Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Ultrasound findings of lung ultrasonography in COVID-19: A systematic review

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ABSTRACT

Purpose: To identify the defining lung ultrasound (LUS) findings of COVID-19, and establish its association to the initial severity of the disease and prognostic outcomes.
Method: Systematic review was conducted according to the PRISMA guidelines. We queried PubMed, Embase, Web of Science, Cochrane Database and Scopus using the terms ((coronavirus) OR (covid-19) OR (sars AND cov AND 2) OR (2019-nCoV)) AND ((“lung ultrasound”) OR (LUS)), from 31st of December 2019 to 31st of January 2021. PCR-confirmed cases of SARS-CoV-2 infection, obtained from original studies with at least 10 participants 18 years old or older, were included. Risk of bias and applicability was evaluated with QUADAS-2.
Results: We found 1333 articles, from which 66 articles were included, with a pooled population of 4687 patients. The most examined findings were at least 3 B-lines, confluent B-lines, subpleural consolidation, pleural effusion and bilateral or unilateral distribution. B-lines, its confluent presentation and pleural abnormalities are the most frequent findings. LUS score was higher in intensive care unit (ICU) patients and emergency department (ED), and it was associated with a higher risk of developing unfavorable outcomes (death, ICU admission or need for mechanical ventilation). LUS findings and/or the LUS score had a good negative predictive value in the diagnosis of COVID-19 compared to RT-PCR.
Conclusions: The most frequent ultrasound findings of COVID-19 are B-lines and pleural abnormalities. High LUS score is associated with developing unfavorable outcomes. The inclusion of pleural effusion in the LUS score and the standardisation of the imaging protocol in COVID-19 LUS remains to be defined.

1. Introduction

A new variant of coronavirus, SARS-CoV-2, has become responsible for the worst global pandemic since the influenza A H1N1 pandemic in 1918 [1]. The first case of human infection was described on December 2019 in the Chinese city of Wuhan [2]. On account of that, SARS-CoV-2 has caused >100 million new cases and 2 million deaths globally from coronavirus 19 disease (COVID-19) until January 31st [3]. Its effect on society as well as the measures taken by governments to try to contain its spread, have pushed the economy into its worst recession since World War II, with an estimated contraction of 5.2% of the World Gross Domestic Product by 2020 [4].

The impact of these statistics has forced researchers around the world into an accelerated search for the natural history of the disease to develop possible tools for the management of the disease. The diagnosis of COVID-19 and the establishment of prognostic markers have become to major focus, in order to determine which patients require admission and to adapt therapeutic measures accordingly. Real-time reverse transcriptase polymerase chain reaction (RT-PCR) and antibody serology have become the reference methods in the diagnosis of infection, but do not provide information on disease severity and prognosis [5].

In this context, thoracic imaging has proven to be a useful diagnostic tool. Although thoracic computed tomography (CT) has been the most studied technique, there is evidence that lung ultrasound (LUS) may be an effective alternative for diagnosing the disease [6]. This imaging

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modality is quick, cost-effective, and does not require ionising radiation. In addition, it can be repeated as many times as necessary to monitor disease progression, and be performed at the patient's bedside (point-of-care ultrasound, POCUS) [7]. However, this evidence remains weak, with no up-to-date systematic review to support its use.

At present, there is an increasing literature on the LUS use in COVID, both in the diagnosis and prognosis of the disease. However, the available information is dispersed, without a detailed compilation of COVID-associated findings and their association with initial disease severity and prognostic outcomes. The purpose of this article is to identify the defining LUS findings of COVID-19, and to establish its association to the initial severity of the disease and prognostic outcomes.

2. Material and methods

2.1. Search strategy

This study was designed according to the 2015 PRISMA (Preferred Reporting Items for Systematic review and Meta-Analysis) guidelines [8] and has been registered in the PROSPERO database under the number CRD42021237210.

The information used in this article was extracted from the electronic databases of PubMed, Embase, Web of Science, Cochrane Database of Systematic Reviews and Scopus. A combination of MeSH and associated terms (COVID-19, ultrasonography) with other methodological terms (lung, LUS) were used in the search, resulting in the terms ((coronavirus) OR (covid-19) OR (sars AND cov AND 2) OR (2019-nCoV)) AND ((“lung ultrasound”) OR (LUS)). This has been enriched by the possibility to analyse the bibliography of relevant studies to add additional publications.

2.2. Articles selection

The studies included span the time frame from 31st of December 2019 to 31st of January 2021. We established as inclusion criteria confirmed cases of SARS-CoV-2 infection in humans by SARS-CoV-2 RT-PCR and/or serology or antigen test. Participants were adults aged 18 years or older, with no other limitations on the included population. As exclusion criteria, we established the following: only original studies conducted in a significant patient sample of at least 10 participants with the characteristics described above were included; studies without a significant sample (e.g. case report), non-original studies (e.g. reviews) and secondary research (narrative review, systematic review and meta-analysis) were excluded. No other limitations by article type, language or publication status (preprint, peer-reviewed or already published) was settled.

2.3. Extraction of data

For data processing, the reference and document management tool Mendeley® and the calculation spreadsheet programme Microsoft Excel® were used. Two independent operators (J.G. and E.G.), were involved in the search, selection and inclusion, with no communication of results between them during the process. In a first search, we screened by title and abstract of the article, and in a second phase according to the full text. Discrepancies between the two researchers were resolved by a third researcher (A.B.).

Data were collected in a data template common to both investigators. The variables collected from the selected studies were title, authors, date, type of study, total number of participants and number of PCR-confirmed COVID-19 cases, characteristics of the included patients (age, sex, BMI, clinical severity, associated comorbidity or any other selection criteria), setting (hospital, primary care, emergency department), time of LUS acquisition, presence or absence of blinding evaluation of LUS images, transducer used, number of fields scanned, ultrasound findings (pulmonary B lines, pleural thickening, pleural irregularity, subpleural consolidation, pulmonary consolidation, pleural effusion, lung ultrasound score (LUS score)) and LUS performance in diagnosing COVID-19 cases and predicting clinical outcomes.

The LUS score is a severity score used in COVID-19 pneumonia, assigning a range of 0–3 to each of the lung fields analysed. Soldati et al. [9] made a standardisation proposal establishing the findings associated with each point, being 0 normal, 1 presence of 3 or more B-lines or pleural irregularity, 2 confluence of B-lines or subpleural consolidation and 3 pulmonary consolidation. Only articles that met this definition were pooled in the study, in order to make their results comparable. For the purpose of comparison, in the cases where studies did not scan the 12 lung fields (dividing each hemithorax into 3 by the midclavicular anterior and posterior line and subdividing each of these fields into upper and lower fields) as proposed by Soldati et al. [9], but instead chose to analyse a smaller or greater number of lung fields, an adapted LUS score was calculated. Specifically, the LUS score of each individual study was multiplied by 12/number of lung areas scanned, so as to obtain the equivalent LUSS if 12 anatomical zones had been scanned.

Clinical outcomes were often varied among different studies, so we collected the following: in-hospital death (or death after a certain follow-up time), need for mechanical intubation, intensive care unit (ICU) admission, development of acute respiratory distress syndrome (ARDS). During the selection phase, in case of overlapping population samples, the most recent study was chosen.

We assessed the quality of the studies included with the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool [10]. Definitions and judgment criteria for each domain were established according the guidelines of the Cochrane Collaboration's “Cochrane Handbook of Systematic Reviews of Interventions” [11]. Two independent reviewers (P.L. and J.P.) evaluated the risk of bias in the included studies by means of a tailored QUADAS-2 tool. Disagreements were discussed and resolved with a senior reviewer (E.G.). Specifically, high risk in each of the 4 domains assessed in QUADAS-2 was defined as follows. In domain 1 (patient selection), high risk of bias was assigned if study design was case–control or if enrolment was non-consecutive; and high risk regarding applicability if the setting of the study or the severity of COVID-19 disease was not clear in all patients of the study. Domain 2 (index test) was established as high risk of bias if LUS images were interpreted without blinding to SARS-CoV-2 PCR, other imaging techniques or clinical data, depending on the study approach, or if a threshold was used that was not pre-specified; and high risk regarding applicability if the LUS acquisition and analysis method was not clear or was not the same for all patients. Domain 3 (reference standard) high risk of bias was determinated if the reference standard was unlikely to correctly classify COVID-19 patients; and high risk regarding applicability if no alterations were made to the definition of a positive SARS-CoV-2 PCR (in terms of cycle threshold or otherwise). Lastly, domain 4 (flow and timing) was settled as high risk of bias if LUS acquisition was not performed within 5 days of the reference standard.

3. Results

According to the established search criteria, we found 1333 articles in the 6 databases described above, to which 2 more articles were added from the bibliography of these studies. 835 duplicate articles were removed. Of the remaining 497 articles, 381 were excluded based on title and abstract information. Finally, of the 115 full-text articles assessed for eligibility, 66 articles were included in our qualitative synthesis and 49 were excluded (Fig. 1).

Quality of included studies, as evaluated by QUADAS-2, is shown in Fig. 2 and Appendix 1. Risk of bias was high in 2 articles ([12,13]) for patient selection, in 2 articles for index test ([14,15]) and in 7 articles for flow and timing ([16–22]). There were high applicability concerns only in one study, specifically in the index test domain ([23]). All studies were considered as low-risk in the reference standard domain, since all of them used SARS-CoV-2 RT-PCR as gold standard. None of the articles

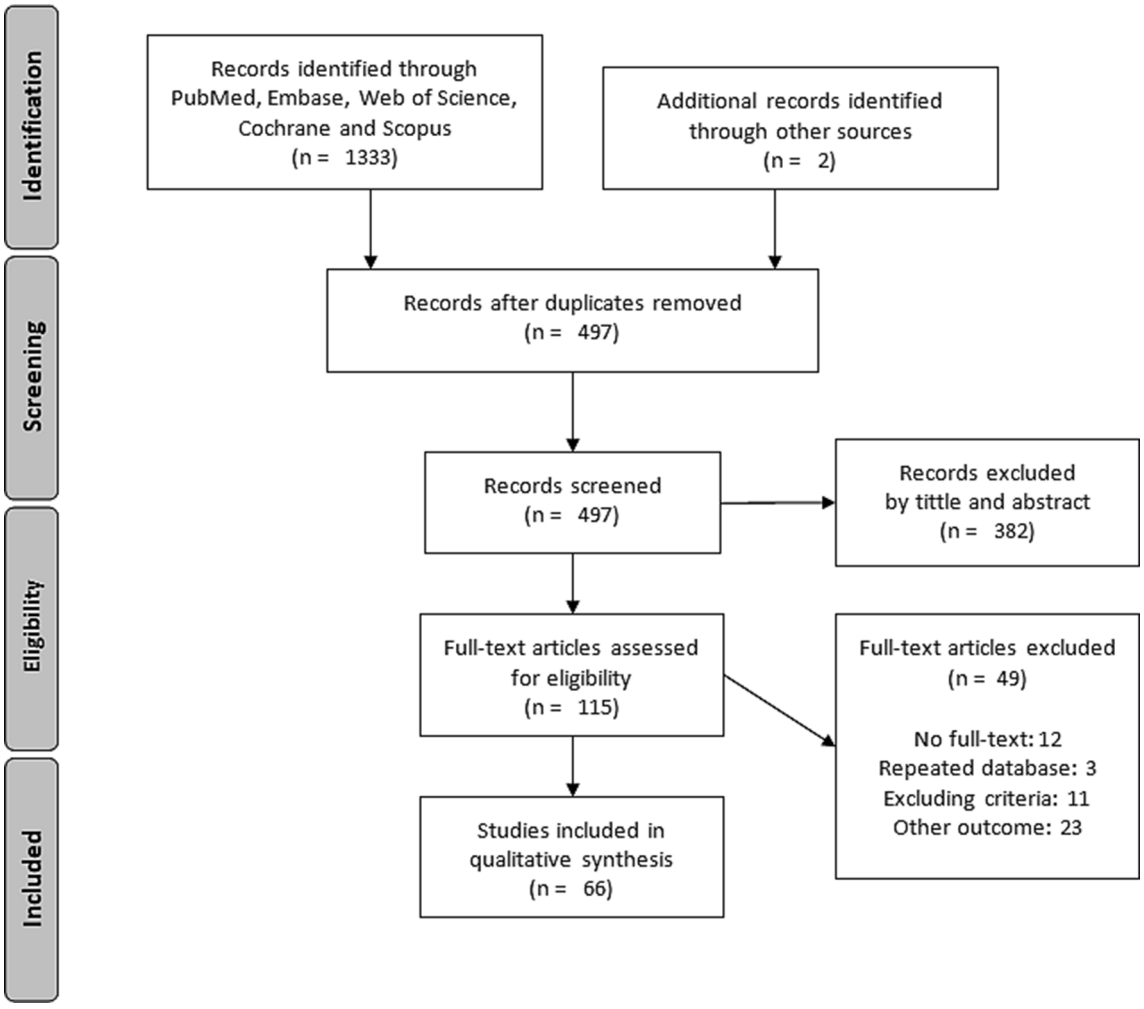

Fig. 1. Article selection flow diagram according to PRISMA guidelines [8].

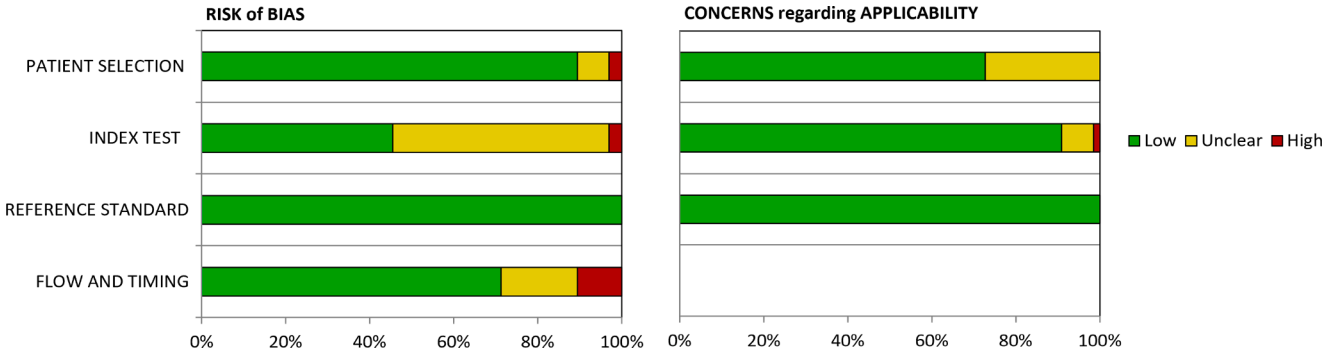

Fig. 2. Quality of included studies as established in the QUADAS-2 tool [10].

included were classified as high risk in two or more categories of the 4 domains.

These 66 studies are distributed as follows: 41 were conducted in Europe, 18 in Asia, 5 in North America and 2 in South America. Among them, 25 (37.9%) were prospective cohorts, 24 (36.4%) retrospective cohorts, 2 (3.0%) retrospective case-control studies and 2 (3.0%) cross-sectional studies; while 13 (19.7%) of them did not make it explicit (although it seems clear that these were also observational studies). According to the area of acquisition, 22 (33.3%) were conducted in the emergency department (ED), 13 (19.7%) in hospitalisation (ICU and ward), 12 (18.2%) in hospitalisation ward, 11 (16.7%) in ICU, 3 (4.5%) in pregnancy hospitalisation ward, 2 (3.0%) in nursing homes, 1 (1.5%) in rehabilitation unit, 1 in ED and ICU and 1 in screening tents. Most images were taken within 24 h of admission (40 articles, 60.6%). The most commonly used protocol consisted in scanning 12 lung areas (35, 53.0%), scanning <12 areas in 16 studies (24.2%) and >12 in 8 studies (12.1%), unspecified in the remaining 7 studies (10.6%). The convex probe was the main probe most commonly used (41 articles, 62.1%), followed by the linear probe (7, 10.6%) and the phased array probe (4, 6.1%); in 14 articles it was not detailed (21.2%). Only 34 (51.5%) articles established a protocol for blinded ultrasound evaluators. The data of the included studies are detailed in Table 1 and Appendix 2.

Table 1
Characteristics of included articles.

Author and publication date	Country and study design	COVID-19 cases and clinical setting	Time of LUS acquisition	Blinding	Age (mean or median, years)	Male cases (%)	BMI (mean or median, kg/m^2)	Scanned regions, main probe and frequency (Hz)
Lu [24], 15/04/2020	China, Retrospective cohort	30, Wards	Within 24 h	Yes, NA	52	53	22.5	12, Convex, 5–2
Yasukawa [25], 24/04/2020	United States, Retrospective cohort	10, Wards	Within 24 h	No	53	70	NA	NA, Phased array
Xing [16], 28/04/2020	China, NA	20, Hospital	After a median time of >5 days	No	NA	60	NA	10, NA
Tan [12], 05/06/2020	China, Retrospective case–control	12, ED	Within 24 h	No	61	33	NA	10, Convex, 3.5–5
Bar [13], 10/06/2020	France, Retrospective case–control	31, ED	Within 24 h	Yes, PCR	67	35	30.0	6, Convex
Pare [26], 19/06/2020	United States, Retrospective cohort	27, ED	Within 24 h	Yes, PCR	53	59	31.7	NA, Convex
Nouvenne [27], 22/06/2020	Italy, NA	26, Wards	Within 24 h	Yes, CT	64	54	NA	8, Convex, 3.5–5
Yassa [28], 30/06/2020	Turkey, Prospective cohort	43, Pregnancy ward	Following a routine fetal assessment	Yes, PCR and clinical data	NA	0	NA	14, Convex, 1–8
Møller-Sørensen [29], 02/07/2020	Denmark, NA	10, ICU	Within 24 h	Yes, NA	53	60	NA	6, Linear, 12
Ye [17], 09/07/2020	China, Retrospective cohort	23, Wards	NA	Yes, Clinical data	60	52	NA	12, Convex, 1–5.5
Deng [30], 14/07/2020	China, Retrospective cohort	128, Hospital	Within 24 h	Yes, Clinical data	65	59	NA	8, Convex, 3.5–5
Bonadia [31], 15/07/2020	Italy, Prospective cohort	41, ED	Within 24 h	No	60	78	NA	14, Convex, 6
Dargent [32], 21/07/2020	France, NA	10, ICU	Within 24 h	No	56	80	32.0	12, NA
Zhang [18], 22/07/2020	China, Retrospective cohort	28, Hospital	After a median time of >5 days	No	60	50	NA	NA, Convex, 1–5
Yassa [33], 28/07/2020	Turkey, Prospective cohort	23, Pregnancy ward	Within 24 h	No	NA	0	NA	14, Convex, 1–8
Veronese [34], 29/07/2020	Italy, NA	48, Nursing home	Within 5 days	No	84	19	NA	12, NA
Zieleskiewicz [35], 29/07/2020	France, Retrospective cohort	100, ED and ICU	Within 24 h	No	61	65	NA	12, NA
Favot [36], 31/07/2020	United States, Retrospective cohort	40, ED	Within 24 h	Yes, NA	69	60	31.0	8, Convex
Gaspardone [19], 08/08/2020	Italy, Prospective cohort	70, Rehabilitation unit	At discharge	No	68	69	25.6	12, Convex
Ottaviani [37], 12/08/2020	France, Prospective cohort	21, Wards	NA	Yes, CT and clinical data	65	76	NA	12, Convex, 5–18
Alharthy [38], 14/08/2020	Saudi Arabia, Prospective cohort	89, ICU	Within 24 h	No	43	84	26.5	12, Phased array, 2–4
Thomaz [39], 21/08/2020	Brazil, Cross-sectional	409, Screening tents	NA	No	41	33	NA	12, Linear, 7.5–10
Lichter [40], 28/08/2020	Israel, Retrospective cohort	120, Hospital	Within 24 h	Yes, NA	65	62	NA	12, Phased array
Iodice [41], 01/09/2020	Italy, Prospective cohort	29, Hospital	Within 24 h	~~No~~. Yes, CT	60	90	NA	NA, Convex, 3.5–5
Dini [42], 02/09/2020	Italy, NA	94, Nursing home	NA	No	NA	NA	NA	12, Convex, 3.5
Gil [43], 04/09/2020	Spain, Cross-sectional	27, ED	Within 24 h	No	48	33	NA	13, Convex, 2–5
Battista [44], 07/09/2020	Italy, Prospective cohort	44, ED	Within 24 h	Yes, PCR	66	66	NA	12, Convex, 2.5–5
Narinx [45], 10/09/2020	Belgium, NA	15, ED	Within 24 h	Yes, PCR	50	60	NA	6, Convex, 5

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Table 1 (*continued*)

Author and publication date	Country and study design	COVID-19 cases and clinical setting	Time of LUS acquisition	Blinding	Age (mean or median, years)	Male cases (%)	BMI (mean or median, kg/m^2)	Scanned regions, main probe and frequency (Hz)
Kalafat [46], 11/09/2020	Turkey, Retrospective cohort	82, Pregnancy ward	NA	Yes, PCR	28	0	27.6	6, NA
Li [47], 15/09/2020	China, Retrospective cohort	91, Hospital	NA	No	59	68	NA	12, Linear, 4–12
Castelao [48], 16/09/2020	Spain, Prospective cohort	63, Wards	Within 5 days	Yes, Chest radiography and clinical data, but not PCR status	61	68	NA	12, Convex, 2–5
Cocconcelli [20], 16/09/2020	Italy, Retrospective cohort	102, Hospital	After a median time of >5 days	No	68	74	25.0	12, Convex, 1–8
Brahier [49], 17/09/2020	Switzerland, Prospective cohort	80, ED	Within 24 h	Yes, Clinical data	62	58	NA	10, NA
Ramos-Hernández [50], 21/09/2020	Spain, Prospective cohort	44, Wards	Within 5 days	No	69	68	NA	8, Convex
Zhu [51], 21/09/2020	China, Prospective cohort	27, Hospital	Within 5 days	No	63	59	NA	10, Convex, 1.5–5
Rojatti [52], 25/09/2020	Italy, Retrospective cohort	41, ICU	Within 24 h	No	62	78	26.7	8, Convex
Marggrander [23], 01/10/2020	Germany, Retrospective cohort	17, Hospital	NA	No	51	65	NA	NA, Convex, 3–5
Bosso [14], 03/10/2020	Italy, NA	26, ED	NA	Yes, PCR	66	69	NA	12, Linear
Colombi [53], 08/10/2020	Italy, Retrospective cohort	341, ED	Within 24 h	No	NA	NA	NA	12, Convex, 1–8
Haaksma [54], 08/10/2020	Netherlands, NA	61, ICU	NA	Yes, Clinical data	66	90	28.5	12, Linear, 5–10
Pivetta [55], 12/10/2020	Italy, Prospective cohort	107, ED	Within 24 h	Yes, PCR	63	55	NA	12, Convex, 3–5
Lieveld [56], 15/10/2020	Netherlands, Prospective cohort	86, ED	Within 24 h	Yes, PCR and CT	63	58	NA	12, NA
Zhu [21], 16/10/2020	China, Retrospective cohort	48, Hospital	After a median time of >5 days	Yes, CT and clinical data	63	54	NA	12, Convex, 3.5–5
Bosevski [57], 22/10/2020	Macedonia, NA	17, ICU	NA	No	57	NA	NA	NA
Sorlini [58], 22/10/2020	Italy, Retrospective cohort	287, ED	Within 24 h	No	NA	NA	NA	12, NA
Jalil [59], 26/10/2020	United States, Retrospective cohort	36, Hospital	Within 24 h	Yes, PCR, clinical data and chest radiography	63	53	30.5	8, NA
Gibbons [60], 29/10/2020	United States, Prospective cohort	83, ED	Within 24 h	No	56	43	NA	8, NA
Li [61], 03/11/2020	China, NA	42, ICU	Within 24 h	No	68	43	NA	NA, Convex, 5
Zotzmann [62], 03/11/2020	Germany, Retrospective cohort	20, ICU	NA	Yes, CT	62	70	28.3	8, Convex, 5–1
Perrone [63], 06/11/2020	Italy, NA	52, Wards	Within 24 h	Yes, Clinical data	64	54	25.3	14, Convex, 3.5–5
Alharthy [64], 13/11/2020	Saudi Arabia, Prospective cohort	171, ICU	Within 24 h	No	47	79	26.4	12, Phased array, 2–4
Haak [65], 18/11/2020	Netherlands, Prospective cohort	24, ED	Within 24 h	Yes, PCR and clinical data	NA	NA	NA	12, Convex, 2–6
Allegorico [66], 01/12/2020	Italy, Retrospective cohort	42, ED	Within 24 h	No	69	69	NA	12, NA
Recinella [67], 03/12/2020	Italy, NA	37, Wards	Within 24 h	No	82	51	23.7	12, Linear, 5–8
Schmid [68], 07/12/2020	Germany, Retrospective cohort	39, ED	Within 24 h	Yes, PCR, clinical data and CT	61	56	26.3	12, NA
Zanforlin [69], 07/12/2020	Italy, Retrospective cohort	46, ED	Within 24 h	No	60	57	NA	20, Convex, 5–2

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Table 1 (*continued*)

Author and publication date	Country and study design	COVID-19 cases and clinical setting	Time of LUS acquisition	Blinding	Age (mean or median, years)	Male cases (%)	BMI (mean or median, kg/m^2)	Scanned regions, main probe and frequency (Hz)
Wangüemert Pérez [70], 17/12/2020	Spain, Retrospective cohort	45, Wards	Within 24 h	No	82	44	NA	12, Convex, 3–5
Ji [22], 22/12/2020	China, Prospective cohort	280, Hospital	After a median time of >5 days	Yes, Clinical data	55	50	23.1	12, Convex, 1–6
Speidel[15], 25/12/2020	Switzerland, Prospective cohort	11, Wards	Within 24 h	Yes, PCR and clinical data	76	73	NA	12 Convex, 4
Ibrahim [71], 04/01/2021	Kuwait, Prospective cohort	77, ICU	Within 24 h	Yes, PCR	53	83	NA	12, Convex, 3.5
Bock [72], 07/01/2021	Denmark, Prospective cohort	12, ED	Within 24 h	Yes, PCR and chest radiography but not to clinical data	68	58	NA	14, Convex, 1–5
Garcia de Alencar [73], 11/01/2021	Brazil, Prospective cohort	180, ED	Within 24 h	Yes, CT and clinical data	60	58	NA	12, Convex, 2–5
Boero [74], 24/01/2021	Italy, Retrospective cohort	274, ED	Within 5 days	No	NA	NA	NA	12, Convex, 2–9
Avdeev [75], 25/01/2021	Russia, Prospective cohort	22, Wards	NA	Yes, Clinical data	49	73	28.7	14, NA
Heldeweg [76], 25/01/2021	Netherlands, Prospective cohort	34, ICU	NA	Yes, CT	63	88	28.2	12, Linear, 10–5
Seiler [77], 26/01/2021	Sweden, Prospective cohort	72, Hospital	Within 5 days	No	65	60	28.0	12, Convex, 2–6

*__BMI__: Body Mass Index; __ED__: Emergency Department; __ICU__: Intensive Care Unit; __NA__: Not Available.

The pooled population studied included a total of 4687 patients with confirmed COVID-19. Among them, 43.7% were male (data not available in 22.1%), the mean age was 58 years and the mean body mass index (BMI) was 26.2 kg/m^2. 64.6% were hospitalised (30.4% in ward or intermediate care unit, 17.4% in ICU and 3.2% in pregnancy ward) and 15.5% were followed up outside the hospital (11.0% at home, 3.0% in nursing home and 1.5% in rehabilitation units). In 19.9% of patients it was not specified (ED patients that were either admitted to hospital or followed at home) (Appendix 3).

The ultrasound findings in the included articles are summarised in Table 2 and detailed in Appendix 4. The findings examined in the largest number of patients were at least 3 B-lines (1828, 39.27%) and confluent B-lines (1753, 37.40%), subpleural consolidation (1400, 29.87%), pleural effusion (2055, 43.84%) and bilateral or unilateral distribution (1615, 34.46%); while the least investigated were separated B-lines (386, 8.24%), white lung (118, 2.52%), fragmented pleural line (341, 7.28%), air bronchogram (228, 4.86%), and pneumothorax (492, 10.50%). According to these studies, among the findings studied in more patients, the most frequent findings in patients with COVID-19 were the presence of B lines (91%), in particular in ICU patients (99%) as well as their confluent presentation (80%), whereas at least 3 B-lines was more common in the ED (83%); followed by pleural abnormalities (84%). However, pleural abnormalities were even more common in ward patients (100%), but with a significant presence in ICU particularly irregular pleural lines (88% and 81% respectively). Consolidations, indicative of more severe disease, were less frequent in all studies (43%) and in ED (38%), and more common in ward and ICU (77%); as were subpleural (30% and 42% vs. 60% and 43% respectively) but not pulmonary consolidations (33% and 0% vs. 36% and 0%). Pleural effusion was an infrequent finding (14%), although slightly more frequent in ward (20%) and ICU (26%) patients, and the distribution of abnormal LUS findings was eminently bilateral (59% overall) in ED, ward and ICU (83%, 92% and 79% respectively).

The adapted LUS score (assuming 12 anatomical zones were scanned, as described above) was higher in ICU patients (22.52) and in the ED (15.10) than in the ward (13.98). Even so, these three hospital services had higher scores than the total number of patients including non-hospital patients (11.27). The included studies also describe the utility of the LUS findings and/or the LUS score in the diagnosis of COVID-19, using RT-PCR as the gold standard. This indicator has a remarkable sensitivity (from 89.48% in all patients to 97.4% in ICU patients) with a moderate specificity (from 62.55% in the ED to 76.32% in the ward, except in ICU with 90.63%). The resulting positive predictive value is also moderate (from 52.63% in ward to 75.66% in overall patients, excluding ICU with 96.15%), while the negative predictive value is considerable (from 84.9% in ED to 93.55% in ICU) (Table 3 and Appendix 5).

A total 16 of the 66 included articles studied the role of LUS score in the prediction of relevant clinical outcomes. Recinella et al. [67] found a hazard ratio (HR) of death for total LUSS12 (LUS score for 12 quadrants) in univariate analysis of 1.168 (95% CI 1.049–1.301). Lichter et al. [40] also calculated the unadjusted HR of death for total LUSS12, which was equal to 1.08 (95% CI 1.02–1.16). Moreover, Garcia de Alencar et al. [74] found an odds ratio (OR) of death for total LUSS12 of 1.13 (95% CI 1.07–1.21), and adjustment by age did not change results and Wangüemert Pérez et al. [71] found an OR of death for total LUSS12 of 1.57 (95% CI 1.10 –2.23) adjusted by sex and age-adjusted Charlson index. All four of these results are similar and statistically significant. Another way of presenting these results is by showing the mean LUS score in patients who died and those who survived. Rojatti et al. [52] shows that LUSS8 was 13.9 ± 2.8 in non-survivors and 10.5 ± 3.6 in survivors (p-value = 0.029), Bosso et al. [14] shows that LUSS12 was 20.9 ± 6.5 in non-survivors and 15.6 ± 4.5 in survivors (p-value < 0.01), and finally Garcia de Alencar et al. [74] shows that LUSS12 was 21.6 ± 4.9 in non-survivors and 16.7 ± 4.9 in survivors (p-value < 0.001). Rojatti et al. results are surprisingly similar to those of Bosso, if we multiply the LUSS8 presented in Rojatti et al. by 12/8 to obtain what the equivalent LUSS12 might have been, we obtain a mean LUSS12 for non-survivors of 20.85 and 15.75 for survivors. Likewise, Bonadia et al. [31] a nLUSS (normalized LUSS) median of 1.43 (IQR: 1.31–1.69) in patients who died and of 1 (IQR: 0.27–1.4) in patients who were discharged. If we multiply this result by 12, to obtain its equivalent LUSS12, we obtain 17.16 in dead patients and 12.00 in patients who were discharged.

Another common reported clinical outcome was the need for invasive mechanical ventilation (IMV) or need for non-invasive respiratory support (NIRS). Lichter et al. [40] reported a HR of mechanical

Table 2
Lung ultrasound findings in COVID-19.

	All studied patients* N/n (%)	Emergency department N/n (%)	Wards N/n (%)	Intensive care unit N/n (%)
B-lines				
Any	867/952 (91)	172/178 (97)	29/31 (94)	118/119 (99)
At least 3	1158/1828 (63)	349/421 (83)	104/137 (76)	58/79 (73)
Separated	236/386 (61)	22/40 (55)	5/30 (17)	174/260 (67)
Confluent	713/1753 (41)	88/132 (67)	32/56 (57)	223/280 (80)
White lung	35/118 (30)	10/12 (83)	20/77 (26)	NA
Pleural abnormalities				
Any	394/468 (84)	21/27 (78)	37/37 (100)	184/208 (88)
Pleural thickening	327/574 (57)	136/175 (78)	39/121 (32)	29/39 (74)
Irregular pleural lines	293/623 (47)	36/95 (38)	10/10 (100)	83/102 (81)
Fragmented pleural line	79/341 (23)	15/24 (63)	33/37 (89)	NA
Consolidations				
Any	304/707 (43)	161/423 (38)	65/84 (77)	40/52 (77)
Subpleural	424/1400 (30)	33/79 (42)	70/117 (60)	42/109 (39)
Pulmonary	221/669 (33)	0/12 (0)	37/103 (36)	0/17 (0)
Other				
Pleural effusion	288/2055 (14)	56/481 (12)	57/285 (20)	92/349 (26)
Air bronchogram	27/228 (12)	17/44 (39)	4/56 (7)	NA
Pneumothorax	30/492 (6)	0/12 (0)	1/30 (3)	7/131 (5)
Distribution				
Bilateral	956/1615 (59)	376/451 (83)	143/156 (92)	70/89 (79)
Unilateral	291/1615 (18)	37/451 (8)	10/156 (6)	19/89 (21)

* Including pregnancy wards, nursing homes, rehabilitation units and patients followed at home.

intubation for total LUSS12 in univariate analysis of 1.2 (95% CI 1.1–1.3), and Garcia de Alencar et al. [74] found an OR of 1.17 (95% CI 1.09–1.26). Ji et al. [22] found a HR of ARDS development for total LUSS12 of 1.049 (95% CI 1.023–1.076); adjusted for age, lymphocytes count and comorbidity. Meanwhile, Castelao et al. [48] found the mean LUSS12 in patients with NIRS 23.5 ± 5.3 and of 13.0 ± 7.2 in patients without NIRS (p-value < 0.001). García de Alencar et al. [74] found the mean LUSS12 in IMV patients to be 21.3 ± 4.9 and in not-IMV patients to be 15.2 ± 7.1 (p-value < 0.001) and in Seiler et al. [78], the LUSS12 was equal to 20.0 in IMV patients and 12.0 in non-IMV patients (p-value < 0.0001). Seiler et al. also found that a LUSS cut-off point of 19.5 had an area under the curve (AUC) of 0.80 (95% CI 0.70–0.90), sensitivity 57% (95% CI 34–77), specificity 82% (95% CI 68–91) for prediction of need of IMV.

Finally, there are some articles, like Perrone et al. [63], which group unfavourable outcomes into the same category, in this case: high-flow oxygen support, ICU admission, death. For these 3 grouped events, they find an adjusted HR of 1.17 (95% CI 1.05–1.29) for total LUSS14; adjusted for comorbidities (>2), age (>65 years), sex (male), and body mass index (≥25 kg/m^2). Boero et al. [75] considers need for IMV, ICU admission, and death as unfavourable outcomes and finds a relative risk (RR) of unfavourable outcome for LUSS12 > 15 of 2.05 (95% CI 1.52–2.77).

According to index test risk of bias, among the studies assessing the diagnostic accuracy of LUS (21 in total), 13 had "low" risk of bias and 8 had "unclear" or "high" risk in one of the QUADAS-2 domains. To assess whether the risk of bias could alter the results of this review, for each domain of QUADAS-2 we compared the diagnostic accuracy of LUS in studies that had "low" risk of bias and studies that had "high" or "unclear" risk of bias. As can be seen in Table 4, sensitivity and specificity results were similar (p value < 0.05 only found in one comparaison, where studies with "low" risk of bias in time and flow domain showed higher sensitivity for COVID-19 diagnosis).

With regard to the comparison between CT scores and LUSS, 5 of the included articles describe the Pearson's r correlation between them. These articles were Nouvenne [27] (r = 0.650), Deng [30] (0.891), Ottaviani [37] (0.935), Zhu [21] (0.820) and Heldeweg [77] (0.795). All these values correspond to moderate to high correlations and they also proved to be statistically significant, with all p values < 0.01. As for studies that simultaneously evaluate LUS and CT diagnostic accuracy, in

Table 4
LUS diagnostic performance according to the QUADAS-2 risk of bias.

		Low risk n (%)	High or unclear risk n (%)	p value
Patient selection	Sensitivity	20 (89.3)	1 (96.8)	0.180
	Specificity	20 (70.1)	1 (62.3)	0.144
Index test	Sensitivity	13 (87.3)	8 (90.9)	0.064
	Specificity	13 (71.0)	8 (69.3)	0.051
Time and Flow	Sensitivity	19 (90.5)	2 (77.5)	0.001*
	Specificity	19 (70.2)	2 (69.0)	0.803

* p < 0.05.

Table 3
LUS findings and diagnostic performance.

	All studied patients* (n = 2543)	Emergency department (n = 580)	Wards (n = 342)	Intensive care unit (n = 179)
LUS score (mean)	11.27	15.10	13.98	22.52
	All studied patients* (n = 2894)	**Emergency Department** (n = 2169)	**Wards** (n = 49)	**Intensive care unit** (n = 109)
Sensitivity % (95% CI)	89.48 (87.80–91.00)	90.83 (89.05–92.41)	90.91 (58.72–99.77)	97.40 (90.93–99.68)
Specificity % (95% CI)	70.16 (67.71–72.53)	62.55 (59.44–65.59)	76.32 (59.76–88.56)	90.62 (74.98–98.02)
Positive Predictive Value % (95% CI)	75.66 (74.13–77.13)	74.64 (73.04–76.17)	52.63 (37.87–66.95)	96.15 (89.48–98.66)
Negative Predictive Value % (95% CI)	86.55 (84.67–88.23)	84.90 (82.37–87.13)	96.67 (81.61–99.48)	93.55 (78.61–98.28)

* Including pregnancy wards, nursing homes, rehabilitation units and patients followed at home.

most of them LUS has higher sensitivity but lower specificity. Sensitivity and specificity between both of them were described in Battista [44] (CT 93.0% and 90.0% vs. LUS 68.0% and 79.0%), Narinx [45] (CT 80.0% and 86.7% vs. LUS 93.3% and 21.3%) and Lieveld [56] (CT 90.0–95.0% and 43.0–69.0% vs. LUS 93.0–94.0% and 7.0–31.0%) respectively.

4. Discussion

Lung ultrasound is a developing technique, not yet as widely implemented as other thoracic imaging modalities (computed tomography, X-ray or even echocardiography [78]) but increasingly used. In particular, its use to study pulmonary involvement in COVID-19 has increasingly risen. Recently, other systematic reviews have been published in an attempt to synthesise the available information and establish stronger evidence in this field [79–82]. However, these studies have only partially described lung ultrasound findings, focusing on the most common findings without exploring the frequency of occurrence of other phenomena. The association of each of these findings with the clinical patient profile and the area of acquisition is yet to be described.

The data collected shows a predominance of B-lines, pleural alterations and bilateral distribution in COVID-19, consistent with previous studies that describe SARS-CoV-2 pneumonia as bilateral, peripheral and patchy lung involvement with posterior and inferior predominance [83,84]. Findings of confluent B-lines, irregularity and pleural thickening are more frequent in ICU patients, which corresponds to higher LUS scores. However, subpleural and pleural consolidations are more frequent on ward. Although subpleural consolidation may reasonably be more represented on the ward, as it is indicative of moderate-severe infection, the higher proportion of pulmonary consolidation relative to ICU is likely to be a bias in the selected articles, due to a variable description of this finding. White lung is possibly over-represented in the ED given the low sample of patients in which it was sought. Pleural effusion is an infrequent finding but is more common in ward and ICU patients, suggesting that its presence may be associated with more severe disease (as the most severe patients are admitted to these two departments and as described in other studies [85]) or with complications of the disease and its management (such as superinfection, prolonged ICU stay or need for mechanical ventilation). However, this finding is not included in the LUS score.

LUS score has classically been the prognostic index used during the COVID-19 pandemic, developed by Soldati [9] and in line with previous work by Rouby [86] and Soummer [87]. However, the included studies have also employed other protocols such as the original Bedside Lung Ultrasound in Emergency (BLUE) protocol [88], the modified lung ultrasound (MLUS) scoring system [12] or adapted LUS scores at the criteria of each author [29,33,63]. It is clear that the LUS score is higher in the ICU, although the fact that it is higher in the ED than in the ward may be due to the possibility that ED patients may be referred to one or the other location, or be discharged. In all of the 16 articles that study the role of LUS score in the prediction of relevant clinical outcomes, the data shows that a higher value of baseline LUS scores is associated with a higher risk of developing unfavorable outcomes, such as death, ICU admission or need for mechanical ventilation. A good correlation between CT results and LUSS is also observed, as well as a higher sensitivity but lower specificity.

It seems that LUS is most reliable to rule out severe lung involvement, given its high sensitivity (89.5%) and negative predictive value (86.6%). It must be considered that this negative predictive value was calculated for an average prevalence of 50.9% of COVID-19 confirmed cases in the pooled population of studies that assessed the validity of LUS as a diagnostic tool in suspected cases, using PCR tests for SARS-CoV-2 as the gold standard. This should not suppose a problem, however, given that the lower expected prevalence of COVID-19 cases in the future will only increase the negative predictive value of LUS. As LUS can reasonably rule out COVID-19 in hospitalised patients, it could enable early detection of non-infected patients after an outbreak on the ward, for instance. Nonetheless, it is also true that LUS specificity (70.2%) and positive predictive value (75.7%) might be too low for standardized clinical practice. Furthermore, if COVID-19 prevalence falls below 25% in suspected cases, the positive predictive value will be <50%. Therefore, LUS could allow early management of a patient with indeterminate radiographic findings or a high clinical suspicion of a false negative RT-PCR, but this statement might only hold true in the pandemic context, when the prevalence of COVID-19 was high.

It is worth mentioning the great variability in the way these data are acquired and presented. Unfortunately, the lack of a standard in the type of probe used, the number of lung fields to be analysed and the reference severity index, have not made possible the quantitative synthesis of these studies in a *meta*-analysis of prognostic variables as intended, making it necessary to use narrative synthesis. Given the heterogeneity in measurement of the LUS score, the selection of the prognostic factors studied and the statistical method applied to calculate the final results, we found no way to even group the prognostic results in a table.

Although it is important to note that, the 7 studies that assessed the role of LUS score in predicting mortality all found a positive association, which was significant when statistical inference tests where applied. Similarly, the 4 studies that investigated the role of LUS score in predicting need for invasive ventilation or need for non-invasive respiratory support, all found a significant association. These results support the utility of LUS not only in early detection of pulmonary involvement in the suspicion of COVID-19, but also in assessing the risk of complications. Therefore, it could potentially be a useful tool in bedside monitoring of disease severity in hospitalised patients.

Some of the potential limitations of this work are those inherent to review studies, with the quality of a review being equal to the studies it includes. In this case, only 25 of the included studies (37.9%) were prospective, and the rest may incur biases such as selection bias. Also the low sample of patients in which some of the findings are described (e.g. separated B-lines, white lung, fragmented pleural line, air bronchogram or pneumothorax) and the absence of an acquisition standard may lead to information bias.

Among the strengths of the study, the fact that the results collected include a wide variety of care areas and up to 4687 patients, showing a more reliable picture of the different manifestations of COVID-19 (a disease characterised by its high clinical variability) may be highlighted [89]. These different areas have been analysed separately, allowing to identify the ultrasound findings reported in each of them (not only the most frequent ones) and the performance of the LUS score in these care environments. The time of acquisition and the existence or not of blinding in each of these studies has also been made explicit.

This study also raises some questions for future work and proposes some recommendations based on the results obtained. Other studies should homogenise the LUS study protocol in COVID: define the type of probe to be used, establish the 12 lung fields as the study standard as suggested [90], contrast the LUS score proposed by Soldati et al. with other scoring systems and confirm its advantage over them. Also, it should come towards an agreement on further studies about the best cut-off points for LUS to categorise the severity of patients according to the severity of initial lung involvement of the disease and expected prognosis; and define the prognostic value of pleural effusion in COVID. Furthermore, the utility of performing a radiological test after lung ultrasound in those patients in which lung ultrasound is less effective (particularly to rule out false positives in phases of the pandemic with low prevalence of COVID-19 infection), and other diagnosis are suspected that require a more detailed anatomical studied should also be studied. We propose the use of the variable death at 30 days and the combined variable poor prognosis (non-invasive mechanical ventilation, invasive mechanical ventilation, ICU admission and death at 30 days) as main prognostic variables.

5. Conclusions

The most frequent ultrasound findings of COVID-19 are the presence of B-lines and pleural abnormalities. LUS score is associated with ICU admission, need for mechanical ventilation and death. The inclusion of pleural effusion in the LUS score and the standardisation of the imaging protocol in COVID-19 LUS remains to be defined.

CRediT authorship contribution statement

Jaime Gil-Rodríguez: Conceptualization, Methodology, Investigation, Writing – original draft, Supervision, Project administration. **Javier Pérez de Rojas:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – review & editing. **Pablo Aranda-Laserna:** Investigation, Formal analysis, Writing – review & editing, Visualization. **Alberto Benavente-Fernández:** Conceptualization, Validation, Writing – review & editing. **Michel Martos-Ruiz:** Writing – review & editing, Visualization. **José-Antonio Peregrina-Rivas:** . **Emilio Guirao-Arrabal:** Conceptualization, Methodology, Investigation, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix 1. Quality of included studies as established in the four domains described in the QUADAS-2 tool

Author and publication date	Risk of bias				Concerns regarding applicability		
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Lu, 15/04/2020	Low	Low	Low	Low	Low	Low	Low
Yasukawa, 24/04/2020	Low	Unclear	Low	Low	Low	Low	Low
Xing, 28/04/2020	Unclear	Unclear	Low	High	Low	Low	Low
Tan, 05/06/2020	High	Unclear	Low	Low	Unclear	Low	Low
Bar, 10/06/2020	High	Low	Low	Low	Unclear	Low	Low
Pare, 19/06/2020	Low	Low	Low	Low	Low	Unclear	Low
Nouvenne, 22/06/2020	Low	Low	Low	Low	Low	Low	Low
Yassa, 30/06/2020	Low	Low	Low	Low	Low	Low	Low
Møller-Sørensen, 02/07/2020	Unclear	Low	Low	Low	Low	Low	Low
Ye, 09/07/2020	Low	Low	Low	High	Low	Low	Low
Deng, 14/07/2020	Low	Low	Low	Low	Low	Low	Low
Bonadia, 15/07/2020	Low	Unclear	Low	Low	Low	Low	Low
Dargent, 21/07/2020	Unclear	Unclear	Low	Low	Low	Low	Low
Zhang, 22/07/2020	Low	Unclear	Low	High	Unclear	Unclear	Low
Yassa, 28/07/2020	Low	Unclear	Low	Low	Low	Low	Low
Veronese, 29/07/2020	Low	Unclear	Low	Low	Low	Low	Low
Zieleskiewicz, 29/07/2020	Low	Unclear	Low	Low	Unclear	Low	Low
Favot, 31/07/2020	Low	Low	Low	Low	Low	Low	Low
Gaspardone, 08/08/2020	Low	Unclear	Low	High	Low	Low	Low
Ottaviani, 12/08/2020	Low	Low	Low	Unclear	Low	Low	Low
Alharthy, 14/08/2020	Low	Unclear	Low	Low	Low	Low	Low
Thomaz, 21/08/2020	Low	Unclear	Low	Unclear	Low	Low	Low
Lichter, 28/08/2020	Low	Low	Low	Low	Unclear	Low	Low
Iodice, 01/09/2020	Low	Low	Low	Low	Unclear	Unclear	Low
Dini, 02/09/2020	Low	Unclear	Low	Unclear	Low	Low	Low

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Author and publication date	Risk of bias				Concerns regarding applicability		
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Gil, 04/09/2020	Low	Unclear	Low	Low	Unclear	Low	Low
Battista, 07/09/2020	Low	Low	Low	Low	Low	Low	Low
Narinx, 10/09/2020	Low	Low	Low	Low	Unclear	Low	Low
Kalafat, 11/09/2020	Low	Low	Low	Unclear	Low	Low	Low
Li, 15/09/2020	Low	Unclear	Low	Unclear	Unclear	Low	Low
Castelao, 16/09/2020	Low	Low	Low	Low	Low	Low	Low
Cocconcelli, 16/09/2020	Low	Unclear	Low	High	Low	Low	Low
Brahier, 17/09/2020	Low	Low	Low	Low	Low	Low	Low
Ramos-Hernández, 21/09/2020	Unclear	Unclear	Low	Low	Low	Low	Low
Zhu, 21/09/2020	Low	Unclear	Low	Low	Unclear	Low	Low
Rojatti, 25/09/2020	Low	Unclear	Low	Low	Low	Low	Low
Marggrander, 01/10/2020	Low	Unclear	Low	Unclear	Unclear	High	Low
Bosso, 03/10/2020	Low	High	Low	Unclear	Low	Low	Low
Colombi, 08/10/2020	Low	Unclear	Low	Low	Unclear	Low	Low
Haaksma, 08/10/2020	Low	Low	Low	Unclear	Low	Low	Low
Pivetta, 12/10/2020	Low	Low	Low	Low	Low	Low	Low
Lieveld, 15/10/2020	Low	Low	Low	Low	Low	Low	Low
Zhu, 16/10/2020	Low	Low	Low	High	Low	Low	Low
Bosevski, 22/10/2020	Unclear	Unclear	Low	Unclear	Low	Unclear	Low
Sorlini, 22/10/2020	Low	Unclear	Low	Low	Unclear	Low	Low
Jalil, 26/10/2020	Low	Low	Low	Low	Low	Low	Low
Gibbons, 29/10/2020	Low	Unclear	Low	Low	Unclear	Low	Low
Li, 03/11/2020	Low	Unclear	Low	Low	Low	Unclear	Low
Zotzmann, 03/11/2020	Low	Low	Low	Unclear	Low	Low	Low
Perrone, 06/11/2020	Low	Unclear	Low	Low	Low	Low	Low
Alharthy, 13/11/2020	Low	Unclear	Low	Low	Low	Low	Low
Haak, 18/11/2020	Low	Low	Low	Low	Low	Low	Low
Allegorico, 01/12/2020	Low	Unclear	Low	Low	Unclear	Low	Low
Recinella, 03/12/2020	Low	Unclear	Low	Low	Low	Low	Low
Schmid, 07/12/2020	Low	Low	Low	Low	Low	Low	Low
Zanforlin, 07/12/2020	Low	Unclear	Low	Low	Unclear	Low	Low
Wangüemert Pérez, 17/12/2020	Low	Unclear	Low	Low	Low	Low	Low
Ji, 22/12/2020	Low	Low	Low	High	Low	Low	Low
Speidel, 25/12/2020	Low	High	Low	Low	Low	Low	Low
Ibrahim, 04/01/2021	Low	Low	Low	Low	Low	Low	Low
Bock, 07/01/2021	Low	Low	Low	Low	Low	Low	Low
Garcia de Alencar, 11/01/2021	Low	Low	Low	Low	Unclear	Low	Low

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Author and publication date	Risk of bias				Concerns regarding applicability		
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Boero, 24/01/2021	Low	Unclear	Low	Low	Low	Low	Low
Avdeev, 25/01/2021	Low	Unclear	Low	Unclear	Low	Low	Low
Heldeweg, 25/01/2021	Low	Low	Low	Unclear	Low	Low	Low
Seiler, 26/01/2021	Low	Unclear	Low	Low	Unclear	Low	Low

Appendix 2. Characteristics of included articles

Characteristics	Number of studies (%)
Continent	
Europe	41 (62.1)
Asia	18 (27.3)
North America	5 (7.6)
South America	2 (3.0)
Study design	
Prospective cohort	25 (37.9)
Retrospective cohort	24 (36.4)
Retrospective case–control	2 (3.0)
Cross-sectional	2 (3.0)
Not specified	13 (19.7)
Clinical setting where LUS was performed	
ED	22 (33.3)
Hospital (wards and ICU)	13 (19.7)
Wards	12 (18.2)
ICU	11 (16.7)
ED and ICU	1 (1.5)
Pregnancy wards	3 (4.5)
Home	1 (1.5)
Nursing home	2 (3.0)
Rehabilitation unit	1 (1.5)
Number of COVID-19 patients included	
10–29	23 (34.8)
30–99	31 (47.0)
100–500	12 (18.2)
Time of LUS acquisition	
Withing 24 h of admission	40 (60.6)
Withing 5 days of admission	6 (9.1)
After a median time of >5 days	5 (7.6)
At discharge	1 (1.5)
Following fetal assessment	1 (1.5)
Not specified	13 (19.7)
Blinded operators	
Yes	34 (51.5)
No	32 (48.5)
Type of blinding	
To clinical data	16 (47.1)
To PCR status	15 (44.1)
To CT scan or chest radiography	12 (35.3)
Not specified	4 (11.8)
Chest anatomical areas scanned	
<12	16 (24.2)
12	35 (53.0)
>12	8 (12.1)
Not specified	7 (10.6)
Main type of ultrasound probe used	
Convex	41 (62.1)
Linear	7 (10.6)
Phased array	4 (6.1)
Not specified	14 (21.2)

*__ED__: Emergency Department, __ICU__: Intensive Care Unit specified

Appendix 3. Pooled characteristics of COVID-19 confirmed patients

Characteristics	Results
COVID-19 confirmed cases (n)	4687
Age (mean years; n)	58 (3581)
Number of studies according to mean/median age (N, %)	
≥25 and <50 years	7 (10.4)
≥50 and <70 years	47 (70.1)
≥70 and <90 years	4 (6.0)
NA	8 (11.9)
Sex (N, %)	
Male	2048 (43.7)
Female	1602 (34.2)
NA	1037 (22.1)
BMI (mean kg/m^2; n)	26.2 (1346)
Hospitalised (N, %)	3028 (64.6)
In wards or intermediate care unit	1423 (30.4)
In ICU	816 (17.4)
Not specified (in wards or ICU)	641 (13.7)
In pregnancy wards	148 (3.2)
Not hospitalised (N, %)	727 (15.5)
Followed at home	515 (11.0)
In nursing home	142 (3.0)
In rehabilitation unit	70 (1.5)
Not specified (ED patients that were either admitted to hospital or followed at home) (N, %)	932 (19.9)

*__N__: Number of articles, __n__: Number of patients, __NA__: Not available.

Appendix 4. Detailed data of lung ultrasound findings from the included studies.

Study	COVID-19 cases (N)	B-lines (%)	At least 3 B-lines (%)	Separated B-lines (%)	Confluent B-lines (%)	White lung (%)	Pleural abnormalities (%)	Pleural thickening (%)	Irregular pleural lines (%)	Fragmented pleural line (%)	Consolidation (%)	Subpleural consolidation (%)	Pulmonary consolidation (%)	Pleural effusion (%)	Air bronchogram (%)	Pneumothorax (%)	Bilateral (%)	Unilateral (%)	LUS score
Lu	30		90	17	50	10		10					20	3	7	3	73	17	10.6
Yasukawa	10	100				50		100	100			50	10	0					
Xing	20	100		55	90		100						50	10			100	0	
Tan	12	100			33	83		100	75	50		42	0	8		0			
Pare	27	89	85				78	78				37							
Nouvenne	26		27		65							65	50	4	8		100	0	15.0
Møller-Sørensen	10	100						100			100			50					
Ye	23													17					6.8
Deng	128	100			66		95					50		9	5	2			12.6
Bonadia	41																		13.4
Dargent	10																		22.0
Zhang	28	100						61					68	4					
Veronese	48																		3.0
Zieleskiewicz	100		96						32		32			6		0	85	11	15.3
Favot	40			55	90							45					85	5	
Gasparedone	70																		7.5
Ottaviani	21	90									62								
Alharthy	89	100		7	8				79			27		22		3	79	21	
Thomaz	722		41		20							5					28	28	1.7
Lichter	120							83				78		8					15.0
Iodice	29	100				17							97				100	0	
Battista	44	100						86			45			18	39		75	25	
Narinx	15		93																
Kalafat	82																		9.2
Li	91	65			62			7					53	43		22			
Castelao	63										83			5			94	6	15.3
Cocconcelli	25																		7.0
Brahier	80		50		60			70			25			25			79	6	10.0
Ramos-Hernández	44		75					25				59		30					7.0
Zhu	27																		11.8
Rojatti	34																		11.2
Marggrander	17		53									29	18	18					
Bosso	26																		18.1

(*continued on next page*)

(*continued*)

Study	COVID-19 cases (N)	B-lines (%)	At least 3 B-lines (%)	Separated B-lines (%)	Confluent B-lines (%)	White lung (%)	Pleural abnormalities (%)	Pleural thickening (%)	Irregular pleural lines (%)	Fragmented pleural line (%)	Consolidation (%)	Subpleural consolidation (%)	Pulmonary consolidation (%)	Pleural effusion (%)	Air bronchogram (%)	Pneumothorax (%)	Bilateral (%)	Unilateral (%)	LUS score
Haaksma	24																		19.0
Zhu	48	71					21				13			4			58	21	5.3
Bosevski	17		47				53						0	6					
Sorlini	287		92								39			8			86	7	
Jalil	36			67	92				92			58		0					
Gibbons	83	98							33										
Li	42		86					76			71			24		10			
Zotzmann	20	95	70		55		95					90		50					
Perrone	52													48					23.8
Alharthy	171			67	83		91							27					
Allegorico	42																		14.0
Recinella	37		100			32	100	41		89		59	46	27			97	3	12.0
Zanforlin	46													2					
Wangüemert Pérez	45																		9.7
Ji	280	89	63		12				35	11			16	2					
Ibrahim	77																		27.0
Bock	12	92	58					75		75	67			17					
Garcia de Alencar	180																		18.7
Boero	211																		13.4
Avdeev	22																		17.8
Seiler	72		96									88	42	6					15.7

Appendix 5. Sensitivity and specificity of LUS in the diagnosis of COVID-19 (using RT-RCP as the gold standard)

Study	LUS sensitivity (%)	LUS specificity (%)	Criteria	Population characteristics (mean n, age, BMI; % male)	
				COVID +	COVID−
Bar	96.8%	62.3%	≥3 B-lines at the upper site; consolidation and thickened pleura at the lower site; and thickened pleura.	31, 66.8 yr, 30.0 kg/m^2; 35%	69, 68.7 yr, 26.4 kg/m^2; 44%
Pare	88.9%	56.3%	Any B-lines were detected.	27, 53.0 yr, 31.7 kg/m^2; 59.3%	16, 50.0 yr, 31.3 kg/m^2; 31.3%
Yassa	72.1%	77.8%	LUS score ≥ 1.	43 pregnant women	9 pregnant women
Yassa	73.9%	94.1%	LUS score ≥ 1.	23 pregnant women	273 pregnant women
Favot	70.0%	75.0%	Nondependent bilateral pulmonary edema (bilateral B-lines with superior count ≥ inferior count and no pleural effusions).	40, 69 yr, 31 kg/m^2; 60%	16, 63 yr, 29 kg/m^2; 63%
Dini	78.7%	57.1%	LUS score ≥ 1.	94	56
Gil	100.0%	80.6%	Any pattern not compatible with A-lines in all intercostal areas.	27, 48 yr; 33.3%	31, 45 yr; 16.1%
Battista	68.2%	78.9%	Not specified.	44, 66 yr; 65.9%	19, 61 yr; 63.2%
Narinx	93.3%	21.3%	≥ 3 B-lines.	15, 49.9 yr; 60.0%	75, 50.5 yr; 42.7%
Bosso	73.1%	90.3%	LUS score > 12.5.	26, 66 yr; 69.2%	27, 65 yr; 70.4%
Colombi	93.5%	28.3%	Not specified.	341	145
Pivetta	94.4%	95.0%	Focal or diffuse interstitial syndrome plus with spared areas, subpleural consolidations, and irregular or thickened pleural line.	107, 62.8 yr; 54.1%	121, 50.3 yr; 43.7%
Lieveld	91.9%	71.0%	≥3 or more B-lines and/or consolidation in two or more zones unilaterally or in one or more zones bilaterally.	86, 63.4 yr; 58.1%	100, 64.1 yr; 58.0%
Sorlini	92.0%	64.9%	(A) Interstitial lung syndrome[1] (B) Interstitial lung pattern[2] (C) White lung (coalescent B lines) in two or more zones. (D) Subpleural consolidations.	287	97
Jalil	86.1%	90.9%	Multifocal confluent B-lines, irregular pleura, and the absence of a moderate or large pleural effusion.	36, 62.5 yr, 30.5 kg/m^2; 52%	33, 65 yr, 29 kg/m^2; 42%
Gibbons	97.6%	33.3%	≥3 B-lines was considered positive. Additionally, the presence of a single confluent B-line encompassing a third or more of the visualized distal intercostal space was considered positive[3].	83, 56 yr; 43.4%	27, 64 yr; 55.6%
Haak	95.8%	59.4%	Irregular pleural line, multiple or confluent B-lines, subpleural consolidations and small pleural effusions.	24	69
Schmid	76.9%	77.1%	Bilateral patchy distribution of one of the following: pleural line irregularity OR ≥ 3 B-Lines per intercostal space OR small subpleural consolidation (<1.5 cm) OR no or small pleural effusion unilateral appearance of two or more of the criteria above.	39, 61 yr, 26.3 kg/m^2; 56.4%	96, 60 yr, 26.3 kg/m^2; 53.1%
Speidel	90.9%	76.3%	LUS score ≥ 8.	11, 76.0 yr; 73%	38, 69.5 yr; 47%
Ibrahim	97.4%	90.6%	(A) Patchy distribution of multiple coalesced and separated B-lines with the light beam sign, with bilateral and well-demarcated separation from large "spared" areas. (B) The pleural is sliding and might appear irregular and fragmented. (C) Multiple small subpleural consolidations are limited to the periphery of the lungs.	77, 53 yr; 83%	32, 68 yr; 50%
Bock	91.7%	64.8%	Lung sliding, lung pulse, lung point, multiple B-lines (≥3 per intercostal space), or thickened or fragmented visceral pleura were present.	12, 68 yr; 58%	71, 63 yr; 46%

References

[1] Centers for Disease Control and Prevention, History of 1918 Flu Pandemic | Pandemic Influenza (Flu) | CDC, (n.d.).

[2] J. Enaa, R.P. Wenzel, A Novel Coronavirus Emerges, Rev. Clínica Española. 220 (2020) 115–116, https://doi.org/10.1016/j.rce.2020.01.001.

[3] Johns Hopkins Coronavirus Resource Center, COVID-19 Map, (n.d.). https://coronavirus.jhu.edu/map.html (accessed 10 June 2021).

[4] M.A. Kose, F. Ohnsorge, C. Pazarbasioglu, C. Arteta, J. Baffes, A. Dieppe, J.-D. Guénette, A. Kabundi, S. Kasyanenko, S.K. Celik, G. Kindberg-Hanlon, P. Kirby, M. Maliszewska, H. Matsuoka, P. Nagle, Y. Okawa, C. Okou, F.U. Ruch, R. Steinbach, N. Sugawara, E. Vashakmadze, D. Vorisek, C.M. Wheeler, L.S. Ye, S. Yu, Y. Chen, Z. Chen, H. Doytchinova, F. Jiang, Y. L, M.H. Macadangdang, J.R.R. Norfleet, I.C. Oymak, V. Papagianni, M.F.S.E. Pereira, S. Shi, K. Temaj, X. Wang, J. Wu, H. Zhao, J. Zhou, R.K. Danda, J.R.R. Norfleet, S. Shi, G. Littler, I. Chand, M. Felsenthal, A. Viveros, G. Littler, A. Maximiliano, Global Economic Propects, 2020.

[5] D. Jarrom, L. Elston, J. Washington, M. Prettyjohns, K. Cann, S. Myles, P. Groves, Effectiveness of tests to detect the presence of SARS-CoV-2 virus, and antibodies to SARS-CoV-2, to inform COVID-19 diagnosis: a rapid systematic review, BMJ Evidence-Based Med. (2020) 1–13, https://doi.org/10.1136/bmjebm-2020-111511.

[6] N. Islam, S. Ebrahimzadeh, J.-P. Salameh, S. Kazi, N. Fabiano, L. Treanor, M. Absi, Z. Hallgrimson, M.MG. Leeflang, L. Hooft, C.B. van der Pol, R. Prager, S.S. Hare, C. Dennie, R. Spijker, J.J. Deeks, J. Dinnes, K. Jenniskens, D.A. Korevaar, J. F. Cohen, A. Van den Bruel, Y. Takwoingi, J. van de Wijgert, J.A. Damen, J. Wang, M.DF. McInnes, Thoracic imaging tests for the diagnosis of COVID-19, Cochrane Database Syst. Rev. 2021 (3) (2021), https://doi.org/10.1002/14651858.CD013639.pub4.

[7] N. Smallwood, M. Dachsel, Point-of-care ultrasound (POCUS): unnecessary gadgetry or evidence-based medicine? Clin. Med. J. R. Coll. Phys. Lond. 18 (3) (2018) 219–224.

[8] L. Shamseer, D. Moher, M. Clarke, D. Ghersi, A. Liberati, M. Petticrew, P. Shekelle, L.A. Stewart, Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation, g7647–g7647, BMJ 349 (2015), https://doi.org/10.1136/bmj.g7647.

[9] G. Soldati, A. Smargiassi, R. Inchingolo, D. Buonsenso, T. Perrone, D.F. Briganti, S. Perlini, E. Torri, A. Mariani, E.E. Mossolani, F. Tursi, F. Mento, L. Demi, Proposal for International Standardization of the Use of Lung Ultrasound for Patients With COVID-19, J. Ultrasound Med. 39 (2020) 1413–1419, https://doi.org/10.1002/jum.15285.

[10] P.F. Whiting, QUADAS-2: A Revised Tool for the Quality Assessment of Diagnostic Accuracy Studies, Ann. Intern. Med. 155 (8) (2011) 529, https://doi.org/10.7326/0003-4819-155-8-201110180-00009.

[11] J. Higgins, S. Green, Manual Cochrane de revisiones sistemáticas de intervenciones. Version 5.1.0, 2011.

[12] G. Tan, X. Lian, Z. Zhu, Z. Wang, F. Huang, Y. Zhang, Y. Zhao, S. He, X. Wang, H. Shen, G. Lyu, Use of Lung Ultrasound to Differentiate Coronavirus Disease 2019 (COVID-19) Pneumonia From Community-Acquired Pneumonia, Ultrasound Med. Biol. 46 (2020) 2651–2658, https://doi.org/10.1016/j.ultrasmedbio.2020.05.006.

[13] S. Bar, A. Lecourtois, M. Diouf, E. Goldberg, C. Bourbon, E. Arnaud, L. Domisse, H. Dupont, P. Gosset, The association of lung ultrasound images with COVID-19 infection in an emergency room cohort, Anaesthesia 75 (12) (2020) 1620–1625, https://doi.org/10.1111/anae.15175.

[14] G. Bosso, E. Allegorico, A. Pagano, G. Porta, C. Serra, V. Minerva, V. Mercurio, T. Russo, C. Altruda, P. Arbo, C. De Sio, F. Dello Vicario, F.G. Numis, Lung ultrasound as diagnostic tool for SARS-CoV-2 infection, Intern, Emerg. Med. 16 (2) (2021) 471–476, https://doi.org/10.1007/s11739-020-02512-y.

[15] V. Speidel, A. Conen, V. Gisler, C.A. Fux, S. Haubitz, Lung Assessment with Point-of-Care Ultrasound in Respiratory Coronavirus Disease (COVID-19): A Prospective Cohort Study, Ultrasound Med. Biol. 47 (4) (2021) 896–901, https://doi.org/10.1016/j.ultrasmedbio.2020.12.021.

[16] C. Xing, Q. Li, H. Du, W. Kang, J. Lian, L. Yuan, Lung ultrasound findings in patients with COVID-19 pneumonia, Crit. Care. 24 (2020) 174, https://doi.org/10.1186/s13054-020-02876-9.
[17] R. Ye, X. Zhou, F. Shao, L. Xiong, J. Hong, H. Huang, W. Tong, J. Wang, S. Chen, A. Cui, C. Peng, Y. Zhao, L. Chen, Feasibility of a 5G-Based Robot-Assisted Remote Ultrasound System for Cardiopulmonary Assessment of Patients With Coronavirus Disease 2019, Chest 159 (1) (2021) 270–281, https://doi.org/10.1016/j.chest.2020.06.068.
[18] Y. Zhang, H. Xue, M. Wang, N. He, Z. Lv, L. Cui, Lung Ultrasound Findings in Patients With Coronavirus Disease (COVID-19), Am. J. Roentgenol. 216 (1) (2021) 80–84, https://doi.org/10.2214/AJR.20.23513.
[19] C. Gaspardone, C. Meloni, A. Preda, D. Romagnolo, L. Brugliera, P. Castellazzi, A. Tettamanti, C. Conte, A. Secchi, F. Maranta, S. Iannaccone, D. Cianflone, Lung Ultrasound in <scp>COVID</scp> -19 A Role Beyond the Acute Phase? J. Ultrasound Med. 40 (2021) 503–511, https://doi.org/10.1002/jum.15425.
[20] E. Cocconcelli, D. Biondini, C. Giraudo, S. Lococo, N. Bernardinello, G. Fichera, G. Barbiero, G. Castelli, S. Cavinato, A. Ferrari, M. Saetta, A. Cattelan, P. Spagnolo, E. Balestro, Clinical Features and Chest Imaging as Predictors of Intensity of Care in Patients with COVID-19, J. Clin. Med. 9 (2020) 2990, https://doi.org/10.3390/jcm9092990.
[21] F. Zhu, X. Zhao, T. Wang, Z. Wang, F. Guo, H. Xue, P. Chang, H. Liang, W. Ni, Y. Wang, L. Chen, B. Jiang, Ultrasonic Characteristics and Severity Assessment of Lung Ultrasound in COVID-19 Pneumonia in Wuhan, China: A Retrospective, Observational Study, Engineering 7 (3) (2021) 367–375, https://doi.org/10.1016/j.eng.2020.09.007.
[22] L. Ji, C. Cao, Y. Gao, W. Zhang, Y. Xie, Y. Duan, S. Kong, M. You, R. Ma, L. Jiang, J. Liu, Z. Sun, Z. Zhang, J. Wang, Y. Yang, Q. Lv, L. Zhang, Y. Li, J. Zhang, M. Xie, Prognostic value of bedside lung ultrasound score in patients with COVID-19, Crit. Care 24 (2020) 700, https://doi.org/10.1186/s13054-020-03416-1.
[23] D.T. Marggrander, F. Borgans, V. Jacobi, H. Neb, T. Wolf, Lung Ultrasound Findings in Patients with COVID-19, SN Compr. Clin. Med. 2 (11) (2020) 2151–2157, https://doi.org/10.1007/s42399-020-00553-0.
[24] W. Lu, S. Zhang, B. Chen, J. Chen, J. Xian, Y. Lin, H. Shan, H. Shan, Z.Z. Su, Z.Z. Su, Z.Z. Su, A Clinical Study of Noninvasive Assessment of Lung Lesions in Patients with Coronavirus Disease-19 (COVID-19) by Bedside Ultrasound, Ultraschall Der Medizin. 41 (2020) 300–307, https://doi.org/10.1055/a-1154-8795.
[25] K. Yasukawa, T. Minami, Point-of-Care Lung Ultrasound Findings in Patients with COVID-19 Pneumonia, Am. J. Trop. Med. Hyg. 102 (2020) 1198–1202, https://doi.org/10.4269/ajtmh.20-0280.
[26] J. Pare, I. Camelo, K. Mayo, M. Leo, J. Dugas, K. Nelson, W. Baker, F. Shareef, P. Mitchell, E. Schechter-Perkins, Point-of-care Lung Ultrasound Is More Sensitive than Chest Radiograph for Evaluation of COVID-19, West. J. Emerg. Med. 21 (2020) 771–778, https://doi.org/10.5811/westjem.2020.5.47743.
[27] A. Nouvenne, M. Zani, G. Milanese, A. Parise, M. Baciarello, E. Bignami, A. Odone, N. Sverzellati, T. Meschi, A. Ticinesi, Lung Ultrasound in COVID-19 Pneumonia: Correlations with Chest CT on Hospital admission, Respiration 99 (7) (2020) 617–624, https://doi.org/10.1159/000509223.
[28] M. Yassa, M.A. Mutlu, P. Birol, T.Y. Kuzan, E. Kalafat, C. Usta, E. Yavuz, I. Keskin, N. Tug, Lung ultrasonography in pregnant women during the COVID-19 pandemic: an interobserver agreement study among obstetricians, Ultrasonography 39 (2020) 340–349, https://doi.org/10.14366/usg.20084.
[29] H. Møller-Sørensen, J. Gjedsted, V. Lind Jørgensen, K. Lindskov Hansen, COVID-19 Assessment with Bedside Lung Ultrasound in a Population of Intensive Care Patients Treated with Mechanical Ventilation and ECMO, Diagnostics 10 (2020) 447, https://doi.org/10.3390/diagnostics10070447.
[30] Q. Deng, Y. Zhang, H. Wang, L. Chen, Z. Yang, Z. Peng, Y.a. Liu, C. Feng, X. Huang, N. Jiang, Y. Wang, J. Guo, B. Sun, Q. Zhou, Semiquantitative lung ultrasound scores in the evaluation and follow-up of critically ill patients with COVID-19: a single-center study, Acad. Radiol. 27 (10) (2020) 1363–1372, https://doi.org/10.1016/j.acra.2020.07.002.
[31] N. Bonadia, A. Carnicelli, A. Piano, D. Buonsenso, E. Gilardi, C. Kadhim, E. Torelli, M. Petrucci, L. Di Maurizio, D.G. Biasucci, M. Fuorlo, E. Forte, R. Zaccaria, F. Franceschi, Lung Ultrasound Findings Are Associated with Mortality and Need for Intensive Care Admission in COVID-19 Patients Evaluated in the Emergency Department, Ultrasound Med. Biol. 46 (11) (2020) 2927–2937, https://doi.org/10.1016/j.ultrasmedbio.2020.07.005.
[32] A. Dargent, E. Chatelain, L. Kreitmann, J.-P. Quenot, M. Cour, L. Argaud, M. Adrish, Lung ultrasound score to monitor COVID-19 pneumonia progression in patients with ARDS, PLoS One 15 (7) (2020) e0236312, https://doi.org/10.1371/journal.pone.0236312.
[33] M. Yassa, C. Yirmibes, G. Cavusoglu, H. Eksi, C. Dogu, C. Usta, M. Mutlu, P. Birol, C. Gulumser, N. Tug, Outcomes of universal SARS-CoV-2 testing program in pregnant women admitted to hospital and the adjuvant role of lung ultrasound in screening: a prospective cohort study, J. Matern. Neonatal Med. 33 (22) (2020) 3820–3826, https://doi.org/10.1080/14767058.2020.1798398.
[34] N. Veronese, L.G. Sbrogiò, R. Valle, L. Marin, E. Boscolo Fiore, A. Tiozzo, Prognostic Value of Lung Ultrasonography in Older Nursing Home Residents Affected by COVID-19, J. Am. Med. Dir. Assoc. 21 (10) (2020) 1384–1386, https://doi.org/10.1016/j.jamda.2020.07.034.
[35] L. Zieleskiewicz, T. Markarian, A. Lopez, C. Taguet, N. Mohammedi, M. Boucekine, K. Baumstarck, G. Besch, G. Mathon, G. Duclos, L. Bouvet, P. Michelet, B. Allaouchiche, K. Chaumoître, M. Di Bisceglie, M. Leone, Comparative study of lung ultrasound and chest computed tomography scan in the assessment of severity of confirmed COVID-19 pneumonia, Intensive Care Med. 46 (9) (2020) 1707–1713, https://doi.org/10.1007/s00134-020-06186-0.
[36] M. Favot, A. Malik, J. Rowland, B. Haber, R. Ehrman, N. Harrison, Point-of-Care Lung Ultrasound for Detecting Severe Presentations of Coronavirus Disease 2019 in the Emergency Department: A Retrospective Analysis, Crit. Care Explor. 2 (2020) 1–7, https://doi.org/10.1097/CCE.0000000000000176.
[37] S. Ottaviani, M. Franc, E. Ebstein, L. Demaria, C. Lheure, M.P. Debray, A. Khalil, B. Crestani, R. Borie, P. Dieudé, Lung ultrasonography in patients with COVID-19: comparison with CT, Clin. Radiol. 75 (877) (2020) e1–877.e6, https://doi.org/10.1016/j.crad.2020.07.024.
[38] A. Alharthy, F. Faqihi, M. Abuhamdah, A. Noor, N. Naseem, A. Balhamar, A.A.A.S. B.A. Al Saud, P.G. Brindley, Z.A. Memish, D. Karakitsos, M. Blaivas, Prospective Longitudinal Evaluation of Point-of-Care Lung Ultrasound in Critically Ill Patients With Severe COVID-19 Pneumonia, J. Ultrasound Med. 40 (2021) 443–456, https://doi.org/10.1002/jum.15417.
[39] T.T. Mafort, A.J. Lopes, C.H. Costa, M.S. Cal, M.C. Lopes, B.R.A. Silva, L.F. Faria, A. C. Faria, W. Costa, R.E.B. Salles, M.C.S. Castro, R. Rufino, Changes in lung ultrasound of symptomatic healthcare professionals with COVID-19 pneumonia and their association with clinical findings, J. Clin. Ultrasound. 48 (2020) 515–521, https://doi.org/10.1002/jcu.22905.
[40] Y. Lichter, Y. Topilsky, P. Taieb, A. Banai, A. Hochstadt, I. Merdler, A. Gal Oz, J. Vine, O.r. Goren, B. Cohen, O. Sapir, Y. Granot, T. Mann, S. Friedman, Y. Angel, N. Adi, M. Laufer-Perl, M. Ingbir, Y. Arbel, I. Matot, Y. Szekely, Lung ultrasound predicts clinical course and outcomes in COVID-19 patients, Intensive Care Med. 46 (10) (2020) 1873–1883, https://doi.org/10.1007/s00134-020-06212-1.
[41] V. Iodice, M. Pisaturo, F.M. Fusco, O. Tambaro, G. Parrella, G.D. Flumeri, R. Viglietti, R. Pisapia, G. Palmiero, E. Bignardi, M. Coppola, C. Rescigno, V. Sangiovanni, Use of lung ultrasound in COVID-19: comparison with ultra-high-resolution computed tomography among 29 patients at "D. Cotugno" hospital, Naples, Italy, Infez. Med. 28 (2020) 346–350.
[42] F.L. Dini, C. Bergamini, A. Allegrini, M. Scopelliti, G. Secco, M. Miccoli, S. Boni, R. Brigada, S. Perlini, Bedside wireless lung ultrasound for the evaluation of COVID-19 lung injury in senior nursing home residents, Monaldi Arch. Chest Dis. 90 (2020) 523–527, https://doi.org/10.4081/monaldi.2020.1446.
[43] A. Gil-Rodrigo, P. Llorens, C. Martínez-Buendía, M.-J. Luque-Hernández, B. Espinosa, J.M. Ramos-Rincón, Diagnostic yield of point-of-care ultrasound imaging of the lung in patients with COVID-19, Emergencias Rev. La Soc. Esp. Med. Emergencias 32 (2020) 340–344.
[44] G.B. Fonsi, P. Sapienza, G. Brachini, C. Andreoli, M.L. De Cicco, B. Cirillo, S. Meneghini, F. Pugliese, D. Crocetti, E. Fiori, A. Mingoli, Is Lung Ultrasound Imaging a Worthwhile Procedure for Severe Acute Respiratory Syndrome Coronavirus 2 Pneumonia Detection? J. Ultrasound Med. 40 (6) (2021) 1113–1123, https://doi.org/10.1002/jum.15487.
[45] N. Narinx, A. Smismans, R. Symons, J. Frans, A. Demeyere, M. Gillis, Feasibility of using point-of-care lung ultrasound for early triage of COVID-19 patients in the emergency room, Emerg. Radiol. 27 (6) (2020) 663–670, https://doi.org/10.1007/s10140-020-01849-3.
[46] E. Kalafat, M. Yassa, A. Koc, N. Tug, K. Baydemir, C. Benlioglu, O.F. Oz, B. Aslan, B. B. Oruc, E. Ozkavukcu, P. Birol, D. Budak, E. Yavuz, G. Cavusoglu, M.A. Mutlu, C. Yirmibes, T. Kuzan, Utility of lung ultrasound assessment for probable SARS-CoV-2 infection during pregnancy and universal screening of asymptomatic individuals, Ultrasound Obstet. Gynecol. 56 (2020) 624–626, https://doi.org/10.1002/uog.23099.
[47] S. Li, Y.-L. Qu, M.-Q. Tu, L.-Y. Guo, Q.-L. Zhang, C.-Y. Lv, R.-J. Guo, Application of lung ultrasonography in critically ill patients with COVID-19, Echocardiography 37 (11) (2020) 1838–1843, https://doi.org/10.1111/echo.14849.
[48] J. Castelao, D. Graziani, J.B. Soriano, J.L. Izquierdo, Findings and Prognostic Value of Lung Ultrasound in COVID-19 Pneumonia, J. Ultrasound Med. 40 (2021) 1315–1324, https://doi.org/10.1002/jum.15508.
[49] T. Brahier, J.-Y. Meuwly, O. Pantet, M.-J. Brochu Vez, H. Gerhard Donnet, M.-A. Hartley, O. Hugli, N. Boillat-Blanco, Lung Ultrasonography for Risk Stratification in Patients with Coronavirus Disease 2019 (COVID-19): A Prospective Observational Cohort Study, Clin. Infect. Dis. 73 (11) (2021) e4189–e4196, https://doi.org/10.1093/cid/ciaa1408.
[50] C. Ramos Hernández, M. Botana Rial, L.A. Pazos Area, M. Núñez Fernández, S. Pérez Fernández, M. Rubianes González, M. Crespo Casal, A. Fernández Villar, Predicción de evolución desfavorable en pacientes hospitalizados por COVID-19 mediante ecografía pulmonar, Arch. Bronconeumol. 57 (2021) 47–54, https://doi.org/10.1016/j.arbres.2020.07.043.
[51] S.-T. Zhu, F.-Y. Tao, J.-H. Xu, S.-S. Liao, C.-L. Shen, Z.-H. Liang, B.-B. Shi, Q. Li, Utility of Point-of-Care Lung Ultrasound for Clinical Classification of COVID-19, Ultrasound Med. Biol. 47 (2) (2021) 214–221, https://doi.org/10.1016/j.ultrasmedbio.2020.09.010.
[52] M. Rojatti, I.B. Regli, A. Zanforlin, E. Ferretti, M. Falk, G. Strapazzon, M. Gamper, P. Zanon, M. Bock, S. Rauch, Lung Ultrasound and Respiratory Pathophysiology in Mechanically Ventilated COVID-19 Patients—an Observational Trial, SN Compr. Clin. Med. 2 (11) (2020) 1970–1977, https://doi.org/10.1007/s42399-020-00536-1.
[53] D. Colombi, M. Petrini, G. Maffi, G.D. Villani, F.C. Bodini, N. Morelli, G. Milanese, M. Silva, N. Sverzellati, E. Michieletti, Comparison of admission chest computed tomography and lung ultrasound performance for diagnosis of COVID-19 pneumonia in populations with different disease prevalence, Eur. J. Radiol. 133 (2020) 109344, https://doi.org/10.1016/j.ejrad.2020.109344.
[54] M.E. Haaksma, M.L.A. Heldeweg, J.E. Lopez Matta, J.M. Smit, J.D. van Trigt, J. S. Nooitgedacht, C.V. Elzo Kraemer, M. van de Wiel, A.R.J. Girbes, L. Heunks, D. J. van Westerloo, P.R. Tuinman, Lung ultrasound findings in patients with novel SARS-CoV-2, ERJ Open Res. 6 (2020) 00238–02020, https://doi.org/10.1183/23120541.00238-2020.

[55] E. Pivetta, A. Goffi, M. Tizzani, S.M. Locatelli, G. Porrino, I. Losano, D. Leone, G. Calzolari, M. Vesan, F. Steri, A. Ardito, M. Capuano, M. Gelardi, G. Silvestri, S. Dutto, M. Avolio, R. Cavallo, A. Bartalucci, C. Paglieri, F. Morello, L. Richiardi, M.M. Maule, E. Lupia, F. Baldassa, P. Baron, G. Bianchi, B. V, A. Conterno, P. Del Rizzo, P. Fascio Pecetto, F. Giachino, A. Iannaccone, P. Ferrera, F. Riccardini, C. Sacchi, M. Sozzi, S. Totaro, P. Visconti, F. Risi, F. Basile, D. Baricocchi, A. Beux, V. Beux, P. Bima, I. Cara, L. Chichizola, F. Dellavalle, F. Grosso, G. Labarile, M. Oddi, M. Ottino, I. Pia, V. Scategni, A. Surra, Lung Ultrasonography for the Diagnosis of SARS-CoV-2 Pneumonia in the Emergency Department, Ann. Emerg. Med. 77 (4) (2021) 385–394, https://doi.org/10.1016/j.annemergmed.2020.10.008.

[56] A.W.E. Lieveld, B. Kok, F.H. Schuit, K. Azijli, J. Heijmans, A. van Laarhoven, N. L. Assman, R.S. Kootte, T.J. Olgers, P.W.B. Nanayakkara, F.H. Bosch, Diagnosing COVID-19 pneumonia in a pandemic setting: Lung Ultrasound versus CT (LUVCT) – a multicentre, prospective, observational study, ERJ Open Res. 6 (4) (2020) 00539-2020, https://doi.org/10.1183/23120541.00539-2020.

[57] M. Bosevski, F. Janusevski, K. Kapsarov, Utility of Combined Echocardiography and Lung Ultrasound for Coronavirus Disease-19 Intensive Care Unit Patients: Case Series, Open Access Maced, J. Med. Sci. 8 (T1) (2020) 408–410, https://doi.org/10.3889/oamjms.2020.5382.

[58] C. Sorlini, M. Femia, G. Nattino, P. Bellone, E. Gesu, P. Francione, M. Paternò, P. Grillo, A. Ruffino, G. Bertolini, M. Cariati, F. Cortellaro, The role of lung ultrasound as a frontline diagnostic tool in the era of COVID-19 outbreak, Intern. Emerg. Med. 16 (3) (2021) 749–756, https://doi.org/10.1007/s11739-020-02524-8.

[59] B.A. Jalil, A. Khan, I.R. Kugasia, M. Ijaz, Lung ultrasound in early SARS-CoV-2 pneumonia and the LUS-CoV criteria, Baylor Univ. Med. Cent. Proc. 34 (1) (2021) 1–4, https://doi.org/10.1080/08998280.2020.1834658.

[60] R.C. Gibbons, M. Magee, H. Goett, J. Murrett, J. Genninger, K. Mendez, M. Tripod, N. Tyner, T.G. Costantino, Lung Ultrasound vs. Chest X-Ray Study for the Radiographic Diagnosis of COVID-19 Pneumonia in a High-Prevalence Population, J. Emerg. Med. 60 (5) (2021) 615–625.

[61] R. Li, H. Liu, H. Qi, Y. Yuan, X. Zou, H. Huang, J. Wan, Z. Lv, Y. Ouyang, S. Pan, X. Zhao, H. Shu, Y. Shang, Lung ultrasound assessment of acute respiratory distress syndrome caused by coronavirus disease 2019: An observational study, Hong Kong, J. Emerg. Med. 28 (2021) 8–14, https://doi.org/10.1177/1024907920969326.

[62] V. Zotzmann, C.N. Lang, T. Wengenmayer, X. Bemtgen, B. Schmid, K. Mueller-Peltzer, A. Supady, C. Bode, D. Duerschmied, D.L. Staudacher, Combining lung ultrasound and Wells score for diagnosing pulmonary embolism in critically ill COVID-19 patients, J. Thromb. Thrombolysis 52 (1) (2021) 76–84, https://doi.org/10.1007/s11239-020-02323-0.

[63] T. Perrone, G. Soldati, L. Padovini, A. Fiengo, G. Lettieri, U. Sabatini, G. Gori, F. Lepore, M. Garolfi, I. Palumbo, R. Inchingolo, A. Smargiassi, L. Demi, E. E. Mossolani, F. Tursi, C. Klersy, A. Di Sabatino, A New Lung Ultrasound Protocol Able to Predict Worsening in Patients Affected by Severe Acute Respiratory Syndrome Coronavirus 2 Pneumonia, J. Ultrasound Med. 40 (8) (2021) 1627–1635, https://doi.org/10.1002/jum.15548.

[64] A. Alharthy, M. Abuhamdah, A. Balhamar, F. Faqihi, N. Nasim, S. Ahmad, A. Noor, H. Tamim, S.A. Alqahtani, A.A.A.S. Bin Abdulaziz Al Saud, D.J. Kutsogiannis, P. G. Brindley, Z.A. Memish, D. Karakitsos, M. Blaivas, Residual Lung Injury in Patients Recovering From COVID-19 Critical Illness, J. Ultrasound Med. 40 (2021) 1823–1838, https://doi.org/10.1002/jum.15563.

[65] S.L. Haak, I.J. Renken, L.C. Jager, H. Lameijer, B. (Britt) Y. van der Kolk, Diagnostic accuracy of point-of-care lung ultrasound in COVID-19, Emerg. Med. J. 38 (2021) 94–99, https://doi.org/10.1136/emermed-2020-210125.

[66] E. Allegorico, C. Buonerba, G. Bosso, A. Pagano, G. Porta, C. Serra, P. Dolce, V. Minerva, F. Dello Vicario, C. Altruda, P. Arbo, T. Russo, C. De Sio, N. Franco, G. Ruffa, C. Mormile, F. Cannavacciuolo, V. Mercurio, G. Gervasio, G. Di Costanzo, A. Ragozzino, L. Scafuri, G. Facchini, F. Numis, The use of chest ultrasonography in suspected cases of COVID-19 in the emergency department, Futur. Sci. OA 7 (2021) FSO635, https://doi.org/10.2144/fsoa-2020-0127.

[67] G. Recinella, G. Marasco, M. Tufoni, M. Brizi, E. Evangelisti, L. Maestri, M. Fusconi, P. Calogero, D. Magalotti, M. Zoli, Clinical Role of Lung Ultrasound for the Diagnosis and Prognosis of Coronavirus Disease Pneumonia in Elderly Patients: A Pivotal Study, Gerontology 67 (1) (2021) 78–86, https://doi.org/10.1159/000512209.

[68] B. Schmid, D. Feuerstein, C.N. Lang, K. Fink, R. Steger, M. Rieder, D. Duerschmied, H.-J. Busch, D. Damjanovic, Lung ultrasound in the emergency department – a valuable tool in the management of patients presenting with respiratory symptoms during the SARS-CoV-2 pandemic, BMC Emerg. Med. 20 (2020) 96, https://doi.org/10.1186/s12873-020-00389-w.

[69] A. Zanforlin, G. Strapazzon, M. Falk, V. Gallina, A. Viteritti, L. Valzolgher, M. La Guardia, F. Ferro, L. Pagani, N. Vezzali, Lung Ultrasound in the Emergency Department for Early Identification of COVID-19 Pneumonia, Respiration 100 (2020) 1–9, https://doi.org/10.1159/000512782.

[70] A.L. Wangüemert Pérez, J.M. Figueira Gonçalves, J.M. Hernández Pérez, Y. Ramallo Fariña, J.C. Del Castillo Rodriguez, Prognostic value of lung ultrasound and its link with inflammatory biomarkers in patients with SARS-CoV-2 infection, Respir. Med. Res. 79 (2021) 100809, https://doi.org/10.1016/j.resmer.2020.100809.

[71] Z.I. Bitar, M. Shamsah, O. Maadarani, O.M. Bamasood, A.Z. Bitar, H. Alfoudri, Q. K. Tran, Lung Ultrasound and Sonographic Subpleural Consolidation in COVID-19 Pneumonia Correlate with Disease Severity, Crit. Care Res. Pract. 2021 (2021) 1–6, https://doi.org/10.1155/2021/6695033.

[72] B. Ask, T.L. Annmarie, B.L. Christian, P. Stefan, Lung ultrasound as a prognostic tool in emergency patients clinically suspected of COVID-19, Dan. Med. J. 68 (2021) A07200551.

[73] J.C.G. de Alencar, J.F.M. Marchini, L.O. Marino, S.C. da Costa Ribeiro, C.G. Bueno, V.P. da Cunha, F. Lazar Neto, R.A. Brandão Neto, H.P. Souza, Lung ultrasound score predicts outcomes in COVID-19 patients admitted to the emergency department, Ann. Intensive Care 11 (2021) 6, https://doi.org/10.1186/s13613-020-00799-w.

[74] E. Boero, S. Rovida, A. Schreiber, P. Berchialla, L. Charrier, M.M. Cravino, M. Converso, P. Gollini, M. Puppo, A. Gravina, G. Fornelli, G. Labarile, S. Sciacca, T. Bove, D. Karakitsos, F. Aprà, M. Blaivas, L. Vetrugno, The COVID-19 Worsening Score (COWS)—a predictive bedside tool for critical illness, Echocardiography 38 (2) (2021) 207–216, https://doi.org/10.1111/echo.14962.

[75] S.N. Avdeev, G.V. Nekludova, N.V. Trushenko, N.A. Tsareva, A.I. Yaroshetskiy, D. Kosanovic, Lung ultrasound can predict response to the prone position in awake non-intubated patients with COVID-19 associated acute respiratory distress syndrome, Crit. Care 25 (2021) 35, https://doi.org/10.1186/s13054-021-03472-1.

[76] M.L.A. Heldeweg, J.E. Lopez Matta, M.E. Haaksma, J.M. Smit, C.V. Elzo Kraemer, H.-J. de Grooth, E. de Jonge, L.J. Meijboom, L.M.A. Heunks, D.J. van Westerloo, P. R. Tuinman, Lung ultrasound and computed tomography to monitor COVID-19 pneumonia in critically ill patients: a two-center prospective cohort study, Intensive Care Med. Exp. 9 (2021) 1, https://doi.org/10.1186/s40635-020-00367-3.

[77] C. Seiler, C. Klingberg, M. Hårdstedt, Lung Ultrasound for Identification of Patients Requiring Invasive Mechanical Ventilation in COVID-19, J Ultrasound Med. 9999 (2021) 1–13, https://doi.org/10.1002/jum.15617.

[78] S. Mongodi, D. De Luca, A. Colombo, A. Stella, E. Santangelo, F. Corradi, L. Gargani, S. Rovida, G. Volpicelli, B. Bouhemad, F. Mojoli, Quantitative Lung Ultrasound: Technical Aspects and Clinical Applications, Anesthesiology 134 (2021) 949–965, https://doi.org/10.1097/ALN.0000000000003757.

[79] S. Pecho-Silva, A.C. Navarro-Solsol, A. Taype-Rondan, J. Torres-Valencia, K. Arteaga-Livias, D.A. Herriman, K. Acosta-Pinzas, G. Valenzuela-Rodriguez, J. J. Barboza, V. Panduro-Correa, Pulmonary Ultrasound in the Diagnosis and Monitoring of Coronavirus Disease (COVID-19): A Systematic Review, Ultrasound Med. Biol. 47 (8) (2021) 1997–2005, https://doi.org/10.1016/j.ultrasmedbio.2021.04.011.

[80] K. Barssoum, V. Victor, A. Salem, A. Kumar, M. Mubasher, M. Hassib, M. Magdi, S. Renjithlal, M. Abdelazeem, M. Shariff, O. Idemudia, M. Ibrahim, A. Mohamed, S. Thakkar, H. Patel, M. Diab, A. Szeles, F. Ibrahim, R. Jha, M. Chowdhury, N. Akula, A. Kalra, N.C. Nanda, Echocardiography, lung ultrasound, and cardiac magnetic resonance findings in COVID-19: A systematic review, Echocardiography (2021) 1–40, https://doi.org/10.1111/echo.15152.

[81] A.O. Peixoto, R.M. Costa, R. Uzun, A.M.A. Fraga, J.D. Ribeiro, F.A.L. Marson, Applicability of lung ultrasound in COVID-19 diagnosis and evaluation of the disease progression: A systematic review, Pulmonology 27 (6) (2021) 529–562, https://doi.org/10.1016/j.pulmoe.2021.02.004.

[82] K. Pillai, S. Hewage, A. Harky, The Role of the Lung Ultrasound in Coronavirus Disease 2019: A Systematic Review, J. Med. Ultrasound 28 (2020) 207, https://doi.org/10.4103/JMU.JMU_87_20.

[83] G. Volpicelli, L. Gargani, Sonographic signs and patterns of COVID-19 pneumonia, Ultrasound J. 12 (2020) 1–3, https://doi.org/10.1186/S13089-020-00171-W.

[84] A. Smargiassi, G. Soldati, E. Torri, F. Mento, D. Milardi, P. Del Giacomo, G. De Matteis, M.L. Burzo, A.R. Larici, M. Pompili, L. Demi, R. Inchingolo, Lung Ultrasound for COVID-19 Patchy Pneumonia: Extended or Limited Evaluations? J. Ultrasound Med. 40 (2021) 521–528, https://doi.org/10.1002/jum.15428.

[85] A. Izcovich, M.A. Ragusa, F. Tortosa, M.A. Lavena Marzio, C. Agnoletti, A. Bengolea, A. Ceirano, F. Espinosa, E. Saavedra, V. Sanguine, A. Tassara, C. Cid, H.N. Catalano, A. Agarwal, F. Foroutan, G. Rada, C. Lazzeri, Prognostic factors for severity and mortality in patients infected with COVID-19: A systematic review, PLoS One. 15 (11) (2020) e0241955, https://doi.org/10.1371/journal.pone.0241955.

[86] J.-J. Rouby, C. Arbelot, Y. Gao, M. Zhang, J. Lv, Y. An, W. Chunyao, D. Bin, C. S. Valente Barbas, F.L. Dexheimer Neto, F. Prior Caltabeloti, E. Lima, A. Cebey, S. Perbet, J.-M. Constantin, C. Arbelot, J.-J. Rouby, H. Brisson, R. Deransy, C. Vezinet, P. Garçon, N. El Hadj Kacem, D. Lemesle, A. Monsel, Q. Lu, O. Langeron, F. Gay, B. Lucena, L. Malbouisson, M.J. Carvalho Carmona, J. Neves, P. de Tarso Roth, G. de Dalcin, P.P. Schettino, A. Biestro, D. Cristovao, J. Salluh, Training for Lung Ultrasound Score Measurement in Critically Ill Patients, Am. J. Respir. Crit. Care Med. 198 (2018) 398–401, https://doi.org/10.1164/rccm.201802-0227LE.

[87] A. Soummer, S. Perbet, H. Brisson, C. Arbelot, J.-M. Constantin, Q. Lu, J.-J. Rouby, Ultrasound assessment of lung aeration loss during a successful weaning trial predicts postextubation distress, Crit. Care Med. 40 (7) (2012) 2064–2072.

[88] D.A. Lichtenstein, G.A. Mezière, Relevance of Lung Ultrasound in the Diagnosis of Acute Respiratory Failure*: The BLUE Protocol, Chest 134 (1) (2008) 117–125, https://doi.org/10.1378/chest.07-2800.

[89] O.P. Mehta, P. Bhandari, A. Raut, S.E.O. Kacimi, N.T. Huy, Coronavirus Disease (COVID-19): Comprehensive Review of Clinical Presentation, Front. Public Heal. (2021) 1034, https://doi.org/10.3389/FPUBH.2020.582932.

[90] F. Mento, T. Perrone, V.N. Macioce, F. Tursi, D. Buonsenso, E. Torri, A. Smargiassi, R. Inchingolo, G. Soldati, L. Demi, On the Impact of Different Lung Ultrasound Imaging Protocols in the Evaluation of Patients Affected by Coronavirus Disease 2019, J. Ultrasound Med. 40 (10) (2021) 2235–2238, https://doi.org/10.1002/jum.15580.