[Original Research]

CHEST

Accuracy of Several Lung Ultrasound Methods for the Diagnosis of Acute Heart Failure in the ED

A Multicenter Prospective Study

Aurélien Buessler, MD; Tahar Chouihed, MD, PhD; Kévin Duarte, PhD; Adrien Bassand, MD; Matthieu Huot-Marchand, MD; Yannick Gottwalles, MD; Alice Pénine, MD; Elies André, MD; Lionel Nace, MD; Déborah Jaeger, MD; Masatake Kobayashi, MD; Stefano Coiro, MD, PhD; Patrick Rossignol, MD, PhD; and Nicolas Girerd, MD, PhD

BACKGROUND: Early appropriate diagnosis of acute heart failure (AHF) is recommended by international guidelines. This study assessed the value of several lung ultrasound (LUS) strategies for identifying AHF in the ED.

METHODS: This prospective study, conducted in four EDs, included patients with diagnostic uncertainty based on initial clinical judgment. A clinical diagnosis score for AHF (Brest score) was quantified, followed by an extensive LUS examination performed according to the 4-point (BLUE protocol) and 6-, 8-, and 28-point methods. The primary outcome was AHF discharge diagnosis adjudicated by two senior physicians blinded to LUS measurements. The C-index was used to quantify discrimination.

RESULTS: Among the 117 included patients, AHF (n = 69) was identified in 27.4%, 56.2%, 54.8%, and 76.7% of patients with the 4-point (two bilateral positive points), 6-point, 8-point (≥ 1 bilateral positive point), and 28-point (B-line count ≥ 30) methods, respectively. The C-index (95% CI) of the Brest score was 72.8 (65.3-80.3), whereas the C-index of the 4-, 6-, 8-, and 28-point methods were 63.7 (58.5-68.8), 72.4 (65.0-79.8), 74.0 (67.1-80.9), and 72.4 (63.9-80.9). The highest increase in the C-index on top of the BREST score was observed with the 8-point method in the whole population (6.9; 95% CI, 1.6-12.2; *P* = .010) and in the population with an intermediate Brest score, followed by the 6-point method.

CONCLUSIONS: In patients with diagnostic uncertainty, the 6-point/8-point LUS method (using the 1 bilateral positive point threshold) improves AHF diagnosis accuracy on top of the BREST score.

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ABBREVIATIONS: AHF = acute heart failure; LUS = lung ultrasound

AFFILIATIONS: From the Emergency Department (Drs Buessler, Chouihed, Bassand, Huot-Marchand, and Jaeger), University Hospital of Nancy, France; Université de Lorraine (Dr Duarte), Institut Elie Cartan de Lorraine, Unité Mixte de Recherche 7502, Centre National de la Recherche Scientifique, INRIA, Project-Team BIGS, Villers-lès-Nancy, France; Université de Lorraine (Dr Chouihed, Duarte, Rossignol, and Girerd), Centre d'Investigations Cliniques Plurithématique 1433, Institut Lorrain du Cœur et des Vaisseaux, Vandoeuvre les Nancy France Groupe choc, INSERM U1116, Faculté de Médecine, 54500 Vandoeuvre les Nancy, France; Emergency Department (Dr Gottwalles), Colmar Hospital, Colmar, France; Emergency Department (Dr Pénine), Charleville-Maizières Hospital, Charleville-Maizières France; Emergency Department (Dr André), Mercy Hospital, Metz, France; Intensive Care Unit (Dr Nace), University Hospital of Nancy, France; Department of Cardiology (Dr Kobayashi), Tokyo Medical

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Dyspnea is one of the most frequent causes of admission to the ED[1] and represents a significant diagnostic challenge for emergency physicians. Acute heart failure (AHF) is one of the most common etiologies of acute dyspnea.[2] Guidelines recommend that diagnosis should be made as soon as possible to promptly begin appropriate early treatment.[3,4] Prognosis is related to initiation time of specific therapies.[5] In-hospital mortality is typically reported to be > 10%[6] and has remained stable in the last 30 years.

Diagnostic approaches include clinical evaluation, chest radiograph, biological tests, and specific biomarkers. Nevertheless, diagnosis remains difficult, especially in ED patients, many of whom feature atypical clinical presentation due to several previous comorbidities and mixed/concomitant etiologies of acute dyspnea.[2] Basset et al[7] developed the Brest score for the diagnosis of AHF in ED patients. However, this score classified 50% of cases in the intermediate probability group, hence supporting the importance of developing and promoting "new tools"[8] that are complementary to clinical scores to achieve a quick diagnosis of AHF in patients admitted for acute dyspnea in the ED.

Ultrasound has gained widespread use in recent years and is now a highly valuable tool in the ED. Lung ultrasound (LUS) is a quick, reliable, and easy-to-use examination that can improve the diagnostic accuracy for dyspneic patients.[9,10] Lichtenstein and Mezière[11] further highlighted the advantages of LUS in ICUs for the evaluation of patients with respiratory distress (ie, the BLUE protocol). Several methods have been secondarily proposed to assess pulmonary congestion using different analysis points, interpretation thresholds, and various assessment conditions.[12-14] However, most of these studies focused on patients outside of the ED.

Given these factors, the current study aimed to evaluate and compare the diagnostic performance of currently available ultrasound protocols for pulmonary congestion assessment (ie, the 4-point [BLUE protocol] and 6-, 8-, and 28-point methods) in patients admitted for acute dyspnea in the ED. The study further aimed to evaluate the diagnostic performance of these methods in patients with intermediate Brest scores (ie, 4-8).

Methods

Study Protocol and Design

This study is a part of the prospective Pathway and Urgent Care of Dyspneic Patient at Emergency Department in Lorraine District (PURPLE) study (CNIL DR-2017-098).[15] Patients admitted to the ED in four different hospitals, including a university hospital, over a 3-month period were included. All patients aged > 50 years admitted for acute dyspnea for whom the treating physician had diagnostic uncertainty based on his or her initial clinical evaluation were included. Exclusion criteria consisted of traumatic dyspnea and systolic BP < 70 mm Hg.

For each patient, the Brest score was calculated,[7] and a standardized LUS was performed. All clinical and ultrasound analysis data were collected by the emergency physicians and entered into the Clinical Research Form of the study.

University, Tokyo, Japan; F-CRIN INI-CRCT (Cardiovascular and Renal Clinical Trialists) (Drs Chouihed, Rossignol, and Girerd), Nancy, France; University of Perugia (Dr Coiro), School of Medicine, Perugia, Division of Cardiology; and Département de Cardiologie (Drs Girerd), Institut Lorrain du Cœur et des Vaisseaux, CHRU Nancy, France.

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CORRESPONDENCE TO: Tahar Chouihed, MD, PhD, University Hospital of Nancy, Emergency Department, Nancy, Lorraine France; e-mail: t.chouihed@gmail.com

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Ultrasound Methods

Ultrasounds were performed by ultrasound-certified emergency physicians. Twenty-eight-point LUS were performed in all patients: for each point, a B-line grading from 0 to 10 was used. Using the data of this 28-point method, patients were able to be classified according to four published methods (Fig 1).[11-13,16]

Four-point method (BLUE protocol)[11]: Two scanning sites on each hemithorax: Second intercostal space, mid-clavicular line and fourth intercostal space, anterior axillary line. A positive point was defined as the presence of at least three B-lines. A positive examination was defined, according to the seminal publication,[17] by the presence of at least three B-lines on each scanning site.

Six-point method[12]: Three scanning sites on each hemithorax: Second intercostal space, mid-clavicular line, fourth intercostal space, anterior axillary line, fifth intercostal space, mid-axillary line. A positive point was defined as the presence of at least three B-lines in a given scanning site.

Eight-point method[13]: Four scanning sites on each hemithorax: Two anterior points, between the sternum and the anterior axillary line, comprising two scanning sites. Two lateral points between the anterior and the posterior axillary line, comprising two scanning sites. A positive point was defined as the presence of at least three B-lines in a given scanning site.

Twenty-eight-point method[16,18]: Sixteen points on the right side and 12 points on the left as described in Figure 1. This examination was used both as a continuous count of overall B-lines as well as in the form of dichotomous variables (≥ 15 or ≥ 30).

A positive point was defined as the presence of at least three B-lines in a given scanning site. The examinations were then categorized

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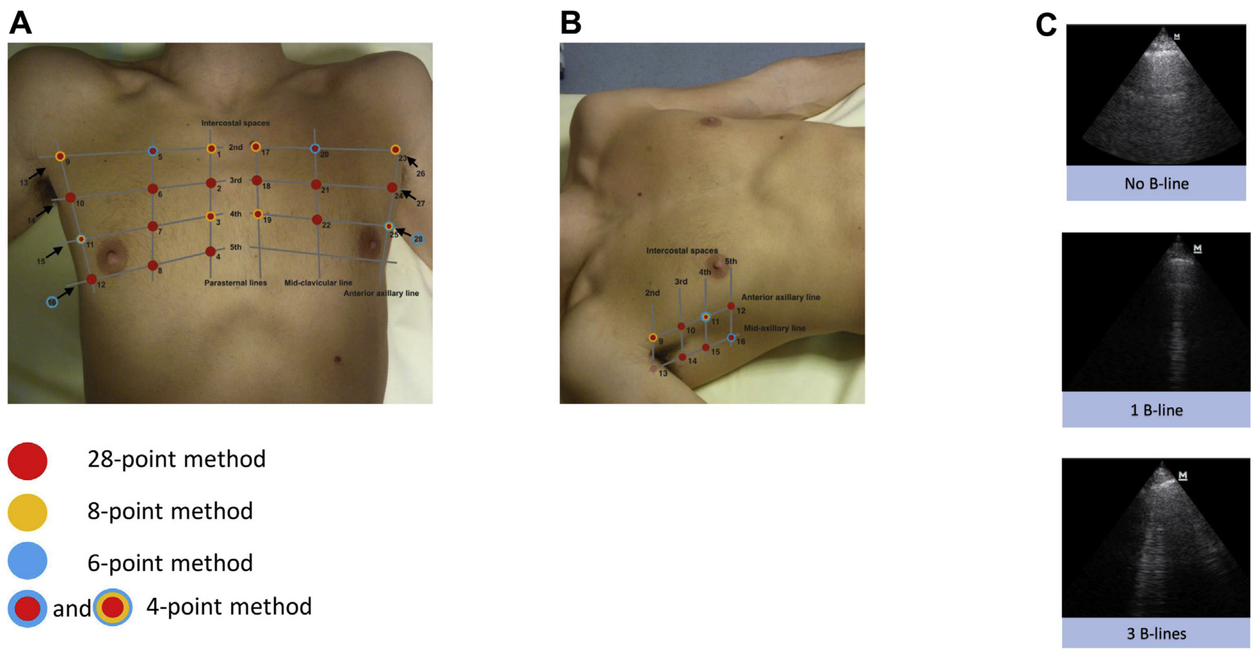

Figure 1 – *A-C, LUS methods: 4- to 28-point method described on a frontal (A) and lateral (B) view. Examples of LUS recordings showing 0 to 3 B-lines (C). LUS = lung ultrasound.*

according to the presence and number of bilateral positive points. We considered two definitions of positive examinations: a positive examination was either defined as at least one positive zone bilaterally (ie, at least one on the right lung and at least one on the left lung) or as at least two positive zones bilaterally. The presence of two positive points on each hemithorax, irrespective of their locations (ie, positive points on the superior part of the right thorax and on the inferior part of the left thorax), qualified for being considered as having "≥ 2 bilateral positive points."

Outcome

Diagnostic outcome was the final diagnosis at discharge collected from the patients' medical records. The final diagnosis of the hospital stay was adjudicated by two senior physicians (emergency physician and cardiologist) blinded to the LUS measurements.

Sample Size

A random sample of 120 patients (60 with AHF and 60 without AHF) was necessary, when the sample C-index was equal to 80%, to achieve a two-sided 95% CI width of 16% (ie, with a lower limit equal to 72% and a upper limit equal to 88%) according to the Hanley and McNeil method. This setting also allows use of a CI width < 0.18 for a C-index equal to 75% and a CI width of 0.14 for a C-index of 0.85.

Statistical Analysis

All analyses were performed by using R software (the R foundation for Statistical Computation). The two-tailed significance level was set at $P < .05$.

Baseline characteristics are described as mean ± SD or median (interquartile range) for continuous variables and frequency (percentage) for categorical variables. Comparison of baseline characteristics according to the AHF and non-AHF groups were conducted by using the nonparametric Wilcoxon test for continuous variables and the χ^2 or Fisher exact tests for categorical variables.

Associations between LUS measurements and AHF were assessed by using logistic regression. ORs with 95% CIs are reported. For certain variables, quasi-complete separation was detected. ORs with CIs were therefore estimated by using a logistic regression model with Firth's penalized likelihood method. This method provides a solution to the phenomenon of monotone likelihood, which causes parameter estimates of the usual logistic regression model to diverge, with infinite SEs.

Individual performance of LUS measurements for diagnosing AHF was assessed by the calculation of the C-index, which is very similar to the area under the curve of the receiver-operating characteristic used on univariable data. In addition, the increase in the C-index was calculated to assess the additional value of LUS measurements in addition to the Brest score for the diagnosis of AHF.

Results

A total of 117 patients were included, 62% of whom had a hospital discharge diagnosis of AHF (n = 73); only 54% (n = 63) had an AHF diagnosis in the ED (three patients with AHF at the ED had a non-AHF discharge diagnosis and 13 had an AHF diagnosis at discharge but not in the ED), however (Table 1). The population was elderly (mean age, 79.6 ± 11.8 years), mainly female (56%), and frequently had comorbidities. The majority of patients were hospitalized subsequent to ED admission (96%; n = 112), primarily in medical wards (n = 68; 58%); 25% (n = 29) were admitted to ICUs, and only 13% (n = 15) were admitted to a cardiology ward. A majority of patients had an intermediate Brest

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score (64%; n = 75), both in the AHF group (67%; n = 49) and in the non-AHF group (59%; n = 26).

Diagnostic Performances in the Overall Study Population

In a first instance, the Brest score had a good diagnostic value when considered as a continuous variable (C-index = 81.8; 95% CI, 74.2-89.4), which subsequently decreased when using BREST score categories (C-index = 72.8; 95% CI, 65.3-80.3).

Among the LUS methods, the 4-point method (two bilateral positive points) had the lowest C-index (63.7; 95% CI, 58.5-68.8), whereas the other methods had very similar C-indices (6-point method for ≥ 1 bilateral positive point, 72.4 [95% CI, 65.0-79.8]; 8-point method for ≥ 1 bilateral positive point, 74.0 [95% CI, 67.1-80.9]; and 28-point method for B-lines ≥30, 72.4 [95% CI, 63.9-80.9]) (Table 2).

The 6-point method (≥ 1 bilateral positive point) had a specificity near 90% with a relatively low sensitivity (56.2%; 95% CI, 41.1-67.8). The 8-point method (≥ 1 bilateral positive point) had a higher specificity (93.2%; 95% CI, 81.3-98.6) and similar sensitivity (54.8%; 95% CI, 42.7-66.5). In contrast, the 28-point method had high sensitivity (B-lines ≥ 15, 89.0 [95% CI, 79.5-95.1]; B-lines ≥ 30, 76.7 [95% CI, 65.4-85.8]) but low specificity (B-lines ≥ 15, 43.2 [95% CI, 28.3-59.0]; B-lines ≥ 30, 68.2 [95% CI, 52.4-81.4]) (Table 2).

For the 6- and 8-point methods, the use of the ≥ 1 bilateral positive point threshold yielded a higher C-index as well as a better sensitivity (13% and 6%, respectively) and moderately lower specificity (–4% and –11%) (Table 2).

Each method provided significant added value to the Brest score as assessed by changes in the C-index. However, the highest increase in the C-index was observed for the 6-point method (6.7; 95% CI, 0.9-12.5; P = .024) and the 8-point method (6.9; 95% CI, 1.6-12.2; P = .010) (Fig 2, Table 3).

Diagnostic Performances With Intermediate Brest Scores

In patients (n = 75) with intermediate Brest scores (4-8), the 4-point method (two positive points bilaterally) had a C-index of 61.2 (95% CI, 55.3-67.1) and an added value to the Brest score of < 5 as measured by an increase in the C-index. In contrast, the 6- and 8-point methods had a C-index > 70 when considering ≥ 1 positive point bilaterally (71.8 [95% CI, 62.4-81.2] and 72.7 [95% CI, 63.9-81.5], respectively).

Similarly to the results in the overall population, the 6- and 8-point methods (≥ 1 bilateral positive point) had a specificity near 90% and a sensitivity near 50%. For the 8-point method, the use of the ≥ 1 bilateral positive point threshold yielded a higher C-index as well as better sensitivity (14% increase) and moderately lower specificity (4% decrease).

A significant increase in C-index over the BREST score was only identified for the 8-point method (increase in C-index = 10.7; 95% CI, 1.7 to 19.7; P = .020). However, the increase in the C-index with the 6-point method had a very similar point estimate (increase in C-index = 8.9; 95% CI, –0.2 to 17.9; P = .054). Importantly, the 28-point method had a lower increase in the C-index of 6.8 (95% CI, –2.6 to 16.1), which was not statistically significant (P = .16) (Fig 2, Table 3).

Discussion

In the present study, the 6- and 8-point methods were found to be the most relevant LUS methods for establishing an AHF diagnosis in the ED. This result was further confirmed among patients with intermediate Brest scores. In addition, all ultrasound methods (particularly the 6- and 8-point methods) provided a diagnostic added value in addition to the Brest score, both in the whole population (increase in C-index 8-point method = 6.9; 95% CI, 1.6-12.2; P = .010) and in patients with intermediate Brest scores (increase in C-index 8-point method = 10.7; 95% CI, 1.7-19.7; P = .020). The main results and techniques used are summarized in Figure 2.

Importantly, we identified a somewhat lower C-index for the diagnosis of AHF than that previously reported in a meta-analysis[19] in which AHF identified on LUS proved to be a diagnostic variable with discriminatory value (positive likelihood ratio, 7.4 [95% CI, 4.2-12.8]; negative likelihood ratio, 0.16 [95% CI, 0.05-0.51]) (e-Tables 2, 3) and for which the authors acknowledged the high statistical heterogeneity for these pooled estimates (I^2 = 78% and I^2 = 99%, respectively). However, contrary to the aforementioned studies, the current analysis was conducted in the specific setting of “real-life” patients admitted to the ED for whom the treating physician had diagnostic uncertainty based on his or her initial clinical evaluation. Our results can be summarized as shown in Figure 3.

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TABLE 1] Characteristics of the Study Population

Characteristic	Population (N = 117)		No AHF (n = 44)		AHF (n = 73)		*P* Value
	No.	Mean ± SD or No. (%)	No.	Mean ± SD or No. (%)	No.	Mean ± SD or No. (%)	
Clinical characteristics							
Age, y	117	79.6 ± 11.8	44	77.0 ± 13.6	73	81.2 ± 10.3	.088
Male sex	117	52 (44)	44	16 (36)	73	36 (49)	.19
Chronic heart failure	117	19 (16)	44	3 (7)	73	16 (22)	.039
Chronic pulmonary disease	117	38 (33)	44	18 (41)	73	20 (27)	.16
SBP, mm Hg	117	137.1 ± 25.0	44	131.8 ± 21.2	73	140.3 ± 26.7	.11
DBP, mm Hg	117	73.1 ± 15.5	44	70.6 ± 12.7	73	74.6 ± 16.9	.18
Heart rate, beats/min	117	93.6 ± 24.6	44	95.8 ± 21.2	73	92.2 ± 26.5	.25
Respiratory rate, beats/min	106	27.3 ± 8.6	39	28.6 ± 10.6	67	26.6 ± 7.3	.54
Spo_2, %	117	93.5 ± 5.8	44	91.7 ± 8.2	73	94.6 ± 3.4	.045
NYHA functional score	117						
NYHA class III		51 (44)		20 (45)		31 (42)	
NYHA class IV		59 (50)		22 (50)		37 (50)	
Jugular venous distension	117	19 (16)	44	1 (2)	73	18 (24)	.0001
Hepato-jugular reflux	117	19 (16)	44	3 (7)	73	16 (22)	.039
Peripheral edema	117	64 (54)	44	18 (41)	73	46 (63)	.026
Lungs auscultation	117		44		73		< .0001
Crackles		52 (44)		4 (9)		48 (66)	
Focal auscultatory findings		18 (15)		12 (27)		6 (8)	
Rhonchi		23 (20)		13 (29.5)		10 (13)	
Wheezing		8 (7)		7 (16)		1 (1)	
Biology							
eGFR MDRD, mL/min/1.73 m^2	116	60.1 ± 27.5	44	71.6 ± 26.7	72	53.1 ± 25.7	.0004
Natremia, mmol/L	115	135.9 ± 5.6	44	135.7 ± 5.9	71	136.0 ± 5.4	.81
BNP, pg/mL	86	946 ± 1017	27	274 ± 281	59	1,254 ± 1,083	< .0001
NT-proBNP, pg/mL	15	2,815 ± 3,741	5	575 ± 448	10	3,936 ± 4,183	.13
Hemoglobin, g/dL	117	12.4 ± 2.0	44	13.2 ± 1.9	73	11.9 ± 2.0	.0004
Hematocrit, %	113	38.6 ± 5.8	43	40.8 ± 5.4	70	37.2 ± 5.6	.0008
Radiology							
Cardiomegaly	117	68 (58)	44	13 (29)	73	55 (75)	< .0001
Pulmonary congestion	117	59 (50)	44	7 (16)	73	52 (71)	< .0001
Pleural effusion	117	35 (30)	44	12 (27)	73	23 (3)	.68
Pulmonary infection	117	39 (33)	44	22 (50)	73	17 (23)	.004
Brest score	117		44		73		
Continuous		5.9 ± 2.7		4.1 ± 2.0		7.0 ± 2.4	< .0001
Categorized							
0-3		22 (19)		17 (38)		5 (7)	< .0001
4-8		75 (64)		26 (59)		49 (67)	
9-15		20 (17)		1 (2)		19 (26)	
Diagnosis: AHF							
ED	117	63 (54)	44	3 (7)	73	60 (82)	< .0001
At hospitalization discharge	117	73 (62)	44	0	73	73 (100)	< .0001
LUS							

(Continued)

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TABLE 1] *(Continued)*

Characteristic	Population (N = 117) No.	Population (N = 117) Mean ± SD or No. (%)	No AHF (n = 44) No.	No AHF (n = 44) Mean ± SD or No. (%)	AHF (n = 73) No.	AHF (n = 73) Mean ± SD or No. (%)	*P* Value
Ultrasound quality	115	7.1 ± 1.6	43	6.9 ± 1.7	72	7.3 ± 1.5	.21
4-point method	117		44		73		
B-line count		8.4 ± 8.9		3.6 ± 3.9		11.3 ± 9.8	< .0001
≥1 bilateral positive point		40 (34)		5 (11)		35 (47)	< .0001
≥2 bilateral positive points		20 (17)		0		20 (27)	< .0001
6-point method	117		44		73		
B-line count		12.6 ± 12.8		5.2 ± 5.4		17.0 ± 13.8	< .0001
≥1 bilateral positive point		46 (39)		5 (11)		41 (56)	< .0001
≥2 bilateral positive points		29 (25)		0		29 (39)	< .0001
8-point method (superomedial point)	117		44		73		
B-line count		15.5 ± 16.6		5.3 ± 5.8		21.6 ± 18.0	< .0001
≥1 bilateral positive point		43 (37)		3 (7)		40 (54)	< .0001
≥2 bilateral positive points		31 (26)		1 (2)		30 (41)	< .0001
28-point method	117		44		73		
B-line count		57.3 ± 58.6		22.0 ± 21.3		78.5 ± 63.6	< .0001
B-lines ≥ 15		90 (77)		25 (57)		65 (89)	< .0001
B-lines ≥ 30		70 (60)		14 (32)		56 (78)	< .0001
Hospitalization	117	112 (95)	44	40 (91)	73	72 (98)	.009
Medical ward		68 (58)		32 (73)		36 (49)	
ICU		29 (24)		7 (16)		22 (30)	
Cardiology ward		15 (12)		1 (2)		14 (19)	

AHF = acute heart failure; BNP = brain natriuretic peptide; eGFR = estimated glomerular filtration rate; MDRD = Modification of Diet in Renal Disease; LUS = lung ultrasound; NT-proBNP = N-terminal pro-B-type natriuretic peptide; NYHA = New York Heart Association; SBP/DPB = systolic/diastolic blood pressure; Spo_2 = blood oxygen saturation.

TABLE 2] Association Between the Different Lung Ultrasound Techniques and AHF Diagnosis (in Univariable Analysis and Following Adjustment on the Brest Score)

Variable	Univariable Association OR (CI 95%)	Univariable Association *P* Value	Adjusted on Brest Score (Continuous) OR (CI 95%)	Adjusted on Brest Score (Continuous) *P* Value
4-point method				
B-line count	1.20 (1.09-1.31)	< .0001	1.22 (1.10-1.36)	.0003
≥ 1 bilateral positive point	7.18 (2.54-20.29)	.0002	7.49 (2.29-24.53)	.0009
≥ 2 bilateral positive points	34.10 (4.46-4381.20)	< .0001	23.96 (2.57-3248.84)	.002
6-point method				
B-line count	1.14 (1.07-1.22)		1.17 (1.08-1.26)	.0002
≥ 1 bilateral positive point	9.99 (3.53-28.26)		12.08 (3.51-41.53)	< .0001
≥ 2 bilateral positive points	59.00 (7.84-7559.37)	< .0001	51.15 (6.08-6740.40)	< .0001
8-point method				
B-line count	1.15 (1.08-1.23)	< .0001	1.15 (1.07-1.24)	< .0001
≥ 1 bilateral positive point	16.57 (4.70-58.38)	< .0001	15.68 (3.87-63.48)	.0001
≥ 2 bilateral positive points	30.00 (3.91-229.96)	.001	38.75 (4.19-358.43)	.001

See Table 1 legend for expansion of abbreviation.

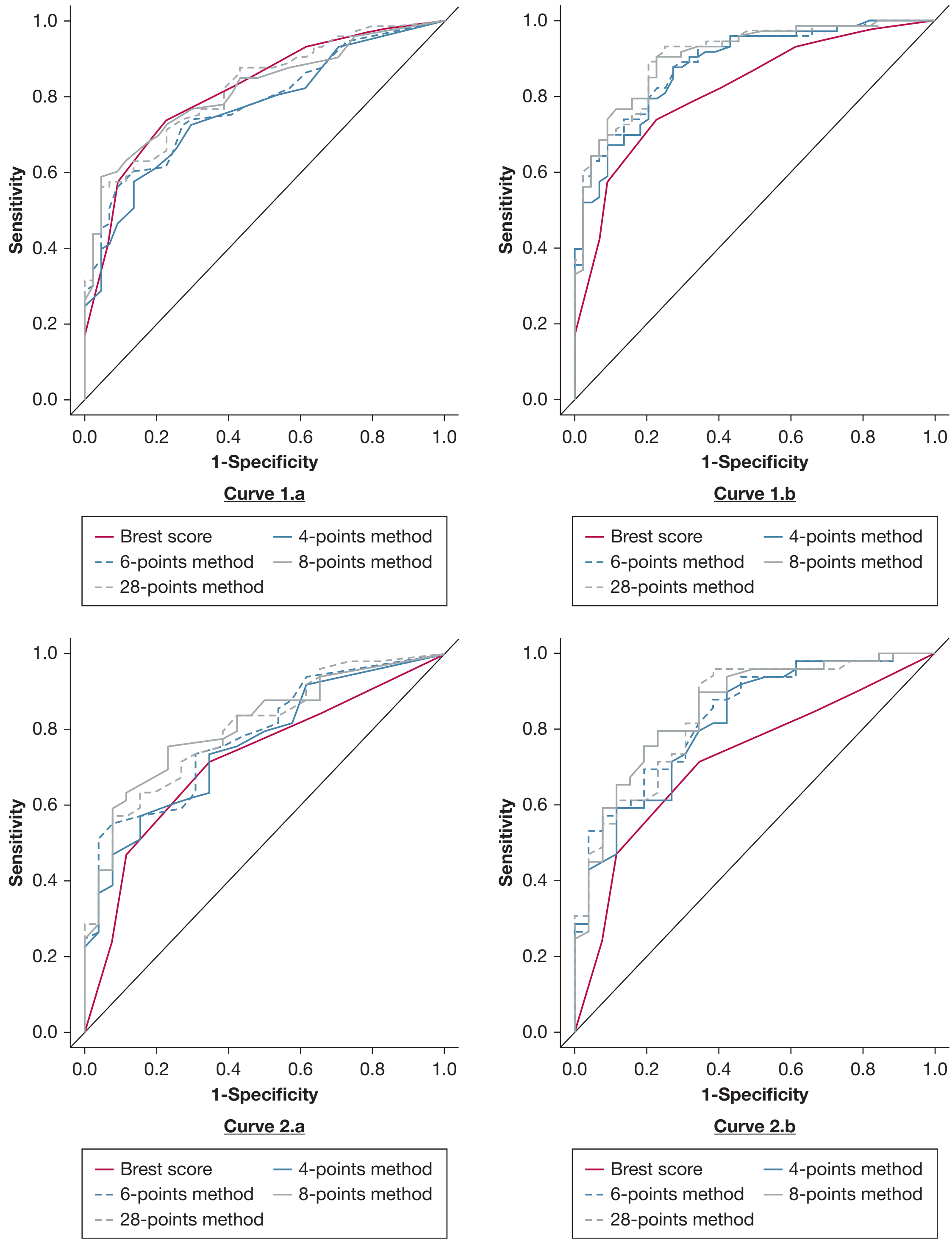

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Figure 2 – *Receiver-operating characteristic curves for acute heart failure diagnosis (B-line count). See* Figure 1 *legend for expansion of abbreviation.*

Brest Score and AHF

Brest score is a clinical score recently developed for AHF diagnosis, with three probability categories: low, intermediate, and high. Our study confirmed its good diagnostic capacity when considered as a continuous value analysis, although it was decreased (C-index, 72.8; 95% CI, 65.3-80.3) when dichotomized as risk categories. Indeed, the Brest score efficiently rules out AHF diagnosis for scores < 4 and affirms the diagnosis for scores > 9. However, for patients with an

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TABLE 3] Diagnostic Performance of the Various LUS Techniques in Conjunction With the Brest Score for Pulmonary Congestion Assessment

	Performance			Diagnostic Value of LUS Techniques in Addition to the Brest Score			
Variable	C-Index Value of the Considered Parameter (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	C-Index Value of Brest Score and Considered Parameter (95% CI)	*P* Value	C-Index Increase in Addition to the Brest Score (95% CI)	*P* Value
Overall population							
Brest score							
Continuous	81.8 (74.2 to 89.4)	…	…	…		…	
Categories (0-3, 4-8, 9-15)	72.8 (65.3 to 80.3)	…	…	…		…	
4-point method							
B-line count	76.7 (68.2 to 85.1)	…	…	88.1 (82.0 to 94.1)	< .0001	6.3 (1.0 to 11.6)	.020
≥ 1 bilateral positive point	68.3 (60.8 to 75.8)	88.6 (75.4 to 96.2)	47.9 (36.1 to 60.0)	86.6 (80.1 to 93.1)	< .0001	4.8 (–0.1 to 9.6)	.053
≥ 2 bilateral positive points	63.7 (58.5 to 68.8)	100.0 (92.0 to 100.0)	27.4 (17.6 to 39.1)	85.3 (78.6 to 91.9)	< .0001	3.5 (0.4 to 6.5)	.026
6-point method							
B-line count	78.2 (70.1 to 86.4)	…	…	89.1 (83.3 to 94.8)	< .0001	7.3 (1.7 to 12.8)	.010
≥ 1 bilateral positive point	72.4 (65.0 to 79.8)	88.6 (75.4 to 96.2)	56.2 (44.1 to 67.8)	88.5 (82.5 to 94.5)	< .0001	6.7 (0.9 to 12.5)	.024
≥ 2 bilateral positive points	69.9 (64.2 to 75.5)	100.0 (92.0 to 100.0)	39.7 (28.5 to 51.9)	88.4 (82.6 to 94.2)	< .0001	6.6 (2.3 to 10.8)	.002
8-point method							
B-line count	81.8 (74.3 to 89.3)	…	….	90.6 (85.2 to 96.0)	< .0001	8.8 (2.8 to 14.7)	.004
≥1 bilateral positive point	74.0 (67.1 to 80.9)	93.2 (81.3 to 98.6)	54.8 (42.7 to 66.5)	88.7 (82.9 to 94.6)	< .0001	6.9 (1.6 to 12.2)	.010
≥ 2 bilateral positive points	69.4 (63.3 to 75.5)	97.7 (88.0 to 99.9)	41.1 (29.7 to 53.2)	88.7 (82.8 to 94.7)	< .0001	6.9 (1.7 to 12.1)	.009
Patients with intermediate Brest score							
Brest score							
Continuous	71.7 (59.9 to 83.6)	…	…	NA	…	…	…
4-point method							
B-line count	75.9 (65.0 to 86.8)	…	…	81.6 (71.7 to 91.5)	< .0001	9.9 (0.1 to 19.6)	.047
≥ 1 bilateral positive point	68.7 (59.3 to 78.2)	88.5 (69.8 to 97.6)	49.0 (34.4 to 63.7)	78.5 (67.8 to 89.2)	< .0001	6.8 (–2.1 to 15.7)	.13
≥ 2 bilateral positive points	61.2 (55.3 to 67.1)	100.0 (86.8 to 100.0)	22.4 (11.8 to 36.6)	76.5 (65.9 to 87.1)	< .0001	4.8 (0.3 to 9.3)	.037
6-point method							
B-line count	78.4 (68.0 to 88.7)	…	…	83.4 (74.0 to 92.7)	< .0001	11.6 (1.9 to 21.4)	.020
≥1 bilateral positive point	71.8 (62.4 to 81.2)	88.5 (69.8 to 97.6)	49.0 (34.4 to 63.7)	80.6 (70.4 to 90.8)	< .0001	8.9 (–0.2 to 17.9)	.054
≥2 bilateral positive points	69.4 (62.5 to 76.3)	100.0 (86.8 to 100.0)	22.4 (11.8 to 36.6)	81.4 (71.9 to 90.8)	< .0001	9.6 (3.1 to 16.1)	.004
8-point method							
B-line count	81.0 (71.2 to 90.8)	…	…	85.4 (76.4 to 94.3)	< .0001	13.6 (3.4 to 23.8)	.009
≥ 1 bilateral positive point	72.7 (63.9 to 81.5)	92.3 (74.9 to 99.1)	53.1 (38.3 to 67.5)	82.4 (72.6 to 92.2)	< .0001	10.7 (1.7 to 19.7)	0.020
≥ 2 bilateral positive points	67.5 (59.6 to 75.3)	96.2 (80.4 to 99.9)	38.8 (25.2 to 53.8)	80.4 (70.3 to 90.4)	< .0001	8.6 (0.9 to 16.4)	0.029

NA = not appropriate. See Table 1 legend for expansion of other abbreviations.

intermediate score (4-8), other complementary tools (biomarkers and/or LUS)[9] seemingly appear necessary to improve diagnostic accuracy.[20]

LUS Methods Using Six or More Scanning Sites

LUS is recommended by international guidelines.[4] It is reliable, reproducible, quick, and easy to use, which prompted its increasing use in patients with acute dyspnea. Its diagnostic performance was reported to be excellent in a large meta-analysis (sensitivity, 94.1% [95% CI, 81.3-98.3]; specificity, 92.4% [95% CI, 84.2-96.4]) for an AHF diagnosis.[21] In addition, Zanobetti et al[22] reported that the diagnostic accuracy of LUS is better for AHF than for other etiologies of acute dyspnea and that 30 min of training is sufficient to provide good expertise.[23,24] However, in these previous studies, a number of LUS methods were used, such that the indicated method in the aforementioned meta-analysis is unclear. Moreover, a head-to-head comparison of each available method for AHF diagnosis was not conducted. In addition, previous studies typically did not specify if the clinical setting of the patients required the use of LUS. Indeed, it is likely that in patients with very unequivocal clinical pictures, the value of LUS is moderate. Importantly, to the best of our knowledge, its added value on top of the Brest score, a recent and powerful clinical diagnostic tool, has not been previously assessed.

In the current study, the 6- and 8-point methods were the most discriminative LUS tools for identifying AHF in elderly patients (mean age, 79.6 years) in whom the ED physicians perceived diagnostic uncertainty. Importantly, in our study, uncertainty was purely physician driven. This explains why only two-thirds of the population would qualify for uncertainty (ie, intermediate risk of HF) using the Brest score. In this "real-life" clinical setting, the 6- or 8-point method significantly increased the discrimination for AHF diagnosis in addition to the Brest score (Table 3) along with an isolated C-index (ie, not taking into account clinical features) > 70. In addition, the diagnostic performance of LUS was maintained in patients with intermediate BREST scores, which further strengthens the ability of LUS to correctly identify AHF in patients with the most clinical uncertainty.

Although the current study reports less evocative C-index values than in previous reports,[19,25] it should be emphasized that only patients with true diagnostic uncertainty were considered in this analysis, which could have decreased the diagnostic performance of LUS. In this particular setting, an isolated C-index $\geq$ 70% together with a significant increase of 6% to 10% in the C-index suggest a strong and clinically relevant improvement in diagnostic accuracy for AHF in actual clinical settings focusing on the most difficult cases. These results further confirm the strong diagnostic ability of LUS.

LUS Methods Using Four Scanning Sites

The BLUE protocol technique, developed in an ICU by Lichtenstein and Mezière,[11] is the most widely used and taught LUS technique. However, in the current study, the diagnostic ability of a 4-point LUS technique for diagnosing AHF was somewhat less than that of other methods which rely on a greater number of scanning points (6-28). The BLUE protocol, relying on four anterior scanning sites to identify AHF, may be less effective in ED patients due to the lower severity of patients with dyspnea (and subsequent pulmonary features/lesions) admitted in the ED compared with patients admitted in ICUs. Patients admitted in the ED are likely to exhibit less extensive pulmonary abnormalities than patients admitted in the ICU and may therefore benefit from LUS techniques involving six or more scanning sites.

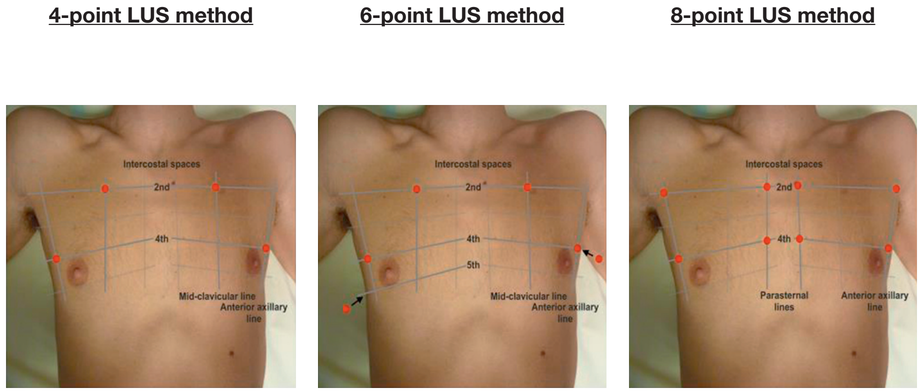
Perspectives

LUS is a new helpful tool in the ED as well as in the prehospital setting. Although echocardiography can assess cardiac dysfunction and filling pressures, the latter requires trained practitioners and can be difficult to perform in the setting of acute dyspnea. Our results show that LUS using a 6- or 8-point method, as in other reports,[26] improves the diagnostic accuracy of AHF in the ED. Notwithstanding, although the specificity of LUS using either a 6- or 8-point method herein was similar to other reports, the sensitivity documented in the current study was only about 50%, which is much lower than the 90.5% (87.4-93) reported by Pivetta et al.[12] However, this previous study was performed by an ED group with extensive experience in LUS, which may have resulted in its higher diagnostic performance. In addition, the differences in diagnostic performance could also be partly related to the absence of identification of lung sliding and condensation in the current study. In addition, LUS alone may not be sufficient to fully identify AHF in patients with high diagnostic uncertainty. Nazerian et al[27] reported a good diagnostic performance for simplified echocardiography performed by emergency

Diagnostic performance of the Brest score and LUS methods

Brest Score

Variables	*Points score*
	+2
Age >65 y	1
Sudden dyspnea	2
Night outbreak	1
Orthopnea	1
Prior CHF episode	2
COPD	–2
Myocardial infarction	1
Pulmonary crackles	2
Pitting leg edema	1
ST abnormalities	1
Atrial fibrillation/flutter	1
Maximal score	**15**



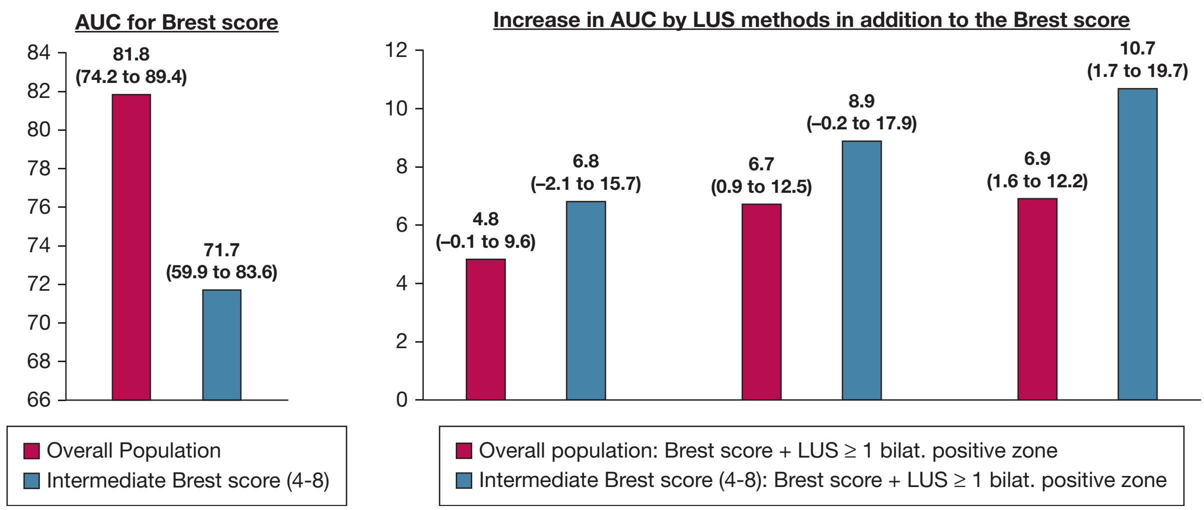


Figure 3 – *Diagnostic performance of the Brest score and LUS methods. See Figure 1 legend for expansion of abbreviation.*

physicians for AHF diagnosis. Other studies also suggest that using the size and collapsibility of the inferior vena cava, or other markers, can improve diagnostic accuracy in dyspneic patients.[28-30] Furthermore, Laursen et al[31] showed that an algorithm using cardiac, vascular, and LUS resulted in an improved early diagnostic accuracy. Thus, the use of an ultrasound-based algorithm rather than an LUS-centered algorithm may be needed to further improve the accuracy of AHF diagnosis. Importantly, studies advocating a multimodal ultrasound approach for improving early diagnostic accuracy do not provide a precise algorithm. We believe that such an algorithm should be validated. It is hoped that the Evaluation of the Feasibility and Accuracy of an Ultrasound Algorithm for Acute Dyspnea Diagnosis in the Emergency Department (EMERALD-US) study will be able to provide reliable evidence regarding an integrated ultrasound algorithm in the field of acute dyspnea admitted in the ED.[32]

Limitations

The present prospective multicenter study has certain limitations. First, various ultrasound devices were used as well as various patient positions[33] (it is, however, likely that most patients were in a semi-seated position), which could have resulted in some heterogeneity. However, given that LUS is likely to occupy an increasing place in emergency settings, including with various ultrasound devices, in various positions, pragmatic studies such as the current one more aptly reflect this intrinsic heterogeneity.

Uncertainty was an inclusion criteria but was purely physician-driven. This could have introduced some heterogeneity in the data as the perception of uncertain situations might vary across physicians.

The adjudicated diagnosis used for the current analysis was based on the hospitalization report extracted from the medical record. This diagnosis could have been influenced by the LUS results. However, the final diagnosis was adjudicated by two senior physicians blinded to the LUS measurements.

Conclusions

The current study suggests that LUS using the 8-point/6-point method improves AHF diagnosis in addition to the BREST score, especially in patients with intermediate BREST scores. Validated algorithms centered not only on the positive diagnosis of AHF but also on the competing diagnosis of dyspnea (eg, pneumonia) using LUS, vascular ultrasound, and simplified echocardiography could further improve LUS diagnostic accuracy in the ED.

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Author contributions: A. B. U. and T. C. had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis, including and especially any adverse effects. A. B. served as principal author. T. C. and N. G. contributed substantially to the study design. K. D., T. C., and N. G. contributed substantially to data analysis and interpretation, and A. B. U., T. C., K. D., A. B., M. H. M., Y. G., A. P., E. A., L. N., D. J., M. K., S. C., P. R., and N. G. contributed substantially to the writing of the manuscript.

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Additional information: The e-Tables can be found in the Supplemental Materials section of the online article.

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