lymphoma. Further investigations are needed to clarify whether there is antineoplastic activity in clarithromycin.

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Financial/nonfinancial disclosures: The authors have reported to CHEST that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

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DOI: 10.1378/chest.10-2768

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Toward a Noninvasive Approach to Early Goal-Directed Therapy

To the Editor:

Although early goal-directed therapy (EGDT) has been a landmark in guiding the approach to patients with sepsis in the ED, few institutions seem willing and able to adopt it for all eligible patients.1 The complexity and invasiveness of the protocol are the most frequently cited barriers. In particular, it has been underlined that many clinicians would not feel comfortable with inserting a central venous catheter (CVC) as a guide to treatment when, for various reasons, they believe that their patients could be treated adequately with a noninvasive approach.

In his counterpoint editorial in a recent issue of CHEST (September 2010), Schmidt2 maintained that the development of alternative goal-directed therapy/resuscitation protocols that are simpler and noninvasive may facilitate implementation. At our institution, we experienced difficulties similar to those described by Mikkelson et al3 since, even after extensive educational interventions in the year 2007, <50% of eligible patients were treated in accordance to the EGDT protocol, in most cases because a CVC was not placed in the patient in the ED. These patients received an inadequate amount of fluids within the first 6 h, probably because when central venous pressure was not measured, only clinical signs were used as a guide to fluid replacement. We are now enrolling patients to a noninvasive protocol that uses inferior vena cava collapsibility >30% and the absence of B lines at lung ultrasound as a guide for fluid challenge.4 CVC placement is reserved for patients who need noradrenaline infusion. A lactate clearance >10% rather than adequate central venous oxygenation values is used as a sign of improving tissue perfusion.5 To date, we have enrolled 27 patients with sepsis whose eligibility was defined as a serum lactate level of ≥4 mmol/L. (seven patients) or systolic BP <90 mm Hg after volume resuscitation (20 patients). Average fluid infusion was 4,120 ± 1,473 mL. A CVC needed to be inserted for the administration of vasoactive drugs in only 44% of cases. Mortality was 44.4% in patients with hypotension and 14.3% in normotensive patients with high lactate levels. Both values are comparable with those published by Rivers6 in his original study. In conclusion, we believe that given the increasing diffusion of clinical ultrasound in the ED, a noninvasive approach such as the one we are using could prove helpful in overcoming many difficulties inherent in the classic EGDT protocol and could favor its well-deserved diffusion.

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DOI: 10.1378/chest.10-2632

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Response

To the Editor:

I appreciate the added perspective of Coen and colleagues regarding my recent counterpoint editorial in CHEST (September 2010) of yet another group reporting difficulty adhering to an early goal-directed therapy (EGDT) protocol despite extensive efforts. Using a novel approach, these authors are studying a dynamic fluid responsiveness predictor (vena caval collapsibility on hand-carried ultrasound examination) in place of the central venous pressure (CVP). This tactic addresses a major failing in conventional EGDT: CVP simply fails to distinguish patients who will respond to fluids from those who will not. For example, in one large study of volume challenges in septic subjects, the positive predictive value of CVP < 8 mm Hg for identifying those who responded was only 47%. The impact of this is that many patients who could respond to further fluids despite a CVP > 8 will be treated with inappropriate blood transfusion or vasoactive therapy. At the same time, many patients who are fluid unresponsive, despite a CVP < 8, will be driven to receive yet more ineffective fluid. These findings mirror those of many other studies published over the past 2 decades showing the physiologic unsuitability of CVP for guiding fluid resuscitation.

In addition to using ultrasound to replace CVP, these investigators then turn the probe on the lungs in an attempt to identify those patients who already have pulmonary edema. A complete goal-oriented ultrasound examination (vena cava plus both lungs) can probably be completed in 3 min, certainly in less time than required for insertion and calibration of a central venous catheter.

Even these possible improvements on EGDT will not lead to superior outcomes if the whole concept of EGDT is flawed. The unusually high mortality in the control group of this study  casts doubt on both the adequacy of control group care and the generalizability of these results to other patients. Finally, a Bayesian analysis of the original trial shows that even a mildly skeptical clinician would conclude that the EGDT trial failed to show benefit.

For many reasons, pending the results of larger, multicenter trials, EGDT should not be considered the standard of care. Meanwhile, creative attempts to meld the commonsense approach of urgent treatment with state-of-the-art knowledge of circulatory physiology will lay the foundation for the future of sepsis therapy: a randomized clinical trial. JAMA. 2010;303(8):739–746.


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Is Pleural Ultrasoundography Better Than Chest Radiograph for Follow-up Resolution of Pneumothorax?

To the Editor:

In a recent issue of CHEST (September 2010), Galbois and colleagues concluded that pleural ultrasoundography (PU) was more accurate and gave faster results than chest radiograph (CXR) in follow-up of pneumothorax resolution. Although we (in the Department of Pulmonary and Critical Care at Louisiana State University) believe that PU is a great diagnostic tool in the ICU, we disagree with some of the findings of their research and have concerns related to its validity.

The study used a single center and single investigator in an operator-dependent technique. CXRs were read by the caring physician rather than by an independent experienced radiologist; this may have led to a bias favoring PU over CXR. The confirmation of pneumothorax was done in most cases by a nonstandard method (aspiration of 10 mL of air) and may have picked up cases of no clinical significance.

Although we understand that the study was designed to evaluate the resolution of pneumothoraces, it can still be criticized for using the same subjects (44 patients), obtaining at least three CXRs and three PUs on each, and counting these tests as independent variables. Furthermore, the use of Fisher exact test for data analysis without establishing independency in this situation is not supported.

The study population was mainly patients with primary spontaneous pneumothoraces (31/44), except for only one subject with dysorphic emphysema in which PU gave false-positive results. The prevalence of severe emphysema in the patient population with pneumothoraces in practice is high, causing concerns about the ability to generalize the findings of this study to the external population.

The sample size of this study was too small, especially when the independency issue stated previously is considered. According to our calculations, for a well-powered study, approximately 320 independent subjects and tests are needed. Finally, the clinical accuracy of the two techniques compared was not assessed in this study.