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Clinical application of Lung Ultrasound for the management of pregnant women with suspicion of COVID-19: a review of literature

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ABSTRACT

COVID-19 is an infectious illness caused by a virus named SARS-CoV-2. Recent studies underlined the need for chest computed tomography (CT) in COVID-19 patients to assess lung involvement. However, CT has a series of disadvantages, such as the need to move the patient from an isolation room to a Radiology Department, the difficulty in protecting and disinfecting the machine, the high cost of the equipment. These disadvantages apply especially to pregnant women, in particular because of the exposure to a significant amount of radiation to the fetus.

In order to avoid these disadvantages, a series of manuscript were published on the alternative use of Lung Ultrasound (LUS) during COVID-19 outbreak. Therefore, we carried out a review of the published studies and case reports, in order to underline the advantages, the correct technique, the typical LUS manifestations of COVID-19 and to help researchers in the diagnosis and monitoring of the disease, especially for obstetricians and gynecologists who already use ultrasound in their clinical practice.

SOMMARIO

COVID-19 è una malattia infettiva causata da un virus chiamato SARS-CoV-2. Studi recenti hanno sottolineato la necessità della Tomografia Computerizzata del torace (TC) nei pazienti COVID-19 per valutare il coinvolgimento polmonare. Tuttavia, la TC presenta una serie di svantaggi, come la necessità di spostare il paziente da una stanza di isolamento a un reparto di radiologia, la difficoltà nella protezione e disinfezione della macchina, l'alto costo dell'attrezzatura. Questi svantaggi si applicano soprattutto alle donne in gravidanza, in particolare a causa dell'esposizione a una quantità significativa di radiazioni al feto.

Al fine di evitare questi svantaggi, una serie di manoscritti sono stati pubblicati sull'uso alternativo dell'ecografia polmonare (LUS) durante l'epidemia di COVID-19. Pertanto, abbiamo effettuato una revisione degli studi pubblicati e dei case reports, al fine di sottolineare i vantaggi, la tecnica corretta, le tipiche manifestazioni LUS di COVID-19 e di aiutare i ricercatori nella diagnosi e nel monitoraggio della malattia, in particolare per gli ostetrici e ginecologi che usano già gli ultrasuoni nella loro pratica clinica.

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an infectious illness caused by a virus named SARS-CoV-2. The first case was reported in Wuhan (1), but rapidly the outbreak spread all over the world. On March 11, 2020, the World Health Organization (WHO) declared COVID-19 as pandemic (2) and 412.755 cases were confirmed from all over the world on March 25, 2020 (3).

The gold standard for COVID-19 diagnosis is real-time reverse transcription polymerase chain reaction (RT-PCR) of viral nucleic acid. However, recent studies underlined the need for chest computed tomography (CT) in COVID-19 patients to assess lung involvement (4,5). Fang et al. reported the CT sensitivity as 98% in diagnosing of COVID-19 pneumonia (6). In addition, CT examination is important not only in diagnosing but also in monitoring COVID-19 patients (7). The typical CT-signs are bilateral distribution of ground glass opacities (GGO) with or without consolidation in posterior and peripheral lungs (8,9).

However, CT has a series of disadvantages, such as the high amount of radiation, the need to move the patient from an isolation room to a Radiology Department with the potential spread of the outbreak. In addition, the difficulty in protecting and disinfecting the machine, as well as the high cost of the equipment with the poor availability in developing countries have to be considered.

These disadvantages apply especially to pregnant women, in particular because of the exposure to a significant amount of radiation to the fetus.

In the last years, a series of studies have shown that Lung Ultrasound (LUS) is able to identify interstitial lung disease and acute respiratory distress syndrome (10-13), even during pregnancy (14). As a result, recent articles were published on the alternative use of LUS during COVID-19 outbreak.

Therefore, we carried out a review of the published studies and case report, in order to underline the advantages, the correct technique, the typical LUS manifestations of COVID-19 and to help researchers in the diagnosis and monitoring of the disease.

Advantages

The use of LUS in the management of patients with COVID-19 has several advantages:

- *avoid moving the patient* (15). This aspect simplifies the management of unstable patients who should be transported by an intensive care to a radiology department;
- *clinical examination and LUS execution by a single operator*. The exam can be performed directly at bed side by a single initial operator, reducing the risk of spreading the outbreak among health professionals (16);
- *establish the severity of the disease*. LUS can distinguish low-risk patients (negative lung ultrasound) from high-risk patients (with pulmonary ultrasound abnormalities), which may require second-level imaging or specific therapies (15);
- *home evaluation* (15). Thanks to the existence of portable ultrasound machines, ultrasound could be performed at home, avoiding hospitalization and overcrowding of hospitals already under pressure;
- *does not use ionizing radiation*. This advantage is particularly important in monitoring those patients who require serial exams (10);
- *less expensive than CT*. LUS is a cheaper than CT scan and more easily to use in developing country (15);
- *use in pregnant women*. LUS has proven to be a reliable method for diagnosing pneumonia in pregnant women, avoiding fetus radiation exposure (17,16).

Disadvantages

A known limitation of LUS is that this technique is unable to find deep lung lesions. In fact, the anomalies must extend to the pleura to be detectable at ultrasound, otherwise the air blocks the transmission of the ultrasound, making the execution of the CT necessary to detect pneumonia (19).

Indeed, average diameter of SARS-CoV-2 is about 120 nm, which allows it to reach the terminal alveoli, determining a peripheral pulmonary pathology (20).

METHODS

In order to allow researchers from all over the world to perform a systematic examination, Soldati et al. proposed a standardized method (21).

During the COVID-19 outbreak, LUS should be performed with a portable convex probe (3.5 mHz), connected wirelessly with a tablet. Although this device processes lower quality images than the new larger ultrasound machines, in this setting,

the wireless ultrasound machine is the most appropriate in order to avoid contamination of the machine and the operator. In fact, these devices can be easily wrapped in disposable plastic covers.
The first operator performs LUS while a second operator, placed at a safe distance from the patient, holds the tablet and freezes images or videos (16).
The protocol (21) requires that the operator analyses 14 areas for 10 seconds:

- posteriorly, along the paravertebral line and bilaterally, in the basal (above the "curtain sign"), middle (inferior angle of scapula) and apical site (spine of scapula);
- anteriorly, along the mid-clavicular line and bilaterally, above and below the internipple line;
- laterally, along the mid-axillary line, above and below the internipple line.

Furthermore, the scans must be:

- intercostals, in order to analyze a large area;
- with focal point set on the pleural line, to optimize the beam shape and to highlight more details;
- with a low mechanical index, to avoid damage to the lungs;
- free of saturation phenomena, due to high echo signal and determining completely white areas;
- without imaging modalities such as Doppler or Contrast;
- with a high frame rate;
- saved in DICOM or video format.

NORMAL AND ABNORMAL LUS PATTERN

In a healthy patient, the only lung structure that can be viewed directly by ultrasound is the pleural line, represented by a hyperechoic horizontal line. This line has horizontal movements synchronized with breathing ("***lung sliding***"). In fact, the air determinates a high acoustic mismatch: the ultrasound beam is reflected and the pulmonary parenchyma is not displayed. This reflection causes the formation of artifacts, called "***A-lines***" and represented by horizontal, parallel and hyperechoic lines (**Figure 1**). As a result, LUS can only evaluate lung disease that has an impact on the pleura (22-24).
In cases of diseases that cause partial loss of the peripheral lung, for example an interstitial pneumonia, the so-called "***B-lines***" are formed (**Figure 2**). They are represented by heterogeneous vertical artifacts probably generated by the variation of the acoustic impedances due to the disease (12,25).

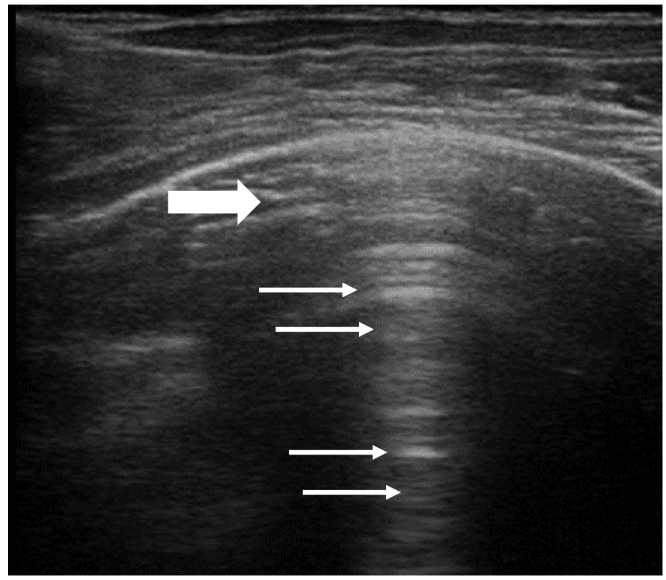

Figure 1. Lung ultrasound findings in a normally aerated lung. It is possible to see the pleural line (white thick arrow) and A-lines (white thin lines)

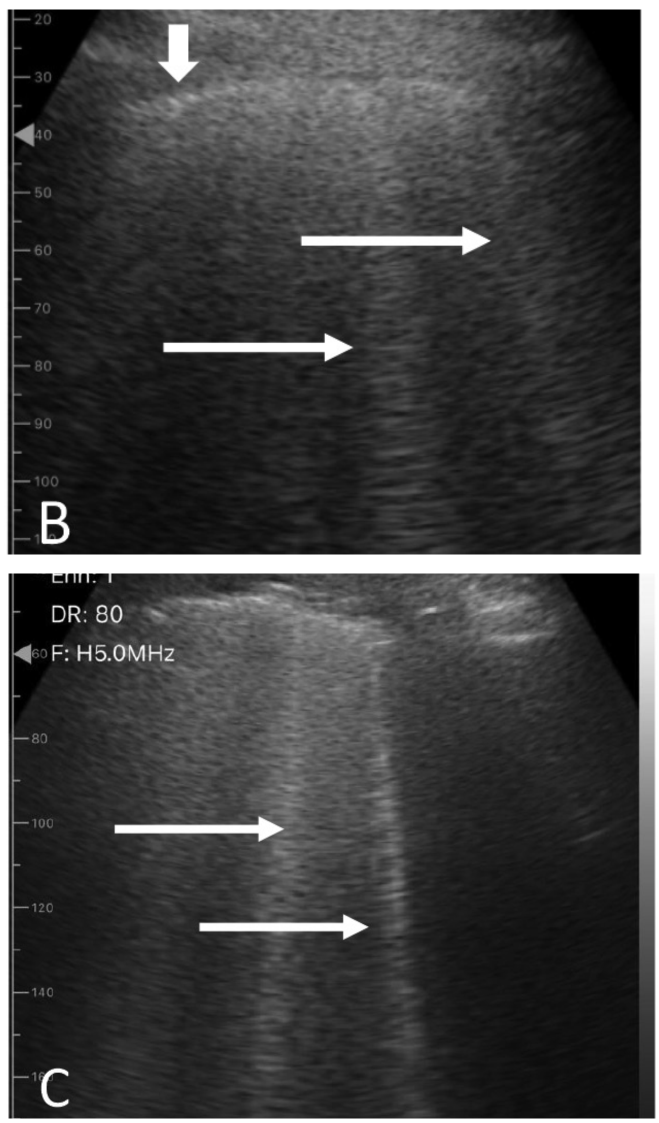

Figure 2. Lung ultrasound scan showing a vertical artifact (B-line, thin arrow) in the context of otherwise normally aerated lung with normal pleural line (white thick arrow)

On the other hand, if the density of the lung parenchyma increases without a consolidative state (12), for example in Acute Respiratory Distress Syndrome (ARDS), LUS highlights a white area in absence of A and B-lines (“***white lung***”) (**Figure 3**).
When the lung collapsed, as in pneumonia or atelectasis, it appears as an irregular hypoechoic area, the ***consolidation*** (12,25), comparable to the liver (**Figure 4**).
Instead, the ***pleural effusion*** is due to collection of fluid in the pleura. It appears completely anechoic or with hyperechogenicity due to blood, pus, fibrin (26).

LUS manifestations of COVID-19

Xu et al. reported that SARS-CoV-2 uses angiotensin-converting-enzyme-2 (ACE2) as the cell receptor, resulting in an interstitial lung damage (27). **Table I** shows the LUS manifestations of COVID-19 in the published articles. The lesions are found mainly in the posterior fields of both lungs (20). The findings identified were:

- B-lines;
- subpleural consolidations;
- thickening of the pleural line with irregularities or discontinuations, probably secondary to the reduced air content of the lung (20);
- regions of white lung;
- air bronchograms and pleural effusions are rare.

Since these findings are shaped following variations in acoustic impedance, LUS indirectly highlights the histopathological changes, which can also be recognized by CT (29).
Furthermore, the results are related to the severity of the disease (19).
Based on published articles (19,20,28), an irregular and rare distribution of B-lines and small white lung regions are found in the early and less severe stages of pneumonia COVID-19. Subsequently, these lesions involve an increased lung surface. Subpleural consolidations with associated areas of white lung appear in the more advanced stages. When these consolidations increase, located mainly in a gravitational position and possibly associated with air bronchograms, they indicate the evolution towards respiratory insufficiency.
Comparing ultrasound images with CT scans, Haung et al. found comparable findings. However, CT showed a superiority in displaying intrapulmonary and apical lesions, while LUS has a greater capacity to detect small peripulmonary lesions and pleural effusion (20).

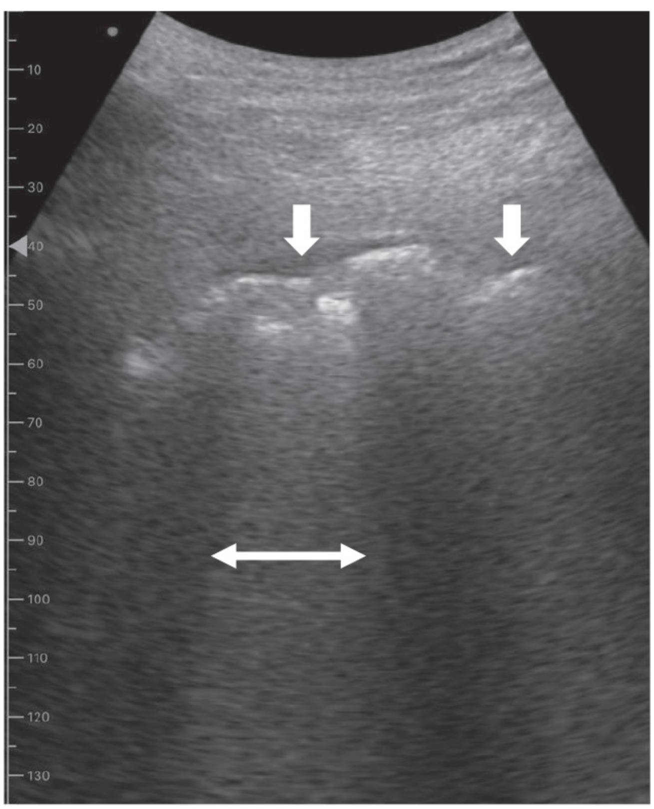

Figure 3. Lung ultrasound scan showing the small subpleural consolidations with areas of white lung. The pleura line is severely broken. Below the point of discontinuity, small consolidated areas (white thick arrow) appear with associated areas of white (double head arrow) in correspondence with the consolidations. The normal A-lines are not visible, nor single vertical artefacts. Conversely, a dense white area is visible below the pleural line (double head arrow).

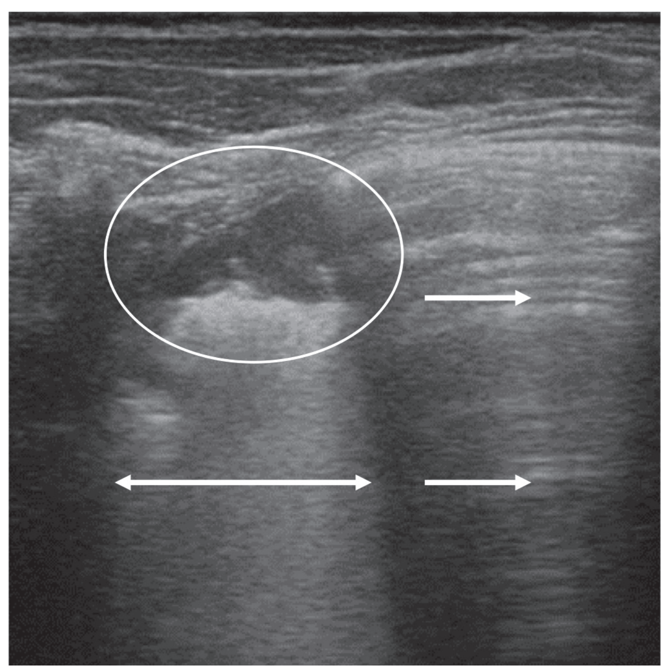

Figure 4. Lung ultrasound scan showing a subpleural consolidation (white circle), characterized by a hypoechoic area below the pleural line (white thin arrow). Below the point of discontinuity, large consolidated areas (white circle) appear with generalized white lung pattern (double head arrow). A-lines (white thick arrow) are visible in the close normal lung.

Table 1. *LUS findings of COVID-19 currently described in literature*

Authors	No. of patients	B-lines	White lung regions	Subpleural consolidation	Thickened pleural line	Air bronchograms	Discontinuous pleural line	Pleural effusion
Inchingolo et al. (16)	1	100% (1/1)	100% (1/1)	100% (1/1)	100% (1/1)	-	-	-
Poggiali et al. (27)	12	100% (1/1)	-	25% (3/12)	-	-	-	-
Huang et al. (19)	20 (examined 12 areas per patient, for a total of 240)	38% (91/240)		22% (53/240)	8% (19/240)	15% (37/240)	15% (36/240)	10% (24/240)
Peng et al. (18)	20	Yes	-	Yes	Yes	-	Yes	Uncommon
Buonsenso et al. (14)	1	100% (1/1)	100% (1/1)	100% (1/1)	100% (1/1)	-	100% (1/1)	-
Soldati et al. (20)	30	Yes	Yes	Yes	Yes	-	Yes	-

LUS Score

In order to allow researchers from all over the world to obtain comparable data, Soldati et al. proposed a LUS score for COVID19- pneumonia (21):

- ***score 0***: there are a **regular pleural line and A-lines**;
- ***score 1***: presence of vertical artifacts. Due to the inflammatory processes and the consequent change in acoustic impedances, the **pleural line appears indented** and below it is possible to identify **B-lines** and **areas of white lung** (12, 13);
- ***score 2***: presence of a **broken pleural line** with **dark and white consolidation areas** underneath. The first is related to the loss of ventilated tissue which is replaced by inflammatory tissue. The second is because of inclusions of air present in phlogistic process (12, 13);
- ***score 3***: presence of a **dense** and **widely extended white lung**.

CONCLUSIONS

Our review demonstrates that LUS is a reliable technique, useful in early diagnosis and monitoring, easier to perform, and less expensive than CT. In particular, LUS is a technique capable of diagnosing and monitoring COVID-19 pneumonia in pregnant women, avoiding excessive exposure to ionizing radiation of CT.

In addition, obstetricians and gynecologists who already use ultrasound in their clinical practice, represent a category of professionals who could easily examine the lung of pregnant patients, selecting those who need to be triaged for specialist care.

Given that COVID-19 is a global health challenge, a greater diffusion of this technique is needed in order to offer this diagnostic surveillance to as many patients as possible. The creation of a shared database is desirable, in order to create an algorithm able to identify the characteristic findings of COVID-19, developing a telemedicine program and sharing the results achieved.

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