Effectiveness of Lung Ultrasound for Diagnosis of Acute Respiratory Distress Syndrome in Mechanically Ventilated Patients

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ABSTRACT

Background: Acute respiratory distress syndrome (ARDS) requires rapid diagnosis for early intervention and improved outcomes. 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 is still uncertain. The objective of the study is to explore the efficacy of lung ultrasound (LUS) for diagnosis of ARDS in mechanically ventilated patients.

Methods: A cross sectional study was conducted among 75 patients in Critical Care Centre, Combined Military Hospital, Dhaka from September 2021 to January 2022. The study was approved by the ethical committee in the hospital. In this study, the Bedside Lung Ultrasound in Emergency (BLUE) protocol for the immediate diagnosis of acute respiratory failure was followed. Purposive sampling technique was used. Data were analyzed by using Statistical Package For Social Sciences (SPSS) version 25.0.

Results: A total of 75 patients were assessed. Among them male were 42(56%) and female 33(44%). The median age of patients was 48 years (Interquartile range 30-60). Primary diagnoses were pneumonia (22.67%), pulmonary oedema (20%), sepsis (20%) and trauma (17.33%). A total of 34(45.33%) patients fulfilled 'CXR-based Berlin Definition' and a total of 36(48%) patients were diagnosed as ARDS by 'LUS-based Berlin Definition'. Considering the 'CXR-based Berlin Definition' as reference standard, sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of lung ultrasound were 85.29%, 82.92%, 80.55%, 87.18% and 84% respectively.

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

Keywords: Acute respiratory distress syndrome (ARDS), Mechanical Ventilation, Bed side lung ultrasound in Emergency protocol (BLUE)

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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, increased lung weight and loss of aerated lung tissue.[1] It results in increased use of critical care resources and healthcare cost[2], as well as high mortality. This mortality and morbidity can be improved by implementing early lung-protective ventilation strategies.[3] To diagnose ARDS, the new "Berlin Definition" is followed, which requires the presence of bilateral opacities on chest X-Ray or computed tomography (CT) scan, not fully explained by effusions, lobar/lung collapse or nodules.[4] However, bedside evaluation of critically ill patients for ARDS is problematic.[5] Thoracic CT scan has the disadvantages of intra- hospital transportation risk, high cost and radiation hazard and cannot be used routinely.[6] Also portable chest X-Ray to detect ARDS has a high probability of incorrect diagnosis.[7] Still, it is the daily reference for lung imaging, despite being a costly, time-consuming imaging modality with radiation risk.[5-7] Bellani found in their study, ARDS continues to be underdiagnosed by ICU clinicians. Thus, an alternate, rapid, readily available, highly sensitive, and specific tool would be of great use for diagnosing ARDS. Fortunately, nowadays, the use of bedside, clinician-performed lung ultrasound (LUS) is increasing in ICUs worldwide.8 Studies have shown that it is a reliable tool for the diagnosis and management of emergency department patients with acute chest diseases.[7] It has shown higher diagnostic accuracy for pleural effusion, consolidation, and interstitial syndrome in cases of ARDS, compared to chest X-ray.[5,8] 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). UIS correlates with a B-line pattern obliterating A-lines.[9] These A-line and B-line patterns have proven to be easily distinguished by a bedside clinician by using lung ultrasound which is useful to screen for or rule out, pulmonary abnormalities consistent with ARDS and can be a reasonable alternative to chest radiography for the detection of interstitial syndrome of ARDS in ICU.[10-12] However, most of the studies compared the efficacy of lung ultrasound with chest X- Ray or CT scan to detect the lung infiltrates, consistent with ARDS; but the performance of lung ultrasound for the ultimate diagnosis of ARDS, using Berlin Definition as the reference standard, remains uncertain. Therefore, this study was conducted to assess the efficacy of lung ultrasound to diagnose ARDS in the intensive care unit.

MATERIALS AND METHODS

The study was a cross sectional study and was conducted in Critical Care Centre, Combined Military Hospital, Dhaka from September 2021 to January 2022. The data were collected by purposive sampling procedure. Patients who were 25 years old or above with acute respiratory failure required invasive mechanical ventilation were included in the study. Informed written consent from legally authorized representatives of patients was also taken. Patients with any structural chest wall deformity, flail chest, burn over the chest, any chest surgery, large dressing over the chest, subcutaneous emphysema, pre-existing lung parenchymal or airway disease & pregnancy were excluded from the study.

In this study, the Bedside Lung Ultrasound in Emergency (BLUE) protocol for the immediate diagnosis of acute respiratory failure was followed. For this study, a 1-5 MHz phased-array probe was used. "Berlin Definition" was

set as the "Gold standard" for ARDS diagnosis and diagnostic accuracy of lung ultrasound was compared to it. 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). Patients diagnosed by the reference standard, 'Berlin Definition' (CXR-based) were classified into mild, moderate and severe ARDS. 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 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).

All collected data were encoded into a statistical software named 'Statistical Package for Social Sciences' (SPSS) version 25.0. Continuous data were expressed as mean ± standard deviation if normally distributed and as median (IQR) if non-normally distributed. Categorical variables were expressed by frequency and percentage. Diagnostic accuracy of 'LUS- based Berlin Definition' was tested against the 'CXR-based Berlin Definition' as the reference standard for ARDS. The significance level was set $p<0.05$ in all cases. To make out the relation between the binary diagnostic test (CXR and LUS) and the presence or absence of ARDS, a 2X2 contingency table was constructed.

RESULTS

This study was done from September 2021-January 2022 at the ICU of the Department of Critical Care Medicine, CMH Dhaka. It was done on 75 acute hypoxic respiratory failure patients, requiring mechanical ventilation in ICU. All of them were assessed by lung ultrasound and chest X-Ray. ARDS was diagnosed in two ways, by the "CXR-based Berlin Definition" and by the "LUS-based Berlin Definition".

The median age of the patients was 48 years (IQR 30-60). Thirty three (44%) patients were female. Male: Female ratio was 1.27:1. Regarding co-morbidities, the majority of study patients had DM 39(52%), followed by HTN 30(40%). Many patients had more than one co-morbidity. Thirty (40%) study patients were smokers. Most common primary diagnoses of study patients during ultrasound assessment were pneumonia (22.67%), pulmonary oedema (20%) and sepsis (20%) (Table-II). Most of them had multiple diagnoses at the same time. The majority of the ARDS patients had moderate ARDS (52.94%). Their median PaO_2/FiO_2, median SpO_2 and median PEEP were 149.25 mm Hg, 94% and 7 cm H_2O respectively (Table-III). Thirty six (48%) patients were diagnosed as a case of ARDS by "LUS-based Berlin Definition". Out of 34 study patients, diagnosed by "CXR-based Berlin Definition" as ARDS, "LUS- based Berlin Definition" could diagnose 29 patients correctly as ARDS and missed the diagnosis in 5 patients. Forty one study patients were excluded for ARDS by "CXR- based Berlin Definition". "LUS-based Berlin Definition" could exclude ARDS in 34 patients correctly and falsely diagnosed 7 patients as ARDS (Table-IV). The sensitivity and specificity of lung ultrasound, used in the Berlin Definition for ARDS diagnosis were 85.29% and 82.92% respectively. Positive predictive value and negative predictive value was 80.55% and 87.18% respectively. The accuracy rate was 84%.

Table-I: Characteristics of the study patients (n=75)

Characteristics	Frequency (%)
Age in years, median [IQR]	48 [30-60]
Sex	
Male	42(56)
Female	33(44)
Pre-existing co-morbidities	
Hypertension	30(40)
Diabetes Mellitus	39(52)
Coronary Artery Disease	20(26.6)
Chronic/end-stage renal failure	05(6.66)
Cerebrovascular Disease	03(4)
Thyroid related disorder	07(9.33)
No comorbidities	10(13.3)
History of smoking	
Smoker	30(40)
Non-smoker	45(60)

*Parentheses ( ) show percentage and [ ] show interquartile range (IQR)

Table-II: Primary diagnoses of the study patients (n=75)

Primary diagnosis	Frequency (%)
Pneumonia	17(22.67)
Sepsis	15(20)
Pulmonary oedema	15(20)
Trauma	13(17.33)
Post-surgery	6(8)
Others	9(12)
Total	75(100)

Table-III: Characteristics of ARDS patients diagnosed by 'CXR-based Berlin Definition' (n=34)

Characteristics	Frequency (%)
Severity of ARDS	
Mild	5(14.7)
Moderate	18(52.94)
Severe	11(32.35)
PaO_2/FiO_2, median [IQR] (mm Hg)	149.25 [25.7- 221.2]
SpO_2, median [IQR]	94 [88-99]
PEEP, median [IQR] (cm H_2O)	7 [5-12]

*Parentheses ( ) show percentage and [ ] show interquartile range (IQR)

Table-IV: The diagnosis of ARDS by 'CXR-based Berlin Definition' & 'LUS-based Berlin Definition' (n=75)

LUS-Based Berlin Definition	CXR-Based Berlin Definition		Total
	ARDS	Not ARDS	
ARDS	29(TP)	7(FP)	36
Not ARDS	5(FN)	34(TN)	39
Total	34	41	75
Sensitivity-85.29%, Specificity-82.92%, PPV-80.55%, NPV-87.18%, Accuracy-84%			

*TP-True Positive, FP-False Positive, FN-False Negative, TN-True Negative, PPV-Positive Predictive Value, NPV-Negative Predictive Value

DISCUSSION

This study was conducted in the ICU of a tertiary-level military hospital of Bangladesh. In this study, to diagnose ARDS, the Berlin Definition was used as the reference standard and ARDS was diagnosed using both chest X-Ray and lung ultrasound. The results from this study showed reasonable sensitivity and specificity of lung ultrasound in the diagnosis of ARDS when used in the Berlin Definition in place of chest X-Ray. In this study, most of the patients were middle aged. Primary diagnosis at the time of assessment was pneumonia (22.67%), pulmonary oedema (20%) & sepsis (20%). The age distribution and primary diagnosis were almost similar to a study conducted in low-income countries.[11] Studies of developed countries showed relatively older age predominance, with pneumonia being the most frequent diagnosis.[12] None of these studies found female prevalence more than males. The findings regarding pre-existing co-morbidities (diabetes mellitus & hypertension being the commonest) were similar to the study carried out in 2018 by See et al.[12] though frequencies are lower. Only 10% patients had no previous co-morbidity.

The majority of the ARDS patients (diagnosed by Berlin Definition) had moderate ARDS (52.94%), with median PaO_2/FiO_2 149.26mmhg, median SpO_2 94% and median PEEP 7 cm H_2O. These findings are similar to previous study conducted in 2015 by Bass CM et al.[10] Increased incidence of moderate ARDS may be the cause of such findings in these studies. According to this study, the sensitivity, specificity, and accuracy of lung ultrasound assessments against the radiographic criteria of ARDS was 85.29%, 82.92%, 84% respectively. Bass showed a slightly lower sensitivity of LUS in detecting ARDS (86%) and specificity was only 38%.[10] In another similar study, See found lower sensitivity (69%) of LUS for ARDS diagnosis.[12] 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. The BLUE protocol algorithm includes an assessment of the lung sliding by ultrasound, along with B-lines. This criterion was removed from the study to avoid false- positive results, because, in trauma patients with chest injuries, there may be loss of lung sliding without the presence of ARDS or cardiogenic pulmonary oedema. 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.[10] Thus limited visualization of posterior lung fields because of the supine position of study patients might have led to 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[9,13] but Copetti et al. scanned each intercostal space in their study and identified ARDS most accurately using lung ultrasound.[13] So, six points examination occasionally may miss the B-lines of ARDS. Bilateral pneumonia and cardiogenic pulmonary oedema can show B-lines bilaterally, without any presence of ARDS. Chest X-Ray diagnosis in ARDS could also be falsely positive due to the limited accuracy, even when interpreted by experts.[12] The presence of basal pulmonary infiltrates and pleural effusion might have further reduced the sensitivity of lung ultrasound, as they are sometimes indistinguishable on chest X-Ray.[12]

This study had several strengths. Most of the studies assessed "the ability of ultrasound to detect ARDS" in optimum condition- imaging was done by expert sonographers and patients were positioned as required for better image acquisition.[5,13] 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 Intensivist, not sonographers, performs 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 to other busy critical care centers. Patients with various diseases and a range of different PaO2/FiO2 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).[10] Using the commonly found probe, this study

showed almost the same or better results than many other studies that used a micro-convex probe.

Alternative methods of imaging for ARDS may be useful in low-resource settings without portable chest radiography capacity. Dependence on traditional tools like chest X-Rays for diagnosing ARDS in these settings may underestimate the incidence of disease.[11] Management strategies that improve mortality in ARDS are lung-protective ventilation and prone positioning, which are cheap, can be implemented even in resource-limited setting and necessitate rapid recognition of ARDS to be implemented successfully. Ultrasound has the advantages of noninvasiveness, immediate implementation, high feasibility, smooth execution, versatility, portability, repeatability, free of radiation, cost-effectiveness. It enables diagnoses to be made with an accuracy superior to that of radiography and is time-saving in dyspneic patients.

CONCLUSION

Lung ultrasound can be a robust and effective tool for rapid and accurate diagnosis of ARDS in intensive care units and it may help to reduce the morbidity and mortality rate from ARDS in emergency situation & intensive care units.

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