

## Original Article

# Role of Lung Ultrasound for Diagnosis of Acute Respiratory Distress Syndrome in Intensive Care Unit

Mayisha Afifa<sup>1\*</sup>, Md Nasir Uddin Ahmed<sup>2</sup>, Mehnaz Ferdous<sup>3</sup>, Md. Mozaffer Hossain<sup>4</sup>

DOI: <https://doi.org/10.3329/bccj.v10i2.62202>

## Abstract:

**Background:** Acute respiratory distress syndrome (ARDS) necessitates rapid recognition for early intervention and favourable outcomes. The Berlin Definition may not be always helpful for ARDS diagnosis in critically ill patients, because of the inability to acquire adequate information from bedside chest X-rays. Lung ultrasound may be a reasonable alternative to chest X-ray for the identification of ARDS, but the effectiveness of lung ultrasound in ARDS diagnosis remains uncertain.

**Objective:** To explore the efficacy of lung ultrasound (LUS) for the diagnosis of ARDS in ICU.

**Methods:** This observational, cross-sectional study was conducted in the ICU, DMCH at the Department of Anaesthesia, Analgesia, Palliative, and Intensive Care Medicine from March 2017 to June 2019. Lung ultrasound was performed on acute hypoxic respiratory failure patients requiring mechanical ventilation. chest X-ray, arterial blood gas analysis, and echocardiography were done to fulfill the Berlin Definition. ARDS was diagnosed by the 'CXR-based Berlin Definition' and 'LUS-based Berlin Definition'.

**Results:** A total of 141 patients were assessed. Their median age was 35 years. Primary diagnoses were sepsis, pulmonary oedema, pneumonia, and trauma. A total of 62 (43.97%) patients fulfilled 'CXR-based Berlin Definition' and a total of 69 (48.93%) patients were diagnosed as ARDS by 'LUS-based Berlin Definition'. Considering the 'CXR-based Berlin Definition' as the reference standard, the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of 'LUS-based Berlin Definition' were 90.3%, 83.5%, 81.2%, 91.7%, and 86.5% respectively.

**Conclusion:** Lung ultrasound can be an effective tool for the diagnosis of ARDS in the intensive care unit.

**Keywords:** Acute respiratory distress syndrome, ARDS, lung ultrasound, LUS, ICU, critically ill.

## Introduction

Acute respiratory distress syndrome (ARDS) is a common, life-threatening disease in the intensive care unit (ICU), characterized by acute inflammatory lung injury, increased pulmonary vascular permeability, and loss of aerated lung tissue<sup>1</sup>. Clinically, it presents with acute hypoxemic respiratory failure and bilateral radiographic infiltrates with no clinical evidence of cardiogenic pulmonary oedema<sup>2</sup>. It results in increased use of critical care resources and healthcare costs<sup>3</sup>, as well as high mortality, about 40%, despite advances in specific therapy<sup>1</sup>. This mortality and morbidity can be improved by implementing early lung-protective

ventilation strategies<sup>4</sup>. Therefore, rapid, appropriate diagnosis of ARDS is very crucial to ensure optimum, life-saving management. To diagnose ARDS, the new 'Berlin Definition'<sup>5</sup> is followed, which consists of four elements: a) Timing- within one week of a known clinical insult or new or worsening respiratory symptoms; b) Chest imaging (chest radiograph/ computed tomography scan)- Bilateral opacities- not fully explained by effusions, lobar/lung collapse or nodules; c) Origin of oedema- Respiratory failure, not fully explained by cardiac failure or fluid overload; need objective assessment (e.g., echocardiography) to exclude hydrostatic oedema if no risk factor present; d) Oxygenation- Mild: PaO<sub>2</sub>/FiO<sub>2</sub> 200 to 300 mmHg with PEEP or CPAP ≥5 cmH<sub>2</sub>O; Moderate: 100 to 200 mmHg with PEEP ≥5 cmH<sub>2</sub>O; Severe: ≤100 mmHg with PEEP or CPAP ≥5 cmH<sub>2</sub>O.

However, applying the 'Berlin Definition' to diagnose ARDS at the bedside can be a great challenge in critically ill patients because of the limitations of conventional lung imaging modalities<sup>6</sup>. Thoracic CT scan has the disadvantages of intra-hospital transportation risk, high cost, and radiation hazard; and cannot be used routinely<sup>7</sup>. The sensitivity and specificity of portable chest X-Ray (CXR) to detect pulmonary abnormalities of ARDS are both approximately 70%, suggesting a high probability of incorrect diagnosis<sup>8</sup>. Although it is the daily reference for lung imaging in an ICU<sup>7,8</sup>, technical limitations in the supine position, suboptimal

1. Specialist, Dept. of Critical Care Medicine, United Hospital Ltd., Dhaka, Bangladesh
2. Assistant Professor, Dept. of Critical Care Medicine, Anwar Khan Modern Medical College & Hospital, Dhaka, Bangladesh
3. Specialist, Dept. of Critical Care Medicine, United Hospital Ltd., Dhaka, Bangladesh
4. Professor and Head, Department of Anaesthesia, Analgesia, Palliative & Intensive Care Medicine, Dhaka Medical College Hospital, Dhaka, Bangladesh

## \*Corresponding Author:

Dr. Mayisha Afifa  
Specialist, Dept of Critical Care Medicine  
United Hospital Ltd, Dhaka, Bangladesh  
Email: [mayisha0607@gmail.com](mailto:mayisha0607@gmail.com)

exposure, and poor quality of bedside anteroposterior chest radiographs may result in mistaken assessment and high interobserver variability<sup>6</sup>. All these factors often result in inaccurate diagnosis and delayed or under-treatment of ARDS patients. Moreover, in some resource-limited ICUs where CT scan or bedside CXR facilities are not available, dependence on these traditional tools may underestimate the incidence of ARDS<sup>1</sup>. Bellani et al. (2016) found in their study that ARDS continues to be underdiagnosed by ICU clinicians, even in the era of the Berlin Definition, leading to increased mortality and morbidity<sup>1</sup>. Thus, an alternate, readily available, highly sensitive and specific tool should be taken into account for the detection of ARDS in ICU.

Fortunately, nowadays the use of clinician-performed, point-of-care ultrasound in ICUs has become popular worldwide as a novel imaging modality, boosting the diagnostic capacity<sup>7,9</sup>. Ultrasound assessment by non-radiologists is increasing because of bedside availability, portability, feasibility, cost-effectiveness, reproducibility of images, and versatility of ultrasound machines<sup>10</sup>. As a radiation-free, non-invasive, real-time imaging modality, LUS offers advantages over CXR<sup>11</sup>. According to 'Bedside Lung Ultrasound in Emergency (BLUE)'-protocol for the immediate diagnosis of acute respiratory failure, the presence of diffuse 'ultrasound interstitial syndrome (UIS)' is needed for the diagnosis of ARDS. UIS correlates with a 'B-line' pattern (vertical artifacts) obliterating 'A-lines' (horizontal artifacts). After brief training, these A-line and B-line patterns have proven to be easily distinguished by a bedside clinician by using LUS<sup>9</sup>. Therefore, several studies<sup>6,9,13,14</sup> have been conducted worldwide to assess the role of lung ultrasound in recognizing ARDS. They found in their study that LUS may be useful to screen for or rule out, pulmonary abnormalities consistent with ARDS at the point of care<sup>9,13</sup> and can be a reasonable alternative to chest radiography<sup>15</sup> and thoracic CT<sup>6</sup> to detect interstitial syndrome of ARDS in ICU. However, most of these studies compared only the efficacy of imaging modalities (LUS, CXR, and CT) to detect the lung infiltrates consistent with ARDS; but apart from a few studies<sup>15,16</sup>, the use of LUS as the imaging modality in Berlin Definition instead of CXR has not yet been systematically studied. In Bangladesh, Leopold et al. (2018) studied the benefits of lung ultrasound to detect ARDS in malaria and sepsis patients in general medical wards only<sup>17</sup>. There is no such study on ICU patients in our country. So, the current study was designed to evaluate the role of lung ultrasound in the diagnosis of ARDS in the ICU. The result obtained from this study might help critical care physicians to diagnose ARDS rapidly & precisely, and thus influence patient management and outcome.

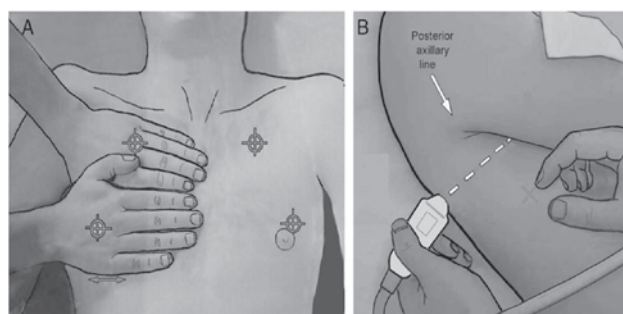
### Materials and methods

This observational, cross-sectional study was carried out in the Department of Anaesthesia, Analgesia, Palliative & Intensive Care Unit, Dhaka Medical College Hospital from March 2017 to June 2019. Before proceeding to collect data, the investigators received 10 hours of point-of-care ultrasound training, which included a demonstration of ultrasound procedures, followed by individual assessment of patients

with different lung diseases by the investigator. Study patients were selected based on the following inclusion & exclusion criteria and their demographics & relevant clinical data were recorded.

- **Inclusion criteria:** Patients with age  $\geq 18$  years, acute hypoxic respiratory failure (onset within one week of a known clinical insult or new/worsening respiratory symptoms) patients requiring invasive mechanical ventilation
- **Exclusion criteria:** Patients with any structural chest wall deformity, flail chest, burn over the chest, any chest surgery, large dressing over the chest, subcutaneous emphysema- impairing ultrasound access; pre-existing lung parenchymal or airway disease; pregnant patients

Bedside evaluation of the lung was performed with a SonoSite M- turbo ultrasound machine (Fujifilm Sonosite Inc., USA), using a 1-5 MHz phased-array probe. The BLUE protocol was followed and six regions underneath six "BLUE" points, three points at each side were evaluated for the presence of B-lines, keeping the patients in the supine position. The "BLUE" points were identified by keeping two hands, on the study patient's body as follows: the little finger of one hand just below the clavicle, fingertips at midline, and another hand just below the upper hand (thumbs excluded). The "upper BLUE-point" corresponded to the middle of the upper hand. The "lower BLUE-point" corresponded to the middle of the lower palm. The posterolateral alveolar and pleural syndrome (PLAPS)-point was the intersection of two lines: a horizontal line continuing from the lower BLUE-point posteriorly and the vertical posterior axillary line<sup>12</sup> (Figure 1).



**Figure 1. A & B. The Bedside Lung Ultrasound in Emergency (BLUE)**

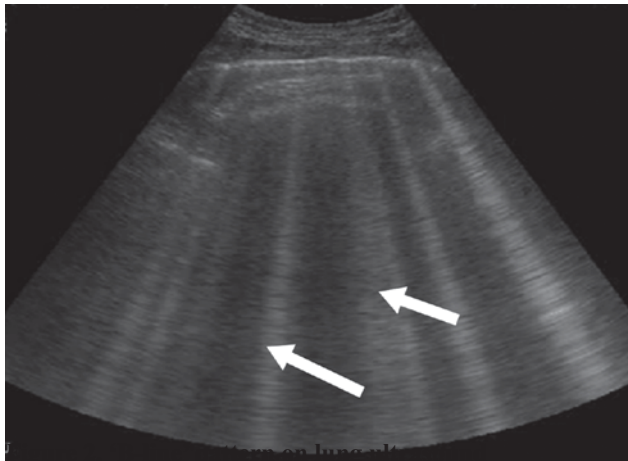
**Points. A. Upper & Lower 'BLUE' points. B. The 'PLAPS' point.<sup>12</sup>**

After the USG procedure, a portable chest radiograph was obtained on the same day, within the shortest possible time to reduce the time-dependent change of the findings. Bedside echocardiography using the same ultrasound machine and ABG analysis was done for all patients.

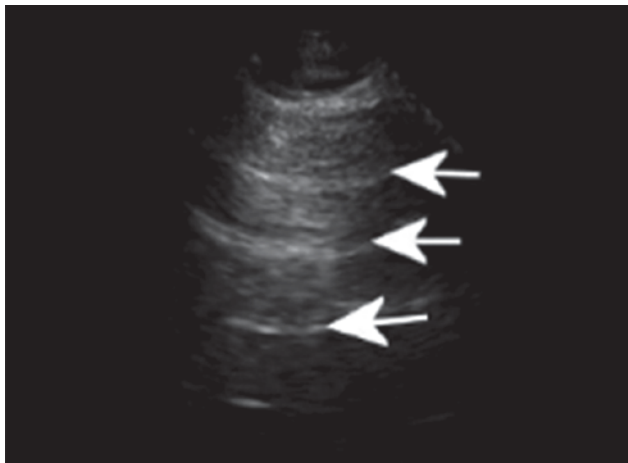
- **Diagnosis of ARDS:** In our study, ARDS was diagnosed in two ways: using the Berlin Definition with chest radiography (CXR-based Berlin Definition) and using lung ultrasound as an imaging modality in Berlin Definition (LUS-based Berlin Definition). The CXR-based 'Berlin Definition' was set as the "Gold

standard' for ARDS diagnosis and the diagnostic accuracy of LUS was compared to it. For both definitions, clinical as well as objective assessment by echocardiography was done to exclude hydrostatic oedema (heart failure and fluid overload). Patients with PEEP  $\geq$ 5 cm H<sub>2</sub>O, having PaO<sub>2</sub>/FiO<sub>2</sub>  $\leq$ 300 mmHg, were considered to fulfill the oxygenation criteria. Patients diagnosed by CXR-based 'Berlin Definition' were classified into mild, moderate, and severe ARDS according to the oxygenation criteria.

For 'CXR-based Berlin Definition', the presence of bilateral opacities in chest X-ray, not fully explained by pleural effusions, lobar/lung collapse, or nodules, was considered as the imaging criterion to detect ARDS. For 'LUS-based Berlin Definition', at least one region of each hemithorax had to be affected by multiple B lines (three B lines or more per rib space) on lung ultrasound to fulfill the imaging criterion<sup>15</sup> (Figure 2). The 'B- line' pattern is 'an elementary signature of the interstitial syndrome,' which can be described by seven criteria. It is always a long comet-tail artifact, arising from the pleural line, moves with lung sliding, and extends up to the edge of the screen. It is well defined, hyperechoic, laser-like line, obliterating the A-lines<sup>12</sup>.



(hyperechoic, vertical lines, shown by arrows)



horizontal lines, shown by arrows)

In a region where ultrasound imaging was difficult to interpret and counting of B- lines was confusing, the region was considered to have A- lines (Figure 3). The 'A-line' pattern is characterized by horizontal reflection artifacts of the pleural line deep into the lung and is seen with alveoli that are physiologically filled with air.

**Statistical analysis**

Statistical analyses were carried out by using the 'Statistical Package for Social Science' (SPSS) version 22.0 [International Business Machines (IBM) Corporation]. Continuous data were expressed as mean  $\pm$  standard deviation if normally distributed and as median (IQR) if not normally distributed. Categorical variables were expressed by frequency and percentage. The significance level was set at p <0.05 in all cases. To make out the relation between the binary diagnostic test (CXR and LUS) and the presence or absence of ARDS, a 2 X 2 contingency table was constructed. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of lung ultrasound to diagnose ARDS were then calculated.

**Results**

A total of 141 patients with acute respiratory failure, who fulfilled the inclusion criteria were selected as the study population. The findings of the study obtained from data analysis are presented below.

The median age of the study participants was 35 years (IQR 25-46) (Table I). 51.1% of them were female. The commonest comorbidity among the study subjects was hypertension (25.5%), followed by DM (17%). Many patients had more than one co-morbidities. 31.9% of the patients were smokers.

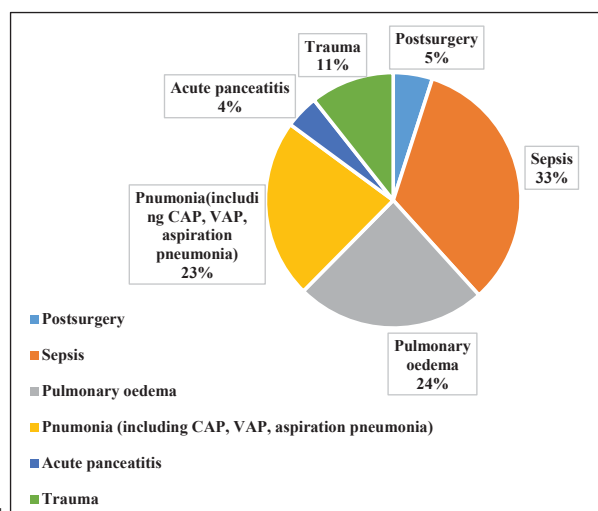
**Table I: Study patients characteristics (N=141)**

Characteristics	Frequency, (%)
Age in years, median[IQR]	35 [25-46]
Gender	
Male	69 (48.9)
Female	72 (51.1)
Pre-existing co-morbidities	
Hypertension	36 (25.5)
Diabetes Mellitus	24 (17.0)
Coronary Artery Disease	12 (8.5)
Chronic/end-stage renal failure	8 (5.7)
Cerebrovascular Disease	6 (4.3)
No comorbidities	55 (39.0)
History of smoking	
Smoker	45 (31.9)
Non-smoker	96 (68.1)

Within () parentheses, percentage (%) over the row in total

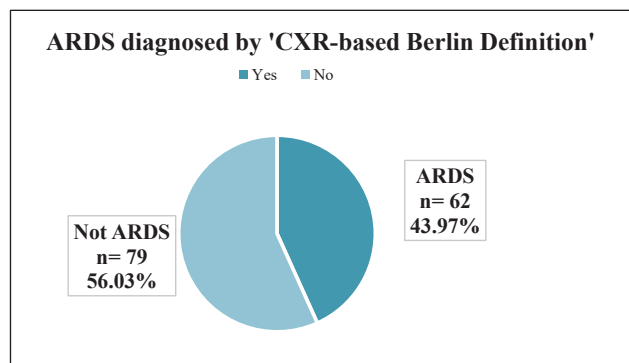
Within [] parentheses, interquartile range (IQR)

Figure 4. shows the primary diagnoses of the study patients. The most common primary diagnoses of study patients during ultrasound assessment were sepsis (33%), pulmonary oedema (24%), and pneumonia (23%). Most of them had multiple diagnoses at the same time.



**Figure 4: Distribution of study patients by primary diagnosis (N=141).**

Figure 5. shows the distribution of study patients diagnosed as ARDS by ‘CXR-based Berlin Definition’. Sixty-two (43.97%) patients were diagnosed as cases of ARDS by ‘CXR-based Berlin Definition’. Among these 62 ARDS patients, the majority had moderate ARDS (48.4%). Their median PaO<sub>2</sub>/FiO<sub>2</sub>, median SpO<sub>2</sub>, and median PEEP were 138.6 mm Hg, 97%, and 12 cm H<sub>2</sub>O respectively ( Table II).



**Figure 5. Distribution of study patients by the presence of ARDS diagnosed by ‘CXR-based Berlin Definition’ (N=141).**

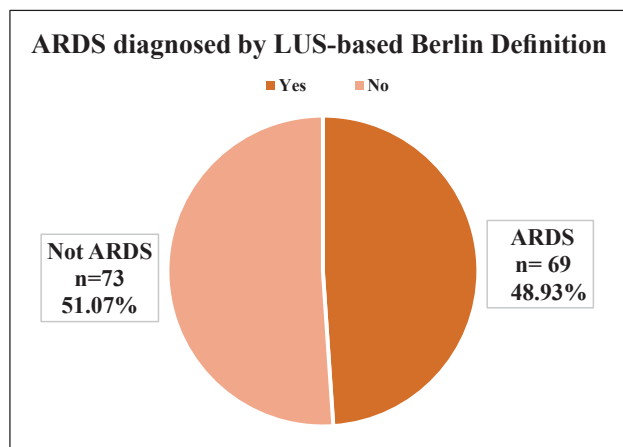
**Table II. Characteristics of ARDS patients diagnosed by ‘CXR-based Berlin Definition’ (n=62)**

Characteristics	Frequency, (%)
Severity of ARDS	
Mild	9 (14.5)
Moderate	30 (48.4)
Severe	23 (37.1)
PaO <sub>2</sub> /FiO <sub>2</sub> , median [IQR] (mm Hg)	138.6 [85.9- 178.3]

SpO <sub>2</sub> , median [IQR] (%)	97 [93.5-99.25]
PEEP, median [IQR] (cm H <sub>2</sub> O)	12 [8- 14]

Within () parentheses, percentage (%) over the row in total  
Within [] parentheses, interquartile range (IQR)

**Figure 6. shows the distribution of study patients diagnosed as ARDS by ‘LUS-based Berlin Definition’. Sixty-nine (48.93%) patients were diagnosed with ARDS by ‘LUS-based Berlin Definition’.**



**Figure 6. Distribution of study patients by the presence of ARDS diagnosed by ‘LUS-based Berlin Definition’ (N= 141)**

Out of 62 study patients, diagnosed by ‘CXR-based Berlin Definition’ as ARDS, ‘LUS-based Berlin Definition’ could diagnose 56 patients correctly as ARDS and missed the diagnosis in six patients. 69 study patients were excluded for ARDS by ‘CXR-based Berlin Definition’. ‘LUS-based Berlin Definition’ could correctly exclude ARDS in 66 patients and falsely diagnose 13 patients as ARDS (Table III).

**Table III. The diagnosis of ARDS by ‘CXR-based Berlin Definition’ & ‘LUS-based Berlin Definition’ (N=141)**

LUS-based Berlin Definition	CXR-based Berlin Definition		Total
	ARDS	Not ARDS	
ARDS	56 (TP)	13 (FP)	69
Not ARDS	6 (FN)	66 (TN)	72
Total	62	79	141

True positive (TP) =56, False positive (FP) = 13, False negative (FN) = 6,

True negative (TN) = 66

From the values of the above table, the sensitivity and specificity of lung ultrasound when used in the Berlin Definition for ARDS diagnosis was calculated as 90.3% and 83.5% respectively. PPV and NPV were 81.2% and 91.7% respectively. The diagnostic accuracy rate was 86.5%.



## Discussion

ARDS is a common cause of mortality in ICU worldwide<sup>9</sup>, warranting prompt diagnosis and management to reduce its potential morbidity, mortality, and economic burden on the patient and the healthcare system. Our study aimed to assess the role of lung ultrasound as a convenient imaging tool for the diagnosis of ARDS in critically ill patients.

In this study, most of the patients were relatively young. Primary diagnosis at the time of assessment was sepsis (33%), pulmonary oedema (24%) & pneumonia (23%). The age distribution and primary diagnosis were almost similar to other studies of low-income countries<sup>13</sup>. Studies of developed countries showed relatively older age predominance, with pneumonia being the most frequent diagnosis<sup>15</sup>. None of these studies found female prevalence more than males. These findings directed to the fact that in DMCH ICU, relatively younger patients get admission to ensure proper resource allocation.

The findings regarding pre-existing co-morbidities (hypertension being the commonest) were similar to previous studies<sup>15</sup>, though frequencies are lower. As a relatively younger age group of patients was studied in this study, the majority of patients (39%) had no co-morbidities.

The majority of the ARDS patients (diagnosed by Berlin Definition) had moderate ARDS (48.4%), with median PaO<sub>2</sub>/FiO<sub>2</sub>, median SpO<sub>2</sub>, and median PEEP 138.6 mm Hg, 97%, and 12 cm H<sub>2</sub>O respectively. These findings are similar to the previous studies<sup>1,9</sup>. Increased incidence of moderate ARDS may be the cause of such findings in these studies.

According to our study, the sensitivity, specificity, and accuracy of lung ultrasound assessments against the radiographic criteria of ARDS were 90.3%, 83.5%, and 86.5% respectively. Bass et al. (2015) showed a slightly lower sensitivity of LUS in detecting ARDS (86 %) and specificity was only 38 %<sup>9</sup>. In another similar study, See et al. (2018) found lower sensitivity (69%) of LUS for ARDS diagnosis<sup>15</sup>. There may be several possible reasons behind the higher sensitivity and specificity of this study. The sample was collected purposively. Clinical, oxygenation, and respiratory failure criteria of the Berlin Definition were used to diagnose ARDS along with lung ultrasound, as an alternative to chest X-ray in this study, which may have resulted in higher specificity. Patients having subcutaneous emphysema were excluded from the study, as they might make the interpretation of ultrasound images difficult, resulting in false assessments. ARDS is a posterior-predominant condition<sup>9</sup>. Thus limited visualization of posterior lung fields because of the supine position of study patients might have led to a few false negative results. Moreover, the 'BLUE' protocol was followed in the present study, which is used for the rapid assessment of acute respiratory failure patients worldwide<sup>12</sup>. On the contrary, Copetti, R., Soldati & Copetti, p. (2008) scanned each intercostal space in their study and identified ARDS most accurately using lung ultrasound<sup>14</sup>. So six 'BLUE' points examination occasionally may miss the B-lines of ARDS. Bilateral pneumonia and cardiogenic

pulmonary oedema can show B-lines bilaterally<sup>12</sup>, without any presence of ARDS. CXR diagnosis in ARDS could also be falsely positive due to the limited accuracy<sup>8</sup>, even when interpreted by experts<sup>15</sup>. The presence of basal pulmonary infiltrates and pleural effusion might have further reduced the sensitivity of lung ultrasound, as they are sometimes indistinguishable on CXR<sup>15</sup>.

This study had several strengths. Most of the studies<sup>12,14</sup> assessed 'the ability of ultrasound to detect ARDS' in optimum conditions- imaging was done by expert sonographers and patients were positioned as required for better image acquisition. However, in this study, lung ultrasound was performed by a critical care resident, keeping the intubated patients only in the supine position. This approach correlated with the reality of ICU where intensivists, not sonographers, perform bedside ultrasound assessment and movement of intubated patients is not possible as required, all the time. In this study, critically ill medical and surgical patients, at risk for ARDS in a large referral center, were methodically evaluated, which suggests the external validity of the study in other busy critical care centers. Patients with various diseases and a range of different PaO<sub>2</sub>/FiO<sub>2</sub> ratios were evaluated; thus, tests of diagnostic accuracy should apply to similar spectra of disease. The two probes, found commonly in a resource-constrained setting, were a phased-array probe (for cardiac, intraabdominal, and obstetric assessment) and a linear probe (for superficial assessments)<sup>9</sup>. Using the commonly found probe, this study showed almost the same or better results than many other studies that used a micro-convex probe.

Like any other scientific study, our study is not without limitations. It was a single-center study, conducted on a limited number of patients. Therefore, findings derived from this study cannot be generalized to the reference population. Further multicenter studies involving a large number of patients would confer greater applicability. Moreover, the interobserver agreement for ultrasound assessments was not taken in the study.

Traditionally, ultrasound study was performed solely by sonologists. However, because of its easy bedside availability, high feasibility, and repeatability, it is gaining popularity among intensivists for rapid diagnosis and quick decision-making<sup>18</sup>. With the advent of cutting-edge technology, sonographic images can be obtained at the patient's bedside even on smartphones by using a compatible ultrasound probe. At present, a lot of structured, comprehensive point-of-care ultrasound (POCUS) training courses (both online and offline) are accessible all over the world, through which physicians can orient themselves with knowledge of ultrasound and improve their expertise & skill to perform POCUS efficiently. This versatile tool enables clinicians to make real-time diagnoses with an accuracy superior to that of radiography and is time-saving in dyspneic patients. Our study showed better performance of Berlin criteria in the detection of ARDS in critically ill patients when lung ultrasound is used as the imaging modality in place of chest X-Ray. Routine use of lung ultrasound in critically ill

ARDS patients should reduce the frequency, number, and radiation hazard of bedside chest radiography and thoracic CT, resulting in decreased cost of patient care in the ICU.

### Conclusion:

Lung ultrasound can be a robust and effective tool for the rapid and accurate evaluation of ARDS at the bedside in intensive care units. Thus it can help the physicians initiate early, life-saving interventions, resulting in improved outcomes for the patients. All critical care physicians should have point-of-care ultrasound training to use this novel, potential diagnostic tool effectively.

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