

# COVID-19: NEW METHODS, RELEVANT RECOMMENDATIONS

## COVID-19: новые методы, актуальные рекомендации

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### Lungs Ultrasound in SARS-Cov-2 Diagnostics: a Prospective Comparative Study of 30 Patients with COVID-19 Pneumonia

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#### ABSTRACT

**INTRODUCTION.** Lung ultrasound has been widely used to diagnose bacterial pneumonia, pulmonary congestion in heart failure, pneumo- and hydrothorax, and other pathological conditions. With the onset of the COVID-19 pandemic, the need for various methods of lung imaging has dramatically increased.

**AIM.** To estimate the value of lung ultrasound in the diagnosis and severity assessment of COVID-19.

**MATERIAL AND METHODS.** Patients with a positive PCR test result for SARS-Cov-2 were included and divided into a moderate, severe, or critical severe group. There were 30 patients involved. All the patients underwent clinical assessment, complete blood count, biochemical blood profile, pulse oxymetry, bedside lung ultrasound, and chest CT scan. To evaluate LUS findings thorax into 16 lung regions and each of these areas was quantitatively scored and summed up in total LUS score. A total severity score for chest CT was compared with the total LUS score.

**RESULT AND DISCUSSION.** All patients had positive LUS findings, as well as positive CT findings. Most common lung ultrasound findings were the following: subpleural consolidations (100.0%, 30/30), large consolidations (73.3%, 22/30) and an irregular pleural line (43.3%, 13/30). A higher total lung ultrasound score was seen in patients with a more severe course of illness and a larger number of lung areas affected; they were older and had a significantly higher incidence of comorbidities and lower SpO<sub>2</sub>. Spearman correlation coefficient revealed a statistically significant correlation between CT chest scan and lung ultrasound –  $r_s=0.52$ ,  $p=0.003011$ .

**CONCLUSION.** During the COVID-19 pandemic, lung ultrasound is a great tool for assessing lung tissue in patients with varying severity of the disease. The advantages of the method are accessibility, ease of implementation and the absence of radiation exposure.

**KEYWORDS:** COVID-19, pneumonia, SARS-CoV-2, computer tomography

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## УЗИ легких в диагностике SARS-Cov-2: проспективное сравнительное исследование 30 пациентов с COVID-19

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### РЕЗЮМЕ

**ВВЕДЕНИЕ.** УЗИ легких широко использовалось для диагностики бактериальных пневмоний, легочного застоя при сердечной недостаточности, пневмо- и гидроторакса, и других патологических состояний. С началом пандемии COVID-19 многократно возросла необходимость в различных методах визуализации легочной ткани.

**ЦЕЛЬ.** Анализ возможности использования УЗИ легких в диагностике и оценке тяжести COVID-19.

**МАТЕРИАЛ И МЕТОДЫ.** Критерием включения было наличие пневмонии, вызванной SARS-Cov-2, подтвержденной ПЦР. Пациенты были разделены на группы по тяжести течения (средней тяжести, тяжелое и крайне тяжелое). Было включено 30 пациентов. У всех пациентов проводились клиническая оценка, общий анализ крови, биохимический анализ крови, пульсоксиметрия, УЗИ легких, компьютерная томография органов грудной клетки. При оценке результатов УЗИ область грудной клетки разделялась на 16 зон, состояние каждой из которых было оценено количественно, результат был суммирован. Полученный результат был сравнен с суммарным баллом поражения по данным компьютерной томографии органов грудной клетки.

**РЕЗУЛЬТАТЫ И ОБСУЖДЕНИЕ.** У всех включенных пациентов выявлялось поражение легких как по УЗИ, так и по компьютерной томографии органов грудной клетки. Самыми частыми находками по УЗИ были следующие: субплевральные консолидации (100%, 30/30), крупные консолидации (73,3%, 22/30) и неровность плевральной линии (43,3%, 13/30). Более высокий балл поражения по данным УЗИ наблюдался у пациентов с более тяжелым течением, большим объемом поражения легких, а также эти пациенты были старше и у них была более низкая сатурация и больше сопутствующих заболеваний. Коэффициент Спирмена показал статистически значимую корреляцию между суммарными баллами поражения по компьютерной томографии органов грудной клетки и по УЗИ ( $rs=,52$ ,  $p= 0,003011$ ).

**ЗАКЛЮЧЕНИЕ.** В период пандемии COVID-19 УЗИ легких представляет большой интерес для оценки состояния легочной ткани у пациентов различной степени тяжести течения заболевания. Преимуществами метода является доступность, простота проведения и отсутствие лучевой нагрузки.

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### INTRODUCTION

An outbreak of the coronavirus disease 2019 (COVID-19) caused an international healthcare crisis, leading to more than six million deaths by July 2022 [1]. The infective agent, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), mainly targets the respiratory system with the development of pneumonia and acute respiratory distress syndrome (ARDS) [2]. A positive polymerase chain reaction test, being highly specific, lacks sensitivity and takes from several hours to days to be performed [3]. Lung visualization, with a chest computer tomography (CT) as a gold standard, is crucial for immediate diagnosis and assessment of the disease severity. Lung ultrasound (LUS), widely used in respiratory and cardiovascular disease, is another imaging modality. In the last two decades LUS has emerged as a very useful tool, not only in intensive care unit (ICU) patients, but also for evaluation of non-ICU lung

pathologies.[4] According to available reports (although their number is currently limited), LUS has a good diagnostic sensitivity and specificity comparable with chest CT scans.[5]

Since the early days of the pandemic, several studies have reported the typical LUS patterns of COVID-19 pneumonia [6]. The most common are B-lines, discrete laser-like vertical hyperechoic artifacts arising from the pleural line to the bottom of the screen without fading, and moving together with the lung sliding. These are the signs of the sonographic interstitial syndrome, which was described in different diseases, including cardiogenic pulmonary edema, interstitial lung diseases, infections, ARDS, etc. [7]. Subpleural and pulmonary consolidations, pleural effusions, and abnormalities of the pleural line were also found [6].

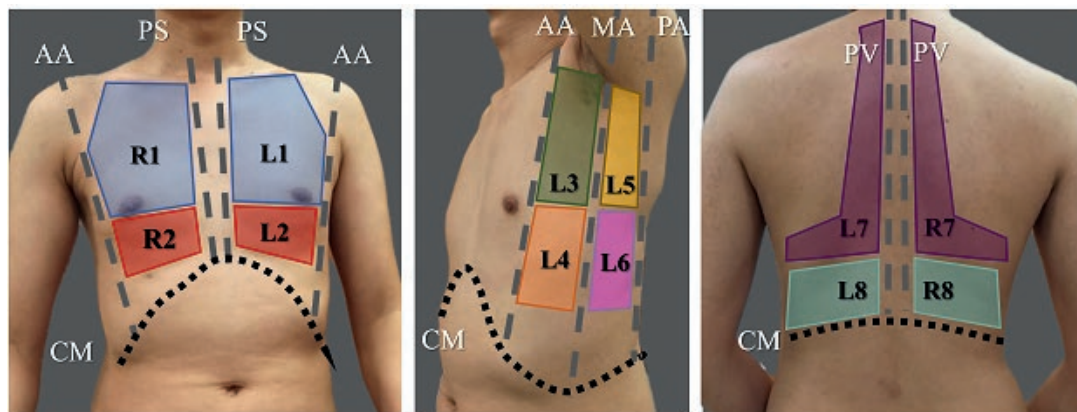
**AIM**

To estimate the value of LUS in the diagnosis and severity assessment of COVID-19 and to compare LUS with chest CT. We also provide a case report, so as to show the sequential LUS findings in the progression of COVID-19 pneumonia together with the clinical, laboratory and chest CT findings.

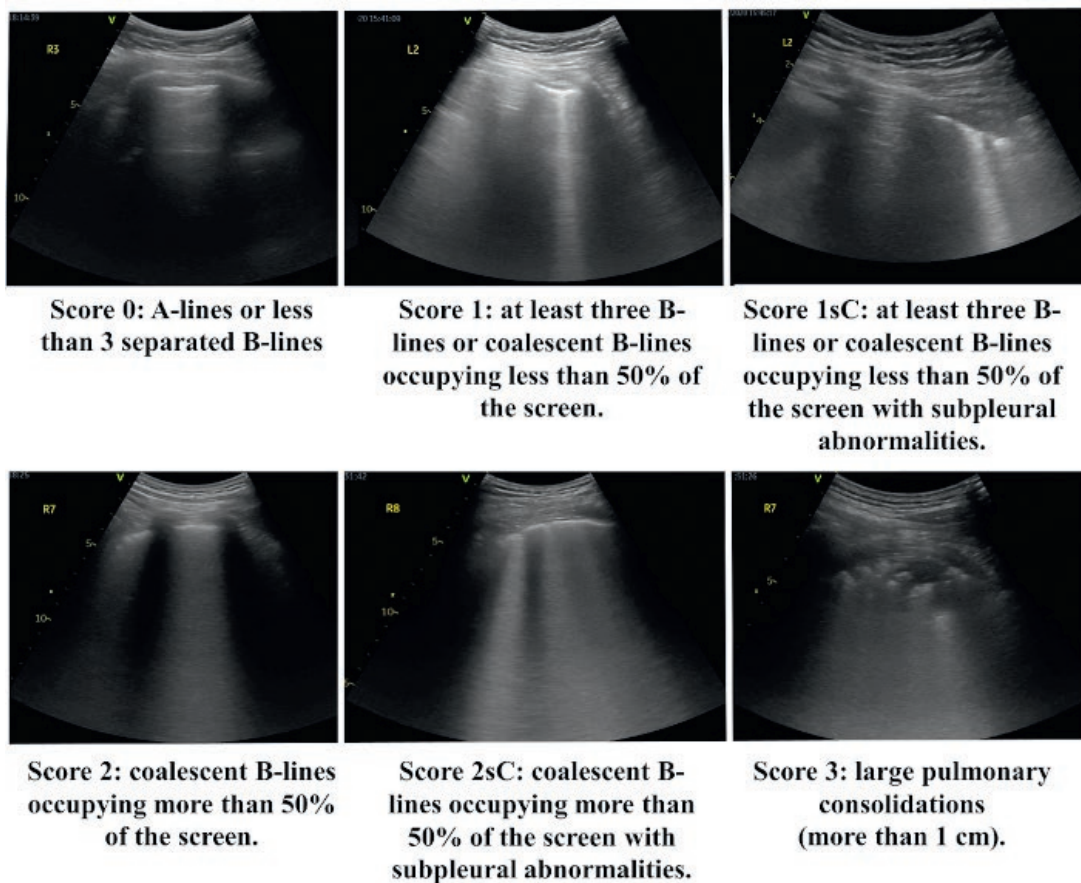
**MATERIAL AND METHODS**

We conducted a pilot study to examine the correlation between LUS findings with chest CT scans and, thus, to evaluate possibility of LUS as a safe bedside alternative in assessing the severity of COVID-19 pneumonia. This study was approved by the local ethics committee of V.V. Vinogradov City Clinical Hospital (Ethics Approval Letter number N3; dated: 09.07.2020). The study involved patients with a positive PCR test result for SARS-Cov-2,

who signed the informed consent form and lasted from May, 2020 until June, 2020. All the patients were classified according to the severity of the disease into a mild, moderate, severe or critically severe group. No negative controls were included in this study. During the hospitalization, all the patients underwent a clinical assessment, a complete blood count, a blood chemistry analysis, a pulse oxymetry, a bedside LUS and a chest CT scan. LUS was performed by the same US system (Vivid iq system (GE, Healthcare, USA) with a convex probe (3,5-5 MHz). A modified Gargani L., et al [8] protocol was used to evaluate our LUS findings: we divided thorax into 16 lung regions and each of these areas we quantitatively scored and summed up in the total LUS score. The scanning technique and scoring system are shown in Figures 1, 2. We also calculated a total severity score (TSS) [9] for each chest CT to compare with the total LUS score.



**Fig. 1.** LUS: 16 scanning areas of left (L1-L8) and right (R1-R8) lungs. PS – parasternal line; AA – anterior axillary line; MA – midaxillary line; PA – posterior axillary line; PS – paraspinal line; CM – costal margin



**Fig. 2.** LUS: scoring system

The statistical analysis was performed using SPSS software (version 21.0, IBM). Quantitative variables were expressed as median [IQR25; IQR75]. All categoric variables were expressed as counts and percentages. We used Spearman correlation coefficient to see whether LUS changes could predict chest CT findings; *p* values < 0.05 were

considered statistically significant. Our study population comprised 30 patients (17 males; median [IQR25; IQR75] age 52 [44;70] years). Table 1 summarizes the baseline clinical characteristics of the patients. Most of the patients (15/30) were classified as those with a severe form of the disease.

**Table 1.** Baseline clinical characteristics of the patients with COVID-19 pneumonia stratified by LUS severity score

Variables	Total population, n=30	LUS score		
		Moderate (n=8)	Severe (n=15)	Critical (n=7)
<b>Demographic Data</b>				
Age, year	52 [44;70]	46.5 [40.3;60]	54 [44.5;64.5]	51 [45.5;74.5]
Males, n (%)	17 (57)	5 (62.5)	8 (53)	4 (57)
BMI, kg/m <sup>2</sup>	29 [26.9;32.7]	27.5 [25.2;28.8]	31.7 [29.3;35.9]	27.1 [24.5;31.2]
Temperature, °C	37.8 [37.2;38.5]	37.5 [36.9; 38.5]	38.4 [37.6; 38.8]	37.6 [36.9;38.0]
SpO <sub>2</sub> (%)	92 [91;94]	94 [93;94]	92 [91;94]	90 [88;92]
<b>Comorbidities</b>				
Hypertension, n (%)	17 (57)	5 (63,5)	9 (60)	3 (43)
Diabetes, n (%)	4 (13)	0 (0)	2 (13)	2 (28)
Coronary artery disease, n (%)	4 (13)	1 (12,5)	2 (13)	1 (14)
Congestive heart failure, n (%)	4 (13)	1 (12,5)	1 (7)	2 (28)
Chronic kidney disease (C3a and higher), n (%)	3 (10)	1 (12,5)	1 (7)	1 (14)
<b>Instrumental Values</b>				
CT stage	2 [2;2]	2 [1;2]	2 [2;2]	2 [2;3]
CT score	7 [6;8]	6.5 [4.5;7.3]	7 [6;8]	9 [7.5;10.5]
LUS score	26.5 [19.3;30]	14.5 [13,5;15,3]	27 [23.5;28]	34 [33.5;35.5]
<b>Laboratory Values</b>				
Lymphocytes	1.05 [0.7;1.4]	1.45 [1.13;1.85]	1.1 [0.7;1.15]	0.7 [0.6;0.7]
CRP, mg/L	79.1 [52.7;108.6]	32.8 [8.4;81]	79.5 [59.4;111.5]	95.4 [79.2;141.4]
D-dimer, ug/L	226.5 [117.5;494]	122.5 [66.5;137.3]	189 [114;525.5]	482 [305;743.8]
<b>Outcomes</b>				
Discharge, n (%)	20 (67)	8 (100)	12 (79)	0 (0)
Additional oxygen supplementation, n (%)	4 (13)	0 (0)	1 (7)	3 (43)
Transfer to ICU, n (%)	4 (13)	0 (0)	1 (7)	3 (43)
Death, n (%)	2 (7)	0 (0)	1 (7)	1 (14)

**Note:** Data are n (%), Median [IQR]. IQR, interquartile range; BMI, body mass index; CRP, C-reactive protein

**RESULTS AND DISCUSSION**

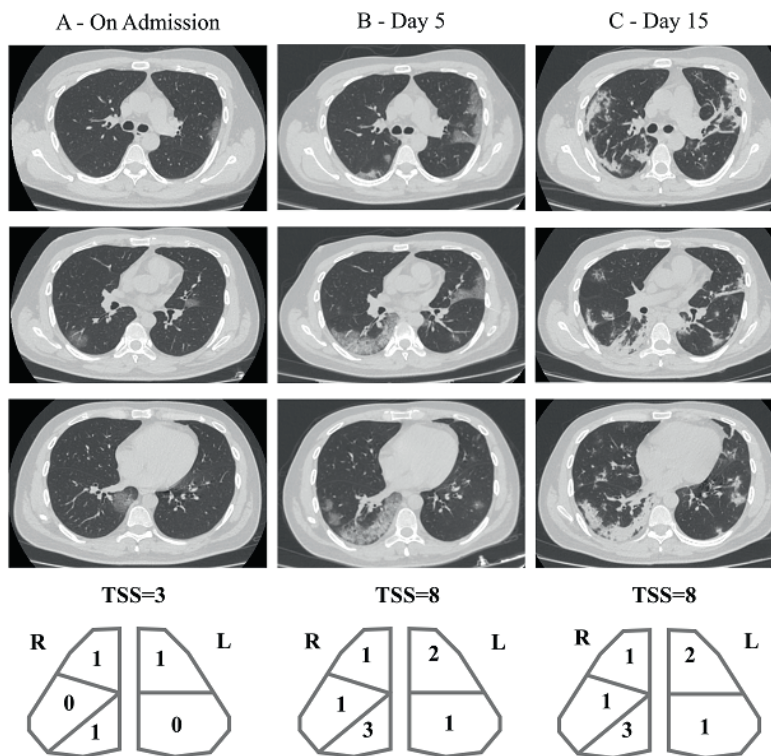
All 30 patients had positive LUS findings, as well as positive CT findings. The most common LUS findings were the following: subpleural consolidations (100.0%, 30/30), large consolidations (73.3%, 22/30) and an irregular pleural line (43.3%, 13/30). A higher total LUS score was observed in patients with more a severe course of the disease and

a larger number of lung areas affected; they seemed to be older and had a significantly higher incidence of comorbidities and lower SpO<sub>2</sub>. Spearman correlation coefficient revealed a statistically significant correlation between the CT chest scan and LUS – *r*<sub>s</sub>=.52, *p*= 0.003011. During hospitalization 1 severe and 1 critical patient with high LUS score died.

**Case Presentation**

A 34-year-old male patient, with no relevant medical history, was admitted to hospital with fever (up to 39.5°C), cough, and progressing fatigue for the past 3 days. He had undergone a maxillary sinusotomy due to chronic sinusitis 2 weeks earlier, and had been taking amoxicillin/clavulanic acid for 10 days. For 2 days he was taking hydroxychloroquine and levofloxacin on the assumption that he had contracted SARS-CoV-2.

On admission his body temperature was 38.3°C, the blood pressure was 120/80 mm Hg, with a pulse rate of 86 beats/min, the respiratory rate was 18/min and the oxygen saturation was 98%. Blood tests were unremarkable. A chest CT was performed, revealing bilateral peripheral ground-glass opacities, a typical radiological picture of COVID-19 infection. The progression of pneumonia on CT is demonstrated in Figure 3.



**Fig. 3.** Chest CT findings. Lower pictures show TSS and the extent of involvement of each of 5 lung lobes, scored as 0 (0%), 1 (1–25%), 2 (26–50%), 3 (51–75%), or 4 (76–100%)

- A – Several irregular rounded ground-glass opacities are seen in both lungs;
- B – The disease progressed, with the elevated number, range, and densities of the lesions. Ground-glass opacities were superimposed with intralobular reticulations resulting in a crazy-paving pattern;
- C – Further progression with increased density of lesions up to consolidations is seen

Subsequently, COVID-19 was confirmed by a positive reverse transcription polymerase chain reaction assay for SARS-CoV-2 in a nasopharyngeal swab. The urine samples for soluble antigens of *Legionella pneumophila* serogroup 1 and *Streptococcus pneumoniae* and sputum culture were negative.

Hydroxychloroquine was canceled because of severe nausea. Prophylaxis of thrombotic complications with enoxaparin was initiated (4 000 IU daily). On Day 2, the patient started taking favipiravir at a loading dose of 1600 mg, followed by 600 mg twice daily. He was also treated with paracetamol 500-1000 mg daily, as the circumstances required. The symptoms, clinical and laboratory findings and treatment are summarized in Table 2.

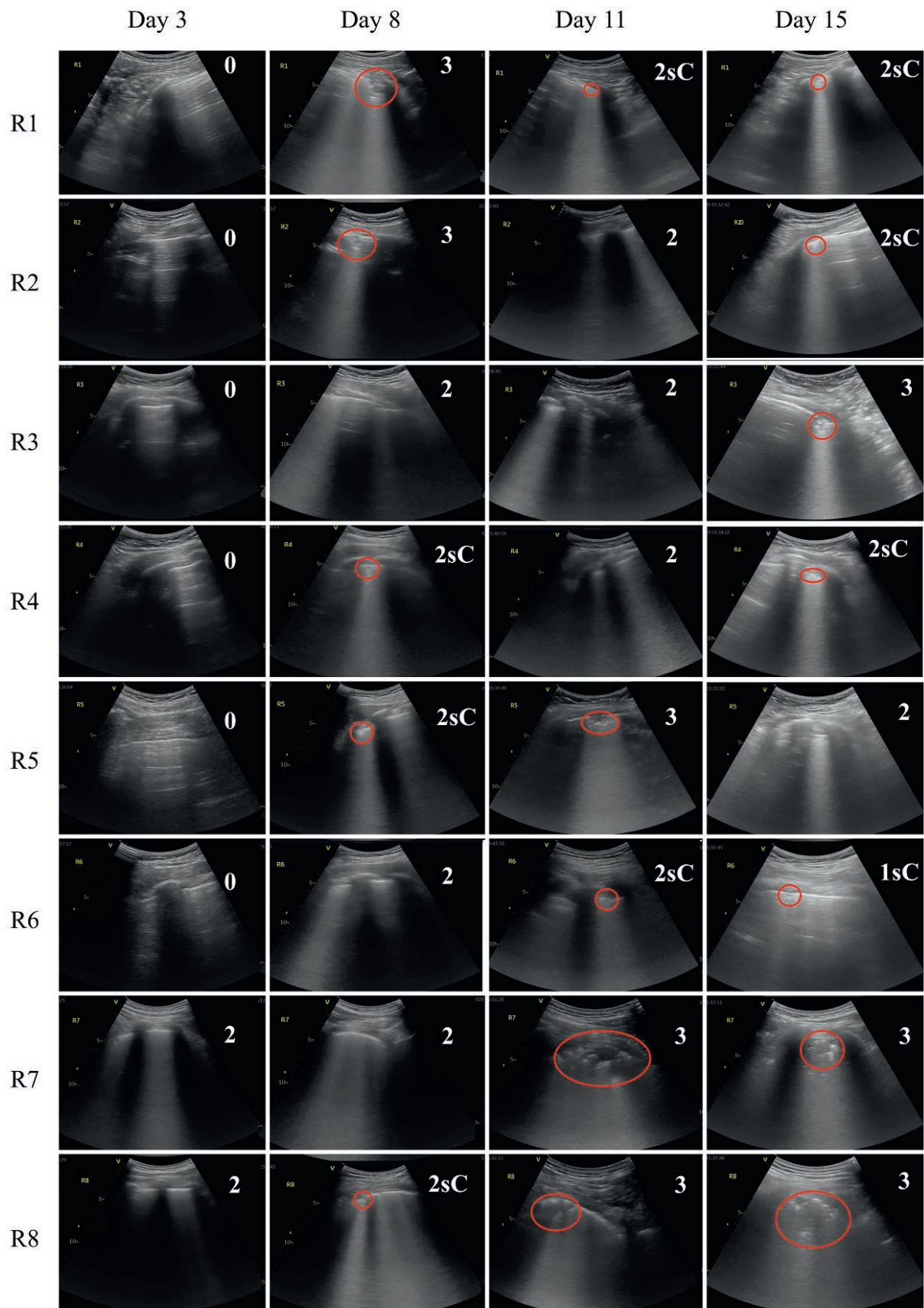
**Table 2. Clinical Course**

Day of hospitalization	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
<b>Lung Visualisation</b>																
Chest CT severity score	3					8										8
LUS severity score				15					34		34					33
<b>Clinical Findings</b>																
SpO2, on air, %	98	98	98	98	97	96	91	92	92	93	93	96	95	96	96	96
SpO2 (on low-flow O2), %							95	97	96	96	96					
Low-flow O2 rate, L/min							5	5	5	5	3					
Body temperature, °C	38.3	37.6	38.4	39.0	38.5	38.0	38.5	38.0	38.0	37.5	37.0	36.6	36.6	36.6	36.6	36.6
<b>Laboratory findings</b>																
	Reference range															
HGB	130-160, g/L	130	129		123		119				122					117
NEU	2-5, 1000/μL	1,5	1,5		1,9		2,2				2,4					4,2
PLT	180-400, 1000/μL	227	206		164		143				333					423
LYM	1.2-3, 1000/μL	1.2	1.8		0.9		0.4				1.2					1.3
CRP	0-5 mg/L	9	10		28		66		108	110	51		15			16
Albumin	35-52 g/L	49			34		34		31		32		32			
LDH	0-248 U/L				361		1110		916		687		673	743		
ALT	0-50 U/L	42	39		64		696	641	554	430	372	371	548	712		355
AST	0-50 U/L	24	27		51		645	500	383	208	135	138	180	274		50
Ferritin	20-250 mcg/L						623		612		725		759			
D-dimer	0-250, ng/mL	33	21						339		269					
<b>Treatment</b>																
Favipiravir				+	+	+										
Enoxaparin		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Paracetamol		+	+	+	+	+										
Prednisolone										+	+	+				
Diclofenac							+	+	+	+						
Ademetionine							+	+	+	+	+	+	+	+	+	+

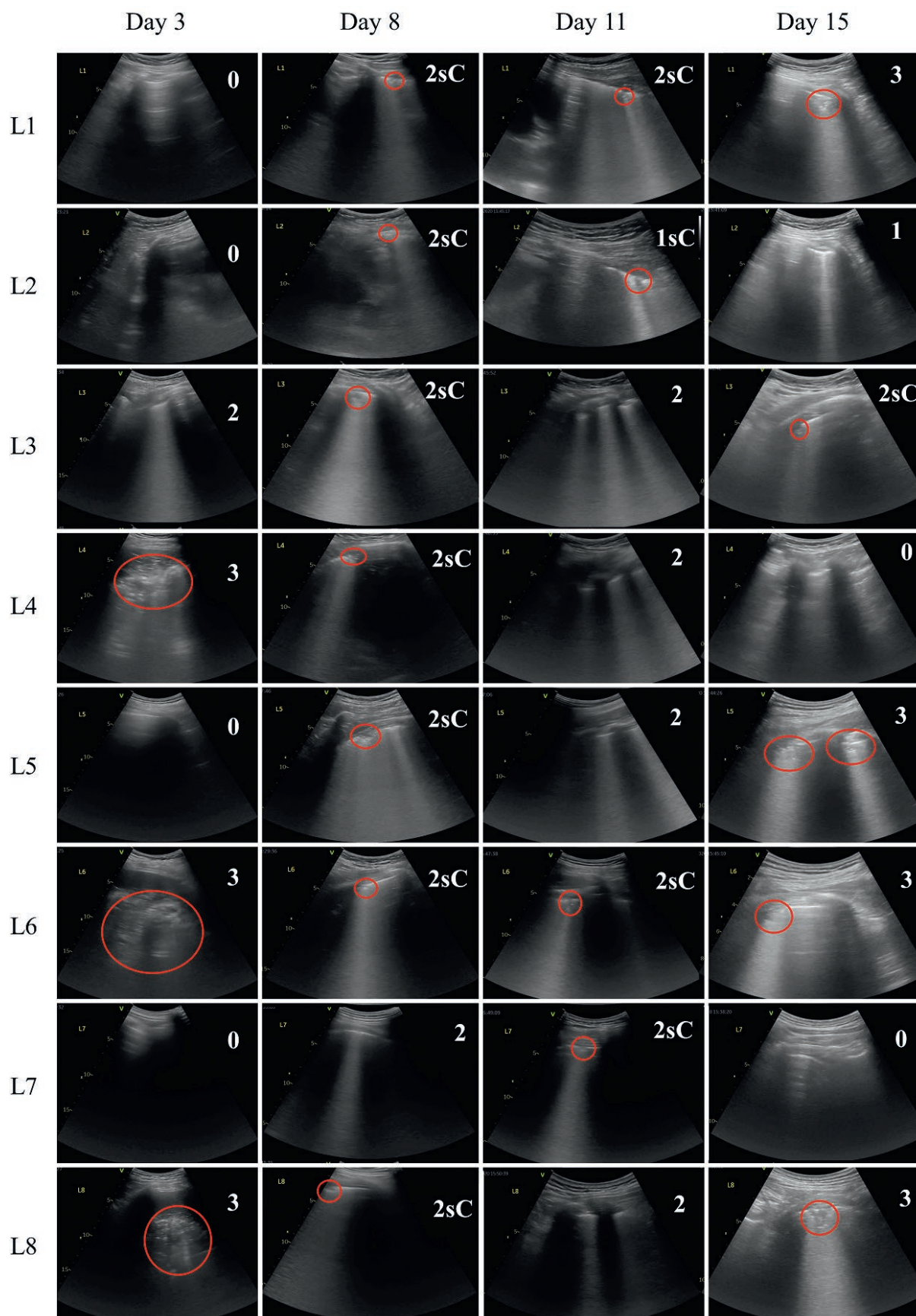
**Note:** SpO2 – oxygen saturation; HGB – hemoglobin; NEU – neutrophils; PLT – platelets; LYM – lymphocytes; CRP – C-reactive protein; LDH – lactate dehydrogenase; ALT – alanine aminotransferase; AST – aspartate aminotransferase

On Day 3, the patient complained of mild shortness of breath, although his oxygen saturation remained 97-98%. The first lung ultrasound was performed, showing coalescent B-lines up to white lung pattern in the posterior

right lung and big consolidations in the basal area of the left lung. Figures 4A and 4B show progressive LUS findings in all areas of both lungs.



**Fig. 4A.** LUS findings: Right lung. Subpleural and pulmonary consolidations are marked with circles. LUS score is indicated in the upper right corner of each picture



**Fig. 4B.** LUS findings: Left lung. Subpleural and pulmonary consolidations are marked with circles. LUS score is indicated in the upper right corner of each picture



He developed mild lymphocytopenia, thrombocytopenia, anemia, and C-reactive protein elevation. By Day 5, he began to desaturate while walking to 93%. The fever persisted, the inflammatory markers increased, and the repeated chest CT showed increased areas of ground-glass opacities, involving about 30% of the lung tissue on both sides. His condition was complicated by toxic hepatitis with alanine aminotransferase and aspartate aminotransferase levels of 696 and 645 U/L accordingly, probably caused by favipiravir. Favipiravir and paracetamol were discontinued, while ademetonine was initiated.

On Day 6, his on-air oxygen saturation lowered to 91% and low-flow oxygen therapy (5 L/min) was started. LUS was repeated, showing abnormal LUS patterns spread to all areas of the lungs, mostly B lines with multiple subpleural consolidations. As the hypoxia and inflammation increased, prednisolone 30 mg twice daily was added to the therapy for 3 days.

His condition improved, the fever subsided and the inflammatory markers and the liver enzymes decreased. By Day 11, supplemental oxygen was discontinued and he was able to maintain the oxygen saturation at 96%. LUS on Day 11 showed the formation of the big consolidations in the basal areas of the right lung.

On Day 15, he was discharged from the hospital with the oxygen saturation at 96% and fatigue as the only remaining complaint. He was scanned at discharge and the right lung consolidations became smaller, while, on the left side, new consolidations appeared in the basal areas. Two months later, he came to a follow-up visit and LUS revealed no abnormalities, except for a small pleural line irregularity and some thickening in the basal areas of both lungs.

During the COVID-19 pandemic, hospitals face immense challenges in terms of staff, time and equipment. LUS is a cheap, quick, feasible and non-invasive visualization method with no exposure to radiation. It appears to be a more sensitive diagnostic option than X-ray [10] and its findings correlate with chest CT [11]. The severity of LUS abnormalities predicts admission to intensive care unit [12], the need for invasive mechanical ventilation [13] or extracorporeal membrane oxygenation [14] and death [12, 13].

The current study shows that the ability of LUS to detect abnormalities in patients with COVID-19 is high and comparable to that of chest CT. Although chest CT provides the best possible imaging of COVID-19 pneumonia, there are certain clinical situations, when the use of LUS can offer additional benefits. In case a mild form of the disease, to avoid excessive use of CT, LUS can be an alternative for screening of pneumonia [15]. Portable devices allow performing LUS in cases of home confinement [16]. It can also be used at admission, to quickly separate patients with possible SARS-CoV-2 infection from other causes of respiratory failure [17]. Another possible application is the progression control of COVID-19 pneumonia in critically ill patients, when LUS allows to monitor changes of lung tissue involvement on a daily basis [18, 19]. LUS combined with echocardiography and lower extremity venous

Doppler makes up an extended ultrasound protocol [19, 20], able to evaluate cardiac and thrombotic complications of COVID-19. LUS can be an opportunity to avoid radiation exposure in pregnant women with COVID-19 [21]. It was also used in a follow up of the convalescents during their rehabilitation period [22]. Post-mortem studies have showed most of pulmonary lesions in patients with COVID-19 start in subpleural regions and are characterized by oedema, alveolar damage, interstitial thickening and consolidation [23] and most of such lesions located subpleurally [24]. Therefore, LUS can identify such pulmonary lesions in a timely and sensitive manner. Most patients in our study showed bilateral and subpleural involvement with large consolidations, which is consistent with chest CT features reported in previous studies [25]. The patients in our cohort also demonstrated the irregular pleural line (43.3%, 13/30) on LUS. These imaging features characterized in our study are similar to those reported in the previous studies targeting the patients with COVID-19 [26].

Although, as compared with other reports, we have not reached a very strong correlation coefficient, in contrast to similar studies [27, 28]. This may be due to the fact that this method highly depends on disease severity, pre-existing lung disease, experience of the operator, has low inter-operator agreement, non-specificity of ultrasound findings that should be considered during a differential diagnosis [29] and potentially, the most important factor is that there is a lack of the standardized protocol for LUS assessment of patients with COVID-19 pneumonia (lack of unifying definitions and discrepancies in the reporting of different lung abnormalities, inability to properly report the extensiveness of LUS findings (both lung areas involved and LUS score) that limits comparison of findings across different studies [30]. As mentioned before, B-lines, a typical COVID-19 pattern, are seen in many diseases, most importantly, heart failure and other forms of pneumonia, especially viral [7]. Also worth mentioning, that all the current studies [5, 10-19, 22] were conducted during a period of extremely high COVID-19 prevalence and that fact could influence specificity and sensitivity of the method. Similar limitations were also found in meta-analyses of LUS in the diagnosis of pneumonia [31]. Another limitation is that our study was a single-centre study with a relatively small sample size, which could limit the generalizability of our findings. Therefore, further multi-centre studies with a larger sample size are needed to assess the prognostic value of the LUS score in patients with COVID-19.

## CONCLUSION

Imaging plays an important role in the diagnosis of COVID-19 and other lung pathology, and LUS is one of the available options for visualisation. Lung ultrasound is a non-invasive, rapid, cheap, repeatable, and sensitive bedside method to detect a wide range of pulmonary pathologies, as well as some others. LUS may be very useful for portable imaging, when CT is not available, for the patients' triage on admission and for monitoring the evolution of pulmonary lesions in critically ill patients.

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Consent of patients (their representatives) to the processing and publication of non-personalized data was obtained.

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