

# The emerging role of lung ultrasound in COVID-19 pneumonia

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## Abstract

In the last decades lung ultrasound (LUS) has become of crucial importance in the evaluation and monitoring of a widely range of pulmonary diseases. One of the major benefits which favours this examination, is that this is a non-invasive, low-cost and radiation-free imaging modality which allows repeated imaging. LUS plays an important role in a wide range of pathologies, including cardiogenic oedema, acute respiratory distress syndrome and fibrosis. Specific LUS findings have proved useful and predictive of acute respiratory distress syndrome which is of particular relevance in the suspicion and monitoring of patients with lung disease. Furthermore, several studies have confirmed the role of LUS in the screening of interstitial lung diseases in connective tissue diseases. Given these data, LUS will likely play an important role in the management of COVID-19 patients from identification of specific abnormalities corresponding to definite pneumonia phases and CT scans findings. In addition, LUS could allow reduction in the exposure of health-care workers to potential infection. Herein, we provide a summary on emerging role of lung ultrasound in COVID-19 pneumonia.

**Keywords:** Lung ultrasound, COVID-19 pneumonia, interstitial lung disease, ILD, CTD-ILD

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## Lung ultrasound role in the evaluation of the lung

There is an emerging evidence base and clinical experience using lung ultrasound (LUS) to evaluate a wide range of pulmonary conditions; whereas, historically, LUS was considered off-limits for lung imaging (1). LUS has recently shown its utility in the detection of a broad range of pathologies including modification of the structure of lung parenchyma from pulmonary oedema, pneumothorax, interstitial fibrosis, and pulmonary diseases characterized by a decrease in lung air content and by an alteration of tissue, air and fluid ratio (2). In these conditions, LUS may detect different artifacts depending on subpleural tissue alterations (3). In normal conditions, parietal and visceral pleura sliding may be detected together with the possible presence of A-lines that reflect the reverberations of the pleura (4). In the case of lung oedema or interstitial lung disease (ILD), both are characterized by the loss of peripheral lung aeration, and therefore the ultrasound beam is reflected creating reverberation artifacts called B lines (also known as “comet-tails”). According to expert recommendations from 2012, B-lines are defined as “discrete laser-like vertical hyperechoic reverberation artifacts arising from the pleural line, extending to the bottom of the screen without fading and moving synchronously with lung sliding” (5). Several studies and reviews have reported the presence of B-lines in cardiogenic pulmonary oedema, acute respiratory distress syndrome (ARDS), and ILD in connective tissue diseases (CTD) (1, 6-9). Although B-lines are a sonographic sign of an interstitial involvement, they may have different aspects and distribution, depending on the pathological subpleural process (cardiogenic edema, ARDS, fibrosis) (4). It is now well known that B-lines appear as diffuse either in cardiogenic edema and in ARDS. However, in ARDS they are frequently associated with an irregular, thickened pleural line, and to the possible presence of subpleural consolidation and areas of sparing (3). Therefore, LUS could help in the differential diagnosis between acute cardiogenic pulmonary oedema and ARDS; showing in ARDS the presence of an inhomogeneous alveolar-interstitial syndrome with spared areas, pleural line abnormalities and lung consolidations. ARDS is characterized by an impairment of the alveolar capillary membrane which leads to an alveolar involvement with ground glass (GG) opacities in the initial phase until the appearance of consolidation. These anatomical modifications may be reflected in the above described LUS findings that seem to be peculiar and strongly predictive of non-cardiogenic oedema also in the early phase (7). In addition, a recent study suggested the utility of LUS in the early investigation for pneumonia in patients with ARDS presenting to the emergency department. The authors reported the correlation of four LUS patterns to different degrees and severity of lung

aeration in ARDS (A-lines, separated B-lines, coalescent B-lines and consolidation) (10). Therefore, LUS may play a key strategic role in ARDS and it could be compared to CT in the evaluation of pneumonia and/or adult ARDS, with the advantage that, it can be frequently repeated at the bed side at low-cost and it is a radiation-free examination (11). In CTD-ILD, LUS is highly sensitive in detecting signs that may have a negative predictive value (12). For this reason, LUS has been considered to have a potential role in ILD either for screening and follow up. However, in CTD many efforts are still to be made to validate LUS as an outcome measure for ILD, in particular in SSc, to both standardize the scanning technique, and to elucidate how to interpret pathological signs other than B-lines as pleura abnormalities (12, 13). B-lines may also be created by a consolidative pneumonia. In this case, apart from the detection of the loss of the pleural line, LUS may show a tissue like pattern which corresponds to the hepatization phase of the disease and the presence of air-bronchograms (3). Clearly, CT scans often represent the “gold standard” in the diagnosis of pneumonia; however, LUS has been demonstrated to have a greater accuracy in the diagnosis of pneumonia compared to plain radiography (14, 15). The loss of lung sliding is detectable in pneumothorax and it is considered specific to this condition if associated with other sonographic signs as the lung-point sign, absence of B lines, and lung pulse (5, 16). In addition, quantification of the amount of pleural fluid within minute quantities by LUS has been described (16, 17). A recent meta-analysis has reported a higher sensitivity and sensibility of LUS compared to radiography in the detection of pleural effusion (18). All together these data confirm the wide use of LUS in a broad range of pulmonary diseases and that this imaging technique has greater or equal diagnostic sensitivity than more traditional techniques as plain radiography. In addition, LUS is a relatively cheap and radiation-free examination which allows regular patient monitoring with the possibility to repeat the examination during follow-up (19). LUS is widely used in intensive care patients with severe (acute) lung diseases (20). Recent data have highlighted the possible use of LUS in the prediction of weaning outcomes in patients undergoing mechanical ventilation (21) using a LUS score. In addition, LUS appears to have a potential role also the early identification of patients which require ventilatory support after major surgery, in particular, through the detection of lung atelectasis (22). In our paper the potential role of LUS in the diagnosis and management of COVID-19 pneumonia is discussed.

### The role of CT in COVID-19 pneumonia

CT scans are widely considered as the current “gold standard” to diagnose COVID-19 pneumonia. A number of studies have identified that CT can identify abnormalities in the early phases, including the detection of subpleural, unilateral, and multifocal GG opacities, and with a slight predominance of lower right lobe. During the course of the disease, CT scans reveal a progression of lesions becoming bilateral, diffuse with a transition to consolidation (with or without pleural effusion). The decrease in GG opacities is associated with the predominance of a reticular pattern with bronchiectasis and irregular interlobular or septal thickening, signs of the development of lung fibrosis (23). These data suggest a crucial role for CT in diagnosis of patients with COVID-19 infection or of those with possible disease. However, the concordance between CT imaging and laboratory results remains unknown to date. In addition, a number of recent studies have reported potential limitations of CT imaging including (but not limited to) the sensitivity of early infection after symptom onset and specific CT features which appear to be related to infection over time (24). Therefore, the role of CT imaging in COVID-19 infection remains debated and needs more supportive evidence, in particular regarding its use in screening asymptomatic patients, also considering the radiation exposure (25).

### The role of LUS in COVID-19 pneumonia

Given these data, the role of LUS in the evaluation and monitoring of patients with the novel COVID-19 pneumonia is emerging. The first cases of pneumonia caused by the novel coronavirus (SARS-Co V-2) breakout in Wuhan, Hubei (China) in December 2019 (26). It rapidly spread all over China and the world and at the end of January 2020, the World Health Organization (WHO) defined the new coronavirus a “Public Health Emergency of International Concern (PHEIC)”. The COVID-19 was declared a pandemic on 11 March 2020 affecting all areas of the world, except the Antarctic continent and with particular incidence in Italy where it still represents a serious challenge to public healthcare structures.

The pathology of COVID-19 pneumonia demonstrated an alveolar damage with edema, proteinaceous exudates, vascular congestion and initial reparative process in two patients subjected to lung lobectomies for cancer and with COVID-19 infection. To note that both patients were asymptomatic for the infection, therefore the above-mentioned changes probably represent the early pulmonary pathology findings (27).

In this context, LUS can acquire relevance in COVID-19 pandemic, also considering the capacity to detect lung lesions before the development of hypoxemia in experimental ARDS models (28). In addition, LUS allows to perform the clinical examination and to acquire lung images by the same clinician with the possibility to cover the probe and decreasing the risk of exposure of health-care workers (29). In this context, recommendations for US transducer and equipment cleaning and disinfection in COVID-19 disease, have recently been published by the UK Intensive Care Society (30). Moreover, the possibility to have a radiation-free imaging technique may play an important role in the evaluation of peculiar categories of patients as in pregnant women. In this context, Moro F et al recently proposed a systematic approach for obstetricians/gynaecologists to perform LUS in pregnant women (31). Recently a case report of a 32-year-old woman, with 35+3-week singleton pregnancy, with COVID-19 infection has been described. Although she initially was afebrile and with a negative reverse transcription polymerase chain reaction (RT-PCR) result, the LUS already showed sign of lung involvement with thick B-lines bilaterally in particular in the basal posterior areas. Patient initially refused hospitalization and went to home against medical advice. Two-days later she still was afebrile, but she complained worsened dyspnoea, LUS was repeated with the detection of imaging findings consistent with interstitial involvement: diffuse thick B-lines and the following CT scan showed signs of COVID-19 pneumonia (32). This case confirmed the vital role of LUS in certain categories of COVID-19 patients in which avoiding radiation exposure from plain radiography is crucial. This case also identified the critical role of imaging investigations in the management of COVID-19 infection as RT-PCR testing can be negative in the early phase, despite the patient having significant lung involvement.

A recent manuscript reported the experience on the use of LUS in 20 patients with COVID-19. The authors reported that, LUS features correlated with CT findings, in particular, the presence of B-lines (multifocal, discrete or confluent) corresponded to CT GG areas and where B-lines had become confluent, CT mirrored pulmonary infiltrating shadows. Pleural effusion was rare, whereas, LUS may detect consolidations when they extend to the pleural surface. In addition, the authors reported focal B-lines in the early stage of the disease, whereas irregular B-lines and thickening of the pleural line were seen in patients with fibrosis and alveolar interstitial syndrome in more severe and progressive stages (33). In COVID-19 pneumo-

**Table 1.** LUS findings in COVID-19 pneumonia patients.

| Study               | Evaluated patients (n)   | Evaluated thorax areas  | Main LUS findings  | Comparison with CT scans or radiography | Suggested potential use   |
|---------------------|--|-------------------------|--|---|---|
| Peng QY, et al.     | 20 patients  | 12 areas                | <ul style="list-style-type: none"> <li>- Abnormal and thickened pleural line</li> <li>- B-lines</li> <li>- Consolidations</li> <li>- Pleural effusion (rare)</li> </ul>  | LUS findings compared to CT scans       | <ul style="list-style-type: none"> <li>- Rapid assessment of COVID-19 pneumonia</li> <li>- Follow-up of lung evolution</li> <li>- Monitoring the response to prone position</li> <li>- Making decisions to weaning form ventilatory support.</li> </ul>   |
| Buonsenso D, et al. | Case report of 1 man with COVID-19 compared to a woman matched for age with fever but COVID-19 negative                | 12 lung areas           | <ul style="list-style-type: none"> <li>- Irregular pleura</li> <li>- Small subpleural consolidations</li> <li>- Irregular vertical artifacts (B-lines)</li> <li>- Lung affected areas with pulmonary spared areas</li> </ul> | Patient was subjected to chest X-ray    | <ul style="list-style-type: none"> <li>- LUS allows to reduce the number of clinicians and health-workers exposed to the patient positive</li> <li>- Screening of patients with clinical signs of infection</li> <li>- Possibility to repeat the examination every 12 or 24 hours</li> <li>- Possibility to perform LUS in the early phase of the disease, probably also before the appearance of the more typical CT findings</li> </ul> |
| Vetruigno L, et al. |  | 6 regions for each lung | <ul style="list-style-type: none"> <li>- B-lines</li> <li>- B-lines with the appearance of "white lung"</li> <li>- Consolidations</li> </ul>   | Not specified                           | <ul style="list-style-type: none"> <li>- Quick examination (5 minutes by an experienced sonographer)</li> <li>- Identification of patients with more severe lung disease</li> <li>- Lung evaluation reducing X-ray and CT scans use</li> </ul>  |
| Kalafat E, et al.   | Case report of a 32-year-old woman, with 35 +3-week singleton pregnancy, with persistent cough and shortness of breath |                         | <ul style="list-style-type: none"> <li>- Thick and bilateral B-lines in the basal posterior lungs area (during the first assessment)</li> <li>- Diffuse B-lines (two days later)</li> </ul>                                  |   |   |

nia, as in all lung diseases, the main limitation of LUS is the detection of pulmonary alterations deep within the lung parenchyma which do not extend to the pleural surface. LUS remains crucial in the detection of all conditions which are characterised by pleural or subpleural tissue alterations and it may be of major utility in the management of COVID-19 patients (33). Recently, a case of a young man with COVID-19 pneumonia who was evaluated by LUS in 12 thorax areas has been reported. Pleural line abnormalities, B-lines, subpleural consolidations, areas of "white lung" and spared areas showing signs of interstitial-alveolar involvement, have been described (34). These data highlight a potential crucial role for LUS in the identification of lung involvement in COVID-19 as this examination allows a rapid assessment and, being radiation-free, it can be repeated regularly (i.e.

within 12-24 hours) (33, 34). In a recent review, typical sonographic findings have been identified in different COVID-19 pneumonia phases. In the pre-disease or in the moderate phase, B-lines are clearly visible, may be adjacent to normal areas with or without small consolidations. In the severe phase, the number of B-lines increases and involves other areas of lung with the involvement of upper and anterior areas and they may become coalescent, and also consolidations may increase in both number and size. The critical phase of COVID-19 pneumonia is characterized by extensive coalescent B-lines with a significant alveolar interstitial syndrome in the posterior-basal areas of lungs (35). LUS may also find a place in the assessment of severity and progression of lung involvement during the infection. In this context, the use of a LUS score in the evaluation of COVID-19 pa-

tients has been recently proposed (36). Patients were evaluated by LUS in three different areas: anterior, lateral and posterior and in each area both superior and inferior segments were analysed. The adopted scoring system assigned one point to the presence of B-lines that when confluent with the appearance of the "white lung" image achieved two points; the presence of consolidation was scored as 3 points. The increase of the score reflected the decrease in lung aeration and the progression of lung severity, suggesting LUS a good examination tool to monitor patient course reducing the use of CT scans and plain radiographs. These data suggest the crucial role of LUS in closely following the patient trajectory in COVID-19 pneumonia which correlates with a worsening of lung involvement (36). The possibility to follow-up patients by LUS could allow clinicians to choose

the more appropriate therapy according to lung severity and evolution of the disease. In this context, a LUS score could have the potential to grade the “severity” of COVID-19 pneumonia through scanning of 12 lung areas (six on each hemithorax) with a maximum score of 36. Previous studies have already demonstrated the potential utility of this score to guide strict follow-up of patients in the assessment of weaning from mechanical ventilation (normal pattern without significant B-lines=0 points; number of B-Lines  $\geq$  3 per rib space=1 point; presence of coalescent B-lines=2 points; consolidations=3 points) (37). It could be anticipated that in COVID-19 patients this score could allow the monitoring of the progression of lung involvement and/or the response to therapy as well as the need of ventilation technique, prone positioning, or changes in treatment in case of clinical worsening (35).

Therefore, these emerging data, together with the previous LUS findings in a broad range of pathologies with similar aspects of lung disease (ARDS, ILD and pneumonia), strongly support the potential rationale for LUS evaluation in the diagnosis and follow-up of COVID-19 lung involvement. COVID-19 clinical presentation can be widely heterogeneous and LUS could be useful in detecting pneumonia in patients with suspicious symptoms as fever and/or cough with a leading role in the *triage* of symptomatic subjects. LUS also has a large emerging role in prognostic stratification, which could allow the monitoring of response to therapeutic intervention such as change in treatments or to prone position (28, 33). LUS may be an invaluable tool to allow the identification of the earliest phases of interstitial damage. These include multiple B-lines, initially separated and after coalescent, in the posterior inferior lung areas. In a subsequent phase of pneumonia, B-lines extend to the anterior areas of the same lobes becoming coalescent posteriorly. This trend may explain the use of the prone position also in the earlier phases, remarking the possible strategic role of LUS in patients’ monitoring. Therefore, LUS may acquire a strategic role also in the earlier phase of the infection, when CT pathological findings are rarer, occurring at a later stage during the disease, including with the appearance of severe features as consolidations, “crazy-paving” pattern, and “revere halo” sign (24). In these earlier stages, patients may be subjected to LUS that can be repeated after 12 or 24 hours when required and/or integrated with a CT scan if LUS findings are not sufficient to answer the clinical query or patient’s symptoms (33). The current utility of LUS in COVID-19 pneumonia are summarized in Table 1, and as reported the 12-zone

LUS assessment is the more used scanning technique allowing a comparison between two examinations to better quantify and compare changes in time (35).

## Conclusion

LUS has showed a promised potential role in the diagnosis and in monitoring of progression and evolution of COVID-19 infection. Recent data have suggested that LUS may be important in the follow-up of COVID-19 pneumonia patients through the scoring of sonography findings which appear to correlate with CT scan alterations according to the different phases and severity of lung involvement. Emerging data from the assessment of COVID-19 pneumonia by LUS could help with the management of other lung disorders as ILD in CTDs. In these diseases, LUS has already been investigated in the screening and detection of the modifications of the lung parenchyma due to ILD. In the future, the adoption of a LUS score system in CTD could also be crucial in routine clinical practice to detect the evolution of ILD from GG opacities to more severe abnormalities.

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