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Lung ultrasound: the possibilities of diagnosing of lung damage associated with the new coronavirus infection COVID-19

Galina V. Nekludova [1, 2, ✉], *Sergey N. Avdeev* [1, 2]

[1] Federal Pulmonology Research Institute, Federal Medical and Biological Agency of Russia: Orekhovyy bul'var 28, Moscow, 115682, Russia

[2] I.M.Sechenov First Moscow State Medical University, Healthcare Ministry of Russia (Sechenov University): ul. Trubetskaya 8, build. 2, Moscow, 119991, Russia

Abstract

This publication is devoted to the ultrasound method of lung examination, which has gained particular relevance during the pandemic of the new coronavirus infection 2019. The lecture discusses the general provisions of lung ultrasound, ultrasonic signs of lung damage, features of ultrasound semiotics in the viral nature of lung lesions, differences from the bacterial nature of lung damage, presents aspects of the use of lung ultrasound during the pandemic of the coronavirus infection 2019. The lecture is based on the experience of domestic and foreign researchers, as well as on the authors' own experience, which demonstrates the value of this method both in intensive care units and in a therapeutic clinic.

Key words: lung ultrasound, ultrasonic artifacts, consolidation, lung damage, coronavirus infection.

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Ультразвуковое исследование легких: возможности диагностики повреждения легких, ассоциированного с новой коронавирусной инфекцией COVID-19

Г.В.Неклюдова [1, 2, ✉], *С.Н.Авдеев* [1, 2]

[1] Федеральное государственное бюджетное учреждение «Научно-исследовательский институт пульмонологии» Федерального медико-биологического агентства: 115682, Россия, Москва, Ореховый бульвар, 28

[2] Федеральное государственное автономное образовательное учреждение высшего образования «Первый Московский государственный медицинский университет имени И.М.Сеченова» Министерства здравоохранения Российской Федерации (Сеченовский Университет): 119991, Россия, Москва, ул. Трубецкая, 8, стр. 2

Резюме

Данная публикация посвящена ультразвуковому методу исследования легких, который приобрел особую актуальность в период пандемии новой коронавирусной инфекции COVID-19. Рассмотрены общие положения ультразвукового исследования легких, ультразвуковые признаки поражения легких, особенности ультразвуковой семиотики при вирусном поражении легких в отличие от бактериального поражения легочной ткани, представлены аспекты применения ультразвукового исследования легких при пандемии коронавирусной инфекции COVID-19. Публикация основана на опыте отечественных и зарубежных исследователей, а также на собственном опыте авторов, продемонстрирована ценность данного метода как в условиях отделения интенсивной терапии, так и в терапевтической клинике.

Ключевые слова: ультразвуковое исследование легких, ультразвуковые артефакты, консолидация, поражение легких, коронавирусная инфекция.

Конфликт интересов. Авторы заявляют об отсутствии конфликта интересов.

Lung ultrasonography (U/S) has become popular mostly in intensive care units and emergency departments and gained acceptance as a useful bedside diagnostic tool for detecting some thoracic pathologies [1–3]. At present, doctors more and more often use lung U/S not only in emergencies, but also in therapeutic divisions as an adjunctive tool to diagnose pulmonary disorders, including pneumonias [4, 5]. *R.Copetti* made a good point by saying that it is high time to consider ultrasound the best stethoscope in our hands [6], and this modality should be as widely introduced in our clinical practice as the stethoscope, which is the symbol of the medical trade and doctors' skills. So far, considerable knowledge and experience has been accumulated suggesting its high diagnostic significance and safety, which is coupled with its convenience and ability to provide rapid information. Ultrasonography can be performed using fixed or portable ultrasound machines with various degrees of technical sophistication.

The following types of transducers can be used: standard convex, micro-convex, and sector transducers with a frequency range of $1 - 6$ MHz and linear transducers with a frequency range of $6 - 12$ MHz reserved for evaluation of superficial structures and the pleura [7, 8]. This examination can be carried out when the patient is sitting or lying if there is a possibility to turn him or her to the side opposite the side being examined.

Depending on the purpose of the examination and time limitations, ultrasound scanning can be done in each lung intercostal space, with 72 zones being examined, or the number of scanned sites can be reduced [9]. It has been shown that reducing the number of scanned zones to 14 does not significantly influence the examination results [10]. For intensive care units, some authors [11] proposed the Bedside Lung Ultrasound in Emergency (BLUE) protocol with only six areas of investigation (three on each side of the thorax). Such units quite often use a more comprehensive protocol with $8 - 12$ zones of examination [12, 13].

During the pandemic of the novel coronavirus infection 2019 (COVID-19), lung U/S stimulated particular interest and become a promising target for further development. Before discussing U/S signs of lung damage in patients with COVID-19, we will look at the overall potential of ultrasonography for examination of the lungs.

At the time of development and introduction of ultrasound diagnostic techniques, doctors avoided using them for a lung examination. Indeed, in normally aerated lung tissue the largest portion of an incident ultrasound signal is reflected from the air. The U/S wave reflection coefficient for air is 750 times higher than for a fluid medium [7]. Thus, unaffected lung tissue cannot be visualised (Figure 1). However, morphological abnormalities and thus changes in the physical properties of lung tissue result in the appearance of acoustic effects that can be detected by ultrasound.

Reduced aeration of lung tissue and its increased density greatly facilitate the transmission of an ultrasound signal to deeper layers of lung tissue, and in zones of consolidated tissue penetration of ultrasound waves is almost 50

times higher [7]. It is important to note that consolidation can be observed not only in various types of pneumonia, but also in other pathologies accompanied by an increase in lung density, such as atelectasis of various causes, pulmonary embolism, tumours, and lung contusion [12]. Consolidation appears as a hypoechoic zone with an ultrasound pattern similar to that of liver (the tissue-like sign). For this reason, this pattern is referred to as lung hepatisation, which actually means consolidation [14]. Nevertheless, ultrasonography fails to detect consolidations that do not extend to the pleura because, as mentioned above, the layer of normally aerated lung tissue reflects ultrasound waves.

Consolidations can be of different shape and size, which is important for differential diagnosis. For example, an inflammatory consolidation appears as an area of irregular shape, which is not true for pulmonary infarction, carcinoma, or metastases. The pleural line over a lung consolidation may be seen as a less well-defined, fragmented hypoechoic line. Inflammatory lesions are separated from normal aerated lung tissue by irregular, interrupted, a bit blurred borders with a staircase appearance [14, 15] (Figure 2).

The air bronchogram sign and its severity are important features of consolidation [14]. This sign is seen as the presence of acoustically dense hyperechoic structures appearing as small linear inclusions, small focal lens-shaped lesions or ramified structures (Figure 2). It is caused by the presence of air in the small bronchi [16, 17]. Areas of consolidation may show either relatively even or uneven distribution of these echo-positive structures. Another possible feature is the dynamic air bronchogram, i.e. hyperechoic structures moving with the respiratory cycle, the presence of which is explained by air movement during inspiration. The dynamic air bronchogram is defined as progression of the air bronchogram in inspiratory time toward the periphery (centrifugally). The presence of this sign in an area of consolidation is the most specific sign of pneumonia and rules out pulmonary atelectasis due to occlusion of a proximal bronchus [15, 18].
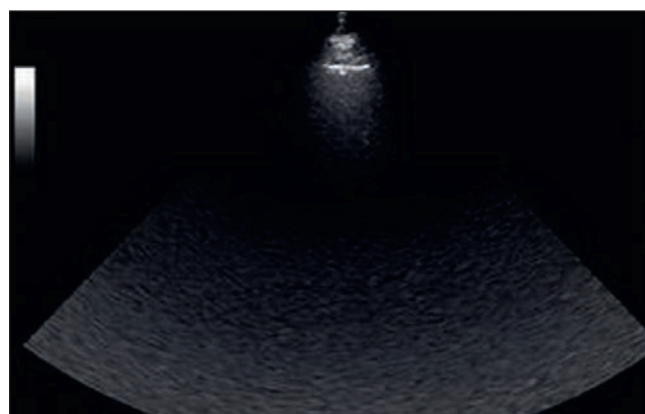

Figure 1. Ultrasound image of unchanged lung tissue (from the personal archive of G.V.Nekludova)

Рис. 1. Ультразвуковое изображение неизмененной ткани легкого (из личного архива Г.В.Неклюдовой)
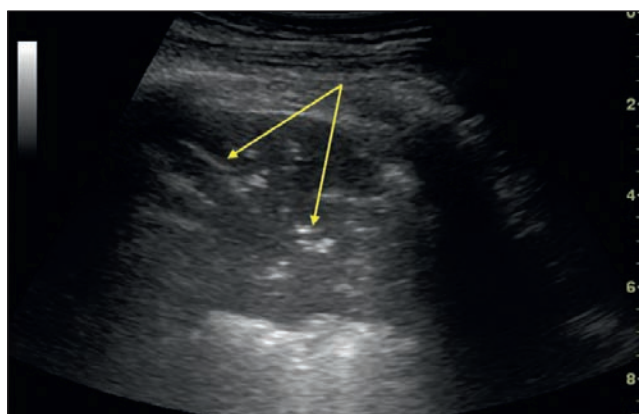

Figure 2. Ultrasound image of the lung consolidate (tissue-like sign), air bronchogram (arrows) (from the personal archive of G.V.Nekludova)

Рис. 2. Ультразвуковое изображение консолидата (*tissue-like sign*) воздушной бронхограммы (стрелки) (из личного архива Г.В.Неклюдовой)
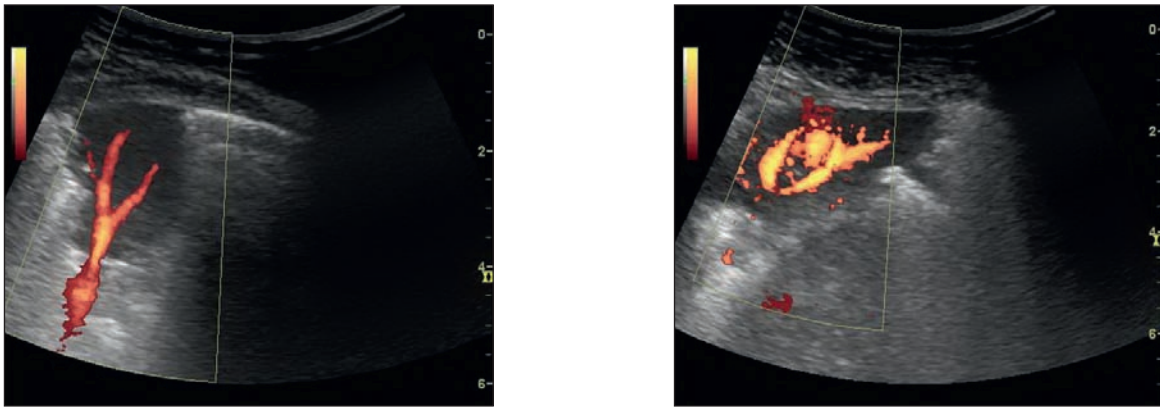
Figure 3. Ultrasound image of blood flow in the lung consolidate. Doppler blood flow analysis in the energy scanning mode shows increased vascularization, regular vascular pattern (from the personal archive of G.V.Nekludova)

Рис. 3. Ультразвуковое изображение кровотока в участке консолидации легочной ткани. Доплеровское исследование кровотока в режиме энергетического сканирования демонстрирует усиление васкуляризации, сосудистый рисунок регулярный (из личного архива Г.В.Неклюдовой)

Lung ultrasound may also show anechoic tubular fluid-containing structures, which represent fluid-clogged bronchioles, with surrounding consolidated lung. This phenomenon is referred to as the fluid bronchogram sign [2, 14]. The presence of this sign and its severity are also helpful diagnostically in identifying the causes of consolidation.

An important step in the evaluation of a consolidation area is an assessment of its vascularity, which could be increased or reduced with either a normal regular (Figure 3) or abnormal distorted vascular pattern [19, 20]. Analysis of these features is important in the differential diagnosis and the identification of the underlying causes of consolidation.

As the attenuation coefficient of ultrasound in fluids is minimal, ultrasonography is highly sensitive and highly specific for the detection of fluid in the pleural cavity and is superior in this regard to chest X-ray [21, 22]. Ultrasound can easily detect pleural effusion and, besides identifying the fluid itself, it can also provide detailed information about its location and nature, amount of fluid, and the condition of the pleural surfaces. It should be noted that lung U/S is more sensitive than chest X-ray for

detecting not only pleural effusion, but also pneumothorax [23, 24].

In addition to identifying certain really existing pulmonary structures, ultrasound scans may show additional ultrasonographic effects representing acoustic artefacts. There are two main patterns of artefacts. The first, called A-lines, is reverberation artefacts that are generated by multiple reflections of the ultrasound waves at the pleura and appear as repetitive, horizontal, hyperechoic lines deep to the pleural line displayed at regular intervals (Figure 4). This artefact is indicative of normal or excessive amount of air in the alveolar spaces [9].

The most important ultrasound artefact is the one called B-lines, which are signs of an increased lung density and its reduced aeration [3, 11, 25]. On ultrasound scans they are seen as hyperechoic lines that originate from the pleural line and traverse the entire ultrasound screen vertically to the opposite edge. These hyperechoic lines extend radially, appear as a laser beam, and move in synchrony with lung sliding (Figure 5). B-lines appear when ultrasound waves reach the interface between a thickened interlobular septa and air-filled alveoli, i.e. the interface between two media with very different acoustic impedance,
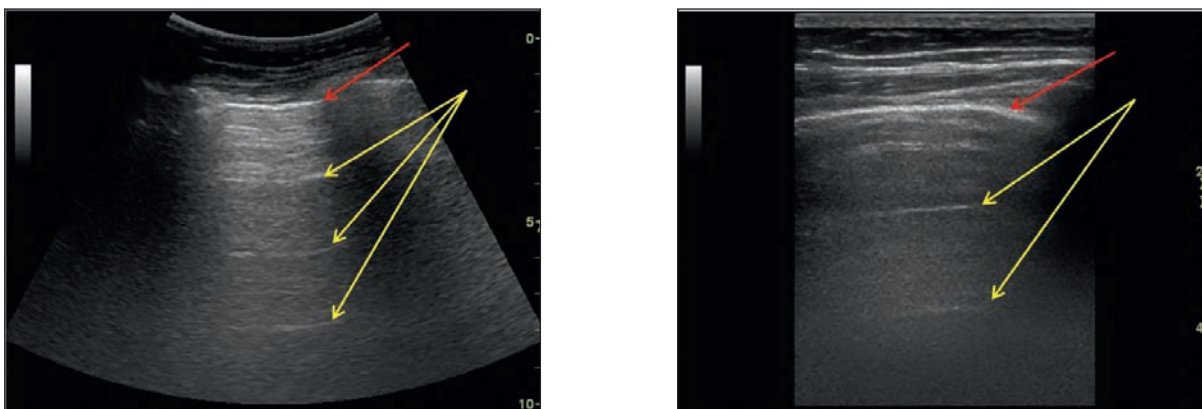

Figure 4. Unchanged lung tissue. Thin echo-positive pleural line (red arrow), A-lines (yellow arrows) (from the personal archive of G.V.Nekludova)

Рис. 4. Неизмененная легочная ткань. Тонкая эхо-позитивная плевральная линия (красная стрелка); А-линии (желтые стрелки) (слева — конвексный датчик, справа — линейный датчик) (из личного архива Г.В.Неклюдовой)
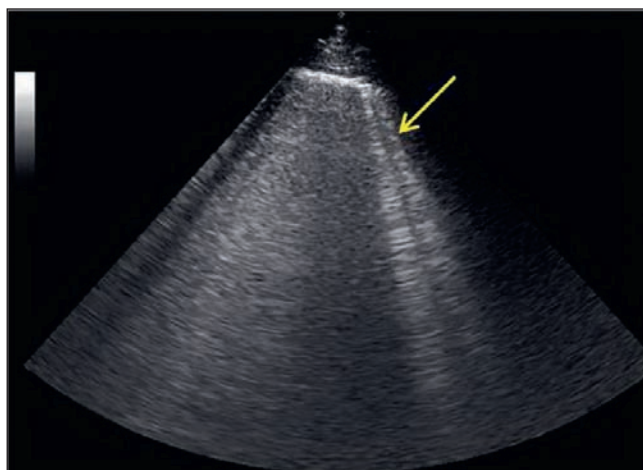
Figure 5. Ultrasound image of the B-line artifact (arrow) (from the personal archive of G.V.Nekludova)

Рис. 5. Ультразвуковое изображение артефакта B-линии (стрелка) (из личного архива Г.В.Неклюдовой)

which results in multiple vertical reverberations. This U/S phenomenon is not a specific sign, but it is characteristic of interstitial changes (interstitial syndrome). For instance, it can be observed in lung atelectasis, pneumonia, lung contusion, pulmonary embolism, diffuse parenchymal lung diseases, cardiogenic pulmonary oedema, and acute respiratory distress syndrome (ARDS) [3]. With progression of interstitial changes, B-lines become more numerous (Figure 6) and confluent (Figure 7), resulting in a single hyperechoic area in the most advanced cases. This phenomenon is referred to as white lung appearance (or the waterfall sign, which is seen when the transducer is placed longitudinally, perpendicular to the ribs) and represents alveolar-interstitial syndrome.

In different cases, depending on the etiology of interstitial syndrome and the severity of the pathogenic process, the pleural line can appear normal (not more than 2 mm thick) or thickened and be regular and smooth or irregular and interrupted [26] (Figures 6, 7).

It should be emphasised that since features and artefacts detected by U/S are not highly specific, they need to be thoroughly and comprehensively assessed together with clinical and laboratory data as well as findings detected by physical examination and additional investigations. This will definitely enlarge the diagnostic potential of sonography and improve the quality of diagnostic services in general.

As mentioned above, it was during the spread of coronavirus infection that this imaging diagnostic modality received enormous attention. What was the reason for such popularity of lung U/S during the pandemic of COVID-19?

Chest computed tomography (CT) is indisputably the tool of choice and the "gold standard" for the diagnosis of pulmonary damage. However, CT is not always available in intensive care units. Moreover, there are some limitations to using CT during a pandemic, including a large number of patients requiring diagnostic testing and treatment, the high infectivity of SARS-CoV-2, risks of transporting patients with hypoxemia and unstable haemodynamics, and difficulties associated with disinfection of CT scanners.

Some pilot studies have already demonstrated a correlation between the results of diagnostic CT and ultrasonography of the lungs in patients with suspected COVID-19-associated pneumonia [27, 28].

In turn, ultrasonography is more sensitive than conventional chest radiography for the detection of interstitial syndrome and subpleural consolidations. Ultrasonography is able to identify very small consolidations (< 0.5 cm) [29]. Moreover, in patients with COVID-19, pulmonary lesions strongly tend toward peripheral (subpleural) distribution, making ultrasonography an acceptable diagnostic tool for COVID-19-associated pneumonias. Also, ultrasound machines are affordable and relatively inexpensive devices, compared to other imaging equipment. Undoubtedly, ultrasound scanners are more mobile. Currently, specialists more and more often use pocket wireless ultrasound devices, which are a lot easier to be disinfected and protect-
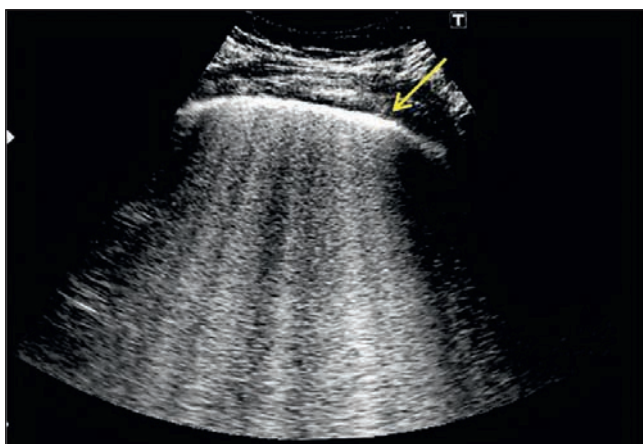

Figure 6. Severe interstitial syndrome, multiple B-lines, thickened pleural line (arrow) (from the personal archive of G.V.Nekludova)

Рис. 6. Выраженный интерстициальный синдром, множественные B-линии, утолщенная плевральная линия (стрелка) (из личного архива Г.В.Неклюдовой)
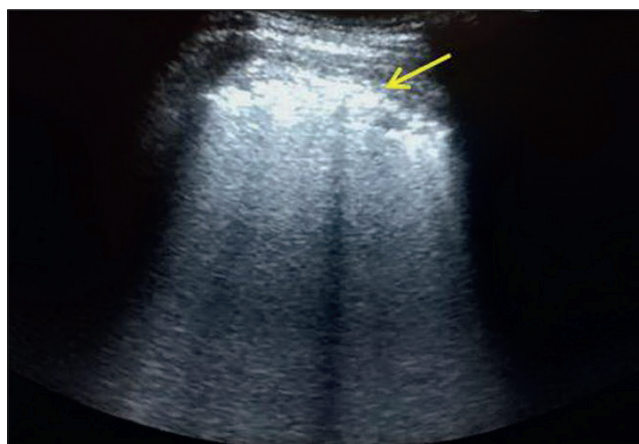

Figure 7. Confluent B-lines, "white lung", thickened, irregular, intermittent pleural line (arrow) (from the personal archive of G.V.Nekludova)

Рис. 7. Сливающиеся B-линии, формирование «белого легкого», утолщенная нерегулярная прерывистая плевральная линия (стрелка) (из личного архива Г.В.Неклюдовой)
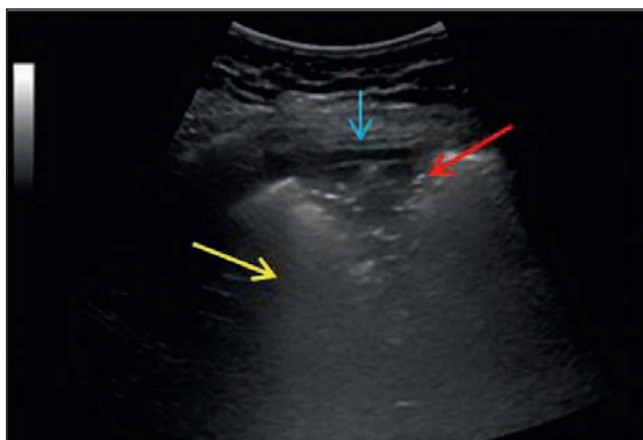
Figure 8. Consolidate with air bronchogram (red arrow) on the background of a pronounced interstitial syndrome, manifested by confluent B-lines (yellow arrow); a small amount of fluid (effusion) in the pleural cavity (blue arrow) (from the personal archive of G.V.Nekludova)

Рис. 8. Участок консолидации с наличием воздушной бронхограммы (красная стрелка) на фоне выраженного интерстициального синдрома, проявляющегося сливающимися B-линиями (желтая стрелка), незначительное количество жидкости (выпот) в плевральной полости (голубая стрелка) (из личного архива Г.В.Неклюдовой)

ed from contamination. An important advantage of ultrasonography is its ability to provide valuable information within a short period of time; besides, it can be used as a bedside method. Being radiation-free, ultrasound examinations can be repeated many times and used for follow-up assessment of the lesions detected.

However, as noted above, U/S signs of lung damage are not highly specific. This raises the question of whether this method can be helpful in the diagnosis of viral pneumonia. Are there any U/S signs specific to pneumonia of viral etiology?

Earlier studies conducted during the type A (H1N1) flu pandemic and outbreaks of avian influenza A (H7N9) analysed specific U/S signs of viral pneumonia and revealed some differences in this regard from bacterial pneumonias. A typical and obligatory feature of viral pneumonia is interstitial syndrome, which manifests by such U/S artefact as B-lines. Another additional sign of viral pneumonias is the presence of small subpleural consolidations [29, 30], while bacterial pneumonias mostly present with areas of consolidation usually seen as larger opacities with air bronchogram. Moreover, bacterial pneumonias are quite often associated with increased vascularity within consolidated lung. It is important to note another significant characteristic of viral lung damage that differentiates it from that in bacterial pneumonias, i.e. a multifocal, mosaic-like (a combination of interstitial syndrome and consolidations) distribution pattern of U/S signs, which are more extended and more often bilateral [31].

Are there any U/S signs specific to pulmonary abnormalities caused by coronavirus infection and not found in other types of viral pneumonia? From the accumulated experience, it is clear that U/S signs as well as CT signs of lung injury observed in patients with coronavirus infection are not specific. This means that ultrasonographic signs identified in patients with COVID-19-associated pneumonia can also be seen in people with other viral infections.

The most consistent and apparently essential finding is the presence of interstitial syndrome; and the greater extension of B-lines (their number and distribution along the pleural line) is correlated with more marked lung involvement as evidenced by morphology and CT [32]. This was proven by a meta-analysis of seven studies. This analysis showed that the pooled frequency of the abnormal B-pattern detected in patients with lung damage caused by COVID-19 was 97%, with a minimum range of frequency reported in different studies (90 to 100%).

The next most frequent sign is abnormalities of the pleural line (its thickening and/or irregularity). The pooled frequency of this sign was 70%, but its frequency reported in different studies ranged significantly from 10 to 100%.

Consolidation (Figure 8) was observed less consistently (its pooled frequency was 39%) and its frequency in different studies varied significantly from 20 to 75%, with minor subpleural consolidations usually with poor blood flow being more frequent (Figures 9 and 10) [28]. Of note, in patients with COVID-19 consolidates are almost always accompanied by signs of interstitial syndrome (multiple separate or confluent B-lines). When isolated consolidations or locally distributed B-lines associated with a consolidation lesion are observed, other underlying causes should be considered.

Pleural effusion is not typical (its pooled frequency was only 14%). This is especially true of a significant pleural effusion, which should prompt consideration of other causes of pleuritis. The same is absolutely true of pneumothorax [33].

These U/S signs, interpreted in combination with clinical data, are quite helpful in detecting lung injury caused by coronavirus and other viruses and differentiating it from bacterial pneumonia. Importantly, in terms of the severity, extent, and nature, U/S findings are correlated with those detected by high-resolution CT [33].

In clinical practice, loss of lung aeration is assessed by semiquantitative analysis of U/S signs. In the context of a pandemic lung examination needs to be performed as promptly as possible, thus it is feasible to modify an U/S protocol and limit the number of chest areas to be scanned to 12 or 14 [31, 34] and in intensive care units this protocol can be reduced even further. The following scoring system is used to assess the severity of lung aeration loss in each area: 0 — normal lung aeration (A-lines or not more than two B-lines), 1 — moderate loss of lung aeration (multiple separated B-lines), 2 — severe loss of lung aeration (coalescent B-lines or white lung appearance in the most severe cases and small subpleural consolidations in some cases), and 3 — consolidation (tissue-like pattern) [31]. Then the sum of all the areas is calculated to obtain the overall score for both lungs.

Some researchers use a modified lung ultrasound scoring system developed for interstitial pneumonia [33].

The severity of U/S-detected loss of lung aeration reflects the following histological changes: the first stage is marked by acute lung damage manifesting as exudative diffuse alveolar damage (DAD), alveolar oedema, formation of hyaline membranes, haemorrhage, and mixed cel-
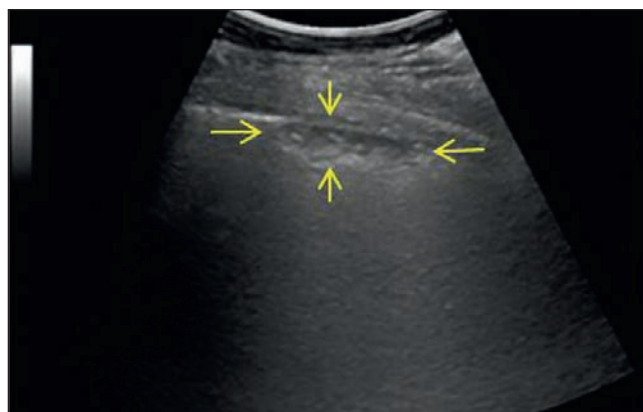
Figure 9. Subpleural consolidate (yellow arrows) on the background of a pronounced interstitial syndrome (confluent B-lines) (from the personal archive of G.V.Nekludova)

Рис. 9. Субплевральный консолидат (желтые стрелки) на фоне выраженного интерстициального синдрома (сливающиеся B-линии) (из личного архива Г.В.Неклюдовой)
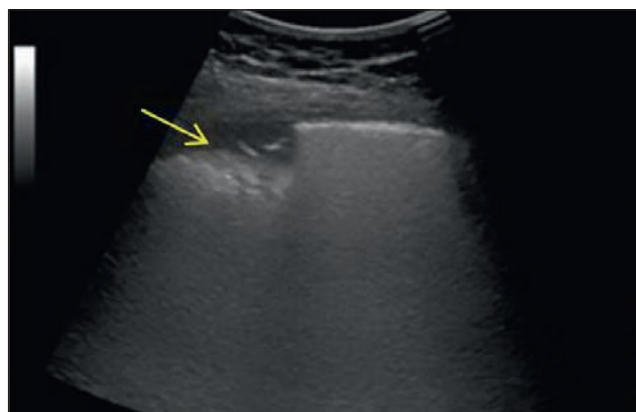

Figure 10. Subpleural consolidate (yellow arrow) on the background of alveolar-interstitial syndrome ("white lung") (from the personal archive of G.V.Nekludova)

Рис. 10. Субплевральный консолидат (желтая стрелка) на фоне альвеолярно-интерстициального синдрома («белое легкое») (из личного архива Г.В.Неклюдовой)

lular inflammatory infiltration; the following stage is characterised by early fibroproliferative changes combined with organisation of exudate, and deposition of loose extracellular matrix; and the next stage is dominated by fibroproliferation [35].

A semiquantitative ultrasound analysis of lung aeration loss not only allows for a one-time assessment of findings, but also offers the option of their follow-up. It can be used as a tool to assess the course and development of the disease, on the one hand, and the efficacy of various therapeutic interventions, on the other. *A.Pagano et al.* [36] used lung ultrasound imaging to assess the changes in lung aeration in patients with ARDS secondary to SARS-CoV-2 with non-invasive continuous positive airway pressure therapy (CPAP). They demonstrated that patients who did not reach an improvement in the oxygenation status with CPAP did not show any U/S signs of improved lung aeration. At the same time, patients whose oxygenation status improved with CPAP demonstrated lung recruitment of various degrees, which means that, besides an increase in lung aeration, in some cases there are probably other pathophysiological mechanisms resulting in the improvement in oxygenation. Thus, lung U/S provided a more comprehensive pathophysiological picture of alterations in patients with ARDS associated with SARS-CoV-2 infection, which helped optimise treatment protocols.

Initiating and maintaining the prone position (PP) is a widely used therapeutic strategy in patients with ARDS associated with COVID-19 [37−39]. PP allows for a more homogeneous overall lung ventilation and pulmonary blood flow, contributing to a reduction in ventilation/perfusion mismatch and improvement in oxygenation [40]. However, due to the individual dynamics of the disease not all patients respond equally positively to PP [38]. In patients with COVID-19 hypoxemic respiratory failure the intensity of positive response to PP is associated with the rate of intubation [41]. There is an increasing number of publications describing the potential of sonography to predict patients' response to PP. Based on the results of previous studies and our own experience, we believe that

it is important to perform not only an overall assessment but also local analysis of the reduction in lung aeration, evaluating it in different regions. The following parameters may be regarded as potential predictors of a positive response to PP: the intensity of lung aeration loss and the area of poorly aerated lung tissue in the posterior portions and the degree of involvement of the anterior portions, as evidenced by ultrasonography. *G.Prat et al.* [42] reported that a normal U/S pattern of both anterobasal lung regions in supine position may predict a positive response to PP in patients with ARDS.

Resolution of the disease and normalisation of lung aeration is accompanied by the appearance of A-lines.

Conclusion

Thus, lung abnormalities associated with COVID-19 do not have any specific ultrasound signs that would be helpful in differentiating them from lung damage in other viral infections. There is, however, a set and combination of U/S findings that can suggest viral etiology of lung injury and distinguish it from that caused by bacterial pathogens. Therefore, in the context of a pandemic the identification of the above described signs may help raise the rate of early diagnosis and facilitate timely therapeutic decisions.

To summarize, during the COVID-19 pandemic lung U/S provides useful information for triage of symptomatic patients (patients with/without pneumonia), assessment of the severity and extent of lung involvement with subsequent identification of critically ill patients and their transfer to an intensive care unit, and monitoring the dynamics of lung injury with treatment [43].

In conclusion, it is important to emphasise that lung U/S is not a replacement for CT of the lungs and should not be viewed as an alternative to the latter. It is a promising adjunctive modality, useful for detecting lung abnormalities, and, in some cases, may substitute for conventional chest radiography, especially when the latter cannot be performed or when multiple examinations are required.

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Author Information / Информация об авторах

Galina V. Nekludova — Doctor of Medicine, Leading Researcher, Federal Pulmonology Research Institute, Federal Medical and Biological Agency of Russia; Associate Professor, N.V.Sklifosovskiy Institute of Clinical Medicine, I.M.Sechenov First Moscow State Medical University, Healthcare Ministry of Russia (Sechenov University); tel.: (916) 296-01-64; e-mail: Nekludova_gala@mail.ru (SPIN: 8956-9125, Author ID: 394036, ORCID: *https://orcid.org/0000-0002-9509-0867*)

Неклюдова Галина Васильевна — д. м. н., ведущий научный сотрудник лаборатории функциональных и ультразвуковых методов исследования Федерального государственного бюджетного учреждения «Научно-исследовательский институт пульмонологии» Федерального медико-биологического агентства; доцент кафедры пульмонологии института клинической медицины имени Н.В.Склифосовского Федерального государственного автономного образовательного учреждения высшего образования «Первый Московский государственный медицинский университет имени И.М.Сеченова» Министерства здравоохранения Российской Федерации (Сеченовский Университет); тел.: (916) 296-01-64; e-mail: nekludova_gala@mail.ru (SPIN-код: 8956-9125, Author ID: 394036, ORCID: *https://orcid.org/0000-0002-9509- 0867*)

Sergey N. Avdeev — Doctor of Medicine, Professor, Corresponding Member of the Russian Academy of Sciences, Chief Pulmonologist of the Ministry of Health of the Russian Federation; Head of the Department of Pulmonology, N.V.Sklifosovskiy Institute of Clinical Medicine, I.M.Sechenov First Moscow State Medical University, Healthcare Ministry of Russia (Sechenov University); Head of Clinical Department, Federal Pulmonology Research Institute, Federal Medical and Biological Agency of Russia; tel.: (916) 614-58-25; e-mail: serg_avdeev@list.ru (SPIN: 1645-5524; Author ID: 194984; ORCID: *https://orcid.org/0000-0002-5999-2150*)

Авдеев Сергей Николаевич — д. м. н., профессор, член-корр. Российской академии наук, главный пульмонолог Министерства здравоохранения Российской Федерации; заведующий кафедрой пульмонологии института клинической медицины имени Н.В.Склифосовского Федерального государственного автономного образовательного учреждения высшего образования «Первый Московский государственный медицинский университет имени И.М.Сеченова» Министерства здравоохранения Российской Федерации (Сеченовский Университет); руководитель клинического отдела Федерального государственного бюджетного учреждения «Научно-исследовательский институт пульмонологии» Федерального медико-биологического агентства; тел.: (916) 614-58-25; e-mail: serg_avdeev@list.ru (SPIN-код: 1645-5524; Author ID: 194984; ORCID: *https://orcid.org/0000-0002-5999-2150*)