Lung ultrasonography for risk stratification in patients with COVID-19: a prospective observational cohort study

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Main points: Our results show that lung involvement visualized with ultrasound correlated to disease severity and that summarising this into a simple ordinal scoring system has potential to discriminate patients requiring hospitalisation and thus better allocate scarce resources.



Abstract

Background

Point-of-care lung ultrasound (LUS) is a promising pragmatic risk stratification tool in COVID-19. This study describes and compares LUS characteristics between patients with different clinical outcomes.

Methods

Prospective observational study of PCR-confirmed COVID-19 adults with symptoms of lower respiratory tract infection in the emergency department (ED) of Lausanne University Hospital. A trained physician recorded LUS images using a standardized protocol. Two experts reviewed images blinded to patient outcome. We describe and compare early LUS findings (acquired within 24hours of presentation to the ED) between patient groups based on their outcome at 7 days after inclusion: 1) outpatients, 2) hospitalised and 3) intubated/death. Normalized LUS score was used to discriminate between groups.

Results

Between March 6 and April 3 2020, we included 80 patients (17 outpatients, 42 hospitalized and 21 intubated/dead). 73 patients (91%) had abnormal LUS (70% outpatients, 95% hospitalised and 100% intubated/death; p=0.003). The proportion of involved zones was lower in outpatients compared with other groups (median 30% [IQR 0-40%], 44% [31-70%] and 70% [50-88%], p<0.001). Predominant abnormal patterns were bilateral and multifocal spread thickening of the pleura with pleural line irregularities (70%), confluent B lines (60%) and pathologic B lines (50%). Posterior inferior zones were more often affected. Median

normalized LUS score had a good level of discrimination between outpatients and others with area under the ROC of 0.80 (95% CI 0.68-0.92).

Conclusions

Systematic LUS has potential as a reliable, cheap and easy-to-use triage tool for the early risk stratification in COVID-19 patients presenting in EDs.

Introduction

The Coronavirus disease (COVID-19) pandemic has overwhelmed the health systems in several high-income settings (1), and is now spreading in the low-income countries. There is a critical need for accessible and low cost methods to stratify risk for evidence-based resource allocation (2). While the majority of COVID-19 patients have a paucisymptomatic or asymptomatic course, some may rapidly deteriorate leading to hospitalisation and the need for respiratory support. It has been suggested that early identification of patients at high risk of respiratory compromise is associated with lower mortality (3). Several studies have shown the predictive value of CT imaging, where the extent and patterns of lung involvement correlated well with severity of COVID-19 on admission to hospital. Other studies have described a progression of lung anomalies on consecutive chest CTs during the course of the disease, with rapid evolution from focal unilateral to diffuse bilateral ground-glass opacities and finally, consolidation (7). However, CT imaging has important limitations in triaging patients during the context of COVID-19, not only due to their limited availability, high cost and exposure to radiation, but more critically, due to their immobile nature, thus necessitating the movement of infectious patients (8). Point-of-care ultrasound applied to lung is a promising alternative diagnostic tool, which can shorten time-to-diagnosis for the aetiology of acute dyspnoea, as well as stratify severity in the Emergency Department (ED) (9). It is widely used in routine practice of Swiss EDs, can be performed at the bedside without radiation exposure and is easy-to-use in patients requiring protective isolation. So far, the use of lung ultrasonography (LUS) in COVID-19 has only been described in cohorts of severe hospitalised patients (10-13). However, it has already shown excellent performance to detect non-COVID-19 pneumonia, compared to CT as a reference standard (14), and matches the discriminative power of CT in patients with acute respiratory distress syndrome (ARDS) (15).

LUS has potential in the pragmatic triage of COVID-19 patients especially in low-resource settings.

This study aims to describe LUS characteristics in a prospective cohort of patients with COVID-19 and explore their predictive capacity for risk stratification.

Methods

Study design and participants

This study is nested in a prospective cohort study of patients with lower respiratory tract infections, which started on February 6th, 2020 in the ED of the Lausanne University Hospital, Switzerland. We prospectively screened consecutive adult patients (age ≥ 18 years) presenting in the ED with an acute lower respiratory tract infection (cough, sputum, dyspnoea or chest pain for <21 days) (16). Patients with COVID-19 confirmed by real time polymerase chain reaction (RT-PCR) for SARS-CoV-2 in a nasopharyngeal swab were included in this study. Patients were excluded if LUS could not be performed within 24 hours of admission or if the patient was receiving therapeutic prone ventilation before the LUS.

The study team collected patient's data using a standardized electronic case report form in REDCap® (Research Electronic Data Capture). We assessed day-7 outcome by checking the electronic health record and we classified patients in three groups: group 1 (outpatients: absence of admission within 7 days of inclusion); group 2 (hospital admission within 7 days of inclusion); group 3 (intubation and/or death within 7 days of inclusion).

Lung ultrasonography

A trained physician (TB) in lung ultrasonography performed all LUS at inclusion in the ED. Acquisition was standardized according to the "10-zone method" (17, 18). Two images (sagittal and transverse) and 5 second videos were systematically recorded in every zone with a Butterfly IQTM, using the lung preset.

The study physician (TB) and an expert radiologist (JYM) standardized the reporting of pathological LUS features based on COVID-19 patterns (Figure 1) (e-Figure 1, e-Figure 2 and Video V1 in the online data supplement) (10, 19). For every zone, the following patterns were reported: (1) normal appearance (A lines, < 3 B lines), (2) pathologic B lines (≥ 3 B lines), (3) confluent B lines, (4) thickening of the pleura with pleural line irregularities (subpleural consolidation < 1 cm) or (5) consolidation (≥ 1 cm). The presence of pleural effusion was also recorded. The LUS score, used as a correlate of loss of lung tissue aeration, as well as a normalized LUS score (nLUS score) corrected for the number of examined zone, were calculated in every patient (15, 19, 20).

Blinded to patient outcome, both physicians independently filled the standardized report. Discordance between the two readers was resolved by a third expert (OP).

Supplementary table 1 shows the potential correlation of visible features between CT and LUS images based on physical explanations behind their generation in several retrospective human studies (11, 21-24) an animal study (25) and biomedical analysis (26).

Statistical analyses

STATA (version 15.0, Stata Corp, College Station, TX, USA) and R Core Team (2019) statistical software were used for analyses.

Differences between the three groups was evaluated by one-way ANOVA, Kruskal-Wallis or chi-squared test, as appropriate. A bilateral p value <0.05 was considered indicative of

statistical significance. The kappa coefficient was calculated to measure the inter-rater agreement between the two LUS readers.

The prognostic accuracy of the LUS score, the nLUS score and the proportion of LUS affected zones to predict outcome was assessed by calculating the area under the receiver operating characteristic curve (AUROC). We determined the optimal nLUS score cut-off by choosing the value with the best sensitivity and a specificity superior to 50%.

Ethics approval

Ethical approval was granted by the Swiss Ethics Committee of the canton of Vaud (CER-VD 2019-02283).

Results

Demographic and clinical characteristics

From the 165 successive adult patients prospectively included in the acute lower respiratory tract infection cohort at the time of ED presentation between March 6 and April 3 2020, 86 patients had a positive nasopharyngeal RT-PCR for SARS-CoV-2 and were included in this nested study (e-Figure 3 in the online data supplement). Six patients were excluded due to >24 hour delay in LUS recording or to ventral decubitus position. The remaining 80 COVID-19 patients included in this analysis were then classified into three groups according to outcome evaluated at day 7 after inclusion: 17 (21%) outpatients without secondary hospitalisation, 42 (52%) patients admitted to hospital and 21 (26%) patients who died or were intubated (15 intubated, 5 deaths, 1 intubated who subsequently died). After inclusion in the ED, 20 patients were discharged home, three of which had a secondary hospitalisation after a median of 3 days (IQR 3.0, 3.5). Five patients were intubated upon inclusion (<24 hours) and eleven were later intubated after a hospital admission with a median duration of 2

days (IQR 2.0, 2.3). Six patients died after a median of 2.5 days of hospitalisation (IQR 1.3, 4.5).

Table 1 shows demographics, clinical characteristics and laboratory results of the study population by group. Overall, the mean age was 62 years (SD 17 years), and 34 (42%) patients were female. Outpatients were significantly younger than patients in the other two groups (mean of 51 years, p=0.002). At inclusion, the median duration of symptoms was 7 days (IQR 6-11) and not different between groups. The most common symptoms were cough (91%), fever (83%) and dyspnoea (75%). Dyspnoea occurred with increasing frequency across severity groups (p=0.014). Heart and respiratory rates were lower in outpatients compared with patients in the other two groups (median 78/min vs 91/min, p=0.002 and 20/min vs 24/min, p=0.002, respectively). Leukocyte count and C-reactive protein were significantly and gradually higher with increasing severity.

Overall, eight patients (10%) had a CT scan and 95% had a chest X-ray. X-rays were abnormal in 76% and outpatients had fewer abnormal X-rays than patients in the other two groups (38.5% versus 84%, p<0.001). Among 10 patients with a normal chest X-ray (9 in the hospitalized group, one in the intubated/death group), 9 had LUS abnormalities.

Lung ultrasonography findings

At ED inclusion, 73 patients (91%) had an abnormal LUS, the proportion of which increased progressively across severity groups to reach 100% in intubated/death patients (p=0.001) (Table 2).

A total of 735 lung zones were explored with LUS in all patients. A median of 10 zones were recorded for each patient (IQR 9, 10); 10 zones (IQR 10, 10) in outpatients, 10 zones (IQR 9, 10) in hospitalised patients, and 8 zones (IQR 8, 10) in intubated/death cases.

LUS examination showed abnormalities in 351/735 (48%) zones; The proportion of involved zones was significantly lower in outpatients compared with patients in the other two groups

(median of 30% [IQR 0, 40], p<0.001). Patients who died or were intubated had the highest proportion of pathological zones (median of 70% [IQR 50, 88]) (Figure 2).

Abnormalities were bilateral in 63 (80%) patients and multifocal in 68 (85%) patients. Abnormalities were predominant in postero-inferior and lateral zones compared with others zones (60/75 [80%, p<0.001] and 61/80 [76%, p<0.001], respectively) (Table 2, Figure 3). With increased severity, lung anomalies affected both apical and basal lung regions (e-Figure 4 in the online data supplement) and were more bilaterally distributed.

The patterns seen on LUS in decreasing severity order were thickening of the pleura with pleural line irregularities (present in 56/80 [70%] of patients), confluent B lines (present in 48/80 [60%] of patients); pathologic B lines (present in 40/80 [50%] of patients) and consolidations (present in 20/80 [25%] of patients) (Table 2, Figure 3).

In terms of the predominant abnormal LUS pattern, outpatients mostly had a "non-confluent B lines" pattern, while the other two groups more frequently presented with "thickening of the pleura with pleural line irregularities" pattern (e-Figure 5 in the online data supplement). While the patterns of "pathologic B lines" and "confluent B lines" were more commonly identified in anterior compared with posterior zones (43/80 [54%] and 24/75 [32%], respectively; p=0.006), "Thickening of the pleural line irregularities" and "consolidation" patterns were more often visualized in posterior compared with anterior zones (53/75 [71%] and 15/80 [19%], respectively; p<0.001) (Figure 3). Pleural effusion was present in 20 (27%) patients, 17 of which (85%) were classified as minor (< 5 mm).

Lung ultrasound score

The median LUS score was 10 (IQR 5, 15) and the median nLUS score was 1.1 (IQR 0.5-1.7). Outpatients had a significantly lower LUS score and nLUS score compared with the two other groups (median nLUS of 0.5 in outpatients versus 1.1 in hospitalized, p<0.001 and versus 1.5 in patients intubated/death, p<0.001)(Figure 4). The nLUS score was not

significantly different between hospitalized patients and those who required intubation or died (median nLUS score 1.1 versus 1.5 p=0.34).

The LUS score, the nLUS score and the proportion of affected zones had a good level of discrimination between outpatients and all admitted patients (including those who were intubated or died) with area under the receiving operating characteristic curve (AUROC) of 0.77 (95% CI 0.63-0.90), 0.80 (95% CI 0.68-0.92) and 0.78 (95% CI 0.67-0.89), respectively. The optimal nLUS score cut-off to differentiate between outpatients and admitted patients including those who were intubated or died was 0.6 (sensitivity 81%, specificity 59%, positive predictive value 88%, negative predictive value 45%, positive likelihood ratio 1.97, negative likelihood ratio 0.32). If this nLUS score had been used at the first ED visit, it would have correctly recommended primary hospitalisation for the three patients who were initially discharged (later returning for secondary hospitalization).

The LUS score, the nLUS score and the proportion of affected zones had a poor level of discrimination between patients who died or were intubated and the other two groups.

Inter-observer consistency of LUS interpretation

The two observers showed good reproducibility for all explored zones with a kappa of 0.74 based on the standardized US report. The reproducibility was excellent to differentiate normal and abnormal zones with a kappa of 0.90.

Discussion

Despite the potential of LUS as a cheap, portable and accessible point-of-care triage tool in acute respiratory disease (especially in low resource settings), a multinational consensus recently stated that the lack of studies limited specific recommendations for the management of COVID-19 patients (27). Using a standardized approach in a prospective ED cohort of 80 patients, we described the characteristics of LUS findings in COVID-19 pneumonia. Most

patients presented abnormal LUS with bilateral and multifocal involvement as previously shown in a large CT scan study (28). The most common patterns seen on LUS in decreasing frequency were thickening of the pleura with pleural line irregularities, confluent B lines, pathologic B lines and rarely, consolidations and minor pleural effusions. Abnormalities affected all lung regions but were more frequent in posterior and inferior zones. LUS findings also evolved with increasing disease severity, both in anatomic scope (progressing from unilateral to bilateral and pan-lung involvement), and pathological type (progressing from the "non-confluent B lines" pattern to "irregular pleural thickening").

Our findings are consistent with the existing literature on radiology presentation in COVID-19 and shed more light on the LUS characteristics of COVID-19. A meta-analysis of 7 small observational studies describing a total of 122 patients evaluated the typical characteristics of LUS in COVID-19. The identified patterns are similar to our study (29). The LUS imaging characteristics described in our and other studies are nonspecific, sharing similarities with those of other viral infections such as influenza and acute respiratory distress syndrome of any cause (15, 30).

Our study is the first analysing the prognostic value of LUS findings in ED COVID-19 patients including outpatients who had less severe disease. So far, studies have only reported LUS findings in hospitalised patients and thus are not useful for early risk stratification and resource allocation in outpatients. We describe a significant relationship between the clinical severity of COVID-19 pneumonia and the anatomic extent and nature of lung pathology detected by LUS, suggesting the utility of LUS in early risk stratification of COVID-19 patients.

We also describe a risk gradient in LUS findings that can be summarised in a simple ordinal scoring system (LUS score) which was able to discriminate between outcome groups in ED

triage. The LUS score can be used to quantify the loss of lung aeration and is thus useful for monitoring patients with ARDS. This simple LUS scoring method may help in assessing COVID-19 disease severity and support ED triage to decide on admission or close monitoring. Previous studies have evaluated the LUS score in COVID-19 patients. In the intensive care unit, the LUS score was higher in patients with refractory respiratory failure compared with others (31). A good correlation existed between the LUS score and a CT scan severity score. Both scores correlated with clinical severity (21, 24). In our study, LUS score also increased progressively according to clinical severity. However, we did not have the power to predict intubation and/or death with a good accuracy.

To our knowledge, our study is the first including the complete range of disease severity, i.e. - outpatients and patients who were intubated or died. Our findings provide additional evidence that the LUS score could be used as a triage tool to decide on admission. The role of LUS to evaluate several respiratory diseases such as pneumonia and ARDS has been widely documented (14, 15). LUS has several advantages over chest CT such as its ease-of-use at point-of-care, low cost, absence of radiation, reproducibility and a reduced risk of nosocomial infection through its portability (reducing patient transport to imaging suites and lengthy disinfection protocol for the CT suite) (32, 33). LUS allows a rapid assessment of severity at presentation in the ED. This study also shows that physicians with basic training in US (1-day theoretical course and 20 supervised acquisitions) are able to identify pathology with excellent concordance compared with experts: a critical proof of concept for its rapid deployment in COVID-19 and for its general use in low resource settings.

This study does not correlate LUS with chest CT imaging. However, current recommendations specify that CT imaging should not be used for screening and is rather reserved for hospitalised, symptomatic patients, with specific indications (34). Interestingly, two studies showed that the LUS and CT scan scores have good agreement in the assessment

of clinical severity (21, 24). Excluding chest CT from the inclusion criteria eliminates a potential selection bias. On the other hand, we cannot propose a direct correlation between CT imaging and LUS.

Acquisition of LUS is dependent on the accessibility of anatomic sites, which is sometimes challenging in respiratory patients unable to mobilise. Indeed, this study reported approximately 15% of missing values in posterior lung regions, which were mostly in severely ill patients. We mitigated this bias by normalising our score according to the number of available zones.

Regardless the discriminatory power of the score reveals that the predictive capacity of accessible zones is already highly informative. Work is underway to identify the most informative zones and devise personalised imputations for such missing values. LUS image interpretation is operator dependant, which is a potential disadvantage of this technique. However, in our study, we found a good agreement between the two observers. Furthermore, using a standardized procedure and a pre-defined scoring method could minimize this limitation.

In conclusion, LUS is a promising tool for early risk stratification in COVID-19. Lung involvement visualized with US correlates with disease severity and summarising this into a simple ordinal scoring system has potential to discriminate patients requiring hospitalisation in the ED and thus better allocate scarce resources.

Work is ongoing to confirm these findings in a larger outpatient cohort.

NOTES

Authors' contributions

TB, OH, NBB: study conception, study design, study performance, study management, data analysis, data interpretation and manuscript writing.

JYM, OP: lung ultrasound images review, data interpretation and critical review of the manuscript.

MBV, HGD: acquisition of the data, interpretation of the data and critical review of the manuscript.

MH: data interpretation, visualisations and critical review of the manuscript.

All authors approved the final version of the manuscript and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

TB had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Competing interests

The authors declare that they have no competing interests.

References

- 1. Tanne JH, Hayasaki E, Zastrow M, Pulla P, Smith P, Rada AG. Covid-19: how doctors and healthcare systems are tackling coronavirus worldwide. BMJ. 2020;368:m1090.
- 2. WHO. Home care for patients with COVID-19 presenting with mild symptoms and management of their contact. The World Health Organisation. 2020.
- 3. Sun Q, Qiu H, Huang M, Yang Y. Lower mortality of COVID-19 by early recognition and intervention: experience from Jiangsu Province. Ann Intensive Care. 2020;10(1):33.
- 4. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. The New England journal of medicine. 2020.
- 5. Mahdjoub E, Mohammad W, Lefevre T, Debray MP, Khalil A, Study Group section s. Admission chest CT score predicts 5-day outcome in patients with COVID-19. Intensive care medicine. 2020;46(8):1648-50.
- 6. Salehi S, Abedi A, Balakrishnan S, Gholamrezanezhad A. Coronavirus Disease 2019 (COVID-19): A Systematic Review of Imaging Findings in 919 Patients. AJR Am J Roentgenol. 2020:1-7.
- 7. Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. The Lancet infectious diseases. 2020.
- 8. Hao W, Li M. Clinical diagnostic value of CT imaging in COVID-19 with multiple negative RT-PCR testing. Travel Med Infect Dis. 2020:101627.
- 9. Zanobetti M, Scorpiniti M, Gigli C, Nazerian P, Vanni S, Innocenti F, et al. Point-of-Care Ultrasonography for Evaluation of Acute Dyspnea in the ED. Chest. 2017;151(6):1295-301.
- 10. Peng QY, Wang XT, Zhang LN, Chinese Critical Care Ultrasound Study G. Findings of lung ultrasonography of novel corona virus pneumonia during the 2019-2020 epidemic. Intensive care medicine. 2020.
- 11. Lu W, Zhang S, Chen B, Chen J, Xian J, Lin Y, et al. A Clinical Study of Noninvasive Assessment of Lung Lesions in Patients with Coronavirus Disease-19 (COVID-19) by Bedside Ultrasound. Ultraschall Med. 2020.
- 12. Poggiali E, Dacrema A, Bastoni D, Tinelli V, Demichele E, Mateo Ramos P, et al. Can Lung US Help Critical Care Clinicians in the Early Diagnosis of Novel Coronavirus (COVID-19) Pneumonia? Radiology. 2020:200847.
- 13. Vetrugno L, Bove T, Orso D, Barbariol F, Bassi F, Boero E, et al. Our Italian experience using lung ultrasound for identification, grading and serial follow-up of severity of lung involvement for management of patients with COVID-19. Echocardiography. 2020.
- 14. Orso D, Guglielmo N, Copetti R. Lung ultrasound in diagnosing pneumonia in the emergency department: a systematic review and meta-analysis. Eur J Emerg Med. 2018;25(5):312-21.
- 15. Mayo PH, Copetti R, Feller-Kopman D, Mathis G, Maury E, Mongodi S, et al. Thoracic ultrasonography: a narrative review. Intensive care medicine. 2019;45(9):1200-11.
- 16. Woodhead M, Blasi F, Ewig S, Garau J, Huchon G, leven M, et al. Guidelines for the management of adult lower respiratory tract infections--full version. Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2011;17 Suppl 6:E1-59.
- 17. Rambhia SH, D'Agostino CA, Noor A, Villani R, Naidich JJ, Pellerito JS. Thoracic Ultrasound: Technique, Applications, and Interpretation. Curr Probl Diagn Radiol. 2017;46(4):305-16.
- 18. Volpicelli G, Elbarbary M, Blaivas M, Lichtenstein DA, Mathis G, Kirkpatrick AW, et al. International evidence-based recommendations for point-of-care lung ultrasound. Intensive care medicine. 2012;38(4):577-91.
- 19. Soldati G, Smargiassi A, Inchingolo R, Buonsenso D, Perrone T, Briganti DF, et al. Proposal for International Standardization of the Use of Lung Ultrasound for Patients With COVID-19: A Simple, Quantitative, Reproducible Method. J Ultrasound Med. 2020.
- 20. Li L, Yang Q, Li L, Guan J, Liu Z, Han J, et al. [The value of lung ultrasound score on evaluating clinical severity and prognosis in patients with acute respiratory distress syndrome]. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue. 2015;27(7):579-84.

- 21. Deng Q, Zhang Y, Wang H, Chen L, Yang Z, Peng Z, et al. Semiquantitative lung ultrasound scores in the evaluation and follow-up of critically ill patients with COVID-19: a single-center study. Acad Radiol. 2020.
- 22. Lomoro P, Verde F, Zerboni F, Simonetti I, Borghi C, Fachinetti C, et al. COVID-19 pneumonia manifestations at the admission on chest ultrasound, radiographs, and CT: single-center study and comprehensive radiologic literature review. Eur J Radiol Open. 2020;7:100231.
- 23. Ye Z, Zhang Y, Wang Y, Huang Z, Song B. Chest CT manifestations of new coronavirus disease 2019 (COVID-19): a pictorial review. Eur Radiol. 2020.
- 24. Zieleskiewicz L, Markarian T, Lopez A, Taguet C, Mohammedi N, Boucekine M, et al. Comparative study of lung ultrasound and chest computed tomography scan in the assessment of severity of confirmed COVID-19 pneumonia. Intensive care medicine. 2020;46(9):1707-13.
- 25. Jambrik Z, Gargani L, Adamicza A, Kaszaki J, Varga A, Forster T, et al. B-lines quantify the lung water content: a lung ultrasound versus lung gravimetry study in acute lung injury. Ultrasound Med Biol. 2010;36(12):2004-10.
- 26. Soldati G, Demi M, Inchingolo R, Smargiassi A, Demi L. On the Physical Basis of Pulmonary Sonographic Interstitial Syndrome. J Ultrasound Med. 2016;35(10):2075-86.
- 27. Rubin GD, Ryerson CJ, Haramati LB, Sverzellati N, Kanne JP, Raoof S, et al. The Role of Chest Imaging in Patient Management during the COVID-19 Pandemic: A Multinational Consensus Statement from the Fleischner Society. Chest. 2020.
- 28. Zhu J, Zhong Z, Li H, Ji P, Pang J, Li B, et al. CT imaging features of 4121 patients with COVID-19: A meta-analysis. Journal of medical virology. 2020;92(7):891-902.
- 29. Mohamed MFH, Al-Shokri S, Yousaf Z, Danjuma M, Parambil J, Mohamed S, et al. Frequency of Abnormalities Detected by Point-of-Care Lung Ultrasound in Symptomatic COVID-19 Patients: Systematic Review and Meta-Analysis. The American journal of tropical medicine and hygiene. 2020;103(2):815-21.
- 30. Testa A, Soldati G, Copetti R, Giannuzzi R, Portale G, Gentiloni-Silveri N. Early recognition of the 2009 pandemic influenza A (H1N1) pneumonia by chest ultrasound. Crit Care. 2012;16(1):R30.
- 31. Zhao L, Yu K, Zhao Q, Tian R, Xie H, Xie L, et al. Lung Ultrasound Score in Evaluating the Severity of Coronavirus Disease 2019 (COVID-19) Pneumonia. Ultrasound Med Biol. 2020.
- 32. Nakajima K, Kato H, Yamashiro T, Izumi T, Takeuchi I, Nakajima H, et al. COVID-19 pneumonia: infection control protocol inside computed tomography suites. Jpn J Radiol. 2020;38(5):391-3.
- 33. Pan L, Wang L, Huang X. How to face the novel coronavirus infection during the 2019-2020 epidemic: the experience of Sichuan Provincial People's Hospital. Intensive care medicine. 2020;46(4):573-5.
- 34. Radiology ACo. ACR Recommendations for the use of Chest Radiography and Computed Tomography (CT) for Suspected COVID-19 Infection 2020 [Available from: https://www.acr.org/Advocacy-and-Economics/ACR-Position-Statements/Recommendations-for-Chest-Radiography-and-CT-for-Suspected-COVID19-Infection.

Figure legends.

Figure 1. Pathological patterns of lung ultrasound observed in COVID-19, with a convex probe and a large field of view, on sagittal scans. Rib shadowing (R) is visible on the sides of the images. **A.** Four B lines (small white arrows) spreading out from the pleural surface. **B.** Confluent B lines (white arrowheads) shaping a curtain covering the depth of the image (white lung). **C.** Thickening of the pleural line with small (< 1 cm) irregularities (small black arrows) **D.** Large consolidation (> 1 cm) (yellow arrow). **E.** Small pleural effusion (large white arrow) forming a hypoechoic line between the thoracic wall and the lung.

Figure 2. Proportion of lung zones affected in the different severity patients groups: outpatients, admitted patients and patients intubated and/or dead.

Boxplot with median and interquartile range.

Figure 3. Distribution of the different lung ultrasound patterns in the different examined lung zones in all patients and according to patient outcome.

Figure 4. Boxplot of the lung ultrasound score and the normalized lung ultrasound score according to patient outcome.

Boxplot with median and interquartile range

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Table 1. Characteristics of study participants at the time of inclusion in the emergency department, classified according to their day 7 clinical outcome.

COX	All patients (n = 80)	Outpatients (n = 17)	Hospitalized patients (n = 42)	Patients intubated or death (n = 21)	p value
Demographics					
Female sex; n (%)	34 (42)	9 (53)	17 (40)	8 (38)	0.608
Age, years; Mean (SD)	62 (17)	51 (18)	62 (17)	70 (10)	0.002
Age distribution					0.002
< 50 years	21 (26)	10 (56)	10 (24)	1 (4.8)	
50-65 years	23 (29)	3 (17)	15 (36)	5 (24)	
> 65 years	36 (45)	4 (24)	17 (40)	15 (71)	
Residence in nursing home; n (%)	8 (10)	0 (0)	4 (10)	4 (19)	0.291
Current smoker; n (%)	1 (1.3)	1 (6)	0 (0)	0 (0)	0.153
Alcohol misuse; n (%)	8 (10)	2 (12)	3 (7)	3 (16)	0.572

	Coexisting disorder; n (%)		5			
	Any	58 (72)	12 (71)	31 (74)	15 (71)	0.961
	Hypertension	39 (49)	6 (35)	23 (54.8)	10 (48)	0.396
	Diabetes	16 (20)	3 (18)	11 (26)	2 (9.5)	0.286
	Obesity	22 (39)	4 (29)	12 (30)	7 (41)	0.606
	Asthma	19 (24)	6 (35)	10 (24)	3 (14)	0.318
	Cardiovascular disease *	10 (12)	1 (5.9)	5 (12)	4 (19)	0.468
	Chronic obstructive pulmonary disease	3 (4)	0 (0.0)	2 (4.8)	1 (4.8)	0.657
	Neurological disorders †	12 (15)	1 (5.9)	4 (9.5)	7 (33)	0.022
	Active cancer	3 (3.8)	0 (0)	1 (2.4)	2 (9.5)	0.244
	Hepatitis or liver cirrhosis	2 (2.5)	0 (0)	1 (2.4)	1 (4.8)	0.644
	Chronic renal failure ‡	3 (3.8)	0 (0)	2 (4.8)	1 (4.8)	0.657
	Chronic inflammatory diseases	4 (5.0)	2 (12)	2 (4.8)	0 (0)	0.253
	Symptoms					
	Duration, days; Median (IQR)	7 [6, 11]	7 [5, 10]	8 [7, 12]	9 [4, 10]	0.485
	History of fever; n (%)	64 (83)	14 (82)	34 (81)	16 (89)	0.750
	Cough; n (%)	71 (91)	16 (94)	39 (93)	16 (84)	0.484
	Dyspnoea; n (%)	59 (75)	8 (47)	33 (79)	18 (90)	0.008
Vital signs at inclusion in emergency department						
	Temperature, °C; Median (IQR)	37.5 (36.8, 38.4)	37 (37, 38)	37.6 (37, 38)	38 (37, 38)	0.626
	Systolic blood pressure, mmHg;	132 (119, 142)	131 (115, 138)	134 (126, 144)	124 (117, 141)	0.079
	Heart rate, bpm; Median (IQR)	85 (78, 97)	78 (75, 83)	90 (81, 99)	91 (82, 98)	0.006
	Respiratory rate, vpm; Median (IQR)	24 (18, 28)	20 (17, 22)	24 (18, 29)	26 (24, 31)	0.001
	Respiratory rate ≥ 22 vpm; n (%)	47 (62)	6 (37)	25 (60)	16 (89)	0.006

Oxygen therapy; n (%)	31 (41)	0 (0)	18 (44)	13 (68)	<0.001
Saturation/fio2; Median (IQR)	4.4 (2.9, 4.6)	4.6 [4.6, 4.6]	4.2 [3, 4.5]	2.6 (1.3, 4.3)	<0.001
Glasgow coma scale < 15; n (%)	2 (2.6)	0 (0)	0 (0)	2 (10)	0.044
Laboratory findings at inclusion in em	ergency department				
Leukocyte count, G/L; Median (IQR)	6.2 (4.9, 8.5)	5 (4.3, 6.0)	6.3 (5.0, 7.3)	8.9 (6.2, 10)	<0.001
Hemoglobin, g/L; Median (IQR)	140 (129, 149)	146 (142, 152)	137 (125, 146)	135 (131, 149)	0.070
Platelet count, G/L; Median (IQR)	209 (162, 282)	223 (163, 256)	210 (165, 294)	185 (158, 275)	0.798
C-reactive protein, mg/L; Median (IQR) 72 (30, 147)	30 (9, 40)	72 (24, 143)	141 (89, 229)	<0.001
Glucose, mmol/L; Median (IQR)	6.6 (5.6, 8)	5.8 (5.2, 6.7)	6.6 (5.6, 7.5)	7.8 (7.0, 9.7)	0.011
Creatinine, µmol/L; Median (IQR)	91 (77, 113)	91 (68, 94)	91 (74, 115)	94 (88, 129)	0.049
Radiologic					
Chest radiograph performed; n (%)	76 (95)	13 (76)	42 (100)	21 (100)	<0.001
Infiltrate on chest radiograph; n (%) 58 (76)	5 (38)	33 (79)	20 (95)	<0.001
CT scan performed; n (%)	8 (10)	1 (6)	4 (9.8)	3 (14)	0.690

^{*} Heart failure, coronary disease. †Stroke, dementia, parkinson. ‡Stade III-V according to CKD classification.

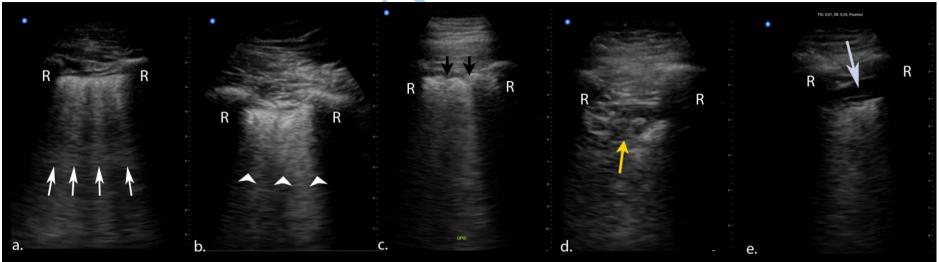
Missing values: smoking status 1, alcohol use 3, obesity 23, duration of symptoms 8, fever 3, cough 2, dyspnoea 1, vital signs 12, blood count 1, C-reactive protein 2, glucose 22, chest radiograph and Ct scan 4.

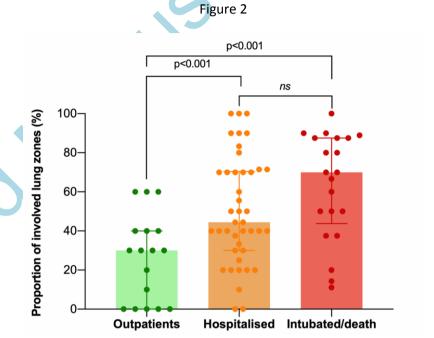
 Table 2. Lung ultrasound characteristics of study participants at inclusion in the emergency department according to clinical outcome at day seven.

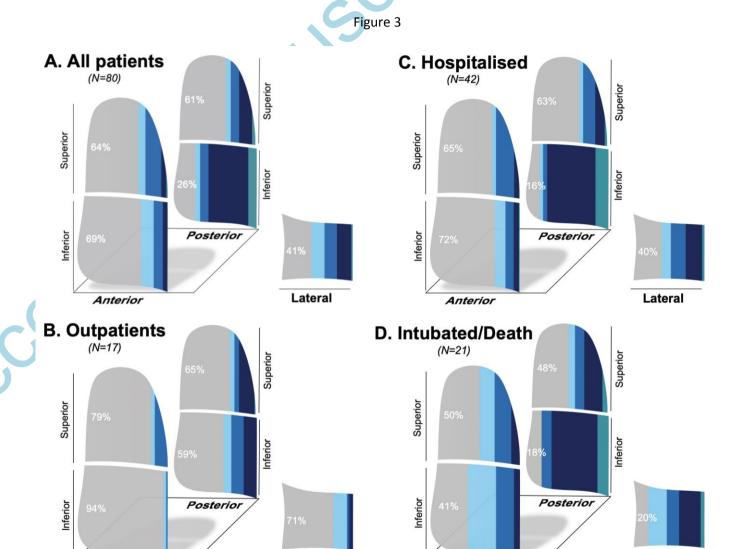
No. (%)	All patients	Outpatients	Hospitalized	Patients intubated or	p value
	(n = 80)	(n = 17)	patients (n = 42)	death (n = 21)	
Abnormal lung ultrasound Distribution	73 (91)	12 (70)	40 (95)	21 (100)	0.003
Multifocal	68 (85)	11 (64)	39 (93	18 (86)	0.023
Bilateral	63 (80)	10 (59)	35 (85)	18 (86)	0.053
Identified patterns					
Normal appearance	76 (95)	17 (100)	39 (93)	20 (95)	0.521
Pathologic B lines (≥3)	40 (50)	7 (41)	16 (38)	17 (81)	0.004

Confluent B lines (White lung)	48 (60)	8 (47)	27 (64)	13 (62)	0.463
Thickening of the pleura with pleural line irregularities	56 (70)	6 (35)	34 (81)	16 (76)	0.002
Consolidations (>1cm)	20 (25)	1 (5.9)	12 (29)	7 (33)	0.209
Pleural effusion	20 (25)	2 (12)	11 (27)	7 (33)	0.515
Bilateral	6 (30)	1 (50)	3 (27)	2 (28)	0.808
< 5 mm	17 (85)	2 (100)	8 (73)	7 (100)	0.236









Lateral

Anterior

Anterior

Lateral

Figure 4

