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ORIGINAL RESEARCH INTENSIVE CARE

Lung ultrasound as an evolving tool in the detection of extravascular lung water following goal-directed fluid therapy in septic cancer patients

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Abstract

Background: Severe sepsis can result in septic shock with a high mortality rate. This study aimed to assess the correlation between B-lines detected by lung ultrasound (LUS) and thoracic fluid content (TFC) and to compare their sensitivity and specificity to predict lung congestion on conventional chest radiograph following early goal-directed fluid therapy in septic cancer patients.

Methods: This study included 30 patients suffering from sepsis admitted to the intensive care unit. They received resuscitation according to the surviving sepsis campaign 2018 guidelines. Lung ultrasonography, TFC, central venous pressure (CVP), and inferior vena cava (IVC) scanning were done upon admission then after 3, 6, and 12 h. Chest X-ray was done after 6 h then at the study end (12 h) and CT chest at 12 h.

Results: B-lines showed a moderate-to-strong positive correlation with TFC, a moderate and positive correlation with CVP, and a negative and weak-to-moderate correlation with IVC collapsibility index. The performance of LUS was good at 6 h (AUC = 0.872, 95% CI = 0.700 to 0.965, P < 0.001), and the optimal cut-off value was 7 with a sensitivity and specificity of 75% and 95.5%, respectively. The sensitivity and specificity increased to reach 100% at 12 h using a cut-off value of 9. Meanwhile TFC had lower AUCs compared to B-lines at the two-time points though the difference was statistically non-significant.

Conclusion: Lung ultrasound can be considered a useful non-invasive bedside tool for early detection of extravascular lung water during the early resuscitation phase of goal-directed fluid therapy in sepsis patients.

Abbreviations: LUS: Lung ultrasound; EVLW: Extravascular Lung Water; TFC: Thoracic fluid content; CVP: Central venous pressure; IVC: Inferior vena cava; AUC: Area under the curve; PAOP: Pulmonary artery occlusion pressure; IVC-CI: Inferior vena cava collapsibility index

Key words: IVC collapsibility; Oncologic; Septic shock; Extravascular Lung Water; Humans; Lung; Pulmonary Edema; Ultrasonography

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1. Introduction

Sepsis represents a challenging serious problem in critical care units.[1] Cancer patients receiving chemotherapy are much more susceptible to sepsis due to their immunocompromised status.[2,3] Management of sepsis aims at restoring the intravascular volume, initiating empirical antimicrobials, and identifying the probable source of infection.[4]

Early fluid resuscitation in sepsis-induced hypoperfusion should start with at least 30ml/kg intravenous crystalloids in the first 3 h targeting a mean arterial blood pressure (MAP) of 65 mmHg and a normalized lactate level.[4] Thus, patients with sepsis admitted to critical care units receive a large volume of fluids on their first day of admission,[5] which can result in volume overload, lung congestion, and accumulation of extravascular lung water (EVLW).[6] About 50% of patients with acute circulatory failure positively respond to fluid resuscitation and show an increase in their stroke volume, while the remainder may have worsened outcomes.[7]

Monitoring septic patients' hemodynamics showed beneficial results as a guide to fluid administration in septic patients.[8,9] Different techniques are adopted for assessing patient response to fluid resuscitation, including transpulmonary thermodilution method, measurements of pulmonary artery occlusion pressure (PAOP), and central venous pressure (CVP) along with the analysis of chest radiography.[10,11] Some non-invasive methods to predict fluid responsiveness include the ultrasound assessment of the inferior vena cava (IVC),[7,12] and the measurement of the thoracic fluid content (TFC) using electrical cardiometry.[13]

Recently, lung ultrasound (LUS) evolved as a novel bedside non-invasive tool for the assessment of lung congestion and extravascular lung water (EVLW).[6] Diagnosis of EVLW accumulation is done through the interpretation of B-Lines, which are discrete, hyperechoic, vertical lines extending without fading from the pleura line to the screen edge.[14,15] B-lines indicate the presence of an interstitial lung syndrome, comprising lung edema, interstitial pneumonia, or fibrosis. The number of B-lines correlates with the severity of congestion.[16]

However, much debate exists as to the role and accuracy of these indices in predicting responsiveness to fluid therapy.[7] The present study aimed to address this point by comparing the diagnostic performance of B-Lines relative to the conventional radiographic assessment in the evaluation of fluid response to early goal-directed therapy in septic cancer patients.

2. Methodology

This diagnostic accuracy study was carried out following the approval of the Institutional Review Board of the National Cancer Institute (IRB approval number 201617028.2P). The study was registered at ClinicalTrials.gov (NCT03676699). The study included thirty cancer patients, consecutively recruited from the critical care unit of the National Cancer Institute after obtaining written informed consent from the guardians of the recruited patients.

Patients were recruited based on the presence of malignancies and a diagnosis of sepsis or septic shock according to the third international consensus definition,[17] with an age range between 18 and 65 y. Exclusion criteria included the American Society of Anesthesiologists (ASA) physical status IV, body mass index > 35 kg/m^2, cardiorespiratory diseases, renal failure, and pulmonary metastases or lung cancer. Additionally, patients with inserted chest tubes or suffering from subcutaneous emphysema were excluded.

Upon identification of sepsis, intravenous fluids were started promptly followed by a central venous catheter, and an arterial line and a urinary catheter were inserted. All patients with CVP < 8 mmHg received 30 ml/kg of intravenous crystalloids over the first 3 h according to Surviving Sepsis Campaign to maintain a MAP ≥ 65 mmHg. Norepinephrine was added in non-responders (either a low dose of < 0.15 µg/kg/min or a high dose ≥ 0.15 µg/kg/min targeting MAP ≥ 65 mmHg) while continuing fluid resuscitation till reaching CVP ≥ 12 mmHg.

Lung ultrasonography, IVC scanning, TFC, and CVP measurement were done upon admission (T0), after the first 3 h (T3), after 6 h (T6), and finally after 12 h (T12) to demonstrate the effect of fluid therapy. Chest radiography (CXR) was done after 6 h (T6) and at the end of the study (T12) to minimize the exposure of

patients to the risk of radiation. A confirmatory Computed Tomography (CT) of the chest was done for all patients after 12 h (T12). Echocardiography was done for all patients included in the study by a cardiologist who was blinded to the study to exclude heart failure as a cause of lung congestion.

Anteroposterior CXR with the patient in the sitting position were obtained after 6 and 12 h. The radiographs were assessed by a senior radiologist who was blinded to the hemodynamics and ultrasound results.

Measurements were taken with the patient in the supine position after zeroing of the transducer.

Measurement of thoracic fluid content:

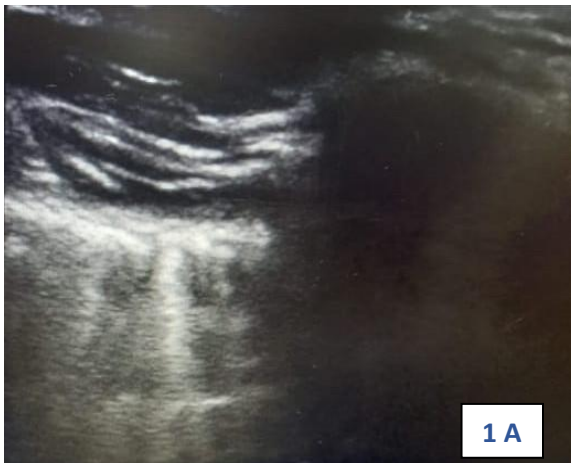
Electrical cardiometry (ICON®; Noninvasive cardiometer device; Osypka Medical, Inc., La Jolla, CA 92037, USA) was used to assess the TFC. The device was connected to the patient through four sensors placed sequentially over the skin of the left side of the neck and left hemithorax. The first and second sensors were placed below the left ear and above the left clavicle. The third and fourth electrodes were placed in the midaxillary line, one at the level of the xiphoid process and the other 5 cm underneath. Values for TFC were assessed and recorded simultaneously during LUS examination.

Lung ultrasound

A SonoSite M-Turbo® ultrasound machine and a 5-1 MHz curved array probe (FUJIFILM Sonosite, Inc.Bothel, WA 98021, USA) were used for all examinations. Patients were scanned while in the supine position. A total of eight quadrants were examined (four quadrants in each hemithorax). Planes of scanning were between parasternal line and anterior axillary line (superior and inferior) as well as between anterior axillary line and posterior axillary line (superior and inferior). A quadrant was defined positive upon confirmation of the presence of three or more B-lines. The patient was considered to have positive B-lines by LUS after the identification of three or more B-lines in three or more quadrants.[16] Ultrasound examination of every quadrant was done by two intensivists who were blind to the details of the images (Figures 1A & 1B). Images were analyzed using the same scoring system.[16]

IVC ultrasound

A SonoSite M-Turbo® ultrasound machine and low-frequency high penetration probe 5-1 MHz curved array probe (FUGIFILM Sonosite, Inc. Bothel, WA 98021, USA) were used for all examinations. Patients were scanned while in the supine position. The end-expiratory and end-inspiratory diameters of the inferior vena cava were measured at 15–20 mm caudal to the hepatic vein junction on a subcostal long-axis view using M-mode. The collapsibility index (IVC CI) was calculated and expressed in a percentage equal to the ratio of the



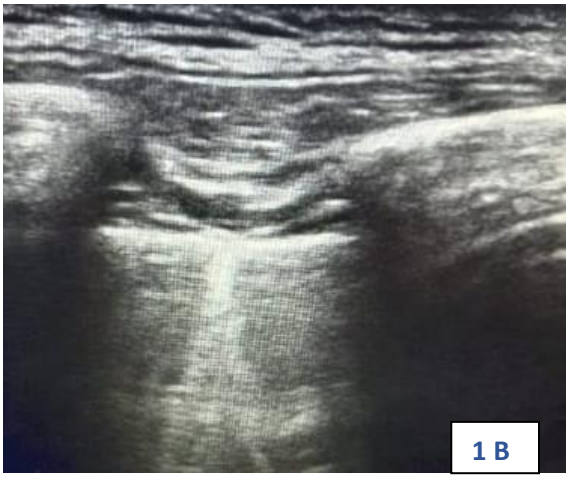


Figure 1 A & B: B-lines detected by LUS

difference between the maximum end-expiratory diameter and the minimum end-inspiratory diameter over the maximum end-expiratory diameter ((IVC max expiratory diam – IVC min inspiratory diam) / IVC max expiratory diam × 100%).[18] The collapsibility index was calculated in percentage, where 0% indicated volume overload and reflected a minimal collapse of IVC while 100 % indicated volume depletion and reflected the complete collapse of the IVC.

Studied outcomes

The primary outcome was to assess the correlation between the B-lines detected by LUS and TFC. Secondary outcomes included the assessment of the sensitivity and specificity of the B-lines in predicting lung congestion on chest radiographs and assessing the correlation between B-lines with IVC CI and CVP measurements.

Statistical analysis

The sample size was calculated using PASS 2008 and assuming a power of 80%, 5% significance level, and an effect size r = 0.5 (representing the correlation between B-lines and TFC). The choice of the effect size was based on the recommendations of Cohen[19,20] who stated that Pearson's correlation coefficients of 0.10, 0.30, and 0.50 indicate small, medium, and large effects, respectively.

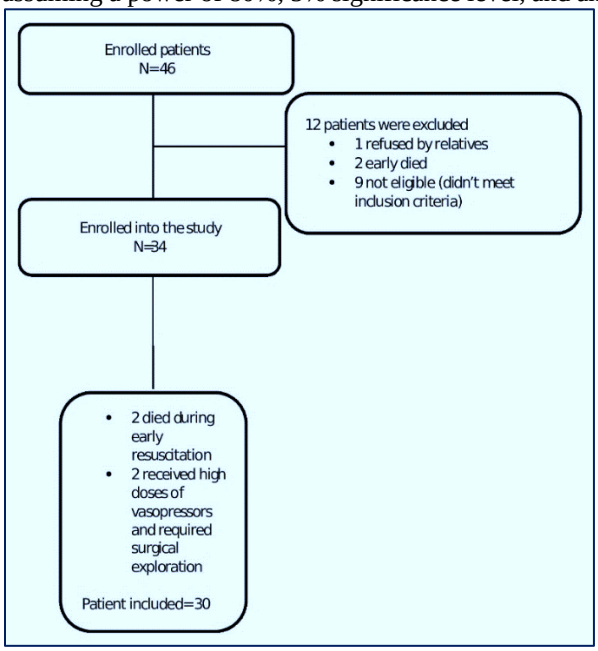


Figure 2: The CONSORT flow chart

The statistical analysis and management of data were done using the Statistical Package for Social Sciences (SPSS), version 26 (IBM Corp., Armonk, N.Y., USA). Continuous numerical variables are summarized according to their distribution as assessed by the Shapiro-Wilk test. Age, MAP, TFC, and IVC CI are presented using mean and standard deviation. SOFA and APACHE II scores as well as B-lines are summarized as medians and interquartile ranges (IQR; expressed as 25^{th} – 75^{th} percentiles). Categorical data (gender, ASA status, cause of admission, and administration of vasoactive drugs) are presented as frequencies. Receiver operating characteristic (ROC) curve was performed and the area under the curve (AUC) is interpreted as excellent discriminatory power (AUC = 0.9 to 1.0), good (AUC = 0.8 to 0.9), fair (AUC = 0.7 to 0.8), and poor (AUC < 0.7). Diagnostic accuracy is calculated in the form of sensitivity (Sensitivity = true positive/ (true positive + false negative) ×100) and specificity (specificity = true negative/ (false positive + true negative) ×100), and accuracy (accuracy = (true positive + true negative) / (all patients) ×100). Repeated measures AONVA, Friedmann's test, McNemar's test, and Cochran's test were used to compare measurements across time points. Spearman's rank-order correlation was carried out between B-lines and different numeric variables. P < 0.05 was considered significant.

3. Results

During the study period, 46 patients were diagnosed with sepsis and admitted to the ICU. Sixteen patients were excluded (one relative refusal to participate, two early deaths, nine patients were not eligible, two deaths during early resuscitation, and two patients required surgical exploration). Thirty patients completed the duration of follow-up and were included in the statistical analysis (Figure 2).

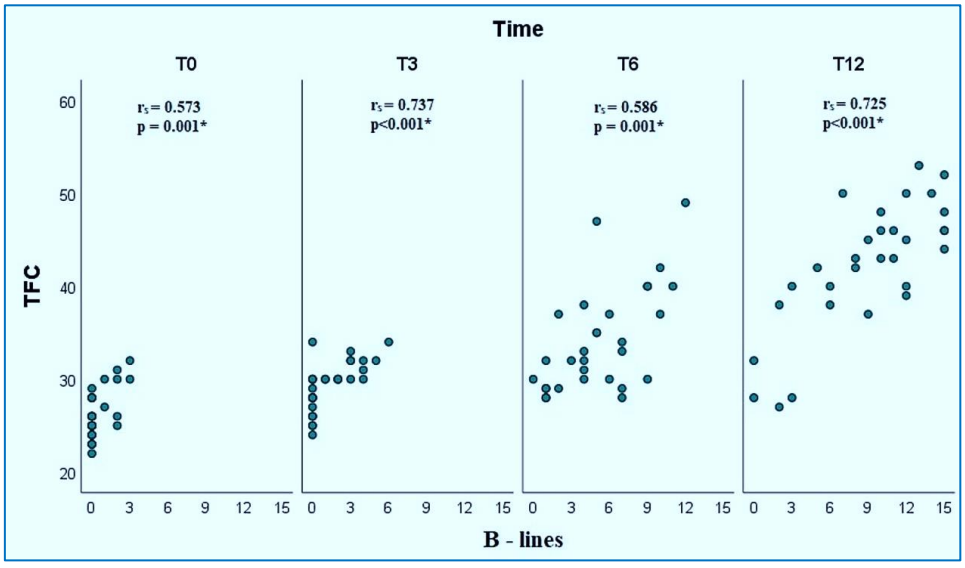


Figure 3: Correlation between B-lines and TFC overtime

The patients' age ranged from 40 to 59 y, with an average (SD) of 50.1 (4.7) y. Most patients were males (60%). Approximately two-thirds (63.3%) were ASA II, whereas the remainder (36.7%) were ASA III. Their initial SOFA score ranged from 8 to 14 (median score 11), while the APACHE score ranged from 11 to 23 (median score 16.5). The most frequent cause of admission to the ICU was postoperative complications (40%), followed by emergency cases (26.7%). The

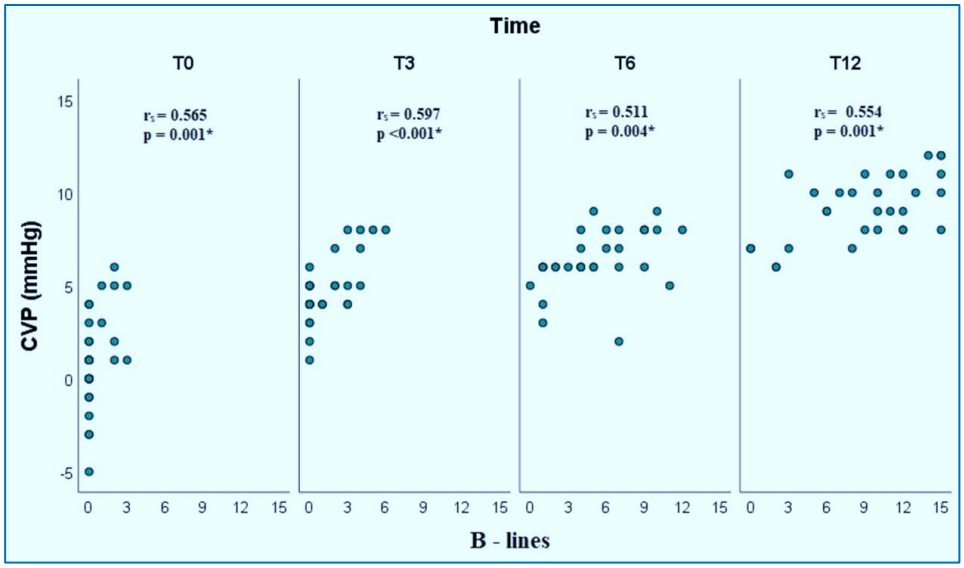


Figure 4: Correlation between B-lines and CVP overtime

LVEF ranged from 51 to 61%, with an average (SD) of 56.8 (3.3). Vasoactive drugs were administered in 53.3% of patients; 40% had low doses while 13.3% had high doses (Table 1).

The assessment of MAP, CVP, TFC, IVC, and B-lines at 0, 3, 6, and 12 h, as well as the chest X-ray, at 6 and 12 h is illustrated in Table 2. There was a gradual increase in MAP, CVP, TFC, and B-lines over time and a gradual decrease in IVC. Significant changes were detected in mean MAP between measurements at 6 and 12 h only ($P < 0.001$). Significant differences in CVP, TFC, and IVC were seen among all the time points ($P < 0.05$), whereas the significant change in the B-lines was detected in measurements after 3 h.

There was a moderate-to-strong positive, significant correlation between the count of B-lines by LUS and TFC measurements throughout the study time at T0, T3, T6, and T12 (rs = 0.573, 0.737, 0.586, and 0.725, respectively, Figure 3). A moderate positive, significant correlation was observed between CVP measurements and B-lines at T0, T3, T6, and T12 (rs = 0.565, 0.597, 0.511, and 0.554, respectively, Figure 4). Moreover, a negative weak to moderate correlation was noticed between B-lines and IVC CI throughout the study, with statistical significance at T0 and T3 (rs = -0.483 and -0.523, respectively), while the correlations at T6 and T12 were weak and non-significant ($P > 0.05$, Figure 5).

CT chest done for all included patients at the end of the study (T12) showed the evidence of B lines in 19 patients (63.3 %).

Comparing between CT chest and chest radiography at 12 h, there was no statistical difference ($P = 0.432$).

Analysis of the ROC curve for predicting lung congestion on chest radiographs demonstrated that the performance of LUS was good (AUC = 0.872, 95% CI = 0.700 to 0.965, $P < 0.001$) at 6 h with a sensitivity of 75%, a specificity of 95.5%, and overall accuracy of 90% at the cut-off value of 7. At 12 h, B-lines had excellent discriminatory power (AUC = 1.000, 95% CI = 0.884 to 1.000, $P < 0.001$), and their sensitivity and specificity increased to reach 100% at a cut-off value of 9. Meanwhile, TFC had a fair-to-good discriminatory power at 6 h (AUC = 0.713, 95% CI = 0.520 to 0.862, p = 0.098) and 12 h (AUC = 0.873, 95% CI = 0.700 to

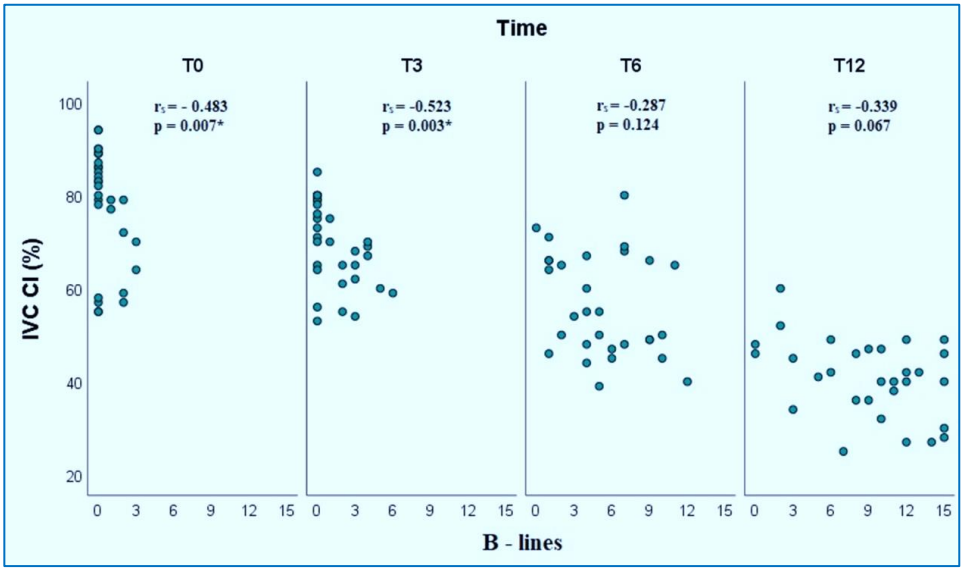


Figure 5: Correlation between B-lines and IVC CI overtime

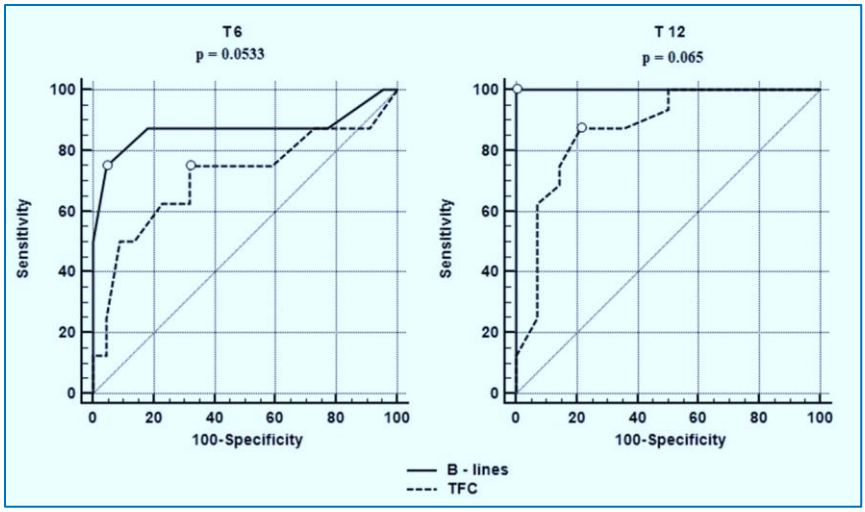


Figure 6: Receiver operating characteristic curves of B-lines and TFC as predictors of lung congestion on radiographs at 6 and 12 h. P-values are derived from comparisons of AUCs of B-lines and TFC.

0.966, P < 0.001) and showed lower AUCs compared to B-lines at the two-time points – though the difference was statistically non-significant (Table 3 and Figure 6).

4. Discussion

The present study aimed to assess the correlation between the B-lines detected by LUS and TFC and to compare its performance in predicting lung congestion on conventional chest radiographs following early goal-directed fluid therapy in septic cancer patients.

The current study results demonstrated that B-lines correlated positively with TFC. This agrees with previous clinical studies which revealed that LUS was a useful non-invasive bedside tool for the detection and assessment of EVLW content, with a positive linear correlation between EVLW and the number of B-lines. Theerawit and colleagues reported a positive correlation between increased EVLW and B-lines in septic patients. [21] A study done on 73 critically ill patients, out of whom 25% were diagnosed with septic shock, reported a positive correlation between the detection of B-lines by LUS and the elevated EVLW diagnosed using the PICCO monitoring system.[22] Hammad and colleagues studied the modulation of fluid management and the early detection of increased EVLW using LUS scoring and TFC measurement in patients with preeclampsia.[23] They verified the strong correlation between LUS and TFC (r = 0.82) for diagnosing increased EVLW.

The results of the current study showed also a moderate positive correlation between CVP measurements and the detection of B-lines by LUS at all study times, while a negative weak-to-moderate correlation was detected between B-lines and IVC CI throughout the study. Hence, although fluid resuscitation was accompanied by improvement of the intravascular status as assessed by the increase in CVP and IVC CI, this was accompanied by an increase in EVLW as demonstrated by the increase in B-lines and TFC. These findings contribute to the explanation of the worsened outcomes which are frequently encountered after fluid therapy in septic patients.[24]

Spevack and colleagues assessed the correlation between LUS with IVC diameters and IVC CI in patients under active treatment of congestive heart failure.[25] They reported the lack of a statistically significant correlation between the detected B-lines and the clinical findings

Table 1: Patients' characteristics and Demographic data

Patients' characteristics		Total patients (n = 30)
Age (y)	Mean ± SD (Min – Max)	50.1 ± 4.7 (40.0 - 59.0)
Sex n (%)	Female	12 (40.0%)
	Male	18 (60.0%)
ASA n (%)	II	19 (63.3%)
	III	11 (36.7%)
SOFA score	Median [IQR] (Min – Max)	11.0 [10.0 - 12.0] (8.0 - 14.0)
APACHE-II score	Median [IQR] (Min – Max)	16.5 [12.0 - 20.0] (11.0 - 23.0)
Cause of admission n (%)	Complicated postoperative case	12 (40.0%)
	Elective surgery	6 (20.0%)
	Emergency surgery	8 (26.7%)
	Medical case	4 (13.3%)
LVEF (%)	Mean ± SD (Min – Max)	56.8 ± 3.3 (51.0 - 61.0)
Vasoactive drug use n (%)	High	4 (13.3%)
	Low	12 (40.0%)
	None	14 (46.7%)

IQR: interquartile range; SD: standard deviation; Max: maximum; Min: minimum; n: number

Table 2: Comparison of the recorded measurements of the studied patients across the time points

Measure		Time 0	3 h	6 h	12 h	p-value
MAP	Mean ± SD (Min - Max)	63.6 ± 7.9 (50.0 - 80.0)	65.3 ± 8.1 (52.0 - 80.0)	69.0 ± 8.7 (58.0 - 87.0)	77.4 ± 8.1 (67.0 - 93.0)	P < 0.001* F p 0-3 = 0.701 p 3-6 = 0.088 p 6-12 < 0.001*
	< 65	18 (60.0%)	12 (40.0%)	15 (50.0%)	30 (100.0%)	P < 0.001* X2 p 0-3 = 0.487
	> 65	12 (40.0%)	18 (60.0%)	15 (50.0%)	0 (0.0%)	p 3-6 = 1.000 p 6-12 < 0.001*
Chest X-ray	0	-	-	22 (73.3%)	14 (46.7%)	P = 0.008* X2
	1	-	-	8 (26.7%)	16 (53.3%)	
CT chest	0				11 (36.6%)	P = 0.432
	1				19 (63.3%)	
CVP	Mean ± SD (Min - Max)	1.1 ± 2.6 (-5.0 - 6.0)	4.9 ± 1.7 (1.0 - 8.0)	6.4 ± 1.6 (2.0 - 9.0)	9.2 ± 1.8 (6.0 - 12.0)	P < 0.001*F p 0-3 < 0.001* p 3-6 < 0.001* p 6-12 < 0.001*
TFC	Mean ± SD (Min - Max)	26.3 ± 2.6 (22.0 - 32.0)	29.3 ± 2.7 (24.0 - 34.0)	34.1 ± 5.6 (28.0 - 49.0)	42.3 ± 6.9 (27.0 - 53.0)	P < 0.001*F p 0-3 < 0.001* p 3-6 < 0.001* p 6-12 < 0.001*
IVC (%)	Mean ± SD (Min - Max)	77.7 ± 12.5 (55.0 - 94.0)	68.8 ± 8.8 (53.0 - 85.0)	56.5 ± 11.0 (39.0 - 80.0)	40.8 ± 8.3 (25.0 - 60.0)	P < 0.001*F p 0-3 < 0.001* p 3-6 < 0.001* p 6-12 < 0.001*
	< 50 %	0 (0.0%)	0 (0.0%)	14 (46.7%)	28 (93.3%)	P < 0.001* X2 p 0-3 = 1.000
	> 50 %	30 (100.0%)	30 (100.0%)	16 (53.3%)	2 (6.7%)	p 3-6 = 0.003* p 6-12 = 0.003*
B-lines	Median [IQR] (Min - Max)	0 [0 - 1] (0 - 3)	0 [0 - 3] (0 - 6)	5 [2 - 7] (0 - 12)	10 [6 - 12] (0 - 15)	P < 0.001*Z p 0-3 = 1.000 p 3-6 = 0.005* p 6-12 = 0.031*

*F: repeated measures ANOVA; IQR: interquartile range; SD: standard deviation; Max: maximum; Min: minimum; n: number; X2: McNemar test (2-repeated measurements) or Cochran's Q test (>2 repeated measurements); Z: Friedmann's test; * significant at P < 0.05; p 0-3: p-value from post-hoc test comparing measurements at T0 and T3; p 3-6:p -value from post-hoc test comparing measurements at T3 and T6; p 6-12:p -value from post-hoc test comparing measurements at T6 and T12.*

although their number decreased with treatment. In a recent study investigating the role of B-lines in the assessment of volume variation in hemodialysis patients, there was a moderate negative correlation with the IVC CI index.[26]

Analysis of the ROC curve in the present study showed a good to an excellent performance of LUS in predicting lung congestion. The performance of B-lines as predictors for lung congestion was assessed by some previous studies in patients with several clinical conditions. A study by Facchini et al.[27] on patients with heart failure reported that B-lines had an AUC of 0.72, and - at a cut-off value of 15 or above - their sensitivity and specificity were 85%, and 84%, respectively. The TFC had an AUC of 0.78 with 85% sensitivity and 81% specificity at a cut-off point of 35 or more. Hammad and colleagues reported that LUS and TFC had a great value in confirming and/ or ruling out pulmonary edema in

Table 3: Analysis of receiver operating characteristic curve for the prediction of lung congestion on chest radiographs

Parameter	6 h		12 h	
	B - lines	TFC	B - lines	TFC
True positive (n)	6	6	16	14
False positive (n)	1	7	0	3
True negative (n)	21	15	14	11
False negative (n)	2	2	0	2
AUC (95% CI)	0.872 (0.700 to 0.965)	0.713 (0.520 to 0.862)	1.000 (0.884 to 1.000)	0.873 (0.700 to 0.966)
P (null hypothesis: AUC = 0.5)	< 0.001*	0.098	< 0.001*	< 0.001*
Cut-off point	> 7	> 33	> 9	> 42
Sensitivity (%)	75.0	75.0	100.0	87.5
Specificity (%)	95.5	68.2	100.0	78.6
Accuracy (%)	90.0	70.0	100.0	83.3

*AUC: area under ROC curve; CI: confidence interval; n: number; TFC: thoracic fluid content; * significant P < 0.05*

patients with preeclampsia.[23] The AUC of TFC in their study was 0.941 (95% CI: 0.849–0.986), with an optimal cut-off value of 40 k ohm−1, 100% sensitivity, and 85.2% specificity whereas the AUC of B-lines was 0.961 (95% CI: 0.887–0.994), with a cut-off value of 15.7, 100% sensitivity and 90.7% specificity.

The use of B-lines to predict lung congestion and to guide fluid therapy in septic patients provides several advantages. Detection of B-lines by LUS is a non-invasive, bedside technique that does not require much expertise and demonstrated good to excellent results while avoiding the hazards of radiation reported with the multiple uses of chest radiographs or computed radiography. However, false-positive results may be encountered as B-lines indicate the presence of interstitial lung pathology (e.g., pulmonary edema, interstitial pneumonia, and pulmonary fibrosis) and thus are not restricted to lung congestion and increased EVLW.[16] In the current study CT was done for confirmation at 12 h after initial stabilization of the patient's condition to ensure patient safety while transporting them to the radiology department. It was observed that all patients found to have positive B-Lines by LUS at 12 h were also confirmed positive by CT. However, 3 patients who were not detected by LUS were found to be positive by CT.

5. Limitations

The main strength point of the present study is addressing the use of B-lines as a predictor of lung congestion that may be used to guide fluid therapy administration in septic patients. However, the study was limited by the relatively small sample size. We performed a ROC curve analysis to assess the diagnostic performance of LUS and TFC as a pilot study, but this analysis requires a larger sample size. Moreover, the exclusion of patients with chronic cardiac or pulmonary conditions may increase the specificity of LUS by decreasing the number of false-positive cases.

6. Conclusion

Lung ultrasound is a feasible, non-invasive bedside tool that can help in the assessment and evaluation of early lung congestion. The authors suggest that the evaluation of the response of goal-directed therapy during the management of cancer patients with sepsis or septic shock can be effectively achieved through the assessment of the intravascular status using CVP and bedside IVC collapsibility index measurements. Meanwhile, the monitoring of the potential sequelae of increased extravascular lung water can be achieved using non-invasive bedside lung ultrasound and the measurement of thoracic fluid content. Since the currently available data are limited, further prospective randomized controlled studies with larger sample sizes are warranted to confirm these findings and provide adequate guidelines for such patients.

7. Data availability

The numerical data generated during this research is available with the authors.

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9. Conflict of interest

Authors declare no conflict of interests. No external or industry funding was involved in this study.

10. Authors' contribution

WE: Put the idea and help in manuscript writing.

MI: Data collection, patient relatives' consent form explanation.

ED: Statistical analysis and results formulation.

MH: Ultrasound technique performance and CT results interpretation.

ES: Manuscript writing, discussion revision and final manuscript revision.

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