

Chapter 4

Imaging Diagnosis of ARDS: How Can We Know the Severity and Prognosis from the Lung Imaging?



Tomoo Kishaba

Abstract Acute respiratory distress syndrome (ARDS) is a critical syndrome and its mortality remains high. Based on Berlin criteria for ARDS, chest imaging plays an important role. For clinicians, evaluation of disease severity and prediction of prognosis are quite helpful for management of ARDS. Chest radiograph is a simple test and first stage of diagnosis for ARDS. Findings of chest radiograph are often affected by patient status, positive pressure ventilation, and stage of ARDS itself. Therefore, integration of clinical condition such as vital sign and ratio of partial pressure of oxygen and fraction of inspired oxygen (P/F ratio) is important. Most important differential diagnosis is congestive heart failure (CHF). Therefore, evaluation of lung water distribution is important. Most robust point of chest radiograph is detection of volume loss comparison with previous film. Chest high-resolution computed tomography (HRCT) is the most useful imaging tool for ARDS. HRCT can distinguish direct injury such as pneumonia, aspiration from indirect injury such as sepsis, burn. Direct injury often shows asymmetric distribution such as unilateral predominant consolidation with air bronchogram. On the other hand, indirect injury more often demonstrates gravity dependent consolidation with subtle ventral ground-glass opacity (GGO). In viewpoint of severity of ARDS, severe ARDS patients show more extensive shadow compared to mild or moderate ARDS. In prediction of prognosis, ARDS have three pathological stages which consist of exudative, fibroproliferative, and fibrotic phase. In chest HRCT, extent of fibrotic shadow such as reticulation and traction bronchiectasis and volume loss are crucial findings which are associated with poor prognosis.

Keywords Acute respiratory distress syndrome · Chest high-resolution computed tomography · Fibroproliferative · Traction bronchiectasis

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1 Introduction

Acute respiratory distress syndrome (ARDS) is a life-threatening syndrome which consists of variable etiology such as pneumonia, sepsis, pancreatitis, trauma [1, 2]. Chest radiograph is a simple and easily applicable tool and diagnosis of ARDS will be possible. However, evaluation of chest radiograph alone has limitation in daily practice for ARDS. According to the Berlin criteria for ARDS, important parameters are both grade of oxygenation and findings of chest imaging [3]. During ARDS, we carefully monitor both clinical parameters such as P/F ratio, laboratory value and extent of imaging findings for evaluation of treatment effect. For patients and physician, crucial issue is to know severity and prognosis of ARDS, which contribute to more adequate management strategy and improve prognosis. In this chapter, I would like to show how we could evaluate severity and prognosis for ARDS using chest radiograph and chest HRCT.

2 Chest Radiograph

Chest radiograph is an initial step of imaging for diagnosis of ARDS. From an imaging point of view, important differential diagnoses are atelectasis, pleural effusion, pneumonia [4]. When we see acute phase of lung injury, chest radiograph often shows normal imaging or subtle GGO. Therefore, next step is chest HRCT in this situation. In initial phase of ARDS, patient often has poor inspiration due to severe distress, which contributes to volume loss like findings. In intensive care unit, we usually order portable chest imaging, cardiomegaly is overestimated and bilateral opacity is often due to pleural effusion. Therefore, portable echo is useful for distinction true parenchymal opacity from pleural effusion with identification of echo-free space and B-line or comet tail artifacts [5–7]. B-line often have positive correlation with chest CT findings of GGO, consolidation or septal thickening. B lines are perpendicular to the pleural line and move synchronously with lung sliding. The presence of 3 or more B lines in 1 intercostal space is considered abnormal and referred to as a B pattern. By contrast, A lines constitute a basic artifact of normally aerated lung described as horizontal repetitive hyperechoic artifacts arising from, and appearing parallel to, the pleural line. In diffuse disease such as ARDS, there is diffuse loss of aeration with multiple B lines and/or areas of consolidation in all lung fields. We often see rapid improvement of bilateral shadow in portable film on positive pressure ventilation status. This phenomenon is caused by high positive pressure end-expiratory pressure (PEEP). We should interpret patient condition through improvement in clinical condition and gas exchange such as P/F ratio.

One of the important role of chest radiograph is to check the position of tracheal tube, central venous line, naso-gastric tube, or other monitoring device [5]. Another important role is to detect ventilator-associated complications especially pneumothorax and ventilator-associated pneumonia (VAP). In patients with positive

pressure ventilation, we sometimes see pneumothorax. Portable chest imaging can miss subtle pneumothorax. Therefore, when we suspect pneumothorax, we can order chest radiograph with Trendelenburg position or erect position. Air tends to accumulate in high area in human body. So, deep sulcus sign is easy to detect pneumothorax using imaging of Trendelenburg position [8]. If we order supine imaging, we might miss small pneumothorax because of bilateral homogeneous opacity with pleural effusion or parenchymal shadow in ARDS patients. In terms of VAP, comparison of previous film and signs of respiratory infection such as fever, purulent secretion, and elevation of inflammation marker are crucial factors for accurate diagnosis [9]. From an imaging point of view, detection of new shadow is important accompanying with exclusion of pleural effusion or atelectasis.

Important differential diagnosis is CHF. CHF usually shows septal lines in lower lung field and peri-bronchovascular thickening in upper lung field [10]. In normal lung, interlobular septum is more evident in anterior ventral portion in upper lung field and near diaphragm. On the other hand, interlobar fissure has scarce septum. Therefore, linear shadow from mediastinum to outer direction in upper lung field or straight line from chest wall suggests septal thickening due to volume overload. In addition, reversed perfusion which is shown by more significance of vascular markings in upper lung field compared to lower lung field. Careful point is acute cardiogenic pulmonary edema often show absence of cardiomegaly. Non-cardiogenic pulmonary edema sometimes show asymmetric fluid overload. In evaluating volume status, vascular pedicle width (VPW) is useful. VPW means distance from outer line of azygos vein to outer line of left subclavian artery [11]. If VPW is over 5 mm, which signifies approximately 1000 ml volume overload with same film condition. Therefore, using difference of VPW combined with physical examination including jugular venous pressure estimation, hepato-jugular reflux, and urine output will provide useful information of volume status of ARDS patients.

In evaluation of severity, severe ARDS patients usually demonstrate more extensive consolidation or GGO rather than mild or moderate ARDS. Trace of imaging trend is quite crucial for both severity and prognosis. Chest radiograph is affected by patient position, depth of inspiration, rotation, inspiration timing, and volume status. Therefore, film condition should be arranged as much as we can. In exudative phase, chest radiograph shows bilateral GGO or consolidation with air bronchogram based on inflammatory exudates in alveolar space [12]. If ARDS phase progress to late exudative phase, we often see more confluent consolidation. More severe the ARDS, more extensive and dense consolidation develop. When ARDS progresses to fibroproliferative phase after 7–10 days, we usually see coarse reticulation and volume loss of bilateral lower lung field [13]. Direct injury such as bacterial pneumonia or aspiration pneumonia often cause asymmetric reticulation because of primary focus in unilateral. On the contrary, indirect injury such as sepsis, pancreatitis, burn usually show symmetric reticulation and volume loss because of systemic intense inflammatory substance. In fibrotic phase of ARDS, we often see diffuse reticulation with persistent volume loss.

In estimation of prediction of prognosis for ARDS, identification of volume loss and diffuse fibrotic change is important. In normal chest imaging, bilateral hilum is

positioned center between apex and dome of diaphragm. If position of hilum is shifted to diaphragm with adequate inspiration, we could judge it volume loss. Atelectasis resembles volume loss. Therefore, accurate distinction between these two process is difficult by chest radiograph alone. Gas exchange usually worse in volume loss and late inspiratory crackles are audible in volume loss [14]. On the other hand, decreased breath sound is evident in atelectasis. From normal volume to volume loss, ARDS phase might be changed exudative to fibroproliferation. In addition to persistent volume loss and hypoxemia, ARDS patients will show poor prognosis with reflection of pathological diffuse alveolar damage (DAD). In evaluating diffuse reticulation, ARDS patients more often show homogeneous distribution of reticulation compared with idiopathic pulmonary fibrosis (IPF). ARDS patients tend to show more central distribution of reticulation rather than IPF. More extensive consolidation or reticulation with significant volume loss is associated with poor prognosis.

3 Chest HRCT

Chest HRCT has advantages for anatomical evaluation of main findings and estimation of extent. Standardization of definition of each imaging findings is quite important. I show definition of major imaging findings of ARDS based on the Fleischner Society [15].

Air bronchogram: An air bronchogram is a pattern of air-filled (low-attenuation) bronchi on a background of opaque (high-attenuation) airless lung. The sign implies (a) patency of proximal airways and (b) evacuation of alveolar air by means of absorption (atelectasis) or replacement (e.g., pneumonia) or a combination of these processes.

Consolidation: Consolidation appears as a homogeneous increase in pulmonary parenchymal attenuation that obscures the margins of vessels and airway walls. Consolidation refers to an exudate or other product of disease that replaces alveolar air, rendering the lung solid.

Ground-glass opacity (GGO): It appears as hazy increased opacity of lung, with preservation of bronchial and vascular margins. It is caused by partial filling of air-spaces, interstitial thickening (due to fluid, cells, and/or fibrosis), partial collapse of alveoli, increased capillary blood volume, or a combination of these, the common factor being the partial displacement of air.

Honeycombing: the appearance is of clustered cystic air spaces, typically of comparable diameters on the order of 3–10 mm but occasionally as large as 2.5 cm. Honeycombing is usually subpleural and is characterized by well-defined walls. Honeycombing represents destroyed and fibrotic lung tissue containing numerous cystic airspaces with thick fibrous walls, representing the late stage of various lung diseases, with complete loss of acinar architecture. The cysts range in size from a few millimeters to several centimeters in diameter, have variable wall thickness, and are lined by metaplastic bronchiolar epithelium.

Reticular pattern: They are interlobular septal thickening, intralobular lines, or the cyst walls of honeycombing.

Traction bronchiectasis and traction bronchiolectasis: Traction bronchiectasis and traction bronchiolectasis, respectively, represent irregular bronchial and bronchiolar dilatation caused by surrounding retractile pulmonary fibrosis. Dilated airways are identified as cysts or microcysts.

Chest HRCT is useful for detection of anatomical location and more accurate extent and distribution of parenchymal shadow rather than chest radiograph (Table 4.1). In one study, the imaging findings provided by CT compared with chest radiograph frequently yielded additional information (66%), with direct influence on patient treatment in 22% of cases [16]. Therefore, HRCT plays an important role for diagnosis, evaluation of severity, and prediction of prognosis of ARDS. ARDS is the most severe form of lung injury. Most important differential diagnosis is CHF. CHF patients often show interlobular septal thickening especially in ventral area in upper lung field and peri-bronchovascular thickening in hilum portion. Mediastinal window of chest CT shows bilateral or right predominant pleural effusion in CHF patients at initial stage. In addition, CHF patients often show enlargement of right pulmonary vein because of volume overload. ARDS is divided into early phase and late phase clinically. Usual threshold between these phases are 14 days [17].

From a pathological point of view, ARDS have three stages which consist of exudative, fibroproliferative, and fibrotic phase.

Exudative phase has extensive inflammation with protein-rich pulmonary edema and hemorrhage. Fibroproliferative phase shows that fibroblast develops with collagen deposition. Fibrotic phase demonstrates lung remodeling with architectural destruction and cystic changes [18]. In exudative phase, ARDS patients show extensive bilateral consolidation in gravity dependent area with GGO (Fig. 4.1). This distribution derived from large difference between intrapulmonary vessel and tissue hydrostatic pressure in dependent area. In addition, dense posterior dependent consolidation can be seen as the syndrome progresses beyond the first week. In early phase, there is air bronchogram with smooth bronchial wall not traction. If adequate intervention is provided during this period, reversibility of consolidation or GGO will be anticipated. When clinical status progresses despite management including lung protective strategy, chest imaging phase shifts to late exudative and enters into fibroproliferative phase.

Table 4.1 Comparison of Chest radiograph and HRCT

	Main findings	Advantage	Disadvantage
Chest radiograph	Bilateral infiltration without cardiomegaly	Easy to perform Detection of volume is more evident	Accurate distribution of infiltration is difficult
Chest HRCT	Bilateral dorsal consolidation with ground-glass opacity	Detail evaluation for anatomical location	Radiation exposure High cost

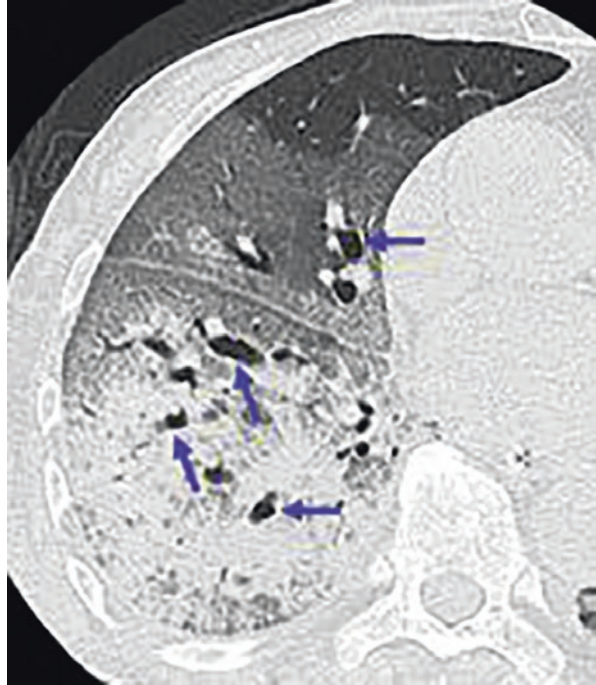
HRCT high-resolution computed tomography

Fig. 4.1 Exudative phase. Dependent airspace consolidation. Adapted from [18]



Fibroproliferative reaction is associated with tissue repair response histologically. This phase is an important turning point which radiological improvement or get worse with clinical condition or gas exchange. CT signs of parenchymal architectural distortion appear with reticulation and bronchiectasis after 2 weeks of ARDS onset. When we see GGO with reticular pattern, which is associated with interlobular septal thickening due to drainage of exudates. Important imaging indicator of transition to fibroproliferative phase is bronchiolectasis, which originates from dilatation of membranous bronchioles. In fibroproliferative phase, chest parenchymal shadow gradually improves in good prognosis group, which suggests adaptive response. On the other hand, traction bronchiectasis within consolidation or GGO appears in spite of treatment, which means maladaptive response and future development of fibrotic phase (Fig. 4.2). Ichikado et al. proposed HRCT score which focus on extent of fibrotic process during fibroproliferative phase [19]. The HRCT score was assigned on a 6-point scale: (I) normal attenuation; (II) ground-glass attenuation; (III) consolidation; (IV) ground-glass attenuation with traction bronchiolectasis or bronchiectasis; (V) consolidation with traction bronchiolectasis or bronchiectasis; and (VI) honeycombing. The presence of each of these six abnormalities in the upper, middle, and lower segments of each lung was independently assessed. The extent of each abnormality was determined by visually estimating the percentage of the affected lung parenchyma in each segment. Each abnormality

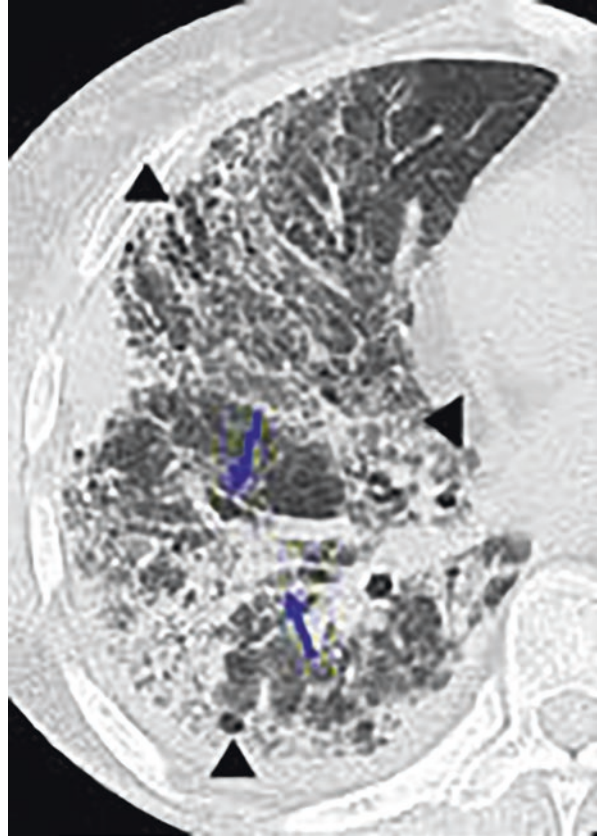
Fig. 4.2 Fibroproliferative phase. Extensive airspace consolidation and ground-glass attenuation with traction bronchiectasis (arrows). Adapted from [18]



score was calculated by multiplying the percentage area by each score. Scores for the six segments were averaged to determine the total score for each abnormality. The overall HRCT score was derived by adding the six abnormality scores. HRCT score have been reported to predict mortality of both pulmonary and extrapulmonary ARDS [20]. According to the multivariate analysis for the association between 60-day mortality and various outcome measure, HRCT score showed most strong predictor of mortality for ARDS [Hazard ratio 1.23 (1.09–1.35), p -value <0.01]. This HRCT score also predict mortality for AE of IPF [21]. Anan et al. showed a simple clinical scoring system consisting of the Acute Physiology and Chronic Health Evaluation (APACHE) II score, P/F ratio, disseminated intravascular coagulation and HRCT scores can predict drug associated ARDS [22]. In terms of traction bronchiectasis, this finding is usually noticed in chronic fibrotic lung disease. Therefore, when we see such findings in ARDS patients, we should call it bronchiectasis or bronchiolectasis alone. Based on current concept, (V) should be replaced by consolidation with bronchiolectasis or bronchiectasis of HRCT score for ARDS patients. HRCT bronchiectasis or bronchiolectasis and lower lobe volume loss may reflect pathological diffuse alveolar damage.

Fibrotic process progresses, ARDS patients shift to next stage, that is fibrotic phase. When we see more central bronchiectasis, which means early stage of fibrotic phase. In this phase, we can see more coarse reticular pattern and small cystic changes (Fig. 4.3). These parenchymal shadows reflect irreversible process such as

Fig. 4.3 Fibrotic phase. Extensive ground-glass attenuation associated with traction bronchiectasis (arrows), coarse reticulation, and cystic changes (arrowheads). Adapted from [18]



remodeling of lung architecture. In addition, we often see persistent GGO or small cystic changes in ventral area. This process is due to overdistension of ventral area with baby lung in severe ARDS [23]. Improvement of oxygenation in ARDS patients is more evident in ventral region [24, 25]. Burnham et al. evaluated HRCT at 1 and 14 days after ARDS onset, average static respiratory compliance over 14 days had negative association with HRCT reticular pattern ($p = -0.46$). Initial static respiratory compliance at 1 day was inversely correlated with HRCT reticulation ($p = -0.38$) and was lower in ARDS patients who showed bronchiectasis on HRCT at 14 days ($p = 0.008$) [26]. Another radiological scoring system showed increased radiologic scores for reticulation were associated with a decreased total lung capacity, forced vital capacity, and diffusing capacity for carbon monoxide ($p < 0.002$) at 180 days after ARDS. This radiological scoring consists of the following; the extent of involvement for each pattern was assigned a numerical score, where 0 = no

involvement; 1 = <5% involvement/minimal/not normal; 2 = 5–25% involvement; 3 = 26–49% involvement; 4 = 50–75% involvement; and 5 = greater than 75% involvement. For each radiologic pattern, the average score (range, 0–20) was calculated by summing all quadrant values for each of slice, adding these values together, and dividing by the number of slices with complete data [27]. Chung et al. also reported that lung involvement of greater than 80%, RA/LA ratio > 1, and varicoid traction bronchiectasis were statistically more common in nonsurvivors than in survivors (respective *p* values of 0.001, 0.008, and 0.038) [28]. Recently, Japanese study of ARDS patients stratified Berlin criteria consists of 153 patients. The severity of this cohort was mild in 42 patients, moderate in 71, and severe in 40 patients. Multivariate analyses revealed that elevated blood lactate level (≥ 2.0 mmol/L) and increased HRCT scores were significantly associated with weaning failure and 30-day mortality of the patients with ARDS [29]. Elevation of lactate is associated with tissue hypoxia and HRCT score reflects both degree of lung injury and fibroproliferation changes.

Finally, we discuss about ventilator-associated complication such as pneumothorax, pneumomediastinum, and ventilator-associated pneumonia. In ventilator management for ARDS patients, lung protective approach such as high PEEP with control of plateau pressure is usually applied. Even if such strategy is introduced, ARDS patients sometimes develop barotrauma because of reduced lung compliance and fragile of visceral pleura associated with intermittent shear stress and persistent inflammation. Chest HRCT provides useful information for early detection of subtle pneumomediastinum to apparent pneumothorax compared to chest radiograph. In terms of VAP, chest HRCT can demonstrate new parenchymal shadow which is distinct from pleural effusion. Patients with the CT score < 235 had a significantly lower incidence of barotrauma (5.0 vs 32.0%; *p* 0.0019) within 28 days after the onset of ARDS than those with CT score of ≥ 235 . The CT score was also independently associated with the occurrence of barotraumas with an odds ratio (OR) of 1.61 by multivariate regression analysis (*p* = 0.018). The percentage of patients complicated with VAP in the higher CT score group tended to be higher than those in the lower CT score groups (51.4% and 35.4%, respectively). Multivariate analysis also demonstrated that the CT score was independently associated with the complication of VAP with an OR of 1.46 (*p* 0.0041).

4 Conclusion

In answers for opening clinical question, we can evaluate the severity of ARDS patients with integration of Berlin criteria and chest imaging texture. Furthermore, we are able to predict mortality of ARDS patients based on the accurate estimation of extent of bronchiectasis or bronchiolectasis.

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