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Ultrasound of the lungs as an actual research method in the conditions of a new coronavirus infection SARS-CoV-2

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Abstract

A literature review of the main issues of ultrasound diagnosis during the period of the SARS-CoV-2 coronavirus infection pandemic. The review shows the key aspects of ultrasound, the experience of foreign colleagues, reflecting the basic principles of ultrasound diagnostics when working with infected patients, the methodology of the distribution of people into the streams with their increased admission to hospitals in a pandemic.

Key words: ultrasound diagnostics, coronavirus infection, ultrasound of the lungs, COVID-19, pneumonia, pandemic.

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Ультразвуковое исследование легких: актуальный метод в условиях новой коронавирусной инфекции SARS-CoV-2

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Резюме

Представлен обзор литературы по основным аспектам проведения ультразвукового исследования легких у больных в период пандемии коронавирусной инфекции SARS-CoV-2, основанным на опыте ведущих научных центров разных стран. Продемонстрирована перспективность применения данного метода у больных с патологией легких, особенно в условиях подобной пандемии.

Ключевые слова: ультразвуковая диагностика, коронавирусная инфекция, ультразвуковое исследование легких, COVID-19, пневмония, пандемия.

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It is hard to imagine current real-life clinical practice without a wide use of imaging diagnostic techniques, particularly ultrasonography (U/S). In recent years, suspected pulmonary abnormalities have been considered as indications for this examination. This method has a whole range of attractive features, such as availability, non-invasive nature, painfulness, absence of direct contraindications, relative easy to use, lack of need for patient preparation, safety, and harmlessness due to its free-radiation nature, demonstrated in a number of studies. These features make it possible to use lung U/S in a wide range of patients, including pregnant and lactating women, adults, children, and patients with implanted pacemakers, metal implants, and other foreign bodies. This modality has become especially popular in these days, when the world is being affected by a "novel" infection and the number of hospitalised patients has risen dramatically.

It is well known that multiple cases of pneumonia of unknown etiology were first reported in workers of the Huanan Seafood Market selling meat and fish, in the Chinese city of Wuhan, in December 2019. On 1 December 2019 the Chinese authorities reported the spread of pneumonia of unknown etiology to the World Health Organisation (WHO). On 30 January 2020 WHO declared multiple cases of coronavirus infection as a public health emergency of international concern. On 11 February 2020 the disease was named COVID-19, which states for coronavirus disease-2019. The International Committee on Taxonomy of

Viruses (ICTV) announced “severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)” as the name of the virus causing this infection [1].

Coronavirus infection is an acute viral disease with a primary lesion of the upper respiratory tract caused by single-stranded, positive-sense RNA virus, belonging to *Betacoronavirus* of the family *Coronaviridae*. It has been spreading around the world in 2019 and 2020, and has been responsible for a huge number of deaths and enormous economic losses [2].

Of note, the identified pathogen was first described as early as the middle of the 20th century. By January 2020, *Coronaviridae* was already viewed as a separate family of viruses including 40 species of enveloped RNA viruses. This family is organised in two sub-families of viruses which infect humans and animals. These viruses are named for the large club-like spikes protruding from their envelope like the spikes of a crown. The latter mediates coronavirus entry through the cell membrane by mimicking molecules to which transmembrane cell receptors bind [1, 2].

At present, there are four known coronaviruses circulating in the human population (HCoV-229E, HCoV-OC43, HCoV-NL63, and HCoV-HKU1), which are always reported among pathogens causing acute respiratory viral infections (ARVI) and are often responsible for mild or moderate respiratory disease. This virus has been classified as a hazard group (HG) 3 pathogen (which corresponds to HG2 in the Russian classification). The virus enters the human body through epithelium in the upper respiratory tract, stomach and intestine. The pathophysiology involves an increased permeability of cell membranes and enhanced outflow of albumin-rich fluid into alveoli caused by the virus. This leads to degradation of surfactant, resulting to alveolar collapse and acute respiratory distress syndrome. Concomitant immunosuppression contributes to the development of opportunistic bacterial and fungal respiratory infections [2].

Computed tomography (CT) is the most informative and highly accurate imaging modality that produces the most detailed images possible of thoracic organs and allows for staging of the disease (classifying it into one of the five stages). It is used in the second step of the diagnostic pathway to confirm the diagnosis after an initial chest radiography has been performed [3].

The high number of infected people in the Russian Federation (as of 8 June 2020 there were 476,658 documented cases) [4] and the resulting enormous burden on the healthcare system suggest the need for the development of additional optimal diagnostic algorithms for pneumonia. The list of mandatory diagnostic examinations. provided in the 2019 Russian Clinical Treatment Guidelines for Pneumonia, does not include ultrasonography (U/S). The provision related to performing lung ultrasonography in 2020 during the COVID-19 pandemic has, however, been modified by including a provisional guidance allowing specialists to use ultrasound to detect pneumonia in the COVID-19 environment [5]. The greatest advantages of this technique involve the following:

- it can be used as a bedside method and in resuscitation divisions;
- it is radiation-free;
- ultrasound devices are easy to disinfect.

There is general agreement that U/S is not acceptable for assessment of lung parenchyma because of a high volume of air in the alveoli and the fact that ultrasound waves are largely scattered in air media. This is, however, true for normal lung tissue, but pathological processes, for example pulmonary oedema, are associated with changes in pulmonary resistance, leading to the appearance of typical structures visualised by ultrasound [6].

The first reports about visualization of lung tissue in pneumonia were made by the Russian scientist *Y.Bogin* as early as fifty years ago [7]. At that time, visualisation of the chest was possible by applying transducers along the standard lines. On ultrasound images pneumonia appeared as inhomogeneous opacities in lung parenchyma [7]. At present, ultrasonography easily differentiates tissues from fluid-filled structures, which appear as diffuse opacities on radiographic images.

Diagnostic ultrasonography can be helpful in obtaining the following clinically important information:

- to detect pleural effusion, to determine the amount of fluid and its relationship to the chest wall, and to choose the optimal puncture point for thoracentesis;
- to detect pleural empyema (its location and extent);
- to detect pneumonia (determine the location, extent, and patterns of pneumonic lesions, identify potential complications, and assess residual abnormalities in the lungs and pleura after achievement of clinical cure);
- to carry out dynamic follow-up of pulmonary and pleural disorders and evaluate the efficacy of treatment;
- to perform differential diagnosis between malignant and benign tumours of the lungs and pleura;
- to monitor the status of the pleural cavity, the degree of lung expansion, and the development of fibrothorax following surgical procedures on the lungs and pleura; and to assess the outcomes of surgical treatment [8].

Ultrasound diagnosis of pneumonia is mainly based on the use of the BLUE (Bedside Lung Ultrasound in Emergency) protocol. In fact, it is a bedside lung ultrasound protocol for emergency situations, which was proposed by *D.A.Lichtenstein* in 2008. This protocol was developed as a 3-minute screening tool to identify the causes of acute respiratory failure in intensive care unit patients. It allows for the differentiation between some pathologies, such as pneumothorax, pulmonary oedema, pulmonary embolism, pneumonia, chronic obstructive pulmonary disease, and asthma [6].

To be able to detect abnormal lung parenchyma on ultrasound scans, it is necessary to have a good understanding of the normal ultrasound lung pattern. In Russia, ultrasound diagnostic procedures are allowed to be performed by doctors specialising in ultrasound diagnostics [9], anaesthesiology and resuscitation [10], emergency medicine [11], or cardiology [12]. The accuracy of the examination depends on the correct choice of a transducer for a particular area of interest. There are three types of transducers: linear with a frequency range of 5 – 15 MHz and the maximum depth of penetration of 10 cm, standard convex with a frequency range of 2 – 7.5 MHz and the maximum depth of penetration of 25 cm, and sector

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with a frequency range of 1.5 – 5 MHz. These types have different ratios of the frequency and depth of penetration. Convex and sector transducers can be used to visualise deep structures, while linear transducers are suitable for visualisation of the pleura [13].

Ultrasound examination is most often performed in supine position, but can also be done in semi-recumbent or lateral positions. Each lung is divided into three zones (anterior, lateral, and posterior) delineated by the parasternal, anterior axillary, posterior axillary, and paravertebral lines.

The ultrasound transducer is placed longitudinally over a lung intercostal space (LIS). Scanning begins anteriorly cranially and progress down to the diaphragm along the parasternal line, with each LIS being scanned. The anterior axillary, posterior axillary, and paravertebral areas are examined in the same way. If any abnormalities are detected in any LIS, this space should be examined more thoroughly.

Key landmarks

The *pleural line*: a thin line representing the pleura, which is seen as a hyperechoic line below the ribs and moves with breathing (Figure 1).

A-lines: repetitive, horizontal, linear arterfacts located at regular intervals behind the pleural line and accompanied by lung sliding; these are signs of the normal lung pattern. A-lines not accompanied by lung sliding are indicative of pneumothorax. *Lung sliding* (demonstrated in B-mode) represents motion of the visceral pleura. This sign is indicative of the normal lung pattern and the absence of pneumothorax (Figure 2).

B-lines: single (⩽ 3 in one LIS) hyperechoic vertical artefacts that originate from the pleural line and appear as a comet tail. They move in synchrony with lung sliding and look like a laser beam. B-lines are indicative of normal lung (Figure 3); however, an increased number of B-lines (> 3 in one LIS) is a marker of pulmonary oedema (interstitial syndrome) (Figures 4, 5). Of note, the detection of B-lines is not 100% specific to COVID-19-associated pneumonia [5].

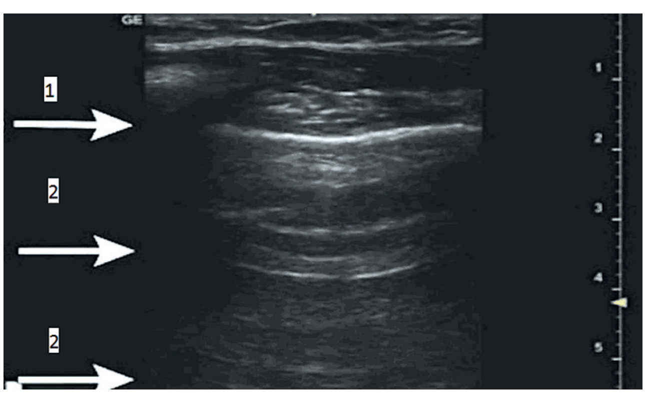

Figure 1. Pleural and A-lines: 1, pleural line; 2, A-line (changes, [14])

Рис. 1. Плевральная и А-линии: 1 – плевральная, 2 – А-линии (с изм., [14])

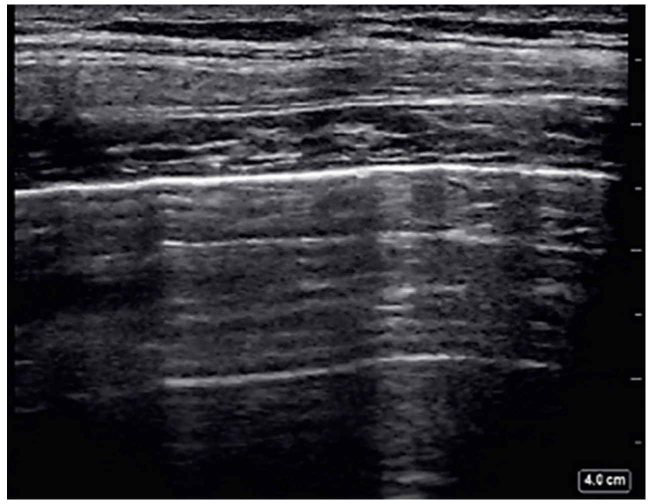

Figure 2. Symptom of pneumothorax of the lung [14]

Рис. 2. Признак пневмоторакса легкого [14]

Figure 3. Normal lung [14]

Рис. 3. Нормальное легкое [14]

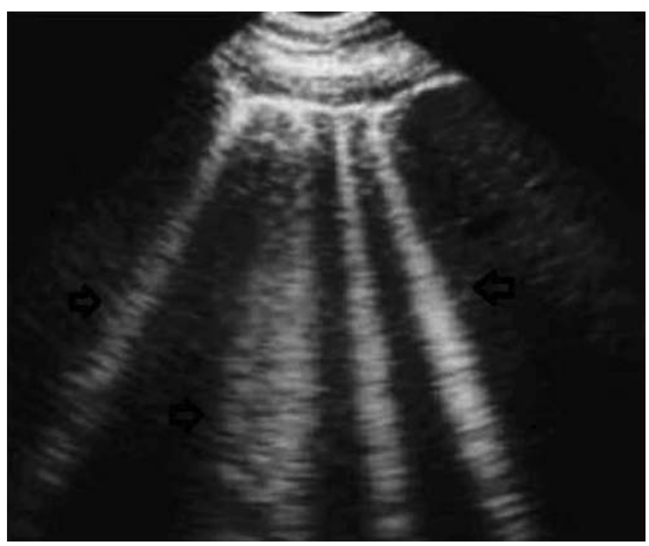

Figure 4. A sign of interstitial pulmonary edema. The arrows indicate B-lines [14]

Рис. 4. Признак интерстициального отека легкого. Стрелками указаны B-линии [14]

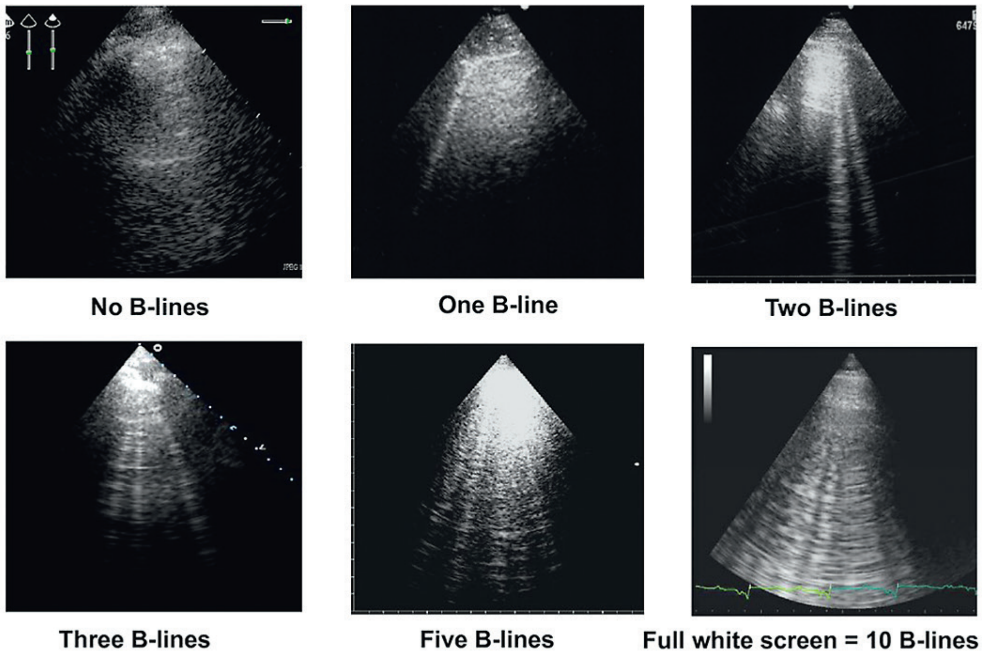

Figure 5. Single and multiple presence of B-lines in the ultrasound picture of the lung [14]
Рис. 5. Единичные и множественные В-линии при ультразвуковом исследовании легкого [14]

The «sea coast» (*Seashore Sign*) (demonstrated in M-mode) is indicative of normal lung sliding and rules out pneumothorax (Figure 6).

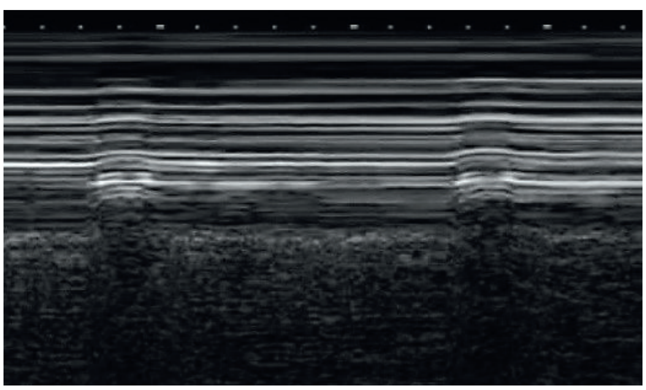

Figure 6. Sign of the "sea coast" in M-mode [14]
Рис. 6. Признак «морского берега» в М-режиме [14]

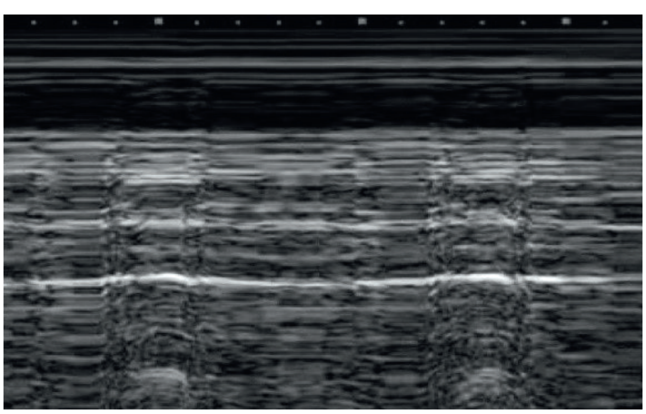

Figure 7. Barcode sign in M-mode [14]
Рис. 7. Признак «штрихкода» в М-режиме [14]

The *barcode sign* (demonstrated in M-mode) indicates the absence of lung sliding and the presence of pneumothorax (Figure 7).

The *quad sign* (*The Quad Sing*) (demonstrated in B-mode) is indicative of pleural effusion. It consists of lines representing the parietal pleura (pleural line), visceral pleura (lung line), and ribs on both sides (Figure 8).

The *sinusoid sign* (*a sign of pleural effusion demonstrated in M-mode*) indicates the movement of the lung line toward the pleural line on inspiration (Figure 9).

The *tissue-like sign*, also known as *lung hepatisation*, indicates lung consolidation (Figure 10). On ultrasound scans, lung tissue takes the appearance of liver tissue.

The *shred sign*, also known as the *fractal sign*, consists of an irregular (shredded) deep border (fractal line) of an area of consolidation. It appears as a hyperechoic border between the consolidated and normal lung tissue (Figure 11).

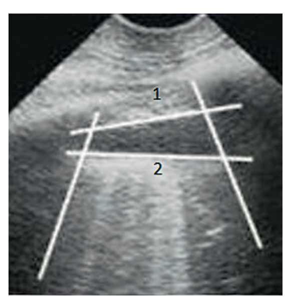

Figure 8. Pleural effusion in B-mode: 1, pleural line; 2, line of the lung (changes, [14])
Рис. 8. Плевральный выпот в В-режиме: 1 – плевральная линия, 2 – линия легкого (с изм., [14])

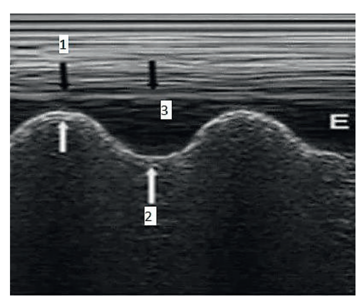

Figure 9. Pleural effusion in M-mode: 1, pleural line; 2, line of the lung; 3, fluid (changes, [14])
Рис. 9. Плевральный выпот в М-режиме: 1 – плевральная линия, 2 – линия легкого, 3 – жидкость (с изм., [14])

Figure 10. Lung consolidation [14]
Рис. 10. Консолидация легкого [14]

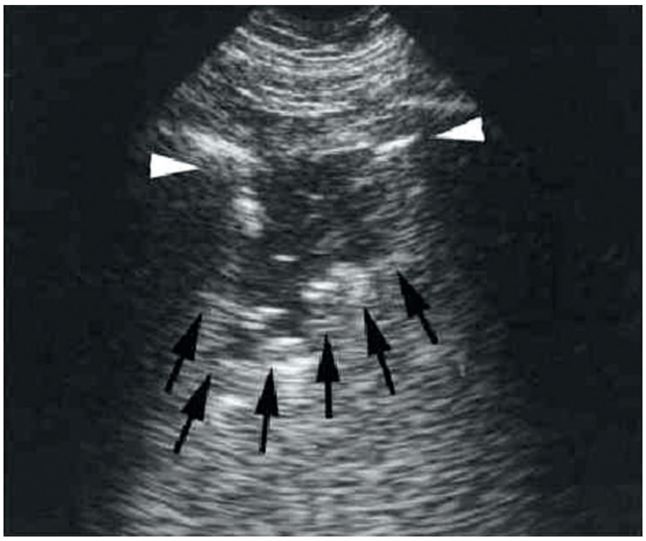

Figure 11. The arrows indicate an uneven, torn line (changes, [14])
Рис. 11. Стрелками указана неровная, рваная линия (с изм., [14])

The key ultrasound signs of COVID-19-associated pneumonia include:

- Irregularity, thickening, and fragmentation of the pleural line and absence of the pleural line along the border of consolidation;
- Appearance of B-lines in a variety of patterns (single, multiple, confluent, i.e. white lung appearance);
- Appearance of A-lines during recovery phase;
- Pleural effusion: uncommon and usually not abundant. It can be of various shape and size, which depends on the amount and distribution of fluid in the pleural cavity;
- Various types of consolidation lesions: local cortical, extended cortical, segmental or lobar [15].

The ultrasonographic features of SARS-CoV-2 pneumonia are related to the stage of disease, the severity of lung injury, and comorbidities. The predominant pattern is varying degrees of interstitial syndrome and alveolar consolidation, the degree of which is correlated with the severity of the lung damage. A recognized limitation of lung ultrasonography is that it cannot detect lesions that are deep within the lung, despite the potential of modern transducers, i.e., the abnormality must extend to the pleural surface to be visible with on ultrasonography examination. Chest CT is required to detect pneumonia that does not extend to the pleural surface [15].

International experience with lung ultrasound

Italian specialists developed a primary assessment protocol to evaluate the health status of people with suspected coronavirus infection. They recommended scanning 14 areas in each patient for 10 s [16], making these scans covering the widest possible surface area. Each area was scored on a 0 – 3 scale, as follows: A score of 0 is given when the pleural line is continuous and regular, with the presence of horizontal artefacts, usually referred to as A-lines. A score of 1 is given when the pleural line is indented, with vertical areas of white visible below. A score of 2 is given when the pleural line is broken and there are small to large areas of consolidation (darker areas) under the broken site with associated areas of white below (white lung pattern). An area is given a score of 3 when the scan shows dense and largely extended white lung tissue, with or without bigger consolidations.

Bedside ultrasound allowed for faster examination, which helped timely assess the need for hospitalisation. This examination was performed in more than 60.000 patients with signs of inflammation (fever and cough) to rule out pneumonia. One of such studies included twelve patients with flu-like symptoms and suspected COVID-19 (nine men and three women; mean age ± standard deviation, 63 ± 13 years old, who were admitted to the Guglielmo da Saliceto Hospital over a period of 4 – 10 days. In two patients ultrasonography detected pulmonary emphysema without concomitant respiratory failure, and three patients had posterior subpleural consolidations. Chest CT scan was performed in all patients and showed a strong correlation with U/S: Five of 12 patients had a crazy-paving pattern, i.e. a combination of ground-glass opacity and interlobular septal thickening. Organizing pneumonia was confirmed in four patients. Lung ultrasound was done by two physicians: one was responsible for the technical procedure, and the other interpreted the images obtained, which also contributed to faster detection of abnormalities [17].

A similar procedure was introduced in a paediatrics department for the evaluation of children with suspected COVID-19, based on the use of lung ultrasound by one paediatrician and another assistant. The paediatrician prepared the ultrasound pocket device, which comprised a wireless probe and a tablet. The probe and tablet were placed in two separate single-use plastic covers. The paediatrician used the probe and did the lung ultrasound, the assistant held the tablet and froze and stored the images, touching neither the patient nor the surrounding materials. The stethoscope was not used because there was a probability to mistakenly touch the patient's mucous membranes with it. This ultrasound procedure was therefore substituted for lung auscultation and significantly reduced doctors' risk of exposure [18].

The National Health Service in England did not even mention lung ultrasound in its clinical guidelines on triage of patients with COVID-19, specifying instead chest X-ray and CT as the first-line diagnostic imaging tools for equivocal cases [16].

Experts of the People's Republic of China (PRC) have recommended performing early chest CT before clinical manifestations for screening suspected patients. However, the high contagiousness of SARS-CoV-2 and the risk of transporting unstable patients with hypoxemia and hemodynamic failure made chest CT a limited option for the patient with suspected or established COVID-19. This explained the introduction of lung ultrasound, which is still an important diagnostic tool even if it has not yet been fully evaluated [15].

Chinese specialists reported that lung ultrasonography gives the results that are similar to those of chest CT and superior to standard chest radiography for evaluation of pneumonia and/or adult respiratory distress syndrome with the added advantage of ease of use at point of care, repeatability, absence of radiation exposure, and low cost. It is useful for rapid assessment of the severity of SARS-CoV-2 pneumonia, detecting the signs of disease progression, and assessing the need for extracorporeal membrane therapy and ventilatory support.

A comparative study of lung U/S and chest CT on a group of 20 patients with COVID-19 demonstrated specific features that can be detected by each of these imaging modalities (see Table) [15].

Table
Computed tomography and ultrasonographic features of COVID-19 pneumonia [15]
Таблица
Особенности пневмонии COVID-19 при компьютерной томографии и ультразвуковом исследовании легких [15]

Lung CT	Lung ultrasound
Thickened pleura	Thickened pleural line (can be observed in interstitial syndrome due to the appearance of artefacts in the initial stage of pneumonia)
Ground-glass shadow (loss of lung aeration and partial collapse of the alveoli) and effusion	B-lines (multifocal or confluent)
Pulmonary infiltrates (lung consolidation due to accumulation of fluid)	Confluent B-lines (in case of the development and progression of alveolar oedema)
Subpleural consolidation	Small consolidation
Translobar consolidation	Both non-translobar and translobar consolidation
Pleural effusion is rare	Pleural effusion is rare
More than two lobes affected	Multilobar distribution of abnormalities
Atypical in lung CT images in the early stage, then diffuse scattered with the progress of the disease, further lung consolidation	B-lines are the main feature in the early stage, mild infection, and in convalescence period; alveolar interstitial syndrome is the main feature in the progressive stage and in critically ill patients; pleural line thickening with uneven B-lines can be seen in patients with pulmonary fibrosis

Conclusion

To summarize, accumulated clinical experience with lung ultrasonography suggests that it is quite a promising and informative method, allowing for a rapid detection of structural lung abnormalities. Expertise of specialists from different countries demonstrates that the results of completed studies made it possible to view lung ultrasound as an important component of primary diagnostic workup for lung damage in patients with COVID-19 infection. It is explained by a number of its advantages, including its availability, ease of use, and high informative value. In addition, it makes it possible to reduce the number of healthcare professionals working in the COVID-19 environment and limit direct contact with patients. However, there is no doubt that further clinical trials are required to evaluate the potential of this technique in different clinical settings.

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