

## Commentary

# Acute lung injury, overhydration or both?

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### Abstract

Acute lung injury or acute respiratory distress syndrome (ALI/ARDS) in the course of sepsis is thought to result from increased pulmonary capillary permeability and resultant edema. However, when the edema is assessed at the bedside by measuring the extravascular thermal volume by transpulmonary dilution, some ALI/ARDS patients with sepsis may have normal extravascular lung water (EVLW). Conversely, a raised EVLW may be present even when criteria for ALI/ARDS are not met, according to GS Martin and colleagues in this issue of *Critical Care*. This commentary puts the findings into a broader perspective and focuses on the difficulty, at the bedside, in recognizing and separating various types of pulmonary edema. Some of these forms of edema, classically differentiated on the basis of increased permeability and cardiogenic/hydrostatic factors, may overlap, whereas the criteria for ALI/ARDS may be loose, poorly reproducible, relatively insensitive and nonspecific, and highly therapy-dependent. Overhydration is particularly difficult to recognize. Additional diagnostics may be required to improve the delineation of pulmonary edema so as to redirect or redefine treatment and improve patient morbidity and, perhaps, mortality. Monitoring EVLW by single transpulmonary thermal dilution, for instance, might have a future role in this process.

In this issue of *Critical Care*, Martin and colleagues [1] describe that, in 29 patients with sepsis, extravascular thermal volume, a measure of extravascular lung water (EVLW) and edema in the lungs, assessed by transpulmonary thermal dilution [2–4], is elevated in many patients even in the absence of criteria for acute lung injury/acute respiratory distress syndrome (ALI/ARDS) according to the Consensus definition [5]. Conversely, about one-third of ARDS patients had normal EVLW (less than 10 ml/kg), as noted previously [6]. The present study underscores the incomplete overlap between edema and ALI/ARDS criteria in the critically ill. How should these findings be interpreted?

ALI/ARDS is defined clinically, on the basis of the Consensus Conference definition, to recognize lung vascular injury and

increased permeability separately from cardiogenic/hydrostatic types of pulmonary edema, but the diagnostic value of these clinical criteria is limited when compared with autopsy findings, for instance [5,7]. With advancing technology, including the non-invasive dual-radionuclide method applicable at the bedside, it has become clear that increased capillary protein permeability in the lungs is indeed a hallmark of ALI/ARDS [8]. However, increased permeability does not necessarily imply edema if, for instance, hydrostatic pressures in the lungs are low or other factors in the Starling equation attenuate the increased transvascular transport of fluid. Conversely, overhydration by aggressive fluid therapy can certainly affect the lungs with resultant pulmonary edema in the absence of increased permeability, but this is hard to recognize at the bedside or to separate from ALI/ARDS. Indeed, overhydration, particularly with crystalloid fluids, is likely to lower plasma colloid osmotic pressure, thereby lowering, even in the absence of increased permeability, the threshold value of hydrostatic pressure – that is, pulmonary capillary wedge pressure – above which interstitial edema and ultimately aveolar flooding develop. Hence, the threshold value of 18 mmHg to define ALI/ARDS according to the Consensus definition is arbitrary; it may be too high and thereby result in the erroneous diagnosis of ALI/ARDS when, in fact, the lungs are flooded by overzealous crystalloids, infused to combat presumed hypovolemia or hypotension. Indeed, a gold standard for diagnosing ALI/ARDS is lacking [5,7], because increased permeability, a potential standard, cannot be assessed in every institution [5]. In contrast, separating ALI/ARDS from cardiogenic edema may not be very hard in the presence of a recent myocardial infarction, pre-existing cardiomyopathy, echocardiographic left ventricular dysfunction, wall motion abnormalities, and a low measured cardiac output with high pulmonary capillary wedge pressure [8].

The key question is therefore whether radiographic pulmonary mechanical and gas exchange abnormalities,

manifested at the bedside, are caused by ALI/ARDS and increased permeability, pulmonary overhydration, or both. This differentiation is important because overhydration may add to morbidity, partly because it prolongs the need for mechanical ventilatory support and the time needed to regain negative fluid balances and mobilization of edema [9]. Indeed, positive fluid balances and high EVLWs may denote an adverse prognosis, in critically ill septic patients [10,11]. It is noteworthy that in Martin and colleagues' study [1] a high EVLW was not necessarily preceded by a more positive fluid balance, in septic (non-ARDS) patients, but in the absence of measured pressure factors it is hard to decide between mildly increased permeability and overhydration, while cardiac causes seem unlikely.

In patients with hypotension, differentiation between ALI/ARDS and overhydration is important for deciding on inotropic support or infusion of fluids. Obviously, intravascular and cardiac underfilling can concur with extravascular (pulmonary) overhydration, making the therapeutic choices difficult in patients needing some therapy for hypotension, low cardiac output, or both, to ensure tissue oxygen delivery. Obviously, this again raises the controversial role of the plasma colloid osmotic pressure, if any, in retaining fluids intravascularly and the associated benefits of colloid fluid therapy. Along these lines, monitoring the EVLW as currently possible by single transpulmonary thermal dilution (PiCCO Plus; Pulsion Medical Systems, München, Germany [2]) could help to guide (fluid) therapy and thereby decrease morbidity and perhaps even mortality, but this contention needs to be confirmed by a prospective study analogous to the study by Mitchell and colleagues [9]. The latter showed less morbidity, and fewer ventilator and ICU days of mechanically ventilated patients monitored with the help of the relatively laborious thermal-dye EVLW measurements (Edwards technology) than those managed with help of a pulmonary artery catheter and repeated pulmonary capillary wedge pressure measurements. In any case, single thermal dilution EVLW has been validated against gravimetric techniques in experimental animals [12].

In conclusion, monitoring EVLW by transpulmonary thermal dilution, which is feasible nowadays [2], can help to manage patients with ALI/ARDS on mechanical ventilation, and can help to decide on withholding intravenous fluids and starting diuretic therapy. Future research should be directed towards improving patient outcome with the help of EVLW monitoring.

### Competing interests

The author(s) declare that they have no competing interests.

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