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Evolution of Techniques and New Protocols for Lung Ultrasound Examination in COVID-19 Pneumonia Patients

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Summary

Competent triage of patients with COVID-19 pneumonia is not only about efficient allocation of hospital resources, but also about making timely decisions that can ultimately save the patient's life. When healthcare facility is overloaded, computed tomography to assess the severity of COVID-19-associated pneumonia in each individual case is not always possible. Alternative solutions, however, are opted.

The aim of the study was to develop Lung UltraSound (LUS) protocols with high diagnostic potential for assessing the severity of pneumonia caused by COVID-19, which can be reliably used instead of CT during triage in an emergency setting.

Materials and methods. We conducted a retrospective analysis of data on 161 hospitalized patients with confirmed pneumonia caused by COVID-19, subjected to both CT and LUS within 24 hours after hospitalization. Three consecutive LUS protocols, including two LUS developed by the NMHC (National Medical Surgical Center) authors, were tested to choose the most reliable protocol for assessing the severity of lung damage in pneumonia caused by COVID-19 (based on correlation with chest CT results). We also checked the applicability of LUS for the prognosis of the disease.

Results. Moderate (<50% CT) and severe (>50% CT) lung damage can be distinguished when using both — the 16-zone and 12-zone LUS NMHC scanning protocols. The AUC for the ROC curves was almost identical: 0.83 (95% CI: 0.75–0.90 and 0.81 (95% CI: 0.73–0.88) for the 16-zone and 12-zone LUS NMHC protocols, respectively. The 16-zone LUS NMHC had an optimal threshold of 20 scores with a sensitivity of 67% and a specificity of 82%, while the 12-zone LUS NMHC provided an optimal threshold of 15 scores with the same sensitivity but lower specificity — only 73%. Neither the 16-zone nor the 12-zone NMHC LUS protocols could predict the outcome.

Conclusion. The newly developed 16- and 12-zone LUS NMHC scanning protocols for patients with pneumonia caused by COVID-19 proved to be easy to implement, demonstrating a strong correlation with CT results. The 16-zone LUS NMHC protocol is probably more relevant for triage of patients with more than 50% of pulmonary tissue involvement based on CT data. Both protocols can be useful in emergency settings and in medical institutions with limited or no access to CT.

Keywords: lung ultrasound; LUS score; COVID-19; pneumonia

Conflict of interest. The authors declare no conflict of interest.

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Introduction

Following the first few months of the COVID-19 pandemic, it has become clear that public health systems are struggling to allocate limited resources during an unprecedented increase in hospitalizations [1]. One of the most difficult tasks is still triaging and identifying patients who require hospitalization. Although PCR testing is still the gold standard for SARS-CoV-2 diagnosis, chest CT is the preferred diagnostic modality for determining disease severity in confirmed cases [2, 3]. Several studies [4, 5] have shown that CT has a diagnostic value in asymptomatic infected patients. However, limited radiology resources and strict decontamination protocols following COVID-19 examinations have jeopardized CT's widespread availability and efficacy [6–8].

Lung ultrasound (LUS) has been proposed as an effective diagnostic tool [11, 12] and is a feasible and inexpensive diagnostic option for COVID-19 pneumonia. Despite its controversial diagnostic value, LUS eventually gained widespread clinical use [13, 14]. The variability of the LUS protocols used and the lack of reproducibility for different operators [2] undermine the validity of using LUS in the triage of COVID-19 pneumonia patients.

Another issue with LUS is the lack of standardized reporting and interpretation systems [15]. The Pirogov National Medical and Surgical Center discovered early in the pandemic that the standard descriptive LUS protocol had moderate to low diagnostic value and was unacceptably time-consuming in triaging patients with COVID-19.

Therefore, the aim of the study was to propose new LUS protocols with high diagnostic performance for determining the severity of lung injury in COVID-19 pneumonia that could be used instead of CT scanning in patient triage in the acute care setting.

Furthermore, to our knowledge, this is the first study to report the results of different LUS protocols performed in the same patients with confirmed COVID-19.

Materials and Methods

We performed a retrospective study using lung ultrasound data from 161 patients with COVID-19 hospitalized between March and May 2021.

This study was approved by the Local Ethical Committee of the Pirogov National Medical and Surgical Center (Protocol No. 11, dated October 26, 2021) and conducted in accordance with the Declaration of Helsinki. Because the data were collected retrospectively and processed anonymously, informed consent was not considered necessary by the Local Ethics Committee of the Pirogov National Medical and Surgical Center.

Patients were initially admitted to the intensive care unit (ICU), and both chest CT and LUS were performed within 24 h of admission.

The diagnosis of COVID-19 was confirmed either by a positive PCR test for SARS-CoV-2 or by a combination of clinical manifestations and radiological signs of infection, even with a negative PCR test on admission.

The exclusion criteria were suspected bacterial infection based on laboratory or radiological findings that developed before admission.

Chest CT evaluation. All enrolled patients underwent chest CT as part of the routine local protocol for suspected COVID-19 pneumonia. A 64-channel Brilliance (Philips Healthcare, Cleveland, OH, USA) or GE Revolution Evo CT scanner was used. The acquisition parameters were 120 kV and 90 mA (±25%). The slice thickness for the lung reconstruction was 1.25 mm. The «lung» filter was used. The extent of lung damage was assessed using a semiquantitative visual CT scoring system (Table 1) based on the volume and characteristics of lung tissue damage (ground-glass opacities and/or consolidation) [16]:

- CT-0, no abnormalities
- CT-1, lung tissue damage <25%
- CT-2, lung tissue damage 25–50%
- CT-3, lung tissue damage 50–75%
- CT-4, lung tissue damage >75%.

Lung UltraSound scales and interpretation. Sonosite Edge II (Fujifilm Sonosite, USA) and Logiq E (GE Healthcare, China) ultrasound devices were used, and a convex transducer was used in the study. The basic mode was «abdominal» and the scan depth was 11–13 cm.

SPSS IBM version 22 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. As appropriate, demographic, clinical, and endpoint variables were presented as means and standard deviations (SD), medians and interquartile ranges (IQR), or numbers (percentages).

To determine the distribution of data, the Shapiro–Wilk test was used. Depending on the normality of the distribution, ANOVA or Mann–Whitney and Kruskal–Wallis *U* criteria were used for comparative analysis.

Spearman's correlation coefficient was used to assess the correlation between data obtained by

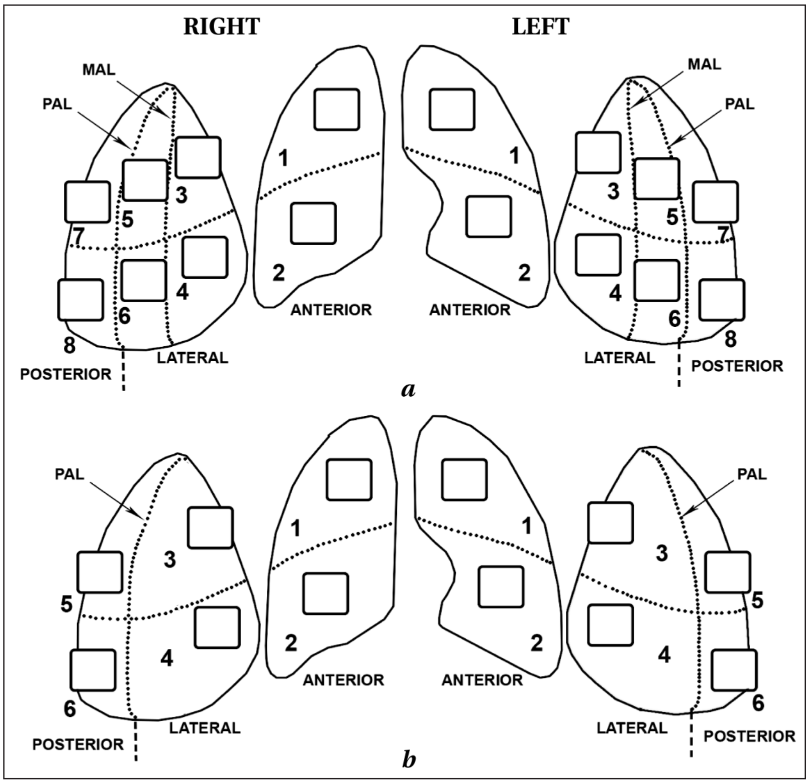

Fig. 1. Lung scheme for the 16-zone LUS and LUS NMHC protocols *(a)* and the 12-zone LUS NMHC protocol *(b)*.
Note. MAL stands for middle axillary line and PAL stands for posterior axillary line. Author's drawing.

Table 1. Scoring protocols for determining the severity of lung damage in COVID-19-induced pneumonia according to LUS results.

Points	Protocol Criteria		
	16-zone LUS	16-zone LUS NMHC	12-zone LUS NMHC
0	Normal lung profile without pleural deformities. Single (<3) B-lines are acceptable	A-lines occupy 100% of the tested area, up to 2 lines per the field of view are allowed. B-lines cannot be confluent or bright, A-lines should be clearly visible against them.	A-lines occupy 100% of the tested area, up to 2 lines per the field of view are allowed. B-lines cannot be confluent or bright, A-lines should be clearly visible against them.
1	Moderate interstitial syndrome, up to 5 B-lines per the field of view. Deformed pleural line.	A-lines occupy >50% of the intercostal spaces per the field of view **or** A-lines occupy 100% of the tested area with multiple B-lines that are clearly visible against the A-lines	A-lines occupy >50% of the intercostal spaces per the field of view **or** A-lines occupy 100% of the tested area with multiple B-lines that are clearly visible against the A-lines
2	Significant interstitial syndrome, subpleural consolidations less than 15 mm*	A-lines occupy <50% of the intercostal spaces per the field of view. **or** The ratio of B-lines to A-lines is 1:1 with subpleural consolidation less than 15 mm	A-lines occupy <50% of the intercostal spaces per the field of view. **or** The ratio of B-lines to A-lines is 1:1 with subpleural consolidation less than 15 mm
3	Large consolidation of more than 15 mm*	Large consolidation greater than 15 mm with or without pleural effusion	Large consolidation greater than 15 mm with or without pleural effusion

Note. * — A threshold value of 15 mm was adopted to differentiate between subpleural and large consolidations [18] detected during ultrasound examination.

LUS and chest CT protocols (as well as between different LUS protocols).

ROC curves were used to compare LUS's ability to discriminate the severity of lung damage detected by CT and predict outcome.

The optimal threshold was determined using the Youden index. The feasibility of using LUS and CT scores for individualized prognosis was evaluated using multivariable logistic regression.

Availability of data and materials. The data are not publicly available because they contain sensitive information about the study participants. Anonymized data supporting the findings of this study are available from the author, I. S. Shcheparev, upon request.

Results

A total of 161 patients with COVID-19 who underwent both chest CT and LUS at hospitalization were included in the study. Their demographic and clinical data are presented in Table 2. The mean duration of symptoms from onset to hospitalization was 10 days (IQR, 3–10).

Of the 161 patients admitted, 59 (36.6%) ultimately required invasive mechanical ventilation and 7 (4.3%) required noninvasive mechanical ventilation. A total of 137 patients (85%) spent at least 1 day in the ICU, with a median length of stay of 5 days (IQR, 3–10). The median length of hospital stay was 8 days (IQR, 3–15).

An example of matched LUS and CT images of a patient with COVID-19 pneumonia used for evaluation is presented in Fig. 2.

In May 2020, the 16-zone LUS protocol together with chest CT was performed in 18 patients (11.1%), while the 16-zone LUS NMHC and 12-zone LUS NMHC protocols were performed sequentially in the remaining 143 patients (88.8%) between March and May 2021. The reason for the small number of patients evaluated by the initially developed descriptive 16-zone LUS was due to several pitfalls of the protocol that were discovered during its clinical application. These included:

1. The high heterogeneity of lung damage observed with the ultrasound transducer made it difficult to count the exact number of B-lines.

2. The presence of areas of intact lung tissue together with large confluent B-lines, which did not allow reliable and clear differentiation of Grade 1 or Grade 2 criteria.

3. Personal protective equipment, including goggles, and their frequent change, which contributed to distractions that interfered with accurate assessment of the ultrasound result.

LUS scores measured using the 16-zone LUS NMHC or 12-zone LUS NMHC protocols in patients

Table 2. Baseline characteristics of hospitalized patients with COVID-19.

Parameter	Value (*N*=161)
Men, n (%)	67 (41.6)
Women, n (%)	94 (58.4)
Age, years	69.2±14.6
SpO_2, %	85.0±12.6
Time from onset of symptoms to hospitalization, days	10 [3–10]
C-reactive protein, mg/L (*N*=154)	97.5 [42.3; 158.5]
NEWS scale, points (*N*=137)	4.8±2.9
LUS protocols used, *N* (%)	161 (100)
16-zone LUS, *N* (%)	18 (11.1)
16-zone LUS NMHC, *N* (%)	143 (88.8)
12-zone LUS NMHC, *N* (%)	143 (88.8)

with varying degrees of CT lung damage differed significantly (P<0.001) (Table 3, Fig. 3), with the median LUS score for the 12-zone protocol tending to be several points lower in all patients graded by CT.

A strong positive correlation was found between 16-zone LUS NMHC results and the severity (%) of lung damage on CT (Spearman correlation coefficient R=0.79, P<0.001) (Fig. 3, *a*), and 12-zone LUS and the severity of lung damage on CT, R=0.78, P<0.001) (Fig. 3, *c*).

Both the 16-zone and 12-zone LUS NMHC protocols showed good performance in discriminating between moderate (less than 50% of lung tissue volume on CT) and severe (>50%) lung damage (Figure 4). The AUC of the ROC curves were almost identical: 0.83 (95% CI, 0.75–0.90) and 0.81 (95% CI, 0.73–0.88) for the 16-zone LUS NMHC and 12-zone LUS NMHC protocols, respectively. The 16-zone LUS NMHC had an optimal threshold of 20 points with a sensitivity of 67% and a specificity of 82%, whereas the 12-zone LUS NMHC had an optimal threshold of 15 points with the same sensitivity but a lower specificity of only 73%.

Seventy-six patients died, 74 (97%) before day 30, 2 patients (3%) after day 30 of treatment, 64 patients were discharged, and outcome data were not available for 3 patients. The AUC of the ROC curves for the 16-zone LUS NMHC (0.67; 95% CI, 0.58–0.76) and 12-zone LUS (0.68; 95% CI, 0.59–0.77) protocols demonstrated moderate ability to predict outcome, as did the AUC for CT (0.65; 95% CI, 0.56-0.74) (Fig. 5). The optimal threshold for 16-zone LUS NMHC and 12-zone LUS NMHC was 12 and 10 points, respectively, with unacceptable specificity of 53 and 55%.

Male sex, older age, and greater percentage of lung damage detected on CT scan on admission were predictors of unfavorable prognosis (Table 4).

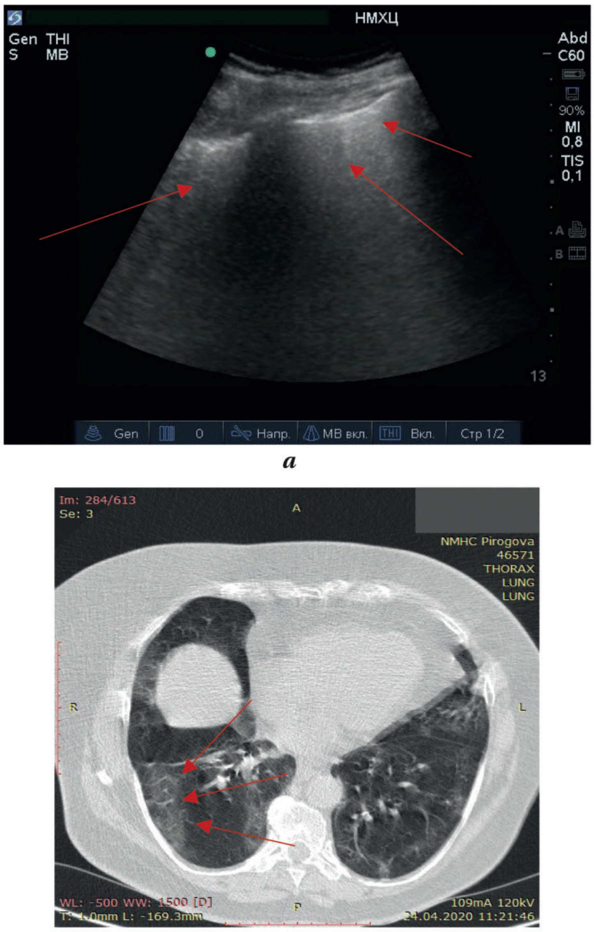

Fig. 2. Example of paired LUS and CT images.
Note. LUS image shows *(a)* multiple confluent B-lines without clearly visible A-lines («corresponds to grade 2»); CT image shows *(b)* a large ground glass-like opacity area.

Discussion

Although LUS cannot be considered the diagnostic modality of choice for patients with COVID-19

Table 3. Correspondence of chest CT scores and LUS scores according to protocols used.

CT scale, points	LUS scale, points				
	Number of patients and protocol options				
	N	16-zone LUS	*N*	16-zone LUS NMHC	12-zone LUS NMHC
0	5	4 (0–0.4)	54	6 (5.7–8.1)	5 (5.0–7.0)
1	4	11 (4.3–15.7)	21	14 (10.4–15.9)	11 (8.7–12.9)
2	1	—	38	21.5 (20.0–23.0)	17.5 (16.0–18.3)
3	8	26.5 (21.7–31.3)	29	23 (21.0–24.5)	18 (16.3–19.1)
4	0	—	1	—	—
0–2*	10	9 (3.0–10.8)	113	12 (11.5–14.5)	10 (9.5–11.8)
3–4**	8	27 (22.6–31.1)	30	22.5 (20.7–24.2)	18 (16.1–18.9)

Note. * <50% of lung damage; ** >50% of lung damage. Data presented as median (interquartile range).

Table 4. Analysis of predictors of mortality in patients with COVID-19.

Parameter	Odds ratio (95% CI)	*P*-value
Male sex	2.13(1.25–3.62)	0.005
Age	1.05 (1.02–1.08)	0.002
Days before hospitalization	1.03 (0.96–1.11)	0.36
SpO_2 on admission	0.98 (0.95–1.02)	0.38
Lung damage on CT, %	0.98 (0.96–0.99)	0.04

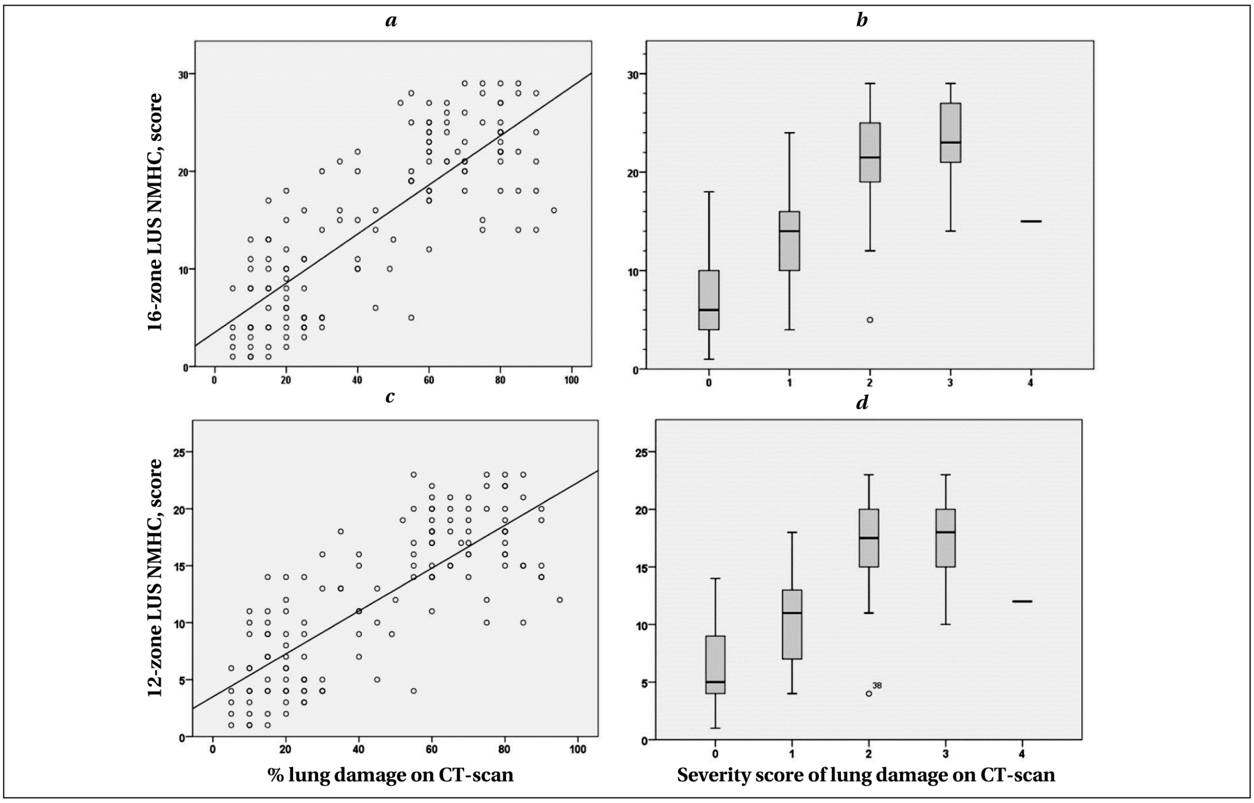

Fig. 3. Correlation of lung damage severity (%) based on CT data with 16-zone *(a)*, 12-zone *(c)* LUS NMHC results; correlation of lung damage severity (scores) based on CT data with 16-zone *(b)*, 12-zone *(d)* LUS NMHC results.

pneumonia, it has been shown to be a reliable tool for patient triage in mass hospitalizations and with limited CT capacity [19, 20]. LUS is relatively easy to use [21] and can be performed at the patient's bedside, minimizing the number of healthcare providers in contact with the patient. However, difficulties can arise in its interpretation in assessing the severity of lung injury and thus in selecting the best treatment strategy. Reliable LUS assessment protocols can be of great value as a diagnostic tool, especially in acute care settings and healthcare facilities with limited access to CT scans. The only systematic review and meta-analysis on this topic concluded that the diagnostic concordance between LUS and

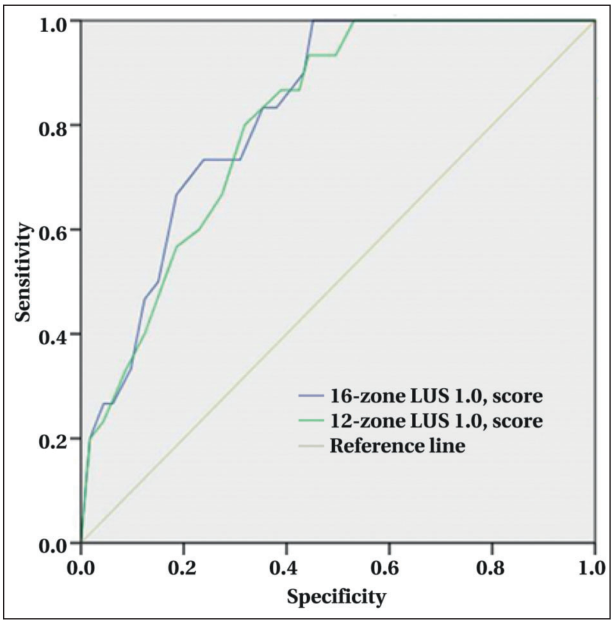

Fig. 4. ROC curve comparison for 16-zone and 12-zone LUS NMHC protocols in patients with >50% lung damage on CT.

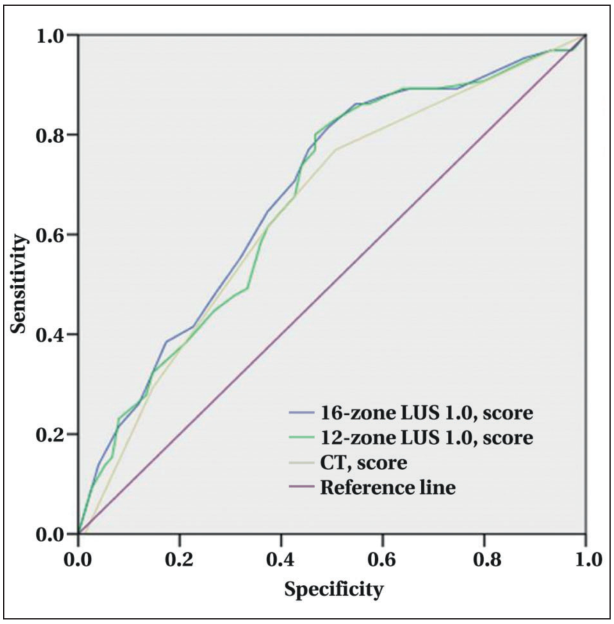

Fig. 5. Comparison of ROC curves for 16-zone, 12-zone LUS NMHC and CT protocols in patients with >50% lung damage on CT.

CT for the diagnosis of lung injury in COVID-19 is high [5]. The quality of the evidence reviewed was considered low; however, LUS has great potential as an alternative to CT in emergency or critical care settings.

Three protocols for LUS evaluation of patients with confirmed COVID-19 were developed and tested. First, a 16-zone LUS protocol was based on the calculation of B-lines, degree of interstitial changes, and size of the subpleural consolidations. The other two protocols, the modified 16-zone LUS NMHC and 12-zone LUS NMHC, were based on the evaluation of A-lines, and B-lines were of secondary importance. It was found that the first LUS protocol was associated with several technical problems related to the evaluation of the results obtained; thus, its implementation did not provide a reliable evaluation and convenience of performance. This protocol was used in 18 patients, and in this limited sample, an increase in the score was noted along with an increase in the CT severity score, which was consistent with the results of the other two protocols tested later in 143 patients.

The 16 zone LUS NMHC and 12 zone LUS NMHC protocols have been proposed as more feasible and reliable scoring systems. Similar LUS protocols have been described in several studies [22, 23]; however, the ratio of vertical to horizontal artifacts was used instead of A-line scoring. In the literature, visible A-lines are not described as a separate feature along with B-lines in the field of view of the ultrasound transducer. We hypothesize that the appearance of A-lines in front of B-lines is only possible with a certain amount of intact lung tissue and that the interpretation of such images does not follow any known guidelines or evaluation protocols.

Therefore, we hypothesized that the evaluation of A-lines instead of the ratio of vertical to horizontal artifacts would be diagnostically significant and easier to perform than in previously described protocols [22, 23].

According to known data, many authors tend to use the 12-zone LUS protocol [23–29]. However, the present study showed that the modified 16-zone LUS NMHC protocol was «slightly better» than the 12-zone LUS NMHC protocol. The performance of the 16-zone LUS NMHC and 12-zone LUS NMHC protocols had a strong correlation with the severity of lung damage on CT, which adds to similar findings from other studies [5, 24, 25, 30–32]. Meanwhile, LUS NMHC with 16 zones was more accurate in differentiating less/more than 50% lung injury. This may support the use of the 16-zone LUS NMHC protocol in the acute care setting to determine prognosis and the need for ICU admission.

Both protocols had moderate prognostic performance with a specificity of 53% for the 16-zone LUS NMHC and 55% for the 12-zone LUS NMHC. There are conflicting data regarding the prognostic value of LUS. In two observational studies [26, 28], a higher LUS score using the 12-zone protocol was not a predictor of mortality. On the contrary, Heldeweg et al [27] showed that a higher LUS score using the 12-zone protocol had a strong association with mortality and ICU stay of more than 30 days.

In this study, the 12-zone LUS NMHC protocol scores were recalculated from the 16-zone LUS NMHC protocol data, which does not allow direct comparison of the data with previous studies.

The main limitations of the study were its retrospective design and the fact that it was not designed to test the hypothesis of clinical equivalence between LUS and CT but rather to test the correlation between these techniques.

Another difficulty was the initial use of a 16-zone LUS protocol, which «evolved» from a local descriptive LUS protocol for non-COVID-19 pneumonia, the continued use of which was abandoned due to a number of technical problems; hence, the small patient sample size. However, the total sample size (161 patients) was larger than that in most published papers, and the two developed LUS evaluation protocols were tested in the same patients.

Conclusion

The developed 16-zone and 12-zone NMHC LUS protocols in patients with COVID-19-associated pneumonia proved to be feasible and strongly correlated with CT findings. The results of the 16-zone and 12-zone NMHC LUS protocols were not predictive of the outcome. Both protocols can probably be adapted for the triage of patients with confirmed COVID-19, especially in the acute care setting and in healthcare facilities with limited or no access to CT.

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