because they derived their estimates using only an ICU patient subset, their findings might understate the improvement that could be

Table 1

Top ICU Community Hospitals

Northwest Medical Center, Tucson, AZ
Summit Medical Center, Oakland, CA
MidState Medical Center, Meriden, CT
Lee Memorial Health System, Fort Myers, FL
St. Anthony's Hospital, Saint Petersburg, FL
JFK Medical Center, Atlantis, FL
Aventura Hospital and Medical Center, Aventura, FL
Winter Park Memorial Hospital, Winter Park, FL
Palm Beach Gardens Medical Center, Palm Beach Gardens, FL
Florida Medical Center, Ft. Lauderdale, FL
Blake Medical Center, Bradenton, FL
Southwest Florida Regional Medical Center, Fort Myers, FL
Orange Park Medical Center, Orange Park, FL
Putnam Medical Center, Palatka, FL
Brandon Regional Hospital, Brandon, FL
Largo Medical Center, Largo, FL
Oak Hill Hospital, Spring Hill, FL
Mease Countryside Hospital, Safety Harbor, FL
Hardin Memorial Hospital, Elizabethtown, KY
North Arundel Hospital, Glen Burnie, MD
Albany Memorial Hospital, Albany, NY
Ellis Hospital, Schenectady, NY
Seton Health System, Troy, NY
Parma Community General Hospital, Parma, OH
Trumbull Memorial Hospital-Forum Health, Warren, OH
Southwest General Health Center, Middleburg Heights, OH
Community Health Partners, Lorain, OH
Grand View Hospital, Sellersville, PA
Westmoreland Regional Hospital, Greensburg, PA
Nazareth Hospital, Philadelphia, PA
Riddle Memorial Hospital, Media, PA
St. Clair Memorial Hospital, Pittsburgh, PA
Jefferson Hospital, Pittsburgh, PA
Baptist Hospital of East Tennessee, Knoxville, TN
Parkridge Medical Center, Chattanooga, TN
Good Shepherd Medical Center, Longview, TX
All Saints Health System, Fort Worth, TX
Wadley Regional Medical Center, Texarkana, TX
Memorial Hermann Baptist Beaumont Hospital, Beaumont, TX
Southwest Texas Methodist Hospital, San Antonio, TX
Shannon Medical Center, San Angelo, TX
Metropolitan Methodist Hospital, San Antonio, TX
Doctors Hospital of Dallas, Dallas, TX
Augusta Medical Center, Fishersville, WA

Table 2

Top ICU Teaching Hospitals

Loma Linda University Medical Center, Loma Linda, CA
Exempla Saint Joseph Hospital, Denver, CO
Hospital of St. Raphael, New Haven, CT
Middlesex Hospital, Middletown, CT
St. Francis Hospital, Wilmington, DE
Cedars Medical Center, Miami, FL
Community Hospital East, Indianapolis, IN
St. Vincent Hospital & Health Services, Indianapolis, IN
Franklin Square Hospital Center, Baltimore, MD
Union Memorial Hospital, Baltimore, MD
Greater Baltimore Medical Center, Baltimore, MD
HealthAlliance Hospital, Leominster, MA
Mount Auburn Hospital, Cambridge, MA
UMASS Memorial Medical Center, Worcester, MA
Providence Hospital and Medical Center, Southfield, MI
Spectrum Health Downtown Campus, Grand Rapids, MI
Bon Secours Cottage Health Services, Grosse Pointe, MI
Sinai-Grace Hospital, Detroit, MI
St. Joseph's Health Center, Syracuse, NY
Park Ridge Hospital, Rochester, NY
Mercy Hospital of Buffalo, Buffalo, NY
Mission Saint Joseph's Health System, Asheville, NC
Summa Health System, Akron, OH
Fairview Hospital, Cleveland, OH
St. John West Shore Hospital, Westlake, OH
UPMC McKeesport Hospital, McKeesport, PA
Chestnut Hill Hospital, Philadelphia, PA
York Hospital, York, PA
St. Luke's Hospital & Health Network, Bethlehem, PA
Hamot Medical Center, Erie, PA
Western Pennsylvania Hospital, Pittsburgh, PA
Lancaster General Hospital, Lancaster, PA
Montgomery Hospital Medical Center, Norristown, PA
Mercy Fitzgerald Hospital, Darby, PA
Easton Hospital, Easton, PA
Crozer-Chester Medical Center, Upland, PA
Lankenau Hospital, Wynnewood, PA
Sacred Heart Hospital, Allentown, PA
Bristol Regional Medical Center, Bristol, TN
Baptist Hospital, Nashville, TN

made if all ICUs performed at the level of the 100 Top Hospitals. They also found that if all ICUs operated at benchmark level:

- the cost of ancillary services alone would be nearly $66 million less annually;
- the most critically ill ICU patients would have substantially better outcomes; and
- deaths for patients on mechanical ventilation for at least four days would lower by more than 8%.

The number of ICU patients is expected to double from its current 5 million level by about 2015. The approximately 75,000 ICU beds in the United States have an average daily occupancy of 45,000-50,000. ICU patients comprise 10% of hospital population but account for 25% of hospital expenditures, which is hardly surprising since ICU patients are usually much more ill than those in the general hospital population.

The study reviewed 15 major teaching hospitals, 25 teaching hospitals with fewer than 400 beds, 20 large community hospitals with more than 250 beds, 20 medium-sized community hospitals with 100-250 beds, and 20 small community hospitals with 25-99 beds. ❖

Research OKs Are Tricky When Dealing with Neonates

Study: Problems in Research Consent Exist

By Cathi Harris

It's no secret that the process of obtaining informed consent for research involving human subjects is never easy. The process is even more complicated, however, when the proposed study participant is a newborn.

"In the neonatal period, it is particularly difficult," says Jon Tyson, MD, a neonatologist and Michelle Bain distinguished professor of medicine and public health at the University of Texas-Houston. Tyson also is a member of the Neonatal Research Network, a federally funded effort to design multicenter trials in neonatal research.

"The fathers are often not there. Even if they are there, if the parents are not married, the father cannot legally consent. The mothers have experienced all of the changes that go on with pregnancy, labor, and delivery. Half of the mothers of our high-risk babies had cesareans, so they have had major surgery with anesthesia. It is an extremely difficult time to get consent in a way in which you feel that there is a meaningful exchange of information."

A recent study by British researchers[1] of 200 parents and 107 neonatologists involved in clinical research in nine European countries found problems with the informed consent process in 70% of cases. In addition, even though most of the parents reported that they felt the informed consent process to be vital, a lower percentage of the doctors placed as high a value on the process.

"Most people think of informed consent as a process that goes on between rational, thinking adults, but that is not always the case," continues Tyson. "Anybody who has a sick child is going to be very distressed. It is a very challenging circumstance."

In addition, it is quite difficult to help the parents distinguish between consenting to participate in a study and consenting to allow a new treatment for their baby, adds Michael Cotton, MD, neonatologist at Duke University in Durham, NC.

"Often they think that giving consent is necessary for their baby continuing to receive care, and that consent will buy them new care," explains Cotton. "You have to be very judicious and very clear in explaining the randomization, that their baby may not get the new treatment, even though their baby may be very, very sick."

The ethical dilemma becomes more apparent to the investigator as well. The parents may want the unproven treatment, and the investigator, who may actually believe in the treatment, must be extremely careful not to unduly influence the decision.

"You [the clinician] may know the lab literature and other studies of the intervention you are now researching; and you know it is probably going to be OK, and you want to go ahead and give it to the baby but you can't because you have to get consent," he says. "You can't get their consent by being biased, by saying, 'If it were my baby, I'd do this.' If you were the baby's doctor you could; but if you are the person obtaining consent, you really shouldn't, because you want it to be their decision and be up to them based on the merits of the study, not on your experience as a parent."

Therefore, on any neonatal consent form, it should specifically state that the baby will continue to get the standard treatment whether the parents agree to enroll in the study, notes Cotton.

"The person obtaining consent is in a tough situation in the [neonatal intensive care unit] because a lot of times the person obtaining consent is the caregiver," he states. "The parent can get confused and think that the research is part of the treatment and one and the same.

That goes to biasing them and making them think that their child's treatment is somehow going to suffer if they do not enroll in the study."

At Duke, researchers try to ensure that the neonatologist treating a baby is not the same investigator getting consent from the parents. In fact, in most publicly funded studies and many new drug trials, the study protocol specifically delineates who should obtain consent from parents, he adds.

Avoiding Miscommunication

Even when a completely objective third party presents the information and there's enough time to thoroughly explain the study protocol, research shows that parents—even when they think they understand the information given—often have serious misconceptions about what they have agreed to do, Cotton continues.[2,3]

"Studies looking at parents and their understanding, the testing done of people after they have had consent obtained from them as to what they actually consented to are really quite striking," he says. "Only about 10-20% get it, and the others really have no idea what they just did. Some people think they signed up for the treatment. Then, you have the parent who says, 'Whatever you say, doc.' And what do you do with that?"

The question of how to handle this remains largely unanswered, says Cotton, and really needs to be studied.

"In the large research study that we are involved in here, one of the things we eventually want to look at is the consent process, but just how we are going to go about it, what questions we should ask, we aren't sure," he says.

Considering that many neonatal trials are conducted to determine the effectiveness and possible side effects of the intervention being studied, some experts question whether the term "informed consent" is even appropriate.

"The very reason you do a clinical trial is because you do not have the information that you need to make the decision that is informed enough to know whether the treatment you receive is beneficial, harmful, or of no effect," explains Tyson. He and Paula Knudson, executive coordinator of the institutional review board at the University of Texas Health Sciences Center, wrote a commentary accompanying a recent *Lancet* article.[4]

The current "default" situation in many NICUs is that, because it is so difficult to perform trials in neonates, and the knowledge base about how to treat newborns with certain illnesses is relatively small, many unproven treatments become part of standard clinical practice in different areas without being studied in well-designed clinical trials, say both Cotton and Tyson.

Many clinicians may feel a frustration that informed consent is hard to obtain, and that, even when obtained, parents may not truly understand the consent they have given anyway, Cotton believes, noting the percentage of physicians in the *Lancet* study not in favor of obtaining full, informed consent from parents.

"There is so much that is individualized to the NICU," he says. "It becomes the standard of care, and that is difficult to randomize. There are just not a lot of big, giant studies in this area."

Currently, there are two efforts, the Neonatal Research Network funded through the National Institutes of Health, and the Vermont-Oxford Network, trying to build databases of clinical information and design study protocols in multicenter, multinational trials to answer questions about certain neonatal therapies. These efforts will help provide more information, but this is still a difficult area.

"Right now, you have this problem that if you require explicit and full disclosure of a treatment in a randomized trial, you don't require the same level of disclosure in clinical practice; you make it much more difficult for the physician to administer the treatment in a trial than in practice," says Tyson. "Then, well-meaning regulations can discourage proper testing and encourage routine clinical use of a therapy of uncertain value."

A key effort in solving this dilemma will be to have ethics committees and institutional review boards that are better informed about the real situations facing neonatal researchers and will develop regulations that address those issues, says Knudson. "I think often they do not understand what the clinician/investigator is facing at the time. And, we are forced to blindly follow the regulations we are given to follow instead of reaching out to determine what the real process actually is." ❖

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