important questions. First, what is the optimal role and timing of the serial measurement of troponin levels in patients with PE? Second, is an elevated troponin level actually more important prognostically than right ventricular dysfunction on an echocardiogram, or is it just equivalent? Third, will other biomarkers, such as brain natriuretic peptide, be more useful, equivalent, or complementary to cardiac troponin levels?

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Practice Guidelines for Noninvasive Positive-Pressure Ventilation

Help or Hindrance?

Clinical practice guidelines have been developed for numerous clinical scenarios, including the management of community-acquired pneumonia, asthma, COPD exacerbations, and many other conditions. The purpose of guidelines is to provide a blueprint for the best clinical practice in a given situation based on current evidence and expert opinion. In this way, guidelines are meant to standardize practice, to serve an educational function, to enhance resource utilization, and, ultimately, to improve patient outcomes. However, the creation of guidelines does not guarantee that these goals will be achieved. In fact, ill-conceived guidelines can promote increased resource consumption without improved outcomes. Thus, evaluation and modification are important components of guideline maintenance to ascertain that they are achieving the desired goals.

The application of noninvasive positive-pressure ventilation (NPPV) lends itself well to clinical practice guidelines. Numerous clinical decisions must be made when initiating and monitoring NPPV, and guidelines have the potential for facilitating the administration of NPPV and for reducing variability in the techniques of application, particularly at less experienced centers. When used optimally, NPPV is applied to carefully selected patients using particular types of equipment and ventilator settings, with appropriate monitoring. Each of these steps can be subjected to guidelines based on evidence, expert opinion, or both.

In the current issue of CHEST (see page 2062), Sinuff et al describe the development, implementation, and evaluation of an NPPV guideline. The authors are to be commended for a carefully per-
formed study exemplifying these critical steps in guideline creation. The guideline was based on a review of the available evidence as well as on opinion from a consensus conference. It was then implemented by being posted throughout hospital wards, and by using physician order sheets as well as nursing and respiratory therapy flow sheets. The authors then assessed the efficacy of the guideline by comparing utilization and outcomes of patients treated for NPPV for 18 months prior to and following the implementation of the guidelines.

The major finding of the study was that guidelines influence clinician behavior with regard to resource utilization and monitoring. After implementation of the guideline, NPPV was used more often in the ICU, arterial blood gases were measured in a higher proportion of patients, and more pulmonary consultations were sought. The authors refrained from specifying ventilator settings in their guideline because of a lack of evidence with which to justify such recommendations. However, they did recommend the initial use of a full-face mask (despite a lack of supportive published evidence), and more patients were treated with full-face masks after than before guideline implementation.

The effects of guidelines on overall patient outcomes were disappointing. The intubation and mortality rates among all patients using NPPV were similar before and after guideline implementation, and hospital and ICU lengths of stay were unchanged. However, a subgroup analysis revealed some promising results. Among patients who met the guideline criteria for NPPV, both the intubation and mortality rates fell by half from 33% before guideline implementation to 16.7% after. In addition, there was a strong trend after guideline implementation for lower intubation rates in the COPD subgroup (38.7% vs 25.6%, respectively) and the chronic heart failure (CHF) subgroup (45.2% vs 23.3%, respectively), and for lower mortality in the CHF subgroup (50% vs 26.1%, respectively). Although these differences were not significant, they suggest the possibilities that guidelines can improve outcomes and that these differences might have reached statistical significance in a larger study.

On the other hand, there were some disturbing results from the subgroup analysis. Specifically, because the authors thought that the evidence supporting NPPV use was sufficient only for patients who had received diagnoses of COPD and CHF, the guidelines categorized patients with other diagnoses as not meeting the criteria for NPPV use. The rate of intubation among patients not meeting guideline criteria increased from 35% before guideline implementation to 100% after (p < 0.0001), and there was a trend for increased mortality rate (20.5% vs 34.3%, respectively). Although the latter increase was not statistically significant, the magnitude of increase was almost as large as the drop in mortality rate among patients meeting the guideline criteria. The concern is that by classifying a sizeable category of patients as “not meeting NPPV criteria,” the authors could have unintentionally encouraged endotracheal intubation in this subgroup, possibly contributing to morbidity and mortality. The authors considered that the increased use of intubation in this subgroup was indicative of “more appropriate” clinical practice, but, lacking a control group, it is equally tenable to argue that some of these intubations were unnecessary and perhaps inappropriate.

Rather than limiting the use of NPPV to patients who have received only a few diagnoses, perhaps the guidelines should have relied more heavily on physiologic and clinical criteria. This would be more in keeping with suggested guidelines from consensus groups as well as some recent clinical reviews. Admittedly, the evidence to support the use of NPPV in patients without COPD or CHF is deficient (with the possible exception of immunocompromised patients). However, it must be recalled that lack of evidence is not tantamount to lack of efficacy. Thus, because the evidence is not firm against the use of NPPV in patients who have received other diagnoses, the guidelines might allow for a trial of NPPV in non-COPD and non-CHF patients who meet other clinical criteria, recommending close monitoring and early intubation if the patient fails to respond favorably.

Another concern about the guidelines is that they may have encouraged the overutilization of resources. Somewhat arbitrarily (because there are no clearly supportive data), the guidelines required the initial use of the ICU with a 1:1 patient/nurse ratio. Although the authors considered the greater use of ICUs with this intensity of nursing as evidence of “improved cardiopulmonary monitoring,” it also could be argued that this represents an excessive use of nursing resources. The study by Plant et al, as well as this writer’s personal observations, indicate that most patients receiving NPPV can be successfully managed in a less intensive setting than an ICU (such as a step-down unit). The guideline requirement of a 1:1 nursing ratio virtually precludes management in such a unit. The guidelines should be flexible on this point, allowing less intensive nursing monitoring (ie, in a step-down unit or even a medical ward) depending on the acuity of the illness. Plant et al found that the mortality benefit in their study was no longer apparent in the subgroup of patients with pH < 7.30. Thus, the guidelines could be reframed to allow management in a less intensive setting.

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setting except for sicker patients (as characterized by low pH, persisting tachypnea, hypoxemia, etc).

Other minor questions about the guidelines regarding the exclusion of certain patients can be raised. For example, patients with pneumothoraces are excluded, with no provision for inclusion once appropriate drainage has been instituted. Also, patients with upper airway obstruction were excluded, yet a historically controlled trial\(^1\) has indicated that NPPV is very effective at avoiding intubation in patients with postextubation respiratory failure, a group of patients in whom temporary upper airway obstruction related to glottic swelling is fairly common. Upper airway obstruction might be considered a relative contraindication, depending on the severity of the obstruction.

Despite these concerns, the guidelines created by Sinuff et al represent an important step forward the formulation of widely applicable guidelines for the implementation of NPPV. As the authors acknowledged in their discussion, guideline creation is a dynamic process. Modifications are made as new evidence becomes available, and in response to evaluations and experience. In addition, guidelines need to be tailored to individual institutions, taking into account staff and technical resource availability, and other unique characteristics. Sinuff et al have established that NPPV guidelines influence clinician behavior and thereby can facilitate the standardization of techniques. In this respect, guidelines are clearly helpful. On the other hand, unless they can be shown to improve the efficiency of resource utilization and/or patient outcomes, they also can be a hindrance, with the potential for needlessly increasing resource utilization. At present, the guidelines for NPPV should be considered a work in progress, with a strong endorsement awaiting better evidence of efficacy.

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Induced Sputum Analysis For T Helper Type 2 Cell Regulation

Closing the Loop

The past decade has seen notable progress in our understanding of allergic asthma. Despite clear advances in dissecting the molecular and genetic factors that contribute to the asthmatic phenotype, morbidity and mortality from asthma, especially in industrialized nations, is increasing.\(^1\)\(^2\) However, there is cause for optimism in the development of new diagnostics and therapeutics. The application of techniques in molecular biology, specifically the investigation of the control of gene transcription, has become routine and accessible. With these applications, we have greater understanding of the early steps in the development of the immune response that is central to expression of the asthmatic phenotype.

Along with this new knowledge comes a myriad of potential new therapeutic targets. Two global controllers of transcriptional programs that define the two types of CD4\(^+\) helper T cells, T helper (Th) type 1 and Th2, have now been identified. \(\gamma\)-Interferon-producing Th1 cells are essential for acquired host defense against many infectious agents. The transcription factor that regulates the development of Th1 cells is T-bet.\(^3\) Th2 cells are responsible for humoral immunity. The transcription factors that dictate their development are GATA-3 and c-Maf.\(^4\)\(^5\) Th2 cells are defined by their synthesis of interleukin (IL)-4, IL-5, IL-9, and IL-13. While both types of Th cells are important for a fully developed acquired immune system, there are circumstances in which the inflammation that accompanies the immune...