



● Review

LUNG ULTRASOUND MAY SUPPORT DIAGNOSIS AND MONITORING OF COVID-19 PNEUMONIA

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Abstract—Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) disease (COVID-19) is characterized by severe pneumonia and/or acute respiratory distress syndrome in about 20% of infected patients. Computed tomography (CT) is the routine imaging technique for diagnosis and monitoring of COVID-19 pneumonia. Chest CT has high sensitivity for diagnosis of COVID-19, but is not universally available, requires an infected or unstable patient to be moved to the radiology unit with potential exposure of several people, necessitates proper sanitization of the CT room after use and is underutilized in children and pregnant women because of concerns over radiation exposure. The increasing frequency of confirmed COVID-19 cases is striking, and new sensitive diagnostic tools are needed to guide clinical practice. Lung ultrasound (LUS) is an emerging non-invasive bedside technique that is used to diagnose interstitial lung syndrome through evaluation and quantitation of the number of B-lines, pleural irregularities and nodules or consolidations. In patients with COVID-19 pneumonia, LUS reveals a typical pattern of diffuse interstitial lung syndrome, characterized by multiple or confluent bilateral B-lines with spared areas, thickening of the pleural line with pleural line irregularity and peripheral consolidations. LUS has been found to be a promising tool for the diagnosis of COVID-19 pneumonia, and LUS findings correlate fairly with those of chest CT scan. Compared with CT, LUS has several other advantages, such as lack of exposure to radiation, bedside repeatability during follow-up, low cost and easier application in low-resource settings. Consequently, LUS may decrease utilization of conventional diagnostic imaging resources (CT scan and chest X-ray). LUS may help in early diagnosis, therapeutic decisions and follow-up monitoring of COVID-19 pneumonia, particularly in the critical care setting and in pregnant women, children and patients in areas with high rates of community transmission. (E-mail: marco.allinovi@gmail.com) © 2020 World Federation for Ultrasound in Medicine & Biology. All rights reserved.

Key Words: Lung ultrasound, COVID-19, Pneumonia, Interstitial syndrome, B-Lines, Acute respiratory disease syndrome.

INTRODUCTION

The novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) hit the central regions of China in late December 2019 and subsequently spread rapidly to multiple countries worldwide. A pandemic outbreak of this virus with rapid human-to-

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human transmission constituted a dire public health emergency.

SARS-CoV-2 disease (COVID-19) is characterized by severe pneumonia and/or acute respiratory distress syndrome (ARDS) in about 20% of infected patients (Chen et al. 2020a; Huang et al. 2020a), with high morbidity and mortality. Herein, we provide an overview of the role of lung ultrasound (LUS) in the early diagnosis, therapeutic decision-making process and follow-up monitoring of COVID-19 pneumonia, representing a reliable alternative to computed tomography (CT) in this setting. Cited retrospective and prospective human studies had institutional review board (IRB) approval. Publications without IRB approval are in compliance with the Declaration of Helsinki.

ROLE OF CT IN COVID-19 PNEUMONIA

Chest CT is considered the routine imaging technique for diagnosis and monitoring of COVID-19 pneumonia. Patients with confirmed COVID-19 pneumonia have characteristic CT features: ground-glass or fine reticular opacities, reticulation, subpleural consolidations, vascular thickening and/or traction bronchiectasis, with peripheral distribution, bilateral involvement, lower lung predominance and multifocal distribution (Bai et al. 2020; Chung et al. 2020; Zhao et al. 2020).

Chest CT has high specificity (Bai et al. 2020) and high sensitivity in the diagnosis of COVID-19 pneumonia, being helpful in early screening of both symptomatic and asymptomatic highly suspected cases (Chen et al. 2020a; Shi et al. 2020) and in patients before negative-to-positive conversion of the reverse transcription polymerase chain reaction (RT-PCR) (Ai et al. 2020; Xie et al. 2020). However, in different studies, 20 of 36 (56%) positive adult patients in the first 2 d after clinical onset (Bernheim et al. 2020), 8 of 99 (8%) symptomatic

adult patients with history of exposure to confirmed cases (Zhao et al. 2020) and 12 of 24 (50%) asymptomatic positive carriers (Hu et al. 2020) had no abnormal CT findings.

Moreover, CT scan is not universally available in emergency departments and is a suboptimal option in the pediatric setting because of the exposure to high-dose radiation and the frequent need for sedation (Miglioretti et al. 2013). Furthermore, in a recent systematic review including 4612 children with COVID-19, 85.7% underwent chest CT scan, and 36% of them had no pathologic CT findings (Liguoro et al. 2020).

The increasing frequency of confirmed COVID-19 cases is striking, and new highly sensitive diagnostic tools are needed in clinical practice. This is particularly true considering that most of the affected/contagious patients are asymptomatic or experience mild symptoms (Li et al. 2020), RT-PCR has a sensitivity of only 71% for SARS-CoV-2 infection (Fang et al. 2020) and a considerable proportion of patients with COVID-19 pneumonia have normal chest radiographs at onset (Ng et al. 2020; Yoon et al. 2020).

LUS: BASICS, SCORING SYSTEMS AND TECHNICAL ASPECTS

Several data have indicated that LUS is an emerging non-invasive bedside technique in the diagnosis of interstitial lung syndrome because it is used to evaluate and quantify the number of B-lines, pleural irregularities and nodules or consolidations (Volpicelli et al. 2012; Soldati and Demi 2017; Demi et al. 2020a). LUS reveals numerous artifacts that physicians recognize and evaluate as part of their diagnosis (Demi et al. 2020b):

A-Lines are motionless and regularly spaced lines horizontal to the pleura (Fig. 1a), and correspond to normal reverberation artifacts of the pleural line.

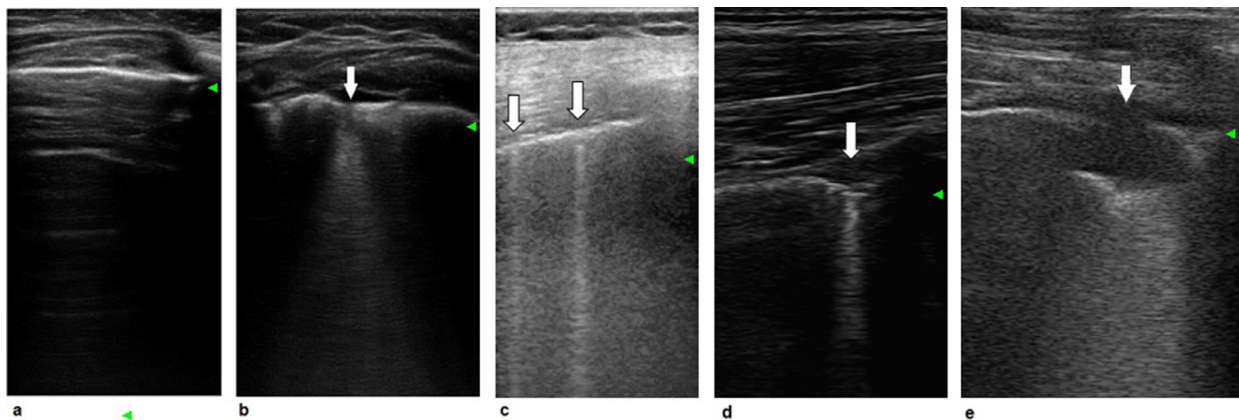


Fig. 1. (a) A-Lines: Lines horizontal to the pleura. (b–e). B-Lines: Linear vertical artifacts that arise from pleural lines (a) with different B-line shapes, for example, a single cone-shaped line (b), a single thin line (c), a single thick line (d) and a subpleural consolidation without air bronchogram (e).

B-Lines are vertical linear artifacts that arise from pleural lines (Fig. 1 a), likely representing ultrasound reverberations generated by the thickened interlobular septa and other subpleural structures (Volpicelli *et al.* 2012). There are several different B-line shapes, for example, the single cone-shaped line (Fig. 1b), single thin line (Fig. 1c) and single thick line (Fig. 1d).

Multiple B-lines are **considered** the sonographic sign of lung interstitial syndrome, and their number increases along with decreasing air content and increasing lung density. An inhomogeneous bilateral pattern of multiple coalescent B-lines and white lung, sometimes with scattered spared areas, characterizes ARDS (Soldati and Demi 2017).

Lung peripheral consolidations are subpleural echopoor regions or regions with tissue-like echotexture (Fig. 1e), with different features: with or without air or fluid bronchogram, vertical artifacts at the far-field margin or hepatization (Volpicelli *et al.* 2012). **Consolidations associated with B-lines are characteristic ultrasound patterns observed in patients with ARDS.**

In clinical practice, especially in the critical care setting, several **scoring systems** have been proposed to quantify the extent of lung involvement, based on the number of chest wall zones used in each system: the 4-zone, 6-zone, 8-zone, 12-zone and 14-zone methods (Fig. 2) are adopted mainly in critical care settings. With the 4-, 6- or 8-zone scoring system (Platz *et al.* 2019), B-lines are counted in multiple intercostal spaces across the thorax, and the presence of three or more B-lines in a single intercostal space is defined as the “B-pattern.” Differently, with the 12-zone scoring system, in each zone a score of 0 is assigned for no B-lines and a score of 1 is assigned for multiple spaced/isolated B-lines, a score of 2 is assigned for diffused coalescent B-lines or “light beam” and a score of 3 is assigned for lung consolidation (Volpicelli *et al.* 2020). Finally, in the 14-zone scoring system, in each zone a score of 0 is assigned for regular pleural line and A-lines, a score of 1 is assigned for an indented pleural line with vertical areas of white below each indent, a score of 2 is assigned for a broken pleural line with vertical areas of white below each small-to-large consolidated area and a score of 3 is assigned for dense and largely extended white lung with or without larger consolidations (Soldati *et al.* 2020b).

Recently, an Italian consensus **proposed a standardization** for the international use of LUS in the management of patients with COVID-19 to use a well-validated terminology related to image artifacts and adopt objective clinical standards for interpretation of imaging features (Soldati *et al.* 2020b).

LUS scanning frequencies, technical adjustments, acquisition protocols, choice of different probes and mechanical indexes have strong effects on the

visualization and counting of lung B-lines (Soldati *et al.* 2020b). Consequently, to avoid misdiagnosis, LUS should be used only by appropriately trained users.

ROLE OF LUS IN DIAGNOSIS OF PNEUMONIA

LUS has been reported to be a promising tool for the diagnosis and follow-up of pneumonia in adults as well as in children (Reissig and Copetti 2014; Pereda *et al.* 2015). In a meta-analysis, LUS exhibited **high accuracy in diagnosing pneumonia** compared with chest CT scan (Long *et al.* 2017). Moreover, in diagnostic performance in **interstitial lung syndrome** (interstitial pneumonia, interstitial diseases and ARDS), LUS is now considered to be similar to CT scan (Asano *et al.* 2018; Patel *et al.* 2018; Man *et al.* 2019; Mayo *et al.* 2019), which is the gold standard method for diagnosis. In particular, a comparative study by Lichtenstein *et al.* (2004) indicated that the **accuracy** of LUS in patients with ARDS was 93% for pleural effusion, 97% for consolidation and 95% for alveolar interstitial syndrome.

The **specificity of B-line evaluation** at LUS is, however, **low** because B-lines can be visualized in any disease process causing interstitial lung disease (*e.g.*, mild to moderate lung congestion, pulmonary edema, pneumonitis, viral pneumonia, pulmonary fibrosis, ARDS) (Dietrich *et al.* 2016; Soldati *et al.* 2019; Demi *et al.* 2020a). Similarly, subpleural consolidations and pleural effusion, which represent anatomic alterations and not artifacts, have low specificity for COVID-19 as they appear in many different conditions. Although the most frequent cause of interstitial pneumonia in areas with high COVID-19 prevalence is SARS-CoV-2, other causes remain possible (atypical bacteria, flu viruses, *etc.*).

ROLE OF LUS IN DIAGNOSIS OF COVID-19 PNEUMONIA

In patients with COVID-19 pneumonia, LUS reveals the typical bilateral pattern of diffuse interstitial lung syndrome, characterized by multiple or confluent B-lines with spared areas, thickening of the pleural line with pleural line irregularity (Fig. 3) and, less frequently, subpleural consolidations and pleural effusion (Buonsenso *et al.* 2020b; Huang *et al.* 2020b; Lomoro *et al.* 2020; Nouvenne *et al.* 2020; Poggiali *et al.* 2020a; Peng *et al.* 2020; Soldati *et al.* 2020a; Volpicelli and Gargani 2020; Volpicelli *et al.* 2020; Xing *et al.* 2020; Yasukawa and Minami 2020).

This pattern was previously described for interstitial pneumonia caused by different etiologies, such as *Chlamydia* (Perrone and Quaglia 2017), *Pneumocystis* (Limonta *et al.* 2019), measles (Volpicelli and Frascisco 2009), influenza virus A H7N9 (Zhang *et al.* 2015) and

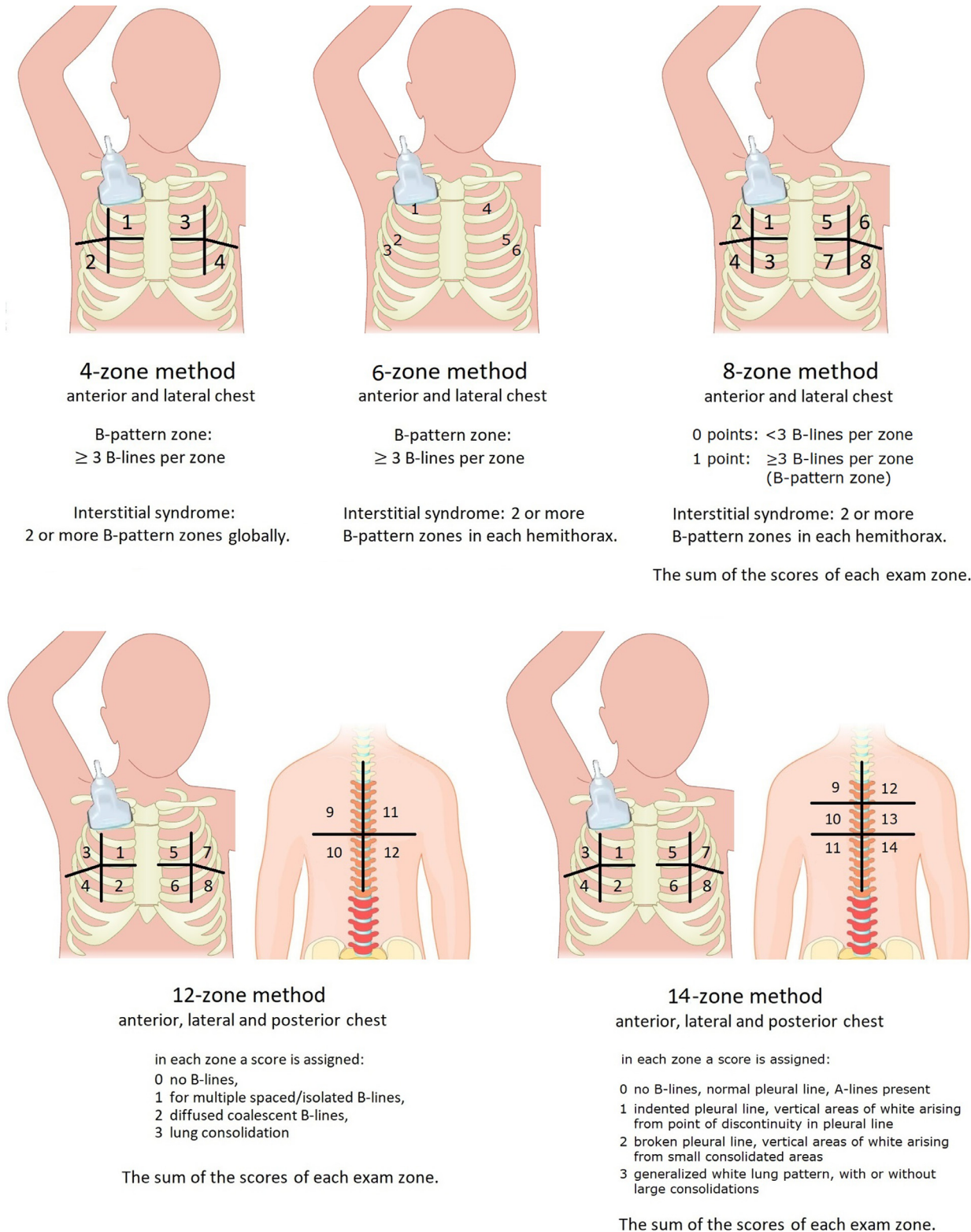


Fig. 2. Different scoring systems used to quantify the extent and characterize the different patterns of lung involvement.

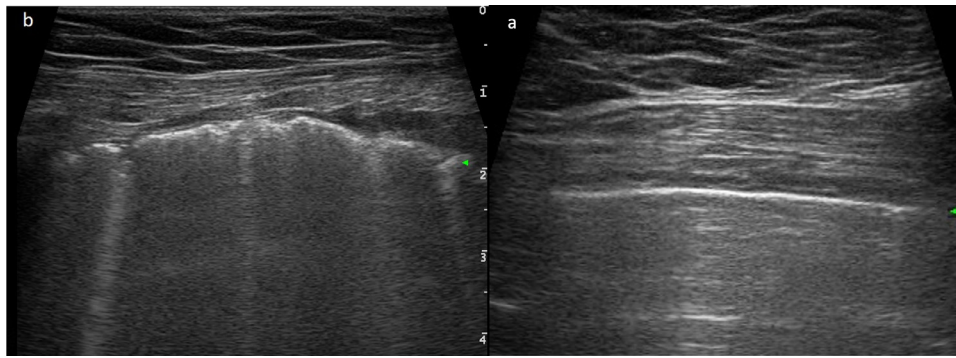


Fig. 3. Ultrasonographic features of normal lung and COVID-19 pneumonia. (a) Normal sonographic lung appearance. Pleural line (hyper-echoic horizontal line, *green arrowhead*) and multiple horizontal reverberations of the pleural line (A-lines). (b) Severe interstitial pneumonia and acute respiratory distress syndrome sonographic appearance. *Green arrowhead* indicates irregular pleural line; *vertical lines* indicate multiple blurred B-lines.

influenza virus H1N1 (Testa et al. 2012; Tsung et al. 2012), supporting the role of LUS in the diagnosis of COVID-19. In COVID-19 pneumonia, different degrees of interstitial syndrome and alveolar consolidation detected by LUS are directly correlated with the severity of the lung injury (Peng et al. 2020; Xing et al. 2020).

There are currently no known findings pathognomonic of COVID-19 on LUS, although Volpicelli et al. recently reported the “light beam,” a broad, lucent, band-shaped, vertical artifact that moves rapidly with sliding, corresponding to the early appearance of “ground glass” (Volpicelli and Gargani 2020; Volpicelli et al. 2020).

LUS can detect the pulmonary dynamic changes associated with COVID-19 pneumonia (Soldati et al. 2020a). In the early stages, the main ultrasound finding is focal B-lines, while, as the disease progresses, B-lines become multifocal and confluent (interstitial lung syndrome), with further development of clear consolidations (Fiala 2020; Soldati et al. 2020b). During convalescence, B-lines and consolidations gradually disappear and are replaced by A-lines (Denina et al. 2020; Peng et al. 2020; Xing et al. 2020).

In this setting, the findings on LUS appear to correlate well with the findings on chest CT scan in patients with COVID-19 pneumonia (Huang et al. 2020b; Lu et al. 2020a; Peng et al. 2020; Poggiali et al. 2020a; Yang et al. 2020b) and can be expected to develop over a similar timeline (Fiala 2020).

The sensitivity, specificity and diagnostic accuracy of LUS have been reported to increase with the severity of COVID-19 pneumonia compared with chest CT scan (Lu et al. 2020).

LUS allows for the evaluation of pleural and peripheral pulmonary lesions, while cannot detect lesions that are deep within the lung, as aerated lung blocks the transmission of ultrasound. However, studies

on chest CT in patients with COVID-19 have revealed that most of the consolidations are generally localized in the peripheral lung (Liu et al. 2020; Yang et al. 2020a, 2020b), which facilitates detection by LUS.

Of note, in a comparative study with chest CT scan, LUS had lower specificity in differentiating patients with COVID-19 and non-COVID-19 pneumonia (Chen et al. 2020b), considering that different pathogens can share similar LUS patterns. However, through rational integration of LUS with the clinical data, good specificity can be achieved in cases of LUS findings suggestive of COVID-19, in relatively young patients or in those without a history of lung disease, in the not-very-early stages of COVID-19 pneumonia (Soldati et al. 2020c).

Compared with CT, LUS has several advantages: It enables bedside assessment, reduces the length of patient stay in the emergency room (reducing health care workers’ exposure to infected patients), prevents exposure to radiation (especially for children and pregnant women), can be repeated during follow-up at low cost and is easily applied in low-resource settings (Volpicelli et al. 2012; Soldati and Demi 2017; Buonsenso et al. 2020a; Denina et al. 2020; Moro et al. 2020). Moreover, CT scan requires transport of the patient, potentially infected and unstable, to the radiology unit with potential exposure of several people, and necessitates proper sanitification of the CT room after use.

LUS CAN GUIDE THERAPEUTIC DECISIONS AND PROCEDURES IN DIFFERENT SETTINGS

The use of bedside LUS allows integration of the information on the state of the lung (sonographic patterns) with all the information from medical history, risk of exposure, clinical examination and blood exams, giving the physician a better characterization of the disease and helping in the decision-making process (Volpicelli

et al. 2020). This multiparametric approach may increase the diagnostic accuracy of LUS for COVID-19 pneumonia, especially in mild to moderate disease or in differential diagnoses with non-COVID-19 pneumonia, for which LUS seems to have lower specificity compared with CT scan (Chen et al. 2020b; Lu et al. 2020a).

Although conclusive data on COVID-19 patients are still lacking, data from studies in different settings of interstitial pneumonia and ARDS may support the role of LUS, especially in areas with high rates of community transmission, guiding therapeutic decisions and procedures in patients with COVID-19 in many critical settings (Soldati et al. 2020b): general practitioners' offices, nursing homes, emergency departments, general internal medicine wards, pulmonology wards, hemodialysis units, obstetrics and paediatrics.

Those general practitioners who are confident using LUS may represent a first important step for patients clinically suspected of having COVID-19 infection, reducing unnecessary emergency department visits. LUS might provide an additional datapoint to the full clinical picture, especially if compared with the limited traditional chest auscultation (Copetti 2016), and allow advanced triage for COVID-19 directly at home (Sho-koochi et al. 2020; Soldati et al. 2020c). The probe can be used as a stethoscope to scan any portion of the lung, providing increased diagnostic accuracy.

Nursing homes are on the front lines of this pandemic, and their residents have been decimated in several countries worldwide. LUS, with a portable ultrasound device, has proven to be an excellent tool for identifying COVID-19 in nursing home residents (Nouvelle et al. 2020), suggesting a potential role for screening patients at high risk in a setting characterized by scarce diagnostic resources.

In emergency departments or in COVID-restricted triage areas for patients clinically suspected of having COVID-19 infection, use of LUS as a primary survey tool in acutely dyspneic or hypoxemic patients provides an immediate evaluation of the lung (Zanobetti et al. 2017; Volpicelli et al. 2020). During the COVID-19 pandemic, LUS, as part of a structured triage system in an emergency department, can help to detect pulmonary and pleural findings early, even in patients without respiratory symptoms and/or fever, especially if pulse oxygen levels are lower than normal values (Poggiali et al. 2020b). For a patient with respiratory failure, a normal LUS could rule out COVID-19 pneumonia and orient the examiner toward different diagnosis (Volpicelli et al. 2020). Conversely, we suggest that patients with LUS findings suggestive of COVID-19 but negative RT-PCR results should be isolated, and RT-PCR should be repeated to avoid misdiagnosis (Soldati et al. 2020c).

In general internal medicine wards and pulmonology wards, LUS might be useful for monitoring the effect of therapeutic drugs (immunosuppressive strategies, antiviral drugs or others) as a bedside and real-time technique, and may decrease utilization of conventional diagnostic imaging resources, reducing exposure of health care workers to SARS-CoV-2 (Yasukawa and Minami 2020).

Patients on hemodialysis are at increased risk of contagion and serious complications during the COVID-19 pandemic (Alberici et al. 2020), because of frequent contact with health care facilities and a high comorbidity burden. Although patients on dialysis have multiple potential etiologies for dyspnea and multiple B-lines at LUS (such as heart failure and fluid overload) and for fever (such as vascular access infection), different LUS patterns detected in COVID-19 patients may help in differential diagnosis in this setting (Reisinger and Koratala 2020; Vieira et al. 2020).

In pregnant woman, LUS may represent a valuable alternative to CT scan during the COVID-19 pandemic (Buonsenso et al. 2020a; Moro et al. 2020; Youssef et al. 2020), particularly because it is mandatory to avoid exposure to radiation in this specific setting, and obstetricians and gynecologists are usually familiar with the use of ultrasound.

In the **pediatric setting**, where LUS is considered as an imaging alternative to CT scan for the diagnosis of childhood pneumonia (Pereda et al. 2015), **LUS could play a central role** in the COVID-19 pandemic. In fact, LUS has been reported to be able to detect lung pathology in children (Denina et al. 2020; Musolino et al. 2020) and neonates (Feng et al. 2020) with confirmed COVID-19, even when asymptomatic, with the same LUS patterns described in adults. Moreover, LUS was found to decrease utilization of conventional diagnostic imaging resources in children with suspected COVID-19 (De Rose et al. 2020). The large number of asymptomatic and mild cases of COVID-19 in children (Lu et al. 2020b; Parri et al. 2020) confirms that chest CT scan and X-ray should not be routinely used. However, further studies in children are needed because LUS reveals conflicting results in early stages and mild forms of COVID-19 pneumonia (Musolino et al. 2020; Scheier et al. 2020).

Although the sensitivity and specificity of LUS in diagnosing COVID-19 pneumonia remain to be determined in larger studies, LUS represents a reliable alternative to CT scan and chest X-ray in all these settings.

Efficient triage of patients with suspected COVID-19 at all health facility levels can help the national response planning and case management system cope with patient influx.

LUS MAY GUIDE THERAPEUTIC DECISIONS AND PROCEDURES IN INTENSIVE CARE UNITS

In hemodynamically or respiratory unstable patients in intensive care, LUS may have major utility in bedside management of COVID-19, to track the evolution of interstitial pneumonia and ARDS, to monitor lung recruitment maneuvers and response to therapies, to identify early possible complications (pneumothorax, over-infections), to guide several invasive procedures and to make decisions on weaning patients from ventilator support (Mojoli *et al.* 2020; Peng *et al.* 2020).

Although data on intensive care unit patients with COVID-19 are scarce, a practical approach based on LUS can be proposed to guide therapeutic decisions in ARDS patients (Bouhemad *et al.* 2015), and different LUS scoring systems may be used to estimate the extent of lung involvement (Volpicelli *et al.* 2020). In fact, a significant reduction in or absence of lung sliding and the evolution to consolidations indicate severe pneumonia or ARDS, suggesting that the patient may require invasive ventilatory support (Copetti *et al.* 2008; Reissig and Copetti 2014). Moreover, LUS score, as an estimate of lung aeration, can be regularly monitored at the beginning and at any time point after therapy for COVID-19 is started (*i.e.*, positive end-expiratory pressure [PEEP] trial or prone position) (Conway *et al.* 2020). An increase in score and/or the presence of posterolateral/inferior consolidations indicate a decrease in aeration, suggesting the need for additional PEEP and recruitment maneuvers, while a decrease in score indicates re-aeration, suggesting the success of interventions and, eventually, weaning from respiratory support (Conway *et al.* 2020). To confirm this, although data on COVID-19 patients are still lacking, PEEP-induced lung recruitment (Lichtenstein *et al.* 2004; Bouhemad *et al.* 2011) and the response to prone positioning (Prat *et al.* 2016; Wang *et al.* 2016) can be adequately estimated with bedside LUS in patients with ARDS.

LUS can be useful in confirming endotracheal tube placement (Das *et al.* 2015; Karacabey *et al.* 2016), which is particularly tricky in the COVID-19 area setting and when an end-tidal CO₂ device is not available, and in detecting pneumothorax (Alrajab *et al.* 2013), which is frequently identified by an anterior extension in the critically ill patient in a recumbent or semirecumbent position.

Even if pleural effusions are not frequent in COVID-19 patients, bedside thoracentesis can be tolerably performed with an echo-guided technique, to promote lung recruitment and ameliorate oxygenation and to reduce the incidence of peri-procedural complications (Mercaldi *et al.* 2013; Rodriguez-Lima *et al.* 2020).

LUS seems to be a more tolerable and more convenient alternative to CT scans in a transportation-limited

setting such as mechanical ventilation or extracorporeal membrane oxygenation. In an urgent situation, such as a patient's sudden deterioration, a quick imaging tool is greatly needed.

In this setting, systematic application of LUS has been reported to decrease utilization of conventional diagnostic imaging resources (Pontet *et al.* 2019; Mojoli *et al.* 2020; Mongodi *et al.* 2020; Vetrugno *et al.* 2020).

RECOMMENDATIONS FOR LUS TO PREVENT SARS-COV-2 TRANSMISSION

Personal protective equipment should be worn when scanning a patient with suspected or confirmed COVID-19 infection. To minimize the risk of potential SARS-CoV-2 transmission, sonographers (i) should assume that every patient has COVID-19 infection; (ii) should wear personal protective equipment, such as face masks (N95/FFP2 or FFP3), waterproof protective gear or goggles, a disposable gown and one or two pairs of disposable gloves (World Health Organization [WHO] 2020); (iii) should drape the ultrasound machine with a plastic disposable wrap, covering probes, cables, couch and keyboard with disposable covers; and (iv) should clean and disinfect the equipment and room with alcohol-based disinfectant cleaner at the end of every exam.

Compared with a portable X-ray or CT machine, ultrasound machines are faster to decontaminate because of their small size. Some physicians have reduced the risk of COVID-19 transmission and minimized decontamination time by using portable, hand-held wireless ultrasound probes attached to sheathed tablet devices, placed in two separate single-use plastic covers (Buonsenso *et al.* 2020b). In the context of the COVID-19 pandemic, portable ultrasound is valuable because it can be transported to remote areas and can be easily sterilized.

LUS should, however, be used only by appropriately trained users, to avoid misdiagnosis and prevent SARS-CoV-2 transmission resulting from non-adherence to appropriate cleaning and disinfection principles.

CONCLUSIONS

LUS may be a first-line diagnostic imaging alternative to chest CT scan and chest X-ray during every step of COVID-19 disease, even before clinical manifestations, particularly in children, pregnant women, critically ill patients that cannot be moved and patients in areas with high rates of community transmission. The combination of sonographic patterns at LUS with clinical and laboratory findings, followed by chest CT for confirmation in selected cases, may help in early diagnosis, therapeutic decisions and follow-up monitoring of COVID-19 pneumonia in both children and adults.

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