JACC: CARDIOVASCULAR IMAGING
VOL. 6, NO. 11, 2013

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER INC.
http://dx.doi.org/10.1016/j.jcmg.2013.08.004

Lung Ultrasound for the Evaluation of Pulmonary Congestion in Outpatients

A Comparison With Clinical Assessment, Natriuretic Peptides, and Echocardiography

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OBJECTIVES The aim of this study was to define the performance of lung ultrasound (LUS) compared with clinical assessment, natriuretic peptides, and echocardiography, to evaluate decompensation in patients with systolic heart failure (HF) in an outpatient clinic.

BACKGROUND Evaluation of pulmonary congestion in chronic HF is challenging. LUS has been recently proposed as a reliable tool for the semiquantification of extravascular lung water through assessment of B-lines.

METHODS This was a cohort study of patients with moderate to severe systolic HF. Receiver-operating characteristic (ROC) analyses were performed to compare LUS with a previously validated clinical congestion score (CCS), amino-terminal portion of B-type natriuretic peptide (NT-proBNP), E/e′ ratio, chest x-ray, and 6-min walk test.

RESULTS Ninety-seven patients were enrolled. Decompensation was present in 57.7% of patients when estimated by CCS, 68% by LUS, 53.6% by NT-proBNP, and 65.3% by E/e′ ≥15. The number of B-lines was correlated to NT-proBNP ($r = 0.72$; $p < 0.0001$), E/e′ ($r = 0.68$; $p < 0.0001$), and CCS ($r = 0.43$; $p < 0.0001$). In ROC analyses, considering as reference for decompensation a combined method (E/e′ ≥15 and/or NT-proBNP >1,000 pg/ml), LUS yielded a C-statistic of 0.89 (95% confidence interval: 0.82 to 0.96), providing the best accuracy with a cutoff ≥15 B-lines (sensitivity 85%, specificity 83%). A systematic approach using CCS, E/e′, NT-proBNP, chest x-ray, and 6-min walk test in different combinations as reference for decompensation also corroborated this cutoff and found a similar accuracy for LUS.

CONCLUSIONS In an HF outpatient clinic, B-lines were significantly correlated with more established parameters of decompensation. A B-line ≥15 cutoff could be considered for a quick and reliable assessment of decompensation in outpatients with HF. (J Am Coll Cardiol Img 2013;6:1141–51) © 2013 by the American College of Cardiology Foundation

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Manuscript received May 8, 2013; revised manuscript received August 19, 2013, accepted August 19, 2013.

JACC: CARDIOVASCULAR IMAGING, VOL. 6, NO. 11, 2013
NOVEMBER 2013:1141–51

Despite impressive improvements in treatment strategies over the past 2 decades, heart failure (HF) morbidity and mortality remain substantially high worldwide (1). Pulmonary congestion, rather than low cardiac output, is considered the leading cause of hospital admissions and death among patients with HF (2,3).

Physical examination is crucial for titrating medical treatment in these patients (4). Unfortunately, this traditional assessment has a good specificity but is not sensitive enough to detect elevated cardiac filling pressures (5). Recently, different clinical congestion scores (CCS) have been developed to evaluate signs of congestion in patients with HF (6–9). However, data comparing these scores with more established tools of decompensation are scarce. The amino-terminal portion of B-type natriuretic peptide (NT-proBNP) is a powerful neurohormonal predictor of prognosis in HF (10) and can be used to titrate therapy (11). Echocardiography can be also used to noninvasively measure left ventricular (LV) filling pressures (12): the ratio of early diastolic mitral inflow velocity to early diastolic velocity of the mitral annulus (E/e′) is one of the most frequently used parameters to assess LV pressures and estimate hemodynamic congestion (13,14).

Lung ultrasound (LUS) through B-line evaluation (formerly ultrasound lung comets) has been recently proposed as a simple, noninvasive, and semiquantitative tool to assess extravascular lung water (EVLW) (15). B-lines have been shown to be correlated to NT-proBNP (16) and E/e′ levels in patients with acute dyspnea (17) and after a stress test (18). LUS can also identify clinically silent pulmonary edema (19,20), suggesting that it could be added to the clinical evaluation to improve hemodynamic profiling and treatment optimization.

To date, no study has evaluated LUS performance for the assessment of pulmonary congestion in outpatients with HF. The aim of this study was to compare B-lines with more traditional methods, such as clinical evaluation, NT-proBNP, and echocardiographic parameters, and determine its performance to assess decompensation in a cohort of outpatients with moderate to severe systolic HF.

ABBREVIATIONS AND ACRONYMS

6MWT = 6-min walk test

CCS = clinical congestion score

CXR = chest x-ray

E/e′ = ratio of early diastolic mitral inflow velocity to early diastolic velocity of mitral annulus

EVLW = extravascular lung water

HF = heart failure

LA = left atrial

LUS = lung ultrasound

LV = left ventricular

NT-proBNP = amino-terminal portion of B-type natriuretic peptide

METHODS

Study design and population. We included 97 consecutive patients followed up in an HF outpatient clinic at the Cardiology Institute of Rio Grande do Sul, Brazil, between November 2011 and October 2012. Inclusion criteria were: 1) age >18 years; 2) LV systolic HF diagnosis for more than 6 months regardless of cause as defined by the Framingham criteria (21) and satisfying the European Society of Cardiology guidelines (22); 3) moderate to severe systolic HF (ejection fraction <45%); 4) no prior diagnosis of pulmonary fibrosis; and 5) absence of congenital heart disease (Fig. 1).

Clinical assessment, NT-proBNP analysis, LUS, echocardiography, and chest x-ray (CXR) were independently performed at the clinical appointment (index evaluation) within a maximum 5-h time delay between the first and last examinations. All patients filled out the Minnesota Living With Heart Failure Questionnaire, a 100-mm analogue visual dyspnea scale, and underwent a 6-min walk test (6MWT) in accordance with standardized methodology. The study protocol was approved by the ethics committee of our institution (protocol UP4467.11). All participants provided written informed consent. We followed the STARD (Standards for the Reporting of Diagnostic) statement for studies of diagnostic accuracy (23).

Clinical congestion score. A previously validated clinical assessment score (7) was used to objectively classify the patients on clinical grounds only. The CCS was calculated by summing up the values obtained in the clinical assessment of HF signs and symptoms, consisting of the following: orthopnea (0 to 4), pulmonary rales (0 to 4), increased central venous pressure (0 to 4), peripheral edema (0 to 4), third heart sound (0 to 1), hepatojugular reflux (0 to 1), and functional class according to New York Heart Association functional classification (1 to 4). The CCS could vary from 1 to 22 points, and patients with ≥3 points were considered decompensated (7).

Natriuretic peptide analysis. Peripheral venous blood samples were obtained from each patient before the index evaluation. NT-proBNP analysis was performed using the Elecsys 2010 analyzer (Roche Diagnostics, Mannheim, Germany). An NT-proBNP >1,000 pg/ml was considered a cutoff marker for decompensated HF.

Echocardiography and LUS. Comprehensive transthoracic echocardiography at rest was performed in all patients using a Vivid-I GE Vingmed ultrasound

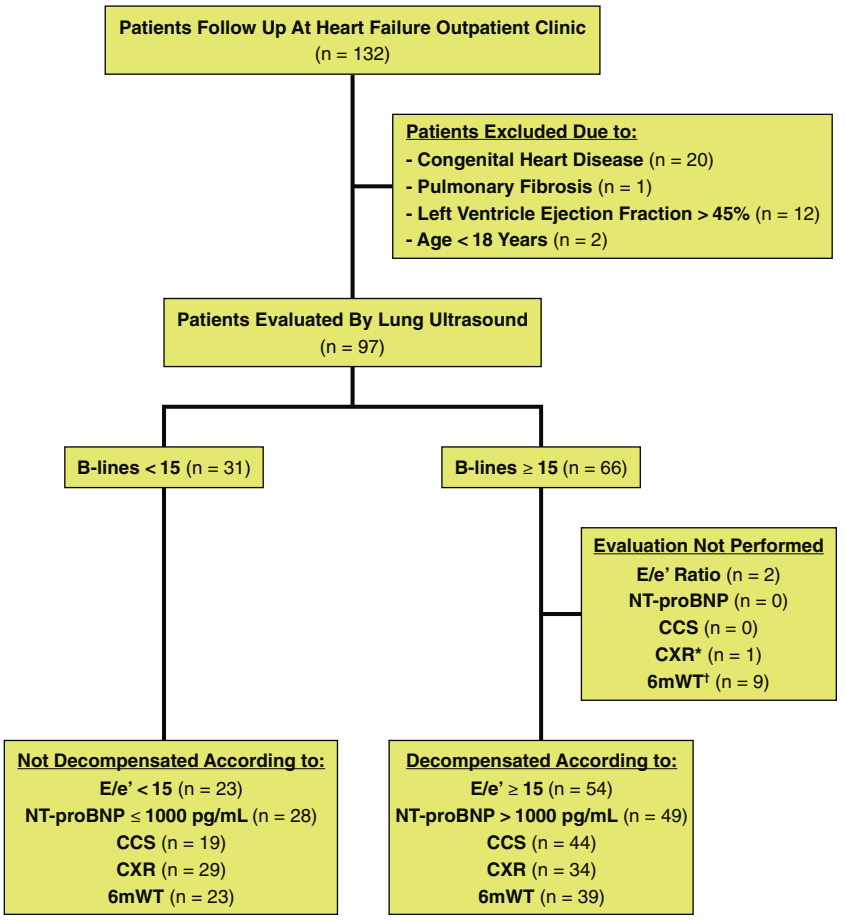
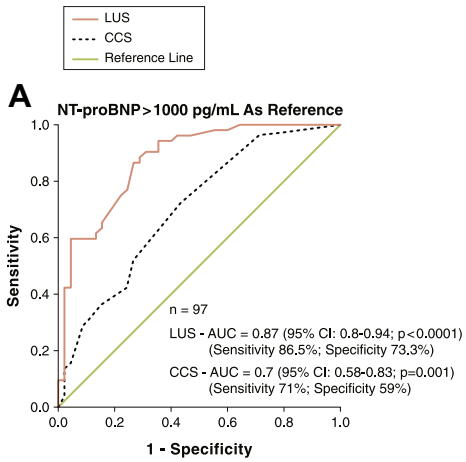


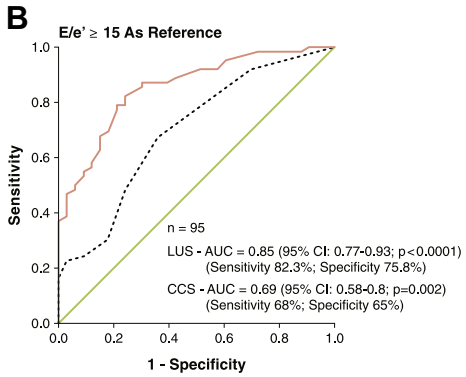
Figure 1. Study Enrollment

*Not possible to evaluate the chest x-ray plain films due to an overpenetration regimen. †Test not performed due to physical disability or medical contraindication. Online Video 1 shows normal lung ultrasound pattern, some A-lines are visible. Online Video 2 shows abnormal lung ultrasound evidencing B-lines, as sign of extravascular lung water. 6mWT = 6-min walk test; CCS = clinical congestion score; CXR = chest x-ray; E/e′ = ratio of early diastolic mitral inflow velocity to early diastolic velocity of mitral annulus; NT-proBNP = amino-terminal portion of B-type natriuretic peptide.

with commercially available cardiac probes (2.5 to 3.5 MHz) to record all examinations. Further independent evaluation was performed offline. LV volumes and ejection fraction were measured by the modified biplane Simpson method according to the American Society of Echocardiography and adjusted for body surface area (24). Diastolic function was determined from the pattern of mitral and pulmonary venous flow velocities measured by pulsed Doppler echocardiography and complemented by septal and lateral mitral annular velocity measured by tissue Doppler imaging (14). The LV filling pressure was determined from E/e′ ratio, with the formula $1.24 \times (E/e') + 1.9$ (13). From the anterograde pulmonary flow acceleration time, we also estimated the mean pulmonary artery pressure and left atrial (LA) pressure using the Mahan and Henry formula (25). Diastolic dysfunction and mitral regurgitation were staged according to the European Association of Cardiovascular Imaging guidelines (14,26).

After the aforementioned routine examination, all patients underwent LUS to assess the presence of B-lines (27). A B-line was defined as a discrete laser-like vertical hyperechoic reverberation artifact that arises from the pleural line extending to the bottom of the screen without fading and moving synchronously with lung sliding (Online Videos 1 and 2) (28). We analyzed the anterior and lateral hemithoraces, scanning along the parasternal, midclavicular, anterior axillary, and midaxillary lines, as previously described





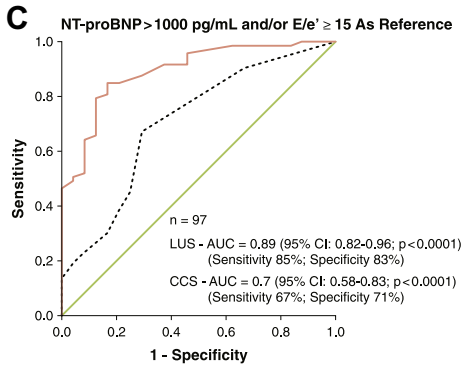


Figure 2. Lung Ultrasound ROC Curves

(A) Receiver-operating characteristic (ROC) curve for lung ultrasound (LUS) and CCS with NT-proBNP >1,000 pg/ml as reference for decompensated heart failure. **(B)** ROC curve for LUS and CCS with E/e′ ≥15 as reference for decompensated heart failure. **(C)** ROC curve for LUS and CCS with NT-proBNP >1,000 pg/ml and/or E/e′ ≥15 as reference for decompensated heart failure. AUC = area under the concentration–time curve; CI = confidence interval; other abbreviations as in Figure 1.

(28). A total of 28 chest sites were scanned, and the total number of B-lines was recorded. Ninety-five patients were analyzed in the supine or near-supine position; 2 patients were orthopneic and the sitting position was preferred. All LUS examinations were recorded and reviewed in a blinded manner.

Chest x-ray. Chest radiographs were obtained in the orthostatic posteroanterior and lateral projections. All plain films were independently evaluated by 2 radiologists recording cardiothoracic index, heart vascular pedicle and vena azygos width, LA enlargement, cephalization, interstitial edema, alveolar edema, pleural effusion, and overall congestion impression.

Statistical analysis. Continuous variables are expressed as mean ± SD or median (25th, 75th percentiles), as appropriate. Categorical variables are presented as counts and percentages. Univariate comparisons were made by chi-square or 2-sample Student *t* test, as appropriate. Differences in the median NT-proBNP concentrations and median number of B-lines were tested with Mann-Whitney nonparametric test. The diagnostic utility of LUS in detecting significant pulmonary congestion was determined using receiver-operating characteristic (ROC) curves, assuming NT-proBNP >1,000 pg/ml, E/e′ ≥15, CCS ≥3, congested CXR, and 6MWT distance <300 m as references for decompensated HF. The results were expressed using the C-statistic. The best threshold was obtained by selecting the point on the ROC curve that maximized both sensitivity and specificity. The correlation between conventional methods and B-line number was assessed with a nonparametric Spearman correlation coefficient analysis. Statistical analyses were performed using SPSS statistics version 19.0.0 (Chicago, Illinois).

RESULTS

Determination of LUS cutoff. There is not a gold standard tool in clinical practice to evaluate decompensation, and multiple parameters are usually combined to increase sensitivity. Therefore, we considered the most used and established parameters as reference to determine the LUS cutoff. Combining NT-proBNP >1,000 pg/ml and/or E/e′ ≥15 yielded a C-statistic of 0.89 for LUS (95% confidence interval [CI]: 0.82 to 0.96), with the best cutoff of ≥15 B-lines providing 84.9% sensitivity (95% CI: 0.7 to 0.9) and 83.3% specificity (95% CI: 0.6 to 0.9) (Fig. 2). A systematic approach including CXR, CCS, E/e′, NT-proBNP, and 6MWT in different combinations (adapted from Gheorghiade et al. [6]) was also used; the best accuracy was yielded

by a cutoff ≥15 B-lines in 9 of 10 different analyses (Online Appendix). This cutoff was also tested assuming NT-proBNP >1,000 pg/ml as a sign of decompensation, with a positive predictive value of 74.2% (95% CI: 0.6 to 0.8) and negative predictive value of 90.3% (95% CI: 0.7 to 0.97). When using E/e′ ≥15 as a reference for decompensation, NT-proBNP and B-lines ≥15 had similar specificity (72.7% and 69.7%, respectively), with a significantly better sensitivity for LUS (87.1%) compared with NT-proBNP >1,000 pg/ml (66.1%).

Clinical, radiographic, and echocardiographic findings. The main characteristics of the patients are listed in Table 1. Decompensation was present in 53.6% according to NT-proBNP, in 57.7% by CCS, and in 37.5% by CXR. An elevated LA pressure estimated by an E/e′ ≥15 was found in 65.3% of patients. The sensitivity of CCS and CXR in detecting elevated LA pressure was 67.1% and 50.8%, respectively. Due to pacemaker stimulation, we were not able to obtain E/e′ and characterize the diastolic function in 2 patients. Restrictive diastolic dysfunction, pseudonormalization patterns, and abnormal relaxation were identified in 41.7%, 28.1%, and 29.2% of patients, respectively. Mitral regurgitation was recognized as mild in 61.9%, moderate in 13.4%, and severe in 2.1% of patients.

LUS findings. LUS feasibility was 100%; mean duration of the examination was 8.7 ± 2.0 min. Significant pulmonary congestion was identified in 68% of patients by LUS (total number of B-lines ≥15). Patients with NT-proBNP >1,000 pg/ml had a significantly higher number of B-lines compared with patients with NT-proBNP ≤1,000 pg/ml (54 ± 36 vs. 17 ± 17; $p < 0.0001$). A higher number of B-lines was also found in patients with E/e′ ≥15 compared with patients with E/e′ <15 (50 ± 34 vs. 8 ± 3; $p < 0.0001$). When stratified by number of B-lines ≥15 and <15, patients showed significant differences between many parameters (Table 2). All patients with B-lines ≥15 presented a pattern of multiple bilateral B-lines, rather homogeneously distributed in all scanned sites (with the exception of sites 18 and 19 occupied in some patients by a larger cardiac area). In this group, there was a significant correlation between the number of B-lines on the right and on the left hemithorax ($r = 0.6$; $p < 0.0001$), as well as a similar number of positive (≥3 B-lines) scans ($p < 0.0001$). A B-line distribution graph is shown in the Online Appendix.

Correlation among clinical, biochemical, and LUS findings. The number of B-lines correlated with NT-proBNP values ($r = 0.72$; $p < 0.0001$) (Fig. 3). Using NT-proBNP as a reference for decompensation, ROC analysis showed a C-statistic of 0.87 for LUS (95% CI: 0.8 to 0.94), with 86.5% sensitivity (95% CI: 0.7 to 0.9) and 73.3% specificity (95% CI: 0.6 to 0.8). The negative predictive value was 82.5% (95% CI: 0.7 to 0.9), whereas the positive predictive value was 79% (95% CI: 0.6 to 0.9) (Fig. 2). The dominant source of discordance was due to abnormal LUS (number of B-lines ≥15) and NT-proBNP ≤1,000 pg/ml. Of these 16 patients, only 2 had an E/e′ <13. The only discordant case with increased natriuretic peptide level and B-lines <15 was associated with the absence of decompensation according to all other methods (Online Appendix). Because the NT-proBNP reference value for decompensated HF is still a source of disagreement, we also performed the analysis using other cutoff points (Online Appendix).

A significant correlation was found between B-lines and E/e′ ($r = 0.68$; $p < 0.0001$) (Fig. 2), CXR ($r = 0.59$; $p < 0.0001$), and CCS ($r = 0.43$; $p < 0.0001$) (Online Appendix). With E/e′ ≥15 as a reference, ROC analysis showed a C-statistic of 0.85 for LUS (95% CI: 0.77 to 0.93), providing the best accuracy with 82.3% sensitivity (95% CI: 0.7 to 0.9) and 75.8% specificity (95% CI: 0.6 to 0.9) (Fig. 2). The negative predictive value was 69.4% (95% CI: 0.5 to 0.8), whereas the positive predictive value was 86.4% (95% CI: 0.7 to 0.9). The dominant source of discordance was an abnormal LUS (number of B-lines ≥15) and an E/e′ <13 (Online Appendix).

DISCUSSION

This study showed that in an HF outpatient clinic, B-lines were significantly correlated with more established parameters of decompensation, suggesting that monitoring chronic HF by LUS can be feasible and accurate in this population. Moreover, our findings suggested a B-line ≥15 value as a reliable cutoff in identifying patients with significant pulmonary congestion.

The recognition and quantification of pulmonary congestion are crucial steps in a thorough evaluation of patients with HF in any clinical setting. LUS seems to be a simple and accurate method for assessing decompensation in an outpatient clinic. The short examination time with 100% feasibility allows this technique to be easily performed during outpatient evaluation. In our study, the time needed to perform each LUS examination was about twice

Table 1. Patient Main Characteristics

	All (n = 97)	B-lines ≥15 (n = 66)	B-lines <15 (n = 31)	p Value
Age, yrs	53 ± 13	55 ± 13	50 ± 13	NS
White	78 (80)	52 (79)	26 (84)	NS
Male	59 (61)	38 (58)	21 (68)	NS
Body mass index, kg/m^2	28 ± 5	28 ± 5	28 ± 4	NS
Heart rate, beats/min	74 ± 13	75 ± 12	73 ± 14	NS
Systolic arterial pressure, mm Hg	120 ± 23	118 ± 23	124 ± 23	NS
Diastolic arterial pressure, mm Hg	75 ± 14	75 ± 14	77 ± 14	NS
Hypertension	52 (53)	36 (54)	16 (51)	NS
Dyslipidemia	43 (44)	30 (45)	13 (42)	NS
Diabetes mellitus	22 (23)	17 (26)	5 (16)	NS
Coronary artery disease	29 (30)	20 (30)	9 (29)	NS
COPD	2 (2)	2 (3)	—	NS
Minnesota questionnaire score	39 ± 22	42 ± 23	33 ± 18	NS
Heart disease etiology				
Dilated cardiomyopathy	52 (54)	35 (53)	17 (55)	
Post-ischemic	26 (27)	16 (24)	10 (32)	
Hypertension	10 (10)	8 (12)	2 (6.5)	NS
Myocarditis	4 (4)	2 (3)	2 (6.5)	
Toxicity—alcohol	3 (3)	3 (4)	—	
Arrhythmia	1 (1)	1 (2)	—	
Chagas	1 (1)	1 (2)	—	
NYHA functional class	2.1 ± 0.8	2.3 ± 0.8	1.9 ± 0.7	
II	49 (50)	34 (51)	15 (48)	
III	22 (23)	16 (24)	6 (19)	0.023
IV	6 (6)	6 (9)	—	
Left ventricular ejection fraction, %	28 ± 7	27 ± 8	31 ± 6	0.004
Indexed left atrium volume, ml/m^2	44 ± 26	47 ± 29	37 ± 18	NS
Electrocardiogram				
Sinus rhythm	75 (77)	47 (71)	28 (90)	0.029
Atrial fibrillation	16 (16)	13 (20)	3 (10)	NS
QRS ≥150 ms	40 (42)	31 (48)	9 (29)	NS
CC, ml/min/1.73 m^2	100 ± 41	97 ± 42	108 ± 40	
<30	1 (1)	1 (1.5)	—	
30–59	15 (15)	11 (15)	5 (16)	NS
≥60	81 (83)	55 (83)	26 (84)	
Sodium, mEq/l	139 ± 3	139 ± 3	139 ± 3	NS
Hematocrit (%)/hemoglobin (g/dl)	40 ± 4/13 ± 1.5	40 ± 4/13 ± 1.5	40 ± 4/13 ± 1.4	NS/NS
Beta-blockers	92 (95)	62 (94)	30 (97)	NS
Target dose	32 (35)	21 (34)	11 (37)	NS
ACE inhibitors	64 (66)	43 (65)	21 (68)	NS
Target dose	23 (36.5)	13 (31)	10 (48)	NS
Angiotensin II receptor blockers	22 (23)	17 (26)	5 (16)	NS
Target dose	15 (71)	11 (69)	4 (80)	NS

Continued on the next page

Table 1. Continued

	All (n = 97)	B-lines ≥15 (n = 66)	B-lines <15 (n = 31)	p Value
Aldosterone antagonist	51 (53)	32 (48)	19 (61)	NS
Diuretics	60 (62)	41 (62)	19 (61)	NS
Digoxin	49 (50)	36 (54)	13 (42)	NS
Calcium antagonists	5 (5)	2 (3)	3 (10)	NS
Nitrates	14 (14)	8 (12)	6 (19)	NS
Hydralazine	5 (5)	3 (4)	2 (6)	NS
Statins	37 (38)	24 (36)	13 (42)	NS
Aspirin	37 (38)	24 (36)	13 (42)	NS
Oral anticoagulants	16 (16)	12 (18)	4 (13)	NS
Amiodarone	10 (10)	8 (12)	2 (6)	NS
Pacemaker/ICD	14 (14)	12 (18)	2 (6)	NS
CRT	5 (5)	4 (6)	1 (3)	NS

Values are mean ± SD or n (%).
ACE = angiotensin-converting enzyme; CC = creatinine clearance; COPD = chronic obstructive pulmonary disease; CRT = cardiac resynchronization therapy; ICD = implantable cardioverter defibrillator; NS = nonsignificant; NYHA = New York Heart Association.

the time that has been previously reported (16,29). This prolongation was mainly because all LUS clips were recorded to be independently and blindly double-reviewed.

Evaluation of decompensation in chronic HF is challenging, even for highly skilled clinicians (30,31). Signs and symptoms provided only a poor sensitivity for the detection of elevated left heart pressures in our series, with similar data (58%) reported in the literature (30). According to a previous study, the main use of a CCS was to predict a decline in the 6-month event-free survival in patients with clear evidence of decompensation (relative risk = 4.8; p = 0.02) (7). However, decompensation is clinically silent in most patients with chronic HF and is often not recognized until conditions develop that require hospital admission; this critical delay in diagnosis justifies the need for more sensitive diagnostic tools (3). The CXR remains by far the most widely used test for detecting pulmonary edema (32), but the absence of radiological evidence for decompensated HF in the chronic outpatient evaluation does not exclude elevated filling pressures (31). This finding was confirmed in our study, with only half of patients with an E/e′ ≥15 being identified by CXR. According to the American Heart Association/American College of Cardiology guidelines, serial CXRs are not recommended in the assessment of pulmonary congestion in chronic HF (4,22). Moreover, serial CXR implies radiation exposure, which should be minimized whenever possible (33,34). Invasive monitoring is the gold standard for evaluating hemodynamic congestion in HF. However, this form of monitoring is clinically impractical, making the use of other noninvasive tools as surrogates for estimating hemodynamic congestion more attractive options.

We showed that B-lines measured by LUS correlated well with NT-proBNP and E/e′. This correlation was not surprising because the presence of B-lines implies more EVLW due to augmented LV filling pressures (17,27,35). Our findings are consistent with those of previous works from other groups, showing that the number of B-lines and their changes after therapy correlate with CXR water score (36), natriuretic peptides (16,37), indexes of diastolic dysfunction (17,38), and intrathoracic impedance monitoring (39). The appropriate reference value of NT-proBNP to use remains a matter of disagreement in the literature. We chose 1,000 pg/ml as a cutoff based on studies that related this value to increased morbidity and mortality (40–45). Because these tests evaluate different pathophysiological mechanisms, it is plausible that their concordance is not complete. Both natriuretic peptides and E/e′ identify hemodynamic congestion, a condition that precedes pulmonary congestion, which is identified by B-lines (46,47). The strength of B-line evaluation is to provide direct insight into the pulmonary interstitium and to be able to differentiate a condition of pure hemodynamic congestion from pulmonary interstitial edema (15). Furthermore, pulmonary congestion is usually, but not always, related to high LV filling pressure, which may

Table 2. Heart Failure Decompensation Parameter Evaluation

	All (n = 97)	B-lines ≥15 (n = 66)	B-lines <15 (n = 31)	p Value
E/e′	23 ± 16	28 ± 18	13 ± 4	<0.0001
LA pressure by E/e′ ratio*	30.5 ± 20.3	36.5 ± 22.0	17.9 ± 5.0	<0.0001
MPAP†	39.1 ± 10.9	42.5 ± 9.8	32.0 ± 9.8	<0.0001
LA pressure‡	22.1 ± 10.5	25.2 ± 9.6	15.0 ± 8.8	<0.0001
NT-proBNP, pg/ml	2,232 ± 2,838	3,070 ± 3,100	450 ± 359	<0.0001
B-lines	36.6 ± 34.2	50.0 ± 34.2	7.9 ± 3.3	<0.0001
6-min walk test distance, m	276 ± 147	241 ± 141	340 ± 139	<0.001
Analogue visual dyspnea scale, mm	20 ± 23	24 ± 25	13 ± 16	<0.05
Clinical congestion on CCS	56 (57.7)	44 (66.7)	12 (38.7)	<0.01
Pulmonary congestion on CXR	36 (37)	34 (52)	2 (6)	<0.0001

Values are mean ± SD or n (%). *Nagueh formula. †Mahan formula. ‡Henry formula.
CCS = clinical congestion scale; CXR = chest x-ray; E/e′ = ratio of early diastolic mitral inflow velocity to early diastolic velocity of mitral annulus; LA = left atrium; MPAP = mean pulmonary arterial pressure; NT-proBNP = amino-terminal portion of B-type natriuretic peptide.

explain some cases of normal NT-proBNP level and/or E/e′ with abnormal LUS (48).

After analyzing LUS and NT-proBNP discordant cases, we realized that these patients were in a "gray zone" for the diagnosis of decompensation by conventional methods. Thus, LUS with number of B-lines ≥15 cutoff appeared to be an additional method to aid in the detection of EVLW, with results similar to those of the multiple-parameter combined assessment. A cutoff based on B-line number has never been previously proposed in outpatients and is somewhat arbitrary. It was at first chosen on the basis of our clinical experience of LUS in patients with HF but then confirmed by statistical analysis. This cutoff of 15 B-lines showed the best accuracy when the reference for decompensation was the combined approach of NT-proBNP >1,000 pg/ml and/or E/e′ ≥15.

LUS is also able to evaluate dynamic changes in EVLW content (37,49). Moreover, this technique is faster to perform, is less expensive, and has lower technical requirements compared with a full echocardiography examination. All of these features make it an attractive clinical tool to introduce in an outpatient HF clinic.

Prospective large-scale randomized (LUS guided vs. standard therapy) outcome studies are

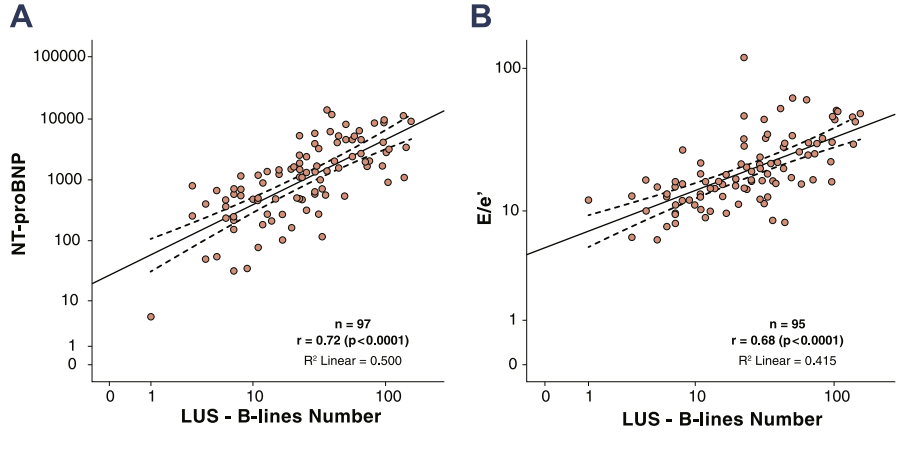


Figure 3. Lung Ultrasound Correlation

Correlation between the number of B-lines and NT-proBNP levels **(A)** and E/e′ values **(B)**. Abbreviations as in Figures 1 and 2.

needed to understand whether B-lines could be implemented in the routine clinical evaluation of outpatients, helping to detect an earlier state of decompensation.

Study limitations. The lack of a true gold standard to verify the presence or absence of pulmonary congestion is an important limitation that does not allow the determination of the real accuracy of LUS, compared with other tests. However, we compared LUS with the most established tools that are used in the real clinical arena in outpatients and found a similar performance.

Sample size is another limitation of this study, and our series may not represent the average patient with HF. Ideally, this study should be repeated in a general cardiology clinic and should include patients with mild systolic HF and patients with only diastolic HF. Furthermore, the detection of B-lines does not necessarily imply their cardiogenic origin. Pulmonary fibrosis and noncardiogenic pulmonary edema, such as acute respiratory distress syndrome, may also result in the presence of B-lines, implying a differential diagnosis that was not present in our study population (50,51).

CONCLUSIONS

In a moderate to severe systolic HF outpatient clinic, B-lines evaluated by LUS were significantly correlated with the CCS, E/e′, and NT-proBNP levels, accurately suggesting decompensation with a B-line ≥15 cutoff. Given its accuracy, LUS could be considered a reliable tool for the assessment of pulmonary congestion in patients with HF; it could be used as an extension of the physical examination and to differentiate hemodynamic from pulmonary congestion. This technique is appealing for the outpatient clinic because it uses simple technology (including pocket-sized devices) and is rapid to perform and interpret. As a possible clinical implication, pharmacological therapy could be tailored as soon as the patient, although asymptomatic, shows a significant increase in the number of B-lines.

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Key Words: B-lines ■ heart failure ■ lung ultrasound ■ natriuretic peptides ■ pulmonary congestion ■ ultrasound lung comets.

APPENDIX

For supplemental videos (and legends), tables, and figures, please see the online version of this article.