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CPAP or NPPV for Acute Cardiac Pulmonary Edema?

ABSTRACT & COMMENTARY

CHADDA AND ASSOCIATES EXPLORED THE HYPOTHESIS THAT noninvasive positive-pressure ventilation (NPPV) would unload the respiratory muscles and improve cardiac and hemodynamic function more effectively than continuous positive airway pressure (CPAP). The study included 6 patients with acute cardiogenic pulmonary edema. In random order, the patients were treated with 5 cm H_2O CPAP, 10 cm H_2O CPAP, and NPPV with an inspiratory pressure of 10 cm H_2O and an expiratory pressure of 5 cm H_2O. Each treatment lasted 20 minutes, and patients were enrolled approximately 1 day after presenting with acute cardiogenic pulmonary edema. Oxygen was administered to maintain $SpO_2 > 90\%$. CPAP and NPPV were applied using an oronasal mask. Respiratory assessments included flow measurements at the mask and pressure from an esophageal balloon catheter. Hemodynamic measurements included heart rate, blood pressure, cardiac output, and pressures from a pulmonary artery catheter.

NPPV reduced the esophageal pressure swings and esophageal pressure time product compared with baseline, whereas there was no reduction in either of these measures with CPAP. NPPV and 10 cm H_2O CPAP both reduced the right and left atrial filling pressures without a change in cardiac index. Chadda et al concluded that both NPPV and CPAP at 10 cm H_2O reduced ventricular preload, and thus improved cardiac performance, but that NPPV was more effective at unloading the respiratory muscles (Chadda K, et al. Cardiac and respiratory effects of continuous positive airway pressure and noninvasive ventilation in acute cardiac pulmonary edema. *Crit Care Med*. 2002;30:2457-2461).

COMMENT BY DEAN R. HESS, PhD, RRT

In the past 10 years, a plethora of high-level evidence has accumulated to support the use of NPPV. In appropriately selected patients, NPPV reduces the need for endotracheal intubation, improves survival, and decreases the risk of ventilator-associated pneumonia.[1-3] The strongest evidence of NPPV's effectiveness is in patients with acute decompensation of COPD. The role of NPPV in patients with acute cardiogenic pulmonary edema is unclear. Although some have

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reported benefit from NPPV in this patient population,[4,5] others have urged caution.[6] Mehta and associates[7] reported a higher rate of acute myocardial infarction (AMI) in patients with acute cardiogenic pulmonary edema who were randomized to receive NPPV as compared to those who received mask CPAP. In patients with acute cardiogenic pulmonary edema, Rusterholtz and colleagues[8] reported a high rate of NPPV failure in patients with AMI. Sharon and associates[9] reported that high-dose nitrates were safer and more effective than NPPV in these patients. There is considerable evidence for the effectiveness of mask CPAP[10] (without NPPV) for the treatment of acute cardiogenic pulmonary edema.

It is against this background that the present study was conducted. Not surprisingly, Chadda et al reported that NPPV unloaded respiratory muscles to a greater extent than CPAP. However, NPPV and CPAP were equally effective in reducing right and left ventricular preload. An appropriate question might be, "So what?" Chadda et al conclude that this study supports the use of NPPV in patients with acute cardiogenic pulmonary edema. I take issue with this conclusion for several reasons. First, this was a short (20-minute) physiologic study. There is no way that we can know if these findings would result in better outcomes in patients receiving NPPV rather than CPAP. Second, the study was conducted almost 1 day after the patients presented with acute cardiogenic pulmonary edema. By the time the patients were enrolled, they had already been treated with diuretics, vasodilators, and inotropic drugs. This is not the time at which most clinicians use either CPAP or NPPV for patients with acute cardiogenic pulmonary edema; rather, we apply this therapy soon after the patient presents to the emergency department.

So how might I apply these findings in my practice? Given the high-level evidence for its use, I will continue to use mask CPAP at 10 cm H_2O for patients with acute cardiogenic pulmonary edema. For those patients who remain hypercarbic with CPAP therapy, I will, as I have in the past, consider the addition of NPPV before intubation. I strongly consider emergent endotracheal intubation for patients with AMI, pulmonary edema, and respiratory failure. ■

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Latest Pulse Oximeters can Improve ICU Process of Care

ABSTRACT & COMMENTARY

Synopsis: *A new-generation pulse oximeter with improved signal-extraction technology had less malfunctioning time than a conventional pulse oximeter placed on the same hand in postoperative cardiac surgery patients and was associated with fewer arterial blood gases and faster FIO_2 reduction.*

Source: Durbin CG Jr, et al. More reliable oximetry reduces the frequency of arterial blood gas analysis and hastens oxygen weaning after cardiac surgery. *Crit Care Med*. 2002;30(8):1735-1740.

DURBIN AND ROSTOW AT THE UNIVERSITY OF Virginia sought to determine whether a latest-generation pulse oximeter (Masimo SET) could improve the process of care in weaning postcardiac surgery patients from ventilatory support, in comparison with a state-of-the-art, previous-generation pulse oximeter (Ohmeda 3740). They recorded data from both oximeters simultaneously in each patient with both sensors applied to the same hand, but randomly withheld the data from 1 device from those taking care of the patient, who were unaware of the true purpose of the study. Outcomes studied were device nonfunctional monitoring time (the percentage of total monitoring time when the monitor was producing unreliable or unusable data according to predetermined criteria), time to extubation, number of ventilator changes, time to an FIO_2 of 0.40, and number of arterial blood gas specimens obtained.

During a 13-month period, Durbin and colleagues entered 86 patients into the study, which was powered to detect a 20% reduction in weaning time with 90% confidence. Data from 4 patients were excluded. Data from the new-generation oximeter were available to clinicians in 43 patients and from the conventional oximeter in 39 patients. Time to extubation was the same in the 2 patient groups, although patients managed according to data from the latest-generation oximeter were weaned to an FIO_2 of 0.40 an average of more than an hour faster than patients managed with the conventional oximeter (means, 176 vs 348 min, $P = 0.0125$) and required fewer blood gases during this time (means, 2.7 vs 4.1 measurements, $P = 0.000015$). There were no differences in the number of ventilator changes during weaning in the 2 patient groups. Durbin et al conclude that use of the new-generation oximeter enables clinicians to manage postoperative cardiac surgery patients in a more efficient and cost-effective manner with respect to oxygen weaning and the use of arterial blood gas measurements.

COMMENT BY DAVID J. PIERSON, MD

Although data showing benefits in terms of patient-relevant outcomes have been lacking, routine monitoring of postoperative patients with pulse oximetry has become the standard of ICU care. Specially designed efficacy studies have demonstrated that it is possible to reduce the number of arterial blood gas measurements through the use of continuous pulse oximetry monitoring, but whether similar reductions occur in everyday practice remains to be seen. By detecting brief episodes of clinically unimportant desaturation that would otherwise have gone unnoticed, continuous pulse oximetry can actually increase the number of blood gas measurements, ventilator adjustments, and other interventions if bedside caregivers do not exercise clinical judgment every time the alarm sounds.

Be that as it may, the new generation of pulse oximeters, exemplified in the present study by the Masimo device, appears to offer a genuine advance in terms of avoiding artifact and providing accurate readings in the presence of hypoperfusion or patient movement. Other studies have demonstrated this improved reliability under laboratory conditions using volunteer subjects, but the Durbin study is the first to my knowledge to show measurable benefit in clinical use.

For example, Gehring and colleagues[1] in Germany connected healthy volunteers to 3 new-generation oximeters and 1 device representing the previous generation and then induced hypoxemia. They generated motion artifacts using a standardized protocol and also reduced finger perfusion by means of an inflatable balloon applied over the brachial artery. Under the conditions of this model designed to mimic clinical situations in which standard oximeters frequently fail to produce reliable readings, the new-generation devices consistently outperformed their predecessor.

In another recent study, Barker[2] evaluated the performance of 20 different pulse oximeter models during standardized hand motion under both normoxic and hypoxic conditions in healthy volunteers. The Masimo SET pulse oximeter exhibited the best overall performance, with the SpO_2 reading remaining within 7% of reference (control) values 94% of the time. Comparable

results with the Agilent Viridia 24C were 84%, with the Agilent CMS at 80%, the Datex-Ohmeda 3740 at 80%, and the Nellcor N-395 at 69%. The Criticare 5040, used by Barker as a representative of an older generation of oximeter, had an indicated SpO_2 within 7% of the control value only 28% of the time.

Continuous monitoring of arterial oxygenation in ICU patients using pulse oximetry can provide early warning of clinical deterioration. It can also detect clinically insignificant physiological fluctuations in saturation, potentially leading to unnecessary interventions. Discriminating between these monitoring outputs remains an important challenge for clinicians at the bedside, both to safeguard patients and to avoid unwarranted expense and discomfort. However, it appears that the new generation of pulse oximeters can help reduce artifact and provide reliable data more of the time in the management of critically ill patients. ■

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Cardiopulmonary Resuscitation on the Wards: Who Survives?

ABSTRACT & COMMENTARY

Synopsis: *In this review of outcomes from cardiopulmonary resuscitation among non-ICU inpatients in 3 urban teaching hospitals, no patient who had an unwitnessed cardiac arrest survived to discharge. Forty-four percent of patients with witnessed respiratory arrest returned to their homes, as compared with 13% of patients with witnessed cardiac arrest (21% for pulseless ventricular tachycardia or fibrillation, and 7% for pulseless electrical activity or asystole).*

Source: Brindley PG, et al. Predictors of survival following in-hospital adult cardiopulmonary resuscitation. *CMAJ*. 2002;167(4):343-348.

Brindley and associates reviewed all cases of attempted resuscitation from cardiac and/or respiratory arrest that occurred during a 2-year period among hospitalized adult patients in all 3 teaching hospitals of the University of Alberta who were not in an ICU, the emergency department, or the operating room. Brindley et al sought to determine current overall survival rates, since existing data were mainly gathered decades ago, and both the hospital inpatient population and available therapies have changed. They also wished to determine associations among patient characteristics, the circumstances of the arrest, and other factors and survival.

There were 247 arrests during the study period, 58% of which were witnessed and 42% unwitnessed. Among patients with witnessed arrests, 48% were initially successfully resuscitated, 22% survived to hospital discharge, and 19% were able to return home. In contrast, only 21% of patients whose arrest was unwitnessed could be resuscitated, and only 1 patient (1%) survived to discharge and was able to return home. This latter patient had an isolated respiratory arrest; no patient who had an unwitnessed cardiac arrest survived to hospital discharge. The type of arrest strongly influenced outcome: Among the 143 patients with witnessed arrests, 44% with respiratory arrest returned home, as compared with 21% of those with pulseless ventricular tachycardia or ventricular fibrillation, and 7% of those with pulseless electrical activity (PEA) or asystole. The risk of not returning home after cardiac arrest was greater for patients whose events occurred on the night shift (11 PM-7 AM) as compared to the day shift (7 AM-3 PM), but age and sex were unrelated to survival.

■ COMMENT BY DAVID J. PIERSON, MD

This study updates survival statistics for in-hospital cardiopulmonary arrest in the context of present-day inpatient severity of illness assessment and resuscitation techniques. Despite these evolutionary factors in inpatient healthcare, outcomes do not appear to have changed much in the last 40 years. Patients who are found already in cardiac arrest do not survive, even if they are initially resuscitated. About 1 patient in 5 who experiences a witnessed cardiac arrest and whose initial rhythm is pulseless ventricular tachycardia or ventricular fibrillation has a good outcome (defined in this study as being able to return home). For patients found initially in PEA or asystole, the chance is much less—only about 7% in this series.

While outcomes from cardiac or respiratory arrest in the ICU were not examined in this study and would likely be different, the present findings underscore the fact that cardiopulmonary resuscitation in patients sick enough to be in the hospital has a generally poor overall result. This is often at variance with what patients and

their families believe. Resuscitation works much more often in the movies and on television. A review of TV medical dramas published in 1996 found that the initial survival rate following cardiopulmonary resuscitation was 75%, with two-thirds of the patients who arrested in the hospital surviving to discharge.[1] As discussed by Brindley et al, these outcomes are 2 to 6 times better than those in any reported study. The onus is thus on physicians and others in the health care system to discuss actual expected survival should cardiac arrest occur and to find out about the expectations of patients and families. ■

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Special Feature

When Survival is Not the Same as Mortality

By Gordon D. Rubenfeld, MD, MSc

In common discourse we use *survival* and *mortality* interchangeably to refer to death. In fact, survival and mortality have very specific, and very different, definitions to a clinical investigator. They require different analyses and different methods to express a treatment effect. Failing to understand the difference between survival and mortality can lead to misinterpreting clinical studies.

Mortality is a probability. The observed data are the number of deaths divided by the total number of patients. For example, in the study by Luhr and colleagues of mortality in acute respiratory failure in 3 Scandinavian countries, 91 of 221 ARDS patients died, for a 90-day mortality of 41.2%.[1] Whether it is reported, mortality is always measured at some specified time. Survival is a rate. The observed data include whether a patient is alive or dead and when he died (or was last seen alive). It is expressed as the number of deaths divided by the amount of time over which all of the study patients were observed. For example, 1.3 deaths per 100 patient-days is a survival rate. The same data can also be expressed by examining the distribution of survival times, for example, as the mean or median survival time in hours, months, or years. Survival is not measured at a specific time, but is truncated by the length of the study. A 5-year study of congestive heart failure cannot show survival time beyond 5 years. A 28-day study of ARDS, at best, can show that a treatment prolongs survival by 28 days.

Often we are interested in the effect of a treatment on outcome. The effect of treatment on *mortality* is usually expressed as the ratio of mortality probabilities (relative risk or risk ratio) or the difference in the mortality probabilities (risk difference or attributable risk). Sometimes it is mathematically advantageous to present the ratio of the odds of death. The odds ratio is usually, but not always, close to the risk ratio.

The inverse of the mortality risk difference is the number needed to treat in order to save 1 life. Mortality differences are very persuasive and convenient ways to express the results of a trial. The treatment and control arms in the low tidal volume ARDS Network study[2] had mortality risks of 31% and 39.8%, respectively. The risk ratio was 0.78, which means that treated patients had 78% of the chance of dying that control patients had, or a 22% (1-risk ratio) reduction in their mortality. This means that 1 life is saved for every 11 patients treated.[2]

The effect of treatment on *survival* is expressed as the difference in median survival. For example, a recent systematic review concluded that cisplatin-based chemotherapy prolongs median survival by 1.5-3.0 months in stage IIIB-IV non-small-cell lung carcinoma.[3] The effect of treatment on survival can also be expressed as a hazard ratio. Hazard ratios look like relative risks with ratios greater than 1 indicating that the treatment is associated with increased rate of death and hazard ratios less than 1 indicating that the treatment is associated with a decreased rate of death. But hazard ratios are not the same as relative risks. A treatment that reduces mortality from 10 deaths per patient day to 5 deaths per patient day will yield a hazard ratio of 0.5 but may only prolong life by a few hours with no difference in mortality at the end of the study. When authors present mortality and survival information along with *P* values in the same sentence, it can be very confusing.

A randomized, double-blind, placebo-controlled clinical trial of adrenal hormone replacement in septic shock was recently published.[4] In this study, 299 mechanically ventilated patients in vasopressor-dependent septic shock with elevated lactate levels were randomized, within 3 hours of shock onset, to receive hydrocortisone 50 mg IV Q 6 hours and fludrocortisone 50 mg per nasogastric tube Q day for 7 days. Relative adrenal insufficiency (nonresponders) was defined as a cortisol increase ≤ 9 ug/dL after

Table

28-Day Outcomes of a Study Assessing Effects of Corticosteroids in Septic Shock[4]

	Treatment mortality	Placebo mortality	Risk ratio (*P* value)	Odds ratio§ (*P* value)	Hazard ratio§ (*P* value)	Difference in median survival
Responders	61%	53%	1.15 (0.49)	0.97 (0.96)	not reported	2.5 days
Nonresponders	53%	63%	0.83 (0.09)	0.54 (0.04)	(0.67) (0.02)	12 days
Total	55%	61%	0.89 (0.26)	0.65 (0.09)	0.71 (0.03)	6.5 days

§ adjusted for baseline cortisol, cortisol response, Mc-Cabe classification, Logistic Organ Dysfunction score, arterial lactate levels and P_aO_2/F_iO_2

administration of ACTH 250 mg IV. The article's abstract states, "In nonresponders, there were 73 deaths (63%) in the placebo group and 60 deaths (53%) in the corticosteroid group (hazard ratio, 0.67; 95% confidence interval, 0.47-0.95; $P = .02$)." With the mortality and survival data placed together in the same sentence, readers may be tempted to infer that the statistically significant *P* value applies to everything in the sentence.

Do corticosteroids reduce mortality by 33% (1-0.67)? Is 1 life saved for every 10 patients treated as suggested by the 63% and 53% mortality data? Neither of these statements is supported by the data. The mortality in the treated group (53%) is not statistically significantly different than the mortality in the placebo group (63%). As the Table shows, corticosteroids improve survival, but have no statistically significant effect on mortality at 28 days in any of the subgroups. Instead of presenting the simple, statistically negative comparison of mortality at 28 days, the authors present a sophisticated regression analysis of mortality. The adjusted odds ratio controls for unlucky randomization when there are chance differences between the treatment and control groups.[5]

In addition to making the analysis less transparent, there is another price for expressing the results of the study as an odds ratio. Corticosteroids in all patients reduced mortality from 61% to 55% with a (not statistically significant) risk ratio of 0.89 or 11% reduction in mortality. How can the adjusted odds ratio make the treatment look like it reduces mortality by 35%, with an odds ratio of 0.65? The answer is that the odds ratio cannot be interpreted as a "percent reduction in mortality" or as a risk ratio when the mortality rates are above 10 or 15%. In this study the mortality rates are over 50%, causing the odds ratio to greatly overestimate the benefit of therapy compared to the risk ratio.

Ideally, survival, mortality, and adjusted analyses should all tell the same story. When they do not, as in this study, readers are left in a quandary. Which analysis tells the truth? At best, critical readers can conclude that corticosteroids prolong time until death in the study patients with septic shock with no statistically significant effect on mortality. In a subset of patients with limited adrenal reserve, therapy prolongs time until death and reduces mortality but only reduces mortality after analysis in a regression model. The truth is that corticosteroids may or may not save lives in septic shock, but this particular study does not provide particularly compelling evidence of efficacy.

This confusion between survival and mortality is common. One of the randomized trials evaluating lung-protective ventilation in ARDS states in the abstract, "After 28 days, 11 of 29 patients (38%) in the protective-ventilation group had died, as compared with 17 of 24 (71%) in the conventional-ventilation group ($P < 0.001$)."[6] Readers may be tempted to think that this *P* value means that the treatment reduces 28-day mortality from 71% to 38%. In fact, this highly significant *P* value comes from the survival analysis and tells us nothing about the comparison of mortality. Comparing the 71% to the 38% mortality in these 53 patients provides a *P* value of 0.03. This is not nearly as persuasive particularly since this study required a $P < 0.001$ for significance based on the number of interim analyses. Again, readers are tempted to apply the compelling *P* values from a survival analysis to the weak statistical evidence from the mortality data.

Why do the survival analyses yield results that conflict with and are often more persuasive than the mortality analyses in these studies? Survival analysis techniques are designed to detect differences in survival time. Imagine a study where everyone is dead at the end of the study. The risk ratio measured at the end of the study for the treatment is 1.0 (no effect) since the mortality is 100% divided by 100%. Survival analysis can take data from this "negative" study and tell us which treatment prolonged life the longest even if everyone is dead at the end of the study. This is extremely useful information if the study is a 5-year study of severe congestive heart fail-

ure and the treatment prolongs median survival by 13 months. Survival analyses can be run on ICU studies that stop observing patients after a relatively short period. In these studies, a statistically significant result with a hazard ratio below 1.0 may mean that the treatment only prolongs survival by a few hours or days. In the corticosteroid study mentioned above, patients who received the treatment, at best, lived 12 days longer than the controls, without any statistically significant effect on mortality at 28 days. In fact, the problem with survival analysis in critical care studies is that they are too sensitive to finding statistically significant differences in time until death that have no clinical significance.[7]

These statistical issues beg an important conceptual question. What is the *right* time point to measure mortality differences in critical care studies? There is nothing magical about 28 days, and the correct time point to measure mortality is often debated. There is always a tradeoff in selecting study end points between sensitivity to treatment effect and clinical significance. End points close to the therapy and disease (7-day mortality, for example) are most likely to detect a specific effect of the treatment but are not clinically significant.[8] Measuring mortality 5 years after critical illness would arguably be more clinically relevant, but would be expensive and might miss important clinical effects that would be washed out by 5 years.

In relying on mortality at some fixed time point we rely on an implicit, and potentially flawed, assumption. While patients in both groups will continue to die after the end of the study, we assume that the *difference* in mortality observed created by the therapy will remain fixed—that the treated patients won't "catch up" to the controls. Survival analysis doesn't fix this problem, because it, too, is truncated at the end of the short-term observation period. Some readers try to surmount this problem by looking at the shape of the survival curves to see if they are "coming together" or not. This is problematic. Although survival curves are rarely drawn with confidence intervals, rest assured that there are few enough deaths toward the tails of the survival curves to make any "eyeball" inferences about coming together or moving apart dangerous. Although the optimal time point for assessing mortality differences in the ICU is unknown, survival analysis will not substitute for better data on the long-term effects of critical illness and its therapies.

Should survival analysis be abandoned from critical care studies? Not at all. Sometimes, investigators are interested in very sensitive outcome measures. Phase II studies of new therapies and studies that identify risk factors for poor outcome are examples of studies in which a very sensitive outcome measure is useful. In these situations a sensitive outcome measure is more important than a clinically significant one because the data will be used to generate and test new hypotheses. Survival analysis can be used to measure "time until" a variety of events. Time until extubation, time until vasopressor withdrawal, or time until developing renal failure can all be studied using survival analysis techniques.

Obviously, decisions to use any treatment in medicine are driven by individual patient, clinician, and hospital factors. However, one of the most important factors is, or should be, the evidence that the treatment is beneficial to patients. In trying to understand this evidence it is extremely important for readers to understand that improving survival may not reduce mortality. ■

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CME / CE Questions

20. For patients with acute cardiogenic pulmonary edema:
a. NPPV unloads respiratory muscles to a greater extent than CPAP.
b. outcomes are better for NPPV than CPAP.
c. preload reduction is greater for CPAP than NPPV.
d. $PaCO_2$ is lower for CPAP than NPPV.
e. All of the above

21. The strongest evidence supporting the use of NPPV is in patients with:
a. acute cardiogenic pulmonary edema.
b. acute myocardial infarction.
c. acute respiratory distress syndrome.
d. severe pneumonia.
e. ACURE exacerbation of COPD.

22. Compared to previously available models, new-generation pulse oximeters have been shown to do which of the following in postoperative cardiac surgery patients?
a. Reduce the incidence of clinically important episodes of hypoxemia
b. Shorten the duration of mechanical ventilation
c. Reduce mortality
d. All of the above
e. None of the above

23. In monitoring postoperative cardiac surgery patients and in comparison with a previous-generation pulse oximeter, a new-generation pulse oximeter with signal-extraction technology has been shown to:
a. reduce the number of arterial blood gas specimens drawn during FIO_2 weaning.
b. shorten the time to an FIO_2 of 0.40.
c. reduce nonfunctional monitoring time.
d. All of the above
e. None of the above

24. After resuscitation from unwitnessed cardiac arrest occurring on the hospital wards, what proportion of patients survived and were able to return to their own homes?
a. 22%
b. 11%
c. 6%
d. 2%
e. 0%

25. Which of the following were associated with poorer survival after cardiopulmonary resuscitation in the hospital?
a. Unwitnessed arrest
b. Asystole
c. Occurrence of the arrest during the night shift
d. All of the above
e. None of the above

26. An ICU study observes patients from ICU admission until day 28 and presents the results of a survival analysis. The authors state, "The hazard ratio associated with the treatment was 0.5 ($P = 0.0001$)." Which of the following must be true?
a. The mortality at day 28 in the treated patients was half that of the controls.
b. The mortality at hospital discharge was statistically significantly different in treated patients compared to controls.
c. The treatment effect is clinically significant.
d. The time from ICU admission until death is different in treated patients and controls.
e. There is a strong placebo effect.

27. All of the following statements are statements about survival *except*:
a. The hazard ratio associated with therapy was 0.87.
b. A Cox proportional hazards model and Kaplan-Meier curve showed a clear advantage of treatment.
c. The probability of death at 28 days, 90 days, and 365 days was greater in older patients.
d. The difference in median time until death was 7 hours ($P < 0.01$).
e. The death rates in both groups were equivalent.

Readers are Invited. . .

Readers are invited to submit questions or comments on material seen in or relevant to *Critical Care Alert*. Send your questions to: Robin Mason, *Critical Care Alert*, c/o American Health Consultants, P.O. Box 740059, Atlanta, GA 30374. For subscription information, you can reach the editors and customer service personnel for *Critical Care Alert* via the internet by sending e-mail to robin.mason@ahcpub.com. ■

CME / CE 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:

Intensivist Care Improves Outcomes

CRITICAL CARE Plus

EXPANDING YOUR FOCUS IN INTENSIVE CARE

IT Reduces Errors and Cuts Costs, Health Legacy Partnership Says

With Better Funding and More Trust, Regional Successes Can Become Nationwide

INFORMATION TECHNOLOGY CAN SUBSTANTIALLY REDUCE MEDICAL ERRORS AND TRANSLATE INTO MAJOR COST savings, says Janet M. Marchibroda, MBA, Chief Executive Officer for the eHealth Initiative/Washington, D.C. Marchibroda, speaking at the Third Annual Health Legacy Partnership (HELP) Conference and eHealth Initiative Annual Meeting, "The technology exists," she says, "But it requires that the communities to work together to realize the greater good that can come from sharing information to support better patient care." She adds that regional initiatives reveal that the key barriers to IT cooperation are funding and lack of trust between health systems.

Implementing an interoperable electronic infrastructure that connects different health care systems including electronic health records could save thousands of lives and at least $80 billion per year, Marchibroda says. She points to a 1999 report by the Institute of Medicine that found between 44,000 and 98,000 people die in hospitals each year as the result of medical mistakes, creating costs of approximately $37.6 billion each year, with $17 billion linked directly to preventable errors. Using findings from a study of two prestigious teaching hospitals, The IOM report further noted that almost 2% of hospital admissions experience a preventable medication error, resulting in an average increased hospital cost of $4,700 per admission or about $2.8 million annually for a 700-bed teaching hospital.

Clinical Data-Sharing Reduces ED Charges

"One study of intensive care patients found that when physicians used a computerized system, the incidence of allergic drug reactions and excessive drug dosages dropped by more than 75%," Marchibroda says. "The average time those patients spent in the unit dropped from 4.9 days to 2.7, slashing costs by 25%."

Marchibroda further notes that one hospital's use of a community-based clinical data-sharing network resulted in a reduction in emergency department charges of $26 per encounter, while switching to electronic records saves annual paper storage costs that range from $4,000 for a small facility to $100,000 for a large center. Brigham & Women's Hospital found that using computerized physician order entry reduced error rates from 10.7 to 4.9 errors per 1000 patient days and potential adverse drug events by 84%.

Weaning Protocols More Successful Using Handheld Computers

A recently published study[1] further points up IT's potential for improving patient care. Researchers who evaluated 352 patients requiring mechanical ventilation in the medical ICU at Barnes-Jewish Hospital/St. Louis found that using interactive weaning protocols on a handheld computer significantly improved clinical outcomes and overall compliance with the weaning protocol. The study's authors observed that using protocols can reduce the occurrence of medical errors and that one evidence-based guideline "recommends the use of interactive education and reminders directed at non-physician healthcare providers when developing weaning protocols. Our experience suggests that the use of handheld computers programmed with an interactive weaning protocol may be one way to follow this recommendation."

Despite such impressive evidence that maximizing use of information technology results in better care at lower cost, the US health care system as a whole has yet to take the IT plunge. However, Marchibroda notes there have

been some stunning successes at the regional level including the Santa Barbara Care Data Exchange and the Indianapolis Network for Patient Care.

The baseline assessment done by the Santa Barbara group before implementing an interconnected infrastructure revealed that physicians who shared the same patient ordered the same drug, lab test or radiology exam 11% of the time; half of the time, the patients followed the duplicate instructions. The assessment also found that one out of every seven admissions resulted from missing information in emergency rooms or primary care settings and one out of every five lab and X-ray tests were duplicated because of medical record retrieval barriers.

Indianapolis Initiative Offers Working Model

Marchibroda describes the Indianapolis initiative as "a working model of our vision of an interconnected, electronic health information infrastructure" and says that the key factors in its success were commitment and involvement of the health systems at the executive level.

Marc Overhage, MD, a practicing clinician and senior investigator at the Regenstrief Institute for Health Care/Indianapolis, is responsible for much of the INPC's success, which he attributes to community vision, outside funding and approaching the project from the clinician's point of view.

"We're fortunate to have very enlightened leadership here," Overhage says. "When we talk to the CEOs here, rather than seeing IT as putting their institutions at risk, they saw it as being good for the patients. And our focus was always on benefits to patient care and the clinical side."

Overhage observes that the fact that Regenstrief began the INPC project as research funded by the National Library of Medicine and the Agency for Health Care Research and Quality meant hospitals didn't have to fork out the money themselves. "We weren't a competitor knocking at the door suggesting we share data, he says. "We were a nonthreatening neutral party."

Resistance to using IT stems from the time and energy getting IT set up requires, and from irrational fears such as the possibility that competing facilities will be able to access data and use it to gain more admissions. "Most hospitals don't have time, energy and sophistication to look at their own data, let alone monitor a competitor's," Overhage says. "But there are always other things the institutional energy could and should be going toward."

IT implementation does carry some financial risk to hospitals. Though reducing emergency room charges by more than $25 per visit benefits patients and payers, "if you're CEO of a hospital that gets 100,000 visits, your revenue would go down by $2.5 million," Overhage notes. "Part of the challenge-which is a fundamental health care problem-is getting the money back to the people who made the investment. And IT can actually reduce the number of hospital admissions hospitals."

Savings-Sharing Programs Could Help

Savings-sharing plans would do a lot to raise CEO enthusiasm, and Overhage says he's heard that Columbia Presbyterian Medical Centers in New York has negotiated such a deal with an insurer whereby the hospital receives a higher rate of reimbursement because it uses physician-order entry.

The health history information ICU physicians and staff have available to them at the time of admission can be pure gold, Overhage observes. But once the first hours of an admission pass and facts about patients' histories are known, the need for outside data drops dramatically as staff focus shifts to data generated internally.

Marchibroda notes that everyone-health systems, practicing clinicians, public health, payers and patients-can derive value from an interconnected, electronic health information infrastructure. "In the last couple of years, technology has evolved that can make this happen," she observes. "Once we have political will and funding we can vastly improve the quality of health care that is delivered in our country." (Contact info: Janet M. Marchibroda [202] 663-8099; Marc Overhage [317] 630-8685.) ■

Reference

1. Iregui M,et al. Use of a handheld computer by respiratory care practitioners to improve the efficiency of weaning patients from mechanical ventilation. *Crit Care Med*. 2002;30(9):2038-2043.

Empowering Nurses Dramatically Lowers Hospital's Staff Vacancy Rate

Luther Middlefort Applies Multiple Strategies to Improve Patient Flow

A POLICY THAT EMPOWERS FRONTLINE NURSES TO temporarily halt admissions when their units don't have enough nursing staff to care for more patients has significantly slashed the nursing vacancy rate at a

Wisconsin hospital. Roger Resar, MD, Physician Change Agent at 300-bed Luther Middlefort Hospital/Eau Claire, reports that the two-year-old policy also increases throughput and improves patient care. "We believe the people who know best how many patients a unit can safely care for are the people who actually taking care of those patients," Resar says.

When the current nursing shortage hit, Resar's hospital began experiencing overall vacancy rates for nurses between 10-12%. In February 2000, Luther instituted its "capping trust" policy, building an Intranet-accessible population board that allows hospital staff to monitor patient census in real-time. Within six months the nursing vacancy rate dropped to 2%.

Resar acknowledges that during the same period Luther Middlefort also raised nursing pay, started nurse internship programs, improved orientation procedures and paid recruitment bonuses to nurses. But, he points out, virtually every other hospital in the country did those exact same things without attaining nearly the degree of staffing success that Luther enjoys. "Our nurses will tell you that capping trust has had a major impact on recruitment and retention," Resar says. "We see a direct relationship between our ability to hire staff in a time of shortage and the fact that we empower our nurses by trusting them to make the right choices."

Multiple Strategies Bring Multiple Successes

Staffing to peak patient demand leaves staff working below potential when patient flow is average-a luxury hospitals can no longer afford-and staffing to the average demand when flow is at peak creates safety risks for patients and staff alike. Resar smoothed operating room flow and reduced the number of patients awaiting post-surgical beds by using variability control methodology shown to improve patient throughput by Eugene Litvak, PhD, professor of health care and operations management at Boston University School of Management.

Litvak's work at two Boston hospitals revealed that although 50% of surgical patients arrive through the emergency room, the 30-35% of patients who arrive for scheduled surgeries exerts far greater influence on the number of available beds. Despite the fact that they receive blocks of time throughout the week in which they can use operating rooms, many surgeons perform most of their scheduled surgeries on Mondays and Fridays in order to free the mid-week for seeing patients in office. When operating room time isn't used, hospital rooms held open for post-op surgical patients remain empty and the facility must absorb the cost of staffing for the unoccupied beds. Once nurses began closing Luther's ICU when they considered it capped, surgeons had to reschedule elective surgeries to below-peak times.

Initial Physician Concerns Disappeared

Resar says that initially, some surgeons worried about re-scheduling surgeries and retaining adequate operating room access. But when he requested that cardiologists and heart surgeons compare their practice revenues before and after capping trust took effect, and physicians found that the new policy was saving them nearly $150,000 per month by making ICU beds available when needed, the capping trust received their wholehearted support. "Our organization is owned and run by physicians," Resar says. "They want to do what's best for the hospital as well as for themselves and their patients."

The new policy also reduced by 9.2% the number of emergency room patients unable to be admitted because of ICU bed shortages. To further control patient census variables, Luther began running all admissions, transfers and discharges through a single coordinator. Physicians can't make "I'll send this patient home if I can use that bed for that one" kind of side deals, Resar says. The hospital's chief of staff, medical director for the ICU and every nursing director who has patient contact now meet at 8:30 every morning to review incoming patient demands and plan for the day.

Resar found additional ways to improve patient flow when he hired a consultant who specializes in Six Sigma, a strategy used in industry that approaches quality improvement by reducing process variations. Three hospital staff teams trained by the consultant applied Six Sigma-based approaches throughout the facility. They suggested building a separate recovery room for the cardiac cath lab and developing other alternatives to using inpatient beds for the 12-16 hours that often follow outpatient procedures. The hospital created more bed space for acute patients by sponsoring a ventilator unit at a nearby nursing home to which chronic patients can be moved. Team members also routinely attend redesign collaboratives at the Institute for Health Care Improvement seeking more ways to decrease patients' length of stay.

Look At the Whole Journey from Health to Death

Resar stresses that improving flow between patients' hospital arrival and departure times isn't enough. As part of a community a hospital must evaluate and optimize the health care other community resources can provide. Patients receiving only comfort care available through a hospice, for example, should not use ICU beds. "If we don't consider the whole journey the patient makes from health to death,

our hospitals will be filled with patients who don't need the level of care we have to offer them," Resar says. (Contact info: Roger Resar [715] 838-3311; Eugene Litvak [617] 358-1633.) ■

Attention Readers

American Health Consultants is happy to announce that we are opening up our *Primary Care Reports* author process to our readers. A biweekly newsletter with approximately 5000 readers, each issue is a fully referenced, peer-reviewed monograph.

Monographs range from 25-35 Microsoft Word document, double-spaced pages. Each article is thoroughly peer reviewed by colleagues and physicians specializing in the topic being covered. Once the idea for an article has been approved, deadlines and other details will be arranged. Authors will be compensated upon publication.

As always, we are eager to hear from our readers about topics they would like to see covered in future issues. Readers who have ideas or proposals for future single-topic monographs can contact Managing Editor Robin Mason at (404) 262-5517 or (800) 688-2421 or by e-mail at robin.mason@ahcpub.com. ■

PHARMACOLOGY WATCH

FDA Approves Claritin For OTC Use For Seasonal Rhinitis

After years of legal wrangling, the FDA has approved loratadine (Claritin, Schering-Plough) as an over-the-counter (OTC) product for the treatment of seasonal rhinitis. Loratadine is considered a nonsedating antihistamine, and its OTC approval was linked with the FDA's work with the National Transportation Safety Board to improve public awareness about the concerns of drowsiness while driving associated with older antihistamines. The OTC switch also comes within months of loss of patent protection for loratadine and the entry into the market of generic equivalents. The OTC switch applies to all 5 formulations of Claritin, and at least 1 generic house plans to market "Reditabs." Meanwhile, Schering-Plough continues to aggressively market desloratadine, the active metabolite of loratadine under the trade name Clarinex, in an attempt to protect its $3 billion Claritin market.

Simpler Atrial Fibrillation Management

Management of atrial fibrillation (AF) may be simpler in the future based on the results of 2 studies published in the December 5, 2002, *N Engl J Med*. The larger of the 2 studies (AFFIRM) enrolled more than 4000 patients in the United States and Canada with AF and at least 1 other risk factor for stroke such as hypertension, coronary artery disease, diabetes, congestive heart failure, or age older than 65. Patients were randomized to a rhythm control strategy with cardioversion followed by amiodarone, sotalol, propafenone, or older antiarrhythmics such as procainamide or quinidine; or a rate control strategy with digoxin, beta-blockers, and/or calcium channel antagonists. All patients in both groups were anticoagulated with warfarin. The primary end point was overall mortality. The 5-year death rate was 23.8% in the rhythm control group and 21.3% in the rate control group (P = 0.08). Rhythm control was associated with more hospitalizations and more adverse drug effects. In the second study from The Netherlands, 522 patients with persistent AF after electrical cardioversion were randomized to treatment aimed at rate control or rhythm control. Both groups received oral anticoagulation, and the composite end point was death from cardiovascular causes as well as bleeding, implantation of a pacemaker, or severe adverse effects of drugs. After a mean duration of nearly 2.5 years, the primary end point occurred in 44 patients in the rate control group (17.2%) and 60 patients in the rhythm control group (22.6%) (P = 0.11). Although both studies showed trends toward adverse outcomes with rhythm control, neither study reached statistical significance. The authors of both studies suggest that a rate control strategy for the treatment of AF is at least as good as the rhythm control strategy. In an accompanying editorial, Michael D. Cain, MD, states that "on the basis of these data, rate control can now be considered a primary approach to the treatment of atrial fibrillation." He also suggests that nonpharmacologic treatments for AF will still be pursued with the goal toward maintaining

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sinus rhythm (*N Engl J Med*. 2002;347:1825-1833; 1834-1840; 1883-1884).

Oral Anticoagulation Vs Aspirin in AF

In a related study, oral anticoagulation was found to be superior to aspirin in preventing stroke in patients with atrial fibrillation (AF) or paroxysmal AF. The study was a pooled analysis of 6 trials of more than 4000 patients who were randomized to receive therapeutic doses of oral anticoagulant or aspirin with or without low-dose oral anticoagulants. Patients receiving oral anticoagulation were significantly less likely to experience stroke (2.4 vs 4.5 events per 100 patient years; hazard ratio [HR], 0.55), ischemic stroke (HR, 0.48), or cardiovascular events (HR, 0.71) but were more likely to experience major bleeding (2.2 vs 1.3 events per 100 patient years; HR, 1.71). Anticoagulant therapy also showed benefit on all-cause mortality but only after 3 years of therapy. Interestingly, more benefit was seen for anticoagulation vs aspirin in patients younger than 75 compared to those 75 years or older. A lesser benefit was also seen for women compared to men. The authors suggest that oral anticoagulation is more effective than aspirin in decreasing the risk of stroke and other cardiovascular events in patients with nonvalvular AF (*JAMA*. 2002;288:2441-2448).

Immunization Does Not Cause Autism

A new study should put an end to concern regarding the MMR (measles, mumps, and rubella) vaccine and its possible link to autism. Researchers in Denmark looked at the records of all children born between January 1991 and December 1998, representing a cohort of almost 540,000 children. Of those, 82% (440,655) received the MMR vaccine. In the cohort, 316 children were diagnosed with autism and 422 were diagnosed with other artistic spectrum disorders. After adjustment for potential confounders, the relative risk for artistic disorder in the vaccinated children compared to the unvaccinated was 0.92 (95% CI, 0.68 to 1.24). The relative risk for other artistic spectrum disorders was 0.83 (95% CI, 0.65 to 1.24). The authors also looked for a possible association between age at the time of vaccination, the time since vaccination or the date of vaccination, and development of artistic disorder and found no relationship. They also found no temporal clustering of cases of autism at any time after immunization (*N Engl J Med*. 2002;347:1477-1482).

Statins May Lower CRP Levels

C-reactive protein (CRP), an inflammatory marker, has shown to be a strong predictor of cardiovascular events, perhaps even more predictive then LDL cholesterol levels (*N Engl J Med*. 2002; 347:1557-1565). Most physicians have looked at these studies with interest but have been unsure what to do with an elevated CRP level in an individual patient. Perhaps even more importantly, it is unclear whether lowering CRP affects cardiovascular outcomes. Until an answer is found to this important question, an increasing body of evidence is suggesting that statins may lower CRP levels.

Simvastatin Reduced CRP Plasma Levels

A recent study reviewed the use of simvastatin in 130 patients with mixed hyperlipidemia and 195 patients with hypertriglyceridemia in a placebo-controlled, double-blind trial. After 6 weeks of treatment with simvastatin 20, 40, and 80 mg, significant reductions in CRP plasma levels were noted vs placebo ($P < 0.05$) (*Am J Cardiol*. 2002;90:942-946). CRP lowering by statins appears to be a class effect with multiple reports of benefit with various statins in the last 2 years.

FDA Actions

Roche's pegelated interferon alfa-2a (Pegasys) has been approved for use in combination with a ribavirin for the treatment of hepatitis C. The drug was approved in October 2002, but Roche has been eagerly awaiting the approval for combination treatment in order to compete with Schering-Plough's Peg-Intron/ribavirin combination for the same indication.

Eli Lilly has received approval to market atomoxetine (Strattera) for the treatment of attention deficit hyperactivity disorder (ADHD). Unlike other drugs for this indication, atomoxetine is not a stimulant and is not listed as a controlled substance. Rather, the drug is a selective norepinephrine reuptake inhibitor, which seems to play a role in regulating attention, impulsivity, and activity levels. Strattera is approved for treatment of ADHD in children, adolescents, and adults.

Eli Lilly has also received approval to market teriparatide injection (Forteo) for the treatment of osteoporosis in postmenopausal women who are at high risk for fracture. Teriparatide is a portion of human parathyroid hormone, which stimulates new bone formation in the spine and hip. The drug is given by daily injection in the thigh or abdomen. ■