Heart and Vessels (2021) 36:518–527
https://doi.org/10.1007/s00380-020-01719-5

ORIGINAL ARTICLE

Prognostic value of pulmonary oedema assessed by lung ultrasound in patient with acute heart failure

Feifei Yang[1] · Qiushuang Wang[1] · Liwei Zhang[1] · Yongjiang Ma[1] · Qiang Chen[1]

Received: 10 April 2020 / Accepted: 23 October 2020 / Published online: 9 November 2020

Abstract

It is very important to assess pulmonary oedema in patients with acute heart failure. The aim of the study was to investigate the accuracy of lung ultrasound in evaluating pulmonary oedema and to explore lung ultrasound in predicting the prognosis. One hundred twenty-four acute heart failure patients were divided into 3 groups, according to the total number of lung ultrasound B-lines groups: B-lines < 15 was the mild pulmonary oedema group (33 cases), 15 ≤ B-lines < 30 was the moderate pulmonary oedema group (33 cases), and B-lines ≥ 30 was the severe pulmonary oedema group (58 cases). The PiCCO monitoring system was used in 11 patients and measured 26 times in different clinical situations. EVLWI have a higher positive correlation with B-lines ($r=0.95$), compared with NT-proBNP and *E*/*e*′ ($r=0.72$, $r=0.62$). During 1 year of follow-up, a multivariate cox regression analysis showed that age, *E*/*e*′ and B-lines ≥ 30 at admission (C-index of 75%) were risk factors for prognosis. 12-month event-free survival showed a significantly worse outcome was observed in patients with ≥ 30 B-lines at admission. B-lines have a good correlation with EVLWI; age, *E*/*e*′ and B-lines ≥ 30 at admission were risk factors for prognosis.

Keywords Lung ultrasound · B-line · Acute heart failure · NT-proBNP · *E*/*e*′

Abbreviations

PiCCO	Pulse indicator continuous cardiac output
EVLW	Extravascular lung water
NT-proBNP	N-terminal pro brain natriuretic peptide
EVLWI	Extravascular lung water index
NYHA	New York Heart Association
EF	Ejection fraction
LVESD	Left ventricular end-systolic diameter
LVEDD	Left ventricular end-diastolic diameter
PAP	Pulmonary arterial pressure
IVC	Inferior vena cava diameter
ROC	Receiver operating characteristic
AUC	Area under the curve

Feifei Yang and Qiushuang Wang are the first authors.

✉ Feifei Yang
cardiofeifei115@163.com

[1] Department of Cardiology, Fourth Medical Center of Chinese, PLA General Hospital, Beijing 100048, China

Introduction

Pulmonary oedema is a major predictor of morbidity and mortality in patients with acute heart failure. Studies have shown that, compared with low cardiac output, pulmonary oedema has a greater impact on the readmissions and death of patients with acute heart failure [1]. How to accurately assess pulmonary oedema in acute heart failure patients has been a challenge. Previously, invasive examination included the right heart catheter and the Swan-Ganz floating catheter, both of which focused on the assessment of pulmonary oedema by measuring pulmonary capillary wedge pressure. However, because this is a technically invasive and complex operation with more complications, it has been used rarely in clinical work. In recent years, PiCCO (pulse indicator continuous cardiac output) through transpulmonary thermodilution with integrated pulse contour analysis can calculate extravascular lung water (extravascular lung water EVLW) accurately to assess pulmonary oedema, which had been confirmed by the lung gravity method, consequently, it has gradually started to replace the two catheter technologies [2, 3]. The previous study of Kitashiro et al. demonstrated that EVLW had good correlations with PCWP ($r^2=0.62$,

$p < 0.05$; $r^2 = 0.73$, $p < 0.05$) during cardiac tamponade and ischaemia, respectively [4].

Lung ultrasound through B-lines, originating from water-thickened interlobular septa, has become a simple, semi-quantitative, non-invasive and bedside tool for evaluating pulmonary oedema. In recent years, lung ultrasound has increasingly attracted the attention of physicians. Our previous study showed B-lines were positively correlated with E/e' ($r = 0.742$, $r = 0.52$) and NT- proBNP ($r = 0.678$, $r = 0.417$), but were negatively correlated with EF ($r = -0.365$, $r = -0.337$) in the preserved ejection fraction heart failure group and reduced ejection fraction heart failure group [5]. However, the correlation between B-lines with EVLW is still unknown in acute heart failure (AHF). Regarding the prognostic value of B-lines, Coiro et al. reported B-lines ≥ 30 is a strong predictor of the primary endpoint (all-cause death or HF hospitalisation) at 3 months [6]. However, the role of B-lines in prognosis needs to be further explored in the long-term follow-up.

In this study, lung ultrasound was used to evaluate the accuracy of pulmonary oedema by comparing the B-lines with the extravascular lung water index (EVLWI), and according to the results of the 1-year follow-up, to explore the role of lung ultrasound in guiding the prognosis in acute heart failure patients.

Methods

Study patients

We included 124 ADHF patients who underwent transthoracic echocardiography, lung ultrasound, chest X ray and NT-proBNP within 24 h of hospitalization at the Fourth Medical Center of Chinese PLA General Hospital between February 2016 and February 2019. Out of the 124 patients, 11 patients underwent PiCCO monitoring (8.87%). We took a total of 26 PiCCO measurements under different clinical conditions, each measurement accompanied with a complete lung ultrasound and echocardiography examinations. Inclusion criteria were as follows: (1) age > 18 years; (2) moderate to severe heart failure (New York Heart Association functional class III, and IV) satisfying the guidelines of European Society of Cardiology [7]. Exclusion criteria were as follows: (1) pulmonary fibrosis, acute respiratory distress syndrome, interstitial pneumonia or pneumonitis; or (2) congenital heart and valve diseases. The study was approved by the Fourth Medical Center of Chinese PLA General Hospital Ethics Committee. All of the patients were informed in advance about the research content and signed an informed consent.

Echocardiography

Transthoracic echocardiography was performed on a Philips CX 50 (Phillips, Bothell, WA, USA) diagnostic bedside ultrasound machine using a 2D probe (S5-1, with a frequency of 1–5 MHz) within 24 h of hospitalization and before discharge. Referring to the recommendations for cardiac chamber quantification by echocardiography [8], left ventricular end-systolic diameter (LVESD), left ventricular end-diastolic diameter (LVEDD), ventricular septal thickness, left atrial diameter, pulmonary arterial pressure (PAP), and inferior vena cava diameter (IVC) were measured. In the apical four-chamber view, the early diastolic fast-wave (E) was measured using pulsed-wave Doppler at the tip of the mitral valve leaflets, and Tissue Doppler was used to measure the mitral annulus diastolic early e ’wave velocity at the ventricular septum and left ventricle lateral wall; these were averaged to calculate the mean early velocity (e'). The ratio of early diastolic mitral inflow velocity to early diastolic velocity of the mitral annulus was calculated for E/e'.

Lung ultrasound

All patients underwent lung ultrasound to determine the presence of B-lines after immediate echocardiography within 24 h of hospitalization and before discharge. According to the recommendations for point-of-care lung ultrasound [9], we adopted the eight chest zones to analyse the anterior and lateral thorax, scanning from the parasternal line to the posterior axillary line between the second to the fourth intercostal spaces, with four zones in each hemi-thorax including the upper anterior, lower anterior chest areas, the upper lateral and basal lateral chest areas, respectively. Eight chest sites were scanned, the B-line score in each zone is from 0 to10, the counting method is shown in Table 1, and the number of B-lines in the eight zones is summed together for the total number of B-lines. According to the total number of ultrasound B-lines groups [10], B-lines < 15 was the

Table 1 B-line Score

Number of B-lines	Score
No B-line	0
One B-line	1
Two B-lines	2
Three B-lines	3
Four B-lines	4
Confluent B-lines 50% ICS	5
Confluent B-lines 75% ICS	8
Confluent B-lines 100% ICS	10

ICS intercostal space

mild pulmonary oedema group (33 cases), 15 ≤ B-lines < 30 was the moderate pulmonary oedema group (33 cases) and B-lines ≥ 30 was the severe pulmonary oedema group (58 cases). All lung ultrasound examinations were performed within 3–5 min by two operators who were blinded to the clinical details. Intra- and inter-observer variability was 6.2% and 7.8%, respectively, and the reproducibility was 96.2%. Three cases had unusable data because of obesity; we excluded the three cases. Lung ultrasound and corresponding *E*/*e′* were showed in Fig. 1.

PiCCO

The PiCCO monitoring system (PULSION Medical System, Munich, Germany) is a device for cardiac output (CO) measurement combined with cardiac preload volume and lung water monitoring. It computes the CO utilizing an arterial pulse contour analysis algorithm after calibration by means of a transpulmonary thermodilution method. A subclavian vein catheter and a right femoral artery catheter were placed and connected to the PiCCO System for monitoring [11]. When measuring, 15 ml of ice water (4 ℃) was injected rapidly from the central venous catheter with an injection time of less than 5 s, and the thermodilution curve was evaluated with arterial catheter inserted in the femoral artery. From the CO we can obtain the intrathoracic thermal volume and the intrathoracic blood volume; from the difference of these two parameters, we can obtain the value of EVLW and EVLWI. The measurement was repeated three times, and the average was recorded. The PiCCO System was used in 11 patients: every patient was measured separately at admission and before discharge, 4 patients were measured once more due to the worsening heart failure, so PiCCO was performed 26 times in total. After each PiCCO measurement, echocardiography and lung ultrasound examination will be performed at the same time within 1 h.

N-terminal pro brain natriuretic peptide analysis

Peripheral venous blood samples were obtained from each patient within 24 h of hospitalization and before discharge. NT-proBNP analysis was performed using the Elecsys 2010 analyser (Roche Diagnostics, Mannheim, Germany).

Statistical analysis

The SPSS 17.0 software package (IBM, Armonk, NY, USA) was used for statistical analysis. All data are expressed as the mean ± standard deviation (SD) for continuous data and as a ratio for categorical data. Group comparisons were performed using one-way analysis of variance (ANOVA), followed by the least significant difference (LSD) t-test. Spearman correlation analysis was used for correlation analysis. $p < 0.05$ was considered to be statistically significant. Univariable analyses and Multivariable analyses by cox regression models were performed to assess the association between each candidate variable and outcome, results were reported as hazard ratios (HR) and 95% confidence intervals (CI). Kaplan–Meier survival curves for HF re-hospitalization

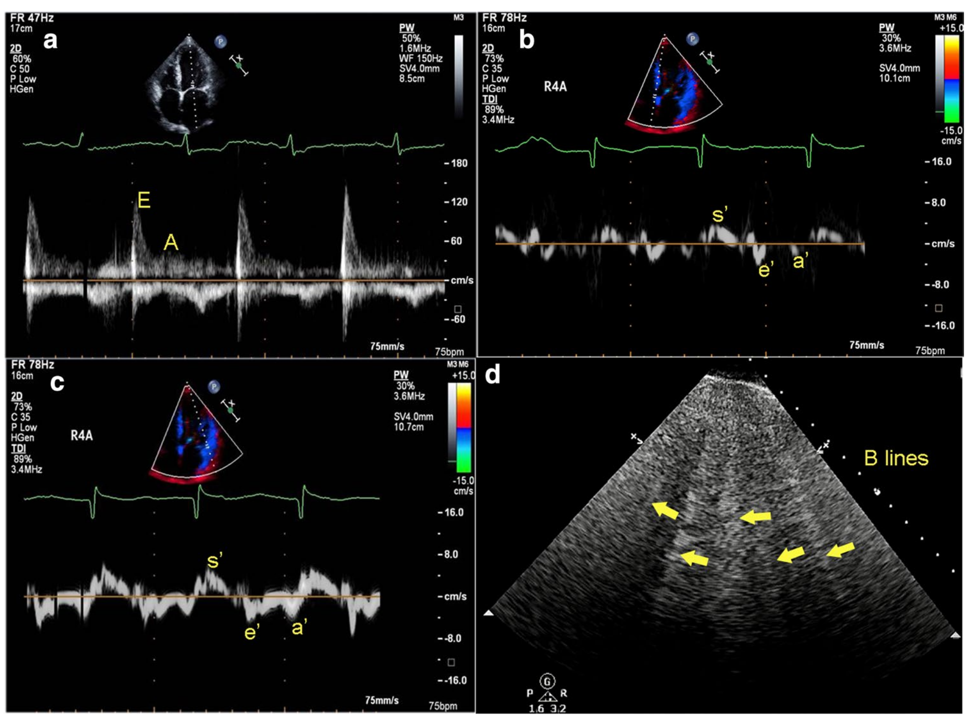

Fig. 1 Lung ultrasound and corresponding *E*/*e′*. **a** In the apical four-chamber view, the early diastolic fast-wave (*E*) was measured using pulsed-wave Doppler at the tip of the mitral valve leaflets; **b** Tissue Doppler was used to measure the mitral annulus diastolic early e 'wave velocity at the ventricular septum and **c** left ventricle lateral wall; **d** B-lines in lung ultrasound

or death in patients with either B-lines ≥ 30 or B-lines < 30 assessed at admission.

Results

Patient characteristics

All 130 enrolled patients underwent lung ultrasound (3–5 min per patient), echocardiography, chest X ray and NT-proBNP within 24 h of hospitalization. Six patients were excluded because of the incomplete data (Fig. 2). Of the remaining 124 patients, 11 patients underwent PiCCO monitoring (8.87%) and made a total of 26 PiCCO measurements in different clinical conditions.

Baseline characteristics for this cohort, grouped by B-lines number, are presented in Table 2.Comparing the clinical data of the three groups, the NYHA grade, Rales ratio, level of NT-proBNP and chest X-ray of the pulmonary congestion ratio were higher in the severe group than in the mild and moderate groups. The usage of digoxin in the severe and moderate groups was higher than in the mild group.

Echocardiography measurements at admission

Comparing the echocardiography measurements of the three groups, the EF of the mild group was significantly higher than that of the moderate and severe groups. The diastolic function index of the severe group, such as *E*/*A*, pulmonary artery pressure and *E*/*e*′ were higher than that of the mild and moderate groups (Table 3).

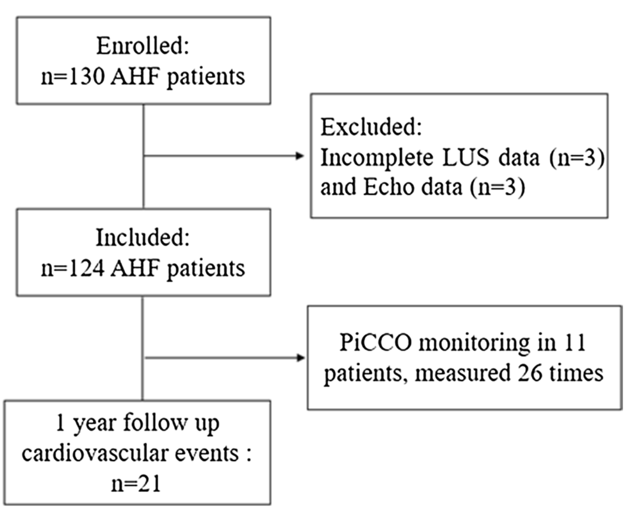

Fig. 2 The flow chart of the study

Correlation between EVLWI and B-lines, NT-proBNP, *E*/*e*′

The correlation between EVLWI and B-lines was the best ($r = 0.95$, $p < 0.001$), followed by NT-proBNP ($r = 0.72$, $p < 0.001$) and *E*/*e*′ ($r = 0.62$, $p < 0.001$) (Table 4, Fig. 3).

Comparison of B-lines, NT-proBNP and echocardiography parameters at admission and discharge

B-lines at discharge and NT-proBNP were significantly lower compared with at admission, EF at discharge was significantly higher than at admission. The left ventricular end systolic diameter, pulmonary artery pressure, *E*/*e*′ and inferior vena cava diameter were significantly lower than at admission (Table 5).

Follow up data: death or rehospitalization

In 1 year of follow-up, 21 cases of cardiovascular events occurred (15 cases were rehospitalized, 6 patients died). Multivariate cox regression analysis showed that age, *E*/*e*′ and B-lines ≥ 30 at admission (C-index of 75%) were the prognostic risk factors; EF at admission was the prognostic protective factor. Twelve-month event-free survival showed a significantly better outcome for those patients with < 30 B-lines at admission, whereas a worse outcome was observed in patients with ≥ 30 B-lines at admission (log rank χ^2 9.794, $p = 0.002$) (Table 6, Fig. 4).

Discussion

Our study showed that B-lines have a good correlation with EVLWI; the correlation of EVLWI with B-lines is better than NT-proBNP, *E*/*e*′. A multivariate cox regression analysis showed that age, *E*/*e*′ and B-lines ≥ 30 at admission (C-index of 75%) were risk factors for prognosis. 12-month event-free survival showed a significantly worse outcome was observed in patients with ≥ 30 B-lines at admission.

Although congestion is considered to be the crucial reason for hospital admission in patients with acute heart failure, a standardized protocol of congestion evaluation is still lacking. The clinical evaluation is often restricted to a simple physical examination including signs and symptoms, relying on a limited set of physical examination findings has met with low sensitivity and poor predictive value [12, 13]. Recently, a position paper by the ESC HF group suggested the use of a flow chart including either clinical, echocardiographic and lung ultrasound measurements to

Table 2 Baseline characteristics of the mild, moderate and severe groups

	Mild (< 15) (*n* = 33)	Moderate (15–30) (*n* = 33)	Severe (≥ 30) (*n* = 58)	*p*
Age (years)	73.24 ± 15.85	66.97 ± 16.64	71.09 ± 16.15	0.278
Male (%)	20 (60.61)	20 (60.61)	39 (67.24)	0.745
BMI	24.35 ± 3.22	25.29 ± 5.09	24.31 ± 3.79	0.500
NYHA Class (%)				< 0.001
II	12 (36.36)	6 (18.18)	2 (3.44)	
III	15 (45.45)	19 (57.58)	26 (44.83)	
IV	6 (18.18)	8 (24.24)	30 (51.72)	
Subtype of HF				0.333
HFpEF	16 (33.33)	13 (27.08)	19 (39.58)	
HFrEF	17 (22.37)	20 (26.32)	39 (51.31)	
Comorbidities				
CAD (%)	26 (78.79)	21 (63.64)	37 (63.79)	0.285
Hypertension (%)	29 (87.88)	21 (63.63)	44 (75.86)	0.071
Hyperlipidaemia (%)	11 (33.33)	14 (42.42)	18 (31.03)	0.538
Smoking (%)	7 (21.21)	4 (12.12)	11 (18.97)	0.165
Diabetes mellitus (%)	15 (45.45)	16 (48.48)	33 (56.90)	0.528
Vitals				
Heart rate (bpm)	76.67 ± 11.66	83.76 ± 17.88	82.29 ± 16.60	0.150
Systolic blood pressure (mmHg)	124.30 ± 22.39	119.27 ± 19.07	122.48 ± 21.19	0.613
Diastolic blood pressure (mmHg)	69.06 ± 12.91	69.67 ± 15.27	68.66 ± 14.58	0.949
Oxygen saturation (%)	97.24 ± 1.75	97 ± 2.49	96.05 ± 4.22	0.192
Rales (%)	12 (36.36)	16 (48.48)*	50 (86.21)#&	< 0.001
Chemistry				
GFR (ml/min/1.73 m^2)	64.17 ± 28.09	68.21 ± 37.84	53.16 ± 33.85	0.139
NT-proBNP (pg/ml)	3408.79 ± 2961.57	4940.39 ± 3086.06	18310.79 ± 8810.83#&	0.015
Congestive X ray (%)	16(48.48%)	26(78.79%)	58(100)#&	< 0.001
Medications				
Beta-blockers (%)	28 (84.85)	29 (87.88)	49 (84.48)	0.92
ACEI/ARB (%)	23 (69.70)	20 (60.61)	40 (68.97)	0.322
Aldosterone antagonist (%)	25 (75.76)	21 (63.64)	46 (79.31)	0.147
Digoxin (%)	1 (3.03)	12 (36.36)*	18 (31.03#	0.002

BMI body mass index; *CAD* coronary artery disease; *ACEI* angiotensin-converting enzyme inhibitor; *ARB* angiotensin receptor blocker

*Mild group compared with moderate group, $p < 0.05$

#Mild group compared with severe group, $p < 0.05$

& Moderate group compared with severe group, $p < 0.05$

detect congestion more precisely [14]. Ultrasonography of the lungs using an echocardiographic probe is potentially useful way to assess pulmonary oedema.

When pulmonary oedema occurs, a layer of high resistance of the gas–liquid interface formed between a pulmonary lobular interval filled with liquid and the alveolar gas; the sound waves in this interface constantly repeated the reflection back and forth, producing a vertical laser beam of high echo bands, extending to the bottom of the screen without attenuation, thus forming a special comet tail sign, also known as the B-line in lung ultrasound. In 1994, Lichtenstein D found an association between a comet tail sign (B-line) and pulmonary interstitial syndrome [15]. In 2004, Jambrik et al. analysed the correlation between the number of pulmonary water B-lines and the extravascular pulmonary water line assessed by chest radiographs and concluded that the correlation was good [16]. Since then, the lung water B-line has been used as a semi-quantitative indicator to assess pulmonary oedema in patients with heart failure and has gradually gained attention.

Lung ultrasound was performed using different scanning regions method in different studies, such as scanning 28 regions, 12 regions, 8 regions, 6 regions or 2 regions [16–18], but the expert consensus document approved

Table 3 Echocardiography measurements of the mild, moderate and severe groups

	Mild (< 15) ($n = 33$)	Moderate (15–30) ($n = 33$)	Severe (≥ 30) ($n = 58$)	p
EF (%)	48.33 ± 9.84	42.82 ± 12.48*	42.07 ± 11.01[#]	0.032
LVEDD (mm)	46.67 ± 5.46	51.55 ± 11.69	50.19 ± 8.44	0.067
LVESD(mm)	33.79 ± 6.58	38.89 ± 12.19	38.81 ± 9.82	0.056
Ventricular septal thickness (mm)	11.84 ± 3.07	11.50 ± 1.49	11.53 ± 1.19	0.744
LA diameter (mm)	37.88 ± 4.62	39.76 ± 8.87	39.09 ± 4.28	0.426
E/A	0.95 ± 0.38	1.01 ± 0.47	1.24 ± 0.55[#&]	0.023
PAP(mmHg)	22.64 ± 11.66	25.48 ± 13.68	33.19 ± 13.50[#&]	0.001
IVC(mm)	17.61 ± 2.24	17.82 ± 3.38	18.48 ± 2.54	0.278
E/*e*′	10.52 ± 4.66	13.29 ± 6.57	17.16 ± 6.79[#&]	< 0.001

EF ejection fraction; *LVEDD* left ventricular end-diastolic diameter; *LVESD* left ventricular end-systolic diameter; *LA* left atrium; *PAP* pulmonary artery pressure; *IVC* inferior vena cava diameter; *E*/*e*′, the ratio of early diastolic mitral inflow velocity to early diastolic velocity of the mitral annulus

[*]Mild group compared with moderate group, $p < 0.05$

[#]Mild group compared with severe group, $p < 0.05$

[&] Moderate group compared with severe group, $p < 0.05$

Table 4 Correlation between EVLWI and B-lines, NT-proBNP, *E*/*e*′

	r	p
B-lines	0.95	< 0.001
NT-proBNP	0.72	< 0.001
E/*e*′	0.62	< 0.001

EVLWI extravascular lung water index; *E*/*e*′, ratio of early diastolic mitral inflow velocity to early diastolic velocity of the mitral annulus

lung ultrasound in 2012 recommended the sonographic technique that ideally consisted of scanning eight regions in the evaluation of interstitial syndrome [19], so our study adopted the eight chest zones to quantify the number of B-lines. In our study, the correlation between EVLWI and B-lines was the best ($r = 0.95$), followed by NT-proBNP ($r = 0.72$) and *E*/*e*′ ($r = 0.62$). The results of this study are consistent with other findings. Hubert et al. reported the correlation between B-lines and LVEDP was higher than that observed for all echocardiographic parameters ($r = 0.62$ for B-lines vs. $r = 0.50$ for all right-or left-sided echocardiographic parameters) [11]. Agricola et al. selected 20 patients undergoing critical cardiac surgery and analysed the correlation between lung ultrasound and PiCCO. It was found that the "pulmonary comet score" was significantly correlated with EVLWI in PiCCO ($r = 0.42$, $p = 0.001$) [20]. Volpicelli et al. reported that critically ill ICU patients also showed a good correlation between B-lines and EVLW, with 81% sensitivity and specificity of 90% for predicting EVLWI [21]. However, the correlation between B-lines and EVLW in acute heart failure has not been reported. Recent studies were focused on the correlation between B-lines, NT-proBNP and *E*/*e*′ in heart failure patients. Miglioranza et al. reported that in patients

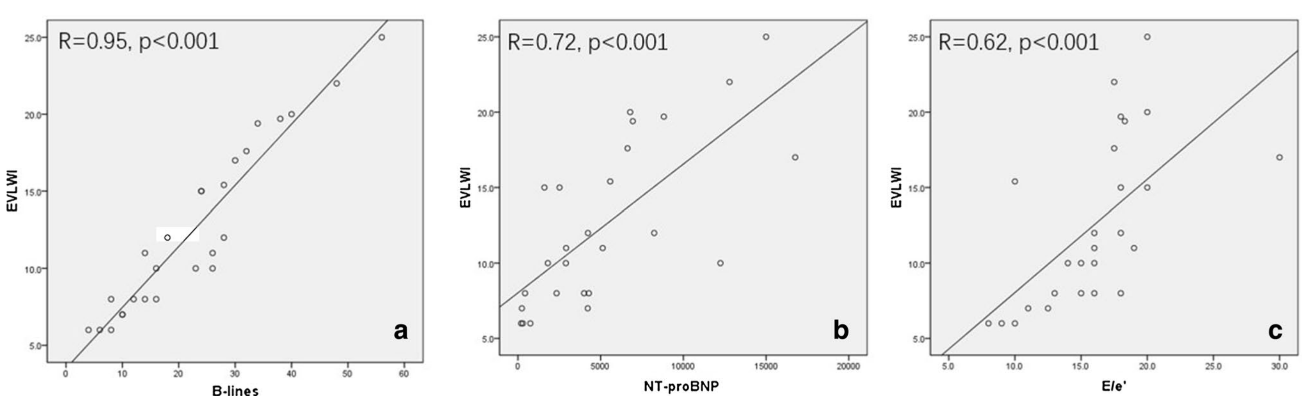

Fig. 3 Correlation between EVLWI and B-lines, NT-proBNP, *E*/*e*′. **a** Scatter plot of the correlation between EVLWI and B-lines; **b** Scatter plot of the correlation between EVLWI and NT-proBNP; **c** Scatter plot of the correlation between EVLWI and *E*/*e*′

Table 5 Comparison of B-lines, NT-proBNP and echocardiography parameters at admission and discharge

	Admission	Discharge	*p*
B-lines	34.16 ± 16.94	22.80 ± 16.36	< 0.001
NT-proBNP (pg/ml)	10458.88 ± 7986.70	6266.70 ± 5478.21	< 0.001
EF (%)	42.89 ± 10.47	46.44 ± 11.17	< 0.001
LVEDD (mm)	48.54 ± 8.44	48.33 ± 8.28	0.641
LVESD (mm)	37.78 ± 9.82	35.83 ± 9.38	< 0.001
LA diameter (mm)	39.30 ± 6.00	38.65 ± 6.07	0.093
Ventricular septal thickness (mm)	11.43 ± 1.37	11.61 ± 2.61	0.479
PAP (mmHg)	29.28 ± 14.79	24.28 ± 12.51	< 0.001
E/*e*′	14.73 ± 8.08	13.37 ± 7.88	0.023
LVC (mm)	18.28 ± 2.72	17.28 ± 2.86	0.003

EF ejection fraction; *LVEDD* left ventricular end-diastolic diameter; *LVESD* left ventricular end-systolic diameter; *LA* left atrium; *PAP* pulmonary artery pressure; *IVC* inferior vena cava diameter; *E*/*e*′, the ratio of early diastolic mitral inflow velocity to early diastolic velocity of the mitral annulus

with chronic heart failure in the outpatient clinic, the number of B-lines and NT- proBNP ($r = 0.72$, $p < 0.0001$) and *E*/*e*′ ($r = 0.68$, $p < 0.0001$) had good correlation [22]. Our previous study showed the correlation between B-lines and *E*/*e*′ was better, especially in the preserved ejection fraction heart failure group compared with reduced ejection fraction heart failure group [5]; similar findings have been reported by Palazzuoli et al. [23]. Moreover, Kobayashi et al. explored the association between these right-sided cardiac parameters and pulmonary congestion in acutely decompensated HF, and their study showed impairments in RV systolic function and RV–PA coupling were associated with a higher number of B-line, both on admission and at discharge [24].

Regarding the value of lung ultrasound in the management of heart failure, Girerd et al. emphasized the value of lung ultrasound for detecting congestion in heart failure patients [25]. In our study, B-lines at discharge were significantly lower compared with at admission, which implies that B-lines can have dynamic change after treatment. During 1 year of follow-up, 21 patients underwent cardiovascular events, including readmission in 15 patients and death in 6 patients. Multivariate analysis showed that age, *E*/*e*′ and B-lines ≥ 30 at admission (C-index of 75%) were risk factors for prognosis, and EF was the protective factor in the prognosis. This study showed that B-lines at admission were related to the prognosis, but B-lines before discharge were not associated with prognosis. Regarding the relationship between B-lines at admission or discharge and prognosis, different studies have different conclusions; there is no consistent conclusion yet. Frassi et al. reported that 290 patients who were hospitalized for dyspnoea or chest pain were followed for an average of 16 months (2.8–29.1) and that the prognosis was worse in patients with a higher number of B-lines at admission; there was a significant difference in the survival rate in patients with B-lines of 0 and B-lines > 30 (70% vs. 19%; $p = 0.007$) [26]. The study of Gargani et al. included 100 patients of dyspnea and/or clinical suspicion of AHF; the results showed B-lines > 15 before discharge (HR 11.74; 95% CI (1.30–106.16) was an independent predictor of events at 6 months [27]. Coiro et al. reported 110 acute HF patients; B-lines ≥ 45 early during HHF were most predictive of outcome (HR = 9.20, 1.82–46.61; $p = 0.007$) [28]. The value of B-lines threshold depends on a number of factors, including clinical status, timing scan, obesity and HF subtypes, so prior studies showed different B-lines threshold.

However, published studies were short-term prognosis for 3 or 6 months. In our study, 12-month event-free survival showed a significantly better outcome for those patients with < 30 B-lines at admission, whereas a worse outcome was

Table 6 Univariate and multivariate cox regression analysis

Univariate	HR (95% CI)	*p*	Multivariate	HR(95% CI)	*p*
Age	1.042 (1.004–1.082)	0.032		1.057(1.007–1.110)	0.026
NYHA Class	1.233 (0.672–2.262)	0.498			
EF at admission	0.977 (0.939–1.017)	0.252		0.893(0.819–0.975)	0.012
EF at discharge	0.992(0.954–1.031)	0.686			
E/*e*′ at admission	1.039 (0.992–1.087)	0.103		1.057(1.021–1.174)	0.011
E/*e*′ at discharge	1.012 (0.963–1.063)	0.631			
NT-proBNP at admission	1.000 (1.000–1.000)	0.005			
NT-proBNP at discharge	1.000 (1.000–1.000)	0.001			
B-lines at admission	1.004 (0.980–1.028)	0.358			
Blines ≥ 30 at admission	7.05 (1.640–30.345)	0.009		13.15 (1.484–116.493)	0.021
B-lines at discharge	0.998 (0.972–1.024)	0.879			
B-lines ≥ 30 at discharge	0.765 (0.309–1.897)	0.564			

EF ejection fraction and *E*/*e*′, ratio of early diastolic mitral inflow velocity to early diastolic velocity of the mitral annulus

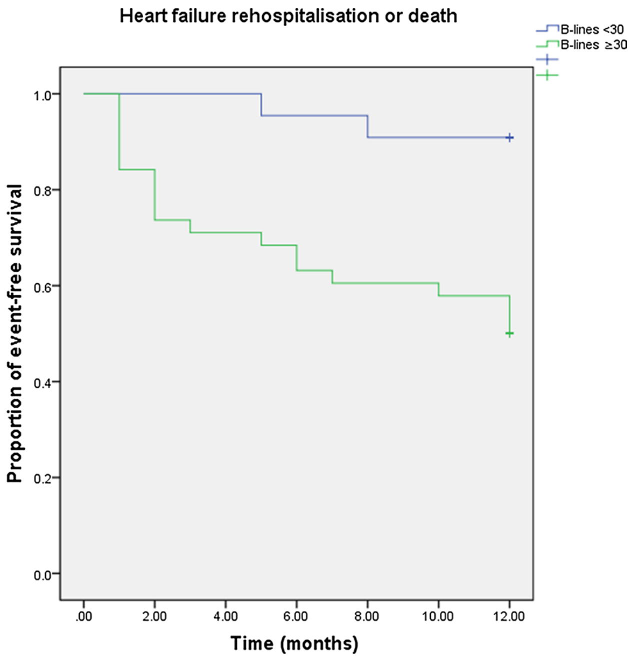

Fig. 4 Kaplan–Meier survival curves for HF rehospitalization or death in patients with either B-lines ≥ 30 or B-lines < 30

observed in patients with ≥ 30 B-lines at admission (log rank χ^2 9.794, $p = 0.002$). This result implies that the higher the number of B-lines, the worse the outcome.

In acute heart failure, some studies showed lung ultrasound could be used to guide therapy. Öhman et al. evaluated a rapid cardiothoracic ultrasound (CaTUS) protocol to guide therapy for acute heart failure; the treatment arm displayed better survival regarding the combined endpoint of 6-month all-cause death or acute heart failure re-hospitalization (log rank $p = 0.017$) [29]. Russell et al. are registering a pilot study which will inform future, larger trial design on lung ultrasound-driven therapy aimed at guiding treatment and improving outcomes in patients with acute heart failure [30]. Of late, the expert consensus document approved lung ultrasound was a useful tool for the assessment of patients with both acute and chronic heart failure; this consensus report will serve as a guide for investigators and clinicians and enhance the quality and transparency of lung ultrasound research in heart failure [19].

Limitations

There are several limitations to our study. First, this was a single-centre study and the number of patients was relatively small, especially of PiCCO patients. Second, B-line is still semi-quantitative method and the need for multiple intercostal collection of images and different zoning methods, different examiners, as well as the patient's body or body position changes, may have a certain impact on the results.

Conclusion

Lung water B-line has a good correlation with EVLWI; B-lines ≥ 30 at admission may be the prognostic risk factor. B-lines can be visualized using the conventional echocardiography probe, and it can illustrate the dynamic change of pulmonary oedema after treatment, so lung ultrasound is highly useful and convenient in the management of heart failure patients.

Author contributions FY and QW participated in the design of the study and performed the ultrasound examinations and analyzed the data. LZ, DH and DS participated in the design of the study and helped to draft the manuscript. YW, YM and QC performed the statistical analysis and helped to draft the manuscript. All authors read and approved the final manuscript.

Funding Clinical Research Support Fund of Chinese PLA General Hospital, Grant no [2018FC-304M-CXYY-01].

Data availability The datasets during and/or analyzed during this study are available from the corresponding author on reasonable request.

Compliance with ethical standards

Conflict of interest The authors have no conflict of interest.

Ethical approval and consent to participate This study was approved by the ethics committee of the Fourth Medical Center of Chinese PLA General Hospital, and written informed consent was provided by all the subjects.

References

1. Gheorghiade M, Abraham WT, Albert NM, Greenberg BH, O'Connor CM, She L, Stough WG, Yancy CW, Young JB, Fonarow GC, OPTIMIZE-HF Investigators and Coordinators (2006) Systolic blood pressure at admission, clinical characteristics, and outcomes in patients hospitalized with acute heart failure. JAMA 296:2217–2226
2. Sakka SG, Rühl CC, Pfeiffer UJ, Beale R, McLuckie A, Reinhart K, Meier-Hellmann A (2000) Assessment of cardiac preload and extravascular lung water by single transpulmonary thermodilution. Intensive Care Med 26:180–187
3. Katzenelson R, Perel A, Berkenstadt H, Preisman S, Kogan S, Sternik L, Segal E (2004) Accuracy of transpulmonary thermodilution versus gravimetric measurement of extravascular lung water. Crit Care Med 32:1550–1554
4. Kitashiro S, Sugiura T, Tamura T, Izuoka T, Miyoshi H, Saito D, Takayama Y, Iwasaka T (1999) Factors associated with increased extravascular lung water in cardiac tamponade and myocardial ischemia. Crit Care Med 27:2229–2233

5. Yang F, Wang Q, Zhi G, Zhang L, Huang D, Shen D, Zhang M (2017) The application of lung ultrasound in acute decompensated heart failure in heart failure with preserved and reduced ejection fraction. Echocardiography 34:1462–1469
6. Coiro S, Rossignol P, Ambrosio G, Carluccio E, Alunni G, Murrone A, Tritto I, Zannad F, Girerd N (2015) Prognostic value of residual pulmonary congestion at discharge assessed by lung ultrasound imaging in heart failure. Eur J Heart Fail 17:1172–1181
7. McMurray JJ, Adamopoulos S, Anker SD, Auricchio A, Böhm M, Dickstein K, Falk V, Filippatos G, Fonseca C, Gomez-Sanchez MA, Jaarsma T, Køber L, Lip GY, Maggioni AP, Parkhomenko A, Pieske BM, Popescu BA, Rønnevik PK, Rutten FH, Schwitter J, Seferovic P, Stepinska J, Trindade PT, Voors AA, Zannad F, Zeiher A, Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology, Bax JJ, Baumgartner H, Ceconi C, Dean V, Deaton C, Fagard R, Funck-Brentano C, Hasdai D, Hoes A, Kirchhof P, Knuuti J, Kolh P, McDonagh T, Moulin C, Popescu BA, Reiner Z, Sechtem U, Sirnes PA, Tendera M, Torbicki A, Vahanian A, Windecker S, McDonagh T, Sechtem U, Bonet LA, Avraamides P, Ben Lamin HA, Brignole M, Coca A, Cowburn P, Dargie H, Elliott P, Flachskampf FA, Guida GF, Hardman S, Iung B, Merkely B, Mueller C, Nanas JN, Nielsen OW, Orn S, Parissis JT, ESC Committee for Practice Guidelines, Ponikowski P (2012) ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail 14:803–869
8. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P, Muraru D, Picard MH, Rietzschel ER, Rudski L, Spencer KT, Tsang W, Voigt JU (2015) Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 28(1–39):e14
9. Volpicelli G, Elbarbary M, Blaivas M, Lichtenstein DA, Mathis G, Kirkpatrick AW, Melniker L, Gargani L, Noble VE, Via G, Dean A, Tsung JW, Soldati G, Copetti R, Bouhemad B, Reissig A, Agricola E, Rouby JJ, Arbelot C, Liteplo A, Sargsyan A, Silva F, Hoppmann R, Breitkreutz R, Seibel A, Neri L, Storti E, Petrovic T, International Liaison Committee on Lung Ultrasound (ILC-LUS) for International Consensus Conference on Lung Ultrasound (ICC-LUS) (2012) International evidence-based recommendations for point-of-care lung ultrasound. Intensive Care Med 38:577–591
10. Picano E, Frassi F, Agricola E, Gligorova S, Gargani L, Mottola G (2006) Ultrasound lung comets: a clinically useful sign of extravascular lung water. J Am Soc Echocardiogr 19:356–363
11. Hubert A, Girerd N, Le Breton H, Galli E, Latar I, Fournet M, Mabo P, Schnell F, Leclercq C, Donal E (2019) Diagnostic accuracy of lung ultrasound for identification of elevated left ventricular filling pressure. Int J Cardiol 281:62–68
12. Palazzuoli A, Evangelista I, Nuti R (2020) Congestion occurrence and evaluation in acute heart failure scenario: time to reconsider different pathways of volume overload. Heart Fail Rev 25:119–131
13. Gheorghiade M, Follath F, Ponikowski P, Barsuk JH, Blair JE, Cleland JG, Dickstein K, Drazner MH, Fonarow GC, Jaarsma T, Jondeau G, Sendon JL, Mebazaa A, Metra M, Nieminen M, Pang PS, Seferovic P, Stevenson LW, van Veldhuisen DJ, Zannad F, Anker SD, Rhodes A, McMurray JJ, Filippatos G, European Society of Cardiology; European Society of Intensive Care Medicine (2010) Assessing and grading congestion in acute heart failure: a scientific statement from the acute heart failure committee of the heart failure association of the European Society of Cardiology and endorsed by the European Society of Intensive Care Medicine. Eur J Heart Fail 12:423–433
14. Mullens W, Damman K, Harjola VP, Mebazaa A, Brunner-La Rocca HP, Martens P, Testani JM, Tang WHW, Orso F, Rossignol P, Metra M, Filippatos G, Seferovic PM, Ruschitzka F, Coats AJ (2019) The use of diuretics in heart failure with congestion-a position statement from the heart failure Association of the European Society of cardiology. Eur J Heart Fail 21:137–155
15. Lichtenstein D (1994) Ultrasound diagnosis of pulmonary edema. Rev Imag Med 6:561–562
16. Jambrik Z, Monti S, Coppola V, Agricola E, Mottola G, Miniati M, Picano E (2004) Usefulness of ultrasound lung comets as a nonradiologic sign of extravascular lung water. Am J Cardiol 93:1265–1270
17. Zhao Z, Jiang L, Xi X, Jiang Q, Zhu B, Wang M, Xing J, Zhang D (2015) Prognostic value of extravascular lung water assessed with lung ultrasound score by chest sonography in patients with acute respiratory distress syndrome. BMC Pulm Med 15:98
18. Enghard P, Rademacher S, Nee J, Hasper D, Engert U, Jörres A, Kruse JM (2015) Simplified lung ultrasound protocol shows excellent prediction of extravascular lung water in ventilated intensive care patients. Crit Care 19:36
19. Platz E, Jhund PS, Girerd N, Pivetta E, McMurray JJV, Peacock WF, Masip J, Martin-Sanchez FJ, Miró Ò, Price S, Cullen L, Maisel AS, Vrints C, Cowie MR, DiSomma S, Bueno H, Mebazaa A, Gualandro DM, Tavares M, Metra M, Coats AJS, Ruschitzka F, Seferovic PM, Mueller C, Study Group on Acute Heart Failure of the Acute Cardiovascular Care Association and the Heart Failure Association of the European Society of Cardiology (2019) Expert consensus document: reporting checklist for quantification of pulmonary congestion bylung ultrasound in heart failure. Eur J Heart Fail 21:844–851
20. Agricola E, Bove T, Oppizzi M, Marino G, Zangrillo A, Margonato A, Picano E (2005) "Ultrasound comet-tail images": a marker of pulmonary edema: a comparative study with wedge pressure and extravascular lung water. Chest 127:1690–1695
21. Volpicelli G, Skurzak S, Boero E, Carpinteri G, Tengattini M, Stefanone V, Luberto L, Anile A, Cerutti E, Radeschi G, Frascisco MF (2014) Lung ultrasound predicts well extravascular lung water but is of limited usefulness in the prediction of wedge pressure. Anesthesiology 121:320–327
22. Miglioranza MH, Gargani L, Sant'Anna RT, Rover MM, Martins VM, Mantovani A, Weber C, Moraes MA, Feldman CJ, Kalil RA, Sicari R, Picano E, Leiria TL (2013) Lung ultrasound for the evaluation of pulmonary congestion in outpatients: a comparison with clinical assessment, natriuretic peptides, and echocardiography. JACC Cardiovasc Imaging 6:1141–1151
23. Palazzuoli A, Ruocco G, Beltrami M, Nuti R, Cleland JG (2018) Combined use of lung ultrasound, B-type natriuretic peptide, and echocardiography for outcome prediction in patients with acute HFREF and HFPEF. Clin Res Cardiol 107:586–596
24. Kobayashi M, Gargani L, Palazzuoli A, Ambrosio G, Bayés-Genis A, Lupon J, Pellicori P, Pugliese NR, Reddy YNV, Ruocco G, Duarte K, Huttin O, Rossignol P, Coiro S, Girerd N (2020) Association between right-sided cardiac function and ultrasound-based pulmonary congestion on acutely decompensated heart failure: findings from a pooled analysis of four cohort studies. Clin Res Cardiol. https://doi.org/10.1007/s00392-020-01724-8
25. Girerd N, Seronde MF, Coiro S, Chouihed T, Bilbault P, Braun F, Kenizou D, Maillier B, Nazeyrollas P, Roul G, Fillieux L, Abraham WT, Januzzi J, Sebbag L, Zannad F, Mebazaa A, Rossignol P, INI-CRCT, Great Network, and the EF-HF Group (2018) Integrative assessment of congestion in heart failure throughout the patient journey. JACC Heart Fail 6:273–285

26. Frassi F, Gargani L, Tesorio P, Raciti M, Mottola G, Picano E (2007) Prognostic value of extravascular lung water assessed with ultrasound lung comets by chest sonography in patients with dyspnea and/or chest pain. J Card Fail 13:830–835
27. Gargani L, Pang PS, Frassi F, Miglioranza MH, Dini FL, Landi P, Picano E (2015) Persistent pulmonary congestion before discharge predicts rehospitalization in heart failure: a lung ultrasound study. Cardiovasc Ultrasound 13:40
28. Coiro S, Porot G, Rossignol P, Ambrosio G, Carluccio E, Tritto I, Huttin O, Lemoine S, Sadoul N, Donal E, Zannad F, Girerd N (2016) Prognostic value of pulmonary congestion assessed by lung ultrasound imaging during heart failure hospitalisation: a two-centre cohort study. Sci Rep 6:39426
29. Öhman J, Harjola VP, Karjalainen P, Lassus J (2018) Focused echocardiography and lung ultrasound protocol for guiding treatment in acute heart failure. ESC Heart Fail 5:120–128
30. Russell FM, Ehrman RR, Ferre R, Gargani L, Noble V, Rupp J, Collins SP, Hunter B, Lane KA, Levy P, Li X, O'Connor C, Pang PS (2019) Design and rationale of the B-lines lung ultrasound guided emergency department management of acute heart failure (BLUSHED-AHF) pilot trial. Heart Lung 48:186–192