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Chapter

Application of Thoracic Ultrasonography for Acute Cor Pulmonale in Acute Respiratory Distress Syndrome Patients

You Shang and Ting Zhou

Abstract

Beneficial therapeutic interventions for acute respiratory distress syndrome (ARDS) include lung protective ventilation; however, ventilator may cause or sometimes worsen acute cor pulmonale (ACP) induced by pulmonary gas exchange disorder and pulmonary vascular dysfunction due to ARDS. The incidence of ACP was 22–50% in mechanically ventilated patients. Currently, point-of-care ultrasound has been widely used in ARDS patients, which becomes much more important in the early detection and management of ARDS and its complications. Application of lung ultrasound combined with echocardiography could monitor respiratory status, hemodynamics, and cardiac function and optimize the ventilation setting in order to protect both lung and right ventricle. This chapter will discuss the pathophysiology of ACP associated with ARDS and the use of point-of-care ultrasound to make protective strategies for lung and right ventricle in detail.

Keywords: acute respiratory distress syndrome, acute cor pulmonale, point-of-care ultrasound, organ protection

1. Introduction

The concept of acute respiratory distress syndrome (ARDS) was first described about five decades ago [1], which is characterized by the acute development of hypoxemia accompanied with bilateral lung infiltrates [2]. ARDS is responsible not only for infections, shock, and multiple organ dysfunction syndromes but also for acute cor pulmonale (ACP) and right ventricular failure in critical ill patients. The mortality of ARDS is 40% approximately in intensive care unit [3], and almost 25% of mechanically ventilated patients could be affected by ARDS [4]. Lung protective mechanical ventilation using low tidal volume and high positive end expiratory pressure (PEEP) and other therapeutic interventions such as fluid restrictive, prone position, neuromuscular blockade, lung recruitment, and sometimes venovenous extracorporeal membrane oxygenation (VV ECMO) for severe cases may be beneficial [5–9]; however, none of them are promising and may cause other complications, for instance, low tidal volume and high PEEP may lead to hypercapnia and consecutive right heart failure [4].

In 1977, it was first found that some ARDS patients accompanied with deleterious effect on pulmonary system and increased pulmonary vascular resistance, or even pulmonary hypertension [10]. Until 2001, it was reported that there was 25% ARDS patients occurring acute cor pulmonale (ACP) when they were receiving lung protective mechanical ventilation with low tidal volume and high positive end expiratory pressure (PEEP) [11]. The incidence of ACP was much higher in severe ARDS patients whose PaO_2/FiO_2 were lower than 100 mmHg. The morbidity was over 50% [12]. In terms of mortality, it was over 60% in moderate to severe ARDS patients (Berlin definition) with ACP, which was defined by transesophageal ultrasound (TEE); however, the incidence was 30% if without ACP [13]. We will discuss it in detail in this chapter.

2. Pathophysiology of acute cor pulmonale (ACP) in ARDS patients

The main function of right heart is maintaining adequate pulmonary perfusion pressure to deliver desaturated mixed venous blood to the respiratory membrane and low systemic venous pressure to prevent organ congestion. The right ventricle is sensitive to changes in afterload because it is anatomically adapted for the generation of low-pressure perfusion [4, 14–16].

Hypoxia induced by ARDS will cause the construction of pulmonary vessels. Pulmonary vasoconstriction could be caused not only by hypoxia but also by damaged pulmonary capillary coagulation, which may result in microvascular obstruction in the lung. In early phase of ARDS, microvascular thrombi could be seen in the histological studies. Those obstructed capillaries could lose their vascular structures in late phase of ARDS [17]. Lung protective mechanical ventilation with low tidal volume may also lead to hypercapnia in ARDS patients, aggravate the constriction of pulmonary arteries, and increase the pulmonary vascular resistance [18]. Furthermore, microvascular obstruction damaged coagulation and inflammation in ARDS contributes to increased afterload of right ventricle and induces right heart failure [19]. When right heart fails to deliver adequate volume to pulmonary circulation, the left heart will be affected with low cardiac output, decreased systemic hypotension, and multiple organ malperfusion.

Mechanical ventilation is also an important determinant to ACP and right ventricular failure; however, there is no robust evidence to support a definitive causal relationship between ACP and respiratory mechanics parameters, such as plateaus pressure, driving pressure, PEEP, and so on. If Vt or PEEP is inappropriate high, pleural pressure will increase and affect venous return of right atrium [20]. Even 6 ml/kg Vt still caused lung overdistension in one-third of ARDS patient [21]. Too low PEEP also results in atelectasis and progressive lung injury [22]. Function of right heart relies on the intrapleural pressure, gas exchange, and balance of lung recruitment and overdistension [13]. A large prospective observational clinical study had been designed to find that there are three physiological and one clinical parameters that could reflect the risk of ACP and would facilitate the attending physician in selecting patients who require echocardiographic assessment and close monitoring. The four variables were as follows: (1) pneumonia as a cause of ARDS; (2) driving pressure (plateau pressure-total positive end-expiratory pressure) >18 cm H_2O; (3) $PaO_2/FiO_2 < 150$ mmHg; and (4) $PaCO_2 > 48$ mmHg. One score for each variable. Patients with a score higher than two had a higher risk of ACP (19, 34, and 74% for risk scores of 2, 3, and 4, respectively) [16].

Damage to either gas exchange or respiratory mechanics may excessive increases preload or afterload of right ventricle, or injury that results in decreased right ventricular contractility [4]. However, due to anatomic structure of right

ventricle, the tolerance of acute increases of afterload is poor, and right heart undergoes dilate to afford it (according to Starling's law). Then, the decrease in right ventricular ejection is responsible for a decrease in left ventricular preload, and right ventricular dilatation is also responsible for left ventricular compression by a septal shift because of the inextensible pericardium [11, 23]. So, decreased left ventricular ejection lowers the cardiac output, systemic blood pressure, and then the coronary artery flow. Decreased coronary artery flow aggravates hypoxia of myocardium; meanwhile, the oxygen consumption of myocardium is increased. When there is an imbalance of oxygen demand and supply, the vicious cycle begins; the more the right heart dilates, the less the right heart coronary blood flow, and the reduced right heart function [4, 24].

In ARDS patients, we try to achieve a balance between maintaining lung open and adequate right heart function; thus, we need to ultrasound to assist us to monitor both lung and heart function at meantime [3].

3. Monitor pulmonary function using point-of-care ultrasound in clinical setting

Point-of-care ultrasound is a readily, minimal invasive, no-radiation and repeatable bedside tool in clinical settings, which has increased widely over the past decade in the intensive care units and plays a very important role in helping intensivists' diagnosing and treating critical ill patients [25].

Point-of-care pulmonary ultrasound scan could be used to assist the diagnosis in the early phase of ARDS. Suspected ARDS could be confirmed by pulmonary ultrasonography scan through the following typical patterns characterized by B-lines, spared areas, pleural line thickening, and subpleural consolidations [26]. The blue protocol indicates the number and thickness of B-lines permitting a semiquantitative evaluation of the amount of extravascular lung water and lung density as well. Lung ultrasound could determine the consolidation of local lung segment, usually in the basal and posterior area, showing hepatization (tissue pattern) in the presence of air bronchograms in 83.3% ARDS patients [27, 28]. Lung ultrasound could also assist intensivists to evaluate proper PEEP in lung recruitment in ARDS patient, avoiding high PEEP induced lung injury. When localized the consolidation of lung segments with lung ultrasound with real-time monitoring, increasing PEEP stepwisely could reduce the degree of nonaerated lung area, while no hemodynamic deterioration was noted [29]. Although CT is considered a valid technique to estimate lung recruitment in ARDS patients by quantifying the amount of tissue according to the different lung recruitment maneuvers, lung ultrasound provides higher safety and available at bedsides and allows continuous monitoring of the nonaerated dependent lung regions, avoiding derecruitment in clinical practice [30, 31].

4. Critical care echocardiography

Ultrasound has been applied in critical ill patients worldwide, which guided the intensivists establish not only all sorts of catheters, like central veins and arteries, but also thoracentesis, peritoneocentesis, and sometimes rachiocentesis. In the other words, ultrasound provides a real-time view and assists the preformation of intensivists under any critical situations. Despite its easily application and availability in any situation, ultrasound has become much more important in management of ARDS patients when evaluating their cardiac function because

those patients had complex interactions among the lung, the ventilation, and the right ventricle [32]. Recently, there were debates about the choice of the modality of echocardiography, either transthoracic (TTE), or transesophageal (TEE). Most documents indicated that TEE is superior to TTE for diagnosis of ACP or right ventricular dysfunction in mechanically ventilated patient with moderate to severe ARDS, as it overcomes technical problems associated with acoustic views and measurements that can usually be performed easily [32, 33]. Another advantage about TEE is providing safely and efficiently when ARDS patients need long duration of prone position or have excessive pneumoderma affecting the ultrasound images [34]. Furthermore, some articles also indicated that TEE has high accuracy than TTE in observing ACP if the patient was mechanical ventilated with high PEEP [33, 35]. Compared to TEE, the sensitivity of TTE for diagnosis of right ventricular dysfunction was only 60% (95% CI, 41–77%) [36]. However, if both TEE and TTE could be chosen in the ICU, the intensivists should consider individual clinical conditions of the patients, experience of using echocardiography, and the clinical settings of the ward. The related invasiveness of TEE should be considered too [37].

As mentioned above, the definition of ACP is acute increased right ventricular afterload, which resulted in right ventricular dilatation and may compromise left ventricular filling. Right ventricular volume overload is defined as dilatation of the right ventricle that could be easily observed with echocardiography, while right ventricular pressure overload is defined as dyskinetic movement of the septum during end-systole. Right ventricular volume and right ventricular pressure could interact with each other [37, 38].

There are many echocardiographic manifestations of ACP. Echocardiography of ACP in an ARDS patient ventilated with a lung protective approach is characterized by (A) a severe dilatation of the right ventricle, a mark, or of right ventricular failure and (B) a paradoxical septal motion with the "D-shape" of the left ventricle, reflecting that right ventricular failure is related to systolic overload (abrupt increase in right ventricular afterload) [32].

Based on the visual image of the right heart provided by two-dimensional echocardiography, assessment of right ventricular size is a widely adopted method, by comparing the right ventricular end-diastolic area (RVEDA) with the left ventricular end-diastolic area (LVEDA) [24, 32, 39]. The RVEDA/LVEDA ratio between 0.6 and 1 indicates moderate ACP, while the RVEDA/LVEDA ratio greater than 1 indicates severe ACP. ACP diagnosis by echocardiographic has been defined as the combination of an RVEDA/LVEDA ratio > 0.6 and the presence of paradoxical septal motion during end-systole on parasternal short axis and apical four-chamber views, which now considered to be gold standard [4, 24, 33].

The statement from the Heart Failure Association and the Working Group on Pulmonary Circulation and Right Ventricular Function of the European Society of Cardiology indicated 12 echocardiographic parameters in the assessment of right ventricular failure, which were (A) pericardial fluid >5 mm in diastole; (B) RV wall thickness > 5 mm; (C) inferior vena cava diameter > 21 mm, inspiration collapse <50% suggests high RA pressure; (D) tricuspid regurgitation peak systolic velocity of TR > 2.8 m/s; (E) tricuspid annular plane systolic excursion TAPSE < 17 mm; (F) right ventricle dilation RVEDD/LVEDD > 1.0, right ventricle basal diameter > 41 mm; (G) right ventricle fractional area change, FAC < 35%; (H) ventricular interdependence: septal shift, D-shaped left ventricle; (I) systolic S′ velocity of tricuspid annulus < 9.5 cm/s by Doppler Tissue Imaging; (J) longitudinal strain of right ventricle free wall < 20%; (K) right ventricular index of myocardial performance, RIMP > 0.54 by Doppler Tissue Imaging; and (L) 3D right ventricular ejection fraction < 45% [40].

5. Right heart protection

Effective treatment of acute cor pulmonale or right heart failure requires an experienced and skilled ICU team to rapidly assess and treat. Lung protective mechanical ventilated strategy could not guarantee to protect the function of right heart for the intensivists. Performing bedside echocardiography could help in tailoring the ventilator management to decrease right ventricular afterload when ACP is detected, thus potentially avoiding further deterioration toward severe ACP [16, 41]. Moreover, within the visual image of the right heart provided by two-dimensional echocardiography, early observation of right ventricular dysfunction using echocardiography could help the intensivists to differentiate the pathophysiology of ACP and make appropriated treatments to optimizing right ventricular preload, increasing right ventricular contractility, and reducing right ventricular afterload, such as therapeutic treatment or prone position [12, 42]. Furthermore, echocardiography could also provide a continuous visual image after the treatments and help to evaluate whether the heart function is improved or not. In other words, with echocardiography, the morbidity and mortality of ACP in ARDS patient might be reduced, and there is a huge need to design more clinical trials using echocardiography in critical ill patients with ARDS.

6. Conclusion

Because of the coupling between lung and heart, the right ventricle is also involved in ARDS either primarily or by the application of mechanical ventilation. Acute cor pulmonale is seen with increasing frequency in the intensive care unit. The incidence of acute cor pulmonale during ARDS is, even if under protective ventilation, not negligible. The use of echocardiography combined with lung ultrasound is important for early detection of acute cor pulmonale and identification of the appropriate ventilator strategy to preserve heart-to-lung interaction. Furthermore, right now, there is no clinical practice guideline or therapeutic intervention focus on the right ventricular protective ventilation strategy in ARDS patients with high risk of ACP. More research should be done to establish how to differentiate patients with high risk of ACP, immediate assessment by echocardiography, and early interventions.

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References

[1] Ashbaugh DG, Bigelow DB, Petty TL, Levine BE. Acute respiratory distress in adults. Lancet. 1967;**2**(7511):319-323. DOI: 10.1016/s0140-6736(67)90168-7

[2] Ranieri VM, Rubenfeld GD, Thompson BT, et al. Acute respiratory distress syndrome: The Berlin Definition. JAMA. 2012;307;(23):2526-2533. DOI: 10.1001/jama.2012.5669, 10.1001/jama.2012.5669

[3] Zochios V, Parhar K, Tunnicliffe W. The right ventricle in ARDS. Chest. 2017;**152**(1):181-193. DOI: 10.1016/j. chest.2017.02.019

[4] Mathieu G, Antoine VB. Hemodynamic monitoring of ARDS by critical care echocardiography. J Emerg Crit Care Med. 2019;**3**:36. DOI: 10.21037/jeccm.2019.07.04

[5] Brower RG, Matthay MA, Morris A, et al. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The New England Journal of Medicine. 2000;**342**(18):1301-1308. DOI: 10.1056/NEJM200005043421801

[6] Guérin C, Reignier J, Richard JC, et al. Prone positioning in severe acute respiratory distress syndrome. The New England Journal of Medicine. 2013;**368**(23):2159-2168. DOI: 10.1056/NEJMoa1214103

[7] Wiedemann HP, Wheeler AP, Bernard GR, et al. Comparison of two fluid-management strategies in acute lung injury. The New England Journal of Medicine. 2006;**354**(24):2564-2575. DOI: 10.1056/NEJMoa062200

[8] Papazian L, Forel JM, Gacouin A, et al. Neuromuscular blockers in early acute respiratory distress syndrome. The New England Journal of Medicine. 2010;**363**(12):1107-1116. DOI: 10.1056/NEJMoa1005372

[9] Bunge JJH, Caliskan K, Gommers D, Reis MD. Right ventricular dysfunction during acute respiratory distress syndrome and veno-venous extracorporeal membrane oxygenation. J Thorac Dis. 2018;**10**(Suppl 5): S674-S682. DOI: 10.21037/jtd.2017.10.75

[10] Zapol WM, Snider MT. Pulmonary hypertension in severe acute respiratory failure. The New England Journal of Medicine. 1977;**296**(9):476-480. DOI: 10.1056/NEJM197703032960903

[11] Vieillard-Baron A, Schmitt JM, Augarde R, et al. Acute cor pulmonale in acute respiratory distress syndrome submitted to protective ventilation: Incidence, clinical implications, and prognosis. Critical Care Medicine. 2001;**29**(8):1551-1555. DOI: 10.1097/00003246-200108000-00009

[12] Vieillard-Baron A, Charron C, Caille V, et al. Prone positioning unloads the right ventricle in severe ARDS. Chest. 2007;**132**(5):1440-1446. DOI: 10.1378/chest.07-1013

[13] Boissier F, Katsahian S, Razazi K, et al. Prevalence and prognosis of cor pulmonale during protective ventilation for acute respiratory distress syndrome. Intensive Care Medicine. 2013;**39**(10):1725-1733. DOI: 10.1007/s00134-013-2941-9

[14] Greyson CR. Pathophysiology of right ventricular failure. Critical Care Medicine. 2008;**36**(1 Suppl): S57-S65. DOI: 10.1097/01.CCM.0000296265.52518.70

[15] Zochios V, Jones N. Acute right heart syndrome in the critically ill patient. Heart Lung Vessel. 2014;**6**(3):157-170

[16] Mekontso Dessap A, Boissier F, Charron C, et al. Acute cor pulmonale during protective ventilation for acute respiratory distress syndrome: Prevalence, predictors, and clinical impact. Intensive Care Medicine. 2016;**42**(5):862-870. DOI: 10.1007/s00134-015-4141-2

[17] Bellingan GJ. The pulmonary physician in critical care * 6: The pathogenesis of ALI/ARDS. Thorax. 2002;**57**(6):540-546. DOI: 10.1136/thorax.57.6.540

[18] Mekontso Dessap A, Charron C, Devaquet J, et al. Impact of acute hypercapnia and augmented positive end-expiratory pressure on right ventricle function in severe acute respiratory distress syndrome. Intensive Care Medicine. 2009;**35**(11):1850-1858. DOI: 10.1007/s00134-009-1569-2

[19] Jardin F, Vieillard-Baron A. Is there a safe plateau pressure in ARDS? The right heart only knows. Intensive Care Medicine. 2007;**33**(3):444-447. DOI: 10.1007/s00134-007-0552-z

[20] Lansdorp B, Hofhuizen C, van Lavieren M, et al. Mechanical ventilation-induced intrathoracic pressure distribution and heart-lung interactions*. Critical Care Medicine. 2014;**42**(9):1983-1990. DOI: 10.1097/CCM.0000000000000345

[21] Reis Miranda D, Klompe L, Mekel J, et al. Open lung ventilation does not increase right ventricular outflow impedance: An echo-Doppler study. Critical Care Medicine. 2006;**34**(10):2555-2560. DOI: 10.1097/01.CCM.0000239118.05093.EE

[22] Duggan M, McCaul CL, McNamara PJ, et al. Atelectasis causes vascular leak and lethal right ventricular failure in uninjured rat lungs. American Journal of Respiratory and Critical Care Medicine. 2003;**167**(12):1633-1640. DOI: 10.1164/rccm.200210-1215OC

[23] Repessé X, Charron C, Vieillard-Baron A. Acute respiratory distress syndrome: The heart side of the moon. Current Opinion in Critical Care. 2016;**22**(1):38-44. DOI: 10.1097/MCC.0000000000000267

[24] Jones N, Burns AT, Prior DL. Echocardiographic assessment of the right ventricle-state of the art. Heart, Lung & Circulation. 2019;**28**(9):1339-1350. DOI: 10.1016/j.hlc.2019.04.016

[25] Corradi F, Brusasco C, Pelosi P. Chest ultrasound in acute respiratory distress syndrome. Current Opinion in Critical Care. 2014;**20**(1):98-103. DOI: 10.1097/MCC.0000000000000042

[26] Lichtenstein DA, Mezière GA. The BLUE-points: Three standardized points used in the BLUE-protocol for ultrasound assessment of the lung in acute respiratory failure. Critical Ultrasound Journal. 2011;**3**(2):109-110. DOI: 10.1007/s13089-011-0066-3

[27] Lichtenstein DA. Lung ultrasound in the critically ill. Clinical Intensive Care. 2005;**16**:79-87. DOI: 10.1080/09563070500131027

[28] Copetti R, Soldati G, Copetti P. Chest sonography: A useful tool to differentiate acute cardiogenic pulmonary edema from acute respiratory distress syndrome. Cardiovascular Ultrasound. 2008;**6**:16. DOI: 10.1186/1476-7120-6-16

[29] Stefanidis K, Dimopoulos S, Tripodaki ES, et al. Lung sonography and recruitment in patients with early acute respiratory distress syndrome: A pilot study. Critical Care. 2011;**15**(4):R185. DOI: 10.1186/cc10338

[30] Bouhemad B, Brisson H, Le-Guen M, et al. Bedside ultrasound assessment of positive end-expiratory pressure-induced lung recruitment. American Journal of Respiratory and Critical Care Medicine.

2011;**183**(3):341-347. DOI: 10.1164/rccm.201003-0369OC

[31] Via G, Lichtenstein D, Mojoli F, et al. Whole lung lavage: A unique model for ultrasound assessment of lung aeration changes. Intensive Care Medicine. 2010;**36**(6):999-1007. DOI: 10.1007/s00134-010-1834-4

[32] Vieillard-Baron A, Prin S, Chergui K, et al. Echo-Doppler demonstration of acute cor pulmonale at the bedside in the medical intensive care unit. American Journal of Respiratory and Critical Care Medicine. 2002;**166**(10):1310-1319. DOI: 10.1164/rccm.200202-146CC

[33] Lhéritier G, Legras A, Caille A, et al. Prevalence and prognostic value of acute cor pulmonale and patent foramen ovale in ventilated patients with early acute respiratory distress syndrome: A multicenter study. Intensive Care Med. 2013;**39**(10):1734-1742. DOI: 10.1007/s00134-013-3017-6

[34] Mekontso Dessap A, Proost O, Boissier F, et al. Transesophageal echocardiography in prone position during severe acute respiratory distress syndrome. Intensive Care Medicine. 2011;**37**(3):430-434. DOI: 10.1007/s00134-010-2114-z

[35] Cook CH, Praba AC, Beery PR, Martin LC. Transthoracic echocardiography is not cost-effective in critically ill surgical patients. The Journal of Trauma. 2002;**52**(2):280-284. DOI: 10.1097/00005373-200202000-00013

[36] Fichet J, Moreau L, Genée O, et al. Feasibility of right ventricular longitudinal systolic function evaluation with transthoracic echocardiographic indices derived from tricuspid annular motion: A preliminary study in acute respiratory distress syndrome. Echocardiography. 2012;**29**(5):513-521. DOI: 10.1111/j.1540-8175.2011.01650.x

[37] Stanko LK, Jacobsohn E, Tam JW, et al. Transthoracic echocardiography: Impact on diagnosis and management in tertiary care intensive care units. Anaesthesia and Intensive Care. 2005;**33**(4):492-496. DOI: 10.1177/0310057X0503300411

[38] Ryan T, Petrovic O, Dillon JC, et al. An echocardiographic index for separation of right ventricular volume and pressure overload. Journal of the American College of Cardiology. 1985;**5**(4):918-927. DOI: 10.1016/s0735-1097(85)80433-2

[39] Frémont B, Pacouret G, Jacobi D, et al. Prognostic value of echocardiographic right/left ventricular end-diastolic diameter ratio in patients with acute pulmonary embolism: Results from a monocenter registry of 1,416 patients. Chest. 2008;**133**(2):358-362. DOI: 10.1378/chest.07-1231

[40] Harjola VP, Mebazaa A, Čelutkienė J, et al. Contemporary management of acute right ventricular failure: A statement from the heart failure association and the working group on pulmonary circulation and right ventricular function of the European Society of Cardiology. European Journal of Heart Failure. 2016;**18**(3):226-241. DOI: 10.1002/ejhf.478

[41] Vieillard-Baron A, Price LC, Matthay MA. Acute cor pulmonale in ARDS. Intensive Care Medicine. 2013;**39**(10):1836-1838. DOI: 10.1007/s00134-013-3045-2

[42] Galiatsou E, Kostanti E, Svarna E, et al. Prone position augments recruitment and prevents alveolar overinflation in acute lung injury. American Journal of Respiratory and Critical Care Medicine. 2006;**174**(2):187-197. DOI: 10.1164/rccm.200506-899OC