



Early View

Review

The use of lung ultrasound in COVID-19

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Please cite this article as: Ivana B, Chiara C, Nicola F, *et al.* The use of lung ultrasound in COVID-19. *ERJ Open Res* 2022; in press (<https://doi.org/10.1183/23120541.00196-2022>).

This manuscript has recently been accepted for publication in the *ERJ Open Research*. It is published here in its accepted form prior to copyediting and typesetting by our production team. After these production processes are complete and the authors have approved the resulting proofs, the article will move to the latest issue of the ERJOR online.

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1. INTRODUCTION

As of mid-September 2022, the novel coronavirus disease (COVID-19) pandemic has infected more than 600 million people and claimed the lives of more than 6.5 million individuals globally [<https://covid19.who.int/>]¹. The early diagnosis of COVID-19 would allow early management and isolation measures, highlighting the need for a rapid, point-of-care diagnosis in every resource setting.

Chest imaging is recommended in symptomatic patients with suspected COVID-19 as a component of the diagnostic workup that otherwise includes clinical and laboratory evaluation. At the beginning of pandemic, in response to member state requests, WHO convened a large international expert group to assist in the development of guidelines on the use of chest imaging in COVID-19 [1]. During the process of guideline development it was identified that the use of chest radiography and chest computed tomography (CT) in COVID-19 management was more established in terms of role, protocols and findings than the use of lung ultrasound (LUS). Therefore, after the publication of the guidelines WHO convened a group of relevant experts from all regions, with due regard to geographic balance and resource-setting representation, to provide an insight in the use of LUS during the COVID-19 pandemic.

In the past few decades, the use of LUS significantly increased, particularly in the evaluation of acute or critically ill patients with a variety of respiratory conditions. Recently LUS has been advocated as a relatively simple procedure that can contribute to the early identification of patients with clinical conditions suggestive for COVID-19, support the decision about hospital admission and inform the therapeutic strategy. This role has been shown in various clinical settings, including primary care facilities, outpatient clinics, emergency departments (ED), hospital wards and intensive care units (ICU) [2, 3]. The possibility of using portable devices to perform LUS in outpatient settings (assisted living facilities, retirement residences, home care) might help health authorities in appropriate resource allocation.

LUS is being used in COVID-19 along with other imaging modalities. Chest computed tomography (CT) has shown a high sensitivity and specificity in detecting COVID-19 [1, 4-7], but its use for diagnostic purposes requires consideration of the ionizing radiation exposure and of the increased risk of virus dissemination due to the patient transfer to the imaging department. Compared with chest CT, chest radiography shows lower sensitivity and similar specificity, is less-resource intensive and can be performed at the point of care if mobile equipment is available. However, it also implies ionizing radiation exposure of patients and staff, albeit with lower doses than chest CT.

This review paper addresses the role of LUS in patients with COVID-19 for diagnosis and disease management, including typical LUS findings for COVID-19, use of LUS in different regions and countries, equipment, capacity building and training needs, as well as advantages and limitations of the use of LUS in COVID-19.

¹ This information is being daily updated at the COVID-19 Dashboard, (WHO website <https://covid19.who.int/>)

2. CLINICAL USE OF LUS IN COVID-19

2.1. Typical LUS findings in COVID-19

COVID-19 pneumonia is characterized by an acute, often bilateral alveolar damage with predominantly peripheral distribution [4, 8]. When using LUS, interstitial pattern, pleural abnormalities, and consolidations are the most frequent findings in COVID-19 pneumonia, with a typically bilateral and patchy distribution and sharply defined spared areas [9-11]. Since pulmonary changes often show subpleural localization and LUS detects abnormalities located near the pleural line, this modality seems particularly suitable for the diagnostic evaluation of COVID-19. Typical LUS findings in patients with COVID-19 pneumonia are shown in Figure 1. Additional examples including LUS video clips showing typical findings have been published [12].

Interstitial involvement

Ultrasound manifestation of interstitial syndrome consists of vertical hyperechoic artifacts called “B-lines”, which originate from the pleural line and usually reach the edge of the screen, moving synchronously with respiration [13]. B-lines are not specific for COVID-19 and may be observed in numerous different pulmonary conditions characterized by reduced aerated/not-aerated space ratio and interstitial involvement due to edema or increased collagen/fibrotic deposition. The distribution of B-lines along with clinical presentation may help discriminate COVID-19 pneumonia from other conditions: bilateral, usually asymmetrical B-lines without a cranial-caudal distribution gradient are the most frequent findings in COVID-19 [10]. In a recent paper of 287 COVID-19 patients admitted to the ED, 92% presented with irregular pleura and interstitial LUS pattern, which was bilateral in 86% of patients [11].

Mild interstitial involvement consists of few scattered B-lines, whereas worse clinical presentation corresponds to more frequent and converging B-lines. In severe interstitial syndrome B-lines are no longer discernible from each other and the converging hyperechoic artifacts result in the “white lung” pattern [14,15].

A particular artifact, called “light beam”, has been described in COVID-19 patients. It consists of a large shining band-form B-line, arising from a portion of normal pleural line in the context of normal A-lines pattern, frequently appearing and disappearing during respiration. This artifact could correspond to ground glass opacities seen on CT during early active disease [16].

Alterations of the pleural line

Pleural line alterations are frequently detected on LUS in COVID-19 [10, 11]. The pleural line often appears thickened, irregular, or fragmented in involved areas, as observed in acute respiratory distress syndrome (ARDS) and interstitial lung disease/pulmonary fibrosis. A reduction or total absence of the normal pleural sliding is observed in association with pleural alterations. Small, sub-centimetric subpleural consolidations can be present together with both B-lines and pleural line alterations.

Consolidations

Consolidative lesions appear when air content in lung tissue drops beneath 10% of normal lung aeration, disrupting the pleural line. In patients with COVID-19 pneumonia, consolidations are often multiple, develop more frequently in the lower posterior regions and may be present with or without air bronchograms [17, 18]. Lobar hepatization, usually found in bacterial pneumonia, is not a frequent finding.

2.2. Additional findings

Two advanced applications of LUS may potentially increase its diagnostic yield: contrast-enhanced ultrasound (CEUS) and elastography.

CEUS uses sulphur-hexafluoride microbubbles as contrast medium to detect perfusion changes at the capillary level. Peripheral areas of low perfusion and peripheral multiple areas of infarction may be detected using CEUS in patients with COVID-19 [19,20].

Ultrasound elastography provides a quantitative assessment of tissue elasticity by analyzing wave propagation in the tissues [21]. Decrease of lung surface wave speed related to interstitial lung edema has been shown using US elastography in an animal model [22].

More evidence must be collected to better define the role of these advanced applications in the clinical work-up of COVID-19 pneumonia.

2.3. Differential diagnosis and complications

Several diseases or complications may affect the management of patients with COVID-19. To properly take these situations into account, LUS findings need to be evaluated and interpreted together with laboratory results, prevalence of the disease during the pandemic phases and patient previous medical history (e.g., comorbidities such as cardiovascular disease, lung interstitial disease or fibrosis) [23].

Viral lung infections: Differential diagnosis with other viral lung infections is difficult since LUS findings are similar in different viral pneumonias i.e., small subpleural consolidations (<0.5 cm), areas of white lung, pleuropulmonary line abnormalities and solitary or confluent B lines [24, 25].

Bacterial pneumonia: The presence of an isolated large lobar consolidation with air bronchograms is consistent with bacterial pneumonia. During the 2009 H1N1 pandemic, LUS was able to distinguish between viral and bacterial pneumonia or coexistence of both diseases, with an agreement between observers of 0.82, which was higher than conventional radiology studies [26]. Numerous studies have evaluated the accuracy of LUS in the diagnosis of pneumonia. Two meta-analyses have shown LUS to achieve sensitivity and specificity >90% for the diagnosis of pneumonia [27, 28].

Pulmonary infarction and pulmonary embolism: Both venous and arterial thromboembolism are frequent in COVID-19 due to excessive inflammation, diffuse intravascular coagulation, hypoxia, and immobilization [29]. High rates of pulmonary embolism have been reported in patients with COVID-19, ranging between 1.6-36% in patients in a non-ICU ward [30, 31] and 14-25% in ICU patients [29, 30]. In patients with significant dyspnea or signs of respiratory failure, a normal LUS can suggest pulmonary embolism [32, 33]. Diagnosis of pulmonary embolism in patients with COVID-19 using LUS is challenging; triangular or rounded pleural-based lesions, generally characteristics of pulmonary embolism [34], are not easy to distinguish from multiple COVID-19 inflammatory abnormalities. CEUS might be helpful for distinguishing pulmonary infarcts from COVID-19 inflammatory lesions [35]. Given the severity of the condition and the potential for a specific therapy, CT pulmonary angiography should be always considered as the imaging exam of choice in patients with suspected pulmonary thromboembolism [36, 37].

Heart failure: Presence of diffuse and symmetrical B-lines with a gravity-related distribution is more consistent with cardiogenic pulmonary edema and is rare in COVID-19 pneumonia. LUS in conjunction with clinical evaluation showed a significantly higher accuracy than chest radiography and natriuretic peptides in differentiating acute decompensated heart failure from non-cardiac causes of acute dyspnea [38]. Moreover, when combined with a more extensive bedside ultrasound examination including the heart, deep veins of the limbs, and inferior vena cava, LUS might be helpful in identifying heart failure [39].

Pleural effusion: Pleural effusion is an uncommon finding in COVID-19 and usually derives from a concurrent condition [11, 18]. Ultrasound is a highly reliable method in the detection, quantification, and follow-up of pleural effusion [40] with the diagnostic accuracy substantially better than for chest radiography¹² [41]. LUS is also helpful for image guided procedures such as thoracentesis or pleural drainage.

Pneumothorax: Spontaneous pneumothorax is rare in non-critically ill COVID-19 patients [42]. It is more common in the early severe COVID-19 patients and was associated with a high mortality rate [43]. The mechanism is unknown, but presumable related to patient self-induced lung injury. The LUS features specific for pneumothorax are: a lack of lung sliding (i.e. the ultrasonographic visualization of the movement of the two layers of the pleura), the absence of B-lines, and the identification of a lung point (i.e. the junction between the margin of the pneumothorax and the normal visceral/parietal pleura coupling, which is 100% specific for pneumothorax and can be used to determine its size) [44]. The performance of LUS for detection of pneumothorax is excellent and superior to chest radiography [45]. LUS is also effective in the monitoring of pneumothorax, especially in critically ill patients, with reported sensitivity ranges from 78-90%, which is significantly higher than the 39-52% reported for chest radiography, while specificity is >98% [45-48].

Subcutaneous emphysema: Subcutaneous emphysema is rare in COVID-19 patients, but can be found in those with severe disease [49], pneumothorax or pneumomediastinum [50] usually as a consequence of invasive mechanical ventilation and barotrauma. During LUS exam, due to subcutaneous gas bubbles,

many reverberation artifacts are present preventing visualization of deeper structures such as the ribs and lung.

2.4. LUS as a triage modality

In addition to clinical and laboratory assessment, chest imaging has been recommended for patients with suspected or confirmed COVID-19 to inform decisions on hospital admission versus home discharge as well as on regular ward versus ICU admission [1].

In outpatients with suspected COVID-19 pneumonia, LUS findings correlate with disease severity and the need for hospital referral [51]. In the ED, LUS has achieved >90% sensitivity and 20-65% specificity for detecting of COVID-19 pneumonia [11, 52]. This suggests that a negative LUS in symptomatic patients is reliable, eliminating the need for more invasive, costly, and time-consuming tests. Additionally, early LUS on adult ED patients with symptoms of lower respiratory tract infection has shown good discrimination between those who can be safely managed as outpatients and those requiring ward admission [53]. Similarly, early ED LUS has shown good differentiation between survivors and patients with fatal outcome. Moreover, the extent and degree of lung aeration loss was related to clinical outcome [54].

A prospective investigation in 120 adult patients with COVID-19 found a higher prevalence of pleural thickening, subpleural consolidations and total LUS score with worsening disease and that LUS findings were predictive of clinical deterioration and associated with mortality [55]. In the ICU, patients with refractory hypoxemia showed a higher prevalence of areas with multiple, coalescent B-lines, lung consolidations and pleural effusions, as well as a significantly higher total LUS score [56]. LUS severity score in hospitalized patients predicted the development of respiratory failure [18]. These findings are consistent with a recent systematic review indicating that the presence 3 or more B-lines on LUS, their confluent presentation and pleural abnormalities were associated with the likelihood of unfavorable outcomes (ICU admission, need for mechanical ventilation or death) [57].

A study using LUS in pregnant women with COVID-19 as the first image modality to reveal lung involvement proved the value of LUS, which prevents ionizing radiation exposure of pregnant patients. This study found that quantification with LUS score correlates well with the patient's symptomatology and with the progression of the disease, anticipating the worsening or the improvement of clinical symptoms [58].

2.5. Diagnostic accuracy of LUS and comparison with other chest imaging modalities

The evidence on diagnostic performance of LUS in diagnosing COVID-19 pneumonia is limited. Several studies conducted in high prevalence settings found that point-of-care LUS is a highly sensitive test [11, 59-61]. An international multicenter study with more than 1400 patients concluded that the integration of LUS patterns of probability with clinical findings allows to rule in or rule out COVID-19 pneumonia at

bedside [23]. This is in line with previous reports of high sensitivity of LUS in diagnosing interstitial syndrome [14, 15]. However, the low specificity is an issue.

Few papers have compared LUS diagnostic performance with other imaging modalities in COVID-19. A systematic review done in April 2021 identified 37 studies that evaluated the diagnostic accuracy of chest CT, chest radiography and LUS in symptomatic patients with suspected COVID-19, which respectively showed a pooled sensitivity of 89%, 72 % and 78 %, and a pooled specificity of 81%, 71% and 76 % [1]. A multi-center prospective study described diagnostic accuracy of LUS comparable with chest CT (AUROC² sensitivity and specificity for LUS 0.81, 91.9% and 71.0% vs 0.89, 88.4% and 82.0% for CT), suggesting that LUS can rule-out clinically relevant COVID-19 pneumonia at ED and facilitate diagnosis of COVID-19 in high prevalence settings [59]. Similarly, LUS was a valuable tool for excluding pulmonary manifestations of COVID-19, especially in patients without a medical history of cardiopulmonary disease (sensitivity and NPV of 100%) [60]. However, CT showed better performance for COVID diagnosis at hospital admission compared to LUS (sensitivity and specificity for CT 90-95 % and 43-69 % vs 94-93 % and 7-31 % for LUS) [61]. Further studies should be conducted in different prevalence settings of COVID-19 to validate these results.

In the pediatric population, LUS might be the preferred imaging modality, especially if performed by experienced operators [62]. The use of chest radiography or chest CT for diagnosis of COVID-19 should be carefully weighed against the harmful effect of radiation exposure during childhood [1]. LUS findings in children are similar to those found in adults [63], being more frequent in moderate or severe cases [64]. In some children with normal chest radiography, LUS and chest CT can detect abnormal findings suggestive of COVID-19 [65, 66].

3. THE USE OF LUS IN COVID-19 IN DIFFERENT REGIONS/COUNTRIES

A recent online survey conducted by the International Society of Radiology showed that the current imaging practice of imaging in COVID-19 differs throughout the world: conventional chest X-ray and CT were the most applied imaging modalities, while LUS was used for bedside imaging and in the ICU, mostly by intensivists, usually using small mobile units for point-of-care ultrasound [67]. A survey conducted in Italy showed that LUS was already extensively used by anesthesiologists and intensivists at the time of the first wave of the COVID-19 pandemic and then, its adoption increased further [68].

A detailed analysis of global trends in the use of LUS in the management of COVID-19 was not available at the time of preparation of this manuscript. Therefore, a literature search was performed for inferring on the use of LUS in different regions, using PubMed and Google Scholar databases with the key words “COVID-19”, “lung ultrasound” and “imaging”. Case series and case reports were included and review papers were excluded. A total of 200 publications from May 2020 to November 2021 met the criteria for

² AUROC: area under receiver operating characteristic curve

the literature review. Detailed information is provided in Appendix A. Figure 2 summarizes the regional distribution³ of these publications and provides information about the individual countries of origin. Figure 3 summarizes the field of application of LUS in the different studies. While the number of published papers may not necessarily reflect the actual routine clinical practice, extrapolation of data from the literature review was considered a suitable approach for inferring trends in the use of LUS in different regions and countries.

Ultrasound is an affordable and widely available imaging modality which has no specific installation requirements. It operates on standard electrical supply and can also be battery operated. Machines are robust, mobile, and potentially portable and require relatively little maintenance. Point-of-care ultrasound (POCUS) can assist emergency and critical care in COVID-19 management [68] and allows for utilization in out-of-hospital settings [69]. A low level of awareness of the many advantages of ultrasound technology mentioned above, and a lack of qualified staff adequately trained to perform LUS may be major barriers to its utilization, in particular for LMICs. Awareness-raising, advocacy and training can help build capacity of local medical professionals to facilitate scaling-up of the use of LUS for COVID-19 management. Tele-medicine could facilitate the use of LUS by creating access to remote expertise for both clinical and teaching purposes. Artificial intelligence based diagnostic ultrasound systems could decrease variability obtaining standardized image acquisitions, improve accuracy of diagnosis, and facilitate future clinical application of LUS, most especially in resource limited settings.

4. EQUIPMENT, CAPACITY BUILDING AND TRAINING NEEDS

4.1. *Technology needs and issues related with US equipment*

LUS does not require dedicated ultrasound equipment or probes. Any commercially available, portable ultrasound device with standard B-Mode imaging is sufficient for transthoracic ultrasound [14, 70]. A pocket-size device may be as effective as standard equipment in the evaluation of interstitial lung diseases [71,72] and can significantly reduce the overall time required to perform a bedside examination [73,74]. Ultrasound units equipped with color Doppler, pulsed-wave Doppler and cardiac functionality are important for evaluation of the heart, lung vascularization and vessels [75]. High-end systems with CEUS, shear wave elastography and image fusion may potentially be useful for bedside monitoring of conditions such as pleural reactive inflammatory effusion or peripheral thrombus embolism in severe cases of COVID-19 infection [19, 76]. Advanced ultrasound modes, including tissue harmonic imaging, compound imaging, different pre- and post-processing techniques, filters, and interpolation algorithms influence the appearance of B-line artifacts and should be turned off or limited to a minimum to allow better visualization of artifacts [77,78]

³ Geographical distribution according to the 6 WHO regionals offices as follows: African Regional Office (AFRO), the Americas Regional Office (AMRO), Eastern Mediterranean Regional Office (EMRO), European Regional Office (EURO), South-East Asia Regional Office (SEARO) and Western Pacific Region (WPRO). Regional of the Americas, South-East Asia Region

Transducer selection significantly affects findings obtained at LUS examination and must take into consideration patient anatomy, size, age, and purpose of the examination [77]. Transducers in multi-frequencies and shapes, including low frequency convex and micro-convex probes, high resolution linear probes and sector (phased-array) cardiac probes are recommended [70, 77]. High-frequency and high-definition linear transducers, thanks to their high superficial definition and low penetration capacity, are preferable for imaging superficial structures and abnormalities (pleural irregularities, pneumothorax, subpleural consolidations and very small amount of pleural effusion), mainly in the anterior fields, or the assessment of chest wall muscles (such as the diaphragm or intercostals). Low-frequency phased-array and convex transducers allow for visualization of the deeper structures, such as consolidations and pleural effusions, as well as for thick parietal wall areas, mainly in the lateral and posterior fields [77-79]. Micro-convex (small surface) probes provide extended view of the pleural surface and deeper penetration [14]. More B-lines are visualized using low-frequency compared to high-frequency probes [77, 78].

4.2. LUS training needs

The use of LUS in the context of the COVID-19 pandemic emphasizes the need for staff with adequate knowledge and skills to perform the procedure properly and safely. A survey conducted in Italy among anesthesiologists and intensivists after the first wave of the COVID-19 pandemic showed that, while residency programs were progressively implementing LUS training, 76.7% of the sample did not undertake any LUS certification [68].

There is no consensus regarding the amount of training or level of competence needed to perform LUS [80]. A systematic review found a limited number of high-quality studies about LUS training and recommended further research with validated theoretical and practical tests for assessment [81]. It was suggested that physicians without previous knowledge of ultrasound could independently and competently perform LUS after at least 10 supervised scans, reaching high levels of accuracy (>95% of correctly interpreted images) [82]. It was also shown that 25 LUS examinations supervised by experts would be enough for trainees without expertise in this procedure to acquire competence [83]. A short formal LUS training for clinicians is feasible and allows operators to achieve good proficiency and correct diagnosis of lung patterns [10, 84-90].

4.3. Standardization of LUS and scoring system

Given the relatively limited number of ultrasonographic patterns and the fast-learning curve, performing LUS may at first appear simple; however, examination needs to be performed in a systematic manner in order to produce as reliable information as possible [13, 91]. A well-known limitation of LUS is that it is highly operator dependent [92, 93]. The use of a clear definition and terminology of ultrasound abnormalities has been suggested to minimize possible errors in the detection of lung disease [13].

A standardized ultrasonographic approach is needed to ensure that most of physicians are able to recognize LUS signs and to limit inter-examiner variability [94]. Examination begins with selection of the probe and image settings, and then continues with partitioning of chest surface to cover all lung areas.

LUS findings are mainly constituted by artifacts produced by air, lung parenchyma, chest wall and pleura [13, 95]; thus, a correct setting of the device is essential: a single-focal point modality should be used, the focus should be set at the level of the pleural line and depth should be set at 6-7 cm from the pleural line. The gain should be regulated to maintain the homogeneity of the echoic image on the whole screen, including the bottom edge. The use of cosmetic filters and specific modalities such as harmonic-imaging, contrast, and compounding should be avoided, and the highest frame rate should be achieved [96].

A standardized approach to lung ultrasound examination in patients with COVID-19 was recently suggested [97]. For patients able to maintain the sitting position, a sequence of 14 evaluations (three posterior, two lateral and two anterior for each hemithorax) was proposed. A more simplified, 12-zone acquisition protocol is generally used in patients not able to keep the sitting position (Figure 4). A longitudinal scan, with the visualization of the so-called “bat sign”, should be performed first, to allow for a correct identification of the pleura within the intercostal space. Since the length of visualized pleura is highly variable among different patients and in the same patient among different intercostal spaces, the reliability of a score based on extension of artifacts per scan may be limited [98]. Hence, a transversal scan allows for a significantly wider window and a more constant pleural length and should be preferred when LUS is performed with the specific aim of a quantitative lung aeration assessment.

Quantification of the loss of aeration has led to different LUS rating systems. The most frequently used system distinguishes four steps of progressive loss of aeration [99-102], each corresponding to an ultrasonographic pattern. In patients with ARDS, this regional lung ultrasound score has shown a good diagnostic accuracy when compared to chest computed tomography and is strongly correlated with tissue density assessed with quantitative computed tomography [103-104]. Each of the lung regions examined by lung ultrasound (generally using the 12-zone approach) is scored from 0 to 3 according to the degree of loss of aeration (Table 1). Dorsal lung segments of upper lobes, located behind the scapula, are the only regions that cannot be explored by lung ultrasound [105]. For each area, points are allocated according to the worst ultrasound pattern observed. A LUS score ranging between 0 and 36 is then calculated as the sum of each region, where a higher score indicates a decreased aeration. This score is a global picture of lung aeration and can be monitored over time and to assess the effects of the interventions. To allow serial comparisons and monitoring, the capture of representative images, possibly stored as video clips, and standardized reporting of the examination are also required (Figure 4).

To better quantify the extension of the disease, a percentage of presence of pathological signs can be assigned to each of the scans (0-30-50-70-100%). A diseased area is defined by the presence of any pathological finding (e.g., separated, and coalescent B-lines, light beams, consolidations); the percentages of diseased lung in each area are added, and the result is then divided by the total number

of scans to obtain a percentage of the whole examination. This approach enables a longitudinal assessment of lesion size and more precise calculation of the proportion of diseased lung [106].

5. INFECTION PREVENTION AND CONTROL MEASURES WHEN PERFORMING LUS

Performing LUS in patients with suspected or confirmed COVID-19 poses specific challenges in terms of infection prevention and control (IPC). The physical proximity to the patient is required during the entire procedure, which is not the case for chest radiography and CT. In LUS the distance between patient and sonographer may be as little as 30–50 cm and patients may be asked to inhale/exhale deeply and hold their breath. The LUS examination time in patients with COVID-19 is usually between 5 and 10 minutes depending on the individual patient as well as on the professional experience [107]. Therefore, effective implementation of IPC measures is critical in LUS procedure to prevent the spread of COVID-19 and ensure safety of both the patients and healthcare providers [108]. Training needs to build IPC competence, including personal protection and equipment disinfection procedures, as well as equipment and accessories management and maintenance.

Standard personal protective equipment and hand hygiene practices must be considered for all ultrasound practitioners and patients [108, 109]. Ultrasound practitioners must continue routine clinical practices for cleaning and disinfection of probes used on critical aseptic fields or contaminated through contact with blood, mucous membranes, or bodily fluids during use [108-110]. All exposed components of the ultrasound machine or probe must be disinfected with an approved low- or intermediate-level instrument-grade disinfectant. Moreover, the use of portable touch screen equipment and single-use gel packets are highly recommended [111]. Suitable IPC measures for the equipment, ultrasound practitioners and patients when performing LUS on patients with suspected or confirmed COVID-19 are summarized in Appendix B.

6. CONCLUDING REMARKS

The fields of application of LUS in the context of the COVID-19 pandemics are numerous, including identification of patients that might benefit from hospital admission and patients with more extensive pulmonary involvement who should be referred to ICU admission, and monitoring of the progression of COVID-19 pneumonia. Additionally, point-of-care ultrasound can serve to identify patients with progressive pulmonary involvement or other thoracic complications (e.g., heart failure, pleural effusion and pneumothorax) requiring transfer to a higher level of medical care and informing therapeutic management. Advanced applications of LUS, such as contrast-enhanced ultrasound and elastography,

can provide information regarding lung peripheral perfusion, areas of infarction and degree of interstitial lung edema.

Since many respiratory illnesses or complications may mimic COVID-19 pneumonia, LUS findings need to be evaluated and interpreted together with laboratory results and prevalence of the disease during the pandemic phases as well as with patient past medical history (e.g., comorbidities such as cardiovascular disease, lung interstitial disease or fibrosis).

LUS is a non-invasive, rapid, and reproducible procedure, involving simple sterilization, can be performed at the bedside, without moving unstable patients, usually by a physician who clinically monitors the patient, allowing interpretation of LUS imaging features along with other significant clinical and laboratory findings. The possibility of performing LUS in outpatient settings is relevant for appropriate resource allocation. LUS does not involve exposure to ionizing radiation and therefore can be used repeatedly on the same patient and is a suitable imaging modality for diagnosis and monitoring of COVID-19 in pediatric patients and pregnant women.

The main limitation to a wider implementation of LUS stands in the need for appropriate expertise and the lack of standardized training programs. Indeed, and especially in the current pandemic context, the issue of the physical proximity between the patient and the ultrasound operator needs to be carefully considered when deciding to implement a LUS service, as well as the need to implement specific infection prevention and control measures. Eventually, while it is widely known that LUS is at least non-inferior to conventional chest X-ray in terms of sensitivity and specificity, and reproducible for the diagnosis of respiratory failure, the interrater agreement for LUS is not as good as for lung CT scan, and the comparative sensitivity/specificity with CT is less than ideal.

In the context of COVID-19 pandemic, the use of LUS might be enhanced by organizing proper and standardized training in different LUS applications for healthcare providers, with particular focus on LMICs. Multi-organ symptoms after COVID-19 acute infection with wide range of different signs and symptoms, from cough and shortness of breath to fatigue, headache, palpitations, chest and joint pain, physical limitations, depression and insomnia, has been considered an escalating health concern, and a global effort is needed to properly address it. Given its characteristics of portability, affordability and relatively ease of access, LUS may be an ideal imaging tool for diagnostic assessment of lung involvement in those patients and also for monitoring of short- and long-term pulmonary changes. There is a potential for applying artificial intelligence in computer-assisted analysis of LUS images, most especially in resource-poor settings with inadequate human resource capacity. Further research exploring those issues might provide a promising avenue for the applicability of LUS in COVID-19 management.

Acknowledgments

The authors thank the following colleagues for their contribution to the preparation of this manuscript:

- Gharbi Hassen (Tunisia): review of the manuscript outline;

- Abramowicz Jacques (USA) and Savoia Paulo (Brazil): manuscript review on behalf of the World Federation of Ultrasound in Medicine and Biology (WFUMB);
- Ribolzi, Francesco (WHO): manuscript review;
- Bokobza Jérôme (France), Fassola Leandro (Argentina) and Fotouh El-daly Ahmad Mohamad Aboul (Egypt): technical input for drafting some of the sections; and
- Antonucci Edoardo (Italy): preparation of figures 4 and 5

Special thanks are expressed to Malumba Richard (Uganda) for his instrumental assistance with the literature review to inform section 3 and Appendix A.

Funding

This project has been partially funded by a voluntary contribution from the Government of Japan to the WHO.

Conflict of interest


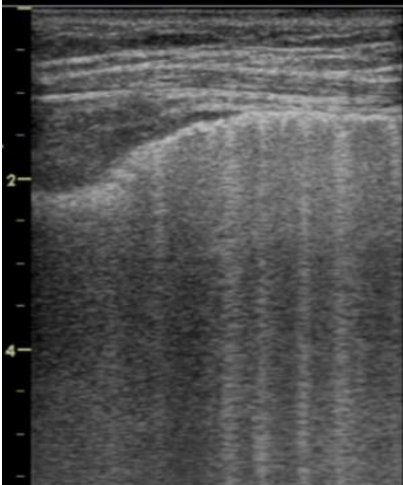
All authors declared their interests according to WHO standard procedures. None of the interests declared were found to be significant.

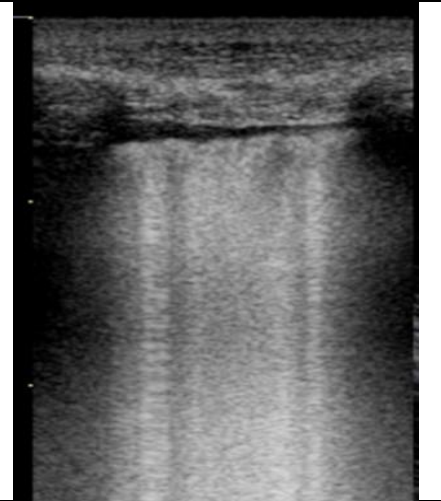

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TABLES

Table 1. Different lung ultrasonographic scores and representative ultrasonographic images (images courtesy of Dr Michele Umbrello).

Score	Aeration	Characteristics	Representative image
0	Normal	The pleural line is continuous and regular. Horizontal artifacts (A-lines), or two or fewer B-lines are present	
1	Moderate loss	The pleural line is indented. Below the indent, three or more well-spaced, non-confluent vertical artifacts (B-lines) are present	

2	Severe loss	<p>The pleural line is broken. Below the breaking point, small-to-large consolidated areas(subpleural consolidations) appear, with associated areas of multiple confluent vertical artifacts (coalescent B-lines)</p>	 This is a B-mode ultrasound image of the lung. A horizontal line representing the pleural line is visible at the top, but it is broken in the middle. Below this broken point, there are several vertical, comet-tail artifacts (B-lines) that are confluent, indicating lung consolidation.
3	Complete loss	<p>The scanned area shows dense and largely extended white lung with tissue-like pattern(consolidation)</p>	 This is a B-mode ultrasound image showing a large area of lung consolidation. The lung tissue appears as a dense, white, tissue-like pattern. There are some yellow markers on the image, including a '5' and a 'V'.

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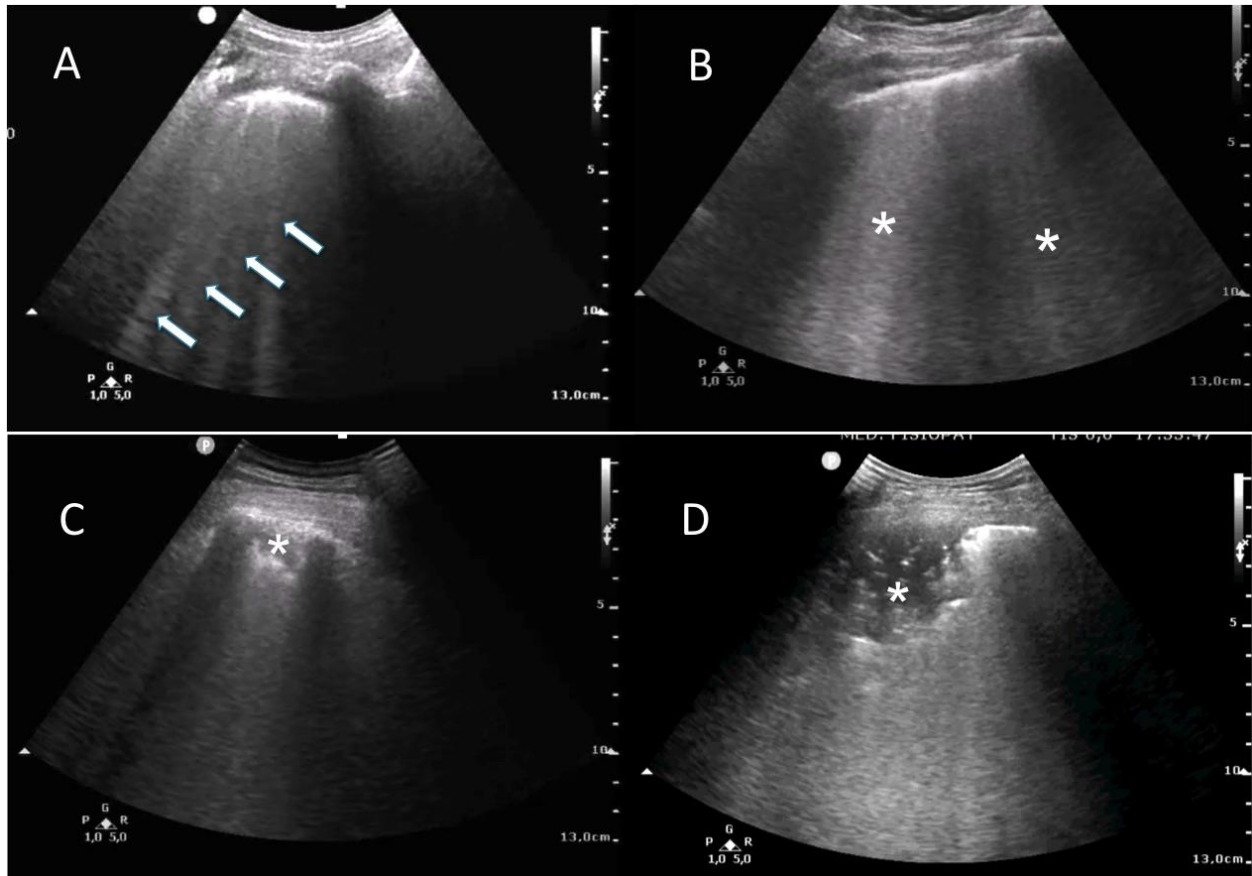
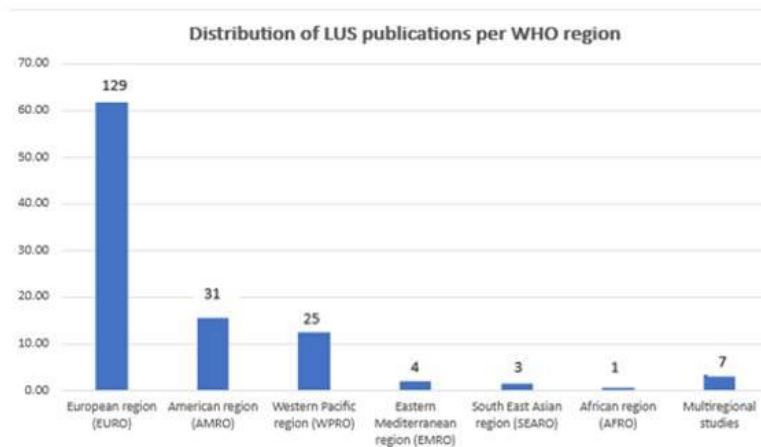


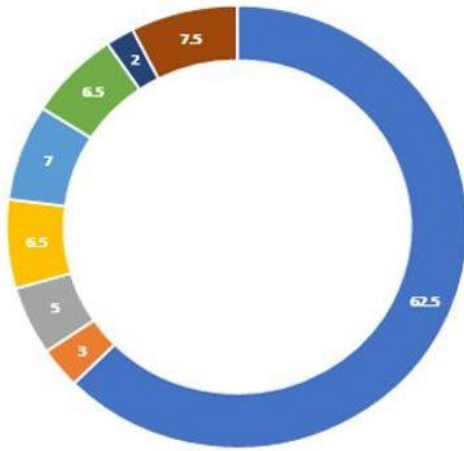
Figure 1. Typical LUS findings in patients with COVID-19 pneumonia: (a) interstitial involvement with separated B-lines (arrows) and irregular pleural line; (b) confluent B-lines (asterisks); (c, d) consolidations (asterisks); (d) air bronchograms (images courtesy of Dr Nicola Flor and Dr Chiara Cogliati).



COUNTRIES INVOLVED IN THE LITERATURE REVIEW	
Country	National articles (+ multinational articles)
Australia	4
Belgium	2 (+2)
Brazil	6
Canada	7 (+3)
China	19
Denmark	4
France	6 (+2)
Germany	11
Greece	1
India	3
Iran	1
Ireland	- (+1)
Israel	3
Italy	15 (+7)
Kuwait	1
Mexico	3 (+1)
Netherlands	- (+1)
Pakistan	1
Peru	1
Poland	2
Portugal	1
Russia	1
Saudi Arabia	1
Singapore	1
South Africa	1
South Korea	1
Spain	15 (+2)
Switzerland	2
Turkey	7
UK	13 (+5)
USA	14 (+5)

Geographical distribution of publications on use of LUS in COVID-19 based on the results of the literature review: the diagram shows the distribution of the publications according to the 6 WHO regional offices for a total of 200 publications on use of LUS in COVID-19, including 187 national articles and 13 multinational papers. Data presented as “EURO” comprise papers published by one single country as well as 6 articles jointly published by more than one European country. The literature review identified 7 inter-regional articles (i.e., papers jointly published by countries from different parts of the world) which were not included in any specific region and are therefore presented separately in this figure. The 31 countries involved in the literature review are listed on the right side together with the number of national articles submitted by each country. The numbers provided between brackets indicate, when appropriate, the number of multinational studies to which a given country has contributed. More detailed information about the reviewed publications is provided in Appendix A.

Clinical applications of LUS in the reviewed studies



Code	Clinical application of LUS	Percentage
	Routine diagnosis of COVID-19 in adults ^(a)	62.5 %
	Diagnosis of COVID-19 in pregnant women	6.5 %
	Diagnosis of COVID-19 in children	5 %
	Monitoring regression of COVID-19 pneumonia	3 %
	Monitoring critically ill patients	7 %
	Prognostication	6.5 %
	Patient triage	2 %
	Other applications (*)	7.5 %

(a) Including evaluation of the diagnostic accuracy of LUS in comparison with lung CT and chest X-ray (CXR)

(b) Other applications: screening, contrast-enhanced ultrasound, application of LUS in nursing homes, "self-ultrasound", guiding therapy, deciding on intubation, wireless ultrasound, assisting in patient resuscitation, application of LUS with artificial intelligence and with robotics.

Figure 3. Specific field of application of LUS in the different studies.

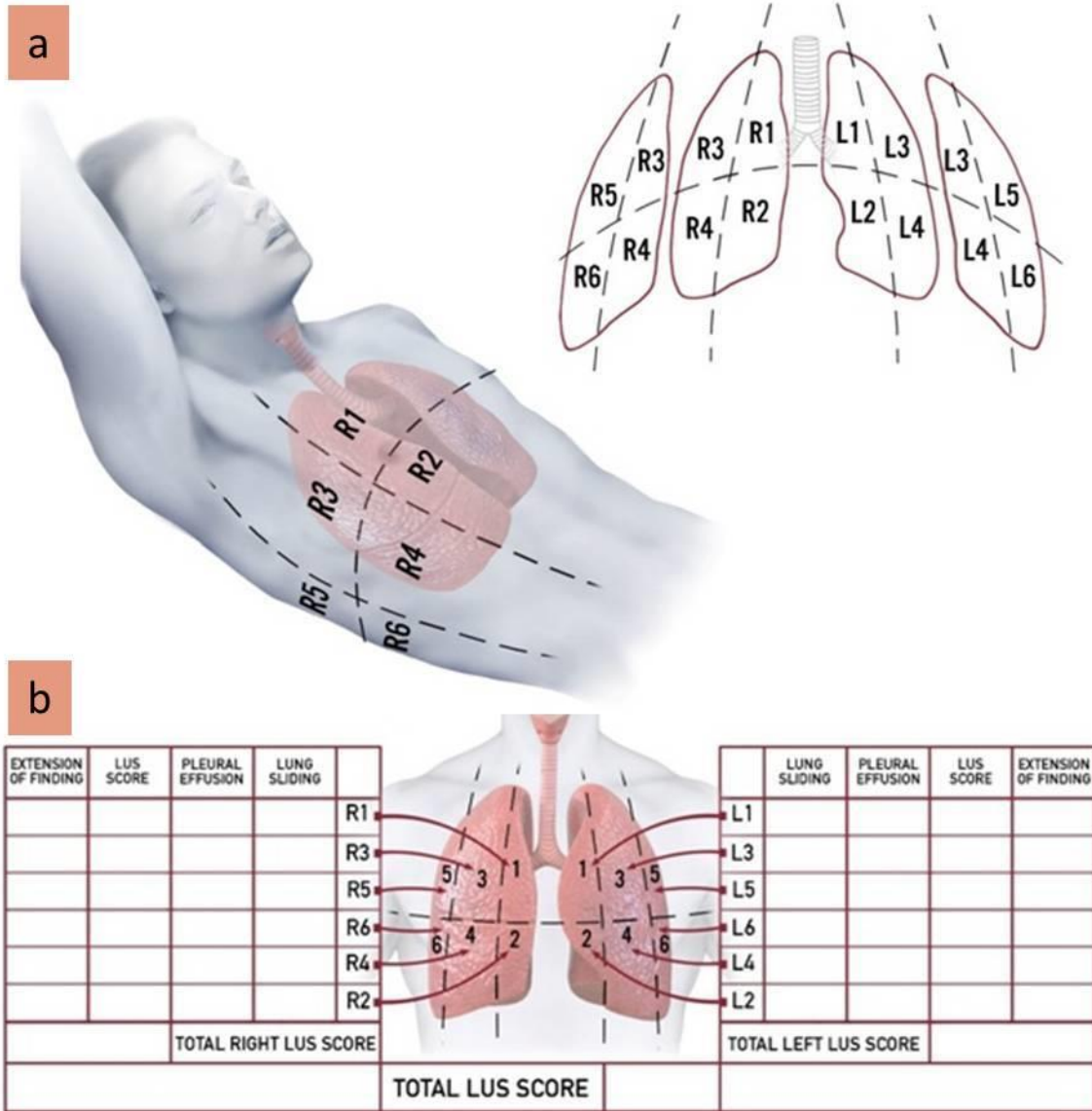


Figure 4. Standardized LUS examination: (a) anatomic landmarks, topographic regions and (b) example of LUS report form. Each hemithorax is divided into anterior, lateral, and posterior region, according to anatomic landmarks (anterior and posterior axillary lines and internipple line): R1 right anterior superior; R2 right anterior inferior; R3 right lateral superior; R4 right lateral inferior; R5 right posterior superior; R6 right posterior inferior; L1 left anterior superior; L2 left anterior inferior; L3 left lateral superior; L4 left lateral inferior; L5 left posterior superior; L6 left posterior inferior. The presence or absence of lung sliding and pleural effusion for each region should be noted. A LUS score ranging from 0 to 3 is assigned according to the degree of aeration loss and the presence of any other pathological sign (extension of findings) allowing calculation of LUS score for left and right lung and total score. LUS report form also may include information about examination quality, mechanical ventilation settings and arterial blood gas results (courtesy of Dr Michele Umbrello).

Appendix A: list of publications reviewed to inform the situation regarding the use of LUS in COVID-19 in different regions/countries

Taking into account that a deep analysis regarding use of LUS in the management of COVID-19 in different countries and regions was not available at the time of preparation of this manuscript, it was considered that extrapolation of data from a review of the studies published on this topic could be a suitable pragmatic approach for inferring on the use of LUS in different regions and countries. However, a limitation of this approach is that the number of published papers may not necessarily reflect the actual routine clinical practice in the use of LUS within that country/region.

Searches were performed using PubMed and Google Scholar databases using the key words “COVID-19”, “lung ultrasound” and “imaging”. Only English-language articles were included in this review. Review papers were not included, since these don’t use primary data, but case series and case reports were incorporated. Each publication was examined noting the field, the objectives, and the country where the study was performed.

A total of 200 publications from May 2020 to November 2021 met the criteria for the literature review (*see table below*). It can be noted that 65% of all the reported data came from Europe and more than 60% of all the papers reviewed were published by five countries: Italy, China, USA, Spain, and UK (including national and multinational studies).

Keeping in mind that more exhaustive searches in other languages and including non-traditional large databases would be needed to improve data collection of trends in use of LUS in low- and middle-income countries (LMICs), this literature review indicates a paucity of data on the use of LUS for COVID-19 management in LMICs.

First author	Title	Journal	Country	Clinical application
Abrams ER	Point-of-Care Ultrasound in the Evaluation of COVID-19. doi: 10.1016/j.jemermed.2020.06.032	J Emerg Med	USA	General application
Agricola E	Heart and Lung Multimodality Imaging in COVID-19. doi: 10.1016/j.jcmg.2020.05.017	JACC Cardiovasc Imaging	Italy	Heart and lung ultrasound
Alharthy A	Prospective Longitudinal Evaluation of Point-of-Care Lung Ultrasound in Critically Ill Patients with Severe COVID-19 Pneumonia. doi: 10.1002/jum.15417	J Ultrasound Med	Saudi Arabia	Follow up in critically ill COVID-19 patients

Allinovi M	Lung Ultrasound May Support Diagnosis and Monitoring of COVID-19 Pneumonia. doi: 10.1016/j.ultrasmedbio.2020.07.018	Ultrasound Med Biol	Italy	LUS for diagnosis and monitoring of COVID pneumonia
Antúñez-Montes OY	Feasibility of Lung Point-of-Care Ultrasound for Patients with COVID-19 in Air Medical Transport: Triage of 2 Initially Suspected Cases on Mexico's Front Line. DOI:10.1002/jum.15414	J Ultrasound Med	Mexico	Triage
Antúñez-Montes OY	Proposal to Unify the Colorimetric Triage System with the Standardized Lung Ultrasound Score for COVID-19. doi: 10.1002/jum.15446	J Ultrasound Med	Mexico	Triage
Antúñez-Montes OY	Routine use of Point-of-Care lung ultrasound during the COVID-19 pandemic. doi: 10.1016/j.medin.2020.04.010	Med Intensiva	Italy	General application
Matthies AK	Diagnostic accuracy of point-of-care lung ultrasound for COVID-19: A systematic review and meta-analysis https://doi.org/10.1101/2021.10.09.21264799	medRxiv	UK	Diagnostic accuracy
Aziz R	Essential notes: The use of Lung Ultrasound for COVID-19 in the intensive care unit doi: 10.1016/j.bjae.2020.09.001	BJA Educ	UK, USA	LUS in ICU
Baig MA	The Rapid COVID Screening (RCS) Tool. doi: 10.29271/jcpsp.2020.Supp1.S56	J Coll Physicians Surg Pak	Pakistan	LUS for screening COVID patients
Baker K	Lung Ultrasound in a COVID Pandemic - Choosing wisely. https://doi.org/10.1002/ajum.12213	Australas J Ultrasound Med.	Australia	General application
Bar S	The association of lung ultrasound images with COVID-19 infection in an emergency room cohort. doi: 10.1111/anae.15175	Anaesthesia	France	LUS in emergency room
Boccatonda A	Can Lung Ultrasound be Used to Screen for Pulmonary Embolism in Patients with SARS-CoV-2 Pneumonia? doi: 10.12890/2020_001748	Eur J Case Rep Intern Med	Italy	General application
Boero E	The role of lung ultrasonography in COVID-19 disease management. https://doi.org/10.1002/emp2.12194	J Am Coll Emerg Physicians Open	Italy, UK, Canada, USA	General application
Bonadia N	Lung Ultrasound Findings Are Associated with Mortality and Need for Intensive Care Admission in COVID-19 Patients Evaluated in the Emergency Department. doi: 10.1016/j.ultrasmedbio.2020.07.005	Ultrasound Med Biol	Italy	LUS findings associated with mortality and need for ICU

Bosso G	Lung ultrasound as diagnostic tool for SARS-CoV-2 infection https://doi.org/10.1007/s11739-020-02512-y	Intern Emerg Med	Italy	General application
Brahier T	Lung ultrasonography for risk stratification in patients with COVID-19: a prospective observational cohort study https://doi.org/10.1093/cid/ciaa1408	Clin Infect Dis	Switzerland	Risk assessment
Buda N	Consensus of the Study Group for Point-of-Care Lung Ultrasound in the intensive care management of COVID-19 patients. doi: 10.5114/ait.2020.96560	Anaesthesiol Intensive Ther	Poland	General application
Buda N	Lung ultrasound in the diagnosis of COVID-19 infection - A case series and review of the literature. doi: 10.1016/j.advms.2020.06.005.	Adv Med Sci	Poland	General Application
Buonsenso D	Clinical role of lung ultrasound for diagnosis and monitoring of COVID-19 pneumonia in pregnant women. doi: 10.1002/uog.22055	Ultrasound Obstet Gynecol	Italy	LUS in pregnancy
Buonsenso D	Effectiveness of rapid lung ultrasound training program for gynecologists and obstetricians managing pregnant women with suspected COVID-19. doi: 10.1002/uog.22066	Ultrasound Obstet Gynecol.	Italy	LUS in pregnancy
Buonsenso D	Point-of-Care Lung Ultrasound findings in novel coronavirus disease-19 pneumoniae: a case report and potential applications during COVID-19 outbreak. 2020 Mar;24(5):2776-2780. doi: 10.26355/eurrev_202003_20549	Eur Rev Med Pharmacol Sci.	Italy	General application
Calvo-Cebrián A	Usefulness of Lung Ultrasound Examinations Performed by Primary Care Physicians in Patients with Suspected COVID-19. doi: 10.1002/jum.15444	J Ultrasound Med	Spain	LUS used by primary healthcare physician
Caro-Dominguez P	Collaborators of the European Society of Paediatric Radiology Cardiothoracic Task Force. Thoracic imaging of coronavirus disease 2019 (COVID-19) in children: a series of 91 cases doi: 10.1007/s00247-020-04747-5	Pediatr Radiol	Spain, USA, UK	LUS in paediatrics
Carrer L	Automatic Pleural Line Extraction and COVID-19 Scoring from Lung Ultrasound Data. doi: 10.1109/TUFFC.2020.3005512	IEEE Trans Ultrason Ferroelectr Freq Control	Italy	LUS and Artificial Intelligence
Casper Falster	Lung ultrasound may be a valuable aid in decision making for	European Clinical	Denmark	General

	patients admitted with COVID-19 disease https://doi.org/10.1080/20018525.2021.1909521	Respiratory Journal		application
Castelao J	Findings and Prognostic Value of Lung Ultrasound in COVID-19 Pneumonia. https://doi.org/10.1002/jum.15508	J Ultrasound Med	Spain	LUS in prognosticating COVID patients
Cho YJ	Lung ultrasound for early diagnosis and severity assessment of pneumonia in patients with coronavirus disease 2019. doi: 10.3904/kjim.2020.180	Korean J Intern Med	South Korea	Early diagnosis and severity assessment
Cocconcelli E	Clinical Features and Chest Imaging as Predictors of Intensity of Care in Patients with COVID-19 doi: 10.3390/jcm9092990.	J Clin Med	Italy	LUS for risk stratification
McDermott C	Sonographic Diagnosis of COVID-19: A Review of Image Processing for Lung Ultrasound doi: 10.3389/fdata.2021.612561	Frontiers in Big Data journal	Canada	General application
Consoli L	2019 novel coronavirus (COVID-19) pneumonia complications: the importance of lung ultrasound. doi: 10.1007/s40477-020-00494-3	J Ultrasound	Italy	General application
Conway H	Personalizing Invasive Mechanical Ventilation Strategies in Coronavirus Disease 2019 (COVID-19)-Associated Lung Injury: The Utility of Lung Ultrasound. doi: 10.1053/j.jvca.2020.04.062	J Cardiothorac Vasc Anesth	UK	LUS in ICU
Dargent A	COVID-LUS study group. Lung ultrasound score to monitor COVID-19 pneumonia progression in patients with ARDS. doi: 10.1371/journal.pone.0236312	PLoS One	France	LUS scoring application
Davidovna KZ	A single-center comparative study of lung ultrasound versus CT during the COVID-19 era doi: 10.4081/mrm.2021.766	Multidisciplinary Respiratory Medicine	Russia	Comparison LUS and CT
de Oliveira RR	Lung ultrasound: an additional tool in COVID-19. doi: 10.1590/0100-3984.2020.0051	Radiol Bras	Brazil	General application
De Rose C	How to Perform Pediatric Lung Ultrasound Examinations in the Time of COVID-19. doi: 10.1002/jum.15306	J Ultrasound Med.	Italy	LUS in paediatrics
Delrio S	Lung ultrasound signs and cytokine profile in Covid-19 patients: a case series DOI: 10.26355/eurrev_202009_22799	Eur Rev Med Pharmacol Sci	Italy	General application
Denault AY	A proposed lung ultrasound and phenotypic algorithm for the care of COVID-19 patients with acute respiratory failure. doi: 10.1007/s12630-020-01704-6	Can J Anaesth	Canada	General application

Deng Q	Semiquantitative lung ultrasound scores in the evaluation and follow-up of critically ill patients with COVID-19: a single-center study. doi: 10.1016/j.acra.2020.07.002	Acad Radiol	China	LUS for score in evaluating critically ill patients
Denina M	Lung Ultrasound in Children With COVID-19.. doi: 10.1542/peds	Pediatrics	Italy	LUS in paediatrics
Di Serafino M	The lung ultrasound: facts or artifacts? In the era of COVID-19 outbreak. doi: 10.1007/s11547-020-01236-5	Radiol Med	Italy	Comparison LUS and CT
Dini FL	Bedside wireless lung ultrasound for the evaluation of COVID-19 lung injury in senior nursing home residents. doi: 10.4081/monaldi.2020.1446.	Monaldi Arch Chest Dis	Italy	Bedside wireless LUS in nursing homes
Duclos G	"No dose" lung ultrasound correlation with "low dose" CT scan for early diagnosis of SARS-CoV-2 pneumonia. doi: 10.1007/s00134-020-06058-7	Intensive Care Med	France	Comparison LUS and CT
Duggan NM	Using Lung Point-of-care Ultrasound in Suspected COVID-19: Case Series and Proposed Triage Algorithm. doi: 10.5811/cpcem.2020.7.47912	Clin Pract Cases Emerg Med	USA	LUS application at POC
Duggan NM	Best Practice Recommendations for Point-of-Care Lung Ultrasound in Patients with Suspected COVID-19. doi: 10.1016/j.jemermed.2020.06.033	J Emerg Med	USA	Proposed LUS protocol
Espersen C	Lung Ultrasound Findings Associated With COVID-19 ARDS, ICU Admission, and All-Cause Mortality. doi: 10.4187/respcare.09108	Respir Care	Denmark	Risk assessment
Farrow R	Early Multi-organ Point-of-Care Ultrasound Evaluation of Respiratory Distress During SARS-CoV-2 Outbreak: Case Report. doi: 10.5811/cpcem.2020.4.47524	Clin Pract Cases Emerg Med	USA	General application
Favot M	Point-of-Care Lung Ultrasound for Detecting Severe Presentations of Coronavirus Disease 2019 in the Emergency Department: A Retrospective Analysis. doi: 10.1097/CCE.0000000000000176	Crit Care Explor	USA	LUS in detecting severe cases
Feng XY	Application of pulmonary ultrasound in the diagnosis of COVID-19 pneumonia in neonates. doi: 10.3760/cma.j.cn112140-20200228-00154	Zhonghua Er Ke Za Zhi	China	General application
Flower L	The Use of Point-of-Care Lung Ultrasound and	J Cardiothorac	UK	General

	Echocardiography in the Management of Coronavirus Disease 2019 (COVID-19).doi: 10.1053/j.jvca.2020.05.009	Vasc Anesth		application (LUS and heart US)
Fonsi GB	Is Lung Ultrasound Imaging a Worthwhile Procedure for Severe Acute Respiratory Syndrome Coronavirus 2 Pneumonia Detection? https://doi.org/10.1002/jum.15487	J Ultrasound Med	Italy	Self-performed LUS
Fox S	Point-of-care ultrasound and COVID-19. 2020 May 14. doi: 10.3949/ccjm.87a.ccc019	Cleve Clin J Med	USA	General application
Frailé Gutiérrez V	Ultrasound in the management of the critically ill patient with SARS-CoV-2 infection (COVID-19): narrative review doi: 10.1016/j.medin.2020.04.016	Med Intensiva	Spain	LUS in ICU
García-Cruz E	Critical care ultrasonography during COVID-19 pandemic: The ORACLE protocol. doi: 10.1111/echo.14837.	Echocardiography	Mexico	General application (LUS and heart US)
Garcia de Alencar JC	Lung ultrasound score predicts outcomes in COVID-19 patients admitted to the emergency department https://doi.org/10.1186/s13613-020-00799-w	Annals of Intensive Care	Brazil	LUS in emergency room
Gaspardone C	Lung Ultrasound in COVID-19 A Role Beyond the Acute Phase? doi: 10.1002/jum.15425.	J Ultrasound Med	Italy	General application
Gil-Rodrigo A	Diagnostic yield of point-of-care ultrasound imaging of the lung in patients with COVID-19 https://europepmc.org/article/med/33006834	Emergencias	Spain	General application
Gino Soldati, MD,	LUS for COVID-19 Pneumonia: Flexible or Reproducible Approach? https://doi.org/10.1371/journal.pone.0256359	Journal of ultrasound in medicine	Italy	General application
Giugno V	Lung Ultrasound (LUS) in COVID-19 Pneumonia: Usefulness in Two Atypical Cases. DOI: 10.12890/2020_001800	Eur J Case Rep Intern Med	Italy	General application
Gopar-Nieto R	Lung ultrasound for the identification of COVID-19 pneumonia. doi: 10.24875/ACM.M20000071	Arch Cardiol Mex	Spain	General application
Gregorio-Hernández R	Point-of-care lung ultrasound in three neonates with COVID-19. doi: 10.1007/s00431-020-03706-4	Eur J Pediatr	Spain	LUS in neonates
Guarracino F	Lung, Heart, Vascular, and Diaphragm Ultrasound Examination of COVID-19 Patients: A Comprehensive Approach. doi: 10.1053/j.jvca.2020.06.013	J Cardiothorac Vasc Anesth	Italy	Comprehensive approach (lung, heart, vascular and diaphragm)

				US)
Hoffmann T	Can follow up lung ultrasound in Coronavirus Disease-19 patients indicate clinical outcome? https://doi.org/10.1371/journal.pone.0256359	Plos one	Germany	General application
Hsiao YH	Using lung ultrasound changes to evaluate the response of recruitment maneuver in a patient recovering from coronavirus disease 2019 with acute respiratory distress syndrome. doi: 10.1097/JCMA.0000000000000418.	J Chin Med Assoc	China	LUS compared to CXR
Inchingolo R	The diagnosis of pneumonia in a pregnant woman with coronavirus disease 2019 using maternal lung ultrasound. doi: 10.1016/j.ajog.2020.04.020	Am J Obstet Gynecol	Italy	LUS in pregnancy
Iodice V	Use of lung ultrasound in COVID-19: comparison with ultra-high-resolution computed tomography among 29 patients at "D. Cotugno" hospital, Naples https://pubmed.ncbi.nlm.nih.gov/32920569/	Infez Med	Italy	Comparison LUS and CT
Jackson K	Lung ultrasound in the COVID-19 pandemic DOI: 10.1136/postgradmedj-2020-138137	Postgrad Med J	UK	General application
Ji L	Response to: Lung ultrasound early detection and monitoring in COVID-19 pneumonia: fact and fiction. doi: 10.1093/qjmed/hcaa166	QJM	China	General application and monitoring
Johri AM	ASE Statement on Point-of-Care Ultrasound during the 2019 Novel Coronavirus Pandemic. doi: 10.1016/j.echo.2020.04.017	J Am Soc Echocardiogr.	USA	LUS at PoC
Jung EM	Contrast enhanced ultrasound (CEUS) to assess pleural pulmonary changes in severe COVID-19 infection: First results. doi: 10.3233/CH-209005	Clin Hemorheol Microcirc	Germany	Contrast-enhanced LUS
Kalafat E	Lung ultrasound and computed tomographic findings in pregnant woman with COVID-19. doi: 10.1002/uog.22034	Ultrasound Obstet Gynecol	Turkey	LUS and CT in pregnancy
Kalafat E	Utility of lung ultrasound assessment for probable SARS-CoV-2 infection during pregnancy and universal screening of asymptomatic individuals doi: 10.1002/uog.23099	Ultrasound Obstet Gynecol	Turkey	LUS in pregnancy
Karagöz A	Accuracy of Bedside Lung Ultrasound as a Rapid Triage Tool for Suspected Covid-19 Cases doi: 10.1097/RUQ.0000000000000530.	Ultrasound quarterly	Turkey	Triage
Karakus O	Detection of Line Artefacts in Lung Ultrasound Images of	IEEE Trans	UK, France	Physics of LUS

	COVID-19 Patients via Non-Convex Regularization. doi: 10.1109/TUFFC.2020.3016092.	Ultrason Ferroelectr Freq Control		
Karl Jackson	Lung ultrasound in the COVID-19 pandemic http://dx.doi.org/10.1136/postgradmedj-2020-138137	Postgrad Med J	UK	General application
Kennedy TM	Lung Point-of-Care Ultrasound in Pediatric COVID-19: A Case Series doi: 10.1097/PEC.0000000000002254	Pediatr Emerg Care	USA	General application
Khalili N	Lung Ultrasound in COVID-19 Pneumonia: Prospects and Limitations. doi: 10.1016/j.acra.2020.04.032	Acad Radiol.	Iran	General application
Kiamanesh O	Lung Ultrasound for Cardiologists in the Time of COVID-19. doi: 10.1016/j.cjca.2020.05.008	Can J Cardiol	Canada	General application
Kiefl D	German recommendations on lung and thoracic ultrasonography in patients with COVID-19 DOI: 10.1007/s00063-020-00740-w	PMID	Germany	Recommendations on LUS applications
Kirkpatrick AW	Lung ultrasonography in a woman with COVID-19: This examination could be remote. doi: 10.1503/cmaj.75302	CMAJ	Canada	General application
Kulkarni S	Point-of-care lung ultrasound in intensive care during the COVID-19 pandemic. doi: 10.1016/j.crad.2020.05.001	Clin Radiol	UK	LUS in ICU
Kunze G	Lungenultraschall bei Patienten mit SARS-CoV-2-Infektion [Lung ultrasound in patients with SARS-CoV-2 infection]. doi: 10.1007/s10049-020-00767-8	Notf Rett Med	Germany	General application
Lerchbaumer MH	Point-of-care lung ultrasound in COVID-19 patients: inter and intra-observer agreement in a prospective observational study https://doi.org/10.1038/s41598-021-90153-2	Scientific reports	Germany	Diagnostic accuracy
Lichter Y	Lung ultrasound predicts clinical course and outcomes in COVID-19 patients doi: 10.1007/s00134-020-06212-1	Intensive Care Med	Israel	LUS in prognosticating COVID patients
Liu RB	Ultrasound on the Frontlines of COVID-19: Report From an International Webinar. doi: 10.1111/acem.14004	Acad Emerg Med.	USA	General application
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Luna Gargani	Why, when, and how to use lung ultrasound during the COVID-19 pandemic: enthusiasm and caution. https://doi.org/10.1093/ehjci/jeaa163	European Heart Journal	UK	General application
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Millington SJ	How I Do It: Lung Ultrasound for Patients with COVID-19 Pulmonary Disease. doi: 10.1016/j.chest.2020.08.2054	Chest	Italy, Canada, USA	General application
Møller-Sørensen H	COVID-19 Assessment with Bedside Lung Ultrasound in a Population of Intensive Care Patients Treated with Mechanical Ventilation and ECMO doi: 10.3390/diagnostics10070447	Diagnostics (Basel).	Denmark	LUS in ICU
Mongodi S	Lung Ultrasound in Patients with Acute Respiratory Failure Reduces Conventional Imaging and Health Care Provider Exposure to COVID-19. doi: 10.1016/j.ultrasmedbio	Ultrasound Med Biol.	Italy	LUS in ICU
Moro F	How to perform lung ultrasound in pregnant women with suspected COVID-19. doi: 10.1002/uog.22028	Ultrasound Obstet Gynecol.	Italy	LUS in pregnancy
Mort DO	Abnormal Lung Point-of-Care Ultrasound (POCUS) in Suspected Cases of COVID-19 pneumonia with Normal Plain Chest Radiographs - A Case Series https://pesquisa.bvsalud.org/controlcancer/resource/pt/mdl-33020762?src=similardocs	Acute Medicine	UK	Comparison LUS and CXR
Musolino AM	Roman Lung Ultrasound Study Team for Pediatric COVID-19 (ROMULUS COVID Team). Lung Ultrasound in Children with COVID-19: Preliminary Findings. doi: 10.1016/j.ultrasmedbio.2020.04.026	Ultrasound Med Biol	Italy	LUS in paediatrics
Musolino AM	The Role of Lung Ultrasound in Diagnosis and Follow-Up of Children with Coronavirus Disease 2019. doi: 10.1097/PCC.0000000000002436	Pediatr Crit Care Med	Italy	LUS monitoring children for COVID
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Nouvenne A	Point-of-Care Chest Ultrasonography as a Diagnostic Resource for COVID-19 Outbreak in Nursing Homes. doi:	J Am Med Dir Assoc	Italy	LUS use in nursing homes

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Ottaviani S	Lung ultrasonography in patients with COVID-19: comparison with CT. doi: 10.1016/j.crad.2020.07.024	Clin Radiol	France	Comparison LUS and CT
Palabiyik F	Imaging of COVID-19 pneumonia in children. DOI: 10.1259/bjr.20200647	Br J Radiol	Turkey	LUS in paediatrics
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Pata D	Chest Computed Tomography and Lung Ultrasound Findings in COVID-19 Pneumonia: A Pocket Review for Non-radiologists. doi: 10.3389/fmed.2020.00375	Front Med (Lausanne).	Italy	Comparison LUS and CT
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Peh WM	Lung ultrasound in a Singapore COVID-19 intensive care unit patient and a review of its potential clinical utility in pandemic. doi: 10.15557/JoU.2020.0025	J Ultrasound	Singapore	LUS in ICU
Peixotoa AO	Applicability of lung ultrasound in COVID-19 diagnosis and evaluation of the disease progression: A systematic review doi: 10.1016/j.pulmoe.2021.02.004	pulmonology	Brazil	General application
Pierce CW	Clarifying the role of lung ultrasonography in COVID-19 respiratory disease. doi: 10.1503/cmaj.75311	CMAJ	Canada	General application
Pierrakos C	Lung Ultrasound for the Guidance of Adjunctive Therapies in Two Invasively Ventilated Patients with COVID-19 doi: 10.4269/ajtmh.20-0538.	Am J Trop Med Hyg	Belgium	LUS in guiding therapy
Qian X	Current Ultrasound Technologies and Instrumentation in the Assessment and Monitoring of COVID-19 Positive Patients. doi: 10.1109/TUFFC.2020.3020055	IEEE Trans Ultrason Ferroelectr Freq Control	USA	General application
Quarato CMI	Diagnosis and monitoring of COVID-19 pneumonia in pregnant women: is lung ultrasound appropriate? doi: 10.1002/uog.22156.	Ultrasound Obstet Gynecol.	Italy, Belgium	LUS in pregnant women with COVID-19

Quarato CMI	Lung Ultrasound in the Diagnosis of COVID-19 Pneumonia: Not Always and Not Only What Is COVID-19 “Glitters” doi: 10.3389/fmed.2021.707602	Frontiers in Big Data journal	Italy	General application
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Reisinger N	Lung ultrasound: a valuable tool for the assessment of dialysis patients with COVID-19. doi: 10.1007/s10157-020-01903-x	Clin Exp Nephrol.	USA	LUS in dialysis
Rojatti M	Lung Ultrasound and Respiratory Pathophysiology in Mechanically Ventilated COVID-19 Patients-an Observational Trial https://doi.org/10.1007/s42399-020-00536-1	Compr Clin Med	Italy	LUS in monitoring ventilated patients
Roy S	Deep Learning for Classification and Localization of COVID-19 Markers in Point-of-Care Lung Ultrasound. doi: 10.1109/TMI.2020.2994459	IEEE Trans Med Imaging	Italy, Netherlands	LUS and Artificial Intelligence
Royer O	Lung Ultrasound Evolution in a Patient with COVID-19 https://doi.org/10.1164/rccm.202006-2572IM	Am J Respir Crit Care Med	Canada	General application
Rubio-Gracia J	Point-of-care lung ultrasound assessment for risk stratification and therapy guiding in COVID-19 patients. A prospective non-interventional study DOI: 10.1183/13993003.04283-2020	European Respiratory Journal	Spain	Risk assessment
Sahu AK	Lung sonographic findings in COVID-19 patients https://doi.org/10.1016/j.ajem.2020.08.080	Am J Emerg Med	India	General application
Sanjeev Bhoi	Point-of-care ultrasound in COVID-19 pandemic http://dx.doi.org/10.1136/postgradmedj-2020-137853	Postgrad Med J	India	General application
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Scheier E	Lung ultrasound cannot be used to screen for Covid-19 in children. doi: 10.26355/eurrev_202005_21145	Eur Rev Med Pharmacol Sci	Israel	LUS in paediatrics
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Schmid M	Lung Ultrasound findings in COVID-19 Pneumonia. doi: 10.3238/arztebl.2020.0335	Dtsch Arztebl Int	Germany	General application
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Shaw JA	Lung Ultrasound in COVID-19: Not Novel, but Necessary doi: 10.1159/000509763	Respiration	South Africa	General application
Shokoohi H	Lung ultrasound monitoring in patients with COVID-19 on home isolation. doi: 10.1016/j.ajem.2020.05.079	Am J Emerg Med	USA, Spain	LUS patient monitoring
Shumilov E	Comparison of Chest Ultrasound and Standard X-Ray Imaging in COVID-19 Patients. doi: 10.1055/a-1217-1603	Ultrasound Int Open	Germany	Comparison LUS and CXR
Skaarup KG	Lung ultrasound findings in hospitalized COVID-19 patients in relation to venous thromboembolic events: the ECHOVID-19 study. doi: 10.1007/s40477-021-00605-8.	J Ultrasound	Denmark	Risk assessment
Smallwood N	Should point-of-care ultrasound become part of healthcare worker testing for COVID? doi: 10.7861/clinmed.2020-0442	Clin Med (Lond).	UK	LUS in testing healthcare workers for COVID
Smargiassi A	Lung Ultrasound for COVID-19 Patchy Pneumonia: Extended or Limited Evaluations? doi: 10.1002/jum.15428	J Ultrasound Med	Italy	Limiting LUS to specific chest regions
Smargiassi A	Lung ultrasonography for early management of patients with respiratory symptoms during COVID-19 pandemic. doi: 10.1007/s40477-020-00501-7.	J Ultrasound	Italy	General application
Smith MJ	Point-of-care lung ultrasound in patients with COVID-19 - a narrative review. doi: 10.1111/anae.15082	Anaesthesia	UK	General application
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Sperandeo M	Diagnosis of coronavirus disease 2019 pneumonia in pregnant women: can we rely on lung ultrasound? doi: 10.1016/j.ajog.2020.06.028	Am J Obstet Gynecol	Italy	LUS in pregnancy
Sperandeo M	Lung ultrasound early detection and monitoring in COVID-19 pneumonia: fact and fiction. doi: 10.1093/qjmed/hcaa165	QJM	China	General application and monitoring
Taccari F	COVID-19 and Lung Ultrasound: Reflections on the "Light Beam". https://doi.org/10.1002/jum.15468	J Ultrasound Med	Italy	Physics of LUS
Tan G	Use of Lung Ultrasound to Differentiate Coronavirus Disease 2019 (COVID-19) Pneumonia from Community-Acquired Pneumonia. https://doi.org/10.1016/j.ultrasmedbio.2020.05.006	Ultrasound Med Biol	China	Modified LUS scoring system
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Tung-Chen Y	Correlation between Chest Computed Tomography and Lung Ultrasonography in Patients with Coronavirus Disease 2019 (COVID-19). DOI: 10.1016/j.ultrasmedbio.2020.07.003	Ultrasound Med Biol	Spain	LUS correlation with CT
Tung Chen Y	Lung Ultrasound Findings in a Covid-19 Patient with Negative Chest CT DOI: 10.1055/a-1248-9068	Ultraschall Med	Spain	LUS and CT application
Tung-Chen Y	Lung ultrasound in the frontline diagnosis of COVID-19 infection doi: 10.1016/j.medcli.2020.06.001	Med Clin	Spain	General application

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Tung-Chen Y	Time course of lung changes on thoracic ultrasound of mild COVID-19 patients. doi: 10.1016/j.eimc.2020.05.002	Enferm Infec Microbiol Clin	Spain	Patient follow-up
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Vazquez Martínez JL	Short report - Usefulness of point-of-care ultrasound in pediatric SARS-CoV-2 infection. DOI: 10.26355/eurrev_202007_22284	Eur Rev Med Pharmacol Sci.	Spain	LUS in paediatrics at POC
Veronese N	Prognostic Value of Lung Ultrasonography in Older Nursing Home Residents Affected by COVID-19 doi: 10.1016/j.jamda.2020.07.034	J Am Med Dir Assoc.	Italy	LUS in nursing homes for prognosticating
Vetrugno L	Our Italian experience using lung ultrasound for identification, grading and serial follow-up of severity of lung involvement for management of patients with COVID-19. doi: 10.1111/echo.14664	Echocardiography	Italy	LUS for grading and monitoring response
Vetrugno L	Lung Ultrasound and the COVID-19 "Pattern": Not All That Glitters Today Is Gold Tomorrow. doi: 10.1002/jum.15327	J Ultrasound Med	Italy	General application
Vetrugno L	The "pandemic" increase in lung ultrasound use in response to Covid-19: can we complement computed tomography findings? A narrative review. doi: 10.1186/s13089-020-00185-4	Ultrasound J	Italy	LUS complementing CT findings
Vieillard-Baron A	Lung ultrasonography as an alternative to chest computed tomography in COVID-19 pneumonia? doi: 10.1007/s00134-020-06221-0	Intensive Care Med	France, Canada	Comparison LUS and CT
Vieira ALS	Role of point-of-care ultrasound during the COVID-19 pandemic: our recommendations in the management of dialytic patients. doi: 10.1186/s13089-020-00177-4	Ultrasound J	Brazil	LUS and dialysis of COVID patients
Volpicelli G	Sonographic signs and patterns of COVID-19 pneumonia. doi: 10.1186/s13089-020-00171-w	Ultrasound J.	Italy	General application
Volpicelli G	What's new in lung ultrasound during the COVID-19 pandemic. doi: 10.1007/s00134-020-06048-9	Intensive Care Med.	Italy, Spain	General application

Volpicelli G	Lung ultrasound for the early diagnosis of COVID-19 pneumonia: an international multicenter study https://doi.org/10.1007/s00134-021-06373-7	Springer	Italy	General application
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Wangüemert Pérez AL	Lung Ultrasound Before and After SARS-CoV-2 doi: 10.1016/j.arbres.2020.07.040.	Arch Bronconeumol.	Spain	General applicatin
Wu S	Pilot Study of Robot-assisted Tele ultrasound Based on 5G Network: a New Feasible Strategy for Early Imaging Assessment during COVID-19 Pandemic doi: 10.1109/TUFFC.2020.3020721	IEEE Trans Ultrason Ferroelectr Freq Control	China	General application
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Yadav A	Lung Ultrasound in COVID-19. doi: 10.1007/s13312-020-1942-3	Indian Pediatr.	India	General application
Yang Y	Lung ultrasonography versus chest CT in COVID-19 pneumonia: a two-centered retrospective comparison study from China. doi: 10.1007/s00134-020-06096-1	Intensive Care Med.	China	Comparison LUS and CT
Yao Z	Lung Ultrasound Findings in Patients with Coronavirus Disease (COVID-19) https://www.ajronline.org/doi/full/10.2214/AJR.20.23513	AJR	China	General application
Yassa M	Lung ultrasonography in pregnant women during the COVID-19 pandemic: an interobserver agreement study among obstetricians. doi: 10.14366/usg.20084	Ultrasonography	Turkey	LUS in pregnancy
Yassa M	Lung Ultrasound Can Influence the Clinical Treatment of Pregnant Women with COVID-19. doi: 10.1002/jum.15367	J Ultrasound Med	Turkey	LUS in pregnancy
Yassa M	Outcomes of universal SARS-CoV-2 testing program in pregnant women admitted to hospital and the adjuvant role of lung ultrasound in screening: a prospective cohort study. doi: 10.1080/14767058.2020.1798398	J Matern Fetal Neonatal Med	Turkey	LUS in pregnancy in screening for COVID pneumonia
Yasukawa K	Point-of-Care Lung Ultrasound Findings in Patients with COVID-19 Pneumonia. doi: 10.4269/ajtmh.20-0280	Am J Trop Med Hyg.	UK	General application
Ye R	Feasibility of a 5G-Based Robot-Assisted Remote Ultrasound	Chest.	China	Robotic LUS

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Youssef A	Lung ultrasound in the coronavirus disease 2019 pandemic: a practical guide for obstetricians and gynecologists. doi: 10.1016/j.ajog.2020.05.014.	Am J Obstet Gynecol	Italy	General application
Yu RZ	Role of 5G-powered remote robotic ultrasound during the COVID-19 outbreak: insights from two cases. DOI: 10.26355/eurev_202007_22283	Eur Rev Med Pharmacol Sci	China	Robotic LUS
Yusuf GT	The use of contrast-enhanced ultrasound in COVID-19 lung imaging. doi: 10.1007/s40477-020-00517-z	J Ultrasound	UK	Contrast-enhanced US
Zanforlin A	How Is COVID-19 Changing Lung Ultrasound? A Survey by the Thoracic Ultrasound Academy. doi: 10.1002/jum.15398	J Ultrasound Med	Italy	General application
Zanforlin A	Lung Ultrasound During the COVID-19 Pandemic: Building a Mobile Lung Ultrasound Unit. doi: 10.1002/jum.15375	J Ultrasound Med	Italy	Mobile Ultrasound
Zhang LN	[Recommendations for the treatment of severe coronavirus disease 2019 based on critical care ultrasound] DOI: 10.3760/cma.j.cn112138-20200219-00098	Zhonghua nei ke za zhi.	China	LUS in ICU
Zhang Y	Lung Ultrasound Findings in Patients with Coronavirus Disease (COVID-19). doi: 10.2214/AJR.20.23513	AJR Am J Roentgenol	China	General application
Zhang Z	The Role of Lung Ultrasound in the Assessment of Novel Coronavirus Pneumonia. doi: 10.1053/j.jvca.2020.04.040	J Cardiothorac Vasc Anesth	China	General application
Zhao L	Lung Ultrasound Score in Evaluating the Severity of Coronavirus Disease 2019 (COVID-19) Pneumonia. doi: 10.1016/j.ultrasmedbio.2020.07.024	Ultrasound Med Biol	China	LUS score to evaluate severity of pneumonia
Zieleskiewicz L	Comparative study of lung ultrasound and chest computed tomography scan in the assessment of severity of confirmed COVID-19 pneumonia. doi: 10.1007/s00134-020-06186-0	Intensive Care Med	France	Comparison LUS and CT
Zieleskiewicz L	Ultrasound findings in patients with COVID-19 pneumonia in early and late stages: Two case-reports. doi: 10.1016/j.accpm.2020.04.015	Anaesth Crit Care Pain Med	France	General application

Appendix B: Infection prevention and control measures

Infection prevention and control measures when performing lung ultrasound on patients with suspected or confirmed COVID-19¹

Equipment (ultrasound machine, probe)

- Clean and disinfect the entire ultrasound machine, particularly the keyboard, screen and the whole probe with an approved low- or intermediate-level instrument-grade disinfectant.
- Cleaning process: remove all debris such as ultrasound gel with paper/cloth, wash with detergent and water, then rinse and dry thoroughly or use a detergent impregnated wipe approved for use on medical devices.
- A dedicated ultrasound machine for scanning COVID-19 patients should be allocated where possible.
- Handheld ultrasound devices should preferentially be used, as they can be completely encased with a probe cover, can be easily cleaned, and do not have a cooling fan.
- If a handheld device is not available, cart-based ultrasound machines should be stripped of all unnecessary items, like printers, baskets, and gel bottles.
- Machines with touch screens are preferable to machines with keyboards or buttons.
- Employ single-use gel packets instead of gel bottles.
- Clean and disinfect computer workstations and desks used by the ultrasound practitioner for reporting.

¹ World Health Organization, 2020. Use of chest imaging in COVID-19.
<https://www.who.int/publications/i/item/use-of-chest-imaging-in-covid-19>

Ultrasound practitioners

- Ultrasound practitioners with specific health problems that place them at greater risk (as detailed by local occupational health guidelines) are to be excluded from performing ultrasound
- Personnel protective equipment such as gloves; masks, protective eyewear, gowns should be worn upon entry into the patient room. Disposable wear should be discarded after use. Reusable wear should be cleaned and disinfected according to manufacturer's guidelines.
- Additional training on PPE for healthcare workers is advised and should include donning and doffing guidance.
- The practitioners should not wear jewelry, arms should be uncovered below elbow
- All ultrasound practitioners should perform hand hygiene before and after all patient contact, contact with potentially infectious material (e.g. bed linen and patient gowns), and before and after removing personal protective equipment (PPE) including gloves.
- Hand hygiene should be performed using an alcohol-based hand rub or washing hands with soap and water for at least 20 seconds. If hands are visibly soiled, use soap and water.
- Personnel who come into contact with COVID-19-positive or COVID-19-suspected patients, especially those working in high-risk environments (e.g. ICU/emergency departments) should don a uniform or scrubs that are not taken home for laundering.
- Ultrasound practitioners should routinely wear closed-toe shoes constructed in a material that can be easily cleaned, and these should be wiped regularly and immediately after coming into contact with a COVID-19-positive patient.

Patients

- It is advisable that confirmed COVID-19- positive patients wear a surgical mask at all times.
- If there is no dedicated system for COVID-19- confirmed patients, it would be preferable to scan at the end of the clinic list so that the equipment undergoes vigorous cleaning and disinfection.
- During the pandemic, it is reasonable not to allow trainees or students to participate.
- Accompanying persons should be limited at the point of procedure unless warranted for the purpose of the examination, for example pediatrics or patients requiring extra care.