

Point-of-care lung ultrasound in the assessment of COVID-19: results of a UK multicentre service evaluation

T Knight, P Parulekar, G Rudge, F Lesser, M Dachsel, A Aujayeb, D Lasserson & N Smallwood

Abstract

Background: Coronavirus disease 2019 has had a dramatic impact on the delivery of acute care globally. Accurate risk stratification is fundamental to the efficient organisation of care. Point-of-care lung ultrasound offers practical advantages over conventional imaging with potential to improve the operational performance of acute care pathways during periods of high demand.

The Society for Acute Medicine and the Intensive Care Society undertook a collaborative evaluation of point-of-care imaging in the UK to describe the scope of current practice and explore performance during real-world application.

Methods: A retrospective service evaluation was undertaken of the use of point-of-care lung ultrasound during the initial wave of coronavirus infection in the UK. We report an evaluation of all imaging studies performed outside the intensive care unit.

An ordinal scale was used to measure the severity of loss of lung aeration. The relationship between lung ultrasound, polymerase chain reaction for SARS-CoV-2 and 30-day outcomes were described using logistic regression models.

Results: Data were collected from 7 hospitals between February and September 2020. In total, 297 ultrasound examinations from 295 patients were recorded. Nasopharyngeal swab samples were positive in 145 patients (49.2% 95%CI 43.5–54.8). A multivariate model combining three ultrasound variables showed reasonable discrimination in relation to the polymerase chain reaction reference (AUC 0.77 95%CI 0.71–0.82).

The composite outcome of death or intensive care admission at 30 days occurred in 83 (28.1%, 95%CI 23.3–33.5). Lung ultrasound was able to discriminate the composite outcome with a reasonable level of accuracy (AUC 0.76 95%CI 0.69–0.83) in univariate analysis. The relationship remained statistically significant in a multivariate model controlled for age, sex and the time interval from admission to scan.

Conclusion: Point-of-care lung ultrasound is able to discriminate patients at increased risk of deterioration allowing more informed clinical decision making.

Keywords

Coronavirus disease 19, Point-of-care, Lung ultrasound

Background

Coronavirus disease 2019 (COVID-19) is a respiratory tract infection caused by a novel coronavirus, SARS-CoV-2.¹ COVID-19 is a heterogeneous disease with a spectrum of severity, ranging from asymptomatic infection to acute respiratory distress syndrome (ARDS), multi-organ failure and death.² In the UK, approximately 20% of hospitalised patients required admission to high dependency or intensive care units (ICU) during the initial wave of infection.³ Adaptations to standard processes of acute care have been required to rapidly risk stratify patients based on the probability of infection and the prospect of deterioration.

Lung ultrasound (LUS) is a useful tool in the clinical assessment of patients with suspected COVID-19.^{4, 5} Pathways designed to cohort patients based on the risk of COVID-19 have been mandated to limit viral transmission during inpatient

admission.⁶ The level of risk is determined at initial triage on the basis of symptoms and history of contact with known cases. This approach is imperfect given the absence of classical syndromic features in a significant proportion of patients.⁷

LUS could potentially be employed to improve the accuracy of this process. Clinical assessment must also anticipate the trajectory of illness to differentiate patients likely to make a full recovery without intervention from patient who would benefit from enhanced monitoring and early escalation of care. LUS may provide prognostic information allowing care to be better calibrated to risk.^{8, 9}

There is a large body of literature defining the role of LUS in respiratory failure and the assessment of critically unwell patients.¹⁰ LUS is highly sensitive for detecting peripheral pathology associated with COVID19, leading to the sonographic signs of a thickened, irregular pleural line, frequent and often

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confluent B lines and peripheral consolidations.¹¹ These have been described in multiple case series.¹²⁻¹⁵ The imperative to minimise transfers between departments and limit unnecessary exposure of health-care workers to the risk of infection has led to calls for increased use of POCUS during the pandemic.⁵

A collaborative national evaluation of the use of POCUS in COVID was jointly commissioned by the Society for Acute Medicine (SAM) and Intensive Care Society (ICS). The evaluation aimed to define how and when POCUS was used in real-world clinical practice and explore the relationship between ultrasonographic features of disease, diagnosis and prognosis.

Methods

A retrospective service evaluation of POCUS was completed between 1st of February 2020 to the 1st October 2020. Service evaluation methodology was employed to define and describe variations in approach and evaluate relationships with outcomes during routine clinical practice.

Invitations to participate were disseminated to hospitals by SAM and ICS. In the UK, the skills and equipment required to integrate POCUS into standard care are concentrated in a relatively small number of hospitals.¹⁶ Accredited POCUS supervisors were approached by email to register their hospitals to participate. This ensured participating hospitals had prior experience in the application of POCUS in acute care. The analysis presented is a sub-set of the national evaluation containing all patients imaged outside of the intensive care unit (ICU). Analysis of the ICU cohort was undertaken separately.

All adult patients (aged ≥ 16 year) presenting to participating hospitals with confirmed or suspected covid-19 were eligible for inclusion. All point-of-care imaging studies obtained as part of routine care were eligible for inclusion. Point-of-care LUS studies were undertaken by competently trained practitioners. Competence was defined as Focused Acute Medical Ultrasound (FAMUS),¹⁷ Focused UltraSound in Intensive Care (FUSIC) accreditation,¹⁸ or equivalent. The decision to undertake LUS was at the discretion of the treating clinician informed by local hospital policy where present. The ultrasound device used was determined by local availability.

Several approaches to point-of-care LUS have been described in the literature.^{19, 20} Protocols differ primarily based on the number of anatomical locations at which images are captured. The most common protocols recommend image capture at 6, or 14 anatomical locations. The choice of protocol used was determined by the treating clinician.

A standardised report was developed to record demographic and ultrasonographic features of each

imaging study. An ordinal four-point scale was used to determine the severity of lung involvement at each anatomical location by semi-quantifying the loss of aeration. The scale has been previously been validated in the ICU.²¹

- Score 0: A-lines or <2 B-lines (considered 'normal' aeration)
- Score 1: ≥ 2 well-spaced B-lines (moderate loss of aeration)
- Score 2: Coalescent B-lines +/- small consolidations <1 cm (severe loss of aeration)
- Score 3: Tissue-like pattern +/- frank consolidation +/- small consolidations >1 cm (complete loss of aeration)

An assessment of the pleural line was recorded and reported as 'normal' or 'abnormal' by the operator. The presence of pleural effusions was reported.

The primary analysis was performed using a 6-point score for all studies. The anatomical locations required to calculate a 6-point score is contained within 12-point and 14-point studies, as such a 6-point score could be calculated in all instances. Comparisons of the diagnostic performance of 6-point and 12-point scans were made from studies in which both scores were available.

The results of nasopharyngeal reverse-transcription polymerase chain reaction (PCR) tests for SARS-CoV-2 obtained on presentation were recorded. Patients without a PCR result were excluded from analysis comparing diagnostic performance of LUS with PCR but included in analysis in relation to prognosis.

The treating clinician was asked to provide a clinical diagnosis at the conclusion of the episode of care when the PCR status was negative or unknown. The clinical diagnosis took into account all available clinical, laboratory and radiological investigations obtained during the episode of care. Cause of death was used when the patient did not survive to hospital discharge. Secondary analysis was undertaken to ascertain the diagnostic performance of LUS applied to patients with a positive PCR or a clinical diagnosis of COVID-19 as the reference standard.

Oxygen saturations determined by peripheral pulse oximetry and the fraction of inspired oxygen (FiO₂) at the time of imaging were recorded. Partial pressure of oxygen (PaO₂) derived from arterial blood gas samples were not recorded in the dataset. Establishing the relationship between arterial samples and LUS performed at different times was deemed problematic. The severity of hypoxia was assessed using the pulse oximetry / FiO₂ (SF) ratio.²² The SF ratio has been shown to correlate with the PaO₂ / FiO₂ ratio and can be used a substitute to identify patients with severe respiratory failure.²³

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Outcomes were assessed and recorded at thirty days after the imaging study.

Mortality and ICU admission were recorded. A composite outcome of death or ICU admission was used to assess the predictive performance of LUS in relation to prognosis. Outcomes were determined locally using the hospital's electronic record.

Statistical analysis

Normally distributed data are described using mean and standard deviation. Non-normally distributed data are described using median value and interquartile range. Count data are provided with a proportion and 95% confidence intervals where appropriate. Bar plots are provided with error bars representing 95% confidence intervals.

Logistic regression was used to explore the relationship between LUS, the PCR result and 30-day outcomes. Multivariate models included age, sex, time interval between admission and study and hospital as fixed effects. Model coefficients are expressed using the odds ratio associated with a one unit increase in score. The discriminatory performance of the ultrasound severity score to predict PCR positivity and adverse outcomes was assessed using receiver operating characteristic curves and reported by calculating the area under the curve (AUC). Standard statistics of diagnostic performance were obtained from a 2 by 2 contingency table. Optimal thresholds were determined by maximisation of the Youden index. Statistical analysis was undertaken using the R statistical software. Mixed effect models were constructed using the lme4 package.

Results

Data were collected from 7 hospitals between February and September 2020. In total 297 ultrasound examinations from 295 patients were recorded. Serial imaging was undertaken for two patients. The low frequency of paired imaging precluded meaningful analysis of changes over time and the second studies were therefore excluded from the analysis.

The median number of LUS studies per hospital was 18 (IQR 3 – 57). Studies were performed in 3 different locations, 45 (15.3%) studies were performed in the ED, 212 (71.9%) were performed on the AMU and 39 (13.2%) were performed on an inpatient ward. Demographic and clinical data are provided in Table 1. The median interval between admission and imaging was 0 days (IQR 0-1). The median recorded duration of symptoms prior to presentation was 6 days (IQR 3-12). The relationship between FiO₂ and peripheral saturations and the classification of patients into SF groups is summarised in Figure 1.

The initial nasopharyngeal PCR for SARS-CoV-2 was positive in 145 patients (49.2% 95%CI 43.5-54.8). The SARS-CoV-2 PCR result was unknown in 24 patients (8.1% 95%CI 5.5-11.8). Death within 30 days of admission occurred in 65 (22.0%, 95%CI 17.6-27.1) patients. The composite outcome of death or intensive care admission at 30 days occurred in 83 (28.1%, 95%CI 23.3-33.5) patients. 30-day outcome was not available for 4 (1.3%) patients.

Distribution of scores

A complete 6-point ultrasound examination was recorded in 294 (99.7%) cases. One study contained missing values in relation to four anatomical zones. Imputation was not undertaken, and the case was excluded from further analysis. Ultrasound assessment was performed using a 12-point protocol in 122 (41.3%) studies.

The distribution of 6-point severity scores stratified by inter-hospital location is provided in Figure 2. The median 6-point severity score was 4 (IQR 3-8) and the modal 6-point ultrasound severity score was zero. 6-point severity scores obtained from ward settings were skewed towards higher scores. The range of 6-point severity scores stratified by hospital and degree of hypoxia is provided in Figure 3. One hospital appeared to provide higher scores within strata suggesting a possible difference in approach to image interpretation at this location. Patient characteristics and outcomes stratified by 6-point severity score are provided in Table 1.

Pleural abnormalities were present in 201 (68.1%, 95%CI 62.6-73.2) studies. Abnormalities were unilateral in 93 (31.5%, 95%CI 26.5-37.0) studies and bilateral in 108 (36.6 95%CI 31.3-42.2) studies. The presence of pleural abnormalities was not recorded

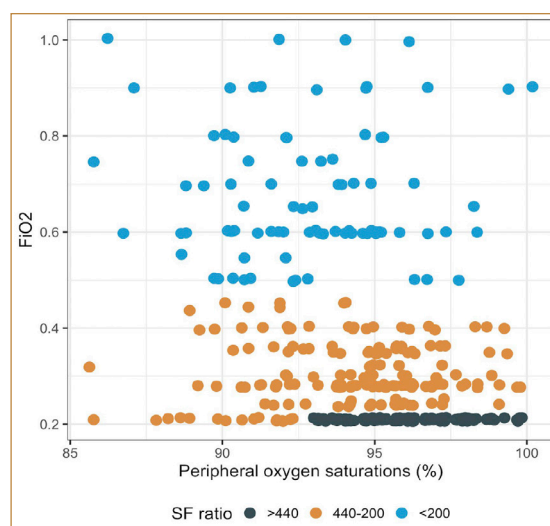


Figure 1. Scatter plot demonstrating relationship between FiO₂ and peripheral oxygen saturations and associated classification based on the SF ratio

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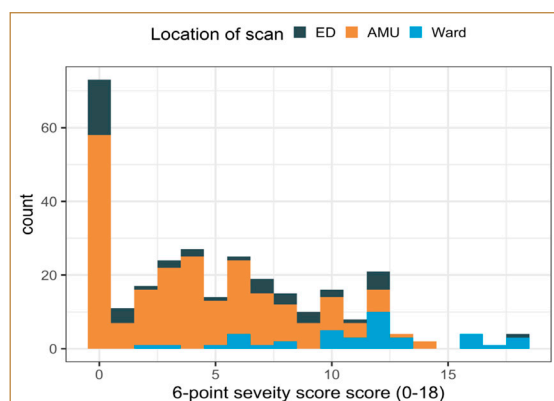


Figure 2. Distribution of 6-point severity scores stratified by location of scan

in 8 (2.7%) studies. Unilateral pleural effusions were present in 14 (4.7%, 95CI 0.28-0.78) studies and bilateral in 19 (6.4%, 95%CI 4.2-9.8) studies.

Diagnosis

In univariate analysis the 6-point severity score and presence of pleural abnormalities were both statistically associated with the presence of SARS-CoV-2 by PCR (p-value < 0.001). The presence of pleural effusion did not show a statistically significant association with the PCR result in univariate analysis.

A multivariate model combining the 6-point severity score, presence of pleural abnormalities and presence of pleural effusions was able to discriminate PCR positivity with reasonable accuracy (AUC 0.77 95%CI 0.71-0.82). The prevalence of SARS-CoV-2 stratified by 6-point severity score quartiles and the presence of pleural abnormalities is provided in Figure 4A.

A total of 52 (17.6%) patients had an ultrasound severity score of zero in combination with normal pleural appearance. An abnormal LUS (presence of B-lines or pleural abnormalities) had good sensitivity but poor specificity for SARS-CoV-2. (sensitivity 93%, 95%CI 87-97, specificity 27%, 95%CI 19-35, positive predictive value 53%, 95%CI 46-60, negative predictive value of 80%, 95%CI 66-91, negative likelihood ratio 0.27).

A secondary analysis was undertaken using a positive SARS-CoV-2 PCR or a clinical diagnosis of COVID at discharge as the reference standard. The discharge diagnosis was felt to be consistent with a diagnosis of COVID-19 in 79 (57.6%) patients with a negative PCR. The multivariate model combining the 6-point severity score and the presence of pleural abnormalities had an AUC of 0.93 (95%CI 0.91-0.96) to predict diagnosis using the revised reference criteria.

12-point ultrasound

12-point imaging studies were provided by 3 contributing hospitals. The mean 12-point score

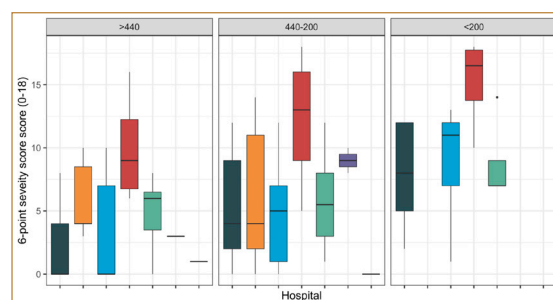


Figure 3. Distribution of 6-point severity scores stratified by hospital and severity of hypoxia as defined by the S/F ratio

was 9.9 (SD 6.9). There was strong correlation between the 6-point and 12-point scores (Pearson correlation 0.93, p value = <0.001). Abnormalities were recorded in 9 (7.4%) patients using a 12-point protocol that were not evident using the 6-point protocol. The mean 12-point score in those with a zero score 6-point study was 3 (SD2.3). The diagnostic performance of 6-point and 12-point studies were compared in the sub-group of patients in which both scores were recorded. There was no statistical difference in performance between the two approaches (6p AUC 0.73 95%CI 0.63-0.82 vs 12p AUC 0.72 95%CI 0.62-0.81).

Prognosis

The relationship between ultrasound and thirty-day outcomes were assessed. In univariate analysis, there was a statistically significant relationship between the 6-point severity score and mortality (unadjusted OR 1.2 95%CI 1.1-1.2). The association between

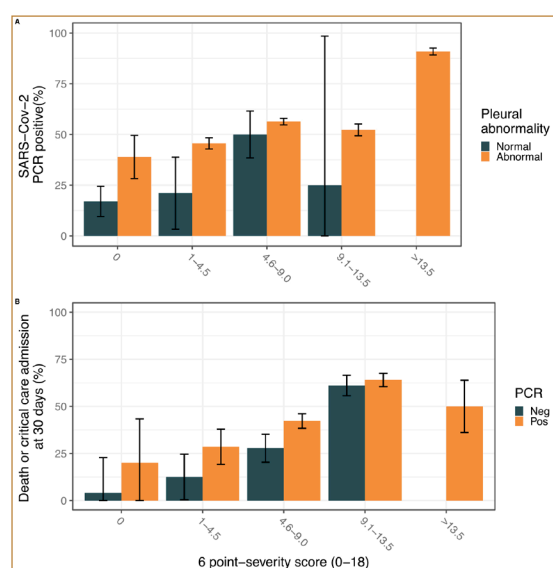


Figure 4. Ultrasound severity score as a prognostic and diagnostic marker

A. Prevalence of SARS-CoV-2 positivity stratified by ultrasound severity score and the presence of pleural abnormalities
B. Relationship between 6-point severity score and thirty-day outcome

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Table 1. Demographic, clinical and outcomes stratified by the composite ultrasound severity score calculated from a 6-point severity score and pleural abnormalities

Characteristic	N	6-point severity score					
		Overall, N = 295 [†]	0, N = 73 [†]	1-4.5, N = 79 [†]	4.6-9.0, N = 83 [†]	9.1-13.5, N = 49 [†]	>13.5, N = 11 [†]
Mean age (years)	292	66 (50, 77)	68 (49, 77)	62 (45, 74)	71 (50, 79)	63 (52, 78)	72 (60, 77)
Unknown		3	0	0	1	2	0
Sex	293						
Male		198 (68%)	42 (58%)	57 (72%)	61 (74%)	33 (69%)	5 (45%)
Female		95 (32%)	31 (42%)	22 (28%)	21 (26%)	15 (31%)	6 (55%)
Unknown		2	0	0	1	1	0
Duration of illness	286	6 (3, 11)	4 (2, 10)	6 (2, 12)	7 (3, 14)	8 (3, 14)	3 (2, 6)
Unknown		9	2	3	1	3	0
SARS-CoV-2 PCR	295						
Neg		145 (49%)	50 (68%)	40 (51%)	36 (43%)	18 (37%)	1 (9.1%)
Pos		126 (43%)	16 (22%)	30 (38%)	45 (54%)	25 (51%)	10 (91%)
Unknown		24 (8.1%)	7 (9.6%)	9 (11%)	2 (2.4%)	6 (12%)	0 (0%)
Interval from admission to study	292	0.00 (0.00, 1.00)	0.00 (0.00, 1.00)	1.00 (0.00, 1.00)	0.00 (0.00, 1.00)	1.00 (0.00, 3.00)	0.00 (0.00, 1.50)
Unknown		3	2	0	0	1	0
Pleural abnormality	295						
Normal		86 (29%)	52 (71%)	19 (24%)	11 (13%)	4 (8.2%)	0 (0%)
Unilateral		93 (32%)	13 (18%)	31 (39%)	26 (31%)	21 (43%)	2 (18%)
Bilateral		108 (37%)	5 (6.8%)	26 (33%)	45 (54%)	23 (47%)	9 (82%)
Unknown		8 (2.7%)	3 (4.1%)	3 (3.8%)	1 (1.2%)	1 (2.0%)	0 (0%)
S/F ratio	295						
>440		117 (40%)	53 (73%)	31 (39%)	28 (34%)	4 (8.2%)	1 (9.1%)
440-200		139 (47%)	20 (27%)	42 (53%)	42 (51%)	30 (61%)	5 (45%)
<200		39 (13%)	0 (0%)	6 (7.6%)	13 (16%)	15 (31%)	5 (45%)
30 day mortality	291	65 (22%)	5 (6.9%)	12 (16%)	25 (30%)	18 (37%)	5 (45%)
Unknown		4	1	3	0	0	0
Death or ICU admission	291	83 (29%)	6 (8.3%)	14 (18%)	29 (35%)	29 (59%)	5 (45%)
Unknown		4	1	3	0	0	0

[†] Median (IQR); n (%)

6-point severity score and 30-day mortality remained significant in the multivariate model (adjusted OR 1.2 95CI% 1.1–1.2). The addition of pleural abnormalities and pleural effusions as predictors did not significantly improve the performance of the model.

The 6-point severity score was statistically associated with death or critical care admission at 30 days in univariate analysis (unadjusted OR 1.2 95CI% 1.1–1.2). The relationship remained statistically significant in a multivariate model

controlled for age, sex and time interval from admission to scan (adjusted OR 1.2 95CI 1.1–1.3)

The 6-point severity score was able to discriminate the composite outcome with a reasonable level of accuracy (AUC 0.76 95%CI 0.69–0.83) in univariate analysis.

Performance was optimised above a threshold severity score of 6. The risk of adverse outcome in patients above this threshold was significantly increased (OR 7.35 95%CI 4.02–13.42). The addition of pleural abnormalities and effusions as

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predictors in the model had a negligible effect on performance.

Death or critical care admission occurred in 5 (7.7%, 95%CI 3.3-16.8) patients with a severity score of zero, of which, 3 patients were PCR positive. Two patients in this group had a negative PCR. In both cases COVID-19 was not recoded on the death certificate as a cause of death. The proportion of patients experiencing the composite outcome within severity score quartiles stratified by PCR positivity is provided in figure 4B and stratified by severity of hypoxia in figure 5. In patients with severe hypoxia there was no obvious relationship between 6-point severity score and outcome. The risk appeared to increase incrementally in the sub-group of patients saturating adequately on room air and the sub-group requiring supplemental oxygen without severe respiratory failure as defined by the S/F ratio.

Discussion

We present the findings of a multi-centre service evaluation of the use of point-of-care LUS during the initial wave of COVID-19. LUS was able to discriminate patients based on the presence of SARS-CoV-2 by PCR and the risk of adverse outcomes with reasonable levels of accuracy. The inclusion of studies obtained from 295 individual patients provides the largest evaluation of LUS in COVID-19 reported to date.

The severity of lung ultrasound findings and presence of pleural abnormalities were associated with the detection of SARS-CoV-2 by PCR. An abnormal LUS examination had a sensitivity of 93% for detection of SARS-CoV-2 by PCR. The specificity of LUS at this threshold was poor. The results suggest LUS should not be used as the sole basis to exclude the presence of SARS-Cov-2 or to dictate decisions in relation to cohorting of care in isolation. The evaluation was undertaken during a period of high community prevalence. The negative predictive value of LUS would be expected to increase as the case rate falls.

LUS demonstrated inferior diagnostic performance to that reported in a recent observational study of 187 patients with suspected COVID compared with PCR as a reference in our evaluation.²⁴ This may reflect differences in methodological approach. Our evaluation provides insight into real world clinical practice and was not specifically designed to assess diagnostic performance. During the evaluation period national guidelines stated only patients admitted for in-patient care should routinely have samples obtained for PCR analysis.²⁵ Implementation of this practice is consistent with the relatively high proportion of patients with normal LUS with unknown PCR results in our

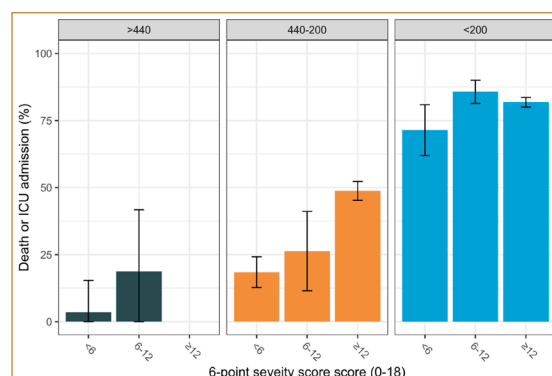


Figure 5. 30 day outcome stratified by 6-point severity score and severity of hypoxia

evaluation. Exclusion of these patients from analysis is likely to have led to biased estimates of diagnostic performance and potential underestimation of sensitivity. The excellent discrimination observed when using clinical diagnosis as the reference standard should be interpreted with caution. The vast majority of patients within the dataset received a clinical diagnosis of COVID-19 creating a skewed class balance resulting in biased predictions. In addition, the clinician determining the clinical diagnosis was not blinded to the LUS results.

Assessing the diagnostic performance of LUS using SARS-CoV-2 PCR as a reference standard is problematic given the poor reliability of detection in samples obtained from nasopharyngeal swabs. An early observational study of 205 patients with high clinical suspicion of COVID-19 based on clinical and radiological criteria detected viral RNA in less than 70% of nasopharyngeal samples.^[26] Comparable rates of adverse outcomes amongst patients in the higher risk ultrasound severity quantiles in the sub-group of patients that received a clinical and radiological diagnosis of COVID-19 could represent misclassification by PCR. Determining whether the poor specificity reflected deficiencies in LUS, poor specification of the ordinal scale used to record results, or the PCR reference standard is unclear.

LUS may provide clinically useful prognostic information. The severity of ultrasonographic findings was shown to correlate with the risk of death and ICU admission independently of the degree of hypoxia. The incremental increase in the risk of adverse outcomes associated with increasing score in patients independent of oxygen at the time of imaging suggests a potential role for LUS in differentiating patients at the lower end of the risk spectrum. The observed risk profile in the patient sub-group requiring supplemental oxygen at the time of imaging, but without severe respiratory failure as defined by the S/F ratio is particularly interesting.

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The risk of death or critical care admission in this group appeared to be well calibrated with ultrasound severity score. The ability to predict deterioration in this group has important implications in relation to decision regarding the most appropriate clinical environment and level of monitoring for ongoing care. This could be used to support the use of care pathways that utilise LUS to inform decisions in relation to the suitability for ambulatory management and target the use of peripheral oxygen saturation monitoring at home.²⁷

Limitations

Service evaluation methodology places strict limits on the generalisability of inference. Our evaluation should be interpreted as hypothesis generating rather than providing definitive answers.

The scale used to measure the severity of ultrasonographic is semi-quantitative and requires a subjective assessment by the operator. We were able to control for clustering at the hospital level but not at the individual operator level. Image interpretation was performed by the treating clinician with access to clinical, laboratory and in some cases radiological information, which may have biased scoring on the severity scale. Inter-rater concordance could not be measured.

We did not record the presence of key covariates now known to influence outcomes in COVID-19, in particular the presence of chronic respiratory disease. The S/F ratio classified a small number of patients receiving high-flow oxygen but with normal peripheral oxygen saturations as severely hypoxic (Figure 1). The severity of hypoxia in this group cannot be quantified. The application of high flow in itself suggests a degree of clinical concern was present at the time of assessment. Inclusion in the high risk group is therefore not unreasonable.

Conclusion

Point-of-care LUS is able to discriminate patients at increased risk of deterioration. The ultrasound severity score appears to be best calibrated with risk in patients receiving oxygen therapy. The evaluation provides further evidence of the clinical utility of point-of-care lung ultrasound which combined with the potential practical advantages provide a strong argument for wider adoption and integration of the practice.

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Declarations

Ethics approval and consent to participate

Specific regulations were released by the Health Research Authority to guide the use of confidential and anonymised patient data for COVID-19 research. [28] The study was conducted in accordance with these regulations. Individual patient consent was not required. The database was managed under clinical governance arrangements and a form review by a Research Ethics Committee was not required. Participating hospitals registered the study with their local audit office and Caldicott Guardian.

Consent for publication

Not applicable

Availability of data and materials

The data that support the findings of this study are available from the Society for Acute Medicine, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the Society for Acute Medicine.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

TK performed data analysis and interpretation and drafted the manuscript text. NS and PP were responsible for the conception and design of the study. PP, FL, GR MD, AA, DSL and NS provided critical review of the article. All authors approved the final manuscript.

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