Editorial

Acute lung injury and acute respiratory distress syndrome: diagnostic hurdles

Carmen Sílvia Valente Barbas

Acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) are spectra of the same disease that reflect the clinical expression of a pulmonary edema with high concentrations of proteins, subsequent to increased permeability of the alveolar-capillary membrane leading to acute respiratory failure. This syndrome occurs in genetically predisposed individuals after exposure to one or more risk factors. The pathophysiological mechanism that accounts for this lesion and subsequent dysfunction of the permeability of the alveolar-capillary membrane can be triggered by direct or primary factors, such as pulmonary infection (bacterial, viral, parasitic, or fungal), pulmonary contusion, aspiration of gastric content, and near drowning, as well as by indirect triggering factors, such as septic syndrome, septic shock, multiple blood transfusions, polytrauma, pancreatitis, and amniotic fluid embolism. The differentiation from the initial insult is important for the concomitant treatment of the causes associated with the development of the alteration of the permeability of the alveolar-capillary barrier, as well as to understand the lesions of the various compartments of the alveolar-capillary membrane: the alveolar epithelium, the interstitial space, and the pulmonary capillary endothelium. Histologically, ALI/ARDS is characterized by diffuse alveolar damage (DAD) with intra-alveolar edema, interstitial edema, and hyaline membrane, as well as, in its chronic phase, by the proliferation of fibroblasts. However, the histological evaluation alone might not suffice to characterize, in detail, the involvement of the epithelial, interstitial, and endothelial compartments, as well as the pulmonary response to aggression. In addition, it is necessary to use electron or laser confocal microscopy, with the aid of endothelial and epithelial immunomarkers, in order to evaluate the degree and extent of the lesion of the alveolar-capillary membrane,[1] also providing better understanding of its pathogenesis. Specific staining or the use of markers of infection might be necessary for the identification of the infectious agent that causes or perpetuates ARDS.

In this issue of the Brazilian Journal of Pulmonology, Pinheiro et al. retrospectively studied 22 deceased patients in the intensive care unit of the University Hospital of the Federal University of Juiz de Fora (in the state of Minas Gerais) who were submitted to autopsy.[2] Of the 22 patients, 10 met the criteria of the American European Consensus Conference (AECC) for the diagnosis of ARDS (arterial oxygen tension/fraction of inspired oxygen < 200, and ALI < 300; bilateral pulmonary infiltrate and pulmonary wedge pressure < 18 mmHg, or absence of clinical evidence of left atrial hypertension), and 7 presented DAD in the histological analysis of the lungs. Positive and negative predictive values for the diagnosis of ARDS were, respectively, 50 and 83%, and positive and negative likelihood ratios were 2.33 and 0.47. In patients who met the AECC criteria for ARDS but did not present DAD in the histological analysis of the lung, the authors found bilateral pneumonia, pulmonary embolism, tuberculosis, and cryptococosis - the last two probably in their disseminated form - as histological diagnoses. Therefore, specialists in ARDS have recently recommended a sophistication of the criteria for the diagnosis of ARDS, since a more complex diagnosis can have therapeutic and prognostic implications, as well as influence the choice and therapeutic response to protective ventilatory strategies. The following diagnoses, not found by the authors, can be differential of ARDS: diffuse alveolar hemorrhage; acute interstitial diseases of various etiologies; eosinophilic pneumonia; and bronchiolitis obliterans.

Patients with ARDS are characterized by alteration of the permeability of the alveolar-capillary membrane. Therefore, it is necessary to understand the triggering of the lesion, as well as the treatment that can help repair it. Specialists in ARDS have recommended that techniques to measure the permeability of the alveolar-capillary membrane be performed, such as determining the ratio between the extravascular lung water/end-diastolic volume, measured using the transpulmonary thermodilution technique, in order to characterize the syndrome and differentiate it from acute cardiogenic edema.[3] A more accurate diagnosis of ARDS will further the programming and study of possible regulating treatments of the inflammatory lesion process, including the regulation of transcription factors and cytokine markers, such as STAT 3,[4] and vascular lesion factors, such as endothelial growth factors. Knowing the alteration level of the permeability of the alveolar-capillary membrane will also help the ventilatory support programming, such as alveolar recruitment maneuvers, as well as

adjustment of positive end-expiratory pressure and tidal air volume, which might influence the prognosis of these severe patients.[5] The diagnosis of ARDS triggering factors, such as infections and traumas, becomes important for the correction of the cause, such as fixation of fractures, no administration of blood products, as well as administration of antibiotic therapy, antiviral drugs, antiparasitic and antifungal agents or anti-coagulants for the concomitant treatment to repair the alveolar-capillary membrane.

More recently, computed tomography scans of the chest, especially those taken using multislice detectors, which can reconstruct the pulmonary imaging in various planes, have helped characterize ARDS, with its typical heterogeneous distribution, with condensation areas in the gravity-dependent regions of the lung, representing pulmonary edema and collapse, and in characterizing interstitial processes and other specific lesions, such as cavitations in mycobacteriosis, small cysts in pneumocystosis, ground-glass halos in fungal lesions, diagnosis of vascular involvement and visualization of the adjustments of positive end-expiratory pressure and tidal volume, as well as responses to alveolar recruitment maneuvers in protective pulmonary ventilatory strategies. Therefore, in patients with immunodeficiency, that is, patients with neoplasms, with transplants, with cirrhosis, or acquired immunodeficiency syndrome, as well as in refractory patients, initial empirical treatment should be performed, with more specific diagnostic procedures for the diagnosis of the triggering cause of ARDS, such as bronchoscopy with bronchoalveolar lavage, with testing and culture for bacteria, mycobacteria, fungi, and testing for virus, such as herpes virus and cytomegalovirus. In cases of clinically suspected viral processes, rapid tests in the nose, mouth and throat should be performed for the influenza virus, the parainfluenza virus, and adenovirus in order to elucidate the diagnosis. In refractory cases, and in cases of progressive clinical and functional worsening, an open lung biopsy can be performed.

Studies in genetics for evaluation of patients at risk of developing ARDS, epidemiological studies to characterize risk factors, sophistication of the diagnosis-centered approach to diagnostic techniques, and specific treatments for lesions of the alveolar-capillary pulmonary membrane, as well as the development of treatments for multiple organ failure, will certainly influence the improvement of the prognosis of these severe patients with ARDS under intensive care.

The attempt to correctly diagnose ARDS, characterizing the alteration of the permeability of the alveolar-capillary pulmonary membrane, should always be performed with the concomitant diagnosis of the triggering cause, such as infections, multiple transfusions, contusions, aspiration of gastric content, pancreatitis and interstitial processes of various etiologies, especially those associated with viral and opportunistic infections. Understanding that the AECC criteria have low diagnostic accuracy for ARDS is essential for intensivists and pulmonologists in order to improve diagnostic investigation and sophisticate therapeutic possibilities for these severe patients hospitalized in intensive care units.

Carmen Sílvia Valente Barbas
Tenured Professor in the Pulmonology Department of the University of São Paulo School of Medicine, and Pulmonologist in the Intensive Care Unit for Adults of the Hospital Israelita Albert Einstein

References

1. Ab`Saber AM, Borges ER, Parra ER, Hoelz C, Teodoro WR, Capelozzi VL, et al. Differences between fatal acute respiratory distress syndrome and fatal alveolar hemorrhage at confocal scanning laser microscopy. Am J Respir Crit Care Med. 2006;A201.
2. Pinheiro BV, Muraoka FS, Assis RVC, Lamin R, Oliveira JCA, Pinto SPS, et al. Precisão do diagnóstico clínico da síndrome do desconforto respiratório agudo quando comparado a achados.de necropsia. J Bras Pneumol. 2007;33(4):423-28.
3. Monnet X, Anguel N, Osman D, Hamzaoui O, Richard C, Teboul JL. Assessing pulmonary permeability by transpulmonary thermodilution allows differentiation of hydrostatic pulmonary edema from ALI/ARDS. Intensive Care Med. 2007;33(3):448-53.
4. Gao H, Ward PA. STAT3 and suppressor of cytokine signaling 3: potential targets in lung inflammatory responses. Expert Opin Ther Targets. 2007;11(7):869-80.
5. Barbas CSV, de Matos GFJ, Pincelli MP, da Rosa Borges ER, Antunes T, de Barros JM, et al. Mechanical ventilation in acute respiratory failure: recruitment and high positive end-expiratory pressure are necessary. Curr Opin Crit Care, 2005;11(1):18-28.