УДК 616.24:[616.98:578.834.1-036.21]-022.14-073.432.1
https://doi.org/10.20538/1682-0363-2022-4-150-159

Lung ultrasound in the diagnosis of COVID-19-associated pneumonia

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ABSTRACT

Over the past decades, lung ultrasound in the diagnosis of lung diseases has become widespread. Ultrasound examination has a number of advantages (no radiation exposure, real-time imaging, clear visualization of the subpleural lung regions and costophrenic angles), which make it possible to use ultrasound to monitor the dynamics of pneumonia in children and pregnant women. Currently, in the context of the COVID-19 pandemic, lung ultrasound is widely used due to its high diagnostic efficiency, which is comparable with classical radiography and X-ray computed tomography (CT) by a number of parameters.

The article describes the method of lung ultrasound and the radiographic pattern of COVID-19-associated pneumonia. It also provides a review of the literature, according to which the severity of pneumonia was determined, depending on the radiographic pattern, and the need for a lung ultrasound was identified.

The article indicates that information on assessment of the radiographic pattern of the lungs at runtime in different variants of the course of coronavirus infection, as well as many methodological issues, including the frequency of second-look lung ultrasound, has not been sufficiently studied.

Keywords: ultrasound, pneumonia, COVID-19, interstitial syndrome, white lung, consolidation, B-lines, pleural line

Conflict of interest. The authors declare the absence of obvious or potential conflicts of interest related to the publication of this article.

Source of financing. The authors state that they received no funding for the study.

For citation: Balabanova A.A., Kurazhov A.P., Zavadovskaya V.D. Lung ultrasound in the diagnosis of COVID-19-associated pneumonia. *Bulletin of Siberian Medicine.* 2022;21(4):150–159. https://doi.org/10.20538/1682-0363-2022-4-150-159.

Ультразвуковая диагностика COVID-19-ассоциированных пневмоний

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РЕЗЮМЕ

В течение последних десятилетий ультразвуковая диагностика заболеваний легких получила широкое распространение. Ультразвуковое исследование (УЗИ) имеет ряд преимуществ: отсутствие лучевой нагрузки, получение изображения в режиме реального времени, отчетливая визуализация субплевральных отделов легких и реберно-диафрагмальных синусов, которые дают возможность использовать ультразвук

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для динамики пневмонии у детей и беременных женщин. В условиях пандемии COVID-19 УЗИ легких получило широкое применение в связи с высокой диагностической эффективностью, сопоставимой по ряду показателей с классической рентгенографией и рентгеновской компьютерной томографией.

Излагается методика УЗИ легких, ультразвуковая картина COVID-19-ассоциированных пневмоний. Предоставлен обзор литературы, согласно которой выявлены степени тяжести пневмонии в зависимости от ультразвуковой картины и необходимость использования УЗИ легких.

Указано, что недостаточно изучены информация об оценке ультразвуковой картины легких в динамике при различных вариантах течения коронавирусной инфекции, а также многие вопросы методического характера, включая периодичность и частоту динамического УЗИ легких.

Ключевые слова: ультразвуковое исследование, пневмония, COVID-19, интерстициальный синдром, белое легкое, консолидация, B-линии, плевральная линия

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии финансирования при проведении исследования.

Для цитирования: Балабанова А.А., Куражов А.П., Завадовская В.Д. Ультразвуковая диагностика COVID-19-ассоциированных пневмоний. *Бюллетень сибирской медицины.* 2022;21(4):150–159. https://doi.org/10.20538/1682-0363-2022-4-150-159.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) [1–3] is a potentially severe acute respiratory infection caused by SARS-CoV-2 (2019-nCoV) [4]. It is a dangerous disease [3], which can occur both as mild [5, 6] and severe [7] acute respiratory infection. The most common complication of the disease is viral pneumonia, which can result in acute respiratory distress syndrome and subsequent acute respiratory failure, most often requiring oxygen therapy and respiratory support [8].

Medical imaging methods are used to identify COVID-19-associated pneumonias and their complications, to carry out differential diagnosis with other lung diseases, to determine severity of the disease and its progression, and to assess therapy effectiveness [6]. The main medical imaging methods for detecting chest pathologies in patients with suspected or confirmed COVID-19-associated pneumonia include lung computed tomography (CT), plain chest radiography (CR), and lung and pleural ultrasound (US).

CT is the gold standard imaging modality for examining patients with suspected or confirmed COVID-19-associated pneumonia. For example, it has been determined that specificity of CT versus US and CR can reach 100% in certain patient groups [9]. At the same time, it should be taken into account that many infectious and non-infectious diseases, such as various HIV-associated lung lesions and interstitial lung disease, can reduce CT specificity in the diagnosis of COVID-19-associated lung lesions [10, 11]. Typical CT changes in the lungs in COVID-19-associated pneumonia are bilateral subpleural ground-glass opacities in the lung tissue or lung consolidation areas of an irregular, sometimes rounded shape with predominantly peripheral distribution in the lungs, which emerge in case of bacterial coinfection [12].

In the Russian Federation, according to the Temporary Guidelines of the Russian Society of Radiologists and Russian Association of Specialists in Ultrasound Diagnostics in Medicine, in the context of the COVID-19 pandemic, the so-called "empirical" visual scale for a rapid assessment of pathological CT changes in the lungs is recommended. It is based on the visual assessment of the approximate volume of the damaged lung tissue and the nature of lung changes [13]. This scale has 5 grades (Table 1).

Table 1

Visual scale for assessing the degree of lung damage detected on CT

Degree of lung damage	Characteristics
CT-0	Normal pattern and the absence of CT signs of viral pneumonia despite typical clinical manifestations and relevant epidemiological history

Table 1 (continued)

Degree of lung damage	Characteristics
CT-1	Mild degree – ground-glass opacities. Lung parenchyma involvement ≤ 25%
CT-2	Moderate degree – ground-glass opacities. Lung parenchyma involvement of 25–50%
CT-3	Severe degree – ground-glass opacities, lung consolidation areas. Lung parenchyma involvement of 50–75%
CT-4	Critical degree – diffuse ground-glass opacities and lung consolidation in combination with reticular changes. Hydrothorax. Lung parenchyma involvement ≥ 75%.

To date, this scale is the mainstay for determining the severity of morphological changes in the lungs in patients with COVID-19-associated pneumonia. Its high efficiency has been proven by its wide use in clinical practice. The only limiting factor for CT is the impossibility of its use in intensive care units and mechanically-ventilated patients.

Another frequently used diagnostic radiology technique in detecting COVID-19-associated pneumonia is plain chest radiography (CR) [14]. This method has lower diagnostic efficiency, but due to its greater availability and lower cost, it has become widespread during the COVID-19 pandemic [15]. Typical CR changes in COVID-19 are multiple diffuse, peripheral, irregularly shaped opacities, localized mainly in the lower lobes of both lungs [16].

Over the past decades, one of the topical issues in diagnostic US has been the assessment of its information value in lung diseases [17–20]. It has been determined that this modality has a high diagnostic value in the assessment of some lung diseases and, in certain clinical situations, outperforms CR in sensitivity and specificity [21]. For example, the results of the study by Russian researchers indicated greater accuracy of US compared with CR in the diagnosis of pneumonia in children, and the same authors provided evidence that in some cases US can compete with CT, for example, in the diagnosis of lung abscess [22]. In addition, lung US has been quite widely used in monitoring pathologies associated with lung tissue, including cardiogenic pulmonary edema, pneumothorax, pleural effusion, atelectasis, pneumonia, and peripheral lung nodules [23–27]. A number of other publications also indicate that, in recent decades, US has been in great demand in the diagnosis of various lung diseases, including, in addition to the above, emphysema and pleural diseases [17–19, 28–30].

It is believed that lung US in patients with suspected or confirmed COVID-19-associated pneumonia is an additional imaging method that does not replace or exclude CR and CT as traditional diagnostic modalities with high information value, proven by many years of clinical practice. In this regard, lung US is not included in the clinical guidelines and standards for the diagnosis and treatment of community-acquired pneumonia [5, 13]. This is partly because the effectiveness of US is largely dependent on the experience and qualifications of the doctor performing the study.

Many researchers provide evidence that US can compete in accuracy with CT in the diagnosis of COVID-19-associated pneumonia [31, 32], and in some aspects it outperforms CR [33]. So, according to a study by R. Gibbons et al. [33], the sensitivity of US in detecting intrapulmonary changes in COVID-19 was 97.6%, while that of CR was only 69.9%. However, lung US was less specific than CR (33.3 and 44.4%, respectively). This study included 143 patients aged 18 years and older with symptoms of COVID-19 (all registered patients had a body temperature of 38 °C or higher, a heart rate of 100 beats per minute or higher, a respiratory rate of 16 breaths per minute or more, SpO_2 less than 94% with cough, dyspnea, myalgia, malaise, ageusia, and anosmia).

It was also previously found that lung US makes it possible to control the course of pneumonia directly at the bedside, including mechanically-ventilated patients [34]. An additional advantage of lung US due to the absence of radiation exposure is the ability to examine pregnant women [35], who may have a more severe course of COVID-19-associated pneumonia [28, 36, 37]. Lung US reveals initial signs of lung damage caused by SARS-CoV-2, which is especially important when triaging patients in the emergency rooms of medical institutions. An increase in the intensity of interstitial changes in the lungs up to the emergence of a white lung in the US scan may be a predictor of a need for intubation and transfer of patients to mechanical ventilation [31]. In such cases, lung US strongly affects the treatment strategy, reducing decision-making time, which is crucial, since the condition of patients with COVID-19 can deteriorate rapidly [34].

LUNG ULTRASOUND TECHNIQUE

Routine lung US is performed using the B-mode with a microconvex transducer with a frequency of 5 MHz. At the same time, it is possible to use linear or convex transducers in the frequency ranges of 5–15 and 3–5 MHz, respectively [17, 38]. The linear transducer is used to detail and better visualize pleural sliding and search for alveolar consolidation [18]. Depending on the severity of the patient's condition, the examination is performed in an upright, sitting or lying position. It is believed that if the patient is mechanically ventilated or in the prone position, then it is necessary to scan the accessible chest areas and note this feature of the US examination in its protocol [39].

To date, a standard technique for lung US has been developed and is actively used [40]. In 2008, D. Lichtenstein developed the so-called BLUE protocol, which is an algorithmic approach to examining the lungs in acute respiratory pathology [18]. Its advantages are simplicity and speed, since it allows to get the main diagnostic information with the maximum ease of performing the study in a short period of time. The basic principle of the BLUE protocol is a simple sonographic evaluation of the lungs. If pulmonary embolism (PE) is suspected, this protocol is extended by a simplified study of lower extremity veins and echocardiography performed to detect extrapulmonary thrombi as possible causes of PE. The study of only anterior lung regions makes it possible to confirm or exclude such conditions as pneumothorax and pulmonary edema within a few seconds. In the absence of US signs of pneumothorax and pulmonary edema, further, according to the diagnostic algorithm, a study of the lower extremity veins and lateral and posterior lung regions is performed in order to diagnose possible pulmonary infarction and pleural effusion [18]. Sonographic signs of PE are pulmonary consolidation, predominantly wedge-shaped or rounded, fluid located directly above the subpleural lung lesion, and local interstitial changes [41].

According to the BLUE protocol [18], when performing a routine lung US examination to diagnose intrapulmonary lesions, the chest is arbitrarily divided into 12 zones. On the right and left, the chest surface is divided into anterior, lateral, and posterior regions, each of which, in turn, is subdivided into upper and lower zones (Table 2). Then the US transducer is placed perpendicular to the ribs or parallel to the intercostal spaces, and all regions accessible for inspection are scanned [18].

To minimize the risk of COVID-19 for medical personnel, lung US is preferably performed directly in the patient's ward quickly and according to a pre-verified protocol, using a portable device. In the study of patients with mild or moderate disease severity, to reduce the time of the examination, lung US is performed in a vertical, hands-behind-the-head position of the patient.

Table 2

Zones and anatomical landmarks in lung US

Surface	Vertical borders	Zones	Horizontal borders
Anterior	From the parasternal to the anterior axillary line	Upper	From the supraclavicular region to the IV rib
		Lower	From the IV rib to the diaphragmatic sinus
Lateral	From the anterior axillary to the posterior axillary line	Upper	From axillary fossa to the IV rib
		Lower	From the IV rib to the diaphragmatic sinus
Posterior	From the posterior axillary to the paravertebral line	Upper	From the II rib to the inferior angle of the scapula
		Lower	From the inferior angle of the scapula to the diaphragmatic sinus

NORMAL LUNG US PATTERN

In normal conditions, lung tissue is visualized in the intercostal spaces and is represented on diagnostic images by multiple parallel hyperechoic lines (called A-lines) due to lung sliding and movements of the visceral pleura [18]. A-lines are located directly below the pleural line, which, in turn, has the form of a thin hyperechoic strip in normal conditions (Fig. 1). Also, in normal conditions, US examination reveals single B-lines (no more than 3 in 1 intercostal space), which are linear vertical hyperechoic comet tail artifacts, coming from the pleural line [17, 18] (Fig. 2). B-lines are formed due to reverberation between the visceral pleura and air in the alveoli on the lung surface and because of thickening of the subpleural interlobular septa [18].

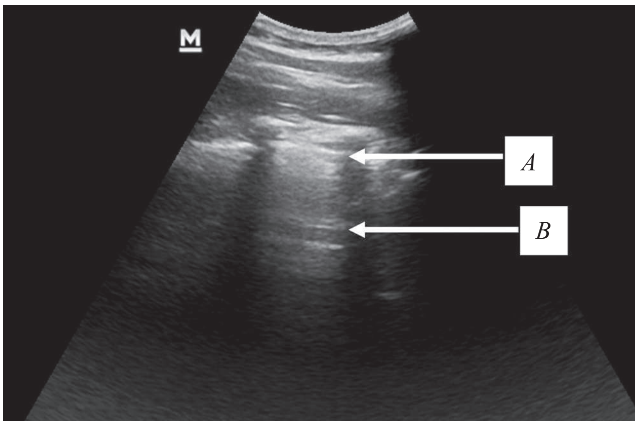

Fig. 1. US pattern of unchanged lung tissue: *A* – pleural line, *B* – multiple parallel white A-lines

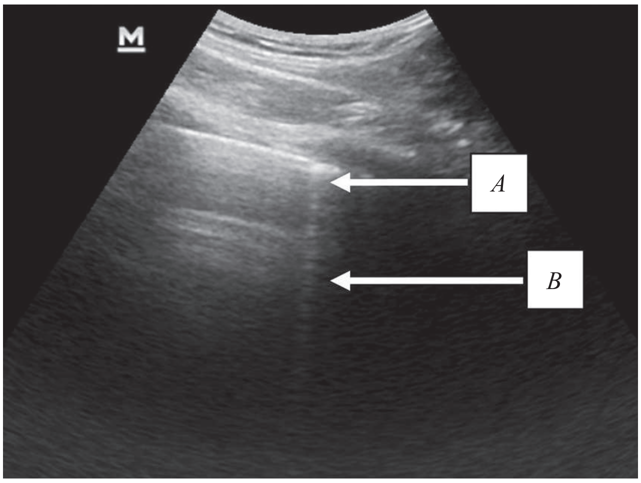

Fig. 2. US pattern of unchanged lung tissue with a single vertical B-line: *A* – pleural line, *B* – single B-line

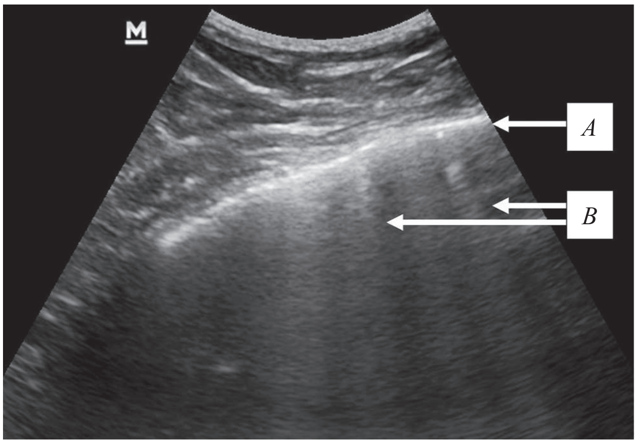

Fig. 3. US pattern of the interstitial syndrome in a patient with COVID-19-associated pneumonia: *A* – thickened pleural line with uneven contours, *B* – multiple vertical B-lines

US PATTERNS OF LUNG CHANGES IN PATIENTS WITH COVID-19-ASSOCIATED PNEUMONIA

For the first time, US patterns of lung lesions in COVID-19 were described by scientists from China [42]. According to their results, the main US signs of lung damage in COVID-19-associated pneumonia were: 1) thickening and uneven costal pleura; 2) different variants of B-patterns in the form of focal, confluent or multifocal B-lines; 3) subpleural and lobar lung consolidation, sometimes with air bronchograms (hyperechoic bright elements representing air trapped in the bronchioles); 4) small rare pleural effusion [42].

To date, it is believed that qualitative US signs of lung tissue damage in COVID-19-associated pneumonia are: 1) interstitial lung disease, 2) white lung, and 3) lung consolidation [43, 44] (Fig. 3–5).

The US pattern of interstitial lung disease is visualization of more than three vertical B-lines in one intercostal space. It is believed that the interstitial syndrome is a consequence of an infectious and inflammatory process that affects the interstitium [45]. In this case, B-lines are usually more pronounced in the lower zones with the same distribution on both sides, and the anterior and upper lateral lung zones are affected to a lesser extent. Besides, in interstitial lung disease, in addition to multiple B-lines, lung US reveals thickening of the pleural line (Fig. 3) [18]. This syndrome occurs due to local changes in the acoustic properties of the lung, caused by changes in the density and subpleural interlobular septa thickening [46–48].

The US pattern of the white lung is commonly understood as visualization of multifocal confluent B-lines, since it was found that an increase in their number reflects an increase in the amount of extravascular lung water, which is observed in interstitial pulmonary edema [49, 50]. Diffuse white lung is characterized by the alveolar – interstitial syndrome, which implies both alveolar and interstitial pulmonary edema [18] (Fig. 4).

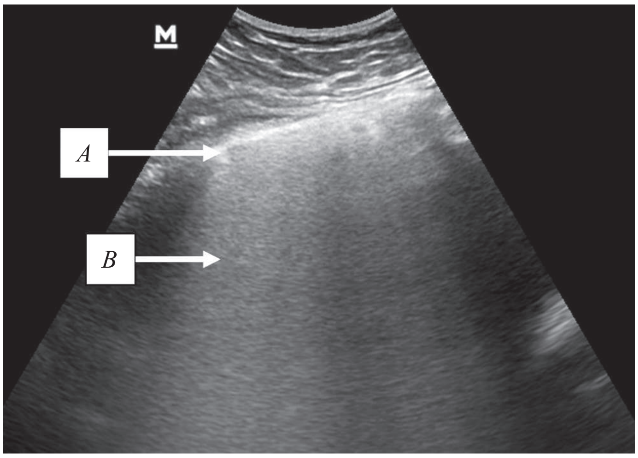

Fig. 4. US pattern of the white lung in a patient with COVID-19-associated pneumonia: *A* – thickened pleural line, *B* – multiple merging vertical B-lines

The alveolar – interstitial syndrome has no physical basis and is well detected by CT scan, as well as by lung US [51–53]. The alveolar – interstitial syndrome occurs in many pathological conditions, including cardiogenic pulmonary edema, bacterial, viral and fungal pneumonia, and chronic interstitial lung disease during an exacerbation [21, 51, 53].

In addition to the visualization of multifocal confluent B-lines, lung US detects an uneven, thickened, interrupted pleural line. This also includes visualization of single hypoechoic areas in the subpleural regions of the lungs corresponding to the alveoli completely filled with fluid [46–48].

Lung consolidation occurs when inflammation spreads to the subpleural lung areas and sonographically manifests itself as uneven thickening and discontinuity of the costal pleura. In addition, hypoechoic areas appear in the subpleural lung regions, which are formed due to the filling of the alveoli with fluid (Fig. 5). The emergence of these hypoechoic areas indicates a loss of lung tissue airiness. Acoustic properties of the lungs become the same as in soft tissues, significantly different from the lungs containing air [46–48].

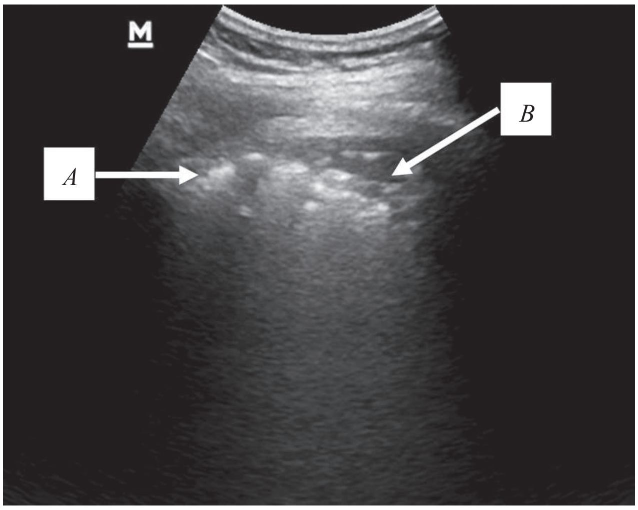

Fig. 5. US pattern of lung consolidation in a patient with COVID-19-associated pneumonia: *A* – thickened interrupted pleural line, *B* – hypoechoic areas in the subpleural lung regions

A study by Chinese scientists [54] showed that in patients with confirmed severe SARS-CoV-2 infection, bacterial and fungal coinfection develops in 25.5 and 10.9% of cases, respectively. In studies by Italian scientists [55], it was found that in 16,654 patients who died from COVID-19, bacterial and fungal coinfection occurred in 11% of cases.

When bacterial coinfection develops, typical US signs of pneumonia are lung consolidation, air bronchogram, pleural effusion, subpleural destruction foci, and compressive atelectasis in combination with pleural effusion [56–58] (Fig. 6).

Another direction of research in the use of US in the diagnosis of COVID-19-associated pneumonia is developing US semiotics of lung damage, depending on the stage of the disease. So, Q.Y.Peng et al. [42] revealed certain correlations of the US pattern with stages of pneumonia caused by SARS-CoV-2 (Table 3).

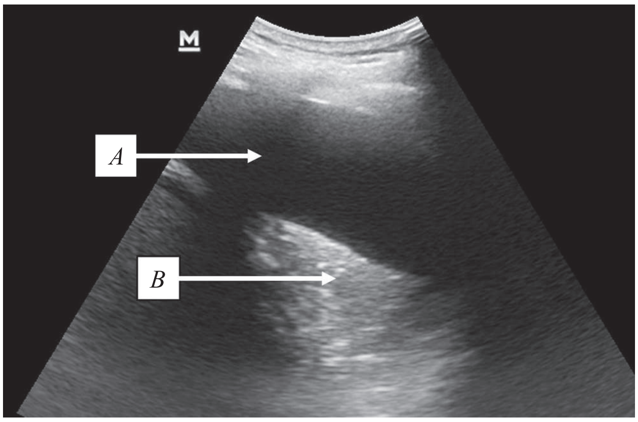

Fig. 6. US pattern of compressive atelectasis in the lower lung regions combined with pleural effusion in a patient with COVID-19-associated pneumonia complicated by bacterial coinfection: *A* – pleural effusion, *B* – area of compressive atelectasis

Table 3

US pattern of lung tissue damage in COVID-19-associated pneumonia depending on the disease severity according to Q.Y. Peng et al. [42]

Stages of pneumonia	US pattern
Initial stage or mild form	Unevenly distributed focal B-lines and an unevenly thickened pleural line are visualized
Stage of progression or moderate form	The number of B-lines in the affected lung zones increases, primarily in the basal lung regions, and then it spreads to other lung zones. The number of B-lines increases and they merge.
Severe form	Lung consolidation areas are visualized. Lung «hepatization» is noted, and pleural effusion emerges
Resolution stage	Reduction of the number of B-lines, emergence of A-lines in the affected lung area

Apart from identifying qualitative US signs of lung damage in COVID-19, attempts were made to perform a semi-quantitative assessment of pathological lung changes in this disease. For example, G. Soldati et al. proposed a scoring scale for assessing the severity of pneumonia caused by SARS-CoV-2, according to lung US data [58]. In accordance with this scale, a semi-quantitative assessment of the degree of lung damage is performed on the scale from 0 to 3 for each of the 12 examined areas (Table 4) [58].

Table 4

US pattern of lung tissue damage in COVID-19-associated pneumonia depending on the degree of lung damage according to G. Soldati et al. [58]

Degree of lung damage	US pattern
0	Normal, the pleural line is smooth and continuous, A-lines are visualized
1	The pleural line has serrated margins; three or more vertical B-lines are visualized under the altered pleural line in one zone
2	The pleural line is interrupted; under the altered pleural line, lung consolidation areas of different sizes are visualized; below them, multiple confluent B-lines (white lung) are detected
3	In the scanned area, increased white lung is detected with or without larger consolidation areas

In this paper [58], the average scores calculated according to the method proposed by the authors was 29.2 ± 7.3 and 20.4 ± 8.5 in patients with and without deterioration of the clinical condition, respectively. Therefore, when conducting the univariate and multivariate analyses, it was found that the total score calculated from the US data was directly associated with the likely deterioration of the patient's condition. Moreover, an overall mean US score above 24 was associated with an almost 6-fold increase in the odds for the deterioration of the patient's condition.

Another foreign study [39] showed that lung US in patients with COVID-19 can be used as a predictor of the disease course and outcome. In this work [39], lung US was performed only in six zones (anterior, anterolateral, and posterolateral on both sides), since the examined patients were in the intensive care unit, and to interpret the US data, a scoring scale for the assessment of the lung damage severity was also proposed (Table 5).

Table 5

US pattern of lung damage in COVID-19-associated pneumonia depending on the degree of severity according to Y. Lichter et al. [39]

Degree of lung damage	US pattern
0	Normal, A-lines are visualized due to normal lung aeration
1	Three or more vertical B-lines are visualized in one zone due to a moderate loss of lung aeration; the pleural line is altered
2	Multiple confluent B-lines are visualized due to a severe loss of lung aeration; the pleural line is altered
3	Lung consolidation areas are visualized; the pleural line is altered

In this study [39], the median scores for patients with mild, moderate, and severe lung damage were 12, 19, and 23, respectively. As a result, the authors of this study obtained a survival curve for patients with COVID-19-associated pneumonia, based on which patients with a score of more than 18 had a 2.6-fold higher mortality risk compared with mortality in patients with a lower score [39].

In turn, another study [59] demonstrated that lung US in the diagnosis of COVID-19 associated pneumonia is comparable to chest CT in terms of sensitivity, which is 93–94%. However, given that lung US can only assess peripheral lung areas [60], this method turned out to have low specificity (less than 50%). In addition, lung US is limited when used in obese patients [61] and depends on the experience and skill of the operator [62].

At the same time, a poorly studied field of lung US in COVID-19-associated pneumonia is a dynamic assessment of the lung sonographic pattern in different forms of coronavirus infection, as well as many methodological issues, including the frequency of second-look lung US.

CONCLUSION

Therefore, in the context of the COVID-19 pandemic, lung US plays an essential role in the diagnosis of COVID-19-associated lung lesions caused by SARS-CoV-2 due to its relatively high diagnostic efficiency (which is comparable in a number of parameters to that of CR and CT) and a possibility of examining non-transported patients and patients with reduced mobility (including pregnant women) during their stay in specialized medical institutions in the absence of radiation exposure. Lung US can also be used as a predictor of the course and outcome of COVID-19-associated pneumonia. At the same time, US patterns of lung damage in this disease and practical methodological aspects of US application require more in-depth study and clarification.

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Received 20.10.2020;
approved after peer review 22.09.2021;
accepted 05.10.2021