

● Review

PULMONARY ULTRASOUND IN THE DIAGNOSIS AND MONITORING OF CORONAVIRUS DISEASE (COVID-19): A SYSTEMATIC REVIEW

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Abstract—The goal of this review was to systematize the evidence on pulmonary ultrasound (PU) use in diagnosis, monitorization or hospital discharge criteria for patients with coronavirus disease 2019 (COVID-19). Evidence on the use of PU for diagnosis and monitorization of or as hospital discharge criteria for COVID-19 patients confirmed to have COVID-19 by reverse transcription polymerase chain reaction (RT-PCR) between December 1, 2019 and July 5, 2020 was compared with evidence obtained with thoracic radiography (TR), chest computed tomography (CT) and RT-PCR. The type of study, motives for use of PU, population, type of transducer and protocol, results of PU and quantitative or qualitative correlation with TR and/or chest CT and/or RT-PCR were evaluated. A total of 28 articles comprising 418 patients were involved. The average age was 50 y (standard deviation: 25.1 y), and there were 395 adults and 23 children. One hundred forty-three were women, 13 of whom were pregnant. The most frequent result was diffuse, coalescent and confluent B-lines. The plural line was irregular, interrupted or thickened. The presence of subpleural consolidation was noduliform, lobar or multilobar. There was good qualitative correlation between TR and chest CT and a quantitative correlation with chest CT of $r=0.65$ ($p < 0.001$). Forty-four patients were evaluated only with PU. PU is a useful tool for diagnosis and monitorization and as criteria for hospital discharge for patients with COVID-19. (E-mail: Vpanduro@unheval.edu.pe) © 2021 World Federation for Ultrasound in Medicine & Biology. All rights reserved.

Key Words: COVID-19, Pulmonary ultrasound, B-Lines, Thoracic radiography, Thoracic tomography.

INTRODUCTION

Since the first cases were described in the province of Hubei in China, coronavirus has become one of the most important infectious diseases of the century, and by the 20th of September 2020, almost 1 million deaths had been reported worldwide (Arteaga-Livias and Rodriguez-Morales 2020). Because it is a new disease, many questions concerning its clinical characteristics, diagnosis and treatment remain (Dhama et al. 2020; Pecho-Silva et al. 2020).

The tools available for diagnosis and monitoring are important to ensure correct clinical decisions and a better comprehension of the evolution of the disease, as well as the possibility of complications in a patient with mild to

moderate disease (Henriquez-Marquez et al. 2021). Diverse authors coincide in that pulmonary ultrasound (PU) can be used in diverse stages of the disease caused by coronavirus disease 2019 (COVID-19), including triage of asymptomatic patients; diagnosis, monitoring and follow-up; evaluation of response to treatment; decision to remove the patient from the mechanical ventilator; and as a criterion for patient discharge (Kristensen et al. 2014; Gargani et al. 2020; Soldati et al. 2020). PU would also have an additional advantage over chest x-ray (CXR) and chest computed tomography (CT), as it is a procedure that can be performed with portable equipment, thereby minimizing patient mobilization and the number of healthcare personnel required and, thus, reducing the number of professionals exposed to a possible contagion (Convissar et al. 2020; Pecho-Silva 2020; Smith et al. 2020).

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Some articles have been published on the use of PU in COVID-19, as have reviews with fewer than 60 patients (Convissar et al. 2020; Smith et al. 2020). The number of articles published has increased rapidly; therefore, it is imperative to have up-to-date data on this topic to facilitate decision-making.

This review aims to systemize the published evidence on the use of PU in the diagnosis and follow-up and as a criterion for discharge of patients with COVID-19, and to evaluate its correlation with other diagnostic procedures such as CXR, chest CT and tests of reverse transcription polymerase chain reaction (RT-PCR).

METHODS

Search strategies

This study was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) checklist. The protocol is available in the Figshare repository (Taype-Rondan 2020). A systematic search was carried out in the following databases (between December 1, 2019 and July 5, 2020), with the following terms:

Pubmed: ("2019/12/01"[Date–Publication]: "2020/07/05"[Date–Publication]) AND (((lung or chest or pulmo* or thora*) and (ultraso* or sonog* or echography)) and (Covid* or SARS* or coronavirus*)).

Scopus: [(TITLE–ABS–KEY (*coronavirus OR sars* OR covid*) AND TITLE–ABS–KEY (ultraso* OR *sonography OR echography)) AND (LIMIT-TO (PUBYEAR, 2020) OR LIMIT-TO (PUBYEAR, 2019)) AND (LIMIT-TO (SUBJAREA, "MEDI")) AND (LIMIT-TO (LANGUAGE , "English") OR LIMIT-TO (LANGUAGE , "Spanish"))].

Google Scholar: (((lung or chest or pulmo* or thora*) and (ultraso* or sonog* or echography)) and (Covid* or SARS* or coronavirus*)).

Selection of studies

For this systematic review, all primary articles were included, including case series for more than one patient and case reports (including letters to the editor), in which PU was part of the diagnostic evaluation and/or clinical follow-up and/or as a criterion for discharge of patients with COVID-19 confirmed by RT-PCR. Studies in which modifications had been made to the conventional PU technique were excluded.

The selection of articles was carried out independently by two investigators (S.P.S., A.C.N.S.). If there was no agreement, a third investigator (J.T.V.) made the decision to include or exclude the study. All studies included in this systematic review were approved by the ethics committee.

Risk of bias

Two authors (K.A.L. and V.P.C.) rated the quality of the studies according to the National Institutes of Health Quality Assessment Tool for case series studies.

Extraction of data

The data from each study was extracted into a Microsoft Excel database designed for this purpose. Country, type of study, the reason PU was performed, population, type of transducer and evaluation protocol used, PU findings and the qualitative and/or quantitative correlation reported between PU and other imaging techniques (CXR or chest CT) were noted.

RESULTS

Search strategy

The search strategy yielded 949 results; 510 duplicates records were removed. Of 439 records screened, 405 were excluded by title and abstract screening. Of 34 full-text articles assessed for eligibility, 6 articles were excluded, and 28 articles were included in qualitative analysis (Alkhafaji et al. 2020; Bar et al. 2020; Buonsenso et al. 2020a, 2020b; Consoli et al. 2020; Denina et al. 2020; Duclos et al. 2020; Farrow et al. 2020; Feng et al. 2020; Huang et al. 2020; Inchingolo et al. 2020; Ji et al. 2020; Lomoro et al. 2020; Lu et al. 2020; Mongodi et al. 2020; Musolino et al. 2020; Nouvenne et al. 2020; Palmese et al. 2020; Peng et al. 2020; Poggiali et al. 2020; Reisinger and Koratala 2020; Shokoohi et al. 2020; Thomas et al. 2020; Tung-Chen 2020; Xing et al. 2020; Yang et al. 2020; Yasukawa and Minami 2020; Yassa et al. 2021) were included (Fig. 1). The studies were classified as follows: 2 retrospective cohort studies included 150 patients, 1 prospective cohort comprised 31 patients, a cross-sectional study comprised 26 patients, 14 case series that included between 3 and 30 patients and 10 case reports. Twenty-six articles were written in English, 1 in German and 1 in Chinese.

The 28 articles included a total of 418 patients with COVID-19 confirmed by RT-PCR. One hundred fifty patients were described in two retrospective cohorts, 31 patients in one prospective cohort study, 26 patients in one cross-sectional study, 201 patients in 14 case series studies and 10 patients in 10 case reports studies. PU was performed in the patients in all 28 articles as part of diagnosis, in 20 for clinical follow-up, in 5 as part of a routine procedure and in 5 as an additional criterion to decide whether to discharge the patient from hospital or discharge from the intensive care unit. Patient age was reported by 22 of 28 articles: one study (Feng et al. 2020) included 5 neonates aged 1 to 18 days, and another 21 articles registered 18 children or adolescents between 1 and 17 years and 395 adults. In 24 of 28 articles, the sex of the patients was noted, finding 203 men and 143

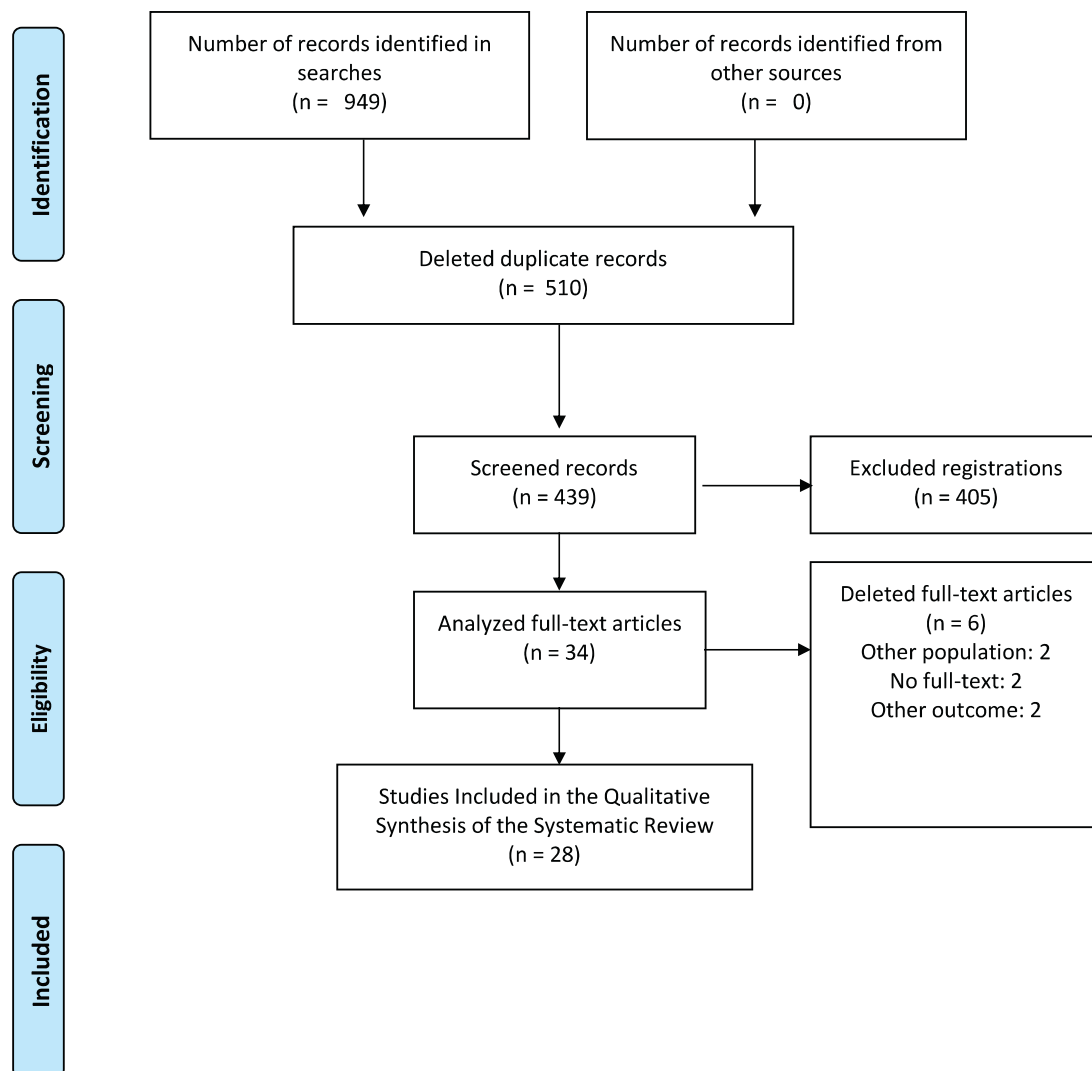


Fig. 1. Article selection flowchart.

women (Alkhafaji *et al.* 2020; Bar *et al.* 2020; Buonsenso *et al.* 2020a; Consoli *et al.* 2020; Denina *et al.* 2020; Duclos *et al.* 2020; Farrow *et al.* 2020; Feng *et al.* 2020; Huang *et al.* 2020; Inchingolo *et al.* 2020; Ji *et al.* 2020; Mongodi *et al.* 2020; Musolino *et al.* 2020; Nouvenne *et al.* 2020; Palmese *et al.* 2020; Poggiali *et al.* 2020; Reisinger and Koratala 2020; Shokoohi *et al.* 2020; Thomas *et al.* 2020; Tung-Chen 2020; Xing *et al.* 2020; Yang *et al.* 2020; Yassa *et al.* 2020; Yasukawa and Minami 2020) (Table 1).

Among the patients included, 13 were pregnant with an average gestation of 23.4 wk (standard deviation: 11.5 wk) at the time of diagnosis (Buonsenso *et al.* 2020b; Inchingolo *et al.* 2020; Yassa *et al.* 2020). It was reported that the 13 fetuses did not present alterations during gestation, and four deliveries were reported with products without infection at birth.

Characteristics of the PU procedure

In 20 of the 28 studies, PU was a bedside procedure; in the remaining 8 studies, patients were transferred to a specific area for the procedure. Nineteen articles reported the transducer used; in 17 of these studies, a linear or convex transducer was used (Bar *et al.* 2020; Buonsenso *et al.* 2020a; Consoli *et al.* 2020; Farrow *et al.* 2020; Huang *et al.* 2020; Inchingolo *et al.* 2020; Ji *et al.* 2020; Lomoro *et al.* 2020; Lu *et al.* 2020; Mongodi *et al.* 2020; Musolino *et al.* 2020; Reisinger and Koratala 2020; Shokoohi *et al.* 2020; Thomas *et al.* 2020; Tung-Chen 2020; Yang *et al.* 2020; Yassa *et al.* 2020). In 15 of the 28 articles, the ultrasound evaluation protocol used was mentioned. In 7 articles, a protocol of 12 zones was used (Buonsenso *et al.* 2020a; Mongodi *et al.* 2020; Musolino *et al.* 2020; Peng *et al.* 2020; Shokoohi *et al.* 2020; Yang *et al.* 2020); in 4 articles a protocol of 6

Table 1. Characteristics of included articles

| No. | Author (country) | Motive | Population N (M F) | Transducer used | Protocol | Chest X-ray correlation* | Chest CT correlation* |
|------------------------------|-----------------------------------|-----------|---|------------------|----------|--------------------------|--------------------------|
| <i>Retrospective cohort</i> | | | | | | | |
| 1 | Mongodi et al. 2020 (Italy) | D, M, Dis | Hospitalized adults in ICU: 84 (65 19) | Linear/sectorial | 12 zones | Superior | Good |
| 2 | Palmese et al. 2020 (Italy) | D, M, Dis | Hospitalized adults in ICU: 66 (36 30) | NR | NR | NP | Good |
| <i>Prospective cohort</i> | | | | | | | |
| 3 | Bar et al. 2020 (France) | D, M | Hospitalized adults: 31 (11 20) | Convex | 8 zones | NP | Good |
| <i>Cross-sectional study</i> | | | | | | | |
| 4 | Nouvenne et al. 2020 (Italy) | D | Hospitalized adults: 26 (14 12) | Linear/convex | 8 zones | NP | Good r=0.65 (p<0.001) |
| <i>Case series</i> | | | | | | | |
| 5 | Lu et al. 2020 (China) | D, M | Hospitalized adults: 30 (NR) | NR | NR | NP | Good |
| 6 | Yang et al. 2020 (China) | D, M | Hospitalized adults: 29 (18 11) | Convex | 12 zones | NP | Superior |
| 7 | Lomoro et al. 2020 (Italy) | D, M, R | Hospitalized adults: 22 (NR) | Linear/convex | NR | Yes, good in 11 | Yes, good in 16 |
| 8 | Peng et al. 2020 (China) | D | Adults: 20 (NR) | NR | 12 zones | NP | Good |
| 9 | Huang et al. 2020 (China) | D, M | Hospitalized adults: 20 (11 9) | Linear/convex | 12 zones | NP | Good |
| 10 | Xing et al. 2020 (China) | D, M | Hospitalized adults: 20 (12 8) | NR | NR | NP | NP |
| 11 | Poggiali et al. 2020 (Italy) | D | Hospitalized adults: 12 (9 3) | NR | NR | NP | Good |
| 12 | Yasukawa and Minami 2020 (USA) | D, M | Hospitalized adults: 10 (7 3) | Sectorial | 6 zones | NP | Yes, good in 1 |
| 13 | Musolino et al. 2020 (Italy) | D, R | Hospitalized children: 10 (6 4) | Linear/wireless | 12 zones | Yes, good in 2 | Yes, good in 1 |
| 14 | Yassa et al. 2020 (Turkey) | D, M, Dis | Hospitalized pregnant women: 8 (0 8) | Convex | 14 zones | 3/8 Good | 5/8 Good |
| 15 | Denina et al. 2020 (Italy) | R | Hospitalized children: 8 (5 3) | NR | NR | Yes, good in 7 | Good |
| 16 | Feng et al. 2020 (China) | D, M | Hospitalized children: 5 (3 2) | NR | NR | Good | Superior |
| 17 | Buonsenso et al. 2020b (Italy) | D, M | Hospitalized pregnant women in ICU: 4 (0 4) | NR | NR | Yes, good in 2 | NP |
| 18 | Shokoohi et al. 2020 (Spain) | D, M | Hospitalized adults in UCI: 3 (1 2) | Linear/wireless | 12 zones | Good | Good |
| <i>Case reports</i> | | | | | | | |
| 19 | Thomas et al. 2020 (USA) | D, M | Hospitalized adult: 1 female | Convex | NR | Good | NP |
| 20 | Buonsenso et al. 2020a (Italy) | D, M | Hospitalized adult: 1 male | Convex/wireless | 12 zones | Good | Good |
| 21 | Reisinger and Koratala 2020 (USA) | D, M | Hospitalized adult: 1 female | Convex/wireless | 6 zones | NP | NP |
| 22 | Ji et al. 2020 (China) | D | Hospitalized adult: 1 female | Convex | NR | NP | Good |
| 23 | Tung-Chen 2020 (Spain) | D, M, Dis | Hospitalized adult: 1 male | Convex/wireless | 8 zones | NP | NP |
| 24 | Inchingolo et al. 2020 (Italy) | D | Hospitalized pregnancy: 1 female | Convex | NR | Good | NP |
| 25 | Farrow et al. 2020 (USA) | D | Hospitalized adult: 1 female | Convex | 6 zones | Good | Good |
| 26 | Alkhafaji et al. 2020 (USA) | D, M | Hospitalized adult: 1 male | Linear | 6 zones | Superior | NP |
| 27 | Duclos et al. 2020 (France) | D, M | Adult in ICU: 1 male | NR | NR | NP | Good |
| 28 | Consoli et al. 2020 (Italy) | D, M | Hospitalized adult: 1 male | Convex | NR | Good | Good |

D = diagnosis; M = monitorization; R = routine; Dis = discharge; ICU = intensive care unit; CT = thoracic (chest) tomography; TR = thoracic radiography; NR = no report; NP = not performed.

* Good or superior correlation based on the author's qualitative report; statistical testing was not performed.

zones was used (Alkhafaji *et al.* 2020; Farrow *et al.* 2020; Reisinger and Koratala 2020; Yasukawa and Minami 2020); in 1 article a protocol with 14 zones was used (Yassa *et al.* 2020); and in 3 articles a protocol of 8 zones was used (Bar *et al.* 2020; Nouvenne *et al.* 2020; Tung-Chen 2020).

Comparison with CXR and chest CT

Two hundred seventy-seven of 418 patients did not undergo CXR (Bar *et al.* 2020; Buonsenso *et al.* 2020b; Duclos *et al.* 2020; Huang *et al.* 2020; Ji *et al.* 2020; Lomoro *et al.* 2020; Lu *et al.* 2020; Musolino *et al.* 2020; Nouvenne *et al.* 2020; Palmese *et al.* 2020; Peng *et al.* 2020; Poggiali *et al.* 2020; Reisinger and Koratala 2020; Tung-Chen 2020; Xing *et al.* 2020; Yang *et al.* 2020; Yassa *et al.* 2020; Yasukawa and Minami 2020), including 7 of the 13 pregnant women. Fifty-six of the 418 patients did not undergo chest CT (Bar *et al.* 2020; Buonsenso *et al.* 2020b; Duclos *et al.* 2020; Huang *et al.* 2020; Ji *et al.* 2020; Lomoro *et al.* 2020; Lu *et al.* 2020; Musolino *et al.* 2020; Nouvenne *et al.* 2020; Palmese *et al.* 2020; Peng *et al.* 2020; Poggiali *et al.* 2020; Reisinger and Koratala 2020; Tung-Chen 2020; Xing *et al.* 2020; Yang *et al.* 2020; Yassa *et al.* 2020; Yasukawa and Minami 2020), including 10 of the 13 pregnant women. Forty-four of the 418 patients underwent neither CXR nor chest CT, being evaluated only with PU and RT-PCR (Bar *et al.* 2020; Buonsenso *et al.* 2020b; Duclos *et al.* 2020; Huang *et al.* 2020; Ji *et al.* 2020; Lomoro *et al.* 2020; Lu *et al.* 2020; Musolino *et al.* 2020; Nouvenne *et al.* 2020; Palmese *et al.* 2020; Peng *et al.* 2020; Poggiali *et al.* 2020; Reisinger and Koratala 2020; Tung-Chen 2020; Xing *et al.* 2020; Yang *et al.* 2020; Yassa *et al.* 2020; Yasukawa and Minami 2020). In the 5 articles that included these 44 patients, the authors did not describe a clinical course different from those of the remaining patients evaluated with CXR and/or chest CT.

Because of the types of articles found in this systematic review, the global quantitative correlation of PU with CXR and/or chest CT could not be assessed; therefore, we report the qualitative result described by the authors. Of the 14 articles that evaluated the qualitative correlation between PU and CXR findings, 12 considered it good and 2 (including the cohort of 84 patients) reported that PU was superior to CXR (Alkhafaji *et al.* 2020; Mongodi *et al.* 2020). Likewise, of the 20 studies that evaluated the qualitative correlation between PU and chest CT, 18 considered it good and 2 reported that PU was superior to chest CT (Feng *et al.* 2020; Yang *et al.* 2020) (Table 1). Only the cross-sectional article reported a quantitative correlation between PU and chest CT, indicating that it was good with $r=0.65$ and $p < 0.001$ (Nouvenne *et al.* 2020).

In total, considering all procedures performed in studies that used CXR or chest CT (even repeat examinations), we found that PU was performed 18 times more than CXR and 12 times more than chest CT. The cohort of 84 patients reported that PU reduced the use of CXR and chest CT by 31.8% before the use of PU to 3.6% after the use of this procedure (Mongodi *et al.* 2020).

Pulmonary ultrasound findings and their correlation with chest CT findings

In Table 2 the PU findings are outlined. All articles (Alkhafaji *et al.* 2020; Bar *et al.* 2020; Buonsenso *et al.* 2020a, 2020b; Consoli *et al.* 2020; Denina *et al.* 2020; Duclos *et al.* 2020; Farrow *et al.* 2020; Feng *et al.* 2020; Huang *et al.* 2020; Inchingolo *et al.* 2020; Ji *et al.* 2020; Lomoro *et al.* 2020; Lu *et al.* 2020; Mongodi *et al.* 2020; Musolino *et al.* 2020; Nouvenne *et al.* 2020; Palmese *et al.* 2020; Peng *et al.* 2020; Poggiali *et al.* 2020; Reisinger and Koratala 2020; Shokoohi *et al.* 2020; Thomas *et al.* 2020; Tung-Chen 2020; Xing *et al.* 2020; Yang *et al.* 2020; Yassa *et al.* 2020; Yasukawa and Minami 2020) reported the presence of B-lines: coalescent, multifocal, diffuse, confluent or “white lung.” Alteration of the pleural line was reported in 25 of 28 articles: irregular, thickened, interrupted. Alteration of the pulmonary parenchyma was reported as presence of lobar, multilobar or noduliform subpleural consolidations with bilateral and posterior distribution. The presence of the dynamic air bronchogram was described in 4 studies (Consoli *et al.* 2020; Huang *et al.* 2020; Mongodi *et al.* 2020; Shokoohi *et al.* 2020). One article did not describe the presence or absence of pulmonary alterations (Inchingolo *et al.* 2020). One article indicated that there were no alterations to the pulmonary parenchyma (Reisinger and Koratala 2020). Pleural effusion was reported in only 1 article (Denina *et al.* 2020). The presence of pneumothorax was reported in only 1 article (Consoli *et al.* 2020).

Table 3 summarizes the PU findings in the 28 articles (Alkhafaji *et al.* 2020; Bar *et al.* 2020; Buonsenso *et al.* 2020a, 2020b; Consoli *et al.* 2020; Denina *et al.* 2020; Duclos *et al.* 2020; Farrow *et al.* 2020; Feng *et al.* 2020; Huang *et al.* 2020; Inchingolo *et al.* 2020; Ji *et al.* 2020; Lomoro *et al.* 2020; Lu *et al.* 2020; Mongodi *et al.* 2020; Musolino *et al.* 2020; Nouvenne *et al.* 2020; Palmese *et al.* 2020; Peng *et al.* 2020; Poggiali *et al.* 2020; Reisinger and Koratala 2020; Shokoohi *et al.* 2020; Thomas *et al.* 2020; Tung-Chen 2020; Xing *et al.* 2020; Yang *et al.* 2020; Yassa *et al.* 2020; Yasukawa and Minami 2020) included in this rapid systematic review, which have been grouped with respect to the location of the lesions: pleural line, presence of B-lines, lung parenchyma or pleural cavity and its comparison with chest CT lesions caused by COVID-19 (Fig. 2).

Table 2. Results of informed pulmonary ultrasound of COVID-19 patients in included articles

| N* | B-Lines | Pleural line | Consolidation |
|-----------------------------|------------------------------------|------------------------|--|
| <i>Retrospective cohort</i> | | | |
| 1 | Yes, multifocal, coalescent | Non-sliding, irregular | Multilobar, lobar, dynamic air bronchogram |
| 2 | Yes, focal and multifocal, diffuse | Irregular, interrupted | Multilobar |
| <i>Prospective cohort</i> | | | |
| 3 | Yes, confluent | Thickened | Consolidated |
| <i>Transversal</i> | | | |
| 4 | Yes, diffuse, coalescent | Irregular | Microconsolidations and consolidations |
| <i>Case series</i> | | | |
| 5 | Yes, interstitial syndrome | NR | Present, lobar, posterior, subpleural, peripheral |
| 6 | Interstitial syndrome | Irregular, thickened | Multilobar, subpleural, posterior |
| 7 | Yes, diffuse | Irregular | Subpleural, bilateral, posterior |
| 8 | Yes, diffuse, bilateral | Thickened, irregular | Subpleural, bilateral, posterior |
| 9 | Yes, coalescent, confluent | Thickened irregular | Nodular consolidation, bronchogram, patches, bilateral |
| 10 | Yes, confluent, diffuse | Irregular, Interrupted | Bilateral, multilobar |
| 11 | Yes, diffuse | Irregular | Subpleural, occasional, bilateral |
| 12 | Yes, confluent, white lung | Irregular | Subpleural, lobar, bilateral |
| 13 | White lung | Irregular | Subpleural, posterior, bilateral |
| 14 | Yes, bilateral, coalescent | Irregular | Subpleural, bilateral, pleural effusion |
| 15 | Yes, confluent | NR | Subpleural |
| 16 | Yes, white lung | Irregular | Small, subpleural |
| 17 | Yes, diffuse | Irregular | Consolidation, bilateral, posterior |
| 18 | Yes, coalescent | Irregular, Thickened | Lobar, bilateral |
| <i>Case reports</i> | | | |
| 19 | Yes, posterior, bilateral | Thickened | Bilateral |
| 20 | Yes, coalescent | NR | Subpleural nodular |
| 21 | Yes, coalescent | Irregular | No |
| 22 | Yes, coalescent | Irregular | Subpleural, present |
| 23 | Yes | Irregular | Subpleural, unilateral |
| 24 | Yes, white lung | Thickened | NR |
| 25 | Yes, diffuse | Irregular | Present |
| 26 | Yes, multifocal | Regular, thickened | Subcentimetric, lobar, posterior |
| 27 | Yes, diffuse and coalescent | Irregular | Multilobar, bilateral |
| 28 | Yes, multifocal and coalescent | Thickened, non-sliding | Pneumothorax, dynamic air bronchogram |

NR = no report.

* According to the numeration in Table 1.

DISCUSSION

Pulmonary ultrasound results

The PU results are similar and consistent among the different articles included in this systematic review, concur simultaneously with the results of the systematic revisions and narratives (Ai et al. 2020; Antúnez-Montes and Buonsenso 2020; Convissar et al. 2020; Fang et al. 2020; Fiala 2020; Fraile Gutiérrez et al. 2020; Mohamed

et al. 2020; Ojha et al. 2020; Smith et al. 2020) and correlate qualitatively with the COVID-19 results observed on chest CT (Ai et al. 2020; Fang et al. 2020; Ojha et al. 2020; Pan et al. 2020), as summarized in Table 3.

Characteristics

Our results indicate that PU has been used at various stages of the disease (diagnosis, follow-up, as an evaluation for discharge and in observation of the resolution of lesions in a progressive manner) in an adequate manner and with benefits for the patient. We included 418 patients, indicating that the use of PU continues to increase in patients with COVID-19; previous reviews have included fewer than 60 patients (Convissar et al. 2020; Smith et al. 2020), and a recent systematic review with meta-analysis included 122 patients (Mohamed et al. 2020) although more evidence is required to define the usefulness of PU at each stage.

The protocol of 12 zones is the most frequently used protocol in the articles reviewed (Buonsenso et al. 2020a; Huang et al. 2020; Mongodi et al. 2020; Musolino et al. 2020; Peng et al. 2020; Shokoochi et al. 2020; Yang et al. 2020), including the study of cohorts of 84 patients. It is followed by the protocol of 6 zones (Alkhafaji et al. 2020;

Table 3. Pulmonary ultrasound findings and their correlation with thoracic tomography in the diagnosis of pleuroparenchymal disease of COVID-19

| Thoracic tomography | Pulmonary ultrasound |
|-----------------------------------|--|
| Pleural thickening | Thickening and irregularity of the pleural wall |
| Subpleural ground-glass opacities | B-Lines (multifocal, discrete, confluent) |
| Reticular interstitial lesions | Confluent B-lines |
| Subpleural consolidation | Subpleural consolidations with dynamic air bronchogram |
| Translobar consolidation | Translobar consolidation |
| Rare presence of pleural effusion | Rare presence of pleural effusion |
| Multilobar, basal, posterior | Multilobar, basal, posterior |

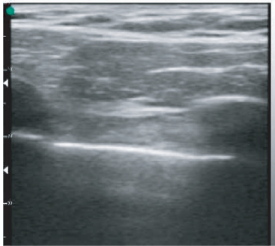
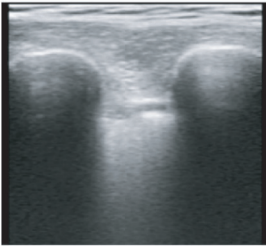
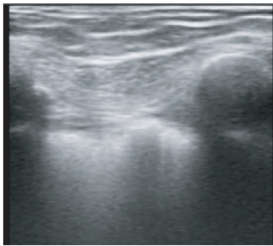
| Pulmonary Phase IIA Image A | Pulmonary Phase IIB Image B | Hyperinflammation Phase Image C |
|---|---|---|
| <ul style="list-style-type: none"> • Development of B-lines. • The pleural line begins to become irregular. • Areas with B-lines are adjacent to normal areas of lung sliding and A-lines.  | <ul style="list-style-type: none"> • B-lines continue to increase in number and distribution. • Thickening and irregularity of the pleural wall. • B-lines (multifocal, discrete, confluent). • Begin to affect the upper and anterior areas of the lungs. • Small consolidations increase in number and size.  | <ul style="list-style-type: none"> • Subpleural consolidations with dynamic air bronchogram. • Extensive coalescent B-lines affect different areas of the lungs. • Confluent B-lines. • Translobar consolidation with or without air bronchograms. • Pleural effusions are small or rare.  |

Fig. 2. Simplified description of the main lung ultrasound findings by stage of COVID-19 disease.

Farrow *et al.* 2020; Reisinger and Koratala 2020; Yasukawa and Minami 2020). However, these differences in the protocols used did not affect the presence or absence of pathological findings on PU or the way the findings were reported. It might be convenient to propose the use of the 12-zone protocol as it is the most widely used. Also, convex and linear transducers were the most frequently used transducers, which is important because most conventional ultrasound are equipped with these transducers.

Other aspects of the use of PU for consideration

PU has other benefits, such as greater availability compared with chest CT and RT-PCR, low cost per examination, ease of access, shorter duration, dynamic and repeated evaluation of pulmonary parenchyma, accessibility to bedridden patients, safety for pregnant women, ease of integration of telemedicine in areas that lack trained specialists and immediate results unlike in RT-PCR (Alkhafaji *et al.* 2020; Bar *et al.* 2020; Buonsenso *et al.* 2020a, 2020b; Consoli *et al.* 2020; Convissar *et al.* 2020; Denina *et al.* 2020; Duclos *et al.* 2020; Farrow *et al.* 2020; Feng *et al.* 2020; Gargani *et al.* 2020; Huang *et al.* 2020; Inchingolo *et al.* 2020; Ippolito *et al.* 2020; Ji *et al.* 2020; Kristensen *et al.* 2014; Lomoro *et al.* 2020; Lu *et al.* 2020; Mongodi *et al.* 2020; Musolino *et al.* 2020; Nouvenne *et al.* 2020; Ojha *et al.* 2020;

Palmese *et al.* 2020; Pan *et al.* 2020; Pecho-Silva 2020; Peng *et al.* 2020; Poggiali *et al.* 2020; Reisinger and Koratala 2020; Schiaffino *et al.* 2020; Shokoohi *et al.* 2020; Smith *et al.* 2020; Soldati *et al.* 2020; Thomas *et al.* 2020; Tung-Chen 2020; Xing *et al.* 2020; Yang *et al.* 2020; Yassa *et al.* 2020; Yasukawa and Minami 2020;).

With respect to the learning process, the authors of some included articles mentioned that its implementation is short and therefore feasible (Ippolito *et al.* 2020; Lu *et al.* 2020; Mongodi *et al.* 2020; Ojha *et al.* 2020; Pan *et al.* 2020; Pecho-Silva 2020; Schiaffino *et al.* 2020; Shokoohi *et al.* 2020; Smith *et al.* 2020; Yang *et al.* 2020). Also beneficial in PU is that cleaning and disinfection of the equipment are much easier and faster for PU than for CXR or chest CT equipment, and the same disinfection protocols are used.

In addition, portable PU equipment is becoming less expensive and has increasing resolution, allowing the transmission of images via Wi-Fi or Bluetooth, so only a single healthcare worker would have to approach the patient to perform the procedure; the rest of the healthcare team can receive the images outside the patient's isolation room without exposing themselves to potential contagion (Antúnez-Montes and Buonsenso 2020; Buonsenso *et al.* 2020a; Fraile Gutiérrez *et al.* 2020; Gargani *et al.* 2020; Mohamed *et al.* 2020; Musolino *et al.* 2020; Shokoohi *et al.*

al. 2020; Tung-Chen 2020). To date, no contraindications to the use of PU or complications associated with its use have been described.

What does the literature say about PU in COVID-19?

So far, PU is a useful tool in diagnosis and monitoring and as a criterion for hospital and ICU discharge for patients with COVID-19. To date, no contraindications to the use of the PU or any complications from its use have been described. PU findings in the different articles were similar, correlated qualitatively well with the tomographic findings and were better than the X-ray findings in patients with COVID-19. PU could, in select cases, replace chest radiography and/or tomography in the diagnosis and follow-up of patients with COVID-19 (Convissar et al. 2020; Smith et al. 2020).

Findings from this study

This review involved the largest number of patients with COVID-19 evaluated with PU to date. PU findings of multifocal, multilobar, subpleural, posterior alterations of the pleural line of the coalescent, irregular, interrupted, thickened type, together with alterations of the pulmonary parenchyma of multilobar or lobar distribution, with dynamic air bronchogram, are frequent findings and consistent with COVID-19 and aid in diagnosis, follow-up and evaluation of response to treatment and as criteria for discharge from the intensive care unit or hospital. PU could replace chest-x ray and could reduce exposure of patients to ionizing radiation and displacement of patients from their rooms, thus exposing fewer staff and other patients to the intranosocomial transmissibility of COVID-19.

Suggested acquisition protocol

- Use convex or linear transducers. The latter are preferable to study the detail of the pleural and subpleural alterations.
- Use a single-focal-point or multifocusing modality and set the focal point on the pleural line.
- Preferably, scans need to be intercostal to cover the widest surface possible with a single scan.
- Evaluate the presence of the artifactual patterns in multiple areas and bilaterally to study the extent of lung surface affected.
- Ideally, 12 areas in total should be evaluated: anterior midclavicular upper and lower on the right and the left; posterior paraspinous (apical, medial and basal), right and left; and lateral axillary (medial), right and left.

Limitations

Some of the limitations of this systematic review have to do with the quality of the evidence that comes from only two retrospective cohort studies, one from a prospective

cohort and one from a cross-sectional cohort, and letters to the editor, case series and case reports. Another limitation is the different evaluation protocols used to perform PU. A final limitation is that PU does not allow the detection of lesions that are not subpleural or peripheral; however, this would also be of little relevance as COVID-19 lesions are usually subpleural or peripheral and therefore evaluable with PU (Convissar et al. 2020; Mohamed et al. 2020; Poggiali et al. 2020; Smith et al. 2020; Soldati et al. 2020).

The studies found indicate more experience with the use of PU in patients with COVID-19, even in pregnant women and children, is accumulating. In addition, they report adequate sensitivity and specificity for the diagnosis of COVID-19, and no articles have been published that have found that PU is not useful or that it is harmful to the patient. This suggests that PU is an advantageous tool. However, studies of higher methodological quality are required to corroborate the current findings.

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