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CONCEPTS

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The role of lung ultrasonography in COVID-19 disease management

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Abstract

Coronavirus disease 2019 (COVID-19) has created unprecedented disruption for global healthcare systems. Offices and emergency departments (EDs) were the first responders to the pandemic, followed by medical wards and intensive care unit (ICUs). Worldwide efforts sprouted to coordinate proper response by increasing surge capacity and optimizing diagnosis and containment. Within the complex scenario of the outbreak, the medical community shared scientific research and implemented best-guess imaging strategies in order to save time and additional staff exposures. Early publications showed agreement between chest computed tomography (CT) and lung sonography: widespread ground-glass findings resembling acute respiratory distress syndrome (ARDS) on CT of COVID-19 patients matched lung ultrasound signs and patterns. Well-established accuracy of bedside sonography for lung conditions and its advantages (such as no ionizing radiation; low-cost, real-time bedside imaging; and easier disinfection steps) prompted a wider adoption of lung ultrasound for daily assessment and monitoring of COVID-19 patients. Growing literature, webinars, online materials, and international networks are promoting lung ultrasound for the same purpose.

We propose 11 lung ultrasound roles for different medical settings during the pandemic, starting from the out-of-hospital setting, where lung ultrasound has ergonomic and infection control advantages. Then we describe how medical wards and ICUs can safely integrate lung ultrasound into COVID-19 care pathways. Finally, we present outpatient use of lung ultrasound to aid follow-up of positive case contacts and of those discharged from the hospital.

1 | BACKGROUND AND CLINICAL SIGNIFICANCE

Since the beginning of the coronavirus disease 2019 (COVID-19) outbreak in December 2019 in China, lung ultrasound has been increasingly utilized in patient assessment and management from triage stations to high dependency or intensive care unit (ICUs). In their publication, Huang et al reported the first recognized lung ultrasound features, which follow a peculiar pattern along the chest in an upper anterior-to-lower posterior crescendo distribution. These features can be condensed into 3 main categories: (1) B-lines that can be fused and fixed due to lack of sliding; (2) pleural line artifacts, which can present as unsmooth, discontinuous, and interrupted; and

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(3) consolidations, which can vary from small and subpleural (either patchy, strip, or nodular) to consolidations with air bronchograms.[1] Soon after, Peng et al described agreement between lung ultrasound findings in COVID-19 patients and the corresponding CT scan images. In particular, they reported the correspondence between lung ultrasound consolidations and CT images, as well as between ground-glass opacities and discrete or multifocal B-lines.[2] These early papers were only the beginning of a series of publications supporting the role of lung ultrasound during the COVID-19 pandemic in multiple settings.

1.1 | Practical advantages of ultrasound in the setting of a pandemic

In the context of COVID-19, the main advantages of lung ultrasound consist of its ability to identify subtle lung alterations early in the course of the infection, even in asymptomatic patients[3], and its ability to monitor the evolution and extension of pulmonary lesions. Given the experience in mechanically ventilated patients, it has been suggested that serial lung ultrasound repeated in a standardized manner, such as the 12-zone method, may help to track the clinical trajectory of the COVID-19 course, titrate therapy, and change ventilatory settings in severely affected patients.[4]

Although CT represents the gold standard to assess lung involvement, with a specificity superior to the nasal swab for COVID-19 diagnosis, sonography may be a valid alternative to both chest X-ray and CT scan standard radiology. Furthermore, lung ultrasound can identify alterations in the lung periphery, which correlate with histopathological findings and are generally identified only by CT, remaining hidden in a large percentage of chest radiographs.[5]

Lung ultrasound can also be performed directly at the bedside by a single operator, reducing the risk of cross contamination, reducing healthcare workers' exposure to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and relieving the personal protective equipment (PPE) shortages experienced in many healthcare facilities.[6]

In the context of an epidemic, there could be many limitations in offering standard radiology imaging. The number of cases may overwhelm the radiological department capacity; patients may be too sick to be transferred, or the shortage of personnel and PPE may limit this possibility; equipment cleaning may slow down the pace of examinations. Finally, in resource-limited settings, there may be no access to standard radiology at all. This context further emphasizes the lung ultrasound features, such as its effectiveness in both diagnosing and monitoring the progression of lung diseases, and viral pneumonia in particular. Lack of ionizing radiation exposure, ease of equipment sterilization, and considerably lower cost make point-of-care ultrasound (POCUS) the ideal choice during epidemics. Moreover, there have recently been developed low-cost portable ultrasound machines. These devices may sharply cut the costs for POCUS applications, both while purchasing and when transporting the equipment. [4]

Additionally, the lack of radiation of lung ultrasound is critically important in patients more vulnerable to radiation exposure, such as pregnant women, in whom lung ultrasound demonstrated to be a safe tool for monitoring COVID-19 disease evolution.[7]

TABLE 1 Potential roles of lung ultrasound in the management of coronavirus disease 2019 (COVID-19)

Out-of-hospital	Correctly addressing patients to the right hospital
Triage	Defining who can be safely discharged
Emergency department	Ruling in or out: recognizing the patients who need admission to the ward
Non-COVID wards	Diagnosing asymptomatic COVID-19 positive patients on a ward
COVID wards	Identifying COVID-19 patients who are likely to deteriorate
Intensive care unit	Setting, monitoring, and weaning from ventilation
Operating room	Better patient risk stratification and selection
Family medicine	Home evaluation and patient follow-up

In this paper, we propose a detailed list of possible clinical and research uses of lung ultrasound in COVID-19, some of which remain unexplored. In particular, we highlight the potential lung ultrasound relevance in a comprehensive series of settings during the COVID-19 outbreak, from out-of-hospital scenarios to hospital settings and finally to outpatient care (Table 1).

2 | POSSIBLE LUNG ULTRASOUND ROLES IN THE EMERGENCY SETTING

2.1 | Lung ultrasound for out-of-hospital patient evaluation and ED triage

At the onset of an unexpected COVID-19 outbreak, EDs working at the front line experienced an uncontrolled and large patient influx. As a result, the risk of infection, both for the healthcare personnel and other ED patients, had to be contained. On the other hand, undertriaging could lead to loss of lives and cross-infections. Identification of those patients who could be safely sent home and self-quarantined was mandatory. In the early phase of the epidemic, an initial patient screening was based on clinical and epidemiological criteria (pretriage). As the infection transmission in the community significantly increased, these criteria lost their utility. Therefore, it became vital to find one or more clinical screening tools able to quickly identify suspected COVID-19 cases, even in the absence of typical symptoms such as fever and cough, and with a high negative predictive value. At the epicenter of the epidemic in Italy, a group of clinicians tried to coordinate their efforts sharing ideas via regular web meetings. Implementation of both lung ultrasound and rapid walking test (RWT) was proposed to improve nurse-led pretriage accuracy. The RWT has been designed to detect silent hypoxemia, comparing peripheral oxygen saturation before and after a 30-meter walk at maximum speed. Patients with desaturation

at RWT were admitted to the ED for further assessment by a clinician. For those patients with a negative RWT, adding an imaging exam such as lung ultrasound could play a crucial role by revealing subtle pathological findings at the time of ED presentation. Hence, the combination of a normal lung ultrasound and a negative RWT could help select patients who could be safely discharged home from triage and reduce ED crowding, reducing the time-consuming wait for swab test results.[8] Later on, Piliego et al[9] proposed a lung ultrasound-guided triage algorithm with the integration of sonographic findings with patient's oxygen saturation on room air and SARS-CoV-2 real-time reverse transcription-polymerase chain reaction (RT-PCR) test. The current application of lung ultrasound into triage flowcharts is limited by the lack of standard scanning protocols and operator experience, which may influence the validity and interpretation of test results. Although prospective studies have not yet validated lung ultrasound-based triage, this concept paves the way for further research efforts aimed at preventing an overwhelmed healthcare system during a possible second wave of a viral pandemic.

Some countries attempted to centralize COVID-19 patients in dedicated facilities maintaining some "COVID-free" institutions but, with the rise of infection incidence, this straight division may no longer be feasible. However, in the out-of-hospital setting lung ultrasound assessment led by trained personnel may help to route more acute patients to the appropriate care center. To this extent, uniform training and scanning protocols are required to yield reliable evaluation. Although aimed at different acute conditions, there are some data suggesting a steep learning curve and promising outcomes in differentiating lung ultrasound patterns of acute heart failure and chronic obstructive pulmonary disease acute exacerbation.[10] Furthermore, out-of-hospital lung ultrasound may reduce extra staff exposure to cross-contamination and contribute to maintaining a clean pathway for non-COVID patients.

2.2 | Lung ultrasound for early COVID-19 diagnosis

The initial decision whether or not to admit a patient based on RT-PCR swab results has gradually lost its value because of low sensitivity of the test,[11] shortage of available tests, and limited processing capacity by laboratories. While awaiting RT-PCR test results, other patients and staff have also been unnecessarily exposed to contamination risk. Although lung ultrasound has shown high sensitivity for pulmonary lesions and can overcome the time gap of swab results, its low specificity remains a burden. Volpicelli et al reported to have identified a new sign, called "light beam," in 48 out of 49 COVID-19 positive patients.[12] This sonographic sign is a band-form finding arising from a large portion of the pleural line creating an "on–off" effect as it appears and disappears from the screen with the respiratory cycle. Signs seen in the lung ultrasound of patients with COVID-19 are similar to those extensively described in patients with other types of lung disorders. What may give specificity to the light beam sign is the distribution of the pattern in the current epidemiological context.[13] However, patients with previous lung conditions where pre-existing sonographic findings could overlap COVID-19 related acute patterns remain a significant challenge. For this reason, Volpicelli et al proposed a classification based on specific lung ultrasound patterns and the presence of clinical confounding factors, which divides ED patients into 4 categories. COVID-19 likelihood would rise starting from the group with a normal lung ultrasound and low probability of infection to the group with bilateral pathological lung ultrasound futures. Lung ultrasound could identify the COVID-19 patients prior to any tests, helping clinicians to establish the correct treatment course, as well as discharge home or early referral to an intensive care physician.[12]

A protocol that incorporates a lung ultrasound scoring system and supplemental oxygen requirement at the time of examination is currently being validated in a multicenter prospective trial in Australia and New Zealand EDs to help risk-stratify suspected COVID-19 patients. The protocol aims to provide instant, objective information of the severity of the disease to the emergency clinician in order to develop appropriate care plan.[14]

To date, the superiority of lung ultrasound alone as compared to a combined score of both sonographic and clinical findings for identification of COVID-19 patients in ED has yet to be investigated. Additional work is needed to overcome the temporal challenge and low sensitivity of the standard tests.

3 | POSSIBLE LUNG ULTRASOUND IMPLICATIONS FOR MEDICAL WARDS

3.1 | Lung ultrasound for the detection of silent COVID-19 infection

In order to reduce cross-contamination and properly allocate resources in the medical wards, some hospitals attempted to implement 3 pathways differentiating COVID-19 from non-COVID-19 patients for each area: those with confirmed infection, those with pending test results but high clinical suspicion and those with a negative swab test. This last group of patients usually followed a "clean track" as they presented with other acute issues (eg, stroke, acute coronary syndrome) and low probability of COVID-19 infection. However, as infection spread became uncontrolled, asymptomatic carriers may have been assigned to this "clean track," becoming an unrecognized contagion source. In this regard, several accidental lung findings suggestive for COVID-19 pneumonia have been reported in asymptomatic patients as incidental findings in radiological examinations performed for other indications.[15] Hence, admitting those patients to a non-COVID ward represented a potential risk for the other patients and the staff.[11] A lung ultrasound performed after the admission in a non-COVID area holds the promise of early detection of sonographic features suspicious for COVID-19 pneumonia, or at least confirmation of the absence of findings consistent with the disease. However, because pre-existent lung conditions could be confounding, patients should be monitored over time. Integration of lung ultrasound findings together with vitals parameters such as oxygen saturation

could be of help in detecting asymptomatic positive patients in the ward. Further research studies are required to confirm this hypothesis.

3.2 | Lung ultrasound for predicting clinical deterioration

Once COVID-19 patients are admitted to the ward, their response to treatments varies markedly. Recent observational data and clinical experience have suggested that there could be different phenotypes of patients with COVID-19, which could explain the wide range of clinical presentations, response to therapies, and outcomes.[16] Early detection of patients who are likely to develop critical illness is crucial and may aid in promptly escalating the level of care and optimizing the use of limited resources.

Liang et al investigated the accuracy of several clinical and radiological variables on admission to the hospital in a risk prediction score based on a cohort of COVID-19 patients in China. From 72 potential predictors, 10 variables were selected as independent predictive factors to estimate the risk of developing critical illness defined as admission to the ICU, invasive mechanical ventilation (IMV), or death.[17]

To date, there are few studies on the prediction risk of admission to the hospital and no published data are as yet available on lung ultrasound as a predictive tool for a patient's deterioration.[18] A methodical approach should be followed, as predictions regarding a patient's condition deteriorating could be unreliable and cause more harm than benefit in clinical decisions. The authors of this review are all committed to producing qualitative and transparent research and wish that such research would adhere to the guideline proposed by the Equator network, that is the transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD).[19]

At present, we are aware of ongoing observational studies in the medical community, which are considering integration of clinical, laboratory, and ultrasound data to develop and validate a prediction tool that can accurately anticipate the need of IMV in patients admitted to hospital.[20] Interestingly, each study is considering a multiorgan sonographic approach rather than solely lung ultrasound, with cardiac and diaphragm ultrasound being the main targets.

4 | POSSIBLE LUNG ULTRASOUND IMPLICATIONS IN INTENSIVE CARE UNIT

4.1 | Lung ultrasound for aeration monitoring in mechanically ventilated patients

The ideal ventilatory management of patients with COVID19-induced ARDS has not been defined yet. In classical ARDS, a distinction between a diffuse and a focal loss of aeration pattern is essential as it correlates to a different response to intrathoracic pressure increase (positive end-expiratory pressure [PEEP], tidal ventilation, or recruitment maneuvers) and hyperinflation risk. Lung ultrasound can discriminate between the 2 patterns and can identify recruitable and nonrecruitable regions of the lung parenchyma.[21] As a result, lung ultrasound may lead clinicians to set a specific ventilation strategy aiming for a better outcome.[22,23] A validated sonographic score (lung ultrasound aeration score) is based on the recognition of 4 different lung aeration patterns. The conversion of these patterns into numerical variables provides quantifiable measures that allow clinicians to follow up aeration changes.[24] A second dynamic score (lung ultrasound re-aeration score), built on the same mechanism, provides data on aeration over time.[25] This latter score correlates tightly with the pressure-volume curve method when assessing PEEP-induced lung recruitment in ARDS patients. [26]

COVID-19-related respiratory failure frequently shows an initially maintained respiratory system compliance, with poor systemic oxygenation (called L phenotype). Some of them may deteriorate to a poorer condition with lower compliance (H phenotype), which resembles classical ARDS.[27] Even though the ideal ventilatory management of COVID-19-induced ARDS (CARDS) has not been defined yet, the aforementioned scores might be used to assess the amount of lung recruitment obtained by a specific ventilation mode, the response to negative fluid balance, and the effects of therapies or prone positioning.[28] Moreover, lung ultrasound may provide daily information about the patient's lung status, reducing the need for repeated chest X-ray and CT scan with their related risks and resource consumption.[29]

4.2 | Lung ultrasound for timing successful weaning in COVID-19 patients

By means of the same scores, lung ultrasound can detect changes in lung aeration occurring during a spontaneous breathing trial (SBT) and predict the risk of post-extubation failure.[30] To date, the available recommendations on weaning plan for ventilated COVID-19 patients follows standard protocols of the general population.[31] As suggested by current experience COVID-19 patients may require prolonged respiratory support with mechanical ventilation.[32] Because aeration loss is only one of the leading causes of weaning failure, lung ultrasound findings should always be correlated to clinical parameters, laboratory results, and radiological imaging.

The usefulness of lung ultrasound in weaning ventilated COVID-19 patients has yet to be investigated. Ideally, lung ultrasound could aid in optimizing aeration condition prior to SBT, to identify and treat other concomitant conditions such as effusion or atelectasis and select the best ventilation support strategy in the postextubation phase, such as high flow nasal oxygen or non-invasive ventilation.

5 | RESEARCH NEEDED AND UNANSWERED QUESTIONS

The uses of lung ultrasound previously discussed follow the worsening status of many patients with COVID-19. However, the authors feel

more research is required of less explored applications beyond the already established role for lung ultrasound.

5.1 | Possible use of lung ultrasound for patient selection in perioperative medicine

A surgical procedure carries a burden of inflammatory response and general anesthesia is correlated with a high risk of pulmonary complications. The physiological surgery-related thrombotic risk might worsen in COVID-19 patients due to a well-described, complement-mediated thrombotic microangiopathy, and surgical risk of these patients may be further increased.[33] Our hypothesis is that the ability to identify asymptomatic infected patients by lung ultrasound prior to surgery may help in patient selection, anesthetic management, and postoperative monitoring. This may be especially helpful for surgical cases admitted from the ED, where a decision between to proceed or to postpone the intervention could be taken according to lung ultrasound findings. In this regard, the Chinese Society of Anesthesiologists recently provided a consensus on POCUS applications for lung, diaphragm, heart and airways in perioperative settings.[34] We think that early detection of COVID-19-positive patients in presurgery settings could avoid poor outcomes, reduce staff exposure to contamination, and improve correct resource allocation, but all these aspects need further investigations.[35,-37]

5.2 | Possible lung ultrasound implications in outpatient care

According to the Imperial College COVID-19 response team, the number of cases has been highly underestimated as the majority of the cases are asymptomatic or manifest minimal symptoms.[38] Safety measures such as home-based self-isolation and lockdown have been adopted in several countries to prevent contagion, learning from Chinese colleagues' experience. However, as the economic and social activities restart, the pandemic cannot be contained solely by hospitals, and further efforts from out-of-hospital healthcare professionals such as general practitioners are required. The feasibility of lung ultrasound in the community has been previously proven, and its application as a screening tool in nursing home has been described.[39,40] In this specific scenario, we hypothesize that 3 main categories of outpatients may benefit from lung ultrasound. The first are those with mild symptoms who do not require urgent medical aid but who would benefit from early finding of any changes on lung ultrasound to predict progression of their disease process and clinical deterioration. The second are those who have been successfully discharged from hospital and may require a proper follow-up over time. The last are the close contacts of a known case who may receive serial lung ultrasound exams to catch any imaging change. Combining the RWT, pulse oximetry, and lung ultrasound scan with a hand-held portable device could ensure a proper home-based assessment and identify patients who might need further medical assistance.

5.3 | The need for lung ultrasound standardization in COVID-19

Recently, an Italian group of experienced sonologists proposed a standardized approach to optimize the use of lung ultrasound in patients with COVID-19, mainly focusing on equipment, procedure, classification, and data sharing.[41] However, some practical factors need to be considered prior to define scanning techniques. An already established lung ultrasound score based on the 6-regions-per-side approach provides a proper assessment of lung aeration.[24] Moreover, the posterior scan regions must be incorporated into the standard scanning technique as they are frequently involved in the disease evolution. Lastly, despite having many sonographic similarities with other well-known lung conditions, COVID-19 pneumonia might have its own specific sonographic findings, or distribution of findings, which may change the classical "white-or-black" approach of POCUS we are used to.

6 | CONCLUSION

Growing evidence supports the utility of lung ultrasound in COVID-19 patients, but data from multicenter observational studies are still lacking. Lung ultrasound may play strategic roles in the management of COVID-19 patients from their initial presentation to ED, during their hospitalization and after discharge in the community. Hence, a rapid, multidisciplinary, and comprehensive effort to find out the more accurate lung ultrasound protocol and its usefulness when adopted alone or integrated to other clinical parameters is urgently needed to improve patient care as well as healthcare workers' safety.

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CONFLICTS OF INTEREST

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