Abstract. – OBJECTIVE: Acute respiratory distress syndrome (ARDS) is a critical disease commonly found in many clinical cases, with a mortality rate of approximately 50%. Early diagnosis and intervention are important for improving ARDS prognosis. In this study, the applications of lung ultrasound in ARDS diagnosis and assessment are reviewed to clarify its key clinical values and application prospects.

MATERIALS AND METHODS: According to the standard diagnosis of ARDS based on the Berlin definition, CXR or CT examination should be conducted. However, both the blurred images of the former, as well as the inconvenience and high risks of the latter, impose restrictions on their application in critically ill patients.

RESULTS: Lung ultrasound was shown to improve safety, effectiveness, lacked radiation, can be performed bedside, and offers dynamic functionality.

CONCLUSIONS: It may be a suitable approach to replace or complement traditional imaging examinations with lung ultrasound.

Key Words: ARDS, Lung ultrasound, COVID-19.

Introduction

As a clinically common critical illness with close to 50% mortality, acute respiratory distress syndrome (ARDS) is a clinical syndrome consisting of lung parenchymal cell damage induced during the onset of non-cardiac diseases, such as serious infection, shock, trauma, and inflammation. In addition to severely endangering the lives of critically ill patients, it affects the quality of survivors’ lives. In this context, emphasis has been placed on early diagnosis and intervention aimed at improving the prognosis of ARDS. Considering the ARDS diagnosis based on the Berlin definition raised in 2012, the imaging criteria include dense shades of both lungs presented by chest x-ray (CXR) or computer topography (CT) scanning, which is accompanied by a failure to fully interpret pleural effusion and collapse or nodule of the pulmonary lobe/lung. Considering that CXR fails to generate clear images owing to the influence of multiple factors, the corresponding accuracy has not been satisfactory. Chest CT is considered the gold standard for ARDS diagnosis. However, it has some disadvantages, including high expenses, high transshipment risks, failure to implement it at the bedside, and unavoidable radiation exposure. Moreover, patients with ARDS caused by strongly infectious human-to-human diseases, such as 2019-nCoV pneumonia, must be isolated and encouraged to go outdoors less frequently. Consequently, the applications of chest CT in critically ill patients are limited.

In this context, it is still difficult to perform early diagnosis and dynamic assessments of ARDS among critically ill patients, as far as imaging is concerned. Owing to its safety, effectiveness, lack of radiation, ability to be conducted bedside, and dynamic functionality, lung ultrasound has been extensively adopted in clinical activities. For the past few years, the clinical application of lung ultrasound has entered a new development stage marked by rapid progress in the promotion of bedside ultrasound, especially the publication of the Expert Consensus by the International Liaison Committee on Lung Ultrasound. Currently, it has become an approach that can replace CXR, and be used to detect and evaluate lung and chest lesions. In light of this background, this study aimed to summarize the influence of bedside ultrasound on the early diagnosis and dynamic assessment of ARDS.
Materials and Methods

Lung Ultrasound

It was once believed that ultrasound cannot penetrate through the lungs or skeletal thorax filled with gas to reflect ultrasonic waves or develop images of the normal subpleural lung parenchyma. According to relevant conventional theories, the lung is considered as a blind spot for ultrasonic testing. However, ultrasonic images and artifacts caused by changes in charge and water content in the pulmonary alveoli and mesenchyma of damaged lungs make pulmonary ultrasonography possible. Since 1997, some researchers have attempted to observe the variations in the ARDS course by virtue of the ultrasonic technique, and it has been gradually proven over time that such a technique is significant for clinical application. Currently, corresponding clinical applications and scientific research are being conducted more profoundly. Under such circumstances, the application values and advantages of lung ultrasound, with the help of analysis of artifacts (e.g., lines A and B), become increasingly obvious in the differential diagnosis of pulmonary consolidation, pulmonary atelectasis, and dyspnea pathogeny that attack critically ill patients.

As ultrasound cannot be transmitted through air-filled tissue, ultrasound of the normal lung does not reveal the lung parenchyma beyond the pleura. Conversely, artifacts are produced owing to the interaction between the air- and fluid-filled lung tissue, resulting in specific ultrasound signs. Common lung pathologies include parenchymal changes, reduced lung ventilation, and/or pleural surface changes. This alters the ultrasound lung pattern, allowing for the detection of pathology using lung ultrasound. Pulmonary ultrasound is based on the analysis of a limited number of artifacts that result in a specific ultrasound pattern rather than a direct display of the lung parenchyma. Pulmonary ultrasound artifacts arise from the pleura; therefore, the pleural line must be clearly detected to avoid errors. In adults, it is located 0.5 cm below the rib line (bat sign) and always corresponds to the mural pleura, while the visceral pleura may or may not be present. The A-line is a horizontal hyperechoic artifact that is a duplication of the pleural line due to ultrasound reverberation between the pleura and probe. The presence of the A-line indicates a high gas volume ratio below the mural pleura and, therefore, may be associated with a normal pulmonary, hyperinflated, or pneumothorax.

Movement of the pleural line synchronized with tidal ventilation is called pulmonary sliding and indicates that the mural and visceral pleura are coated, with the latter sliding beneath the former. The M-mode allows a more precise analysis of pulmonary glide and shows the “seashore sign”. If the pulmonary glide is not present, a “pulmonary pulse” can usually be observed on both ultrasound and M-mode: the visceral pleura moves only in response to propagating cardiac activity and not in response to tidal ventilation. Anterior lung sliding and lung pulsation were performed to rule out pneumothorax and provide information about regional tidal ventilation. In M-mode, the absence of a pulmonary glide/pulse is manifested as the “stratospheric sign”. The pulmonary point is an alternation of normal and aborted pulmonary glides with an exclusive A-line and is specific for pneumothorax; it corresponds to the point at which the collapsed lung contacts the parietal wall at each inspiration. The B-lines always arise from the pleural line and move with the lung slide. They are usually well-defined, long, and extend to the bottom of the screen, erasing the A lines, and hyperechoic. More than two B lines per scan form a B pattern, historically known as a “lung rocket,” which is compatible with interstitial syndrome. Three or four B lines are associated with thickened subpleural interlobular septa, and five or more are associated with areas of hairy glass, suggesting severe interstitial syndrome.

Results

Diagnostic Significance of Lung Ultrasound in ARDS

Through the B-line, lung ultrasound can monitor increases in interstitial and alveolar fluids
in patients with ARDS. It is characterized by at least three mixed hyperechoic shadows perpendicular to the pleural line. They extend to the bottom of the screen without attenuation and synchronously move along with the lung sliding. As ARDS-associated pulmonary lesions are influenced by gravity, non-uniformity is usually found in diseased regions, pathological processes, and pathologic changes. Existing focal changes include diffuse lesions; while some regions are severely damaged, some other regions have mild impairment, and some others are free of such influence. The pathological physiology of the disease determines the distribution patterns of the B line and produces ultrasonic manifestations, which are especially critical for differential diagnosis. Caused by primary lung injuries, the B-line of ARDS is formed by abnormalities adjacent to the surface of the visceral pleura. Moreover, these abnormalities are directly induced by lung injuries. Among patients with ARDS, pulmonary ultrasonography findings show different characteristics due to differences in lung tissue dysfunction for the activation of gasification in a non-gravity-dependent lung field, the B-lines were non-uniformly distributed on both sides. Specifically, while multiple B-lines exist in some lung fields, they merge in some regions. In these cases, there may be normal lung tissues denoted by the A-line between them, manifested as an interstitial syndrome of nonuniform distribution. On the backside of the lung field, the B-lines are distributed more densely and even manifest as “white lungs.” The consolidation region usually appears in the backside lung field, especially at the pars basilaris, and is also combined with a static/dynamic air bronchogram. In regions with merged B-lines, the phenomena of “lung sliding” may reduce or disappear in most cases. Pleural lines combined with multiple small consolidations become irregular, thickened, and rough.

By virtue of lung ultrasound, all lung characteristics of ARDS determined by early CT can be found, such as non-uniform pulmonary interstitial syndrome with undamaged sites, abnormal changes of pleural lines, commonly seen lung consolidation, pulmonary atelectasis, and pleural effusion. As proven by relevant research, the findings of lung ultrasound are consistent with the pathophysiological conditions shown by CT scanning, and lung ultrasound also turns out to be more sensitive and specific than CXR examinations, as far as the corresponding diagnosis is concerned. Once ultrasound technology is applied to patients with acute lung injury (ALI)/ARDS, the number of CXR/CT examinations is substantially reduced. Therefore, lung ultrasound has important clinical values. As suggested by the Expert Consensus published by the International Liaison Committee on Lung Ultrasound, ARDS diagnosis can be made according to the following ultrasound signs: subpleural consolidation of the anterior wall, weakening or disappearance of lung sliding, normal pulmonary parenchyma (the corresponding site not involved in the lesion), signs of pleural line abnormalities (irregular segmental thickening of the pleural line), and non-uniform thickening of B-lines. On this basis, lung ultrasound may replace or complement conventional chest imaging in the ICU to a great extent.

**Dynamic Assessment of ARDS Based on Lung Ultrasound**

After performing a definite diagnosis of ARDS according to the Berlin definition, disease severity is frequently assessed based on the oxygenation index (PaO2 /FiO2) and positive end-expiratory pressure. Moreover, oxygenation index is susceptible to various factors. Considering that the lung water content in ARDS is closely related to the oxygenation index and prognosis, it is extremely important to assess the lung water content. The pathophysiological characteristics of ARDS include an increase in pulmonary vascular permeability and progression from pulmonary interstitial edema to alveolar edema. In some opinions, extravascular lung water (EVLW) is selected as a new index for differentiating ARDS severity; once EVLW exceeds 10 mL/kg, pulmonary edema can be definitively diagnosed; and for EVLW beyond 15 mL/kg, it indicates severe ARDS. To perform EVLW measurement, pulse indicator continuous cardiac output (PiCCO) technology should be adopted. However, the accuracy of this technology, which is expensive and invasive, is influenced by arrhythmia, aortic valvular diseases, and improper manipulation. According to another study based on a mouse model of ALI, the number of B-lines was positively correlated with the ratio of wet weight to dry weight (W/D) of lung tissues (r=0.834; p<0.001). In the mouse ALI/ARDS model, lung ultrasound can be used to assess EVLW. By monitoring the number of B-lines during lung ultrasound, abnormal changes can even be found at an early phase before oxygenation changes, including EVLW.
At present, the lung ultrasound scoring method is commonly used in clinical practice. Specifically, both lungs were divided into 12 regions; each region was assigned a value between 0 and 3 according to the number of B-lines, their distribution, and whether any subpleural consolidation existed. The aggregate sum of the scores graded for these 12 regions serves as the lung ultrasound. It has been reported in relevant research that lung ultrasound scoring is strongly correlated with EVLW content measured by the transpulmonary thermodilution technique. Therefore, lung ultrasound can be used to assess the severity of ARDS based on the relevant ultrasound signs. Undoubtedly, it is likely that it will become a routinely used tool for the non-invasive assessment of EVLW in patients with ARDS.

Discussion

Patients with coronavirus disease of 2019 (COVID-19) are classified as mild, common, severe, and critical due to factors such as the severity of lung disease and the degree of systemic organ involvement. In patients with early or mild COVID-19, the lesion may be a focal interstitial infiltrate with localized pleural thickening at the site of the lesion with discrete B-lines posteriorly, suggesting interstitial lung inflammation. Progressive COVID-19 may show interstitial and alveolar infiltrates in multiple lobes of the lung with multiple focal B-lines on ultrasound and progression to ARDS. Zhu et al used a semi-quantitative lung ultrasound score: 0 for the A-line, 1 for the discrete B-line, 2 for the fused B-line, and 3 for pulmonary solidity. This score is related to the ratio of alveolar “water” to “air”. The higher the percentage of water, the higher the score, and the more severe the lung lesions. This study found a significant gradient in lung ultrasound scores among the mild, severe, and critically ill patients. This suggests that lung ultrasound scores can be used to assess the severity of disease in COVID-19.

The Brandão Neto et al. study on lung ultrasound in patients with COVID-19 in the emergency department found that lung ultrasound was similar to lung CT and that lung ultrasound scores correlated well with mortality, tracheal intubation rates, and ICU transfer rates, and could be used to predict patient prognosis. Lung ultrasound is useful for repeated screening multiple times a day to compare patients before and after lung disease progression and to fully understand whether lung disease is worsening or improving. At the same time, it can reduce the disadvantages of transferring patients to the imaging department for examination, such as the risk of transferring critical patients and radiation.

Conclusions

In addition to guiding early treatment, lung ultrasound also assists clinical doctors in not only rapid diagnosis but also dynamically evaluating ARDS occurrence and development. For ARDS management in the ICU, lung ultrasound may replace bedside CXR and reduce the number of chest CT examinations. With the rapid development of the ultrasonic technique and increasingly more profound investigations on ARDS pathogenesis, the application of lung ultrasound will be increasingly accepted by more doctors and will become more popular for the diagnosis and treatment of ARDS, as well as to assess ARDS.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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Ethical Approval

The study did not involve human participants and ethics approval is not applicable.

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