4. Shapiro N, Howell MD, Bates DW, et al: The association of sepsis syndrome and organ dysfunction with mortality in emergency department patients with suspected infection. *Ann Emerg Med* 2006; 48:583–590, 590.e1
5. Fries M, Weil M, Sun S, et al: Increases in tissue Pco2 during circulatory shock reflect selective decreases in capillary blood flow. *Crit Care Med* 2006; 34: 446–452
6. Trzeciak S, McCoy JV, Phillip Dellinger R, et al; Microcirculatory Alterations in Resuscitation and Shock (MARS) investigators: Early increases in microcirculatory perfusion during protocol-directed resuscitation are associated with reduced multi-organ failure at 24 h in patients with sepsis. *Intensive Care Med* 2008; 34:2210–2217
7. Negovsky VA: The second step in resuscitation–the treatment of the 'post-resuscitation disease'. *Resuscitation* 1972; 1:1–7
8. Bernard SA, Gray TW, Buist MD, et al: Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. *N Engl J Med* 2002; 346:557–563
9. Hypothermia after Cardiac Arrest Study Group: Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. [erratum appears in *N Engl J Med* 2002; 346:1756]. *N Engl J Med* 2002; 346:549–556
10. Gaieski DF Neumar RW Fuchs B et al: Haemodynamic management strategies are not explicitly defined in the majority of therapeutic hypothermia implementation studies. *Resuscitation*. 2012; 83:835–839
11. Adrie C, Adib-Conquy M, Laurent I, et al: Successful cardiopulmonary resuscitation after cardiac arrest as a "sepsis-like" syndrome. *Circulation* 2002; 106:562–568
12. van Genderen ME, Lima A, Akkerhuis M, et al: Persistent peripheral and microcirculatory perfusion alterations after out-of-hospital cardiac arrest are associated with poor survival. *Crit Care Med* 2012; 40:2287–2294
13. Donnino MW, Miller J, Goyal N, et al: Effective lactate clearance is associated with improved outcome in post-cardiac arrest patients. *Resuscitation* 2007; 75:229–234
14. Trzeciak S, Rivers EP: Clinical manifestations of disordered microcirculatory perfusion in severe sepsis. *Crit Care* 2005; 9(Suppl 4) :S20–S26
15. Bateman RM, Walley KR: Microvascular resuscitation as a therapeutic goal in severe sepsis. *Crit Care* 2005; 9(Suppl 4):S27–S32

Predicting who will develop acute respiratory distress syndrome following trauma: Why bother?*

Acute lung injury (ALI) is a common and devastating complication of acute illness or injury with an in-hospital mortality of approximately 40%. Epidemiologic studies suggest that there are approximately 200,000 cases of ALI in the United States each year, associated with 75,000 deaths (1). Furthermore, ALI accounts for 3.5 million hospital days, long-term decrease in quality of life, and enormous costs related to intensive care and rehabilitation. ALI has of course been the focus of intense research efforts, and significant progress has been made in ventilator management and in supportive treatment. Surprisingly, however, efforts at preventing ALI are still in their infancy. ALI represents a major public health problem, and effective prevention of ALI has the potential not only to save and improve lives but also to lead to significant cost savings for the healthcare system by preventing the development of the full-blown syndrome.

A recent workshop on the future of research into ALI, sponsored by the National Heart Lung Blood Institute, stressed the importance of prevention in future research (2). The clinical syndrome of ALI generally occurs as a complication of an initial predisposing acute injury, such as pneumonia, aspiration, sepsis, trauma, shock, or massive transfusion (3). But, only a fraction of patients with these initial injuries (10%–30%) will go on to develop ALI (4, 5). In many of those who will eventually suffer from ALI, the presentation is delayed. At hospital admission, only 30% of patients who will eventually have ALI fulfill the diagnostic criteria (6). The remaining patients go on to develop ALI a median of 2 days after hospital presentation (interquartile range 1–4 days). This period of time between hospital presentation and development of ALI is the window of opportunity for interventions to prevent the development of ALI.

During the period between hospital admission and the development of ALI, healthcare delivery factors, including delayed treatment of infection and shock, fluid and transfusion strategies, prevention of common intensive care unit complications, and management of mechanical ventilation, may be as important as individual biology in determining the development and outcome of ALI. Recently, Li and colleagues (7) from the Mayo Clinic published their experience of 8 yrs of implementing these best practices. They demonstrated a reduction in the age- and sex-specified prevalence of acute respiratory distress syndrome (ARDS) in Olmsted County, which decreased from 81 to 38.3 cases per 100,000 person-years. This decrease was largely driven by the prevention of hospital-acquired ARDS, whereas the prevalence of community-acquired ARDS remained essentially unchanged.

In this issue of *Critical Care Medicine*, Watkins and colleagues (8) present a new predictive model for the development of ARDS after trauma. The model was derived in a cohort of severely injured trauma patients who participated in a randomized controlled trial, conducted between the years 2003 and 2004. This trial was designed to evaluate the effect of leukoreduced vs. standard blood transfusions on post-traumatic infection and found no effect. The model was then validated in a separate cohort of patients collected prospectively between 2003 and 2010. The final model includes patient age and severity of illness (Acute Physiology and Chronic Health Evaluation II and Injury Severity Score), as well as specifics of the injury and treatment (blunt injury, pulmonary contusion, flail chest, and need for massive transfusion). Importantly, all

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of these data elements should be available either immediately at admission or very soon afterwards. The resultant score performed reasonably well with an area under the receiver operator characteristic curve of 0.79 in the derivation cohort and 0.71 in the validation cohort and was superior to previously published efforts (9, 10).

Is this score important to the bedside clinician? Will this score influence treatment of individual patients? The short answer is "not right now." There is only one element of the score that is potentially modifiable, massive transfusion, an area that is already the subject of intense ongoing research in the trauma community. Li and colleagues (7) demonstrated that an aggressive strategy of implementing best practice measures, including restricting transfusion, can lead to a reduction in the prevalence of ARDS. One would hope that these measures, which are appropriate for nearly all patients, are either already in place or else in the process of being implemented in well-directed ICUs. In fact, the current study by Watkins et al (8) validates this approach and suggests that these measures are effective. The incident rate of ARDS in the validation cohort, collected between the years 2003 and 2010, is significantly lower (24%) than that in the derivation cohort, which was collected earlier, from 2003 to 2004 (35%). This improvement was observed in spite of the fact that the validation cohort was significantly sicker.

The true importance of this work by Watkins and colleagues is in its future potential use in facilitating research into the prevention of ALI. Such future studies, testing pharmacological interventions aimed at preventing the development of ALI, will not be feasible in unselected patient populations. To do so would require enrollment of thousands of patients at huge cost both in terms of money spent and opportunity lost. Success in these future trials will depend on the rapid identification of high-risk patients using well-developed and validated scoring systems. Once these patients are identified, and all current best practice interventions are implemented, potential new pharmacological interventions targeted at the specific population may be tested (11). Work such as that presented by Watkins et al in this issue of *Critical Care Medicine* is the crucial first step in that process.

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REFERENCES

1. Rubenfeld GD, Caldwell E, Peabody E, et al: Incidence and outcomes of acute lung injury. *N Engl J Med* 2005; 353:1685–1693
2. Spragg RG, Bernard GR, Checkley W, et al: Beyond mortality: Future clinical research in acute lung injury. *Am J Respir Crit Care Med* 2010; 181:1121–1127
3. Hudson LD, Milberg JA, Anardi D, et al: Clinical risks for development of the acute respiratory distress syndrome. *Am J Respir Crit Care Med* 1995; 151(2 Pt 1):293–301
4. Fowler AA, Hamman RF, Good JT, et al: Adult respiratory distress syndrome: Risk with common predispositions. *Ann Intern Med* 1983; 98(5 Pt 1):593–597
5. Gong MN, Thompson BT, Williams P, et al: Clinical predictors of and mortality in acute respiratory distress syndrome: Potential role of red cell transfusion. *Crit Care Med* 2005; 33:1191–1198
6. Gajic O, Dabbagh O, Park PK, et al: U.S. Critical Illness and Injury Trials Group: Lung Injury Prevention Study Investigators (USCIITG-LIPS): Early identification of patients at risk of acute lung injury: Evaluation of lung injury prediction score in a multicenter cohort study. *Am J Respir Crit Care Med* 2011; 183:462–470
7. Li G, Malinchoc M, Cartin-Ceba R, et al: Eight-year trend of acute respiratory distress syndrome: A population-based study in Olmsted County, Minnesota. *Am J Respir Crit Care Med* 2011; 183:59–66
8. Watkins TR, Nathens AB, Cooke CR, et al: Acute respiratory distress syndrome after trauma: Development and validation of a predictive model. *Crit Care Med* 2012; 40:2295–2303
9. Navarrete-Navarro P, Rivera-Fernández R, Rincón-Ferrari MD, et al: GITAN multicenter project: Early markers of acute respiratory distress syndrome development in severe trauma patients. *J Crit Care* 2006; 21:253–258
10. Miller PR, Croce MA, Kilgo PD, et al: Acute respiratory distress syndrome in blunt trauma: Identification of independent risk factors. *Am Surg* 2002; 68:845–850; discussion 850
11. Litell JM, Gong MN, Talmor D, et al: Acute lung injury: Prevention may be the best medicine. *Respir Care* 2011; 56:1546–1554