



Diagnostic Performance of 6-Point Lung Ultrasound in ICU Patients: A Comparison with Chest X-Ray and CT Thorax

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Abstract

Objective: To evaluate the diagnostic performance of a rapid bedside 6-point lung ultrasonography (LUS) performed by an intensive care unit (ICU) physician for detection of four common pathological conditions of the lung, such as alveolar consolidation, pleural effusion, interstitial syndrome and pneumothorax, in critically ill patients and its comparison with bedside chest X-ray (CXR) and high-resolution computed tomography (CT) scan of the thorax. Volume of pleural effusion measured by LUS and CT thorax was also compared.

Methods: This was a cross-sectional, observational study of 90 adult patients with an acute lung injury score of ≥ 1 admitted to the medical-surgical ICU. They were examined by CXR and 6-point LUS as per BLUE protocol at bedside, followed by CT thorax in the radiology department.

Results: The sensitivity of 6-point LUS for detecting alveolar consolidation, pleural effusion, interstitial syndrome and pneumothorax was 76%, 88%, 83% and 89%, respectively, which was remarkably higher than that of CXR. The specificity of LUS was 100% for all pathologies, which was again notably higher than that of CXR except for interstitial syndrome for which it was 88.5%. Measurement of volume of pleural effusion by LUS was comparable and had a strong absolute agreement with CT thorax.

Conclusion: 6-Point LUS can be a useful diagnostic tool and is better than CXR in diagnosing respiratory pathologies in critically ill patients. Owing to the comparable diagnostic performance of LUS and CT scan and with increasing evidence in favour of LUS, the requirement of CT thorax can be reduced. Radiation hazards associated with CXR and CT, as well as potentially risky transfer of patients to CT room, can also be minimised.

Keywords: 6-Point BLUE protocol, chest X-ray, CT scan thorax, lung ultrasound, point of care ultrasound

Introduction

The most common imaging modality for lungs in intensive care units (ICUs) is bedside chest X-ray (CXR) as it is inexpensive and readily available, but has several limitations, namely, changes in lung parenchymal density due to suboptimal exposure and rotation leading to incorrect interpretation of lung disease, exposure without adequate inspiration leading to obscuration of lung bases and day-to-day variation in film exposure leading to difficulty in comparing serial CXR (1, 2). CXR has also been found to have low sensitivity for diagnosing various pathologies in ICU patients (3, 4).

Thoracic computed tomography (CT) scan is the gold standard for lung imaging, but this technique is expensive, carries radiation hazard and requires transportation of critically ill patients from ICU to radiology department that carries a significant risk and may not always be possible because of the haemodynamic and respiratory instability of the patient.

Literature suggests that lung ultrasonography (LUS) can have diagnostic accuracy better than CXR and comparable to CT scan in diagnosing lung pathologies (3, 5-9). Ultrasonography (USG) was conventionally performed by radiologists, but is now gaining popularity amongst intensivists as it can help in early diagnosis and quick therapeutic decision-making because of its easy bedside availability (10, 11). Most of the studies in the literature have targeted individual lung pathologies (3, 6, 8, 9), but those comprehensively evaluating diagnostic accuracy of point of care LUS in detecting all lung pathologies together in comparison with CXR and CT scan are limited (4).

We studied 6-point BLUE protocol because it is easy to learn, and the scan is completed in a shorter time, thus allowing quick therapeutic decision-making. Studies in the literature have evaluated the performance of 8 and 12 scan points (6, 8), but, to our knowledge, there are no studies comprehensively evaluating the performance of 6-point LUS in detecting commonly encountered lung pathologies in the ICU.

The aim of the present study was to evaluate the diagnostic performance of 6-point LUS, performed by an ICU physician, for detection of four common pathological conditions of the lung, namely, consolidation, pleural effusion, pneumothorax and interstitial syndrome, in critically ill patients and

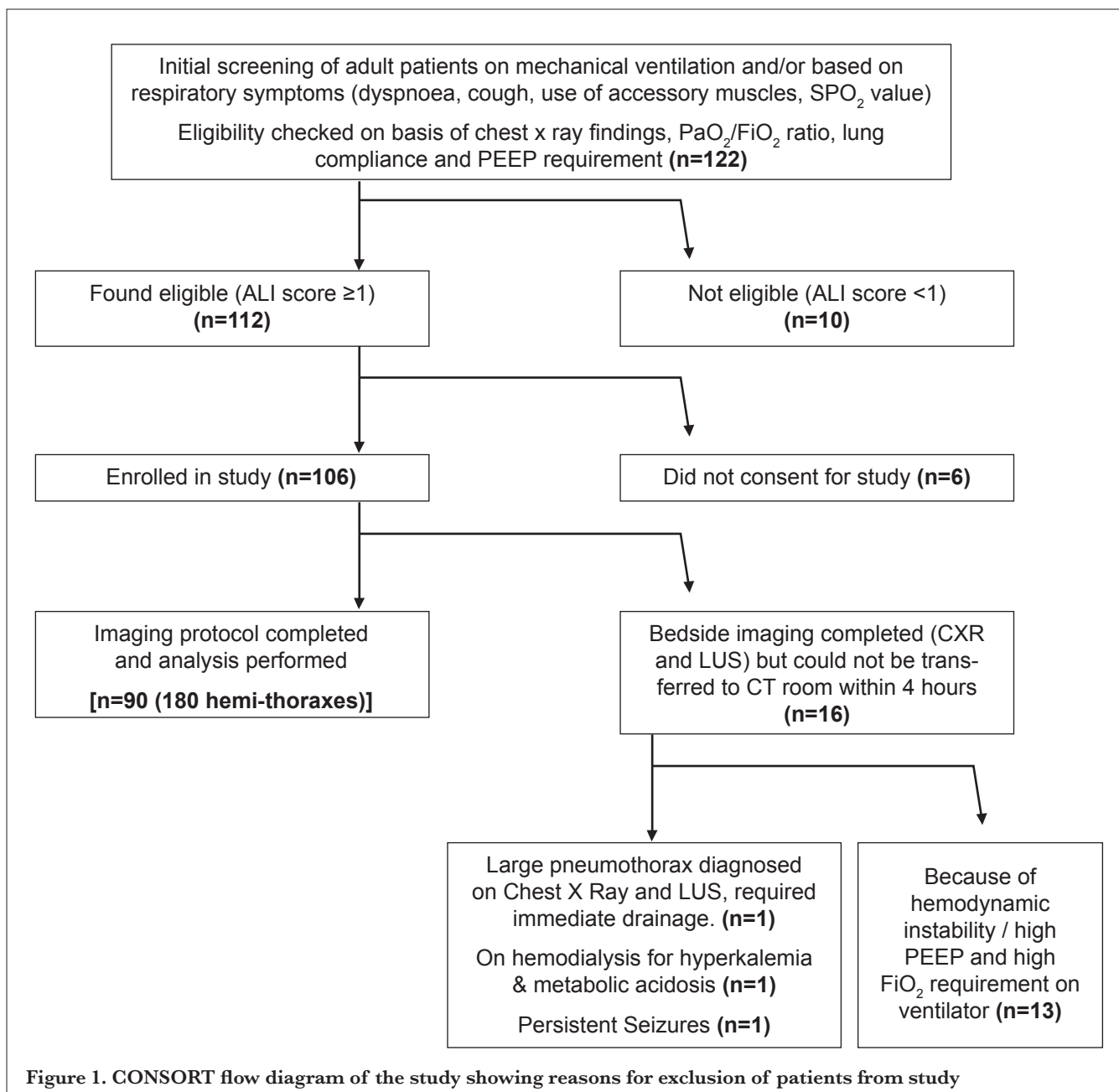


Figure 1. CONSORT flow diagram of the study showing reasons for exclusion of patients from study

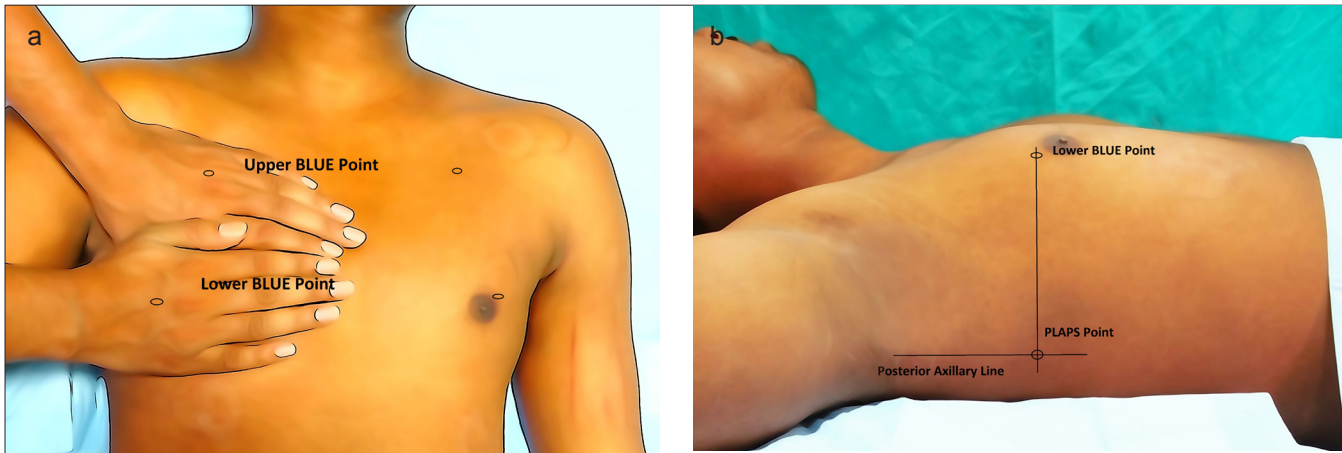


Figure 2. a,b. (a) Two hands equivalent to the size of patient's hand were placed over the anterior chest wall in such a manner that the little finger of the upper hand lies just below the clavicle, fingertips at parasternal border, and lower hand was kept adjacent to the upper hand excluding thumbs. The middle point of the upper hand constituted 'upper BLUE point', and the middle point of the palm of the lower hand constituted 'lower BLUE point' (marked by black circles). (b) A perpendicular line was drawn from lower BLUE point towards posterior axillary line, and the intersection of these two lines was labelled as Postero Lateral Alveolar and/or Pleural Syndrome (PLAPS) point. These points roughly follow the anatomy of the lung and avoid the heart as much as possible. Upper and lower BLUE points are for examination of the anterior surface of the lung, and PLAPS point is for lateral and posterior surfaces of the lungs

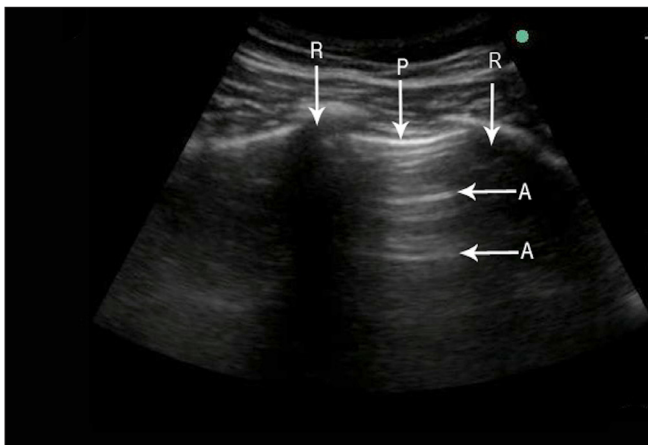


Figure 3. USG pattern generated by normal lung. Pleural line (P) is seen between rib shadows (R). Various repetition lines known as A lines (A) can be seen parallel to the pleural line, placed at a regular interval equal to the distance between skin and pleural line. Normal pattern also includes lung sliding, which is the sliding movement of visceral pleura over parietal pleura (not seen here)

its comparison with bedside CXR and high-resolution CT scan thorax. Another objective was to compare the volume of pleural effusion measured by LUS with that by CT thorax.

Methods

This was a hospital-based cross-sectional, observational study conducted in a tertiary care medical institute between July 2016 and August 2017. The study was approved by the institute ethics committee (IEC reference no. 2016-80-MD-91). Informed con-

sent was obtained from the patient or next of kin before enrolment to the study. Adult patients admitted to our medical-surgical ICU who had evidence of lung pathology as demonstrated by an acute lung injury (ALI) score of ≥ 1 were included (12, 13). The primary outcome of the present study was to determine the usefulness of 6-point LUS in ICU patients by comparing its diagnostic performance with CXR and CT scan thorax.

Patients were subjected to imaging protocol consisting of bedside CXR and LUS, followed by CT scan thorax. Findings of LUS were compared with those of CXR and CT thorax, and this completed our study protocol. Patients with lung injury were selected as it would have been unethical to subject those with normal lung to an expensive diagnostic tool, such as CT scan, that also carries radiation hazard and transportation risk.

The consort diagram of the study is shown in Figure 1 mentioning reasons of exclusion from the study.

Description of imaging protocol

After admission, bedside CXR in anteroposterior view using a portable equipment MobileArt eco MUX 10 (Shimadzu (Asia Pacific) Pte. Ltd., Japan) and arterial blood gas analysis were performed. The ALI score of patients on facemask/spontaneous respiration was calculated using two parameters, i.e. consolidation on CXR and $\text{PaO}_2/\text{FiO}_2$ ratio, whereas for patients receiving invasive mechanical ventilation, all four parameters were taken into consideration (Consolidation on CXR, $\text{PaO}_2/\text{FiO}_2$ ratio, positive end expiratory pressure (PEEP) required on ventilator and lung compliance). A radiologist who was blinded to the clinical condition, as well as

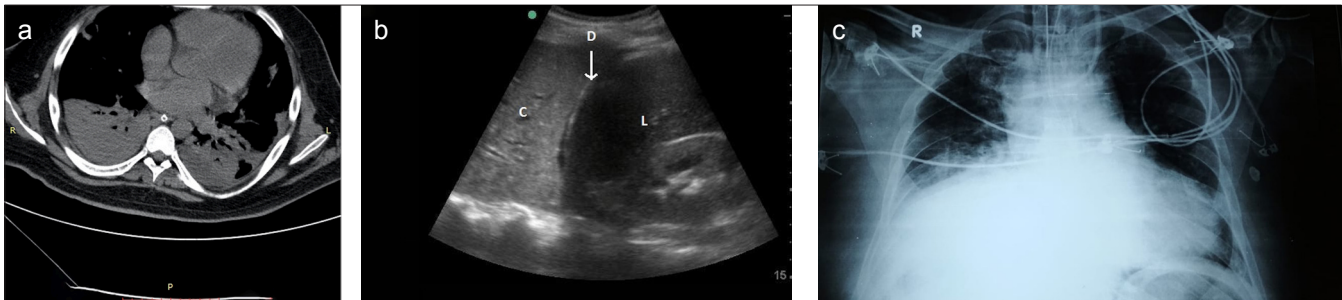


Figure 4. a-c (of Patient A). (a) CT thorax of a patient with consolidation of the right and left lower zones (right lower zone consolidation being more extensive than left). (b) LUS in same patient at right PLAPS point showing alveolar consolidation (C) of the right lower zone (seen as isoechoic tissue-like structure) separated from liver (L) by diaphragm (D), caused by loss of lung aeration. (c) Suboptimal CXR due to rotation, showing obscured right costophrenic angle and diffuse haziness in the right lower lung zone, which may either be due to pleural effusion or collapse-consolidation or even due to an enlarged liver pushing up the diaphragm (as it is difficult to differentiate between pleural effusion and consolidation on CXR)

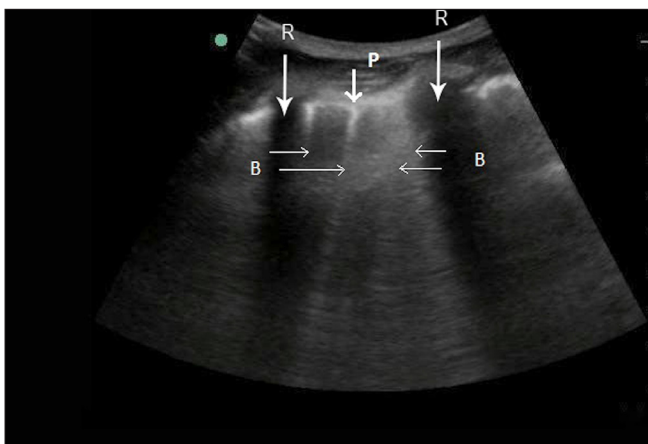


Figure 5. LUS findings in interstitial syndrome; appearance of 'B lines' extending downwards from the pleural line (P) up to the bottom of ultrasound screen. Regularly distanced B lines (B) between two adjacent ribs (R), three or maximum of four in number denote interstitial pathology; mean distance between them is 7 mm corresponding to pleural projections of interlobular septa

USG and CT scan findings of the patient recorded the CXR finding. Assessment of the quality of CXR was based on five parameters: inclusion (anatomic inclusion of the entire thoracic cage), rotation, film exposed in adequate inspiration or not (to assess the entire lung fields, especially lung bases), adequate penetration and presence of any external artefacts.

Subsequent to CXR, 6-point LUS (three in each hemithorax) was performed as described in the BLUE protocol (*Bedside Lung Ultrasonography in Emergency*). In our ICU, we have adapted this 6-point protocol as it is quick and is reported to have >90% accuracy in detecting common pathologies in critically ill patients (14). The intensivist performing LUS had >2 years of experience in performing LUS (10) and was blinded to CXR and CT scan findings of the patient. Nomenclature and method of marking 6 points for LUS on the patient's chest has been described in Figure 2a and b. Imag-

ing was performed using a curvilinear probe (2-5 MHz) with SonoSite M-turbo portable USG machine (Fujifilm SonoSite Inc., Bothell, WA, USA). Upper and lower BLUE points were examined in supine position, and PLAPS point was examined in 30° head up position. Upper and lower BLUE points were examined in supine position to facilitate the detection of pneumothorax, and PLAPS point was examined in semirecumbent position to diagnose and precisely quantify minimal pleural effusion. Intubated and non-intubated patients were examined in the same position to maintain uniformity across all patients in the study group. The transducer pointer was either directed cephalad or to the patient's right. This process was repeated for each point on the other side.

LUS images were standardised as per the image characteristics described in the BLUE protocol (15). Upon sagittal placement of an ultrasound transducer on the chest wall over an intercostal space, the following structures and artefacts were identified in that image: (1) subcutaneous tissues and intercostal muscles, (2) superior and inferior ribs with posterior acoustic shadowing, (3) a hyperechoic homogeneous twinkling horizontal line between two rib shadows, called the 'pleural line' that moves synchronously with respiration and (4) hyperechoic horizontal lines parallel to the pleural line, called 'A lines' that are repetition of the pleural line, placed at a regular distance equal to the skin-pleural line distance (Figure 3) (15). Alveolar consolidation was defined as isoechoic tissue-like structure (i.e. liver) caused by loss of lung aeration (Figure 4b) (16). Interstitial syndrome was diagnosed by the appearance of 'B lines' that are vertical lines extending downwards from the pleural line, extending up to the bottom of ultrasound screen. They erase A lines and move along with the pleural line. Regularly distanced B lines between two adjacent ribs that are 3 or maximum of 4 in number denote interstitial pathology (Figure 5), whereas irregularly distanced B lines that are >4 in number denote alveolar-interstitial pathology (Figure 6b) (15, 16). Detection of B lines in <2 areas per hemithorax or limited to one hemithorax indicates 'limited interstitial syndrome'

and favours diagnosis of isolated pulmonary conditions, such as pneumonitis; in contrast, if B lines are present on at least two areas on both hemithoraxes, it favours the diagnosis of ‘diffuse interstitial syndrome’, such as pulmonary oedema or acute respiratory distress syndrome (ARDS).

Pneumothorax was diagnosed based on two sonographic features: absence of lung sliding on 2D imaging (no movement of the pleural line) and presence of stratosphere sign or bar code sign on M mode (Figure 7b) (17, 18). Presence of local lung sliding, sea shore sign on M mode or B lines excluded the diagnosis of pneumothorax. Pleural effusion was determined as a hypoechoic or anechoic homogeneous structure in the dependent zones along with hyperechoic shadow of collapsed lung (Figure 8b, c). Inspiratory shift of visceral pleura towards the pleural line on M mode produces a characteristic sine wave pattern in pleural effusion called as ‘sinusoid sign’ (15, 16). USG quantification of pleural effusion volume was calculated using the formula: $V \text{ (mL)} = 16 \times D \text{ (mm)}$, where V is the volume of pleural effusion in mL, and D is the distance in millimeters between mid-height of the diaphragm and visceral pleura in end-expiration (19).

Subsequent to LUS, patients were transported to the radiology department for CT scan thorax with 64 slice multidetector channel (Brilliance CT; Philips Medical Systems, The Netherlands). Patients who could not be transported to CT room within 4 hours of bedside imaging because of haemodynamic instability, high positive end-expiratory pressure (PEEP) and high FiO_2 requirement on ventilator or ongoing lifesaving clinical management not permitting patient’s transfer, were excluded from the study. A maximum of 4 hours delay was accepted, similar to that reported in the literature previously (4). Scans were obtained in the supine position from the apex of thorax to the lung bases. Assessment included thin multi detector high resolution computed tomography performed and reported by a second radiologist who was blinded to CXR and LUS findings, as well as clinical condition, of the patient.

Statistical analysis

Sample size estimation was done with help of Two sided McNemar Test to detect a difference of 0.20 in the sensitivity between LUS and CXR. The sensitivity of LUS and CXR was assumed to be 0.75 and 0.55 respectively based on previously

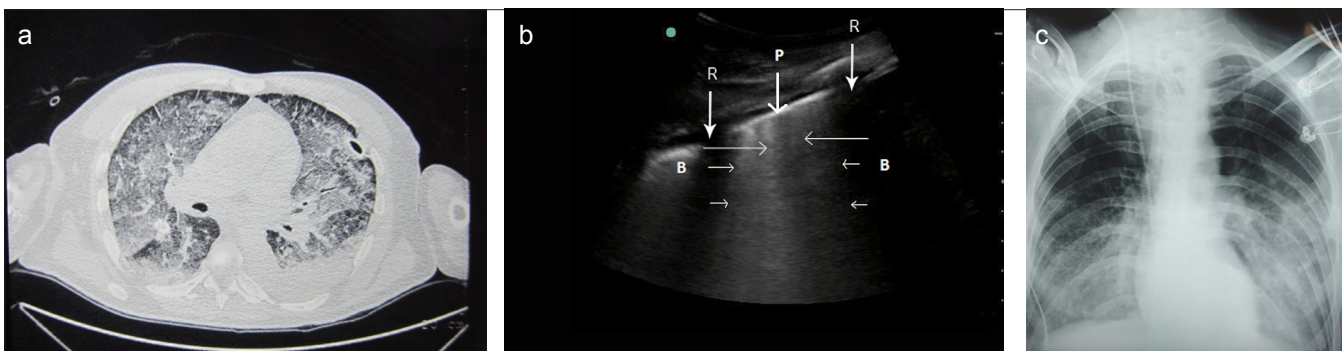


Figure 6. a-c (of Patient B). (a) Ground glass opacification of lung parenchyma on CT thorax of a patient with alveolar-interstitial syndrome. (b) LUS at lower BLUE point showing >4 B lines (b) between adjacent ribs (R) with unequal distances between them, suggesting an alveolar-interstitial pathology, similar to that of CT thorax in the same patient. (c) Sub-optimal CXR with rotation showing haziness in the lower half of lung fields on both sides, favouring the diagnosis of consolidation or pleural effusion (not correlating with CT or LUS findings)

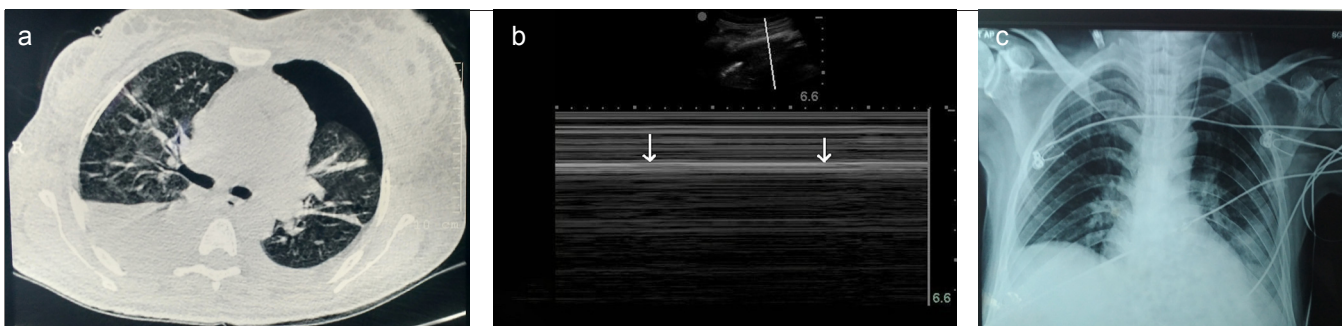


Figure 7. a-c (of Patient C). (a) CT scan of a patient showing large pneumothorax in left hemithorax. (b) M mode across the pleural line (white arrows) with absent lung sliding during LUS at left upper BLUE point, generated ‘Bar code pattern’, in the same patient diagnosing pneumothorax. (c) CXR of the same patient with a rotated film showing blunting of right costophrenic angle but with no evidence of pneumothorax

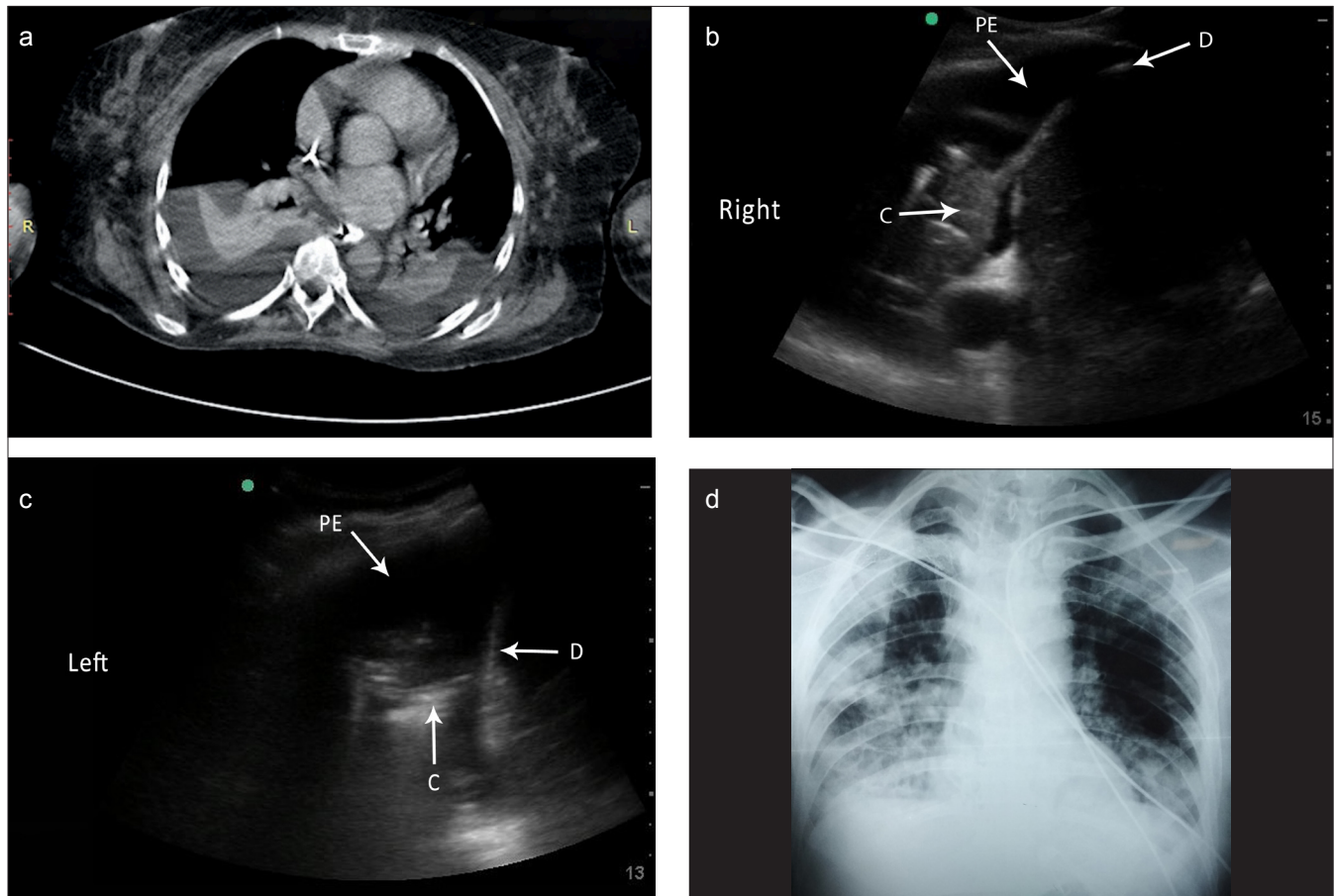


Figure 8. a-d (of Patient D). (a) CT thorax of a patient showing bilateral pleural effusion with consolidation. (b) LUS at right PLAPS point in the same patient showing pleural effusion (PE) seen as hypoechoic or anechoic homogeneous structure along with hyperechoic shadows of underlying collapsed lung with consolidation (C) above diaphragm (D). (c) LUS at left PLAPS point with pleural effusion and underlying collapsed lung. (d) CXR was suggestive of bilateral lower zone consolidation and right-sided pleural effusion

available data in the literature. The proportion of the positive cases (by CT, gold standard method) was 0.6. The proportion of discordant pairs was 0.475 [$\text{Sensitivity_LUS} (1 - \text{Sensitivity_CXR}) + \text{Sensitivity_CXR} (1 - \text{Sensitivity_LUS})$]. The sample size was estimated to be 163 hemithoraxes to achieve a statistical significance level of 0.05 with 80% power. Considering the fact that it may not be possible to complete the study protocol in every enrolled patient, we incremented the sample size by 30%, making it 212 hemithoraxes, i.e. 106 adult patients. Sample size was calculated using 'Power Analysis and Sample Size, version-8' software (PASS-2008).

IBM Statistical Package for the Social Sciences, version 23 (IBM SPSS Statistics Corp.; Armonk, NY, USA) was used for data analysis. Normality of continuous data was tested, and a variable was considered normal when standard deviation was <0.5 mean. Demographic data, such as age, body weight, body mass index and lung injury score, were presented as mean \pm standard deviation, and measured values of pleural effusion were presented as median (interquartile range). Categorical

data were presented as frequency (%). Measurements of diagnostic accuracy, i.e. sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy and its 95% confidence interval, were measured using cross table analysis. Wilcoxon signed-rank test was used to analyse the difference in measurements of pleural effusion volume by LUS and CT scan. Intraclass correlation coefficient was calculated to test the absolute agreement between LUS and CT scan. A p-value <0.05 was considered as statistically significant.

Results

A total of 180 hemithoraxes from 90 patients were included in the analysis. Demographic characteristics and primary diagnosis of these patients are shown in Table 1.

Thirty (33.3%) X-ray films out of 90 were of suboptimal quality, as 9 were not in full inspiration and all 30 were rotated. In contrast, LUS images acquired were of optimum resolution to interpret findings in all patients. LUS required removal of surgical dressing in 4 patients.

Table 1. Demographic characteristics and diagnosis at the time of admission

	Mean±SD	Range
Age (years)	47.66±16.21	18-79
Gender (%)	Male: 67 (74.4%), female: 23 (25.6%)	
Body weight (kg)	57.2±10.49	42-106
BMI (kg/m ²)	22.67±3.75	16.80-34.65
Lung injury score	1.89±0.76	1.0-3.75
Diagnosis at admission and no. of patients	Postoperative acute respiratory failure: 22 Acute severe pancreatitis with respiratory failure: 8 Malignancy with suspected lung metastasis: 6 Acute exacerbation of COPD: 9 Liver disease with respiratory failure: 16 Polytrauma with respiratory distress: 8 Sepsis/multiorgan dysfunction syndrome: 17 Interstitial lung disease: 4	

BMI: body mass index; COPD: chronic obstructive pulmonary disease

Table 2. Diagnostic performance of lung ultrasound compared with chest X-ray for diagnosing various lung pathologies

Pathology	Performance of chest X-ray in diagnosing individual pathology						Performance of lung ultrasound in diagnosing individual pathology					
	Visualised on CXR (no. of hemithoraxes)	Confirmed to be truly existing later on, i.e. true positive (no. of hemithoraxes (%))	Not found to be existing later on, i.e. false positive (no. of hemithoraxes (%))	Not visualised on CXR (no. of hemithoraxes)	Confirmed to be truly absent later on, i.e. true negative (no. of hemithoraxes (%))	Found to be actually present later on, i.e. false negative (no. of hemithoraxes (%))	Visualised on LUS (no. of hemithoraxes)	Confirmed to be truly existing later on, i.e. true positive (no. of hemithoraxes (%))	Not found to be existing later on, i.e. false positive (no. of hemithoraxes (%))	Not visualised on LUS (no. of hemithoraxes)	Confirmed to be truly absent later on, i.e. true negative (no. of hemithoraxes (%))	Found to be actually present later on, i.e. false negative (no. of hemithoraxes (%))
Consolidation	81	53 (65.4%)	28 (34.6%)	99	44 (44.4%)	55 (55.6%)	82	82 (100%)	0	98	72 (73.5%)	26 (26.5%)
Pleural effusion	74	62 (83.8%)	12 (16.2%)	106	39 (36.8%)	67 (63.2%)	113	113 (100%)	0	67	51 (76.1%)	16 (23.9%)
Interstitial syndrome	28	21 (75%)	7 (25%)	152	89 (58.6%)	63 (41.4%)	81	70 (86.4%)	11 (13.6%)	99	85 (85.9%)	14 (14.1%)
Pneumothorax	0	0	0	180	171 (95%)	9 (5%)	8	8 (100%)	0	172	171 (99.4%)	1 (0.6%)

CXR: chest X-ray; LUS: lung ultrasonography

Table 2 compares the performance of LUS with CXR in diagnosing various lung pathologies. LUS had higher rate of true positive and true negative findings, as well as lower rate of false positive and false negative findings, than CXR.

Table 3 shows the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of three imaging modalities in detecting various pathologies. CXR was unable to differentiate between consolidation and pleural effusion in 18 hemithoraxes, so they were considered having both consolidation and pleural effusion on CXR. Figure 4c

shows the CXR of one such patient with probable diagnosis of either pleural effusion or consolidation-collapse or even an enlarged liver pushing up the diaphragm. LUS demonstrated it to be consolidation of the right lower zone (Figure 4b), and CT thorax confirmed the findings of LUS in the same patient (Figure 4a).

Alveolar consolidation was found in 108 hemithoraxes on CT scan (Table 3); out of these, LUS could detect it in 82 hemithoraxes. Out of 26 consolidations missed on LUS, 14 were located in the left lower lobe, 6 in the right lower lobe and 3

Table 3. Diagnostic performance of LUS in comparison with CXR and CT scan thorax for various lung pathologies for each hemithorax

Pathology		CT+ (no. of hemithoraxes)	CT - (no. of hemithoraxes)	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%) (95% CI)	NPV (%) (95% CI)	DA (%) (95% CI)
Consolidation	LUS+	82	0	75.9	100	100	73.5	85.6
	LUS-	26	72	(66.6-83.4)	(93.6-100)	(94.4-100)	(63.4-81.6)	(79.7-90.0)
	CXR+	53	28	49.1	61.1	65.4	44.4	53.9
	CXR-	55	44	(39.3-58.9)	(48.9-72.4)	(53.9-75.4)	(34.6-54.8)	(46.6-61.1)
Pleural effusion	LUS+	113	0	87.6	100	100	76.1	91.1
	LUS-	16	51	(80.4-92.5)	(91.3-100)	(95.9-100)	(63.9-85.3)	(86.1-94.5)
	CXR+	62	12	48.1	76.5	83.8	36.8	56.1
	CXR-	67	39	(39.2-56.9)	(62.2-86.8)	(73.0-91.0)	(27.8-46.8)	(48.8-63.2)
Interstitial syndrome	LUS+	70	11	83.3	88.5	86.4	85.9	86.1
	LUS-	14	85	(73.3-90.3)	(80.0-93.9)	(76.5-92.7)	(77.1-91.8)	(80.3-90.4)
	CXR+	21	7	25.0	92.7	75.0	58.6	61.1
	CXR-	63	89	(16.5-35.8)	(85.1-96.7)	(54.8-88.5)	(50.2-66.4)	(53.8-67.9)
Pneumothorax	LUS+	8	0	88.9	100	100	99.4	99.4
	LUS-	1	171	(50.7-99.4)	(97.3-100)	(59.7-100)	(96.3-99.9)	(96.1-99.7)
	CXR+	0	0	0	100	0	95.0	95.0
	CXR-	9	171	(-)	(62.9-100)	(-)	(90.4-97.5)	(90.8-97.4)

CT: computed tomography; CI: confidence interval; CT+: detected by CT scan thorax; CT-: not present on CT scan thorax; CXR+: detected by chest X-ray; CXR-: not seen on chest X-ray; LUS+: detected by lung ultrasonography; LUS-: not detected by lung ultrasonography; PPV: positive predictive value; NPV: negative predictive value; DA: diagnostic accuracy

each in the right middle and right upper lobe on CT. While LUS detected 100% of the consolidations involving ≥2 lobes (as detected by CT scan), it could only detect 59% of them that were limited to one lobe (Table 4).

Fifty-one hemithoraxes were diagnosed to have interstitial pathology on LUS as they had 3-4 B lines between two adjacent ribs; CT scan confirmed the diagnosis as pneumonitis or interstitial fibrosis. Nineteen hemithoraxes had findings suggestive of alveolar-interstitial syndrome (pulmonary oedema or ARDS) as they had >4 closely placed B lines on LUS. CT scan concurred LUS diagnosis by demonstrating ground glass opacities of pulmonary oedema or ARDS, and at the same time, CXR was found to be a less sensitive modality to diagnose interstitial syndrome (Figure 6a, b and c).

Barring one patient who was excluded from the analysis, CXR could not detect pneumothorax in any patient, making it again a poorly sensitive modality for diagnosing this pathology. All clinically significant pneumothoraxes were detected by LUS. Figure 7a shows the CT scan of a patient with left pneumothorax. LUS of the same patient in M mode demonstrated barcode sign at the left upper BLUE point (Figure 7b), whereas CXR could not demonstrate pneumothorax (Figure 7c).

Out of 90 patients, 69 were receiving mechanical ventilation with endotracheal tube, and 21 were breathing spontaneous-

ly (17 on O₂ by facemask, 2 on intermittent bi-level positive airway pressure and 2 on tracheostomy with O₂ via T-piece). Diagnostic performance of LUS and CXR was analysed separately in these two subgroups of patients, and results are shown in Tables 5 and 6. LUS had better sensitivity, specificity and diagnostic accuracy in diagnosing various pathologies in patients receiving mechanical ventilation than spontaneous respiration.

Difference between median fluid volume detected by CT scan and USG was statistically insignificant. There was a strong absolute agreement in pleural effusion measurement between LUS and CT thorax (Table 7).

Discussion

Our results demonstrate that LUS imaging protocol used in the present study yielded greater sensitivity and diagnostic accuracy than CXR, as well as had >85% accuracy than CT thorax, in detecting common lung pathologies. After enrolment, 15% of patients could not be transferred timely to CT room (Figure 1). Data emphasise the need of a reliable point of care imaging modality as intrahospital transfer of critically ill patients is not always possible. Furthermore, transfer is not without risks as the incidence of overall, as well as critical, adverse events during such transfers has been reported to be as high as 78% and 22%, respectively (20). Although portable

No. of lobes involved in a hemithorax	No. of hemithoraxes with consolidation on CT scan	No. of hemithoraxes with consolidation on LUS	Sensitivity of LUS (compared with CT scan)
1	64	38	59.4%
2	30	30	100%
3 (right hemithorax only)	14	14	100%

CT: computed tomography; LUS: lung ultrasonography

Pathology		CT+ (no. of hemithoraxes)	CT- (no. of hemithoraxes)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	DA (95% CI)
Consolidation	LUS+	68	0	81.9	100	100	78.6	89.1
	LUS-	15	55	(72.0-89.5)	(93.5-100)	(-)	(69.9-85.3)	(82.7-93.8)
	CXR+	39	22	47.0	60.0	63.9	42.9	52.2
	CXR-	44	33	(35.9-58.2)	(45.9-73.0)	(54.4-72.5)	(35.8-50.2)	(43.5-60.7)
Pleural effusion	LUS+	92	0	92.9	100	100	84.8	94.9
	LUS-	7	39	(86.0-97.1)	(91.0-100)	(-)	(73.2-91.9)	(89.8-97.9)
	CXR+	47	11	47.5	71.8	81.0	35.0	54.4
	CXR-	52	28	(37.3-57.8)	(55.1-85.0)	(71.3-88.0)	(29.1-41.4)	(45.7-62.9)
Interstitial syndrome	LUS+	58	8	87.9	88.9	87.9	88.9	88.4
	LUS-	8	64	(77.5-94.6)	(79.3-95.1)	(78.9-93.3)	(80.6-93.9)	(81.9-93.2)
	CXR+	18	7	27.3	90.3	72.0	57.5	60.1
	CXR-	48	65	(17.0-39.6)	(81.0-96.0)	(53.4-85.2)	(53.4-61.5)	(51.5-68.4)
Pneumothorax	LUS+	3	0	100	100	100	100	100
	LUS-	0	135	(29.2-100)	(97.3-100)	(-)	(-)	(97.4-100)
	CXR+	0	0	0	100	0	97.8	97.8
	CXR-	3	135	(0-70.7)	(97.3-100)	(-)	(97.8-97.8)	(93.8-99.6)

CT: computed tomography; CI: confidence interval; CT+: detected by CT scan thorax; CT-: not present on CT scan thorax; CXR+: detected by chest X-ray; CXR-: not seen on chest X-ray; LUS+: detected by lung ultrasonography; LUS-: not detected by lung ultrasonography; PPV: positive predictive value; NPV: negative predictive value; DA: diagnostic accuracy

CT scanners are available for bedside scan, this technology is not widely available and is mostly used for neuroimaging until now (21).

We found that one-third of CXR images were of suboptimal quality, as reported previously (22, 23), whereas LUS images were of sufficient resolution for interpretation in all cases. In our study, the diagnostic accuracy of CXR was 54% for detecting consolidation. Moreover, it was unable to differentiate between consolidation and pleural effusion in approximately 22% of CXR films. The major advantage of imaging with LUS is its ability to differentiate between consolidation and pleural effusion, which may not always be possible with CXR. Figure 8 shows the comparative findings of CXR, LUS and CT thorax in a patient where CXR was suggestive of bilateral lower zone consolidation and right-sided pleural effusion (Figure 8d). On the other hand, LUS showed bilateral pleural effusion with underlying collapsed lungs (Figure 8b and c),

and these findings were corroborated by CT thorax (Figure 8a). Inability of CXR to differentiate between consolidation and pleural effusion has been reported in the literature previously by Vignon et al., where patients admitted in the ICU with apparently normal CXR had moderate to severe pleural effusion, and conversely those with suspected pleural effusion on CXR had extensive consolidation and no effusion on LUS (5).

LUS had 86% diagnostic accuracy in detecting alveolar consolidation and was able to differentiate between effusion and consolidation. Our study had lower sensitivity but higher specificity of LUS in detecting alveolar consolidation than that reported in the literature, which may be because we performed LUS on 6 points rather than 12 points (6, 8).

All 26 hemithoraxes with consolidations missed on LUS were limited to one lobe only, which could be due to three reasons.

Table 6. Diagnostic performance of LUS in comparison with CXR and CT scan thorax for various lung pathologies in non-mechanically ventilated patients

Pathology		CT+ (no. of hemithoraxes)	CT - (no. of hemithoraxes)	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%) (95% CI)	NPV (%) (95% CI)	DA (%) (95% CI)
Consolidation	LUS+	14	0	56	100	100	60.7	73.8
	LUS-	11	17	(34.9-75.6)	(80.5-100)	(-)	(49.8-70.6)	(57.9-86.1)
	CXR+	14	6	56	64.7	70.0	50.0	59.5
	CXR-	11	11	(34.9-75.6)	(38.3-85.8)	(52.9-82.9)	(36.3-63.8)	(43.3-74.4)
Pleural effusion	LUS+	21	0	70.0	100	100	57.1	78.6
	LUS-	9	12	(50.6-85.3)	(73.5-100)	(-)	(43.6-69.7)	(63.2-89.7)
	CXR+	15	1	50.0	91.7	93.8	42.3	61.9
	CXR-	15	11	(31.3-68.7)	(61.5-99.8)	(68.9-99.0)	(33.0-52.2)	(45.6-76.4)
Interstitial syndrome	LUS+	12	3	66.7	87.5	80.0	77.8	78.6
	LUS-	6	21	(40.0-86.7)	(67.6-97.3)	(56.9-92.4)	(64.2-87.3)	(63.2-89.7)
	CXR+	3	0	16.7	100	100	61.5	64.3
	CXR-	15	24	(3.6-41.4)	(85.8-100)	(-)	(56.6-66.3)	(48.0-78.5)
Pneumothorax	LUS+	5	0	83.3	100	100	97.3	97.6
	LUS-	1	36	(35.9-99.6)	(90.3-100)	(-)	(85.8-99.5)	(87.4-99.9)
	CXR+	0	0	0	100	0	85.7	85.7
	CXR-	6	36	(0-45.9)	(90.3-100)	(-)	(85.7-85.7)	(71.5-94.6)

CT: computed tomography; CI: confidence interval; CT+: detected by CT scan thorax; CT-: not present on CT scan thorax; CXR+: detected by chest X-ray; CXR-: not seen on chest X-ray; LUS+: detected by lung ultrasonography; LUS-: not detected by lung ultrasonography; PPV: positive predictive value; NPV: negative predictive value; DA: diagnostic accuracy

Table 7. Comparison of measurement of pleural effusion volume by LUS and CT scan thorax

	Pleural effusion on LUS (ml)		Pleural effusion on CT scan (mL)		P value (Wilcoxon signed-rank test)	Absolute agreement# (95% CI)
	Median (IQR)	Min-Max	Median (IQR)	Min-Max		
Right hemithorax	288 (208-688)	80-1312	260 (132-630)	50-1400	0.589	0.981* (0.969-0.989)
Left hemithorax	320 (208-506)	160-1440	250 (150-485)	50-1500	0.080	0.983* (0.969-0.990)
Both hemithoraxes	304 (208-640)	80-1440	250 (150-500)	50-1500	0.096	0.982* (0.974-0.988)

#Absolute agreement between LUS and CT scan measured values of pleural effusion using intraclass correlation coefficient. *Significant at p<0.001. CT: computed tomography; CI: confidence interval; IQR: interquartile range; Min: minimum volume measured; Max: maximum volume measured; LUS: lung ultrasonography

First, some of them were not extending up to the pleural surface (6, 24). In other words, normally aerated lung tissue was present between consolidation and pleural surface, producing 'A' pattern on LUS causing deep located consolidation to be missed. Second, it could be because of overlapping adjacent regions (heart and air in fundus of stomach that could be exaggerated by gastroparesis in the critically ill) as we found high incidence of consolidations missed on the left lower lobe. CT thorax of two patients even demonstrated the diaphragm being pushed up due to air in fundus of distended stomach. We presume that the quality of LUS examination on the left side may be improved by decompressing the stomach. Third,

it could be because of their small size. Consolidations located in the upper lobes of lungs are more likely to be missed, but the reasons are not well defined (25). The specificity of LUS for detecting consolidation was 100% in our study as there was no false positive case.

Our study demonstrated superiority of LUS over CXR in detecting pleural effusion as reported in previous studies (9, 26, 27). False negative results with LUS were mainly due to small pleural effusions that were not of much clinical significance (50 to 150 mL). In our study, the minimum effusions detected by LUS were 80 ml on the right side and 160 mL on the left side.

Literature suggests that the measurement of pleural effusion on the right side yields more consistent results, and that of left-sided effusion produces more variable results, which may be because of the heart occupying the left hemithorax (5).

A considerable number of patients admitted to the ICU are diagnosed with type of pathologies where extra vascular lung water content is increased (fluid accumulation in interstitial space and alveoli), leading to impaired gaseous exchange and respiratory distress. Their radiological appearance depends upon whether fluid accumulation is only in the interstitium or alveoli plus interstitium and is known as interstitial syndrome or alveolar-interstitial syndrome, respectively (28). Out of 14 hemithoraxes with interstitial syndrome that were missed on LUS, 6 had large pleural effusion (>1000 mL) that might have prevented the appearance of B lines on USG as they arise from the pleural line, and parietal and visceral pleural lines are separated in effusion. Eleven hemithoraxes were diagnosed to have interstitial syndrome on LUS that were absent on subsequent CT scan. This finding was similar to that of Vercesi et al. (29) who also found a higher number of false positive cases of moderate to severe ARDS when diagnosed by LUS. There is a possibility that B lines could have resolved because of ongoing respiratory management (e.g. use of diuretics and application of PEEP during mechanical ventilation) received by these patients as B lines have been shown to resolve as quickly as an hour following haemodialysis in patients with renal failure (30).

Literature has suggested >90% sensitivity and >95% specificity of LUS in diagnosing pneumothorax (11, 31). False positive cases of pneumothorax on USG have been reported in the literature in patients with chest trauma and subcutaneous emphysema (6). Our study had no such cases leading to 100% specificity of LUS in detecting pneumothorax. A slightly lower sensitivity of LUS in detecting pneumothorax in our study could be because of a small number of hemithoraxes with pneumothorax.

LUS had better sensitivity, specificity and diagnostic accuracy in diagnosing various pathologies in patients receiving mechanical ventilation than in those on spontaneous respiration in our study. We could not determine any reasons for this difference in our study. In addition, there is a paucity of data on factors that can alter LUS findings with different breathing modes. Antonio et al. (32) have described the behaviour of LUS findings during spontaneous breathing trial that provided some insight on changes in LUS findings with change in breathing mode. More studies are required that would be sufficiently powered to detect the difference in LUS finding with different breathing modes to determine any possible factors contributing to the difference between these two subsets of patients.

Our study has few limitations. First, we studied patients with lung injury with an ALI score of ≥ 1 . Results might have differed if patients with normal lung were also enrolled. We only had 6 hemithoraxes out of 180 who had no lung pathology on CT scan, and we reported the same by LUS also. Although the number of hemithoraxes with normal lung is small in our study, results suggest that the likelihood of reporting normal lung as diseased by LUS would be low.

Second, the time delay between LUS and CT scan might have contributed to the difference in radiological findings between them in some cases. This is rather inevitable because of logistic issues involved in transferring these patients to CT room. We kept this time delay up to 4 hours as reported previously in the literature and excluded patients who could not be transferred to CT room within this time frame to maintain comparability (4).

Finally, we performed LUS at 6 points that might have contributed to lower sensitivity of LUS in our study than that in the literature, but at the same time, this has not lowered its specificity. This limitation can partly be overcome by examining patients at a greater number of intercostal spaces. Posterior regions of lower lobes can be appreciated better in lateral decubitus, but positioning a critically ill patient may not always be possible (33).

On the positive side, a 6-point scan could be completed in a shorter time that would be immensely useful in evaluating patients with respiratory distress in the ICU, and a detailed scan can be performed later after clinically stabilising patients. It is simpler to learn and does not require change in patient position. Future studies can be planned to compare the feasibility and diagnostic performance of this 6-point protocol with that of more widely described 8- or 12-point protocol of LUS.

Conclusion

A 6-point LUS can be a useful screening tool in diagnosing respiratory pathologies in critically ill patients as it has better diagnostic performance than CXR in detecting commonly found lung pathologies in critically ill patients. LUS can measure pleural effusion with similar accuracy as that of CT scan. Owing to the comparable diagnostic performance of LUS and CT scan and with increasing evidence in favour of LUS, the requirement of CT thorax may be minimised. Radiation hazards associated with CXR and CT, as well as potentially risky transfer of ICU patients to CT room, can also be reduced.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Sanjay Gandhi Post Graduate Institute of Medical Sciences (IEC reference no. 2016-80-MD-91).

Informed Consent: Written informed consent was obtained from patient or next of kin before enrolment in this study.

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