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Lung ultrasonography results statistically agree with computed tomography in COVID-19 pneumonia cases from a private hospital in southern Brazil

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ABSTRACT

Introduction: Computed tomography (CT) scans can both exclude other pathological conditions and display a high level of sensitivity for COVID-19 pneumonia. Although LUS has the potential to replace these methods in patient evaluation, issues remain as to whether it can be considered a reliable surrogate in the clinical decision process.

Objective: To compare the performance of lung ultrasonography (LUS) with that of lung computed tomography (CT) scans in patients with suspected COVID-19 for the presence of interstitial pneumonia and the degree of lung injury.

Methods: In a cross-sectional clinical study, LUS and CT were compared for the presence of interstitial pneumonia and the degree of lung injury in patients with suspected COVID-19. Pearson's correlation analysis was performed to measure the degree of association between the two methods. Bland–Altman plot was applied. *P*-values ≤ 0.05 were considered significant.

Results: A good correlation between LUS and CT scan was obtained for estimates of lung injury in pneumonia in a group of COVID-19 patients ($R^2 = 0.7186$; $p < 0.01$). Agreement between LUS and CT values is assessed by constructing the Bland-Altman plot and all data points fall within ± 1.96 times the standard deviation of the difference between the results of the two methods. This corroborates that there is a strong agreement between the two methods.

Conclusions: LUS, as compared to CT scans, is an effective method to estimate degrees of lung injury in patients with suspected Covid-19 in the emergency department.

Keywords: *COVID-19; Computed Tomography; Lung Ultrasonography; Pneumonia*

INTRODUCTION

Critical care ultrasonography has gained importance in the ICU (intensive care unit) and emergency department (ED) scene over the last decade[1]. It was initially used in the evaluation of the trauma patient to disclose intra-abdominal bleeding, an approach known as the FAST examination[2]. Ultrasound-assisted deep vein puncture and bedside echocardiography follow suit. As a novel use of ultrasonography beyond the boundaries of the radiological department, the exploration of the lung somewhat lagged. The virtual absence of lung ultrasonography (LUS) uses in the realm of conventional radiology and the idea that air hampers the transmission of sound set this modality aside from the other areas of point-of-care ultrasonography. Only recently has it come of age and revealed itself as an area deserving attention in the investigation of the critically ill[3,4].

COVID-19 patients are progressively being evaluated for pulmonary compromise in emergency departments and intensive care units by LUS rather than chest XR (X-Ray) or CT (computed tomography) scan. While the

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former underperforms lung ultrasonography, the latter imposes the hindrances of patient dislocation, ionizing radiation, and waiting times for results. Although LUS has the potential to replace these methods in patient evaluation, issues remain as to whether it can be considered a reliable surrogate in the clinical decision process[5].

Decisions concerning COVID-19 patients are, firstly, whether to investigate patients presenting with respiratory symptoms in the ED and, secondly, whether discharge them from the ED or admit them to the hospital. Rarely if ever, in the course of COVID-19 disease, decisions about oxygen therapy, advanced support of respiratory function, use of anti-inflammatory drugs, anticoagulants, or antibiotics are made based on lung imaging, apart from pulmonary angiography in embolism-suspected patients. Instead, respiratory function, inflammatory markers, coagulation tests, and white blood cell counts help the clinician in therapeutic decisions. Having said that, and acknowledging that imaging is but a small part in conveying the information needed for the decision of discharging patients without investigation from the ED and about the need for admission, LUS may perform well as compared to chest XR and lung CT scans, provided that its capacity to estimate degrees of lung involvement correlate and agree with CT scans. Furthermore, US (ultrasonography) may add valuable information on alternative diagnoses of respiratory failure[6] LUS can provide quite sensitive data for lung interstitial syndrome making it a valuable alternative to other methods[7,8].

LUS could also be used in the follow-up of patients already admitted for COVID-19 pneumonia, especially when worsening of the clinical picture and lowering lung function demands an explanation. Despite its low sensitivity for interstitial syndrome, chest XR has been used on COVID-19 patients to exclude alternative diagnoses. CT scans can both exclude other pathological conditions and display a high level of sensitivity for COVID-19 pneumonia. We, therefore, decided to compare the performance of LUS with that of lung CT scans in patients with suspected COVID-19 for the presence of interstitial pneumonia and the degree of lung injury.

METHODS

In a cross-sectional clinical study, LUS and CT were compared for the presence of interstitial pneumonia and the degree of lung injury in patients with suspected COVID-19. We ranked the degree of lung compromise with the US by assigning values for pleural lesions, the intensity of B lines, and consolidation. The investigators determined the scores for both methods blinded.

For the pleural line, we attributed a value of 0 for normal, 1 for irregular pattern, and 2 for the broken line. For the presence of B lines, we attributed 0 for absent, 1 for non-confluent B lines, 2 for confluent B lines, and 3 for white lung pattern. For the presence of consolidation, we attributed 0 for absent and 1 for presence. The values obtained for each of these variables were computed for each point of the LUS examination, namely points A, B, PLAPS for the right and left lung totalizing a maximum of 36 possible points per patient. We compared these zones with topographic equivalents on CT Scans. Accordingly, CT was evaluated for ground glass opacities (GGO), consolidation and/or atelectasis, crazy paving pattern, and pleural effusion. Topographic equivalents with LUS were chosen representing in a gross mode the A, B, PLAPS points, respectively corresponding to the upper lobes, the middle lobe on the right or lingula on the left, and the lower lobes. For parenchymal opacities, in a visual scale score, we attributed value 0 for normal, 1 for up to 25% of lung compromise, 2 for 26-50%, 3 for 51-75%, and 4 for more than 75% lung compromise, applied to 6 parts of lung representing in a gross mode the A, B, PLAPS bilaterally, and to each one of the lesions. The sum was the final score, totalizing a maximum of 24 possible points per patient. We also used a specific software (Siemens Healthcare CT Pneumonia Analysis) to compare the quantitative percentage of lung compromise. Pleural effusion was considered present or absent.

The enrolment period ran from March to November 2020. Patients of both sexes, aged 18 years old and above on the day of evaluation at the ED were included. Those with previous heart and lung disease were not excluded. Active flu symptoms, fever, or desaturation not immediately explained by previous conditions were the clinical criteria for inclusion. Some of these patients were known to be positive for SARS-CoV-2 infection by previous testing. Those first tested at the department had the results available only on the days following evaluation. All participants signed an informed consent form and this study was approved by the Institutional Review Board of the National Health Council of Brazil (approval number 4.497.118).

Data were analyzed using the Statistical Package for Social Sciences (SPSS, version 23.0, Chicago, IL) and R studio available in R platform (http://www.R-project.org/). The Kolmogorov-Smirnov test was used to assess the type of distribution of quantitative variables. Pearson's correlation analysis was performed to measure the degree of association between the two methods. Bland–Altman plot was generated to provide a graphical visualization of the agreement between the two measurement methods[9]. The mean values (X-axis) were plotted against the difference between the two methods (Y-axis) to identify any systematic bias and possible outliers.

Horizontal lines were drawn at the mean difference and at the limits of agreement, defined as the mean difference plus and minus 1.96 times the standard deviation of the differences. All statistical tests in this study were two-sided and *p*-values ≤ 0.05 were considered statistically significant.

RESULTS

During the application of the protocol, 22 patients were analyzed, the data are detailed below. Male patients were 68.2% and the median age was 59 years (interquartile range [IQR]: 41.5 – 68.0). Comorbidities detected were, in order of frequency: hypertension (52.4%), unspecified cancer (23.8%), respiratory disease (19%), obesity (19%), smoking (9.5%), unspecified diabetes (4.8%), hypothyroidism (4.8%), liver disease (4.8%), immunodeficiency (4.8%), and depression/anxiety (4.8%). All patients had a positive RT-PCR test for COVID-19. During hospitalization, the median oxygen saturation of the patients was 95% (IQR: 94-98%), with a median respiratory rate of 20 respiratory movements per minute (IQR: 19-21) with 4 of these patients requiring mechanical ventilation during the period.

A good correlation by Pearson coefficient analysis between LUS and CT scan was obtained for estimates of lung injury in pneumonia in a group of COVID-19 patients ($R^2 = 0.7186$; $p < 0.01$) (**Figure 1**).

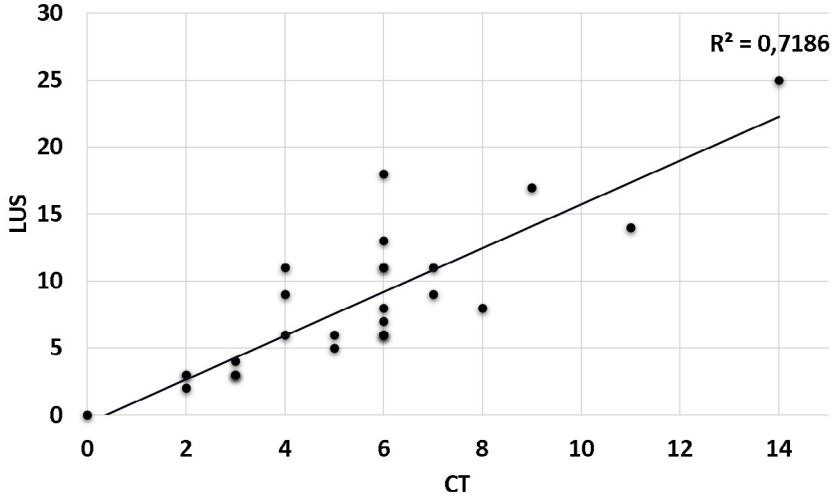

Figure 1: Pearson correlation coefficient analysis between LUS (lung ultrasonography) and CT (computed tomography).

Agreement between LUS and CT values is assessed by constructing the Bland-Altman plot (**Figure 2**). X-axis suggests the mean of LUS and CT. Y-axis was plotted by the difference between LUS and CT. All data points fall within ± 1.96 times the standard deviation of the difference between the LUS and CT values. This corroborates that there is a strong agreement between the two methods.

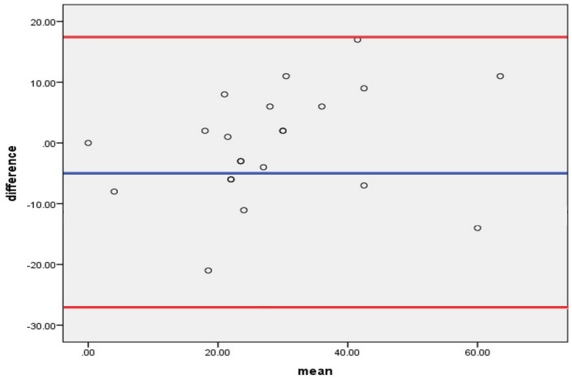

Figure 2: Bland-Altman plot for LUS (lung ultrasonography) and CT (computed tomography) results.

DISCUSSION

We studied patients being investigated at the ED for the possibility of COVID-19 infection and for clinical evaluation that resulted in discharge or admission. It is therefore unsurprising that 100 % of the patients tested positive for SARS-CoV-2 at the time of image acquisition. Some of these patients were already known to be RT-PCR positive for having been tested days before their visit to the ED. A good correlation between LUS and CT scan was obtained for estimates of lung injury in pneumonia in a group of patients with suspected COVID-19. Also, agreement between LUS and CT values was detected by Bland-Altman plot. The interstitial syndrome has been well characterized in LUS, expresses itself by the pattern of B lines, and correlates with above-normal levels of water in the lungs. Allinovi et al[10], reviewing the literature concluded that LUS can detect the interstitial lung syndrome through the evaluation and quantitation of B lines, pleural irregularities, and consolidations This syndrome is associated with intra-alveolar and interstitial fluid, a result of either hydrostatic or inflammatory edema. That said, the presence of B lines is an artifact of unspecific etiology in LUS. However, patterns of distribution amongst lung zones, like the A/B combination that suggests pneumonia, the clinical setting in which B lines are observed, namely patients with suspect heart failure, infection, or lymphangitic carcinomatosis, or, as in our series, the epidemiological context of the COVID-19 pandemic, all convey the necessary specificity for this finding to attain diagnostic utility. Accordingly, specificity increases with CO-RADS level[11].

In addition to the epidemiological context, specificity can also be affected by the definition of what is a US positive finding. Narinx et al.[12], considered US examination positive for COVID-19 when B lines were found in only one of the BLUE protocol areas. The use of a score might result in improvements in specificity. LUS has been acknowledged as high in COVID-19, whereas sensitivity scores are low[11]. However, in this meta-analysis, positivity for COVID-19 in LUS examinations is either not mentioned or constructed on limited criteria. According to the present study, specificity found by Fonsi et al[13], was significant (79%). In this context, the interstitial lung syndrome on the LUS examination of patients with a very low likelihood of alternative etiologies strongly suggests SARS-CoV-2 infection, as was the case in our series. However, not all RT-PCR-positive patients will display an abnormal LUS examination, as some patients are evaluated in the pre-pneumonic phase of their disease, and some never really develop pneumonia as part of the clinical picture of COVID-19. This explains some of the false negative results found with LUS. Accordingly, previous studies[14,15] in retrospective research with patients evaluated with LUS at the ED, found that amongst 31 RT-PCR-positive patients, 28 were detected by LUS and of 15 diagnosed by LUS, 11 were confirmed by RT-PCR positive for SARS-CoV-2. COVID-19 suggestive findings at LUS in RT-PCR negative patients may result from RT-PCR sampling in upper airways when the infection is no longer active at this site, but in the lung parenchyma, where bronchoalveolar lavage sampling may be positive[16]. Trauer et al[17] stress the importance of the background on which LUS is used for precise accuracy of LUS in COVID-19, as both sensitivity and specificity may be influenced by disease severity, pre-existing lung disease, scanning protocol, operator experience, disease prevalence, and reference standard. These limitations are being observed, and in the appropriate context, LUS can help to sort out patients to be discharged or admitted for further observation, without the need for a CT scan. This decision can be easily taken provided LUS is available in the ED, with the added advantage of avoiding a radiological approach. LUS will not tell a COVID-19 patient apart from others displaying the same interstitial features, although in the appropriate context, COVID-19 can be assumed and it accurately quantifies severity. Decisions that apply specifically to COVID-19 patients can only be implemented in the high-prevalence scenario.

The main interest of this study was to explore the capacity of LUS to quantify lung injury in COVID-19 pneumonia. We compared our score with a corresponding CT scan score, used as a gold standard. Zones A, B, and PLAPS on either side of the chest of the LUS examination were compared with topographic equivalents of the radiological examination. Scores for the whole lung were compared through correlation and agreement. We opted for a model of 6 views, although other authors prefer more extended examinations with up to 14 views[10] improved accuracy with these more extended approaches is to be demonstrated and, in our understanding, may compromise the intrinsic and distinguishing expeditiousness of the LUS examination.

We have found more B-line artifacts than consolidation. This may be because B lines are found in the early stages of the disease, whereas consolidation tends to appear later. This association has been explored in a study by de Almeida Monteiro et al[18] that opted for an original model to explore the capacity of LUS to detect patterns of the severity of lung injury in COVID-19 pneumonia, relating LUS findings to pathological specimens

obtained soon after death. Their comparison found a good correlation between subpleural and pulmonary consolidation and fibrosis, a link that could be a marker of gravity and prognosis in these patients; given the fact that fibrosis is related to a poorer outcome. On the other hand, although it is worth remembering the capacity of LUS to detect consolidation, pleural effusion, and heart failure, CT scans could probably outperform LUS when a wider differential diagnosis of respiratory conditions is entertained. Amongst the weaknesses of this study is the small number of patients investigated, although statistically significant agreement and correlation were disclosed between the methods. Also, it can be argued that the method employed to compare LUS and CT scans is new and that its reliability proper is at stake. To compensate for this objectionable feature, we most extensively explained how we constructed the scores and how they were matched. Furthermore, we acknowledged that our score is not always easily applicable. For instance, differences between confluent B lines and white lungs are not always easy to define. For the same reason, irregular and broken pleural lines are often a subtle difference. But we understand that these discriminations are often possible to establish and represent different levels of damage that should be explored. Finally, COVID-19 is no longer either a frequent or serious condition presenting at ED, although this model could be potentially applied to other conditions presenting as interstitial lung syndrome. We concluded that LUS, as compared to CT scans, is an effective method to estimate degrees of lung injury in patients with suspected COVID-19 in the ED.

Authorship

Luiz C. Pallarés and Ana P. Zanardo designed and implemented the study. Jonas M. Wolf performed the statistical analyses. Luiz C. Pallarés, Ana P. Zanardo, V. de Souza, and Jonas M. Wolf. Luiz C. Pallarés, Ana P. Zanardo, V. de Souza, and Jonas M. Wolf wrote the first draft of the manuscript and contributed to the literature review and discussion of the results. All authors contributed to and have approved the final manuscript.

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Conflicts of interest

The authors declare no conflicts of interest.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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