Lung Ultrasound Integration in Assessment of Patients with Noncritical COVID-19

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Objectives—Performing lung ultrasound during the clinical assessment of patients with suspicion of noncritical COVID-19 may increase the diagnostic rate of pulmonary involvement over other diagnostic techniques used in routine clinical practice. This study aims to compare complications (readmissions, emergency department [ED] visits, and length of outpatient follow-up) in the first 30 days after ED discharge in patients with confirmed COVID-19 who were managed with versus without lung ultrasound.

Materials and Methods—Prospective, observational, analytical study in noncritical patients with confirmed respiratory disease due to SARS-CoV-2, assessed in the ED of a tertiary Spanish hospital in March and April 2020. We compared 2 cohorts, differentiated by the use of lung ultrasound as a diagnostic tool. Complications were assessed (hospital admissions, ED revisits and days of outpatient follow-up) at 30 days postdischarge.

Results—Of the 88 included patients, 31% (n = 27) underwent an initial lung ultrasound, while 61 (68%) did not. In 82.5% of the patients evaluated with ultrasound, the most predominant areas affected were the posterobasal regions, in the form of focalized and confluent B-lines; 70.4% showed pleural irregularity in these same areas. Use of the lung ultrasound was associated with a greater probability of hospital admission (odds ratio 5.63, 95% confidence interval 3.31 to 9.57; p < 0.001). However, it was not significantly associated with mortality or short-term complications.

Conclusions—Lung ultrasound could identify noncritical patients with lung impairment due to SARS-CoV-2, in whom other tests used routinely show no abnormalities. However, it has not shown a prognostic value in these patients and could generate a higher percentage of hospital admissions. More studies are still needed to demonstrate the clear benefit of this use.

Key Words—COVID-19; pneumonia; lung; ultrasonography; point-of-care; emergency departments

Introduction

The emergence of the SARS-CoV-2 (COVID-19) pandemic has mobilized the scientific community to quickly create a global research network on the topic, which has proven crucial for generating knowledge and helping to control the disease.1,2,3 The data available show that most people infected with COVID-19 have mild symptoms, although the precise proportion

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Abbreviations
CI, confidence interval; CT, computed tomography; ED, emergency department; IQR, interquartile ranges; OR, odds ratio; SD, standard deviation

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of these cases is difficult to estimate. This population group has a greater potential to transmit the disease than patients with more severe symptoms, so their early detection could decisively contribute to containing the spread of the virus.

Together with blood and molecular tests, imaging examinations constitute a basic pillar for diagnosis. In those with mild to moderate symptoms, respiratory involvement is mostly assessed by conventional chest radiograph and computed tomography (CT). The latter is the gold standard, revealing the characteristic ground glass opacities and bilateral pneumonia that predominate in peripheral posterobasal regions. The diagnostic precision reaches a sensitivity of up to 98% and a specificity of 25%, with a positive and negative predictive values of about 65% and 83%, respectively, at 6 to 11 days after symptom onset. In the case of the chest radiograph, the most commonly described presentation is characterized by basal consolidations, which become apparent 10 to 12 days after the appearance of the first symptoms. However, the sensitivity of this technique is limited for COVID-19–induced pneumonia.

In light of this situation, the lung ultrasound has been increasingly used in China, the USA and Europe, as a method that provides dynamic and accessible information, reduces the risk of transmission, and improves sensitivity. Although the correlation between CT and lung ultrasound findings has not been demonstrated in studies with strong statistical power, theoretically, the peripheral location of the lung damage makes the ultrasound a valid alternative technique. In other instances of pneumonia, this method has shown to be comparable to the CT.

In intensive care units, ultrasounds are the accepted diagnostic tool to monitor patients for acute respiratory distress syndrome secondary to SARS-CoV-2 pneumonia. However, this tool may also be a useful first-line diagnostic tool for early detection of the disease in noncritical patients, reducing the risk of short-term described complications.

Thanks to the portability of the equipment and clinical training of professionals in lung ultrasound, this technique is being introduced in many areas of patient care. However, more studies are necessary to establish the prognostic value of ultrasound findings.

We hypothesize that performing an ultrasound during the clinical assessment of patients suspected of mild to moderate lung affection due to COVID-19 could improve the early diagnosis of lung damage in this disease and possibly help identify the cases at risk of an unfavorable evolution. Thus, the primary objective is to compare complications (hospital admissions, emergency department [ED] revisits, and length of outpatient follow-up) in the first 30 days after ED discharge in patients with confirmed COVID-19 who were managed with versus without lung ultrasound.

**Material and Methods**

Prospective analytical cohort study in patients with suspected of having COVID-19 who presented to the ED at the General University Hospital of Alicante in March and April 2020. The study included adults (≥18 years) with COVID-19 confirmed by nasopharyngeal aspirate with real time-polymerase chain reaction (RT-PCR). All patients had noncritical symptomology with a nonpathological or inconclusive chest radiograph on assessment by a radiologist. Participants were divided into 2 cohorts: the first underwent clinical, analytical, radiological, and lung ultrasound assessment; in the second, lung ultrasound was not performed. Exclusion criteria were patients with a lung pathology that complicated interpretation of the ultrasound and those for whom data could not be obtained. We calculated a sample size to obtain 80% power and a significance level of 5%, considering that 7% to 10% of patients with positive RT-PCR would experience complications, based on data published up to 14 May 2020 by the Ministry of Health Centre for Coordination of Alerts and Emergencies. However, all patients evaluated with ultrasound with a positive RT-PCR result were included. They were compared with another group that did not undergo ultrasound, maintaining a ratio above 3:1.

Demographic, clinical, and analytical variables were collected. Outcome variables were destination upon discharge from the ED (hospital admission, home hospital unit, preventive medicine, primary health care, medical hotel) and the patient’s evolution over the next 30 days (ED revisits at 72 hours and at
We studied the ultrasound findings that have been associated with lung damage from SARS-CoV-2 since the beginning of the pandemic\textsuperscript{17,24,25}: interstitial pattern with focalized B-lines (separated and/or coalescent in severe cases, denominated as “white lung”), with patchy distribution of lesions alternating with normal areas, in the form of A-lines. Some authors have described an ultrasound sign in patients in the initial phase of lung damage, presenting as a “light beam,” which consists of vertical bands of B-lines shaped like light beams that appear and disappear with breathing (on–off phenomenon). The presence of this sign in the early stages of illness could minimize the disassociation between clinical and radiological presentation.\textsuperscript{8} At a pleural level, there are irregularities, such as fragmentation and subpleural consolidations, which may even be translobar in cases that are severe or with superinfections. The described ultrasound patterns and their distribution could help determine the severity and spread of the damage in a semi-quantitative way.\textsuperscript{17,18,25} Together with clinical signs and symptoms, these patterns (whether appearing alone or in combination) can be considered compatible with COVID-19 (Figure 1).

The clinicians who performed the ultrasound were unaware of the results of the RT-PCR and decided to manage the patient based on the ultrasound findings.

Patients with ultrasound findings showing lung involvement were treated according to the protocols established by the hospital’s commission on infectious diseases, with antibiotics and hydroxychloroquine. In the ultrasound group, the clinician decided hospital admission based on ultrasound findings. Patients who presented bilateral ultrasound involvement were considered patients with bilateral pneumonia. Following the indicated hospital protocols, those patients with suspected COVID with bilateral radiological involvement were admitted to the hospital. For this reason, patients with negative radiography but bilaterally affected ultrasound were treated as patients with bilateral pneumonia and, therefore, admitted. Patients with unilateral involvement, both radiographic and ultrasound, could be discharged with outpatient management.

The rest of the data were obtained from the electronic health record (Orion Clinic).
**Statistical analysis**

A descriptive analysis was performed; qualitative variables were expressed as absolute and relative frequencies, and quantitative variables as medians and interquartile ranges (IQR). Qualitative variables were compared using the chi-squared or Fisher’s exact test, as appropriate, and quantitative variables, using the Mann–Whitney U test. The estimated magnitude of association was expressed as a crude odds ratio (OR) with 95% confidence interval (CI). Analyses were performed using SPSS software, v.26 (IBM, New Castle, NY, USA).

**Ethical aspects**

The study complied with the ethical principles of the Declaration of Helsinki for medical research in

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**Figure 1.** Lung ultrasound in patients with COVID-19, according to the scoring system devised by Soldati et al. (A) Score 0. A-lines, regular pleura: pattern of equidistant, horizontal lines (thin arrow), parallel to pleura. Compatible with normal findings. Linear pleural line in the presence of pleural sliding*. (B) Score 1. Irregular focalized/pleural B-lines: pattern of B-lines, vertical lines that reach the depth of the field and start at the (discontinuous) pleural line. They appear in patches and alternate with areas of a normal pattern. In the initial phases, they can appear and disappear with breathing (light beam). The pleural line is fragmented*. (C) Score 2. Confluent B-lines and/or subpleural consolidation: in “white lung” (thick arrow), the B-lines converge and the pleural irregularity is increased, generating a pattern of consolidation**. (D) Score 3. Translobar consolidation: in severe cases or in the presence of superinfection, subpleural consolidation has a hepatized, tissue-like appearance.
humans, and the medical research ethics committee of the General University Hospital of Alicante approved the protocol (reference PI2020-070). In light of the urgent need to collect data, the requirement to obtain informed consent from participants was waived.

Results

Participant characteristics

The study included 88 patients with a mean age of 51.2 years (standard deviation [SD] 18.1): 27 (31%) received a lung ultrasound during their exploratory clinical assessment, while 61 (68%) did not (Figure 2).

None of the patients required admission to the ICU or mechanical ventilation therapy since the sample collected consisted of individuals with mild symptoms, which in turn represents the highest percentage of those affected by COVID-19.

Ultrasound findings

Figure 3 shows the distribution of ultrasound findings. Our analysis of the cohort receiving lung ultrasound showed the proportion of each region affected. In 82.5% of the patients evaluated with ultrasound, the most predominant areas affected were the posterobasal regions, in the form of focalized and confluent B-lines; 70.4% showed pleural irregularity in these same areas.

Damage was predominantly in the posterobasal areas and took the form of focalized and confluent B-lines (85.2% of cases in the R1 region, 77.8% in R2, and 88.9% each in L1 and L2). A score of 2 (confluent B-lines presenting as white lung, with pattern of subpleural consolidation) was most prevalent in these regions (63% in R1, 48.1% in R2, 25.9% in L1 and 44.4% in L2).

Tables 1 and 2 show participants’ baseline and analytical characteristics. The only difference between the 2 groups was obesity, which was more frequent in patients evaluated by ultrasound.
Table 1. Baseline characteristics of patients with positive RT-PCR for COVID-19 and attended in the emergency department

| Variables                              | Total N = 88 | Yes N = 27 | No N = 61 | p value |
|----------------------------------------|--------------|------------|-----------|---------|
| Age in years, mean (SD)                | 51.2 (18.1)  | 50.2 (18.6) | 51.5      |         |
| Gender, n (%)                          |              |            |           |         |
| Women                                  | 48 (54.5)    | 17 (63)    | 31 (51.7) | 0.33    |
| Men                                    | 40 (45.5)    | 10 (37)    | 29 (48.3) |         |
| Contact with COVID-19                  | 53 (60.22)   | 17 (63)    | 35 (57.4) | 0.79    |
| Comorbidities                          |              |            |           |         |
| Hypertension, n (%)                    | 21 (23.9)    | 8 (29.6)   | 13 (21.3) | 0.4     |
| Diabetes mellitus, n (%)               | 10 (11.4)    | 3 (11.1)   | 7 (11.5)  | 0.99    |
| Obesity, n (%)                         | 14 (15.9)    | 8 (29.6)   | 6 (9.8)   | 0.028   |
| Lung disease, n (%)                    | 10 (11.4)    | 3 (11.1)   | 7 (11.5)  | 0.99    |
| NSAIDs, n (%)                          | 2 (2.3)      | 1 (3.7)    | 1 (1.6)   | 0.52    |
| ACE inhibitors, n (%)                  | 6 (6.8)      | 2 (7.4)    | 4 (6.6)   | 0.99    |

RT-PCR: real time-polymerase chain reaction; COVID-19: coronavirus disease 2019; NSAID: nonsteroidal anti-inflammatory drug; ACE: angiotensin-converting enzyme; SD: standard deviation

Table 2. Clinical and analytical variables in patients attended at the emergency department

| Variables                              | Total N = 88 | Yes N = 27 | No N = 61 | p value |
|----------------------------------------|--------------|------------|-----------|---------|
| Clinical variables                     |              |            |           |         |
| Duration of symptoms at diagnosis, days, median (IQR) | 4.5 (2.25–7) | 5 (3–10) | 4 (2–7) | 0.63 |
| Dyspnea, n (%)                         | 68 (77.3)    | 20 (74.1)  | 48 (78.7) | 0.77 |
| Cough, n (%)                           | 72 (81.8)    | 23 (85.2)  | 49 (80.3) |         |
| Fever, n (%)                           | 64 (72.7)    | 16 (59.3)  | 48 (78.7) | 0.06 |
| Loss of smell/taste, n (%)             | 15 (17)      | 7 (25.9)   | 8 (13.1)  | 0.22 |
| Diarrhea n (%)                         | 13 (14.8)    | 6 (22.2)   | 7 (11.5)  | 0.21 |
| Myalgia, n (%)                         | 40 (45.5)    | 10 (37)    | 30 (49.2) | 0.29 |
| Contact with COVID-19, n (%)           | 53 (60.22)   | 17 (63)    | 35 (57.4) | 0.79 |
| Analytical variables, median (IQR)     |              |            |           |         |
| Leucocytes (cells/μL)                  | 6210 (4970–78075) | 6210 (5555–8165) | 6250 (4540–9442) | 0.46 |
| Lymphocytes (cells/μL)                 | 1535 (1180–20675) | 1550 (1002–2050) | 1530 (1205–20175) | 0.81 |
| C-reactive protein (mg/dL)             | 0.94 (0.2–2.1) | 1.18 (0.1–4.62) | 0.69 (0.19–1.2) | 0.21 |
| Procalcitonin (ng/mL)                  | 0.05 (0.03–0.08) | 0.05 (0.04–0.08) | 0.05 (0.02–0.08) | 0.88 |
| Lactate dehydrogenase (U/L)            | 189.5 (160.75–243.75) | 204.5 (164.5–217.75) | 177.5 (150–217.75) | 0.078 |
| Ferritin (μL)                          | 140 (49.5–380.25) | 139.5 (0–555) | 153 (7725–255.75) | 0.82 |
| D-dimer (ng/mL)                        | 0.39 (0.32–0.6) | 0.425 (0.33–0.58) | 0.466 (0.24–0.81) | 0.36 |
| Troponin I (ng/L)                      | 5 (5–8)      | 5 (5–7)    | 6 (5–75)  | 0.53 |
| Pro-BNP (pg/mL) median (IQR)           | 53 (21–96)   | 54.5 (29.5–71.25) | 43 (17–85.5) | 0.95 |

BNP: B-type natriuretic peptide; IQR: interquartile range

Clinical evolution
Table 3 summarizes the results for the clinical evolution in each study group. The only outcome associated with the performance of the ultrasound was the decision to admit the patient to hospital (OR 5.63, 95% CI 3.31 to 9.57, p < 0.001).

Discussion
This study compares 2 cohorts of noncritical patients with COVID-19 who were evaluated with or without lung ultrasound, at 30 days follow-up. Lung ultrasound could be useful for early diagnosis of lung
involvement treatment decision. The use of this technique was associated with a greater probability of hospital admissions, but it did not show a relationship with mortality; therefore, a prognostic value of ultrasound has not been demonstrated in these patients. There were no differences in the incidence of

Figure 3. Distribution of scores, according to the system proposed by Soldati et al. in each of the regions explored by ultrasound in patients with positive RT-PCR.
complications at 30 days postdischarge, between both groups. The peculiarity of our study is that it includes noncritical patients, who are the majority of those affected by COVID-19. In our center, use of the ultrasound conditioned the decision to admit patients for closer clinical management, while other studies have pointed to its role in controlling transmission\textsuperscript{26} in the early phases of the disease.\textsuperscript{27,28} In part, this may be due to the early adoption of protective measures in patients with ultrasound findings that are suggestive of lung damage. The results show that the lung ultrasound identified more lung impairments missed by radiograph and routine care, which led to more hospitalizations, despite having noncritical symptoms. This fact could imply a higher risk due to hospitalization and an increase in healthcare costs. Although the detection of lung involvement is higher with ultrasound, the increase in hospital admission of these patients did not show a clear benefit and there were no differences in prognosis between 2 groups. The difficulty in assessing mortality in our study may be due to the limited sample and population with low severity disease. More studies are needed to evaluate its prognostic value.

The most frequent findings in this initial phase of COVID-19--induced lung damage were confluent B-lines presenting as white lung, with a pattern of subpleural consolidation.\textsuperscript{17,18,20,21,24,25,26} The distribution of the lesions observed in our patients coincides with previously published studies.\textsuperscript{17,18,20,21,24,25,26} While the lung ultrasound was not significantly predictive of our outcome variables, some limitations should be considered when drawing conclusions. First of all, the sample size was small, and the size could not be adjusted to what was estimated, so it is

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**Table 3.** Evolution of patients attended in the emergency department

| Variables                                      | Total N = 88 | Yes N = 27 | No N = 61 | p value |
|------------------------------------------------|--------------|------------|-----------|---------|
| **Destination upon discharge**                 |              |            |           |         |
| Hospital admission, n (%)                      | 16 (18.2)    | 15 (55.6)  | 1 (1.6)   | < 0.001 |
| Home hospital unit, n (%)                      | 9 (10.2)     | 4 (14.8)   | 5 (8.2)   | 0.45    |
| Primary health care, n (%)                     | 76 (86.4)    | 23 (85.2)  | 53 (86.9) | 0.99    |
| Medical hotel, n (%)                           | 39 (44.3)    | 13 (48.1)  | 26 (42.6) | 0.63    |
| **Evolution at 30 days**                       |              |            |           |         |
| Revisit to emergency department                |              |            |           |         |
| At 72 h                                        | 11 (12.5)    | 2 (7.4)    | 9 (14.8)  | 0.49    |
| At 30 days                                     | 26 (29.5)    | 5 (18.5)   | 21 (34.4) | 0.13    |
| Death                                          | 0 (0)        | -          | -         | -       |
| Days to discharge from the preventive medicine service, median (IQR) | 26.5 (19–34.75) | 25 (21–35) | 27 (175–34.5) | 0.48    |

IQR: interquartile range
possible that the power of the study differs from that initially calculated. The main reason is the context of the country-wide lockdown in effect at the time of the study, so that few patients with mild symptoms presented to emergency health services. A second limitation is that the ultrasound is a somewhat operator-dependent technique, which could give rise to some variations in the results. To minimize the risk of this bias, a single, experienced professional read all the results, with potential for 2 experts to review them with blinding maintained at all times. Thirdly, in a pandemic situation, the high prevalence of respiratory infection attributed to SARS-CoV-2 could have generated a bias because ultrasound findings are not apt to determine etiology, so all findings compatible with COVID-19 were considered as such. Finally, the changing management protocols, together with the heterogeneous management of the disease at different care levels and in different Spanish regions, could limit the application of conclusions. Detecting lung damage in this group of patients is the main objective, to begin early isolation and treatment. Taken together, our results support the possible utility of including the lung ultrasound in the early diagnostic process of noncritical SARS-CoV-2 patients. However, more studies are needed to confirm its prognostic value and justify the integration of the ultrasound at different care levels, due to its contribution to increasing hospital admissions and more risks and higher healthcare costs generated.

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