Comparison Between Lung Ultrasound and Computed Tomographic Findings in Patients With COVID-19 Pneumonia

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Abbreviations

COVID-19, coronavirus disease 2019; CT, computed tomography; GGO, ground glass opacity; LUS, lung ultrasound; RT-PCR, reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; US, ultrasound

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Objectives—The aim of this study was to describe findings from lung ultrasound (LUS) and computed tomography (CT) in health professionals with coronavirus disease 2019 pneumonia and to evaluate the associations of the findings of both tests.

Methods—This cross-sectional observational study evaluated 45 health professionals who were initially seen in screening tents and had a diagnosis of coronavirus disease 2019 as confirmed by a reverse transcription polymerase chain reaction and lung involvement diagnosed by LUS. Subsequently, these individuals were admitted to the hospital, where chest CT was performed. Aeration scores were obtained for the LUS examinations based on the following findings: more than 2 B-lines, coalescent B-lines, and subpleural consolidations. A subjective assessment of the extent of lung disease on CT was performed on the basis of the percentage of lung parenchyma involvement as follows: 25% or less, 25% to 50%, and greater than 50%.

Results—Regarding LUS signs, more than 2 B-lines, coalescent B-lines, and subpleural consolidations were present in 73.3%, 68.2%, and 24.4% of cases, respectively. The main findings on CT were ground glass opacities, a crazy-paving pattern, and consolidations (66.7%, 20%, and 20% of cases); 17.8% of cases had examinations without abnormalities. Patients with more than 2 B-lines on LUS had more ground glass opacity areas on CT ($P = .0007$), whereas patients with subpleural consolidations on LUS had more consolidations on CT ($P < .0001$). In addition, patients with higher LUS aeration scores had more extensive disease on CT ($P < .0001$).

Conclusions—Lung ultrasound can detect lung injury even in the presence of normal CT results. There are associations between the abnormalities detected by both methods, and a relationship also exists between LUS aeration scores and the disease extent on CT.

Key Words—computed tomography; coronavirus disease 2019; COVID-19; lung ultrasound; pneumonia; severe acute respiratory syndrome coronavirus 2

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the cause of coronavirus disease 2019 (COVID-19), which was declared a pandemic several months ago.[1] The genome is similar to that of the RNA virus group that caused SARS and Middle East

respiratory syndrome.[2] Severe acute respiratory syndrome coronavirus 2 has a tropism specific to the lower respiratory tract in the initial stage of the disease, although it causes severe pneumonia in a low percentage of cases.[3] Thus, the identification of individuals with suspected COVID-19 as early as possible is crucial in the attempt to interrupt the transmission route and thus control the spread of the pandemic.[4]

Some chest imaging modalities, including lung ultrasound (LUS) and computed tomography (CT), have gained prominence in evaluating lung involvement in COVID-19 in patients with respiratory manifestations. However, the benefits and potential risks of each modality should be considered according to the context in which the patient is evaluated and the stage of disease progression. In the current state, CT is the imaging modality of choice for the imaging diagnosis of COVID-19 pneumonia, which is characterized by the preponderance of ground glass opacity (GGO) abnormalities at disease onset, followed by the development of the crazy-paving pattern and, finally, an increase in the areas of consolidation in a more advanced disease course.[5–7] Despite its usefulness, chest CT is not available in many institutions, and the disinfection of the CT scanner after use by a patient under investigation or with COVID-19 results in a delay in the care of other patients who require CT.[8] Furthermore, exposure to radiation and the limited mobility of the CT scanner may restrict the usefulness of CT scans, especially during this public health emergency with limited medical resources. Thus, in a pandemic situation, LUS may represent a valuable option to reduce the pressure on radiodiagnostic services that offer CT, especially in the context of screening patients in temporary-care structures, taking into account the imbalance between demand and imaging method availability.[9]

Coronavirus disease 2019 pneumonia is a common complication in SARS-CoV-2 infection and can be assessed by LUS in the treatment of patients with suspected lung injury.[1,4] Lung ultrasound has the advantages of being a mobile, fast, and noninvasive technology; it does not expose the patient to radiation, has the possibility of repeatability, and can be used in screening tents or campaign hospitals.[8,10] Moreover, in the COVID-19 context, an LUS examination can be performed by a clinician next to the patient, which reduces the exposure of health professionals to SARS-CoV-2 and avoids transmission of the virus during transport to other areas.[10] Although LUS signs are nonspecific when considered in isolation, the observation of some aspects may increase the diagnostic power of this modality in high-prevalence areas, and some asymptomatic or slightly symptomatic patients may have notable LUS findings, with a high probability of those findings indicating COVID-19.[3,11] Because LUS can identify changes in lung tissue that correlate both with histopathologic lesions and with CT findings, its role may be relevant in the context of the COVID-19 pandemic.[12] Despite the numerous advantages of LUS, there is still not sufficiently clear information to determine its diagnostic value in COVID-19, especially when comparing ultrasound (US) signs with chest CT findings. Thus, the purpose of this study was to describe LUS and CT findings in health professionals with COVID-19 pneumonia and to evaluate the associations of the findings of both tests.

Materials and Methods

Participants

This cross-sectional observational study evaluated 286 health professionals aged 18 years or older with a diagnosis of COVID-19 confirmed by a reverse transcription polymerase chain reaction (RT-PCR) and lung involvement diagnosed by LUS. These individuals were initially seen in screening tents set up at the Piquet Carneiro Policlinic, State University of Rio de Janeiro, where an RT-PCR was performed for all individuals, and an LUS examination was performed for those with at least 1 respiratory symptom, persistent fever in the last 3 days, pulse oximetry (oxygen saturation) below 95%, or a combination of these signs. Depending on the medical evaluation results, patients were admitted to the Pedro Ernesto University Hospital, State University of Rio de Janeiro, where chest CT was performed. We only included patients who underwent both LUS and chest CT examinations with an interval between the examinations of 24 hours or less in the study (n = 45).

The study was approved by the National Research Ethics Commission under number CAAE-30135320.0.0000.5259. All of the participants signed an informed consent form.

Lung Ultrasound

Lung ultrasound examinations were performed using an Aplio XG device (Toshiba Medical Systems, Tokyo, Japan) equipped with a 7.5–10-MHz multifrequency linear transducer or 3.5–5-MHz convex transducer in the B-mode. The transducer used in all analyses was a low-frequency convex device; this transducer was selected because it allows evaluations of patients with different body shapes and standardization of the results.[13] These examinations were performed by a team of 6 clinicians with experience in the method (3 with 12 years of experience, 2 with 10 years of experience, and 1 with 7 years of experience). Each examination was performed by 2 physicians, who were blinded to each other's initial findings. These examinations were performed sequentially by each of 2 physicians and, after the US examinations were completed, a consensus among them was reached in cases of disagreement. The US examinations were performed in 6 areas of each hemithorax (2 anterior, 2 lateral, and 2 posterior). The examinations were performed with the patients in a standing position. The LUS images were examined for the following signs: more than 2 B-lines, coalescent B-lines, and subpleural consolidations. To classify lung injury by LUS, weights ranging from 1 to 3 were assigned for each of the 6 areas and for each LUS finding as follows: 1, more than 2 B-lines; 2, coalescent B-lines; and 3, subpleural consolidations. The sum of all 6 areas evaluated in the LUS represented the aeration score.[11]

Computed Tomography

Chest CT scans were performed with a helical CT scanner with 64 channels (Brilliance 40; Philips Healthcare, Cleveland, OH). The scanning time was set at 4 seconds, with a current of 458 mA in the x-ray generator and a voltage of 120 kV. The examination was performed with the patient in the supine position and during inspiratory apnea. Each acquisition consisted of a block with 250 to 400 cross sections (2 mm thick), with a distance of 1 mm between sections. The images were represented in a square matrix of 768 rows and 768 columns. The gantry was maintained without any inclination, and an iodinated contrast medium was not used. The CT scans were independently evaluated by 3 radiologists (all with >20 years of experience with the method), and a consensus was reached in cases of disagreement. The tomographic patterns of disease probability were evaluated according to the classification previously described by the consensus of the Radiological Society of North America[14]: typical for viral infection (including COVID-19), indeterminate, atypical, and negative for lung disease. The CT scans were also temporally evaluated by the categories described by Pan et al,[5] who estimated the stage of disease progression as follows: stage 1 (0–4 days), initial; stage 2 (5–-8 days), progression; stage 3 (9–13 days), peak; and stage 4 (≥14 days), absorption. In addition, a subjective evaluation of the extent of lung disease was performed on the basis of the percentage of lung parenchyma involvement as follows: 25% or less (A), 25% to 50% (B), and greater than 50% (C).

Statistical Analysis

The normality of the data distribution was assessed by the Shapiro-Wilk test, and because a substantial number of variables did not have a normal distribution, nonparametric tests were selected. The median and interquartile range or frequency values and percentages were used to express the results. The inferential analysis consisted of the Kruskal-Wallis analysis of variance for comparisons between subgroups or the Mann-Whitney test for comparisons between 2 subgroups. The Dunn multiple-comparison test was applied to identify which subgroups differed significantly from each other. Categorical data were compared by the χ^2 or Fisher exact test. The significance level adopted was 5%. The statistical analysis was performed with SAS version 6.11 software (SAS Institute Inc, Cary, NC).

Results

Among the 45 participants who were initially evaluated by LUS and who were admitted to the hospital and underwent a chest CT examination within 24 hours after undergoing the LUS examination, 17 (37.8%) were men, and 28 (62.2%) were women, with a median age of 44 (interquartile range, 36–53) years; 6 (13.3%) were older than 60 years. Respiratory symptoms were present in 26 (57.8%) participants, while 13 (28.9%) had diagnosed comorbidities (including diabetes, cardiovascular disease, and chronic

lung disease). In our sample, 11 (24.4%) patients required supplemental oxygen, and 10 (22.2%) had respiratory failure or a sufficiently severe presentation to be admitted to the intensive care unit.

Regarding LUS signs, more than 2 B-lines were present in 33 (73.3%) cases; coalescent B-lines were present in 28 (68.2%) cases; and subpleural consolidations were present in 11 (24.4%) cases. The median sum of all 6 areas evaluated by LUS represented an aeration score of 6 (3–10). When LUS signs were compared with clinical data, we observed that patients with respiratory symptoms had higher aeration scores than those without respiratory symptoms (10 [8–13] versus 3 [2–5]; $P < .0001$). We observed that patients with comorbidities had more areas of subpleural consolidation on LUS and higher aeration scores than those without comorbidities (53.8% versus 12.5%; $P = .006$; 13 [10–15] versus 4.5 [2–7]; $P < .0001$, respectively). We also observed that patients with respiratory failure or a sufficiently severe presentation to be admitted to the intensive care unit had more areas of subpleural consolidation on LUS and higher aeration scores than those without these characteristics (80% versus 8.6%; $P < .0001$; 14.5 [11–16.5] versus 3 [2–4]; $P < .0001$).

The CT scan findings were classified as typical and indeterminate for lung disease in 29 (64.4%) and 8 (17.8%) participants, respectively. Interestingly, 8 (17.8%) patients had normal CT findings, despite changes observed with LUS. When the abnormal CT scans (n = 37) were categorized on the basis of the classification of Pan et al,[5] 25 (67.6%) cases were stage 1, and 12 (32.4%) were stages 2 and 3; no cases were stage 4. Ground glass opacities, the crazy-paving pattern, and parenchymal bands were observed in 30 (66.7%), 9 (20%), and 8 (17.8%) cases. In these CT examinations, consolidations, the halo sign, and subpleural lines were observed in 9 (20%), 7 (15.6%), and 3 (6.7%) cases. Regarding disease extent on CT, 31 (68.9%), 11 (24.4%), and 3 (6.7%) cases were

Figure 1. Association between patients with more than 2 B-lines on LUS and patients with GGOs on CT ($P = .0007$).

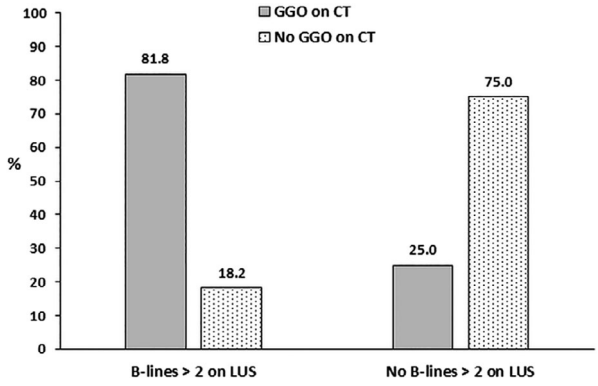
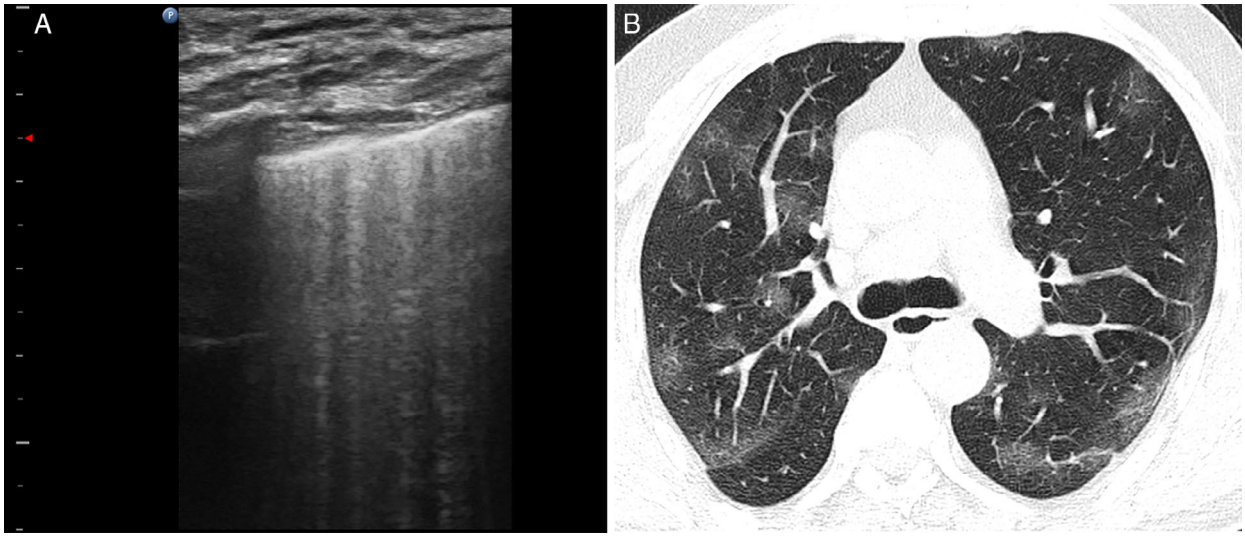


Figure 2. A 48-year-old female nurse was admitted with complaints of cough and high fever for 2 days. Lung ultrasound showed multiple B-lines (**A**), whereas chest CT showed GGOs in both lungs (**B**).



classified as A, B, and C. When the CT findings were compared with the clinical data, we observed that a higher percentage of patients with respiratory symptoms, compared with those without respiratory symptoms, had a lung disease extent of greater than 25% on CT (53.8% versus 0%; $P < .0001$). We also observed that patients with comorbidities, compared with those without comorbidities, had a lung disease extent of greater than 25% on CT (76.9% versus 12.5%; $P < .0001$).

We also evaluated the relationship between LUS signs and CT findings. In this analysis, patients with more than 2 B-lines on LUS had more GGO areas on CT than those without more than 2 B-lines on LUS (Figures 1 and 2). Patients with subpleural consolidations on LUS had more areas of consolidation on CT than those without subpleural consolidations on LUS (Figure 3). In this study, confluent B-lines on LUS were not associated with any specific CT finding. Finally, we evaluated the associations between the LUS aeration score and the various classifications by chest CT (Table 1). Interestingly, patients with higher LUS aeration scores had more extensive and more advanced disease on CT.

Additionally, we evaluated the LUS findings of the 241 patients who underwent LUS examinations without CT scans. In this sample, more than 2 B-lines were present in 187 (77.6%) patients; coalescent B-lines were present in 61 (25.3%) patients; and subpleural consolidations were present in 16 (6.6%) patients. The median sum of all 6 areas evaluated by LUS corresponded to an aeration score of 4 (2–6). When compared with 45 patients undergoing CT, we observed that patients without CT scans had fewer coalescent B-lines, fewer areas of subpleural consolidation, and lower aeration scores on LUS (25.3% versus 62.2%; $P < .0001$; 6.6% versus 24.4%; $P = .0001$; 4 [2–6] versus 6 [3–10]; $P < .0001$, respectively).

Figure 3. Association between patients with subpleural consolidations on LUS and patients with areas of consolidation on CT ($P < .0001$).

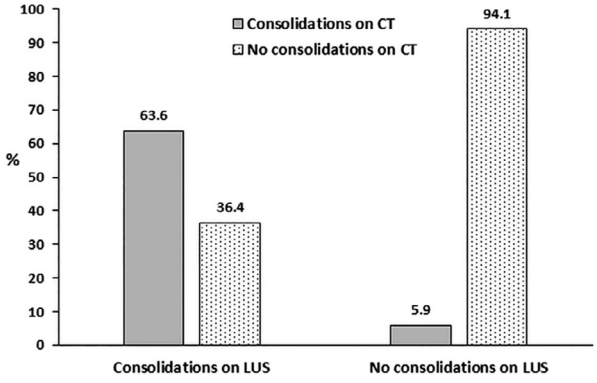


Table 1. Aeration Scores on LUS According to the Various Classifications Assessed by Chest CT

CT Finding	n	Aeration Score on LUS	*P*
Probability pattern			.026
Negative	8	2.5 (2–7)	
Undetermined	8	5 (1.5–7.8)	
Typical	29	10 (5–13)	
Pan category			.39
Stage 1	25	6 (2.5–10.5)	
Stages 2 and 3	12	9 (4.3–13.3)	
Pulmonary involvement, %			< .0001
<25	31	4 (2–6)	
25–50	11	10 (10–13)	
>50	3	27 (24–41)	

Data are presented as median (interquartile range) where applicable.

Discussion

Because of the spread and extremely rapid advancement of COVID-19, early screening, comprehensive detection, and infection monitoring by imaging methods are required, especially with regard to COVID-19 pneumonia caused by SARS-CoV-2. In this context, LUS has been increasingly used as a promising tool for the evaluation of COVID-19 pneumonia lesions, as these lesions show a predominantly peripheral distribution, rendering detection by LUS more appropriate.[15,16] In this study, the following were the main findings: In health professionals with COVID-19 pneumonia, LUS was a very sensitive test for the detection of lung lesions; almost 20% of our cases involved normal CT results despite changes on LUS. Patients with respiratory symptoms or comorbidities had more extensive disease on both LUS and CT. There was a relationship between the LUS aeration score and the extent of lung disease on CT. In addition, we observed an association between more than 2 B-lines on LUS and GGO areas on CT

as well as between subpleural consolidations on LUS and consolidation areas on CT. To our knowledge, this was the first study that evaluated the associations between LUS and CT findings in detail, considering the extent of lung involvement in a more representative sample.

The combination of US signs within certain patterns and their correlation with SARS-CoV-2 identification methods in different COVID-19 phenotypes may allow effective characterization of lung involvement and assist in patient screening and admission.[3] In this sense, we used LUS together with clinical evaluations and RT-PCR assays in screening tents to detect COVID-19 pneumonia in patients who had at least 1 respiratory symptom, persistent fever in the last 3 days, oxygen saturation below 95%, or a combination of these signs. In fact, LUS can help inform clinical decision making for patients with COVID-19 and the management of their associated lung injury.[17] In individuals with respiratory symptoms in high-prevalence areas, the combination of clinical and anamnestic data with LUS signs may represent an important aid to assess pulmonary involvement by SARS-CoV-2, especially in places where CT is not available.[18]

Importantly, almost 20% of our participants had normal CT findings within the first 24 hours after undergoing LUS examinations, with high sensitivity of LUS for the detection of COVID-19 pneumonia.[19]In line with our findings, Bernheim et al[20] observed that 20 (56%) of 36 symptomatic patients with COVID-19 evaluated in the initial phase (0–4 days) had normal chest CT findings. These authors observed that with the progression of time after symptom onset, chest CT findings consistent with COVID-19 were more frequent, including a greater extent of lung involvement. By evaluating 29 patients with COVID-19 pneumonia using LUS and CT divided into 12 regions (interval between tests ≤12 hours), Yang et al[15] observed that in a total of 540 lung regions, 340 (63%) had abnormal signs on LUS, whereas only 209 (38.7%) had abnormal findings on CT. By evaluating 51 patients with confirmed or highly clinically suspected COVID-19, Tung-Chen et al[21] observed radiologic signs compatible with COVID-19 pneumonia in 40 patients on LUS and in 37 patients on chest CT. Other studies have also shown the high sensitivity of LUS in the detection of lung lesions caused by SARS-CoV-2 at different times during disease progression.[18,22]

In COVID-19 pneumonia, histopathologic lesions involve the distal regions of the lung, with characteristics including edema, alveolar damage, interstitial thickening, and gravitational consolidations.[12] Therefore, the imaging diagnosis of COVID-19 pneumonia is facilitated by a surface imaging technique.[17] Thus, the greater sensitivity of LUS relative to CT can be explained at least in part by the fact that SARS-CoV-2 induces lesions in the lung periphery, rendering such lesions particularly suitable for LUS investigations.[3] In fact, the lung characteristics of patients with COVID-19 pneumonia are ideal for LUS, since the manifestations are visible in the posterior and inferior areas of the lung and in the subpleural areas, which can be reached by US.[19]Furthermore, LUS is highly sensitive to variations in the balance between air and fluids in the lung, and because COVID-19 pneumonia is characterized by alveolar-interstitial damage with inflammatory exudation and edema, it can be clearly detected by LUS.[15]

Although LUS is highly sensitive for the detection of multiple lung disorders, including COVID-19 pneumonia, this method does not depict pathognomonic signs related to SARS-CoV-2 in the lungs; therefore, abnormal signs in COVID-19 pneumonia should be interpreted with caution.[23] In fact, abnormal LUS signs in COVID-19 pneumonia such as B-lines and consolidations are present in many other interstitial and alveolar-interstitial lung diseases, including viral pneumonia of different etiologies (eg, H_1N_1 and H_7N_9 influenza viruses), *Pneumocystis jirovecii* pneumonia, idiopathic or secondary pulmonary fibrosis, hypersensitivity pneumonitis, congestive heart failure, and diffuse alveolar hemorrhage.[18,23,24] Integration of clinical data, epidemiologic findings, and LUS signs is necessary for the differential diagnosis between COVID-19 pneumonia and other conditions with similar US manifestations. Thus, LUS signs must be considered in the context of the pandemic, and laboratory tests to confirm COVID-19 are still required to support clinical decision making.

In this study, the most common signs on LUS were focal B-lines, which were present in almost two-thirds of the cases. Because LUS examinations were performed during the first approach to patients, it is

possible that focal B-lines are among the main characteristics in the initial stage of COVID-19. Our findings are in agreement with a study by Yasukawa and Minami,[8] who observed that all patients had thick irregular pleural lines and B-lines. The histopathologic aspect of initial COVID-19 pneumonia is characterized by alveolar damage and irregular inflammatory components, which correlate with B-lines on LUS in several ways.[3,9] In our sample, subpleural consolidations on LUS were observed in less than 25% of cases, unlike in the sample studied by Xing et al,[25] who observed this finding in 50% of cases. However, it is important to note that these authors evaluated 20 patients with COVID-19 pneumonia at different stages of the disease, most of whom were in critical condition, whereas the patients in our study were evaluated by LUS at an earlier time point, even before hospitalization. It is also worth noting that patients with respiratory symptoms or comorbidities had higher aeration scores and more subpleural consolidations on LUS, which indicates that there may be a relationship between clinical findings and LUS signs.

Although chest CT findings may be normal or indeterminate during the very early stage of COVID-19, the initial findings usually include only GGO areas, and then areas of consolidation appear in the lungs with disease progression.[26] The most common finding in our sample was GGOs, observed in almost 70% of cases; this indicated a characteristic of our sample, which predominantly involved cases still in an early phase of COVID-19. This fact was corroborated by the classification of Pan et al[5]; 67.6% of the cases were stage 1 when the classification method was applied to our sample. We observed consolidation areas in only 20% of cases; these lesions are more frequent and have a greater extent in critically ill patients and indicate that the alveoli are filled with inflammatory exudation.[27] Importantly, patients with respiratory symptoms or comorbidities had more extensive disease on CT, which supports the importance of evaluating tomographic data in light of clinical findings.

A relationship exists between LUS and chest CT findings in patients with COVID-19. In fact, in our study, there was an association between more than 2 B-lines on LUS and GGO areas on CT as well as between subpleural consolidations on LUS and consolidation areas on CT, which was in agreement with the previous observations by Peng et al[26] and Lomoro et al.[28] In COVID-19, early-diagnosed B-lines may be a sign of the acute phase of GGO lesions during the early dissemination of active disease, when limited areas of lesions alternate with preserved lung parenchyma.[3,8] The presence of consolidations, whether on LUS or CT, probably correlates with the disease progression and severity based on previous studies of tomographic findings in patients with COVID-19.[3] As most patients with COVID-19 develop GGO-like lesions with a peripheral distribution that progress over time to form more consolidated changes, LUS may detect many symptomatic patients who require hospitalization.[29,30] Finally, we observed associations between the LUS aeration score and the types of patterns/percentage of involvement on CT, which demonstrates that the methods are complementary when lesions are analyzed in their entirety.

The strengths of this study included the prospective evaluations with both LUS and CT within 24 hours of each other as well as the independent reviews of images by more than a single physician. However, similar to other studies, ours also had limitations. First, the study included only health professionals, thus presenting the possibility of a sampling bias; however, our institution has developed a program to exclusively evaluate health professionals because of the considerable vulnerability of this population to SARS-CoV-2 infection. Second, our sample consisted of patients known to have COVID-19, limiting the LUS evaluation as a screening modality. Additionally, similar to almost all studies evaluating the role of LUS in COVID-19 pneumonia, our study was potentially subject to a selection bias, given that LUS examinations were performed only in patients known to have positive RT-PCR results for SARS-CoV-2. Third, we did not evaluate the evolution of LUS and chest CT images of the study population. Finally, although LUS has several advantages over other imaging modalities, it cannot detect deeper lung lesions because aerated lungs block US transmission,[26] and LUS is more operator dependent; thus, the correlation between LUS signs and CT findings is of great interest. Despite these limitations, we think that our study can serve as a theoretical framework for the design of studies aiming to evaluate LUS as a screening test. Accordingly, inclusion of all patients suspected of having COVID-19, including those with negative test results, which to our knowledge has not yet been rigorously reported in the literature, will be important.

Furthermore, our study may serve as a foundation for future longitudinal studies to further explore LUS and chest CT findings in patients with COVID-19.

In conclusion, this study showed that in a sample of health professionals with COVID-19 pneumonia still at an early stage, LUS detected lung lesions even in the presence of normal CT findings. Patients with respiratory symptoms or comorbidities tended to have more changes on LUS and more extensive disease on CT. There was a relationship between the abnormalities detected by the imaging modalities, especially between the presence of more than 2 B-lines on LUS and GGO areas on CT and between subpleural consolidations on LUS and consolidation areas on CT. In addition, there was an association between the LUS aeration score and the extent of the disease on CT.

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