

Correlation between hypoxaemia and lung ultrasound score in patients presenting to an emergency department with interstitial syndrome: a prospective physiological study

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In emergency departments (EDs), physicians are often confronted with conditions that lead to interstitial syndrome (IS), which is an interstitial tissue disease of the lungs.¹ Viral and bacterial pneumonia, pulmonary oedema of haemodynamic origin, and permeability-induced and chronic diffuse parenchymal lung disease are types of IS.² In IS, the involvement of the pulmonary interstitium leads to decreased pulmonary aeration and eventually to hypoxaemia, which is suggestive of IS severity. The ratio between arterial partial pressure of oxygen (P_{aO_2}), measured by arterial blood gas (ABG) analysis, and the fraction of inspired oxygen (F_{iO_2}) is indicative of hypoxaemia³ and defines the severity of acute respiratory distress syndrome.⁴ However, in addition to being painful, ABG sampling is invasive.

Lung ultrasound is a non-invasive, non-irradiating, low cost, and readily available tool that can be used at the patient's bedside. It has been found to be useful in the evaluation of critically ill patients.⁵ Ultrasonographic evaluation of IS is based on the presence of B-lines^{1,2,6} and is defined by the presence of three or more B-lines between two ribs.⁶ The lung ultrasound score (LUSS) is based on a quantitative assessment of B-lines⁷ that reflects lung aeration.⁸ Research findings confirm that LUSS is an effective measure of lung aeration in different intensive care unit situations such as re-aeration induced by antibiotics in ventilator-associated pneumonia⁹ and assessment of positive end-expiratory pressure-induced lung recruitment.¹⁰ In a weaning trial, LUSS was found to be a predictor of post-extubation distress.¹¹ LUSS can also be used to effectively quantify lesions and predict mortality associated with acute respiratory distress syndrome.^{12,13} During the recent coronavirus disease 2019 (COVID-19) pandemic, numerous trials have demonstrated that LUSS is associated with disease severity and mortality in COVID-19 patients.¹⁴

Recently, two small case series highlighted a correlation between P_{aO_2}/F_{iO_2} values and LUSS: one with 37 patients who had acute respiratory distress syndrome and were hospitalised in an intensive care unit,¹⁵ and the other with 33 patients who had COVID-19.¹⁶ If this correlation is

ABSTRACT

Objective: To assess for the presence of a correlation between lung ultrasound score (LUSS) and ratio between arterial partial pressure of oxygen (P_{aO_2}) and the fraction of inspired oxygen (F_{iO_2}) in patients presenting to an emergency department (ED) with interstitial syndrome (IS).

Design: Prospective, multicentre, physiological study.

Setting: Four Belgian hospitals: one tertiary academic centre and three secondary centres.

Participants: A convenience sample of adult patients who presented to an ED with acute dyspnoea and needed an arterial blood gas (ABG) analysis (those with a LUSS < 2 were secondarily excluded).

Main outcome measure: Correlation between P_{aO_2}/F_{iO_2} and LUSS determined using Pearson correlation.

Results: In total, 162 adult patients were included. A statistically significant negative linear correlation between P_{aO_2}/F_{iO_2} and LUSS was found (correlation coefficient, -0.4860 [95% CI, -0.5956 to -0.3587]; $P < 0.0001$).

Conclusions: Our data provide evidence of a statistically significant negative linear correlation between P_{aO_2}/F_{iO_2} and LUSS for ED patients with lung IS. Given the representativeness of P_{aO_2}/F_{iO_2} for hypoxaemia and the fact that hypoxaemia indicates IS severity, our findings suggest that LUSS could contribute to the evaluation of IS severity. If confirmed by future studies that include patient follow-up, a non-invasive approach using LUSS could decrease the need for ABG analysis in patients who do not require repeated measurement of ABG values other than P_{aO_2} , and thereby improve patient comfort.

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confirmed in a larger population of patients presenting to EDs with any kind of acute IS, LUSS could become a useful tool for evaluating P_{aO_2} in these patients and addressing IS

severity. This could eventually diminish the need for ABG sampling, to determine P_{aO_2} , during patient follow-up.

The primary objective was to determine whether there is a correlation between P_{aO_2}/F_{iO_2} and LUSS in patients presenting with IS to an ED. One secondary objective was to determine whether there is a correlation between arterial partial pressure of carbon dioxide (P_{aCO_2}) and LUSS in patients presenting with IS to an ED. The presence of pleural effusions was identified as the main potential confounding factor before the study. Its influence on the correlation between P_{aO_2}/F_{iO_2} and LUSS was tested as another secondary objective.

Methods

Design and setting

This prospective, physiological study took place in four centres in Belgium: one tertiary academic centre (Cliniques Universitaires Saint-Luc) and three secondary centres (Grand Hôpital de Charleroi, Hôpital de Jolimont, and Hôpital de Lobbes). Patients were recruited by convenience sampling between 1 April and 30 August 2021.

Patients aged over 17 years who presented to an ED with acute dyspnoea and for whom ABG analysis was indicated by the physician in charge were potentially eligible for inclusion. Patients were excluded if they had a history of chronic obstructive pulmonary disease or another condition responsible for chronic IS, or if lung ultrasound was not feasible for anatomical reasons. Inclusion and exclusion criteria are listed in Table 1.

If a patient met the inclusion criteria, an independent investigator performed a lung ultrasound to calculate their LUSS. Lung ultrasound was performed at the patient's bedside within 10 minutes of sampling for ABG analysis to minimise any possible bias caused by therapeutic measures or respiratory support initiated during that period. The study did not require patient follow-up.

The primary endpoint was correlation between P_{aO_2}/F_{iO_2} and LUSS. The key secondary endpoints were correlation between P_{aCO_2} and LUSS, and influence of pleural effusion on correlation between P_{aO_2}/F_{iO_2} and LUSS.

Four types of ultrasound machines were used: CX50 (Philips), Sparq (Philips), Clarius pocket-sized handheld ultrasound (Clarius) and Venue Go point-of-care ultrasound (GE Healthcare). The abdominal or lung setting in combination with a curvilinear probe were mandatory to perform lung ultrasound. In the COVID-19 pandemic context, sanitation standards in the institutions were followed by the investigators. Three types of blood gas analysers were used: Automatic QC Cartridge (Siemens), ABL90 FLEX (Radiometer) and ABL800 FLEX (Radiometer).

To calculate the LUSS, the thorax was virtually divided into 12 thoracic zones — six zones on each side as shown in Figure 1. The anterior and lateral zones were evaluated in the dorsal decubitus position, and the posterior zones were evaluated in the contralateral decubitus position. For each zone, a score from 0 to 3 was determined (Table 2, Figure 2). LUSS, which ranges from 0 to 36, was calculated by adding together the scores given to each of the 12 zones. Patients scoring less than 2 were empirically considered to have no IS and were thus secondarily excluded from the study. Investigators also reported the presence of a unilateral or bilateral pleural effusion. In all cases, LUSS was not communicated to the physician in charge of the patient.

The six investigators (EV, GM, AF, LP, FG, FD) were blinded to information relating to any other procedure used for diagnosis by the physicians involved in the care of patients included in the study, including results of ABG analysis. They were trained in performing lung ultrasound and self-evaluated their confidence in calculating a LUSS using a 5-point Likert scale (Table 3). All of them strongly agreed that they were qualified to calculate a LUSS.

Patient identifying information and data were collected on a paper case report form, then anonymised, and then registered on a secure computer file for data analysis.

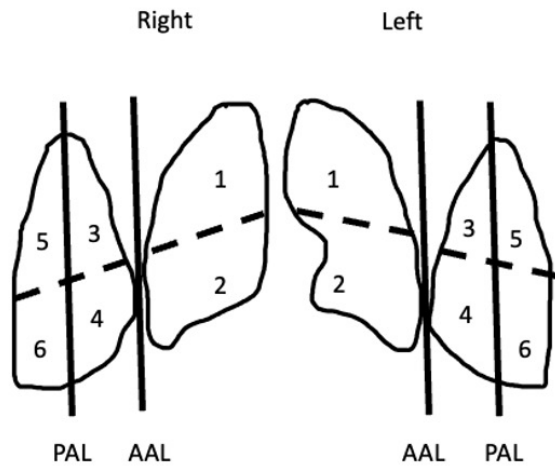
Statistical analysis

The Pearson formula was used to calculate the minimum sample size of 161 patients required to reach a confidence interval of 0.95 with a correlation index of 0.6. Data analysis was performed using JMP Pro 16.0.0 software (SAS Institute). Continuous variables are expressed as mean values and standard deviations. Discrete variables are reported

as categories and expressed as numbers and percentages. The Pearson correlation was used to measure the linear correlation between continuous variables, and correlations are expressed as correlation coefficient and 95% confidence interval. Comparisons between quantitative data were

Table 1. Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
- Acute dyspnoea - Age > 17 years - Arterial blood gas analysis indicated - Signed consent obtained	- Chronic obstructive pulmonary disease - Chronic interstitial syndrome - Lung ultrasound not feasible

Figure 1. Thoracic zones used for lung ultrasound

AAL = anterior axillary line; PAL = posterior axillary line.

performed with a χ^2 test, and between-group comparisons between continuous data with a Wilcoxon–Mann–Whitney test. The significance threshold was set with a P value of < 0.05 . Multiple linear regression was used to test the effects of continuous variables on LUSS and $\text{PaO}_2/\text{FiO}_2$.

Study approval and registration

Before the inclusion of patients, the study protocol was approved by the principal institutional review board: Comité d'Éthique Hospitalo-Facultaire Saint Luc-UCL (2021/10FEV/062). Secondly, the protocol was approved by the institutional review boards of the three other participating hospitals. The study was registered on ClinicalTrials.gov (NCT04813900). This article was

written according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement guidelines.¹⁷

Results

Patients and availability of data

A flowchart showing patient screening and enrolment is provided in Figure 3. A total of 179 patients who met all the inclusion criteria underwent a lung ultrasound, 17 patients with no IS (LUSS < 2) were secondarily excluded, and 162 patients were included in the final data analysis. Population characteristics of those included in the analysis are summarised in Table 4. Data for the primary and secondary endpoints were available for all 162 included patients.

Primary endpoint

A statistically significant negative linear distribution of the bivariate between $\text{PaO}_2/\text{FiO}_2$ and LUSS was found with a correlation coefficient of -0.4860 (95% CI, -0.5956 to -0.3587) and $P < 0.0001$ (Figure 4). Most of the study population were patients who had COVID-19 ($n = 116$). For these patients, the correlation between $\text{PaO}_2/\text{FiO}_2$ and LUSS was also statistically significant (correlation coefficient, -0.5226 [95% CI, -0.6436 to -0.3761]; $P < 0.0001$). Acute heart failure was the second most frequent diagnosis ($n = 28$). In this subgroup, the correlation between $\text{PaO}_2/\text{FiO}_2$ and LUSS was also statistically significant (correlation coefficient, -0.6047 [95% CI, -0.7978 to -0.2991]; $P = 0.0007$). A statistically significant correlation between $\text{PaO}_2/\text{FiO}_2$ and LUSS was shown for patients assessed by five of the six lung ultrasound operators ($P < 0.05$). The sixth operator evaluated nine patients for whom no statistically significant correlation was found between $\text{PaO}_2/\text{FiO}_2$ and LUSS ($P = 0.05$).

Table 2. Definitions of scores 0–3 for the purposes of calculating lung ultrasound scores*

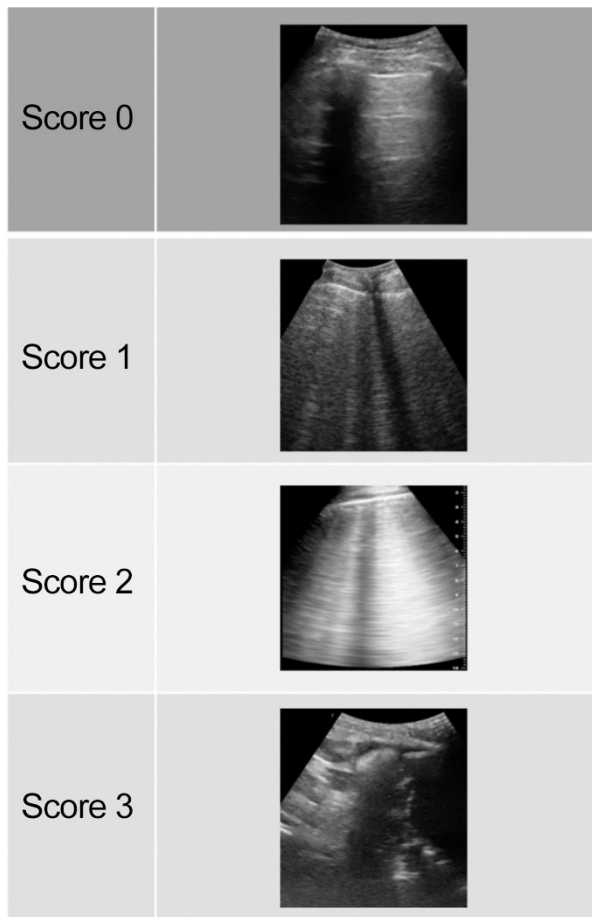
Score	Description
0	Normal aeration of the lung with the presence of A-lines, persistent pleural sliding, and fewer than three B-lines
1	Interstitial syndrome, resulting in moderate loss of aeration with three or more B-lines spaced 7 mm apart
2	Alveolar-interstitial syndrome, resulting in severe loss of aeration with coalescent B-lines spaced less than 3 mm apart
3	Alveolar consolidation, leading to a complete loss of aeration with an ultrasonographic tissue-like pattern

* Lung ultrasound scores range from 0 to 36; they are calculated by adding together the scores given to each of the 12 thoracic zones.

Secondary endpoints

No statistically significant correlation between PaCO_2 and LUSS was found ($P = 0.49$) (Figure 5). The presence of pleural effusion ($n = 28$) had no statistically significant influence on the correlation between $\text{PaO}_2/\text{FiO}_2$ and LUSS ($P = 0.07$) (Figure 6). In the subgroup of patients ($n = 16$) with elevated PaCO_2 (> 45 mmHg or > 6 kPa), there was a statistically significant influence of the presence of pleural effusion

Figure 2. Lung ultrasound images that illustrate scores 0–3 for the purposes of calculating lung ultrasound scores*



* Lung ultrasound scores range from 0 to 36; they are calculated by adding together the scores given to each of the 12 thoracic zones.

on the correlation between $\text{PaO}_2/\text{FiO}_2$ and LUSS ($P = 0.0069$) (Figure 7).

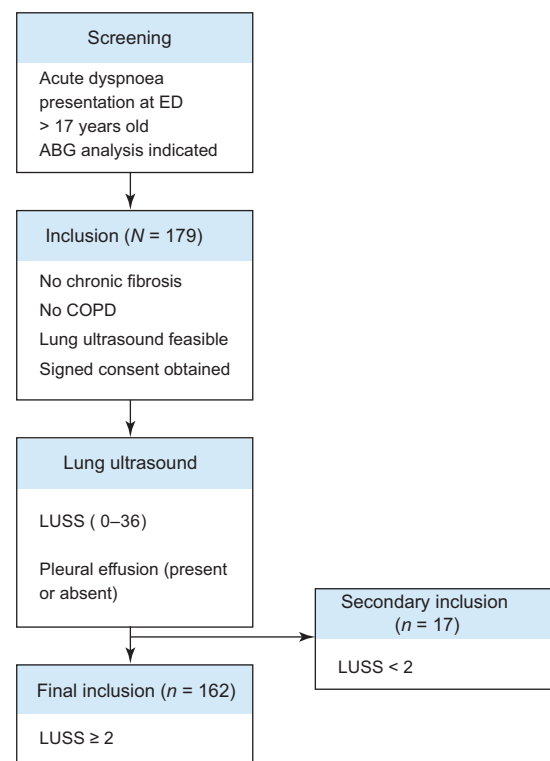
Additional analyses

A statistically significant negative linear correlation between $\text{PaO}_2/\text{FiO}_2$ and respiratory rate was shown (correlation coefficient, -0.2778 [95% CI, -0.4143 to -0.129]; $P = 0.0003$). There was no statistically significant influence of elevated respiratory rate (> 20 breaths/min) on the correlation between $\text{PaO}_2/\text{FiO}_2$ and LUSS ($P = 0.05$) (Figure 8). However, there was a statistically significant correlation between LUSS and respiratory rate (correlation coefficient, 0.3487 [95% CI, 0.2056 to 0.4773]; $P < 0.0001$). There was no statistically significant correlation between $\text{PaO}_2/\text{FiO}_2$ and haemoglobin level ($P = 0.18$) or between $\text{PaO}_2/\text{FiO}_2$ and body temperature ($P = 0.05$). Likewise, no statistically significant

Table 3. Likert scale used by operators to self-assess their ability to calculate the lung ultrasound score

Rating	Response to statement "I am qualified to calculate a lung ultrasound score"
1	Strongly disagree
2	Disagree
3	Undecided
4	Agree
5	Strongly agree

Figure 3. Study flowchart



ABG = arterial blood gas; COPD = chronic obstructive pulmonary disease; ED = emergency department; LUSS = lung ultrasound score.

correlation was found between LUSS and haemoglobin level ($P = 0.73$) or between LUSS and body temperature ($P = 0.72$).

Discussion

Although the correlation between $\text{PaO}_2/\text{FiO}_2$ and LUSS has previously been investigated in small series of acute respiratory distress syndrome and COVID-19 patients in

Table 4. Study population characteristics (n = 162)

Characteristics	Mean (SD) or n (%) [*]
Age (years)	64.1 (16.4)
Sex	
Male	90 (55.6%)
Female	72 (44.4%)
Comorbidities	
History of heart failure with reduced ejection fraction	28 (17.3%)
History of heart failure with preserved ejection fraction	8 (4.9%)
Chronic kidney failure	18 (11.1%)
Pulmonary arterial hypertension	12 (7.4%)
Asthma	9 (5.6%)
History of pulmonary infectious disease	19 (11.7%)
Final diagnosis [†]	
COVID-19	116 (71.6%)
Acute heart failure	28 (17.3%)
Bacterial pneumonia	11 (6.8%)
Pulmonary embolism	4 (2.5%)
Non-specific bronchopneumopathy	3 (1.9%)
Neoplasia	3 (1.9%)
Sepsis	2 (1.2%)
Anaemia	2 (0.6%)
Other [‡]	4 (2.5%)
Pao ₂ /Fio ₂	280.7 (77.6)
Lung ultrasound score	9.2 (5.0)
Pleural effusion	28 (17.3%)
Unilateral	15 (9.3%)
Bilateral	13 (8.0%)
Respiratory rate (breaths/min)	24.8 (6.5)
Elevated (> 20 breaths/min)	110 (67.9%)
Heart rate (beats/min)	94 (19.7)
Systolic blood pressure (mmHg)	136.8 (22.8)
Temperature (°C)	37.2 (1.2)
Haemoglobin level (g/L)	133 (22.0)
Creatinine level (µmol/L)	119.3 (176.8)
Arterial pH	7.46 (0.05)
Arterial lactate level (mmol/L)	1.5 (1.1)
Paco ₂ (mmHg)	35.3 (7.9)
Low Paco ₂ (< 35 mmHg or < 4.7 kPa)	89 (54.9%)
Normal Paco ₂ (35–45 mmHg or 4.7–6.0 kPa)	57 (35.2%)
Elevated Paco ₂ (> 45 mmHg or > 6.0 kPa)	16 (9.9%)
Fio ₂ (%)	25.2 (15.1)
Oxygen supplementation type	
No supplementation	142 (87.7%)
Nasal cannula	13 (8.0%)
Non-rebreather mask	6 (3.7%)
High flow nasal cannula	1 (0.6%)

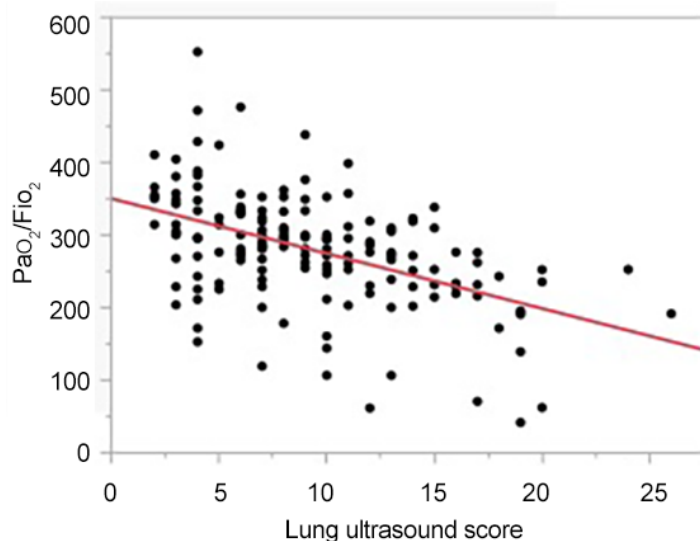
* Continuous data are expressed as mean (SD), and discrete data as number (percentage). † More than one diagnosis was possible. ‡ Including one pneumothorax, one lung contusion, one acute kidney failure, and one central vertigo. COVID-19 = coronavirus disease 2019; Fio₂ = fraction of inspired oxygen; Paco₂ = arterial partial pressure of carbon dioxide; Pao₂ = arterial partial pressure of oxygen; SD = standard deviation.

intensive care units,^{15,16} this study is the first to evaluate this correlation in patients presenting to an ED with acute dyspnoea. The presence of a statistically significant negative linear correlation between Pao₂/Fio₂ and LUSS in patients who have IS is consistent with LUSS reflecting Pao₂/Fio₂ in an ED context. The coefficient of −0.4860 in our population of patients is considered a moderate correlation.¹⁸ If further strengthened during patient follow-up, the correlation between Pao₂/Fio₂ and LUSS could be used to promote the use of lung ultrasound as a non-invasive procedure to assess IS evolution and severity for patients in wards or in countries where access to ABG analysis is difficult.

Although we included patients presenting with different types of acute IS, our study population was mostly comprised of COVID-19 patients, which is representative of the current ED situation. A moderate correlation was also demonstrated in this subgroup. The evolution of the COVID-19 pandemic could further influence this representativeness in the future. In the acute heart failure subgroup, the correlation was also moderate, although the confidence interval was larger due to the small number of patients. Although shown to be moderate, these correlations should be evaluated using appropriately calculated sample sizes for each subgroup. Our study was not designed with these subgroup analyses as primary outcome measures.

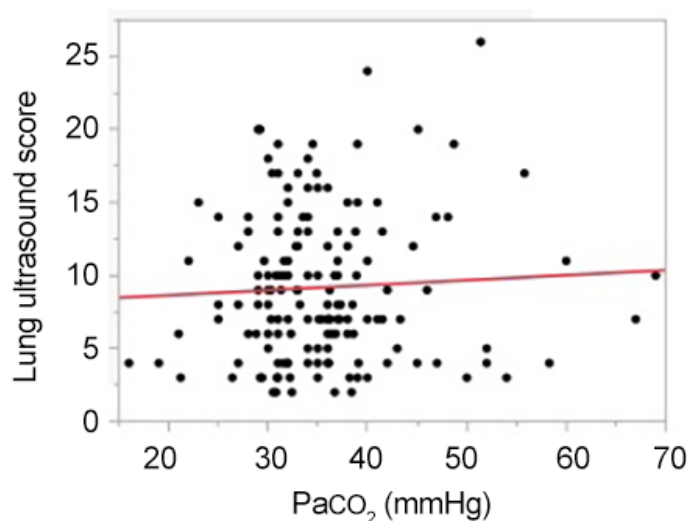
According to the Bohr equation, PaCO₂ is determined

Figure 4. Negative linear correlation between P_{aO_2} to F_{iO_2} ratio and lung ultrasound score



F_{iO_2} = fraction of inspired oxygen; P_{aO_2} = arterial partial pressure of oxygen.

Figure 5. Absence of correlation between lung ultrasound score and P_{aCO_2}



P_{aCO_2} = arterial partial pressure of carbon dioxide.

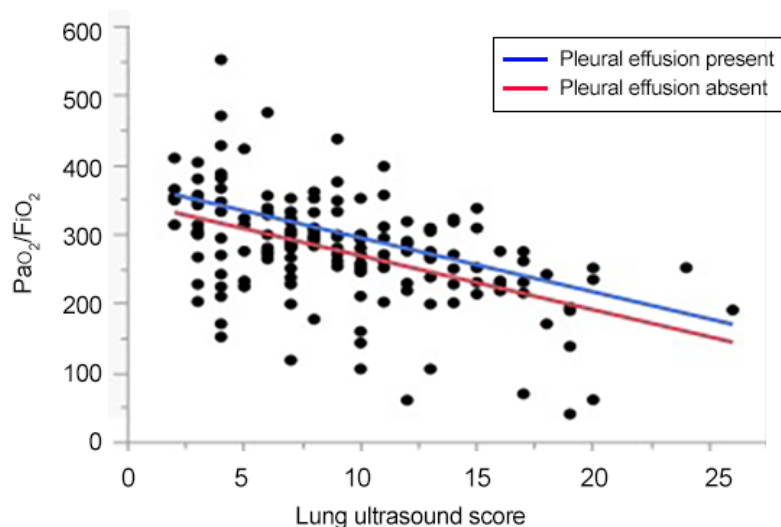
P_{aCO_2} value less than 35 mmHg (4.7 kPa) may be explained by the high proportion of patients presenting with an elevated respiratory rate (> 20 breaths/min). For most patients, elevated respiratory rate is consistent with the presence of acute dyspnoea. The exclusion of patients suffering from chronic obstructive pulmonary disease and chronic fibrosis may also explain the small number of included patients with elevated P_{aCO_2} (> 45 mmHg or > 6 kPa), which accounts for conditions affecting alveolar ventilation. These arguments throw light on the selection of patients in accordance with the inclusion criteria.

Although the presence of pleural effusion was suspected to influence LUSS before the study because of the eventual associated presence of atelectasis, resulting in a lung ultrasound condensation image and possibly increasing the LUSS, it had no statistically significant influence on the correlation between P_{aO_2}/F_{iO_2} and LUSS. This finding suggests that LUSS could be used to assess P_{aO_2} in the same way for patients with and without pleural effusion. Owing to the small number of patients with pleural effusion in our study, this needs to be confirmed. The low prevalence of pleural effusions in COVID-19 patients¹⁹ may explain the small number of pleural effusions in our study population. The pleural effusion size was regrettably not assessed, even though it could have influenced this result. In the subgroup of patients with elevated P_{aCO_2} , the presence of pleural effusion had a statistically significant influence on the correlation between P_{aO_2}/F_{iO_2} and LUSS. This result should, however, be confirmed in a larger population.

In addition, respiratory rate was identified as a potential confounding factor secondary to data analysis. No statistically significant influence of elevated respiratory rate on the correlation between P_{aO_2}/F_{iO_2} and LUSS was found. The respiratory rate variation is indeed independently correlated with P_{aO_2}/F_{iO_2} and LUSS. This suggests that LUSS could be used to evaluate P_{aO_2} regardless of the patient's respiratory rate. This could,

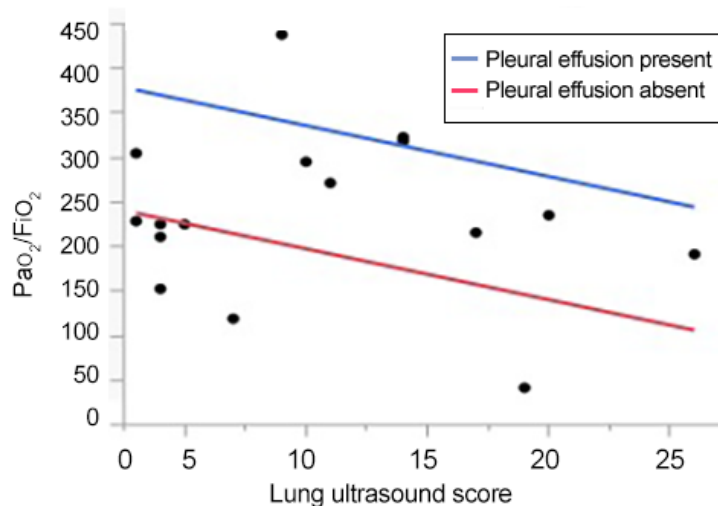
by alveolar ventilation and carbon dioxide production. Therefore, the absence of a statistically significant correlation between P_{aCO_2} and LUSS is consistent with the fact that LUSS represents lung aeration rather than alveolar ventilation.⁹ The large number of included patients with a

Figure 6. Negative linear correlation between P_{aO_2} to F_{iO_2} ratio and lung ultrasound score in patients with or without pleural effusion



F_{iO_2} = fraction of inspired oxygen; P_{aO_2} = arterial partial pressure of oxygen.

Figure 7. Negative linear correlation between P_{aO_2} to F_{iO_2} ratio and lung ultrasound score in patients with or without pleural effusion in a population with elevated P_{aO_2}



F_{iO_2} = fraction of inspired oxygen; P_{aO_2} = arterial partial pressure of oxygen.

failure.²⁰ In our study, four different ultrasound machines were used. Probe settings and type were standardised to minimise variability in lung ultrasound technique. However, the operator could choose between the abdominal setting and the lung setting depending on their routine of use and to improve their B-line visualisation. This could eventually be considered a bias. Since lung ultrasound was not repeated for the same patient, variation over time was not addressed. The six investigators self-evaluated their level of expertise in calculating LUSS, all scoring 5 on a 5-point Likert scale, which allowed us to reduce the influence of lung ultrasound expertise on the LUSS calculation. For one operator, however, there was no statistically significant correlation between P_{aO_2}/F_{iO_2} and LUSS for included patients. This is possibly due to the small number of patients in this subgroup rather than the operator's expertise. In this study, lung ultrasound images were not reviewed. Inter-rater variability in the calculation of LUSS was therefore not objectively assessed.

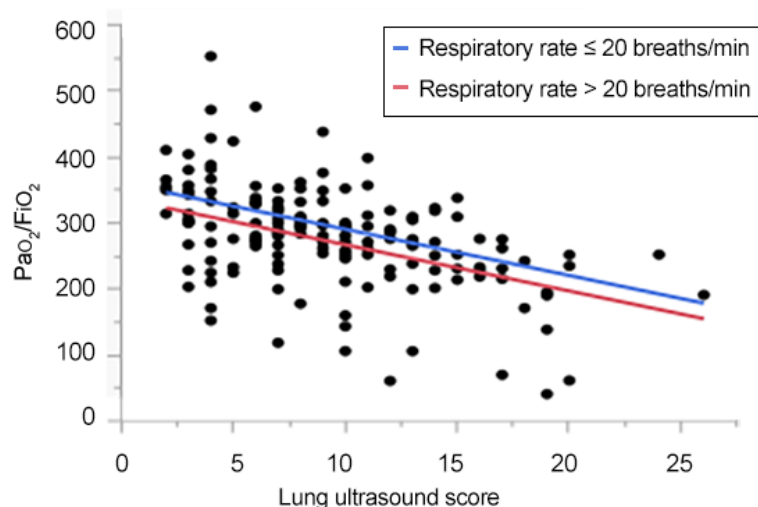
The multicentre nature of this study is a key strength, as it allowed many patients to be included over a short period. The sample size of 161 patients required to reach a 95% confidence interval with a correlation index of 0.6 was also achieved. However, the study was conducted by convenience sampling during the COVID-19 pandemic, which could have generated a patient selection bias due to the small number of lung ultrasound operators available for this study. Contrary to other countries, Belgian emergency physicians are not all familiar with point-of-care ultrasound, and many do not have expertise in lung ultrasound. To avoid convenience sampling, a similar study should be performed in EDs with

lung ultrasound operators available 24 hours a day. In this study, investigators were all trained in lung ultrasound and self-evaluated as qualified to calculate LUSS. Although no refresher course on lung ultrasound was given before the study, the investigators' selection could be seen as a strength. All investigators were blinded to the patients'

however, be influenced by the absence of a predefined method to measure respiratory rate in this study.

A recent study showed that the ultrasound probe, evaluation time and ultrasound operator's level of expertise might affect the assessment of B-lines in patients presenting with acute dyspnoea and suspected acute heart

Figure 8. Negative linear correlation between PaO_2 to FiO_2 ratio and lung ultrasound score in patients with low-normal or elevated respiratory rate



FiO_2 = fraction of inspired oxygen; PaO_2 = arterial partial pressure of oxygen.

clinical evaluation, including ABG results, and were independent of patient care to avoid any influence on LUSS calculation. This could be seen as a strength given the absence of clinical influence in this physiological study. Nevertheless, use of blinded investigators is not representative of LUSS calculation in a real-world clinical practice setting. It is therefore likely that different levels of lung ultrasound expertise would have influenced our results. Lung ultrasound expertise is highly variable among physicians of different medical specialties and possibly influenced by different clinical settings.

The consideration of the influence of two important potential confounding factors —presence of pleural effusion and respiratory rate— on the primary outcome is also a strength of our study. By contrast, the influence of other confounding factors such as body temperature and haemoglobin level on $\text{PaO}_2/\text{FiO}_2$ and LUSS was evaluated independently rather than directly in relation to the primary outcome, which could be seen as a limitation.

The diagnoses that we used in our analysis were based on the ED discharge report and not ascertained by an adjudication committee, which is a limitation. In the specific case of COVID-19 diagnosis, there was high variability in the diagnostic methods used in accordance with institutional procedures. This study was nevertheless a physiological study evaluating the correlation between $\text{PaO}_2/\text{FiO}_2$ and LUSS for any patients presenting to an ED with IS, regardless of their diagnosis.

The physiological nature of this study meant that there was no patient follow-up, which could also be seen as a limitation. However, the statistically significant correlation results for several aetiologies of IS hints at a possible correlation between $\text{PaO}_2/\text{FiO}_2$ and LUSS over time for the same patient. However, future studies should confirm this correlation during patient follow-up.

Conclusion

This physiological study shows a statistically significant correlation between $\text{PaO}_2/\text{FiO}_2$ and LUSS in a population of patients with IS who presented with acute dyspnoea to an ED. The presence of pleural effusion did not have a statistically significant influence on this correlation. If this correlation is confirmed by other studies using repeated measures of $\text{PaO}_2/\text{FiO}_2$ and LUSS on the same patient, further evidence could be provided to improve

patient comfort by diminishing the need for repeated ABG sampling to determine PaO_2 , during patient follow-up. LUSS could subsequently become a non-invasive tool to address IS evolution and severity.

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Competing interests

All authors declare that they do not have any potential conflict of interest in relation to this manuscript.

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