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# Relationship between lung consolidation size measured by ultrasound and outcome in ICU patients with respiratory failure

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## Abstract

**Background** Lung ultrasound has been extensively used to assess the etiology of respiratory failure. Additionally, lung ultrasound-based scoring systems have been proposed to semi-quantify the loss of lung aeration in the ICU. The one most frequently used distinguishes four steps of progressive loss of aeration (scores from 0 to 3) and 3 scores mean tissue-like pattern. However, the burden of consolidation is not considered as tissue-like pattern is defined as 3 scores independently of its dimension. In this study, we present an ultrasound method for quantitative measurement of consolidation size and investigate the relationship between consolidation size and outcome in ICU patients with respiratory failure.

**Methods** A total of 124 patients in ICU were prospectively enrolled and 13 patients were excluded due to failure to obtain LUS measurements. Among the remaining 111 patients, 17 patients were non-intubated, and 94 patients under sedation and analgesia were intubated. All patients underwent lung ultrasound examination for the measurement of lung consolidation size between 24 and 48 h after ICU admission. Lung consolidation size was assessed by consolidation area index (CA), which was determined by tracing the maximum cross-sectional area of the region of consolidation. The Cox-regression model was constructed for 28- and 90-day mortality.

**Results** Consolidation size was successfully evaluated in all patients. The CA was 24.2cm$^2$[15.9–36.6] (median [25th -75th percentiles]). CA was negatively correlated with $PaO_2/FiO_2$ ratio ($r$=-0.26, $P<0.0001$). Upon univariate and multivariate analysis, only CA [Odds ratio (OR) 1.04, 95% CI 1.01–1.08, $P=0.004$] and APACHEII (OR 1.14, 95% CI 1.05–1.25, $P=0.002$) were the risk factors for ICU mortality. Patients with substantial CA (> 29.4cm$^2$) had a higher risk of death in 28-day [Hazard ratio (HR) 4.35, 95%CI 1.70-11.11; Log-rank $P=0.017$] and 90-day mortality (HR 4.10, 95%CI 1.62–10.39; Log-rank $P<0.01$).

**Conclusions** The proposed CA parameter, determined by lung ultrasound, was readily accessible at the bedside. It is noteworthy that a larger CA was correlated with impaired oxygenation and increased mortality rates among ICU patients. Further investigation is required to establish the merits of incorporating CA into lung ultrasound assessments in the ICU.

**Trial registration** ClinicalTrial.gov, Identifier NCT05647967, Date: Dec 13, 2022, retrospectively registered.


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**Keywords** Lung ultrasound, Consolidation area, Mortality

## Introduction

Lung consolidation is a common complication characterized by high prevalence and high fatality in critically ill patients. Its underlying etiology ranges from pneumonia, atelectasis, pulmonary edema and other extrapulmonary diseases [1]. Computed tomography (CT) is the conventional imaging techniques for the evaluation of lung consolidations; however, CT scan necessitates transporting patients to go outside for the examination and cannot be performed at the bedside in real time. For critically ill patients, such transportation poses significant risks [2]. Lung ultrasound (LUS) can easily detect consolidated lung areas in diffuse lung injury at the bedside [3, 4], nevertheless, quantitative assessment of lung consolidation size is seldom evaluated in clinical settings.

In recent years, various LUS-based scoring systems have been proposed to semi-quantify the loss of aeration, and the one most frequently used distinguishes four steps of progressive loss of aeration, each corresponding to a score: score 0 means A lines or ≤ 2 B lines; score 1 means ≥ 3 well-spaces B-lines; score 2 means coalescent lines; score 3 means tissue-like pattern [5]. This rating system focuses on the degree of ventilation loss, and the evidence employed in clinical contexts primarily involves the deleterious side effects of fluid resuscitation [6], assessment of lung recruitment [5], and antibiotics-induced re-aeration [7]. The quantitative assessment of lung consolidation has rarely been described.

In this study, we present an ultrasound method for quantitative measurement of consolidation size and investigate the relationship between consolidation size and outcome in ICU patients with respiratory failure.

## Methods

### Study population

The study population consisted of adult patients (aged > 18 years) who were admitted to the ICU. Patients who presented with acute respiratory failure and pulmonary consolidation on previous chest imaging (LUS, radiography, or CT scan) between November 2021 and September 2023 were eligible for inclusion. Acute respiratory failure was defined by at least one of the following criteria: $PaO_2/FiO_2$(P/F ratio) < 300 mmHg, breathing frequency > 30 breaths/min, and involvement of many potential causes of hypoxemia (e.g., sepsis, atelectasis, pneumonia, and acute exacerbation of chronic lung disease). The exclusion criteria were hemodynamic instability, pulmonary artery hypertension, pregnancy, severe thoracic trauma and failure to obtain the LUS measurements.

This study was strictly carried out in accordance with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Peking Union Medical College Hospital (PUMCH) (Approved date: Aug 2, 2022; No. I-22PJ140). In our study, seventeen non-intubated patients signed informed consent themselves, while the remaining intubated patients, under sedation and analgesia, had their informed consent signed by their next of kin. For participants whose initial consent was obtained from next of kin, attempts were made to obtain retrospective consent once they regained decision-making capacity.

### Lung ultrasound examination

Ultrasound examination (DC-40 S, Mindray, Shenzhen, China) was performed within 24–48 h of ICU admission if consolidation had been confirmed on radiography (Chest-x-ray or lung CT). All images were obtained using a 2–5 MHz abdominal transducer, with the image depth was set at 16 cm. As previously documented [8, 9], a supine position lung ultrasound examination protocol was applied in the study. Firstly, the target consolidation area is identified based on the location of abnormalities in the chest X-ray or CT scan, and a comprehensive 12-zone lung screening is conducted to ensure no areas are overlooked. Secondly, the maximum consolidation area is determined by adjusting the ultrasound probe angle to obtain the most representative view. Finally, the size of lung consolidation was quantified by measuring the consolidation area (CA), which is determined by delineating the maximal cross-sectional area of the consolidated region.

LUS was blindly performed and analyzed by two ICU expert physician who were certified for the Chinese Critical Ultrasound Study Group (CCUSG) and the World Interactive Network Focused on Critical UltraSound (WINFOCUS). The inter-rater reliability for measured values was evaluated using Intraclass Correlation Coefficient. Two investigators blindly evaluated 50 patients' ultrasound images, and the ICC was calculated using two-way random-effects model for absolute agreement. The ICC for the total measured values was 0.85(95%CI 0.78–0.91). Statistical analysis was performed using SPSS IBM Version 26.

### Other parameters

The basic demographic information, including sex, age, etiology for admission, sequential organ failure assessment score, central venous pressure, laboratory tests were collected from the Critical Care Monitor System in PUMCH. Moreover, the clinical Pulmonary Infection

Score (CPIS) [10] score was obtained. The primary clinical outcomes of this study were the P/F ratio, 28-day, and 90-day mortality rates. The length of ICU stays, and duration of intubation were the secondary outcomes.

### Statistical analysis

As previously documented [11], by estimating the prevalence of an overall hospital mortality of 30% for the study population and 20 ± 10% of CA in survivors, a sample of 96 patients was required to detect a difference of 10% in CA between the survivors and the nonsurvivors with a power of 0.8 and alpha of 0.05. Continuous variables are presented as medians and quartiles (25th and 75th percentiles), and categorical variables are presented as numbers and percentages. Differences in categorical variables were analyzed using Fisher's exact test, and differences in continuous data were analyzed using the Mann-Whitney test. Correlations were tested using a simple linear regression model (reported with the correlation coefficient r) or Spearman rank correlation, as appropriate. Sensitivity, specificity, and area under the receiver operating characteristic curves were calculated to determine the diagnostic performance of CA. A $P$ value < 0.05 was regarded as statistically significant and statistical analyses were performed using SPSS IBM Version 26 (Armonk, NY: IBM Corp).

**Table 1** Demographic and clinical characteristics of the population($n$ = 111)

| Baseline Characteristics | Total($n$ = 111) |
|---|---|
| Age(yr) | 65.0[55.0-74.5] |
| Female sex, N (%) | 43(38.7%) |
| APACHEII | 17.0[13.0–24.0] |
| SOFA | 8.0[5.0-10.7] |
| Cause of lung injury, N (%) | |
| Pneumonia | 27(24.3%) |
| Sepsis | 21(18.9%) |
| Surgery | |
| Cardio-surgery | 27(24.3%) |
| Abdominal surgery | 18(16.2%) |
| Thoracic surgery | 9(8.1%) |
| Neurosurgery | 3(2.7%) |
| Other | 6(5.4%) |
| $PaO_2/FiO_2$(mmHg) | 267.7[219.7-302.8] |
| $PaCO_2$(mmHg) | 38.3[35.5–41.5] |
| RR (breath/min) | 18.0[15.5–22.0] |
| PEEP ($cmH_2O$) | 6.0[0–8.0] |
| HR (beats/min) | 85.0[74.0-99.3] |
| CVP (mmHg) | 6.5[5.0-8.3] |
| MAP (mmHg) | 82.0[75.0–90.0] |
| PI (%) | 1.5[0.9–2.3] |
| Lactate(mmol/L) | 1.3[0.9–2.2] |
| Vasopressor supports, N (%) | 55(49.5%) |
| Positive culture, N (%) | 60(54.1%) |
| ICU stay(d) | 7.0[4.0–12.0] |
| Duration of Intubation(d) | 3.0[1.0–7.0] |
| Death within 28 days, N (%) | 14(12.6%) |
| Death within 90 days, N (%) | 20(18.0%) |

Note: values are presented as the median [25th and 75th percentiles] or number (%). RR = Respiratory rate. HR = Heart rate. CVP = Central venous pressure. PEEP = Positive end-expiratory pressure. MAP = Mean arterial pressure. PI = Perfusion index. APACHEII = Acute Physiology and Chronic Health Evaluation II score. SOFA = Sequential Organ Failure Assessment

## Results

### Characteristics of subjects

From November 2021 to September 2023, a total of 124 patients were enrolled in the study. Thirteen patients were excluded, among whom four had no consolidation found and nine could not undergo ultrasound examination due to chest wounds. 111 patients were recruited (male: female, 63:48; age, 65.0 [55.0-74.5] years), among whom17 patients were non-intubated, and 94 patients under sedation and analgesia were intubated. The median time between the admission to the ICU and the start of the LUS test was 29.6 h in the study group.

Twenty patients (18.0%) died within the 90-day follow-up period, of whom 14(12.6%) died within 28 days. The causes of lung injury included pneumonia (21/111, 18.9%), sepsis (21/111, 18.9%), and aspiration (6/111, 5.4%). Positive specimen cultures for *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Aspergillus*, and *Staphylococcus aureus* were found in 60 patients (54.1%). Of these patients, the median P/F ratio was 267.7 [219.7-302.8] mmHg. Other descriptive data is presented in Table 1.

### Relationship between consolidation size and oxygenation index

LUS examination revealed that lung consolidations were found in all patients (100.0%) and the median CA was 24.2 [15.9–36.6]$cm^2$. Figure 1A-G showed an illustrative picture of the consolidation size for different etiology of respiratory failure. In these patients, severe pneumonia triggered by interstitial lung disease, or aspiration showed higher consolidation area index (Fig. 1K). On multivariate analysis, the etiology of respiratory failure was associated with consolidation area index(β:3.24; 95%CI 2.73 to 3.76; $P$ = 0.014).

By dividing patients according to the P/F ratio, four groups showed a gradually increasing trend of CA (19.2$cm^2$ [12.7–30.4] vs. 23.2$cm^2$ [16.2–31.3] vs. 38.9$cm^2$ [19.6–43.2] vs. 39.1$cm^2$ [18.9–39.1], normal vs. moderate $P$ = 0.002, normal vs. severe $P$ = 0.001, mild vs. moderate $P$ = 0.003, Fig. 1H). Spearman's rank correlation analysis was performed to assess the relationship between CA and P/F ratio, and the result showed CA was negatively correlated with P/F ratio (rho=-0.356, $P$ < 0.001, $N$ = 111) (Fig. 1J). P/F ratio data were $log_{10}$-transformed to

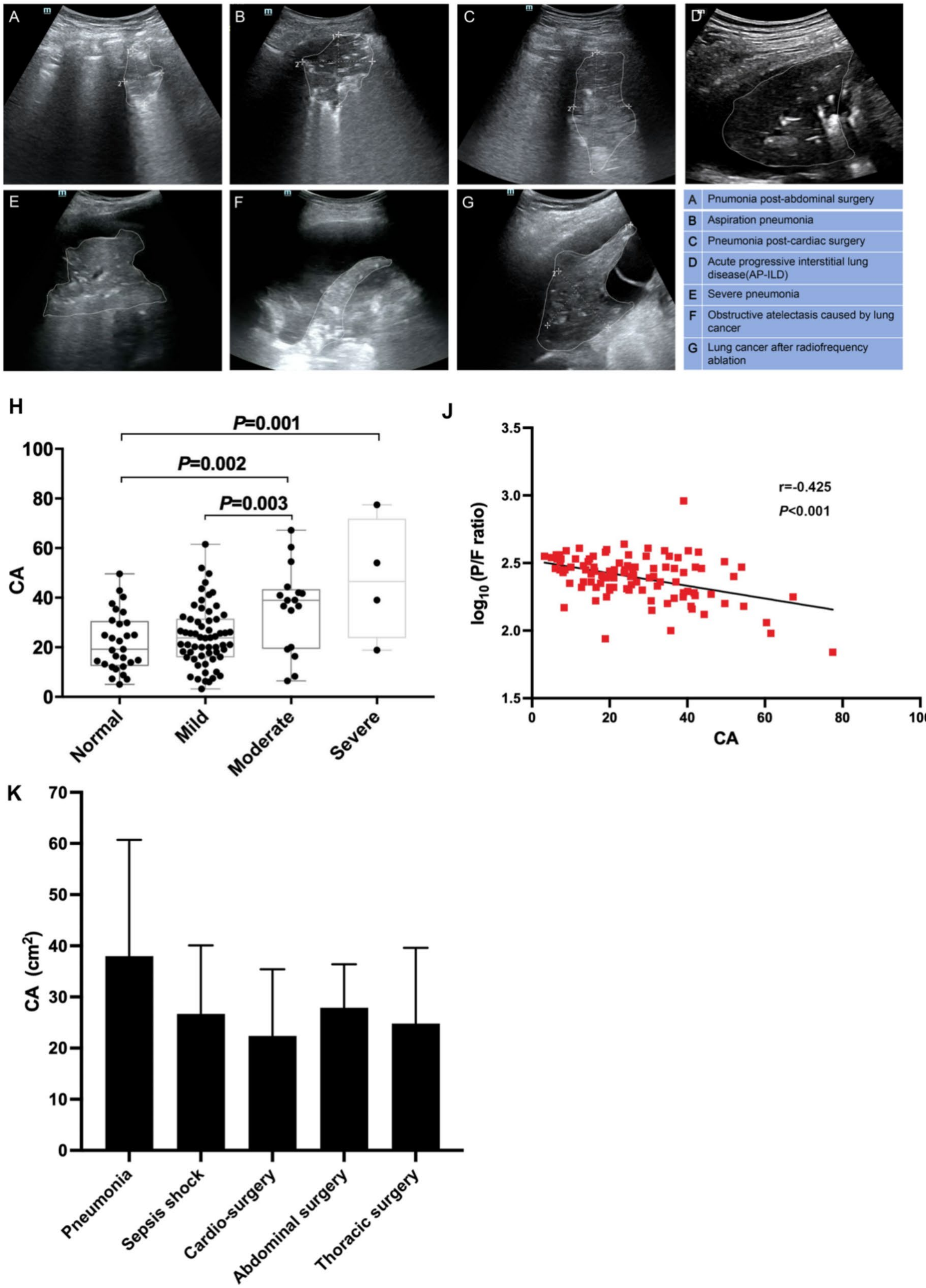


**Fig. 1** Illustrative pictures of consolidations attributable to different etiology and the correlation between CA and oxygenation. One picture for various etiologies of consolidation is shown from A to G. H. Comparisons of CA among the four groups. J. The correlation between $\log_{10}$(P/F ratio) and CA. K. The distribution of CA among different respiratory disorders. CA = consolidation area; P/F ratio = $PaO_2/FiO_2$

**Table 2** Comparisons of demographic and clinical characteristics for ICU mortality

| Baseline characteristics | Survivors | non-Survivors | *P* |
|---|---|---|---|
| | ***n*** **= 91** | ***n*** **= 20** | |
| Age(yr) | 60.2 ± 16.3 | 73.6 ± 8.9 | **< 0.001** |
| Female sex (%) | 38(41.8) | 6(30.0) | 0.450 |
| APACHEII | 16.9 ± 6.3 | 24.9 ± 5.8 | **< 0.001** |
| SOFA | 7.5 ± 3.9 | 11.1 ± 5.0 | **0.006** |
| RR (breath/min) | 18.6 ± 4.1 | 18.4 ± 4.7 | 0.842 |
| P/F ratio(mmHg) | 276.1 ± 73.5 | 237.4 ± 70.3 | **0.038** |
| $PaCO_2$(mmHg) | 39.2 ± 5.7 | 38.0 ± 7.2 | 0.418 |
| HR (beats/min) | 86.3 ± 16.0 | 91.4 ± 17.2 | 0.224 |
| CVP ($cmH_2O$) | 6.3 ± 2.7 | 7.5 ± 4.0 | 0.315 |
| MAP (mmHg) | 83.6 ± 12.8 | 86.1 ± 12.8 | 0.442 |
| CA ($cm^2$) | 24.1 ± 13.3 | 34.7 ± 14.6 | **0.003** |
| ICU stay(d) | 9.1 ± 8.5 | 22.8 ± 12.0 | **0.013** |
| Duration of Intubation(d)[a] | 4.6 ± 5.9 | 20.1 ± 10.1 | **0.003** |

Note: [a] The non-intubated patient was deleted in the analysis

**Table 3** Univariate and multivariate Cox proportional hazards analysis of risk factors for 90-day mortality

| Variables | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| | **Odds ratio (95%CI)** | ***P*** | **Odds ratio (95%CI)** | ***P*** |
| Age | 1.045[0.990–1.103] | 0.108 | 0.943[0.890–1.033] | 0.088 |
| Sex | 0.646[0.183–3.817] | 0.608 | | |
| APACHEII | 1.167[1.041–1.308] | **0.008** | 1.148[1.051–1.255] | **0.002** |
| SOFA | 1.130[0.937–1.362] | 0.201 | | |
| $PaCO_2$(mmHg) | 0.828[0.718–0.955] | **0.010** | 0.531[0.359–0.786] | **0.015** |
| P/F ratio(mmHg) | 0.998[0.990–1.006] | 0.677 | | |
| HR (beats/min) | 1.005[0.959–1.052] | 0.859 | | |
| CVP ($cmH_2O$) | 1.113[0.821–1.509] | 0.491 | | |
| MAP (mmHg) | 1.022[0.956–1.094] | 0.522 | | |
| Lactate(mmol/L) | 1.800[1.143–2.833] | **0.001** | 1.207[1.047–1.392] | **0.012** |
| Duration of intubation(d) | 1.239[0.995–1.544] | **0.056** | 1.021[0.999–1.044] | 0.061 |
| ICU stay(d) | 0.843 [0.683–1.041] | **0.113** | 0.876[0.805–0.954] | **0.022** |
| CA ($cm^2$) | 1.061[1.021–1.102] | **0.002** | 1.048[1.015–1.082] | **0.004** |

Note: CA consolidation area; HR heart rates; CVP central venous pressure; MAP mean arterial pressure

normalize the distribution [11, 12], and the transformed values was linearly related to CA ($r$=-0.425, $P < 0.0001$).

### The consolidation size as predictor of mortality

Over a follow-up period of 79.8[54.9-104.7] days, twenty (20/111, 18.0%) patients died, which included 13 cases of septic shock, 6 cases of cardiac shock and 1 case of hemorrhagic shock. The nonsurvivors exhibited higher levels of CA (34.7[20.1–49.3] vs. 24.1[10.8–37.4], $P = 0.003$) as well as age, APACHEII, SOFA, P/F ratio, ICU stay and duration of intubation than the survivors (Table 2). Upon the univariate analysis, APACHEII($P = 0.008$), $PaCO_2$($P = 0.010$), lactate($P = 0.001$) and CA($P = 0.002$) were significantly associated with patient survival. Variables were introduced into a multivariable binary logistic regression model if significantly associated with mortality at day 30, using the univariate analysis when the p value was < 0.2. Further multivariate analysis showed that APACHEII, $PaCO_2$, lactate, ICU stay, and CA were independent predictors of patient survival, whereas, P/F ratio, SOFA, duration of intubation was no longer significant (Table 3).

In the receiver operating characteristic (ROC) analysis, a threshold of CA > 29.4 $cm^2$ (AUC 0.73, 95% CI 0.63–0.81) had a specificity of 87.36% in predicting 90-day mortality (Fig. 2A). Thus, the size of consolidation was arbitrarily separated into small group(CA ≤ 29.4$cm^2$) and substantial group(> 29.4$cm^2$), and we found that the substantial group had a higher risk of death within 28 days mortality[Hazards ratio(HR) 4.35, 95% CI 1.70-11.11; log-rank $P = 0.017$) and 90 days (HR 4.10, 95% CI 1.62–10.39; log-rank $P = 0.0029$) than the small CA group (Fig. 2B).

## Discussion

This cohort study, mainly performed in critically ill patients with respiratory failure, yielded several findings: [1] consolidation area index of the biggest consolidation was negatively correlated with oxygenation; [2] Larger

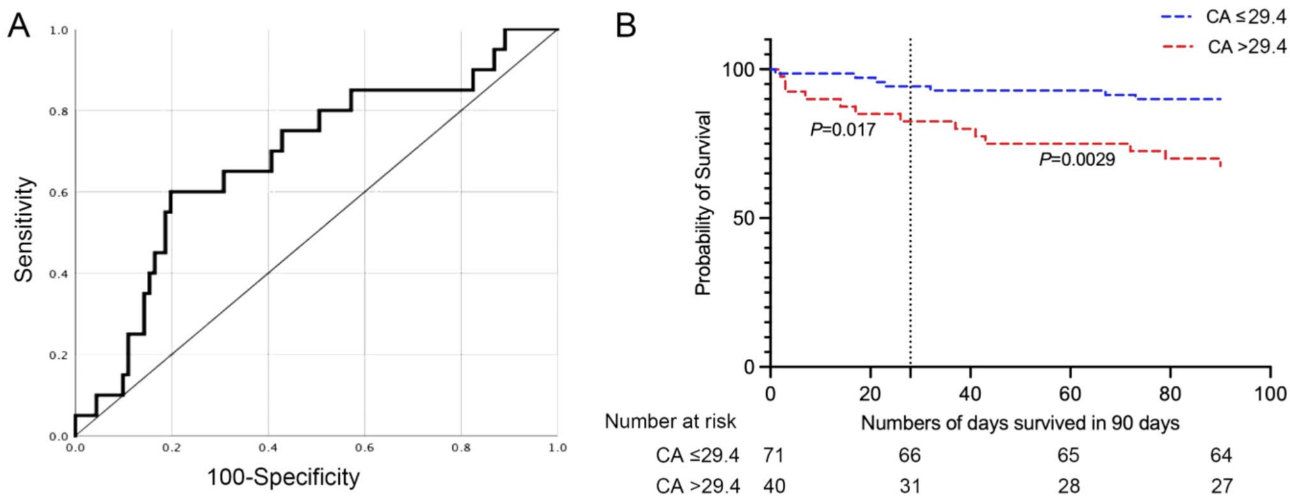


**Fig. 2** The consolidation size as predictor of mortality. A ROC curve comparing the ability of CA for ICU mortality. B Kaplan-Meier survival curves over 28 and 90 days after ICU admission stratified by the CA. The dashed line indicates the 28-day

consolidation size (CA > 29.4cm$^2$), especially 24 h after admission to ICU, showed worse prognosis. The first finding was novel and partially consistent with previous data reporting correlations between LUS scores and oxygenation metrics [13]. The second finding reinforced clinicians' understanding of the poor prognosis associated with bulk consolidation and the need for timely intervention.

Lung ultrasound rating systems had been employed in different clinical contexts. The one most frequently used distinguishes four steps of progressive loss of aeration, each corresponding to a score. This score is computed in six regions per hemithorax, and the global lung ultrasound score corresponds to the sum of each region's score and ranges from 0 to 36 [5]. Following a successful weaning trial, a score exceeding 17 demonstrates high predictability for post-extubation distress, whereas a score below 13 indicates high predictability for successful weaning [11]. And higher points were proved to be correlated with poor prognosis in ARDS, including longer period of intubation and ICU stay [12, 13]. However, a weakness of this scoring system was that consolidation was arbitrarily deemed as three points regardless of its dimension and location. Thus, a quantitative indicator for consolidation was warranted.

In 2000, Lichtenstein DA firstly proposed that the depth of consolidation was measured by the distance from the pleural line to its deepest edege [4]. And in the critical neonatal patients, the consolidation depth was proved to be correlated with the type of neonatal respiratory disorders [14]. Moreover, dimension of lung consolidation was also assessed by tracing the consolidation area above the diaphragm and a transversal view [15].

In our study, the worse oxygenation index seen in larger consolidation size could be explained by the corresponding larger aeration loss, and patients with pneumonia triggered by acute interstitial lung disease and aspiration pneumonia suffered from the relatively larger size. Although the correlation between CA and P/F ratio is not very strong, we believe that multiple factors could affect the oxygenation apart from the ventilation, such as the regional pulmonary perfusion, cardiac output, interstitial lung disease, heart-lung coupling dynamics and so on. Besides, the lower oxygenation index within larger consolidation size could be attributable to the different regional perfusion patterns (D pattern and S pattern) [15, 16], which eventually influenced the mismatch of ventilation and perfusion. Given the relatively small differences among the respiratory disorders, future exploration about the regional perfusion of consolidation is urgently needed.

In previous study, the dorsal aeration loss after major surgery showed poor clinical outcomes for dorsal atelectasis in patients [17]. Similarly, we found that patients with larger consolidation size, especially over 29.4cm$^2$, suffered from poor prognosis including higher 28- and 90-day mortality, which indicated that early therapeutic intervention should be implemented on improving lung aeration and/or reorienting blood flow (fiberbronchoscopy, recruitment maneuver, prone/lateral position) [18].

This study has several limitations. First, this study was conducted at a single center, which limits the generalizability of the results. The sample sizes of patients with severe respiratory failure were small, which might have led to the lack of statistical differences. Therefore, a larger multi-center study is warranted. Second, the calculation of consolidations was two-dimensional area rather than the three-dimensional volume in our study, which might underestimate the real volume of consolidation. Further exploration of the three-dimensional(3D) ultrasound is required, like the 3D EIT for lung morphology [19]. Third, lung ultrasound rating systems had been employed in different clinical contexts and partially corresponded to the global lung ventilation. Combination of CA and LUS calculating scores might better evaluate the clinical outcomes. Fourth, simply comparing this new ultrasound score with the P/F ratio and patient outcomes is limiting, as it does not structurally analyze the possibility of different consolidation types: atelectasis, infection, VILI, post-operative pulmonary complications. In the future, more different consolidation types would be considered.

## Conclusion

The proposed CA parameter, determined by lung ultrasound, was readily accessible at the bedside. It is noteworthy that a larger CA was correlated with impaired oxygenation and increased mortality rates among ICU patients. Further investigation is required to establish the merits of incorporating CA into lung ultrasound assessments in the ICU.


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N/A.


#### Author contributions
HWH and DWL prepared the final copy of the manuscript and ultrasound images. HWH, NW and QLW performed the ultrasound examination. HH, DWL, NW, QLW, YC, ZQZ and YL drafting the manuscript for important intellectual content and interpretation for data.


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#### Data availability
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### Declarations

#### Ethics approval and consent to participate
This was a single-center prospective cohort study in the intensive care unit (ICU) of the Perking Union Medical College Hospital in Beijing, China. This study was strictly carried out in accordance with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Peking Union Medical College Hospital (Approved date: Aug 2, 2022; No. I-22PJ140). In our study, seventeen non-intubated patients signed informed consent themselves, while the remaining intubated patients, under sedation and analgesia, had their informed consent signed by their next of kin.

#### Consent for publication
Not applicable.

#### Competing interests
The authors declare no competing interests.


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### Publisher's note