Translating Clinical Research Into Clinical Practice in the Intensive Care Unit: The Central Role of Respiratory Care

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Critical care is entering a phase of rapid introduction of treatments that have demonstrated efficacy for reducing mortality and morbidity. Until recently the principal question facing intensivists was "Does this treatment work?" Though that question is still important, we now must address the same challenges other fields, notably cardiology, face in *implementing* these practices at the bedside. This report reviews the literature on the chasm between evidence and practice, on the barriers to implementing effective practices in the intensive care unit, and novel strategies to overcome those barriers. Hundreds of thousands of patients die each year in intensive care units in the United States, and it is essential that we take a programmatic approach to addressing their health care needs. *Key words: quality assurance, health care, health services research, guideline adherence, evidence-based medicine.* [Respir Care 2004;49(7):837–843. © 2004 Daedalus Enterprises]

Introduction

I would like to thank the Egan family and I would like to thank Ray Masferrer and the entire American Association for Respiratory Care (AARC) family for this prestigious and important award. Isaac Newton said, "If I have seen far, it is because I have stood on the shoulders of giants." I'm not sure that I have the same vision that Isaac Newton had when he spoke of Euclid and Pythagoras, but I too have had the opportunity to stand on the shoulders of giants in our field. They include people such as Neil MacIntyre at Duke University, where I was a medical resident, and Len Hudson and Dave Pierson at the University of Washington, where I did my pulmonary and critical care training. More importantly, it includes a lot of respiratory therapists (RTs) along the way who have had the "pleasure" of teaching me a lot of bedside respiratory care and clinical physiology in the middle of the night at the bedsides of critically ill patients.

I think it's a particularly exciting time to be an RT. We are at the dawn of an exciting era of evidence-based critical care that is being led by evidence on respiratory care. I'm going to talk about a scary chasm between what we should do, what we say we do, and what we really do. I'm

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going to take you through a working example of trying to bridge that chasm, including the barriers that we've encountered in trying to close the chasm between evidence and practice in the real world, and to talk about some practical solutions that you can do in your own intensive care units (ICUs).

How Many Patients Do I Need to Treat to Save One Life?

The story of evidence-based practice in the ICU does not begin very well. In the terms of clinical epidemiology we talk about the "number needed to treat," which is the number of patients I need to treat with a given therapy to save one life. For example, across a broad range of patients with suspected acute myocardial infarction, thrombolytic therapy reduces mortality from 11.5% to 9.6%, a difference of 1.9%.[1] Therefore, for every 52 patients with suspected acute myocardial infarction (1/0.019) one life will be saved by thrombolytic therapy. In critical care the story starts out a little bit worse than that. Clinical trials of human growth hormone with critically ill patients forced us to invent a new measure, the "number needed to treat to take a life."[2] That's because human growth hormone, applied as it was in the studies, increased mortality. We have some data that increasing oxygen delivery to certain septic patients, at least late in the course of their illness, increases mortality.[3] For every 5 people we treated in that fashion we would take one life. Well, that's bad news. Let's look at pulmonary artery catheterization—a diagnostic procedure that has been performed for over 30 years. Recent evidence on the number needed to treat to save a life in the ICU with a pulmonary artery catheter or care guided by that catheter suggests that the number is infinite because the studies show no evidence of benefit.[4,5] So you can treat or monitor as many people as you want, but we don't have any evidence that it reduces mortality. Five or 10 years ago this talk would end right here. There really was no problem translating evidence into clinical practice in the ICU because the evidence base supporting any specific approach to mechanical ventilation, weaning, sedation, or transfusion was so small. Of course, that does not mean there was no evidence to support critical care practice—simply that the evidence was not particularly strong.

I'm happy to say that today this is a much longer talk. Many of you are aware of the landmark studies that have, or should have, changed critical care practice. These are the studies that show the risks of transfusing non-leukoreduced blood, the benefits of a low-tidal-volume, low-pressure strategy in managing acute lung injury (ALI), the importance of protocol-based weaning that includes daily spontaneous breathing trials, and the benefits of noninvasive mechanical ventilation for COPD exacerbations.[6–9] Of course, that is only a sample of the important clinical trials that have finally demonstrated that specific ICU therapies can save lives. It is important to note that, at least in North American ICUs, all of you are the ones who are responsible for providing, at the bedside, many of these treatments. For every 5 COPD-exacerbation patients you treat with noninvasive ventilation, you save one life. For every 11 ALI patients that you place on a low-tidal-volume ventilation protocol that targets a tidal volume (V_T) $<$ 6 mL/kg of predicted body weight and plateau pressure $<$ 30 cm H_2O, you save one life. Let me describe how incredibly effective these treatments are. For the most part our colleagues in cardiology are talking about numbers-needed-to-treat between 30 and 100 for patients receiving various treatments for acute myocardial infarction. So now that we know that we have extremely effective therapies that that can save lives, it is reasonable to ask whether we are using them or whether we are just talking about using them.

Who Cares About Intensive Care?

Is the ICU even worth focusing on as a place for implementing effective practice? There is an Internet Web site that lists acute respiratory distress syndrome (ARDS) as a rare disease.[10] If that is so, perhaps there are not very many lives to be saved in correctly managing ALI and ARDS. Well, I certainly don't believe that's the case. Chris Goss and the ARDS Network have reported on the incidence and outcome of ALI based on ARDS Network screening.[11] Derek Angus and his colleagues in Pittsburgh studied hospital discharges data to estimate the incidence of severe sepsis.[12] Critical illness syndromes account for a large number of deaths in the United States. There are about 383,000 cases of severe sepsis and 180,000 cases of ALI each year in the United States. The mortality rates of those syndromes are between 30 and 60%. Hundreds of thousands of patients die in ICUs each year who could be saved. That won't surprise any of you who care for patients in the ICU, but it clearly shows that if you're going to focus your efforts on improving care to save lives, the focus of that intervention ought to be in the ICU.

So what does all this mean? When one compares the attributable mortality from critical illness syndromes to the attributable mortality from more familiar diseases, the effect of critical illness syndromes on the public health becomes apparent (Table 1). This table appears in the background section of every single grant that I write. Note that the figures for the attributable mortality from asthma and breast cancer are on the Center for Disease Control Web site, but you won't find the mortality figures for ARDS or sepsis there.

Table 1. Attributable Mortality of Critical Illness Syndromes Versus Other Diseases

Disease	Attributable Mortality
Acute lung injury	17,000–43,000
Acute respiratory failure	60,000–120,000
Breast cancer	41,528
HIV	14,802
Asthma	4,657

HIV = human immunodeficiency virus (Data from Reference 13).

Table 2. Rates of Use of Effective Therapy Among Eligible Patients With Acute Coronary Syndromes

Therapy	Rate of Use (%)
Aspirin	67–83
Thrombolytic therapy	43–64
Heparin	24–63
ACE inhibitors	59–65
Beta blocker	21–60

ACE = angiotensin-converting enzyme (Adapted from Reference 15).

The Chasm Between Evidence and Practice

So we know the ICU is an important place, where lots of deaths occur. We know that we have effective therapies to implement there. I think the next important question is, are we really using those therapies? Are we implementing effective practices in the ICU? The Institute of Medicine recently published 2 important reports that raise issues about the quality of medical care in the United States. In 1999 the Institute published *To Err Is Human: Building a Safer Health System,*[14] and in 2001 it published *Crossing the Quality Chasm: A New Health System for the 21st Century*.[15] You probably know the earlier report as the publication that started the furor over medical error. But of those 2 publications I find *Crossing the Quality Chasm* a far scarier read; it has examples from every medical field that known effective practices are not being used. Whether it's screening mammography, pneumococcal vaccination, hypertension control, or management of acute myocardial infarction, we are not implementing effective treatments. Even in fields where the evidence base is extremely mature, such as care of acute coronary syndromes, patients do not routinely receive effective treatments (Table 2).

What about critical care? Well, we look great. The reason we look great is because we're not even mentioned in *Crossing the Quality Chasm*, in which there are 15 references to "intensive care," 3 of which refer to telemedicine ICUs, and the other 12 are anecdotes about other ICU practices. There are zero references to sepsis and there is only one reference to ARDS, which refers to a study about translating computerized protocols for ARDS. In fact, if you look through the literature on application of evidence-based guidelines to ICU practice, we continue to look terrific, because no one's really looked. An important study from a group at Johns Hopkins reviewed the literature on why physicians don't follow evidence-based clinical practice guidelines.[16] They identified knowledge barriers (lack of familiarity with evidence), attitude barriers (lack of agreement with specific guidelines or guidelines in general, lack of motivation, lack of confidence that guidelines improve outcomes), and behavioral barriers (system factors, guideline factors, and environmental factors). After an extensive literature review of 76 articles, 120 surveys, and 293 barriers they found *none* that specifically related to critical care. They couldn't find any barriers specific to implementing effective practices in the ICU that met their search criteria.

I'll review the small number of studies available on this subject. One study from the United Kingdom was about implementing noninvasive ventilation for COPD exacerbations.[17] It found that 52% of hospitals failed to provide noninvasive ventilatory support for COPD exacerbations. In the 48% of hospitals that did provide it, respondents thought it was underused. Importantly, the investigators found a variety of barriers to implementing noninvasive ventilation. They thought the staff weren't trained adequately to use it, that there were financial barriers in terms of hiring enough staff to implement it, and that some staff were not persuaded by the current evidence of the benefits of noninvasive ventilation. This is particularly surprising since a lot of the data supporting noninvasive ventilation for COPD comes from the United Kingdom. Like the United States, the United Kingdom has implemented limitations on residents' clinical hours, and the survey disclosed that that limited the use of noninvasive ventilation. Other financial cutbacks led to reduced staff hours for physiotherapists and nurses, who are essential to the effective implementation of noninvasive ventilation. It is extremely important to identify these barriers, because solutions will need to be targeted to the specific problems. For example, many of the barriers identified in that study on noninvasive ventilation have solutions that need to be addressed at the policy, staffing, and reimbursement level rather than at the individual hospital level.

There is fairly compelling evidence that use of the semi-recumbent position reduces the risk of ventilator-associated pneumonia. The data may not be overwhelming, but the intervention is certainly inexpensive and safe.[18] Deborah Cook and her colleagues presented one of the few studies on why we have trouble implementing this simple

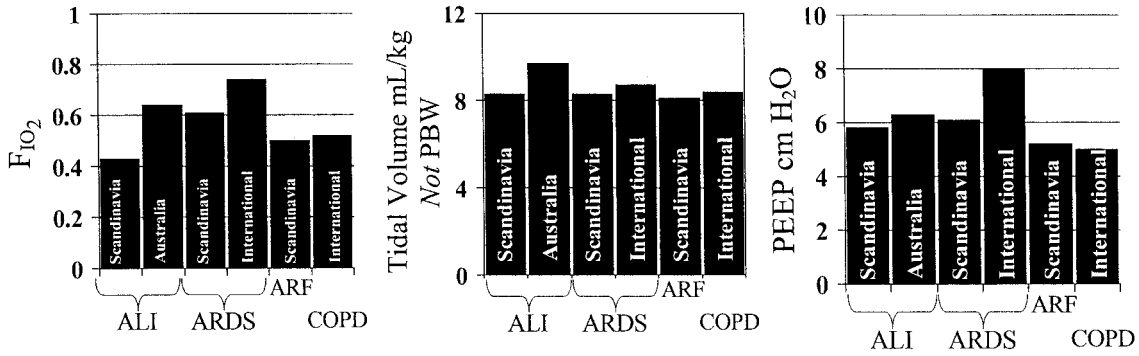

Fig. 1. Comparison of tidal volume, positive end-expiratory pressure (PEEP), and fraction of inspired oxygen (F_{IO_2}) in large cohorts of mechanically ventilated patients. ALI = acute lung injury. ARDS = acute respiratory distress syndrome. ARF = acute respiratory failure. COPD = chronic obstructive pulmonary disease. (Data on Scandinavia, Australia, and International are from References 21, 22, and 23, respectively).

intervention.[19] My favorite finding in the study was that, on the one hand, the nurses thought that the main deterrent to implementing semirecumbency was that physicians were not ordering semirecumbency, while on the other hand physicians thought the main deterrent was nursing preference. We must address such "disconnects" in communication and perception.

Of course you are all aware of the ARDS Network study that showed for the first time in a large multicenter clinical trial that a ventilator intervention can reduce ALI mortality.[8] In that study a V_T of 6 mL/kg of predicted body weight and plateau pressure < 30 cm H_2O was associated with a 31% mortality, and a V_T of 12 mL/kg predicted body weight was associated with 40% mortality. Given that we have few other interventions that have been shown to reduce ALI mortality, this is a big deal. Unfortunately, but perhaps not surprisingly, hospitals do not appear to be implementing lung-protective ventilation for ALI.[20] And the story for mechanical ventilation of ARDS patients is even worse. One of the criticisms of the ARDS Network trial was that it tested a hypothesis that we supposedly already knew to be true—that large V_T is injurious and that ALI patients should be ventilated with lower V_T and lower pressure than other patients.[21] However, data from a large number of mechanically ventilated patients indicate that it is a lesson we have not learned very well. Figure 1 compares 3 heterogeneous cohorts of mechanically ventilated patients who had ALI, ARDS, acute respiratory failure, or COPD.[22–24] Note that the V_T is in mL/kg of *measured* body weight, not *predicted* body weight, so you can add about 20% to the V_T values. On average we ventilate everyone with about 8 mL/kg, about 50% oxygen, and positive end-expiratory pressure (PEEP) of about 5 cm H_2O, *regardless of their diagnosis*. The recommendation to treat ALI patients with lower V_T and lower pressure *preceded* the ARDS Network data that showed that doing so saves lives.[25] It seems that "everyone knows" that we should use lower V_T to treat ALI; however, patients with ALI in large heterogeneous international cohorts receive about the same ventilator settings as patients with other causes of acute respiratory failure. And remember that (at least a decade ago) the average adult male in the United States was 69 inches tall and weighed 180 pounds and the average adult female was 63.7 inches tall and weighed 152 pounds. That 8 mL/kg (average ARDS ventilator settings around the world) would provide the man with a 650 mL V_T, whereas the ARDS Network findings indicate that he should receive 430 mL (ie, 33% lower), and the woman would receive 550 mL V_T, whereas the ARDS Network findings indicate that she should receive 330 mL (ie, 23% lower). Thus the average V_T used with ARDS patients reflects considerable deviation from the conclusions of the ARDS Network study. Of course, we don't know whether those deviations are clinically important, and those averages have fairly substantial deviations around the mean, suggesting that some patients were receiving V_T in the range of 10–12 mL/kg predicted body weight.

Why Don't We Do What We're Supposed to Do?

If we agree that there is strong evidence for effective ICU treatments, and we agree that we are not implementing many of those treatments, and that—compared to other fields—we have not really examined why we aren't changing our practice, let's move on to consider the barriers that are preventing us from changing our ICU practice. I think one of the more interesting issues is *recognition*. In the ICU we treat clinical syndromes such as ARDS, sepsis, and multiple organ failure. These aren't diseases that are readily diagnosed with blood tests. They are syndromes that, arguably, up until recently were not that important to diagnose. Of course it is important to diagnose infection or hypovolemia or hypoxemia, but until recently (I would argue) the diagnosis of ALI was irrelevant because we did not have a specific therapy to offer patients who had that

diagnosis. Similarly, though it is essential to diagnose infection, deciding whether a patient meets criteria for severe sepsis is only important if you have a therapy such as activated protein C or corticosteroids to offer. We know there are problems in the definition and recognition of ALI.[26,27] One study at a Veterans Hospital in Puerto Rico identified 21 patients who met criteria for ARDS, but only 4 of those patients had that diagnosis entered in the chart.[28] Recognizing critical care syndromes has always been difficult—but now it is clinically important.

RTs spend a lot of time documenting in the medical record. The AARC recommends charting over 50 variables in mechanically ventilated patients, including standard factors such as ventilator settings and obscure data such as pallor and skin color.[29] Very little is known about how these recommendations are used in practice. My colleague Saadia Akhtar was interested in whether a group of community and academic hospitals in King County, Washington, implemented those guidelines. She surveyed respiratory therapy directors and examined both blank flow sheets and ICU flow sheets from ARDS patients. There were 3 important findings:

1. The surveyed directors thought they were doing a better job than they really were.
2. There was tremendous variability in which of the AARC-recommended variables were actually charted and how often they were charted.
3. Important variables were not being charted for ARDS patients. For example, though nearly every chart recorded F_{IO_2}, peak inspiratory pressure, and PEEP, only 10 of 17 hospitals routinely recorded plateau pressure, 3 of 17 routinely recorded intrinsic PEEP or total PEEP, and none recorded V_T in mL/kg.[30] If RTs don't chart it, physicians can't act on it! Of course, if no one asks RTs to chart it then they probably won't. It seems clear to me that the AARC should revisit this list of documentation guidelines and consider revising them based on which variables we now have evidence for following.

Let's look at one more (and rather interesting) barrier. Many of the interventions we have been talking about so far are protocols—ways of organizing and implementing practice. They aren't new ventilators, new drugs, or new devices. We know who will market a new, expensive, antiplatelet drug or coronary stent for acute myocardial infarction. We know who will market a new, fast-acting sedative drug, percutaneous tracheostomy kit, or sepsis drug. The pharmaceutical and medical device industry has a very competent and efficient marketing and sales system. But who will market turning down V_T? Who will market turning *off* sedation? Who will market daily spontaneous breathing trials? In fact, we know quite a bit about changing clinical behavior.[31] Perhaps the most humbling fact that we've learned from those studies is that what I and most of my academic colleagues spend a great deal of time doing (namely, giving lectures and writing reports) has very little effect on what all of you do. Interventions that are effective are prompts or reminders that occur at the time a decision needs to be made, feeding back data to providers on current practice and combining multiple interventions (Table 3).

Table 3. Effectiveness of Various Interventions on Changing Clinical Practice

Little or No Effect	Variable Effect	Consistently Effective
Education	Feedback on practice	One-on-one detailing
Pamphlets	Local opinion leaders	Reminders
Lectures	Local consensus on practice	Combinations of interventions

(Adapted from Reference 31).

A Peek at a Possible Solution

Let me tell you a little about a study that is in progress. It is called the King County Lung Injury Project: Improving Ventilator Management. In it we are trying to increase the use of lung-protective ventilation with ALI patients. To identify the barriers to implementing lung-protective ventilation, we studied RTs and nurses who should have a lot of knowledge about it: the nurses and RTs at ARDS Network sites. In a study that is in press at *Critical Care Medicine*[32] we identified barriers to implementing lung-protective ventilation with the ARDS Network protocol including: physician reluctance to give up control over ventilator settings; failure to recognize ALI; lack of knowledge about the benefits of lung-protective ventilation; lack of a written protocol to implement lung-protective ventilation; and nurse and RT concerns about patient comfort, tachypnea, respiratory acidosis, and hypoxemia. So we knew we would have to address each of those. At each site we recruit RTs and nurses to serve as "screeners"; they undergo computer-based training on how to identify ALI. Each day they prompt/remind physicians that certain patients benefit from lung-protective ventilation. It is important that this is merely a prompt: physicians can practice as they see fit. The goal of the intervention is not to tell physicians what to do but to make it easy for them to provide lung-protective ventilation when they want to. We work with each site to develop a set of lung-protective-ventilation orders. Because nurses and RTs are concerned about patient comfort during lung-protective ventilation, we also developed a training video that includes interviews with ALI survivors and their families. Dean Hess, a

well known RT educator from Massachusetts General Hospital, helped us make the training video that gives RTs tips for implementing lung-protective ventilation. Finally, we provide data on implementation to each site as they progress, so they know how well they are doing. What is important about this study is that it primarily involves community hospitals that have a wide range of organization of ICUs. The study is about three-quarters completed, and the preliminary data look promising.

Conclusion

These are exciting times for respiratory care personnel, but they are times that place new responsibilities on all of you. The benefits of RT-based interventions such as lung-protective ventilation, noninvasive ventilation, and protocol-based weaning make implementing these at the bedside essential. You must be skilled enough, educated enough, and there must be enough of you at the bedside to take an active role in protocol implementation. You must be able to work in multidisciplinary teams to develop local protocols, to understand the physiologic and clinical principles that inform protocols so that you know which patients don't fit the protocols, and you must know the evidence well enough to constructively engage your colleagues and ensure that evidence is implemented into practice. In essence, you have to live up to the responsibility that running the protocols places on you.

The ICU is a high-mortality, high-cost, target-rich environment for improving the quality of care. We now have the luxury of a growing evidence base in critical care that makes the question "Are we implementing effective practices?" as important as the question "Which practices are effective?" Many of the current effective practices in the ICU are "low tech." Protocol-based, they require a team management approach. Because they are not marketed by industry, they've got to be "marketed" by all of you here today. There are limited data on whether effective practices are being implemented in ICUs and on how to change ICU practice, but the evidence base is growing. So the ICU presents unique challenges to people like me who want to study it, which makes for exciting research.

I will conclude by acknowledging the numerous people who worked with me over the years, particularly my "right and left hands," Ellen Caldwell, and the RTs, nurses, and physicians at all of our hospital sites, who have all been terrific to work with.

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