

Lung Ultrasound Predicts Well Extravascular Lung Water but Is of Limited Usefulness in the Prediction of Wedge Pressure

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ABSTRACT

Background: Pulmonary congestion is indicated at lung ultrasound by detection of B-lines, but correlation of these ultrasound signs with pulmonary artery occlusion pressure (PAOP) and extravascular lung water (EVLW) still remains to be further explored. The aim of the study was to assess whether B-lines, and eventually a combination with left ventricular ejection fraction (LVEF) assessment, are useful to differentiate low/high PAOP and EVLW in critically ill patients.

Methods: The authors enrolled 73 patients requiring invasive monitoring from the intensive care unit of four university-affiliated hospitals. Forty-one patients underwent PAOP measurement by pulmonary artery catheterization and 32 patients had EVLW measured by transpulmonary thermodilution method. Lung and cardiac ultrasound examinations focused to the evaluation of B-lines and gross estimation of LVEF were performed. The absence of diffuse B-lines (A-pattern) *versus* the pattern showing prevalent B-lines (B-pattern) and the combination with normal or impaired LVEF were correlated with cutoff levels of PAOP and EVLW.

Results: PAOP of 18 mmHg or less was predicted by the A-pattern with 85.7% sensitivity (95% CI, 70.5 to 94.1%) and 40.0% specificity (CI, 25.4 to 56.4%), whereas EVLW 10 ml/kg or less with 81.0% sensitivity (CI, 62.6 to 91.9%) and 90.9% specificity (CI, 74.2 to 97.7%). The combination of A-pattern with normal LVEF increased sensitivity to 100% (CI, 84.5 to 100%) and specificity to 72.7% (CI, 52.0 to 87.2%) for the prediction of PAOP 18 mmHg or less.

Conclusions: B-lines allow good prediction of pulmonary congestion indicated by EVLW, whereas are of limited usefulness for the prediction of hemodynamic congestion indicated by PAOP. Combining B-lines with estimation of LVEF at transthoracic ultrasound may improve the prediction of PAOP. (ANESTHESIOLOGY 2014; 121:320-7)

VOLUME expansion is often the main target to improve the hemodynamic control of critical conditions, but balancing administration of fluids to avoid pulmonary edema on one extreme and hypoperfusion on the opposite is particularly felt as a challenge. Volume overload is always considered a risk in the management of critically ill patients. Technology helps the clinician providing invasive methods to measure crucial parameters at bedside that allow accurate assessment and monitoring of the hemodynamic status. These methods are commonly used in the intensive care unit (ICU) to guide fluid therapy and vasoactive/inotropic drug support, which may be decisive to improve cardiac function and tissue perfusion. Invasive approaches, such as pulmonary artery catheterization, transpulmonary thermodilution PiCCO system, central venous catheterization, transesophageal echocardiography, and others, are largely used after admission to the ICU. However, during the

What We Already Know about This Topic

- An association between the absence of B-lines detected by lung ultrasound and a low level of wedge pressure (pulmonary artery occlusion pressure) has been established.

What This Article Tells Us That Is New

- A multicenter, prospective, observational investigation of 73 critically ill patients admitted to four Italian University hospitals had patients examined with transthoracic ultrasound 10 min before invasive (pulmonary artery catheters or PiCCO systems) hemodynamic measurements were made. This study confirmed that there was not always an association between the elevation of the pulmonary artery occlusion pressure and finding of B-pattern in the lungs, but there was a better specificity between the detection of B-pattern by ultrasound and detecting elevated extravascular lung water by PiCCO.

primary evaluation of critically ill patients in the emergency department that precede ICU admission, therapeutic decisions cannot rely on invasive procedures. Fluid therapy is

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usually decided at bedside on the basis of simple clinical data and few basic instrumental examinations such as bedside chest radiography, electrocardiogram, blood examinations, and blood gas analysis. Even in the hands of expert physicians, these methods cannot be considered accurate enough for assessing and monitoring the real hemodynamic status of the patient. Imprecise monitoring may easily lead to iatrogenic catastrophic consequences, such as pulmonary edema due to overhydration, impairment of pulmonary blood gas exchange, or others.

Point-of-care lung ultrasound has a great potential for guiding the hemodynamic management of critically ill patients. B-lines have been acknowledged as sonographic signs of pulmonary interstitial and alveolar edema in critical and emergency care.¹⁻⁴ Some studies showed that B-lines may be used to predict extravascular lung water (EVLW) and pulmonary artery occlusion pressure (PAOP).^{5,6} However, although EVLW is a direct sign of *pulmonary congestion*, PAOP estimates the pressure in an area that extends from the lung capillaries to the left ventricle and underlies *hemodynamic congestion*.^{7,8} Despite a recent study has shown a tight correlation between absence of B-lines at lung ultrasound and low levels of PAOP,⁶ the hypothesis that elevated PAOP may not necessarily lead to extravasation of fluid into the lung interstitium and B-lines should be considered.

To further investigate the relation between B-lines and PAOP or EVLW, we designed a multicenter study to observe a cohort of critically ill patients representative of many different hemodynamic conditions and pulmonary diseases. Moreover, we wanted to assess whether adjunct of a focused cardiac gross estimation of the left ventricular ejection fraction (LVEF) by transthoracic ultrasound may improve the diagnostic potential of lung ultrasound for B-lines on predicting high or low levels of PAOP and EVLW.

Materials and Methods

This is a multicenter, prospective, observational study on critically ill patients admitted from October 2008 to April 2010 to the ICU of four Italian University hospitals (San Luigi Gonzaga Hospital and Molinette Hospital in Torino, Maggiore della Carità Hospital in Novara, and Vittorio Emanuele Hospital in Catania). The Institutional Review Board approved the multicenter study protocol (number 12884 to 64, Orbassano, Torino, Italy) before the enrollment of the first patient. The Ethic Committee waived the requirement for informed consent of unconscious/sedated patients. Of all the patients admitted to the ICU, those requiring hemodynamic invasive measurements at the discretion of the attending physicians facing complex clinical situations were consecutively enrolled to the study. Exclusion criterion was the impossibility to perform a complete heart/lung transthoracic ultrasound examination, such as extensive dressings, pneumothorax, fibrothorax, or completion pneumonectomy. The lung ultrasound examination was performed by an experienced investigator within 10 min before

the hemodynamic measurements. Only after the completion of the ultrasound examination, a second independent physician totally unaware of the ultrasound results performed the hemodynamic measurement. This blinding procedure was always strictly observed.

Invasive Procedures

Hemodynamic measurements were performed by standardized methods in all the four participating centers and were targeted to the assessment of the PAOP and/or the EVLW values by using the Swan-Ganz catheter and the PiCCO system, respectively. There were no shared guidelines on the choice of the two methodologies across the different ICUs. Both techniques are in use in the ICUs involved in the study. Investigators participating in the study were all senior intensivists with at least 5 yr of experience in advanced hemodynamic monitoring.

Pulmonary Artery Occlusion Pressure. A 7.5-French right-heart balloon flotation catheter (Swan-Ganz) was introduced *via* the jugular, femoral, or subclavian veins into the pulmonary artery. Correct catheter placement was checked by chest radiography and the zero level was checked before measurement of PAOP. Real-time airway pressure curves were always available together with hemodynamic curve tracings at the bedside for the evaluation of PAOP at end-expiration. All measurements were averaged over five cardiac cycles.

Extravascular Lung Water. The EVLW was measured by means of the transpulmonary thermodilution method (PiCCO system). A 5-French thermistor-tipped catheter was placed into the right femoral artery and connected to the PiCCO system for monitoring. After calibration, a 10-ml bolus of cold 5% dextrose solution was injected through a central venous catheter, and the thermodilution curve was evaluated by the arterial catheter inserted in the femoral artery. The mean of three consecutive boluses was considered. An arterial pulse contour analysis algorithm computes the cardiac output which allows calculation of the intrathoracic thermal volume and the intrathoracic blood volume. The EVLW value was obtained from the difference of these two latter parameters and divided by the predicted body weight.⁹

Outcome Variables. Patients were classified as having elevated PAOP and EVLW if any measurements were respectively greater than 18 mmHg and greater than 10 ml/kg during the study period. For PAOP value, this is the usual cutoff point used in clinical practice and recently further indicated to differentiate cardiogenic pulmonary edema from acute respiratory distress syndrome (ARDS).^{6,10} The value of EVLW is based on previous clinical studies that established this value as a threshold for acute lung injury.^{9,11,12}

Ultrasound Techniques

The following ultrasound devices were used: MyLab 40 ultrasound system and MyLab 30CV (Esaote Italia, Milan, Italy), GS50 portable unit (Philips, Hamburg, Germany),

M-Turbo (SonoSite, Bothell, WA), and HDI 3000 (ATL, Bothell, WA).

Lung Views. A curvilinear 2 to 5 MHz probe was used for intercostal lung views through oblique scans. Lung ultrasound was targeted to the evaluation of lung sliding and multiple B-lines. The standardized eight anterior-lateral areas examination was used.¹³ Multiple B-lines, that is, at least three B-lines in a single longitudinal scan, on at least two areas per side represent a sign of diffuse interstitial syndrome (the “B-pattern”). The B-pattern can be related to cardiogenic pulmonary congestion, ARDS, pulmonary fibrosis, or interstitial pneumonia.^{1,2,5} Absence of multiple B-lines with regular sliding is the “A-pattern.” This latter lung ultrasound pattern is a sign of normally aerated or hyperinflated lung and rules out pulmonary edema and other causes of interstitial syndrome.⁶ Detection of multiple B-lines but limited to less than two scans per side or limited to one side was still not considered B-pattern because it is the sign of “focal” interstitial syndrome. This condition indicates a focal interstitial involvement, sometimes around isolated pulmonary consolidations, such as pneumonia, infarction, or contusion.¹⁴ For convenience and hemodynamic similarity, the focal interstitial syndrome was still considered A-pattern. We also compared results by using another criterion for B-pattern, which is detection of bilateral prevalent B-lines in the anterior chest zones. This latter criterion is the same used in the study by Lichtenstein *et al.*,⁶ who limited the lung ultrasound examination for B-lines to the anterior chest.

Cardiac Views. A phased-array 2 to 4 MHz cardiac probe or, alternatively, the same probe used for lung views was used for the study of the heart through the subcostal, parasternal long-axis, and apical four-chamber views. The subcostal view was initially used to evaluate the LVEF by visual estimation of gross wall contraction. The LVEF was visually considered normal or impaired.^{15,16} Impaired function was diagnosed after the eyeballing visual estimation of reduced function corresponding to an LVEF less than 55%, without further distinction between poor and moderate reduction. The other two cardiac views were used in case of doubtful diagnosis or difficult visualization.

Statistical Analysis

Descriptive analysis was carried out using common measures of synthesis. Values are expressed as means \pm SD. Continuous variables (measured PAOP and calculated EVLW) were transformed into dichotomous variables to identify test-positive and test-negative patients. Each ultrasonography study was considered positive when the B-pattern at lung examination and the impaired LVEF at cardiac views were detected. The combined lung and cardiac ultrasonography was considered positive when both examinations were positive. Statistical significance was set at 5% for every test used and reported 95% CI. Statistical analysis was performed with MedCalc v12.3.0 (MedCalc Software, Ostend, Belgium).

Results

The study enrolled 73 patients. Descriptive analysis of the patients is reported in tables 1 and 2. Forty-one patients underwent PAOP measurement, whereas EVLW was assessed in the other 32 patients. Lung and cardiac ultrasonography was feasible in all patients. No data were rejected.

Ultrasound Results

Overall, 25 patients showed B-pattern at lung ultrasound, whereas, of the remaining, 12 patients showed a focal pattern and 36 complete absence of significant B-lines in the anterior-lateral chest areas. Thirty-one patients showed reduced LVEF at cardiac examination. Patients showing B-pattern at lung ultrasound had also a lower $\text{PaO}_2/\text{FiO}_2$ (175.3 ± 76.1 vs. 238.2 ± 83.0 ; $P < 0.01$). The cardiac index measured invasively was significantly lower in patients with a diagnosis of reduced LVEF at focused cardiac ultrasound (2.66 ± 0.8 vs. 4.43 ± 1.48 l min⁻¹ m⁻²; $P < 0.001$).

Table 1. Patient Characteristics

Characteristics	Values			P Value
	Overall	PAOP	EVLW	
Patients, No.	73	41	32	
Sex				
Male	50	31	19	
Female	23	10	13	
Age, yr				
Mean \pm SD	62 \pm 15	63 \pm 15	62 \pm 14	0.83
Range	23–88	28–84	23–88	
Invasive ventilation				
Patients, No.	66	34	32	
PEEP, cm H ₂ O	0–15	0–15	0–15	
Tidal volume, ml/kg				
Mean \pm SD	7.7 \pm 2.1	7.3 \pm 2.3	8.0 \pm 1.9	0.17
APACHE II	21.6 \pm 8.5	21.7 \pm 8.1	21.5 \pm 9.2	0.91
$\text{PaO}_2/\text{FiO}_2$	213.2 \pm 85.7	241.9 \pm 96.4	184.4 \pm 56.2	<0.01*

*A P value < 0.05 was considered statistically significant for the difference between the two groups.

APACHE = Acute Physiology and Chronic Health Evaluation; EVLW = extravascular lung water; PAOP = pulmonary artery occlusion pressure; PEEP = positive-end expiratory pressure.

Table 2. Patient Diagnoses

Diagnoses	No.
Septic shock	19
Liver transplant	18
Cardiogenic pulmonary edema	10
Respiratory failure from chronic pulmonary disease	10
Pneumonia	5
Cardiogenic shock or cardiac arrest	3
Hemorrhagic shock from aortic rupture	3
Respiratory failure (other)	2
Severe trauma	1
Acute pancreatitis	1
Cerebral hemorrhage	1

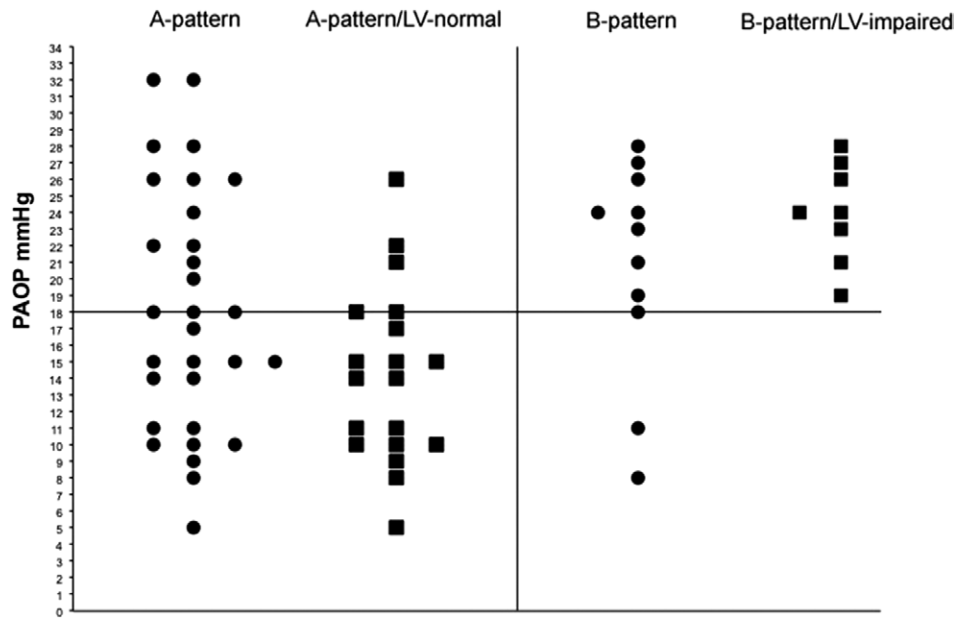


Fig. 1. Comparison with pulmonary artery occlusion pressure (PAOP) levels considering a cutoff point at 18 mmHg: on the *left*, the group of patients showing A-pattern at lung ultrasound and the subgroup showing A-pattern combined with normal left ventricular (LV) ejection fraction estimated at focused cardiac ultrasound; on the *right*, the group showing B-pattern and the subgroup showing B-pattern combined with reduced LV ejection fraction.

Comparison with PAOP Level

Twenty-one patients of 41 had PAOP 18 mmHg or less. The A-pattern was detected in 18 of these patients and in 12 patients with high PAOP (fig. 1), showing a sensitivity of 85.7% (CI, 70.5 to 94.1%) with positive predictive value of 60.0% (CI, 43.6 to 74.6%) and a specificity of 40.0% (CI, 25.4 to 56.4%) with negative predictive value of 72.7% (CI, 56.3 to 84.9%). Considering the criteria for the B-pattern used in the study by Lichtenstein *et al.*, sensitivity and specificity dropped to 76.2% (CI, 52.8 to 91.8%) and 35.0% (CI, 15.4 to 59.2%), respectively. A normal LVEF was found in 19 patients with low PAOP and 3 patients with high PAOP. The combination of A-pattern and normal LVEF was detected in 16 patients with low PAOP and 3 patients with high PAOP. The combination of diffuse B-lines and reduced LVEF was never found in patients with low PAOP and detected in eight patients with high PAOP (fig. 1). Fourteen patients had no concordance between lung and cardiac ultrasound examination. Thus, the combination of A-pattern and normal LVEF showed a sensitivity of 100% (CI, 84.5 to 100%) with positive predictive value 84.2% (CI, 64.3 to 94.6%) and a specificity of 72.7% (CI, 52.0 to 87.2%) with negative predictive value 100% (CI, 84.5 to 100%). The acute and chronic condition affecting each patient with PAOP greater than 18 mmHg, respectively, showing A-pattern or B-pattern, are reported in tables 3 and 4.

Comparison with EVLW Level

Twenty-one patients of 32 had EVLW 10 ml/kg or less. The A-pattern was detected in 17 of these patients and in 1 patient with high EVLW (fig. 2), showing 81.0% sensitivity

(CI, 62.6 to 91.9%) with positive predictive value 94.4% (CI, 78.7 to 99.2%) and 90.9% specificity (CI, 74.2 to 97.7%) with negative predictive value 71.4% (CI, 52.6 to 85.3%). The combination of cardiac evaluation for the LVEF with lung examination did not improve the accuracy of lung ultrasound standing alone in predicting the level of invasive EVLW.

Discussion

Hemodynamic management of critically ill patients is a challenge. Invasive procedures may help, but during the first examination that precedes admittance to an ICU, attending physicians facing unstable patients are called to fundamental therapeutic decisions based on few instrumental and clinical data. Focused ultrasonography performed at bedside has a great potential for the noninvasive evaluation of pulmonary congestion and cardiac function and thus adding crucial information for a gross hemodynamic assessment in the emergency setting.

One previous study showed that the number of B-lines at lung ultrasound has a positive linear correlation with invasive PAOP and EVLW.⁵ This study was performed on selected patients without pulmonary diseases, who underwent cardiac surgery. Exclusion of patients with pulmonary diseases represented a great limitation because B-lines are not only the signs of cardiogenic congestion but are also detected in fibrosis, ARDS, and interstitial pneumonia. Thus, when B-lines are considered signs of high cardiac filling pressures, some pulmonary conditions may cause false-positive ultrasound results. In the following years, other experimental

Table 3. Diagnoses at Admission and Chronic Preexisting Conditions in the Group of Patients with Elevated PAOP Showing A-pattern at Lung Ultrasound

Patient ID	Acute Diagnosis	Preexisting Condition	PAOP, mmHg
NV05	Acute coronary syndrome	COPD, normal cardiac function	20
MO18	Liver transplant	Moderate mitral insufficiency	21
VE05	Severe respiratory failure	Pulmonary hypertension	22
NV13	Acute coronary syndrome with acute decompensated heart failure	Chronic heart failure	22
NV15	Multivessel coronary artery disease, acute decompensated heart failure	Normal cardiac function	24
MO17	Liver transplant	Normal cardiac function	26
NV11	Multivessel coronary artery disease, acute decompensated heart failure	Chronic heart failure	26
NV18	Artery bypass grafting in left main coronary artery disease	Chronic heart failure	26
NV07	Multivessel coronary artery disease, acute decompensated heart failure	Chronic heart failure	28
NV17	Multivessel coronary artery disease, acute decompensated heart failure	Chronic heart failure	28
NV10	Acute coronary syndrome with acute decompensated heart failure	Chronic heart failure	32
NV16	Artery bypass grafting in left main coronary artery disease	Chronic heart failure	32

COPD = chronic obstructive pulmonary disease; PAOP = pulmonary artery occlusion pressure.

Table 4. Diagnoses at Admission and Chronic Preexisting Conditions in the Group of Patients with Elevated PAOP Showing B-pattern at Lung Ultrasound

Patient ID	Acute Diagnosis	Preexisting Condition	PAOP, mmHg
NV03	Acute respiratory failure, pneumonia, septic shock	Normal cardiac and pulmonary function	19
NV01	Acute respiratory failure, pneumonia, septic shock	Normal cardiac and pulmonary function	21
NV02	Acute respiratory failure	COPD	23
NV06	Acute coronary syndrome, pulmonary edema	Normal cardiac and pulmonary function	24
NV08	Aortic rupture	Normal cardiac and pulmonary function	24
NV09	Acute respiratory failure, sepsis	Normal cardiac and pulmonary function	26
NV14	Acute respiratory failure, pneumonia	COPD, Chronic heart failure	27
NV12	Aortic valve insufficiency	Chronic heart failure	28

COPD = chronic obstructive pulmonary disease; PAOP = pulmonary artery occlusion pressure.

and physical models have further demonstrated a good correlation between B-lines and lung water content, but the experimental design on patients has never been investigated more.^{17–19}

Another study performed in the ICU in critically ill patients showed that the pattern without predominance of bilateral B-lines in the anterior chest accurately indicates invasive PAOP level below the threshold of 18 mmHg.⁶ Their results, combined with evidences drawn by other studies, allow to conclude that the A-pattern indicates a dry lung.²⁰ As a consequence, a lung ultrasound pattern without predominance of B-lines in the anterior chest indicates that the patient may tolerate fluid administration.²¹

Our data show that the A-pattern reliably predicts low EVLW, and thus confirming that lung ultrasound may be used to indicate tolerance to fluid loading. However, the comparison with PAOP has proven to be the wrong model to draw this conclusion. In our patients, lung ultrasound prediction of low PAOP resulted in very low specificity due to

many cases showing high PAOP but still absence of B-lines. This finding stands in contrast with most of the existing literature.^{5,6,22} However, at least one other study, performed in stable patients with chronic heart failure, showed the lack of a significant relation between the number of B-lines and the levels of invasive PAOP²³ and the authors concluded that the discrepancy with results of other studies might be explained by different size and type of study populations. Moreover, they also speculated that there might be an association between B-lines and PAOP but only in patients with acute decompensated heart failure. Pulmonary edema is not only the consequence of the lung filtration pressure but also depends on the water permeability of the alveolar-capillary membrane.²⁴ Patients with pulmonary edema due to decompensated heart failure usually have both increased PAOP and increased transpulmonary gradients.²⁵ Indeed, a condition of low PAOP but increased permeability may manifest with noncardiogenic edema, whereas, at the opposite, high PAOP levels but low permeability may explain resistance to

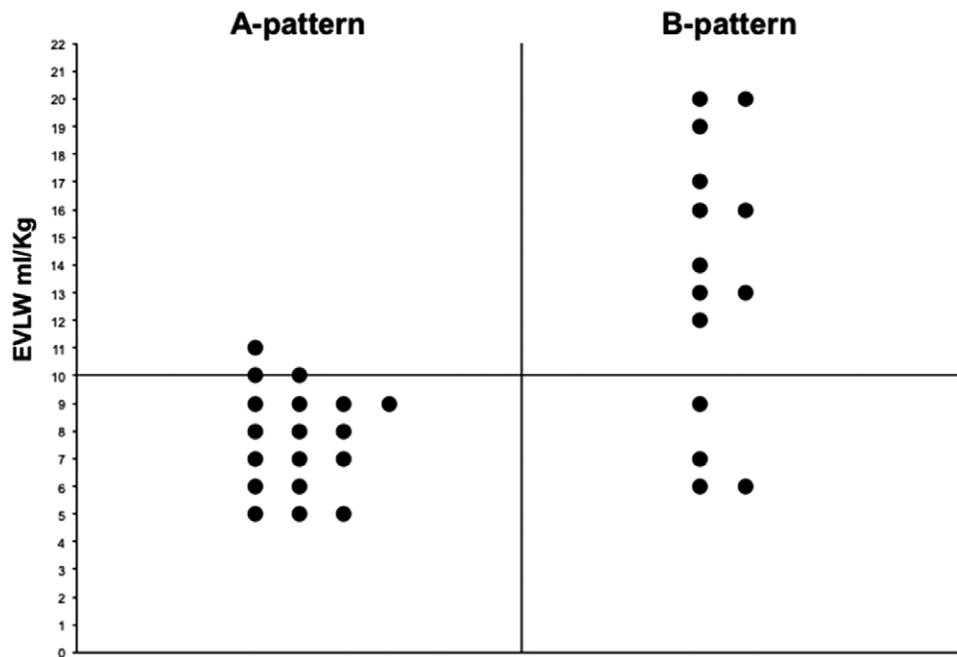


Fig. 2. Comparison with extravascular lung water (EVLW) levels considering a cutoff point at 10 ml/kg: on the *left*, patients showing the A-pattern, whereas on the *right*, patients showing B-pattern after lung ultrasound.

transpulmonary leakage of fluids. For example, patients with chronic heart diseases may show a higher threshold for the development of pulmonary edema despite elevated cardiac filling pressure.^{23,26} Extending the observation to critically ill patients enrolled from different ICUs may have increased the variability of lung conditions observed, and probably explains why we obtained lower specificity of B-lines for predicting low PAOP, if compared with other single-center studies. Indeed, in our study, those patients with high PAOP who showed the A-pattern were mainly affected by chronic heart diseases (table 3), whereas combination of high PAOP and B-pattern was detected mainly in patients affected by respiratory diseases and sepsis but normal cardiac function (table 4).

Hence, PAOP level and pulmonary fluids are not necessarily linked. From the perspective of predicting the tolerance to a fluid challenge, the most important condition to be checked remains the fluid excess at the lung level, which may be occasionally irrespective of the PAOP level. Rather, PAOP is probably more related to the cardiac function. Indeed, in our study, the combination of analysis of B-lines with a gross estimation of the left ventricle function improved the ultrasound prediction of PAOP levels. The B-pattern combined with reduced LVEF was highly predictive of high PAOP. This latter data, if confirmed in a larger population, may be relevant for the differential diagnosis of ARDS.

The comparison between B-lines and EVLW showed a far better specificity. This is not surprising because these two parameters indicate the same phenomenon, that is, fluid in the lung.¹⁹ Although PAOP identifies hemodynamic overload, a condition that may precede pulmonary congestion,

EVLW is a useful method to measure the accumulation of parenchymal lung edema more accurately than PAOP for measuring nonhydrostatic edema.^{7,27} Similarly, B-lines identify fluids that accumulate in the lung at the expense of alveolar air, irrespective of a cardiogenic or noncardiogenic mechanism.⁸ The contribution of B-lines is to provide direct insight into the pulmonary interstitium, even if limited to the lung periphery, and to detect conditions of fluid accumulation not linked to cardiac left ventricle filling pressure. In our patients, high EVLW was always combined with positive lung ultrasound except one case with a borderline level of EVLW (11 ml/kg). Perhaps, a different cutoff for high EVLW could further improve the sensitivity of B-lines. Extending the study population and testing different cut-off values may probably contribute to assess the real relation between B-lines and EVLW calculated by the PiCCO technology.

This study has many limitations. Although the threshold for PAOP is supported by literature, there is no perfect consensus on the abnormal value of EVLW. The value we used as cutoff for EVLW is the higher threshold found in literature. Using a lower threshold, it has found that the number of false-negative cases in our study would have been greater.

Our approach was only qualitative although other authors demonstrated that it is possible to score B-lines to investigate the quantitative relation with PAOP and EVLW.⁵ However, the aim of our study was not to compare two sophisticated methodologies by investigating the linear relation between B-lines and EVLW. Rather, we wanted to evaluate the usefulness of lung ultrasound as a simple noninvasive bedside method for a rough and simplified estimation of the

hemodynamic status before invasive tests are performed in critically ill patients.

Another limitation is the small number of cases studied. Although the multicenter enrollment from different ICUs may be considered a strength of this study, the number of cases enrolled remained below than was expected and is too small to allow definitive conclusions. The original design, which was to measure both the PAOP and EVLW on each patient, turned out not feasible during the study because never sustained by a real clinical need. However, our study population included a wide range of conditions, from the septic to heart failure patients, from ARDS to posttransplant patients, which is representative of the population of many emergency departments and ICUs.

The two groups of patients evaluated for EVLW and PAOP were matched for demographic and clinical characteristics, with the exception of the $\text{PaO}_2/\text{FiO}_2$ level that was worse in the EVLW group. This discrepancy certainly introduces a bias that should be considered in the evaluation of our data. However, this difference was expected because the choice of the invasive monitoring method was independent and reflects the disposition of the intensivists involved in the study to use the PiCCO system for the invasive monitoring of patients with most severe signs of respiratory failure.

Finally, the combination of lung with cardiac ultrasound was only limited to estimation of the LVEF. A more deep insight into the cardiac function by ultrasound would certainly add more reliable data to predict PAOP. A future study should consider a more comprehensive echocardiographic examination to better characterize those patients who show different lung ultrasound pattern but similar PAOP and EVLW.²⁸ In our study, measuring the mitral Doppler inflow E wave velocity to annular tissue Doppler Ea wave velocity ratio would have been informative to distinguish those patients with isolated left ventricular diastolic dysfunction.^{29,30} This latter condition may have a deep influence in the relation between B-lines and PAOP. However, although the gross evaluation of LVEF coupled with B-lines assessment is an easy-to-learn technique, a more advanced echocardiographic study that includes evaluation of the diastolic function needs advanced skill and is more expensive in terms of cost and time.

Conclusion

Lung ultrasound for B-lines represents a useful bedside tool for the first assessment of the hemodynamic status of the critically ill patient. The A-pattern at lung ultrasound predicts low EVLW, whereas it cannot be used alone to predict low PAOP. Only the combination of the A-pattern at lung ultrasound and the normal LVEF estimated by focused cardiac ultrasound reliably indicates low PAOP. Thus, in the first approach to critically ill patients, the concept of using ultrasound to guide fluid resuscitation to avoid deleterious effects on the lung function is confirmed. However, a different relation of B-lines with PAOP or EVLW indicates that

lung ultrasound may be used to rule-out pulmonary congestion but not hemodynamic congestion.

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Competing Interests

The authors declare no competing interests.

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References

1. Lichtenstein D, Mézière G, Biderman P, Gepner A, Barré O: The comet-tail artifact. An ultrasound sign of alveolar-interstitial syndrome. *Am J Respir Crit Care Med* 1997; 156:1640–6
2. Volpicelli G, Mussa A, Garofalo G, Cardinale L, Casoli G, Perotto F, Fava C, Frascisco M: Bedside lung ultrasound in the assessment of alveolar-interstitial syndrome. *Am J Emerg Med* 2006; 24:689–96
3. Volpicelli G, Silva F, Radeos M: Real-time lung ultrasound for the diagnosis of alveolar consolidation and interstitial syndrome in the emergency department. *Eur J Emerg Med* 2010; 17:63–72
4. Xirouchaki N, Magkanas E, Vaporidi K, Kondili E, Platakis M, Patrianakos A, Akoumianaki E, Georgopoulos D: Lung ultrasound in critically ill patients: Comparison with bedside chest radiography. *Intensive Care Med* 2011; 37:1488–93
5. Agricola E, Bove T, Oppizzi M, Marino G, Zangrillo A, Margonato A, Picano E: "Ultrasound comet-tail images": A marker of pulmonary edema: A comparative study with wedge pressure and extravascular lung water. *Chest* 2005; 127:1690–5
6. Lichtenstein DA, Mézière GA, Lagoueyte JF, Biderman P, Goldstein I, Gepner A: A-lines and B-lines: Lung ultrasound as a bedside tool for predicting pulmonary artery occlusion pressure in the critically ill. *Chest* 2009; 136:1014–20
7. Picano E, Gargani L, Gheorghide M: Why, when, and how to assess pulmonary congestion in heart failure: Pathophysiological, clinical, and methodological implications. *Heart Fail Rev* 2010; 15:63–72
8. Volpicelli G, Melniker LA, Cardinale L, Lamorte A, Frascisco MF: Lung ultrasound in diagnosing and monitoring pulmonary interstitial fluid. *Radiol Med* 2013; 118:196–205
9. Berkowitz DM, Danai PA, Eaton S, Moss M, Martin GS: Accurate characterization of extravascular lung water in acute respiratory distress syndrome. *Crit Care Med* 2008; 36:1803–9
10. Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, Camporota L, Slutsky AS; ARDS Definition Task Force: Acute respiratory distress syndrome: The Berlin Definition. *JAMA* 2012; 307:2526–33
11. Holm C, Tegeler J, Mayr M, Pfeiffer U, Henckel von Donnersmarck G, Mühlbauer W: Effect of crystalloid resuscitation and inhalation injury on extravascular lung water: Clinical implications. *Chest* 2002; 121:1956–62

12. Sakka SG, Klein M, Reinhart K, Meier-Hellmann A: Prognostic value of extravascular lung water in critically ill patients. *Chest* 2002; 122:2080–6
13. 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, Breitzkreutz 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): International evidence-based recommendations for point-of-care lung ultrasound. *Intensive Care Med* 2012; 38:577–91
14. Volpicelli G: Lung sonography. *J Ultrasound Med* 2013; 32:165–71
15. Randazzo MR, Snoey ER, Levitt MA, Binder K: Accuracy of emergency physician assessment of left ventricular ejection fraction and central venous pressure using echocardiography. *Acad Emerg Med* 2003; 10:973–7
16. Moore CL, Rose GA, Tayal VS, Sullivan DM, Arrowood JA, Kline JA: Determination of left ventricular function by emergency physician echocardiography of hypotensive patients. *Acad Emerg Med* 2002; 9:186–93
17. Corradi F, Ball L, Brusasco C, Riccio AM, Baroffio M, Bovio G, Pelosi P, Brusasco V: Assessment of extravascular lung water by quantitative ultrasound and CT in isolated bovine lung. *Respir Physiol Neurobiol* 2013; 187:244–9
18. Jambrik Z, Gargani L, Adamicza A, Kaszaki J, Varga A, Forster T, Boros M, Picano E: B-lines quantify the lung water content: A lung ultrasound *versus* lung gravimetry study in acute lung injury. *Ultrasound Med Biol* 2010; 36:2004–10
19. Soldati G, Inchingolo R, Smargiassi A, Sher S, Nenna R, Inchingolo CD, Valente S: *Ex vivo* lung sonography: Morphologic-ultrasound relationship. *Ultrasound Med Biol* 2012; 38:1169–79
20. Soldati G, Copetti R, Sher S: Sonographic interstitial syndrome: The sound of lung water. *J Ultrasound Med* 2009; 28:163–74
21. Lichtenstein D: Fluid administration limited by lung sonography: The place of lung ultrasound in assessment of acute circulatory failure (the FALLS-protocol). *Expert Rev Respir Med* 2012; 6:155–62
22. Agricola E, Picano E, Oppizzi M, Pisani M, Meris A, Fragasso G, Margonato A: Assessment of stress-induced pulmonary interstitial edema by chest ultrasound during exercise echocardiography and its correlation with left ventricular function. *J Am Soc Echocardiogr* 2006; 19:457–63
23. Platz E, Lattanzi A, Agbo C, Takeuchi M, Resnic FS, Solomon SD, Desai AS: Utility of lung ultrasound in predicting pulmonary and cardiac pressures. *Eur J Heart Fail* 2012; 14:1276–84
24. Gehlbach BK, Geppert E: The pulmonary manifestations of left heart failure. *Chest* 2004; 125:669–82
25. Aronson D, Eitan A, Dragu R, Burger AJ: Relationship between reactive pulmonary hypertension and mortality in patients with acute decompensated heart failure. *Circ Heart Fail* 2011; 4:644–50
26. Chakko S, Woska D, Martinez H, de Marchena E, Futterman L, Kessler KM, Myerberg RJ: Clinical, radiographic, and hemodynamic correlations in chronic congestive heart failure: Conflicting results may lead to inappropriate care. *Am J Med* 1991; 90:353–9
27. Sibbald WJ, Short AK, Warshawski FJ, Cunningham DG, Cheung H: Thermal dye measurements of extravascular lung water in critically ill patients. Intravascular Starling forces and extravascular lung water in the adult respiratory distress syndrome. *Chest* 1985; 87:585–92
28. Bouhemad B, Nicolas-Robin A, Arbelot C, Arthaud M, Féger F, Rouby JJ: Isolated and reversible impairment of ventricular relaxation in patients with septic shock. *Crit Care Med* 2008; 36:766–74
29. Bouhemad B, Nicolas-Robin A, Benois A, Lemaire S, Goarin JP, Rouby JJ: Echocardiographic Doppler assessment of pulmonary capillary wedge pressure in surgical patients with postoperative circulatory shock and acute lung injury. *ANESTHESIOLOGY* 2003; 98:1091–100
30. Combes A, Arnoult F, Trouillet JL: Tissue Doppler imaging estimation of pulmonary artery occlusion pressure in ICU patients. *Intensive Care Med* 2004; 30:75–81