Embracing Dissemination and Implementation Research in Cardiac Critical Care

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In both high- and low-resource settings, high-quality health care can be ensured when routine clinical practices are based on high-quality evidence that underpins trustworthy clinical practice guidelines (CPGs). The United States Institute of Medicine (IOM) has defined CPGs as statements that include recommendations for patient care that are informed by a rigorous systematic review of the evidence and an assessment of the benefits and harms of alternative care options [1,2]. Typically, however, many routine practices and guideline recommendations are based on insufficient or low-quality evidence, while others are based solely on expert opinion. For example, in a review of all CPGs issued by the American College of Cardiology and American Heart Association from 1984 to September 2008, Tricoci et al. [3] showed that recommendations based solely on expert opinion, case studies, or "standard of care" (level of evidence C) were the most frequently encountered. Although important improvements have been proposed in the CPG development process [4] since the publication of the IOM standards, many challenges persist, including gaps in available evidence and also CPG implementation. The field of cardiac critical care (CCC) is no exception to these challenges [5].

Embracing dissemination and implementation (D&I) research is one approach to improving the quality of care delivered in CCC. As shown in Figure 1, our conceptualization of implementation research begins with (1) a rigorous systematic review of available evidence to identify interventions and practices of proven effectiveness that can inform the writing of CPG recommendations [6], (2) the identification of gaps in the available evidence that can inform new knowledge generation in the pre-clinical and clinical translational research arena (T1 to T3), and (3) the identification of gaps in CPG implementation that can inform post-clinical D&I research (T4 translation research) [7,8]. In this schema, T4 research includes specific observational or interventional studies to identify strategies that lead to a sustained, increased uptake of evidence-based practices and deimplementation of "evidence-free" practices. From this perspective, 2 examples are presented whereby embracing D&I research can help accelerate improvements in the quality of care delivered in critical care settings. A third example that serves as a model for successful D&I research is also provided.

NONINVASIVE POSITIVE PRESSURE VENTILATION IN CRITICAL CARE

The benefits of noninvasive positive pressure ventilation (NPPV) in selected patients were first described in 1936 by Poulton [9] and have since been firmly established and are increasingly recognized as beneficial for some patients with acute respiratory failure [10–13]. In patients without contraindications who present with acute respiratory failure secondary to cardiogenic pulmonary edema or exacerbations of chronic obstructive pulmonary disease (COPD) complicated by hypercapnic acidosis, current guidelines make a strong recommendation for an immediate use of NPPV (grade 1A recommendation) [14]. Despite the strength of the recommendation on the basis of high-quality evidence supporting the first-line use of NPPV in these settings, the majority of patients do not receive this intervention.

In one review of patients who had intensive care unit admitting diagnoses of COPD or heart failure and met explicit criteria for a trial of NPPV, only 20 of 59 patients (33.9%) received a trial of NPPV; the remaining 39 patients (66%) were intubated [15]. Similarly, a survey of the directors of respiratory care of all 81 acute care hospitals in the states of Massachusetts and Rhode Island between September 2002 and January 2003 found an overall utilization rate for NPPV of 20% of ventilator starts, with enormous variation in the estimated utilization rates among different hospitals, from none to >50% [12]. Congestive heart failure and COPD constituted 82% of the diagnoses of patients receiving NPPV; nevertheless, NPPV was still used in only 33% of these patients receiving any form of mechanical ventilation [12]. The investigators concluded that the low utilization rates and marked variation within the region reflected multiple implementation challenges, including a lack of physician knowledge, insufficient respiratory therapist training, and inadequate equipment [12]. More recent surveys of the emergency departments of 300 hospitals (representing a total of 88,258 hospital beds) in Spain [16], hospitals with academic emergency medicine residencies in the United States [17], physicians and respiratory therapists from 3 hospitals in each of 21 Veterans Affairs networks in the United States [18], and a retrospective cohort study using data from the 2006 to 2008 Nationwide Emergency Department Sample [19] all confirm a need for improvement in the utilization of NPPV. The Nationwide Emergency Department Sample data showed that NPPV use for acute exacerbations of COPD increased from 14% in 2006 to 16% in 2008 ($p = 0.049$), but use varied widely among hospitals, ranging from 0% to 100%, with a median of 11% [19]. The survey from Spain showed that fewer than half of emergency departments offered NPPV, and among them, only 1 in 3 had protocols for the use of NPPV [16]. Again, barriers to greater use of NPPV included a lack of physician familiarity, availability of respiratory therapy, appropriate equipment in the emergency department, and time required for setup [16–18,20].

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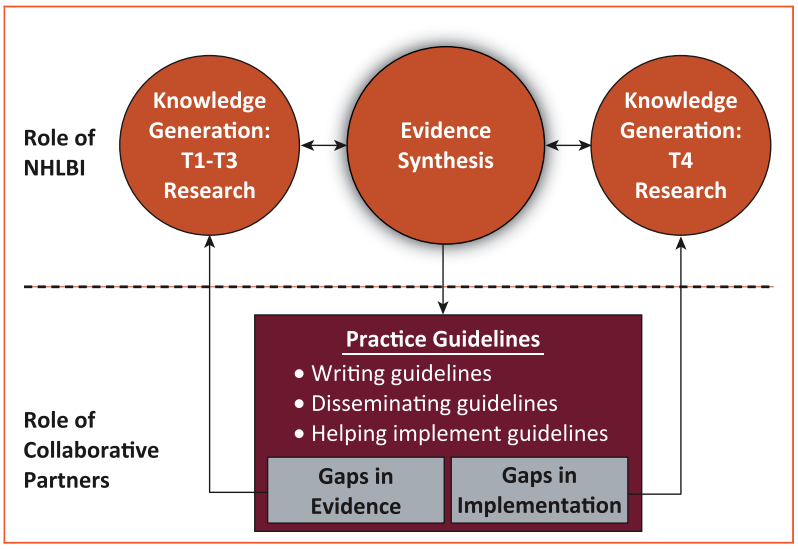

FIGURE 1. The National Heart, Lung, and Blood Institute is committed to supporting rigorous systematic review and synthesis of available evidence to underpin a collaborative partnership model for developing clinical practice guidelines. During this process, identified gaps in evidence can inform new knowledge generation in the pre-clinical and clinical translational research arena (T1 to T3). Similarly, gaps in implementation can inform post-clinical dissemination and implementation (T4 translation) research. This figure does not show the appropriate research studies that are needed to demonstrate whether guidelines applied in practice as intended actually yield the expected clinical and population health impact.

INHALED OXYGEN THERAPY IN ACUTE MYOCARDIAL INFARCTION

The underutilization of NPPV in patients who meet explicit criteria for benefit contrasts sharply with the widespread administration of inhaled oxygen at normal pressure delivered by face mask or nasal cannula in the critical care of patients with acute myocardial infarctions (AMIs) and other acute coronary syndromes for which compelling evidence of benefit is lacking. A recent evidence review by the Cochrane Heart Group found no conclusive evidence from randomized controlled trials to support the routine use of inhaled oxygen in patients with AMIs [21]. None of the 3 randomized controlled trials included in the review demonstrated that oxygen therapy in patients with AMIs did more good than harm on clinical outcomes [21]. In fact, there were more deaths among patients on inhaled oxygen therapy than among those on air, suggesting the possibility of harm although this finding was not statistically significant, because of the small number of deaths recorded [21]. In a recent editorial in which Lauer and Bonds [22] reflected on this issue, they commented that "it is hard to believe that after so many decades we do not know whether this therapy is beneficial, neutral, or harmful."

Despite this lack of compelling evidence, the 2007 American College of Cardiology and American Heart Association guidelines recommended the routine administration of supplemental oxygen to all patients with non–ST-segment elevation acute coronary syndromes during the first 6 h after presentation on the basis that it is safe and may alleviate hypoxemia [23]. In the most recent American guidelines for the management of acute coronary syndromes with and without ST-segment elevation, oxygen therapy is recommended for the subset of patients with cyanosis, arterial oxygen saturation $< 90\%$, respiratory distress, or other high-risk features of hypoxemia (level of evidence C) [24,25]. The European Society of Cardiology guidelines for the management of AMI in patients presenting with ST-segment elevation also recommends oxygen therapy in patients who are "breathless, hypoxic, or who have heart failure" [26] and for patients with acute coronary syndromes and non–ST-segment elevation in whom oxygen saturation is $<90\%$ (level of evidence C) [27]. In both the American and European guidelines, the lack of compelling evidence of benefit for supplemental oxygen administration to all patients with acute coronary syndromes is explicitly recognized [24,26,27]. In particular, the 2013 American guideline for ST-segment elevation AMI provided ample caution in the use of supplemental oxygen and explicitly called for more research to be conducted [25]. That call may soon be answered by Hofmann et al. [28], who recently described a "registry-based clinical trial" (Determination of the Role of Oxygen in Suspected Acute Myocardial Infarction) that is designed and powered to assess the value of supplemental oxygen in patients with AMIs.

TIMELY REPERFUSION: A MODEL OF DISSEMINATION AND IMPLEMENTATION RESEARCH SUCCESS

The old adage, time is muscle, has been used to emphasize the importance of timely reperfusion after thrombotic coronary artery occlusion to minimize total ischemic time, maximize myocardial salvage, and reduce morbidity and mortality in the setting of AMI. This concept has led to important performance metrics, such as first medical contact–to–device, door-to-balloon (D2B), door-to-needle, and door-in–door-out times [25]. In the United States, primary percutaneous coronary intervention (PCI) is the recommended method of reperfusion when it can be performed in a timely fashion by experienced operators (level of evidence A) [25], with a recommended ideal first medical contact–to–device time system goal of 90 min or less (level of evidence B) [25]. Most national and international practice guidelines also recommend that the time from hospital arrival to balloon reperfusion, the D2B time, should be as short as possible and should not exceed 90 min [25,26] or 60 min in primary PCI hospitals [26].

A decade ago, only one-third of United States patients received primary PCI within 90 min, and another third received the intervention more than 120 min after arriving at a hospital [29]. These disappointing practice findings

highlighted significant systems- and provider-level delays that adversely affected timely reperfusion with primary PCI. The national attention these data generated helped galvanize several public and private stakeholder actions important in the field of D&I research. Krumholz et al. [30] summarized these actions and reported the remarkable improvements seen between 2005 and 2010. First, the Centers for Medicare and Medicaid Services initiated public reporting of the percent of patients treated within guideline-recommended times. The National Heart, Lung, and Blood Institute provided funding for research to understand and identify systems- and organization-level factors important in improving D2B times [31]. The American College of Cardiology worked with national partners to launch a national campaign to improve D2B times by advocating the implementation of key strategies proven effective in reducing delays [32]. The American Heart Association also launched an additional national initiative to improve systems of care and reduce delays in timely reperfusion in patients with ST-segment elevation AMIs [33]. As a result of these complementary and synergistic actions from multiple stakeholders acting at multiple levels, D2B time declined from a median of 96 min in the year ending December 31, 2005, to a median of 64 min in the 3 quarters ending September 30, 2010 [30]. Correspondingly, the percent of patients with DB2 times of <90 min or <75 min more than doubled from 44.2% to 91.4% and from 27.3% to 70.4%, respectively [30]. Importantly, the declines in median times were greatest among groups that had the highest median times at baseline, including patients older than 75 years, women, and blacks, thus contributing to reductions in related disparities [30,34].

PERSPECTIVES FOR FUTURE RESEARCH

The 3 examples cited here highlight distinct but interrelated perspectives involved in embracing D&I research in a critical care setting. In the case of NPPV, there is significant underutilization of an intervention that has compelling evidence of effectiveness in cardiogenic pulmonary edema and COPD exacerbations. Novel strategies need to be identified that can lead to accelerated and sustained adoption of NPPV as the intervention of choice for eligible patients. In contrast, the widespread administration of supplemental oxygen in the setting of AMI is a practice based on insufficient evidence. Appropriately designed clinical trials are needed that can provide definitive evidence to either support this widespread use or lead to deimplementation of the practice. The third example, from coronary reperfusion, provides hope that successful translation of research findings into clinical and public health practice is feasible, affordable, and sustainable and may even lead to the reduction and possible elimination of related health disparities. However, the conclusion that successful translation of research findings into widely applied CPGs leads to the desired clinical and public health outcomes, including the elimination of health disparities, should not be assumed but should be formally and rigorously tested.

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