

# BMJ Open Exploring the correlations of lung ultrasound with delirium and other clinical outcomes in older patients with respiratory failure admitted in acute geriatric units (ECO-AGE): protocol for a multicentre, prospective, observational study from the GRETA Group (Gruppo di Ricerca in Ecografia Toracica nell'Anziano) of the Italian Society of Gerontology and Geriatrics (SIGG)

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## ABSTRACT

**Introduction** Point-of-care lung ultrasound (LUS) can assist in diagnosing acute respiratory diseases for its high accuracy and immediate availability at the bedside, including older patients with frailty. Delirium represents a frequent complication of hospitalisation in this setting, frequently triggered by acute respiratory diseases. LUS may therefore help identify individuals at risk of delirium, but the association between LUS abnormalities and delirium remains unexplored.

**Methods and analysis** This study is a prospective, observational, multicentre study, with the main objective of assessing the correlation between LUS abnormalities and incident delirium during hospitalisation (primary outcome). The secondary objectives are to assess correlations between lung and diaphragm ultrasound parameters and clinical outcomes including duration of delirium, severity of respiratory failure and mortality. 480 patients aged ≥65 years old, urgently hospitalised after an emergency department visit for acute respiratory complaints, will be recruited in eleven acute geriatric wards located in eight teaching hospitals across Italy. LUS examinations will be performed by skilled clinicians prior to treatment whenever feasible, and in any case within 48 hours from admission. They will also undergo comprehensive geriatric

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This multicentre, prospective study investigates the potential association between lung ultrasound (LUS) abnormalities and delirium onset in older patients hospitalised for acute respiratory diseases.
- ⇒ Delirium assessment is conducted according to gold-standard criteria, while LUS evaluation may enable the detection of respiratory abnormalities even in frail and functionally impaired individuals.
- ⇒ While reproducible by skilled operators, LUS depends on operator expertise, which may limit result generalisability.
- ⇒ The study is non-interventional and does not assess the impact of LUS performance on patient-related outcomes and its cost-effectiveness.

assessment, and daily delirium assessment through the 4-AT tool. The association between LUS abnormalities, related parameters (LUS score, Pleural Effusion Score) and outcomes will be assessed by linear and logistic regression models.

**Ethics and dissemination** Ethics Committee approval of the coordinating centre (Comitato Etico Territoriale



Lombardia 3, reference ID 4369\_20.03.2024\_M) and collaborative centres has been obtained. All participants will provide written informed consent. Study results will be publicly available following peer-reviewed publication in international scientific journals.

**Trial registration number** NCT06670118.

## INTRODUCTION

Lung ultrasound (LUS), performed at the patient's bedside by trained clinical examiners following the principles of point-of-care ultrasonography (POCUS), has progressively entered medical practice in the last twenty years as a technological supplement to physical examination.<sup>1–3</sup> In acute-care and emergency-urgency settings, LUS contributed to establishing a novel care paradigm, enabling clinicians to confirm the suspected clinical diagnosis, or at least to rule in or rule out the most common causes of acute respiratory symptoms.<sup>4–6</sup> This advance improved the diagnostic process and the appropriateness of referral to specialist imaging services for consultative ultrasonography or traditional chest imaging examinations,<sup>3</sup> including X-rays, whose diagnostic performance is generally considered inferior to LUS<sup>7–9</sup> and high-resolution CT.

According to studies conducted in acute-care geriatric wards, the diagnostic advantages of LUS are also present in older patients with multimorbidity, frailty or disability.<sup>10–12</sup> LUS is technically feasible at the bedside and accurate for detection of the main pleuro-parenchymal abnormalities even in patients with poor performance status,<sup>12</sup> where the diagnostic accuracy of radiographic scans is generally low,<sup>13</sup> enabling quicker diagnosis and initiation of appropriate treatment.<sup>14</sup> In older patients with frailty and multimorbidity, LUS can also be used for continuous monitoring of evolving clinical conditions, such as for assessing the response to intravenous diuretic treatment in acute congestive heart failure or pleural effusion.<sup>15</sup> In these complex patients, LUS examination can be finally complemented by ultrasound evaluation of diaphragm thickness and motility, both of which are frequently impaired in older patients with physical frailty and sarcopenia, possibly contributing to the pathophysiology of acute respiratory failure.<sup>16 17</sup>

Delirium is a severe neuropsychiatric condition characterised by an acute and fluctuating change in attention, awareness and other cognitive and perceptual disorders.<sup>18</sup> Importantly, delirium is almost always triggered by underlying acute medical conditions, which determine the release of several inflammatory mediators and other neuroendocrine changes that ultimately lead to brain dysfunction.<sup>19</sup> In older patients, acute respiratory diseases such as pneumonia, acute exacerbations of chronic obstructive pulmonary disease and acute heart failure often present with delirium as the sole symptom, with typical signs like dyspnoea, fever or cough often absent.<sup>20</sup> Studies have shown that delirium affects over 30% of patients requiring non-invasive ventilation for acute respiratory conditions and was a common complication during SARS-CoV-2 pandemic waves.<sup>21 22</sup>

The pathogenesis of delirium is multifactorial and not fully understood. However, it is widely accepted as resulting from the interplay between predisposing factors, such as dementia and frailty,<sup>23 24</sup> and acute stressors such as infections.<sup>19 23</sup>

Currently, no ultrasonographic markers of delirium are established for routine clinical use.<sup>19</sup> However, previous studies have reported an association between interstitial pulmonary involvement detected by lung LUS and elevated inflammatory markers—both known risk factors for delirium.<sup>25 26</sup>

Hence, we propose that subclinical pulmonary abnormalities detectable by LUS, including interstitial syndrome or inflammatory consolidation, may reveal subsequent delirium onset in a selected group of patients. These ultrasonographic findings may likely reflect underlying systemic inflammation and metabolic dysfunctions associated with delirium. Identifying such markers could have important implications, enabling timely interventions and improving clinical outcomes.

Building on these considerations, we hypothesise that LUS patterns on hospital admission could help identify patients at high risk of developing delirium following acute respiratory diseases. Additionally, we hypothesise that LUS findings may be associated with adverse clinical outcomes, including prolonged need of oxygen therapy, non-invasive ventilation and mortality.

## METHODS AND ANALYSIS

### Study design, setting and objectives

A non-sponsored, multicentre, prospective observational study was designed, without involving the use of drugs, experimental procedures or treatments. Bedside LUS is already part of usual clinical practice for the diagnostic workup and clinical management of older patients with acute respiratory symptoms in all the participating centres. The study acronym is ECO-AGE (Exploring the Correlations of lung ultrasound with delirium and other clinical Outcomes in the Acute GERiatric setting).

It will be conducted in seven internal medicine or geriatric wards devoted to the care of acute older patients admitted from emergency departments (EDs) and located in teaching hospitals from eight Italian cities (Monza, Parma, Pisa, Florence, Rome, Ferrara, Ravenna and Forlì). The participating centres share similar ultrasound equipment and expertise, with clinicians certified in clinical ultrasonography and experience in performing thoracic ultrasound. The participating centres belong to the Gruppo di Ricerca sull'Ecografia Toracica nell'Anziano network on thoracic ultrasound in the elderly of the Italian Society of Gerontology and Geriatrics (SIGG). The Monza centre has the role of Coordinator of the study, and the Monza hospital (Fondazione Istituto di Ricovero e Cura a Carattere Scientifico San Gerardo dei Tintori), a public teaching and research institution, is the study sponsor. The key regulatory and scientific information on

the study is summarised in the WHO Minimum Dataset sheet provided as online supplemental file 1.

The primary objective of the study is to investigate the potential association between LUS findings and the occurrence of delirium in older patients hospitalised for acute respiratory diseases.

The secondary objectives of the study are:

- i. To assess the prevalence of the various respiratory conditions identified through LUS.
- ii. To assess the clinical correlations of different LUS patterns and their association with adverse outcomes, including delirium duration, severity of respiratory failure, length of hospital stay and in-hospital mortality.
- iii. To assess the correlation between diaphragm ultrasound parameters and adverse clinical outcomes, including delirium duration, severity of respiratory failure, length of hospital stay and in-hospital mortality.

### Study population

Patients aged  $\geq 65$  years old admitted from emergency room (ER) with acute respiratory complaints or strong clinical suspicion of respiratory illness, and for whom bedside LUS is clinically indicated, will be assessed for eligibility. Exclusion criteria include a diagnosis of delirium during the initial evaluation on admission or ER assessment, terminal illness, patients with a body mass index (BMI)  $\geq 40 \text{ kg/m}^2$  and clinical conditions that may compromise LUS image quality. A more detailed outline of inclusion and exclusion criteria is provided in [table 1](#).

### LUS examination

LUS examinations will be conducted as early as possible following hospital admission, prior to treatment whenever feasible, and in any case within 48 hours, by a research team member with formal ultrasound certification and at least 6 months of LUS experience. Each participating

centre will have a minimum of two qualified operators. Alternatively, LUS may be conducted by medical residents from the research team under the supervision of a certified senior physician with LUS experience.

Evidence indicates that basic LUS skills can be acquired quickly, and that even inexperienced operators can achieve accurate diagnoses of common respiratory illness after only a few supervised examinations.<sup>27–29</sup> To ensure consistency among operators and centres' procedures, a web-based survey featuring multiple LUS videos will evaluate interoperator agreement in interpreting LUS abnormalities. Additionally, to ensure consistency and reproducibility among different centres, a standardised protocol for image acquisition will be implemented. Participants will undergo LUS examination in the sitting position. Assistance from a second operator will be allowed for patients with severe mobility impairments to maintain the sitting position. For bedridden patients, LUS examinations will be performed with passive mobilisation in the sitting position by auxiliary operators when feasible. If required, at the investigators' discretion, LUS will include an assessment of the diaphragm motility and thickness, with patients laying supine. During ultrasonographic evaluation, operator(s) will be blinded to the patient's clinical diagnosis.

Portable ultrasound systems equipped with 3.5–5 MHz convex and 7.5–12 MHz linear probes, available in all the participating centres, will be used. The ultrasound systems will also be supplied with specific settings for pulmonary imaging.

In compliance with the recommendations by Soldati *et al.*<sup>30</sup> each hemithorax will be ideally divided into six regions (posterior inferior, posterior superior, lateral inferior, lateral superior, anterior inferior and anterior superior). Each of the 12 regions will be systematically scanned using both convex and linear probes, in longitudinal and transversal directions in intercostal spaces.

**Table 1** Patient eligibility criteria

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> <li>▶ Age <math>\geq 65</math> years</li> <li>▶ Direct admission from the emergency room or emergency medical services</li> <li>a. Presence of acute respiratory symptoms/signs, including at least one of the following: dyspnoea or cough</li> <li>b. oxygen saturation less than 94%, or respiratory rate <math>\geq 22</math> breaths per minute, or arterial oxygen tension/fractional inspired oxygen <math>&lt; 300</math>)</li> <li>c. clinical suspicion of acute respiratory illness (pneumonia, acute congestive heart failure, pulmonary oedema, acute COPD, pleural effusion, pneumothorax) following a normal routine clinical examination</li> <li>▶ Indication to perform bedside lung ultrasound (LUS) for clinical reasons within 48 hours of admission</li> </ul>	<ul style="list-style-type: none"> <li>▶ Delirium on admission to the medical ward, evaluated with the 4-AT test during baseline comprehensive geriatric assessment</li> <li>▶ Delirium already diagnosed during emergency room or emergency medical service evaluation</li> <li>▶ Refuse to sign the informed consent form or consent to data collection and processing for the study purposes.</li> <li>▶ Terminal illness of any aetiology, with an estimated prognosis of survival not exceeding 3 months.</li> <li>▶ Previous open thoracic or cardiothoracic surgery that technically compromises the quality of LUS images.</li> <li>▶ Refusal to undergo LUS examination, or opposition to examination due to cognitive impairment or psychiatric conditions.</li> <li>▶ Patients with BMI <math>&gt; 40 \text{ kg/m}^2</math>.</li> </ul>

BMI, body mass index; COPD, chronic obstructive pulmonary disease.

**Table 2** Summary of the guidelines for interpretation of LUS findings

Normal LUS*	Abnormal LUS
<p>All of the following must be present:</p> <ul style="list-style-type: none"> <li>▶ Hyperechoic pleural line with sliding movement synchronous with respiration and linear artefacts (A-lines or less than three B-lines in each scanning field).</li> <li>▶ Absence of parenchymal consolidations.</li> <li>▶ Absence of pleural effusions.</li> </ul>	<p>At least one of the following must be present:</p> <ul style="list-style-type: none"> <li>▶ Presence of diffuse vertical comet-tail artefacts (B-lines), indicative of diffuse interstitial syndrome, due to acute congestive heart failure/pulmonary oedema or severe interstitial pneumonia.</li> <li>▶ Presence of focal vertical comet-tail artefacts (B-lines), indicative of mild/moderate interstitial pneumonia or bacterial pneumonia with early-stage consolidations.</li> <li>▶ Presence of parenchymal consolidations with dynamic air bronchogram, indicative of bacterial pneumonia.</li> <li>▶ Presence of parenchymal consolidations with static air bronchogram, indicative of atelectasis, cancer or pulmonary infarction.</li> <li>▶ Presence of subpleural consolidations, indicative of early-stage bacterial pneumonia, mild interstitial pneumonia or chronic pleural abnormalities.</li> <li>▶ Subpleural anechoic flap, indicative of pleural effusion.</li> <li>▶ Absence of pleural line sliding or presence of lung point, indicative of pneumothorax.</li> </ul>
<p>*Normal LUS in a patient with cough, dyspnoea or hypercapnic respiratory failure allows the diagnosis of chronic obstructive pulmonary disease exacerbation. LUS, lung ultrasound.</p>	

The ultrasound images will be interpreted according to the international consensus recommendations,<sup>12</sup> summarised in [table 2](#).

The severity of interstitial syndrome will be graded assessing the number and distribution of B-lines, in accordance with the LUS Score method<sup>30</sup>: a rating of 0–4 will be assigned to each of the 12 examined thoracic regions, and then all rates will be summed to obtain the final score.

In case of pleural effusion, its severity will be estimated by counting the number of intercostal spaces in which the effusion is visible, measuring the maximal depth of the anechoic flap and calculating the Pleural Effusion Score (PEF), a validated semiquantitative method that can be easily applied during LUS without particular training.<sup>31</sup> If pulmonary consolidations are present, their number, location and ultrasound appearance (subpleural consolidations vs parenchymal consolidations with dynamic air bronchogram) will be recorded.

LUS examination may be possibly completed, under the investigator's judgement, with ultrasonographic assessment of diaphragm motility and thickness, following the methodology suggested by the literature<sup>16 17</sup> and briefly outlined in [box 1](#).

In case of diagnostic uncertainty persisting after LUS examination, patients will be referred to a specialist imaging service for consultative ultrasound or traditional radiologic imaging (X-ray or CT), under the clinical judgement of the treating physician.

### Delirium assessment

Delirium will be screened daily during hospital stay using the 4-AT by a physician blind to LUS findings.<sup>32</sup> The 4AT is a widely used and validated test with good sensitivity

and specificity for detecting delirium.<sup>33</sup> It includes an assessment of alertness, an abbreviated mental test, an assessment of attention by recalling months of the year backwards and an assessment of acute changes or fluctuating course. Each item is scored based on the patient's clinical status and responses. The total score categorises patients as follows: possible delirium, either superimposed or not on pre-existing dementia (total score  $\geq 4$ );

### Box 1 Methodology of diaphragm ultrasound assessment

Diaphragm will be visualised with the patient laying supine, by positioning the convex probe in the right hypochondrial region immediately under the ribcage, directing the ultrasound beam upwards as to visualise the liver parenchyma with the gallbladder at the centre of the image. The diaphragmatic cupola will then be visualised as a hyperechoic line separating the liver from the thoracic region. The M-mode function of the ultrasound machine will then be activated to visualise the diaphragmatic excursion in one dimension. The extent of this excursion will be measured on quiet breathing (tidal volume) and on maximal inspiration. A linear probe in B-mode function will then be used to measure diaphragmatic thickness. The probe will be positioned in the 9th or 10th right intercostal space, to identify the curtain sign at the apposition zone (ie, the area of insertion of diaphragm on the thoracic cage). The diaphragm will then be visualised immediately under this zone, as two parallel hyperechoic lines. The M-mode function of the ultrasound machine will be activated again, and the distance between the two hyperechoic lines corresponding to the upper and lower limit of the diaphragm muscle will be then measured on quiet breathing and on maximal inspiration.

Each measure of diaphragm excursion and thickness will be repeated three times by the same operator. The average of each series of measurements will be considered for the analyses.

possible cognitive impairment (total score 1–3) and unlikely delirium (total score 0). If the screening results in a total score  $\geq 4$ , a formal diagnosis of delirium will be made according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria.<sup>18</sup> Delirium duration will be assessed by counting the total number of days when delirium is present. Delirium psychomotor subtypes (ie, hyperactive, hypoactive and mixed) will be assessed using the Delirium Motor Subtype Scale (DMSS) and included in data collected for the study.<sup>34</sup> The DMSS is a scale comprising 11 motor items (4 rating hyperactive and 7 hypoactive symptoms) that demonstrated good correlation with objective motor behaviour measures. It can be administered by any healthcare professional familiar with patient's behaviour and is applicable for assessing symptoms over the previous 24 hours or longer. The symptoms are evaluated as either present or absent, and to meet the subtype criteria, at least two symptoms from either the hyperactive or hypoactive list must be present. Patients meeting criteria for both hyperactive and hypoactive criteria will be classified as having a mixed subtype, while those exhibiting neither will be categorised as having a non-motor subtype.

### Data collection

In addition to data related to ultrasound and delirium assessment, investigators will collect data on age, sex, race, weight, height, BMI, smoking habits, main diagnosis on hospital admission, comorbidities from a prespecified comprehensive list, regular pharmacological therapies. If height measurement is not feasible, BMI will be estimated using the Chumlea formulas adapted for the Italian population.<sup>35</sup>

Mobility performance will be assessed through either questioning or, at the discretion of the centre, using the Cumulated Ambulation Score<sup>36</sup> and Physical Activity Scale for the Elderly.<sup>37</sup> Level of consciousness will be assessed with the modified Richmond Agitation and Sedation scale.<sup>38</sup> Frailty will be assessed on admission with the Clinical Frailty Scale, using the classification tree of Theou *et al*, that proved good reliability even in the hands of relatively inexperienced assessors.<sup>39</sup> Additionally, the Primary Care Frailty Index will be evaluated.<sup>40</sup> Preadmission functional status will be assessed through the Activities of Daily Living (ADL) and instrumental ADL. Cognitive function will be assessed on admission using the Short Portable Mental State Questionnaire<sup>41</sup> and the Informant Questionnaire on Cognitive Decline in the Elderly.<sup>42</sup>

Data collection will also include arterial blood gas analysis parameters and level of oxygen flow administered on admission, and baseline blood test results, including haemoglobin, platelet count, white cell count, creatinine, urea, sodium, potassium, estimated glomerular filtration rate, C reactive protein and procalcitonin. Relevant findings from chest X-rays or CT performed in the ER or during hospital stay will be recorded.

### Endpoints

The occurrence of delirium during hospitalisation is the primary endpoint of the study. Secondary endpoints include: (1) the prevalence of acute heart failure, pneumonia, pneumothorax and pleural effusion; (2) the duration of delirium (measured in days), duration of oxygen therapy, arterial oxygen tension/fractional inspired oxygen ratio from blood gas analyses, need for and duration of non-invasive ventilation, length of hospital stay and in-hospital mortality and (3) the correlation between ultrasound measurements of diaphragm excursion and thickness as well as the listed adverse outcomes. All these endpoints will be assessed by collecting relevant information from clinical records. Additionally, readmissions and mortality within 3 months from discharge will also be assessed as secondary endpoints, through a follow-up phone call to the patient or their caregiver. The correlation between LUS abnormalities and the LUS score, and each of the primary and secondary endpoints will be examined.

### Sample size

Based on a previous systematic review and meta-analysis,<sup>43</sup> we expect a 20% delirium prevalence in older patients with acute respiratory failure. Assuming a 15% difference in the proportion of patients experiencing delirium between those with normal and abnormal LUS patterns, and a power of 80% and a level of significance of 0.05, a minimum sample size of 420 patients was estimated, including a 10% drop-out rate. This sample size would enable the detection of a statistically significant difference of 15% in the proportion of patients experiencing delirium between the two groups.

### Data management

Data will be collected on electronic case record forms (CRFs) hosted on the platform RedCap licensed to the SIGG. The identity of participants will be pseudoanonymised on electronic CRFs, with only the head investigators of each centre able to match ID codes in the database to individual identities.

Data quality monitoring will be managed by the coordinating centre (Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy). Regular meetings will be held between data management personnel and head investigators of each participating centre, to address and solve data quality issues. Interim statistical analyses may be done once 50% of the planned sample size is reached.

In compliance with the Good Clinical Practice (GCP) rules, the guidelines of the Italian Data Protection Authority and the General Data Protection Regulation of the European Union, accession to data will be granted only to authorised personnel explicitly delegated by each centre's principal investigator or to officers conducting monitoring procedures or GCP inspections arranged by regulatory authorities.

### Statistical analysis

The statistical analysis will be performed using SPSS software (V.3.5.2; statistical package for social science V.27;



IBM) and R studio software (V.4.2.2, The R Foundation for Statistical Computing, Vienna, Austria). Data will be presented as frequency percentiles or mean and SD. Differences between the means of two continuous variables will be evaluated using Student's t-test or one-way analysis of variance in the case of parametric continuous variables  $>2$ , while differences between categorical variables will be evaluated using the  $\chi^2$  test. Linear and logistic regression analysis will be carried out to calculate ORs and 95% CIs referring to the association between delirium (dependent variable, both as continuous variable of the 4-AT or categorical variable) and abnormal LUS (independent variable). A multivariate analysis will be performed accounting for confounders (sex, age, length of hospital stays) and established markers of clinical severity, including the National Early Warning Score 2 (NEWS2) score, comorbidity burden and frailty status. Results will be further stratified by frailty degree and age tertiles. A sensitivity analysis will also be conducted to assess whether the timing of LUS in relation to treatment initiation influences its association with delirium. Furthermore, to explore the potential mediating role of illness severity and frailty in the association between LUS findings and delirium, a mediation analysis will be performed using appropriate regression-based methods, adjusting for relevant covariates such as age, sex, comorbidity burden and baseline cognitive status. In the case of missing data less than 5%, mathematical imputation calculations will be performed. A  $p \leq 0.05$  will be considered statistically significant.

### Patient and public involvement

None.

### ETHICS AND DISSEMINATION

This study protocol has been reviewed and approved by the Ethics Committee of the Coordinating Centre (Comitato Etico Territoriale Lombardia 3, Lombardy Region, Italy) under the ID 4369\_20.03.2024\_M. Local Ethics Committee approval has also been obtained by each collaborating centre. The study will be conducted in compliance with the Declaration of Helsinki and its later amendments. Due to the study's observational design, no risk of harm is envisaged for participants. Thoracic ultrasound is a safe non-invasive procedure that is already in use in each of the participating centres for the clinical management of acute respiratory illness, so the conduction of the study implies no experimental procedures in addition to usual clinical practice. No additional patient visits or examinations are planned for the study.

Participation in the study will only be offered to individuals who meet all the inclusion criteria and none of the exclusion criteria. Information on the study aims, objectives, methodology, risks and benefits for participants will be provided by investigators both orally and in written form through a study-specific information sheet. Eligible patients will be given time to contemplate their

participation, allowing them to seek clarification from investigators before signing the informed consent form and consent to data treatment form.

The findings of the study will be shared with all the investigators of each participating centre. Results will be presented in scientific meetings and public clinical conferences. The study will result in at least one publication in an international peer-reviewed medical journal.

### DISCUSSION

This study will improve the understanding of the prognostic implications of LUS findings in older patients hospitalised with acute respiratory illness. Previous research has primarily focused on the diagnostic utility of LUS and its integration into respiratory failure management pathways.<sup>44</sup> However, LUS can provide important information also on the pathophysiological alterations of respiration,<sup>44</sup> which are often multifactorial in older individuals with frailty and multimorbidity.<sup>45</sup> Establishing a potential correlation between LUS parameters—such as LUS score or PEF score—and patient outcomes—including mortality, length of oxygen supplementation, need for non-invasive ventilation and length of hospitalisation—could support the role of LUS in prognostic evaluation, integrating the findings of the comprehensive geriatric assessment.

The potential role of LUS findings in identifying the risk of delirium in older patients with respiratory illness may be particularly relevant. Delirium is increasingly recognised as a marker of frailty,<sup>46</sup> and its occurrence during hospitalisation is associated with increased mortality risk, functional worsening and cognitive impairment.<sup>47 48</sup> However, reliable biomarkers of delirium risk are still lacking in everyday practice.<sup>49</sup> In this regard, LUS may provide a practical, non-invasive tool for early recognition of patients at risk during hospitalisation. Although all older patients should be monitored for delirium, early identification of those at higher risk—for example, based on LUS and frailty—may support targeted preventive strategies and prioritisation in resource-limited settings.

Our study has some limitations. The non-interventional design does not allow us to assess the impact of LUS implementation on patient-related outcomes or address the cost-effectiveness of the technique. Furthermore, LUS is an operator-dependent technique, which may limit the generalisability of our findings to clinical and organisational settings where point-of-care ultrasound is not part of standard practice. However, the relatively fast learning curve of LUS technique should be considered, as it could contribute to its wider diffusion. The rigorous LUS examination protocol and interoperator agreement assessment can further mitigate this concern. It is also important to note that aging itself can be associated with LUS findings which may be mistakenly interpreted as pathological, when they actually represent artifacts related to physiological lung aging.<sup>50</sup> For example, older adults may exhibit absent A-lines or non-confluent B-lines

on LUS images, even in the absence of acute respiratory illness.<sup>51</sup> This could introduce a potential source of bias in the association between LUS findings and clinical outcomes, including delirium. Finally, we acknowledge that the exclusion of patients with severely limited acoustic windows may introduce a selection bias. Specifically, this may lead to an overestimation of LUS performance by systematically excluding cases in which image acquisition is technically challenging. While such exclusions are necessary to ensure adequate image quality and diagnostic reliability, they may limit the external validity of our findings and should be taken into account when interpreting the generalisability of the results.

In conclusion, this study has the potential of opening new avenues for clinical applications of LUS in detecting delirium risk and may provide indications for further implementation of POCUS in older patients.

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#### REFERENCES

- Volpicelli G, Elbarbary M, Blaivas M, *et al*. International evidence-based recommendations for point-of-care lung ultrasound. *Intensive Care Med* 2012;38:577–91.
- Demi L, Wolfram F, Klersy C, *et al*. New International Guidelines and Consensus on the Use of Lung Ultrasound. *J Ultrasound Med* 2023;42:309–44.
- Díaz-Gómez JL, Mayo PH, Koenig SJ. Point-of-Care Ultrasonography. *N Engl J Med* 2021;385:1593–602.
- Staub LJ, Mazzali Biscaro RR, Kaszubowski E, *et al*. Lung Ultrasound for the Emergency Diagnosis of Pneumonia, Acute Heart Failure, and Exacerbations of Chronic Obstructive Pulmonary Disease/Asthma in Adults: A Systematic Review and Meta-analysis. *J Emerg Med* 2019;56:53–69.
- Islam M, Levitus M, Eisen L, *et al*. Lung Ultrasound for the Diagnosis and Management of Acute Respiratory Failure. *Lung* 2020;198:1–11.
- Mojoli F, Bouhemad B, Mongodi S, *et al*. Lung Ultrasound for Critically Ill Patients. *Am J Respir Crit Care Med* 2019;199:701–14.
- Chiu L, Jairam MP, Chow R, *et al*. Meta-Analysis of Point-of-Care Lung Ultrasonography Versus Chest Radiography in Adults With Symptoms of Acute Decompensated Heart Failure. *Am J Cardiol* 2022;174:89–95.
- Chan KK, Joo DA, McRae AD, *et al*. Chest ultrasonography versus supine chest radiography for diagnosis of pneumothorax in trauma patients in the emergency department. *Cochrane Database Syst Rev* 2020;7:CD013031.
- Kameda T, Mizuma Y, Taniguchi H, *et al*. Point-of-care lung ultrasound for the assessment of pneumonia: a narrative review in the COVID-19 era. *J Med Ultrasonics* 2021;48:31–43.
- Ticinesi A, Scarlata S, Nouvenne A, *et al*. The Geriatric Patient: The Ideal One for Chest Ultrasonography? A Review From the Chest Ultrasound in the Elderly Study Group (GRETA) of the Italian Society of Gerontology and Geriatrics (SIGG). *J Am Med Dir Assoc* 2020;21:447–54.
- Linsalata G, Okoye C, Antognoli R, *et al*. Pneumonia Lung Ultrasound Score (PLUS): A New Tool for Detecting Pneumonia in the Oldest Patients. *J Am Geriatr Soc* 2020;68:2855–62.
- Ticinesi A, Lauretani F, Nouvenne A, *et al*. Lung ultrasound and chest x-ray for detecting pneumonia in an acute geriatric ward. *Medicine (Baltimore)* 2016;95:e4153.
- Esayag Y, Nikitin I, Bar-Ziv J, *et al*. Diagnostic value of chest radiographs in bedridden patients suspected of having pneumonia. *Am J Med* 2010;123:88.



- 14 Laursen CB, Sloth E, Lassen AT, *et al.* Point-of-care ultrasonography in patients admitted with respiratory symptoms: a single-blind, randomised controlled trial. *Lancet Respir Med* 2014;2:638–46.
- 15 Rivas-Lasarte M, Álvarez-García J, Fernández-Martínez J, *et al.* Lung ultrasound-guided treatment in ambulatory patients with heart failure: a randomized controlled clinical trial (LUS-HF study). *Eur J Heart Fail* 2019;21:1605–13.
- 16 Siniscalchi C, Nouvenne A, Cerundolo N, *et al.* On Behalf Of The Parma Post-Graduate Specialization School In Emergency-Urgency Medicine Interest Group On Thoracic Ultrasound. Diaphragm Ultrasound in Different Clinical Scenarios: A Review with a Focus on Older Patients. *Geriatrics (Basel)* 2024;9:70.
- 17 Scarlata S, Di Matteo E, Finamore P, *et al.* Diaphragmatic ultrasound evaluation in acute heart failure: clinical and functional associations. *Intern Emerg Med* 2024;19:705–11.
- 18 *Diagnostic and statistical manual of mental disorders: fifth edition text revision DSM-5-TRTM.*
- 19 Wilson JE, Mart MF, Cunningham C, *et al.* Delirium. *Nat Rev Dis Primers* 2020;6:90.
- 20 Lipowski ZJ. Delirium in the elderly patient. *N Engl J Med* 1989;320:578–82.
- 21 Trevisan C, Remelli F, Fumagalli S, *et al.* COVID-19 as a Paradigmatic Model of the Heterogeneous Disease Presentation in Older People: Data from the GeroCovid Observational Study. *Rejuvenation Res* 2022;25:129–40.
- 22 Fu X, Wang L, Wang G, *et al.* Delirium in elderly patients with COPD combined with respiratory failure undergoing mechanical ventilation: a prospective cohort study. *BMC Pulm Med* 2022;22:266.
- 23 Ormseth CH, LaHue SC, Oldham MA, *et al.* Predisposing and Precipitating Factors Associated With Delirium: A Systematic Review. *JAMA Netw Open* 2023;6:e2249950.
- 24 Bellelli G, Triolo F, Ferrara MC, *et al.* Delirium and frailty in older adults: Clinical overlap and biological underpinnings. *J Intern Med* 2024;296:382–98.
- 25 Fu B, Zhang P, Zhang J. Diagnosis and Prognosis Evaluation of Severe Pneumonia by Lung Ultrasound Score Combined with Serum Inflammatory Markers. *Mediterr J Hematol Infect Dis* 2023;15:e2023057.
- 26 Franchi R, Okoye C, Morelli V, *et al.* Utility of lung ultrasound in selecting older patients with hyperinflammatory phase in COVID-19 pneumonia. A monocentric, cross-sectional pilot study. *JGG* 2023;71:1–7.
- 27 See KC, Ong V, Wong SH, *et al.* Lung ultrasound training: curriculum implementation and learning trajectory among respiratory therapists. *Intensive Care Med* 2016;42:63–71.
- 28 Imanishi J, Iwasaki M, Ujiro S, *et al.* Accuracy of lung ultrasound examinations of residual congestion performed by novice residents in patients with acute heart failure. *Int J Cardiol* 2024;395:131446.
- 29 Breunig M, Hanson A, Huckabee M. Learning curves for point-of-care ultrasound image acquisition for novice learners in a longitudinal curriculum. *Ultrasound J* 2023;15:31.
- 30 Soldati G, Smargiassi A, Inchingolo R, *et al.* Proposal for International Standardization of the Use of Lung Ultrasound for Patients With COVID-19: A Simple, Quantitative, Reproducible Method. *J Ultrasound Med* 2020;39:1413–9.
- 31 Lindner M, Thomas R, Claggett B, *et al.* Quantification of pleural effusions on thoracic ultrasound in acute heart failure. *Eur Heart J Acute Cardiovasc Care* 2020;9:513–21.
- 32 4AT - Rapid Clinical Test for Delirium Detection. 4AT - rapid clinical test for delirium. Available: <https://www.the4at.com> [Accessed 8 Nov 2023].
- 33 Shenkin SD, Fox C, Godfrey M, *et al.* Delirium detection in older acute medical inpatients: a multicentre prospective comparative diagnostic test accuracy study of the 4AT and the confusion assessment method. *BMC Med* 2019;17:138.
- 34 Meagher D, Moran M, Raju B, *et al.* A new data-based motor subtype schema for delirium. *J Neuropsychiatry Clin Neurosci* 2008;20:185–93.
- 35 Donini LM, de Felice MR, de Bernardini L, *et al.* Prediction of stature in the Italian elderly. *J Nutr Health Aging* 2000;4:72–6.
- 36 Kristensen MT, Jakobsen TL, Nielsen JW, *et al.* Cumulated Ambulation Score to evaluate mobility is feasible in geriatric patients and in patients with hip fracture. *Dan Med J* 2012;59:A4464.
- 37 Washburn RA, McAuley E, Katula J, *et al.* The physical activity scale for the elderly (PASE): evidence for validity. *J Clin Epidemiol* 1999;52:643–51.
- 38 Chester JG, Beth Harrington M, Rudolph JL, *et al.* Serial administration of a modified Richmond Agitation and Sedation Scale for delirium screening. *J Hosp Med* 2012;7:450–3.
- 39 Theou O, Pérez-Zepeda MU, van der Valk AM, *et al.* A classification tree to assist with routine scoring of the Clinical Frailty Scale. *Age Ageing* 2021;50:1406–11.
- 40 Vetrano DL, Zucchelli A, Onder G, *et al.* Frailty detection among primary care older patients through the Primary Care Frailty Index (PC-FI). *Sci Rep* 2023;13:3543.
- 41 Pfeiffer E. A short portable mental status questionnaire for the assessment of organic brain deficit in elderly patients. *J Am Geriatr Soc* 1975;23:433–41.
- 42 Harrison JK, Stott DJ, McShane R, *et al.* Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) for the early diagnosis of dementia across a variety of healthcare settings. *Cochrane Database Syst Rev* 2016;11:CD011333.
- 43 Shao SC, Lai CC, Chen YH, *et al.* Prevalence, incidence and mortality of delirium in patients with COVID-19: a systematic review and meta-analysis. *Age Ageing* 2021;50:1445–53.
- 44 Scarlata S, Okoye C, Zotti S, *et al.* Advancing healthcare through thoracic ultrasound research in older patients. *Ageing Clin Exp Res* 2023;35:2887–901.
- 45 Occhipinti M, Larici AR, Bonomo L, *et al.* Aging Airways: between Normal and Disease. A Multidimensional Diagnostic Approach by Combining Clinical, Functional, and Imaging Data. *Ageing Dis* 2017;8:471–85.
- 46 Bellelli G, Moresco R, Panina-Bordignon P, *et al.* Is Delirium the Cognitive Harbinger of Frailty in Older Adults? A Review about the Existing Evidence. *Front Med* 2017;4:188.
- 47 Mazzola P, Tassistro E, Di Santo S, *et al.* The relationship between frailty and delirium: insights from the 2017 Delirium Day study. *Age Ageing* 2021;50:1593–9.
- 48 Gandossi CM, Zambon A, Ferrara MC, *et al.* Frailty and post-operative delirium influence on functional status in patients with hip fracture: the GIOG 2.0 study. *Ageing Clin Exp Res* 2023;35:2499–506.
- 49 Lozano-Vicario L, Garcia-Hermoso A, Cedeno-Veloz BA, *et al.* Biomarkers of delirium risk in older adults: a systematic review and meta-analysis. *Front Aging Neurosci* 2023;15:1174644.
- 50 Ciccacese F, Chiesa AM, Feletti F, *et al.* The Senile Lung as a Possible Source of Pitfalls on Chest Ultrasonography and Computed Tomography. *Respiration* 2015;90:56–62.
- 51 Chiesa AM, Ciccacese F, Gardelli G, *et al.* Sonography of the normal lung: Comparison between young and elderly subjects. *J Clin Ultrasound* 2015;43:230–4.