

Clinical update

Ultrasound of extravascular lung water: a new standard for pulmonary congestion

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Extravascular lung water (EVLW) is a key variable in heart failure management and prognosis, but its objective assessment remains elusive. Lung imaging has been traditionally considered off-limits for ultrasound techniques due to the acoustic barrier of high-impedance air wall. In pulmonary congestion however, the presence of both air and water creates a peculiar echo fingerprint. Lung ultrasound shows B-lines, comet-like signals arising from a hyper-echoic pleural line with a to-and-fro movement synchronized with respiration. Increasing EVLW accumulation changes the normal, no-echo signal (black lung, no EVLW) into a black-and-white pattern (interstitial sub-pleural oedema with multiple B-lines) or a white lung pattern (alveolar pulmonary oedema) with coalescing B-lines. The number and spatial extent of B-lines on the antero-lateral chest allows a semi-quantitative estimation of EVLW (from absent, ≤ 5 , to severe pulmonary oedema, > 30 B-lines). Wet B-lines are made by water and decreased by diuretics, which cannot modify dry B-lines made by connective tissue. B-lines can be evaluated anywhere (including extreme environmental conditions with pocket size instruments to detect high-altitude pulmonary oedema), anytime (during dialysis to titrate intervention), by anyone (even a novice sonographer after 1 h training), and on anybody (since the chest acoustic window usually remains patent when echocardiography is not feasible). Cardiologists can achieve much diagnostic gain with little investment of technology, training, and time. B-lines represent 'the shape of lung water'. They allow non-invasive detection, in real time, of even sub-clinical forms of pulmonary oedema with a low cost, radiation-free approach.

Keywords Oedema • Lung • Ultrasound • Water

B-lines for imaging pulmonary congestion

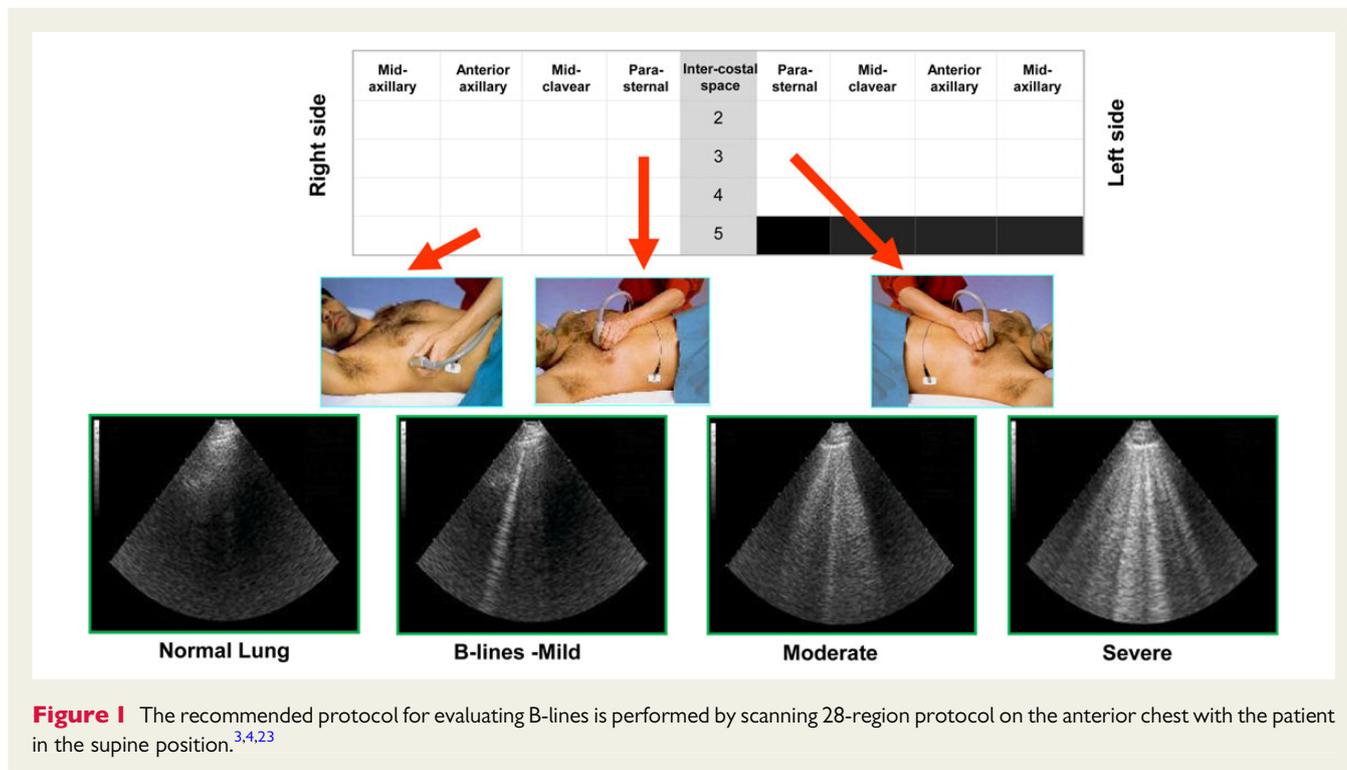
Pulmonary congestion is an almost universal finding in patients with acute heart failure. It may be related to heterogeneous mechanisms such as fluid retention with weight gain in patients with reduced ejection fraction and/or fluid redistribution to the lungs, usually without weight variation, in patients with preserved ejection fraction and a noncompliant cardiovascular system.¹ Clinical symptoms and signs of pulmonary congestion resulting in interstitial and alveolar oedema are a late event in acute heart failure syndrome. The identification of pulmonary congestion with a reliable and objective non-invasive imaging biomarker would confer a pathophysiological, diagnostic, therapeutic, and prognostic advantage to the clinical cardiologist.¹ In patients with impending acute heart failure syndrome, there is often a relatively long incubation period, of days and weeks, during which there is a gradual accumulation of extravascular lung

water (EVLW), a term used to describe water within the lungs but outside pulmonary vasculature. Detection and treatment of pulmonary congestion before it is clinically evident can prevent hospitalization and progression of heart failure. Post-discharge freedom from pulmonary congestion is associated with a better prognosis. Therefore, the possibility to image pulmonary oedema at a sub-clinical stage remains an attractive and elusive goal. Several clinical, radiological, and non-imaging methods are currently used for evaluating pulmonary fluid retention, but they are late and inaccurate (physical examination), insensitive and imprecise (chest X-ray), too complex for real time, repeated measurements in sick patients (computerized tomography), or inadequately validated and not widely available (conductance measurements with cardiac devices).¹ Lung ultrasound (LUS) assessment of EVLW by B-lines provides an excellent alternative,^{2,3} expanding the already established role of transthoracic echocardiography in heart failure.⁴ B-lines can be visualized using the cardiac transducer and appear on the

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antero-lateral chest scan as multiple laser-like signals arising from the hyper-echoic pleural line, changing throughout the respiratory cycle, with a to-and-fro movement synchronized with respiration (Figure 1). The normal lung is black (no signal); the abnormal wet lung with interstitial pulmonary oedema is black and white (with some B-lines departing from the pleural line); and the lung with alveolar pulmonary oedema is white (confluent B-lines in a fully echogenic lung).

The original term of comet-tail artefacts² was subsequently used interchangeably with ultrasound lung comets.⁴ Following the consensus on terminology and standards, B-lines is now preferred.⁵

The term comets intuitively refers to the eye-catching pictorial image, spreading like a rocket or the tail of a comet from the ultrasound transducer to the edge of the screen. B-lines may sound more familiar for radiologists, as the ultrasound counterpart of the well-known radiological Kerley B-lines, a sign of EVLW on chest X-ray. The analogy is however imperfect, because A-lines on chest X-ray (departing from the hila out to the periphery of the lung) are also a sign of abnormal accumulation of EVLW. In contrast, with LUS, 'A-lines' refer to the normal appearance of horizontal, equidistant, parallel artefacts originating at regular intervals from the pleural line (visceral and parietal pleura) (Table 1).

The number of B-lines in the antero-lateral chest scan is usually summed to generate a quantitative or semi-quantitative B-line score (Table 2). Up to 2 B-lines per single intercostal space, or up to 5 in the comprehensive antero-lateral chest scan can be a normal finding,^{2,4} more frequent in the latero-basal areas.

Genesis and determinants of B-lines

In analogy with the counterpart of radiological B-lines, it was initially proposed that the acoustic interface generating B-lines is the

Table 1 Primer of lung ultrasound for cardiologists

Sign	Description	Meaning
A-lines	Horizontal, parallel lines beyond the pleura	Normal artefacts
B-lines	Vertical, comet-tail-like lines fanning out from pleural line	EVLW accumulation
Pleural line	Echo dense line	Parietal and visceral pleura
Pleural effusion	Echo-free pleura-lung space	Pleural effusion

Table 2 Scoring of B-lines

Score	Number of B-lines	EVLW
0	≤5	Absent
1	6–15	Mild degree
2	16–30	Moderate degree
3	>30	Severe degree

sub-pleural interlobular septa thickened by oedema.^{2,3,4} This anatomical model is conceptually helpful and appealingly simple, but probably an oversimplification. According to the biophysical model developed from *in vitro* and *ex vivo* models, the origin of B-lines is not from a precise anatomic structure (interlobular septa) but rather from reflections of discrete air/fluid interfaces between collapsed,

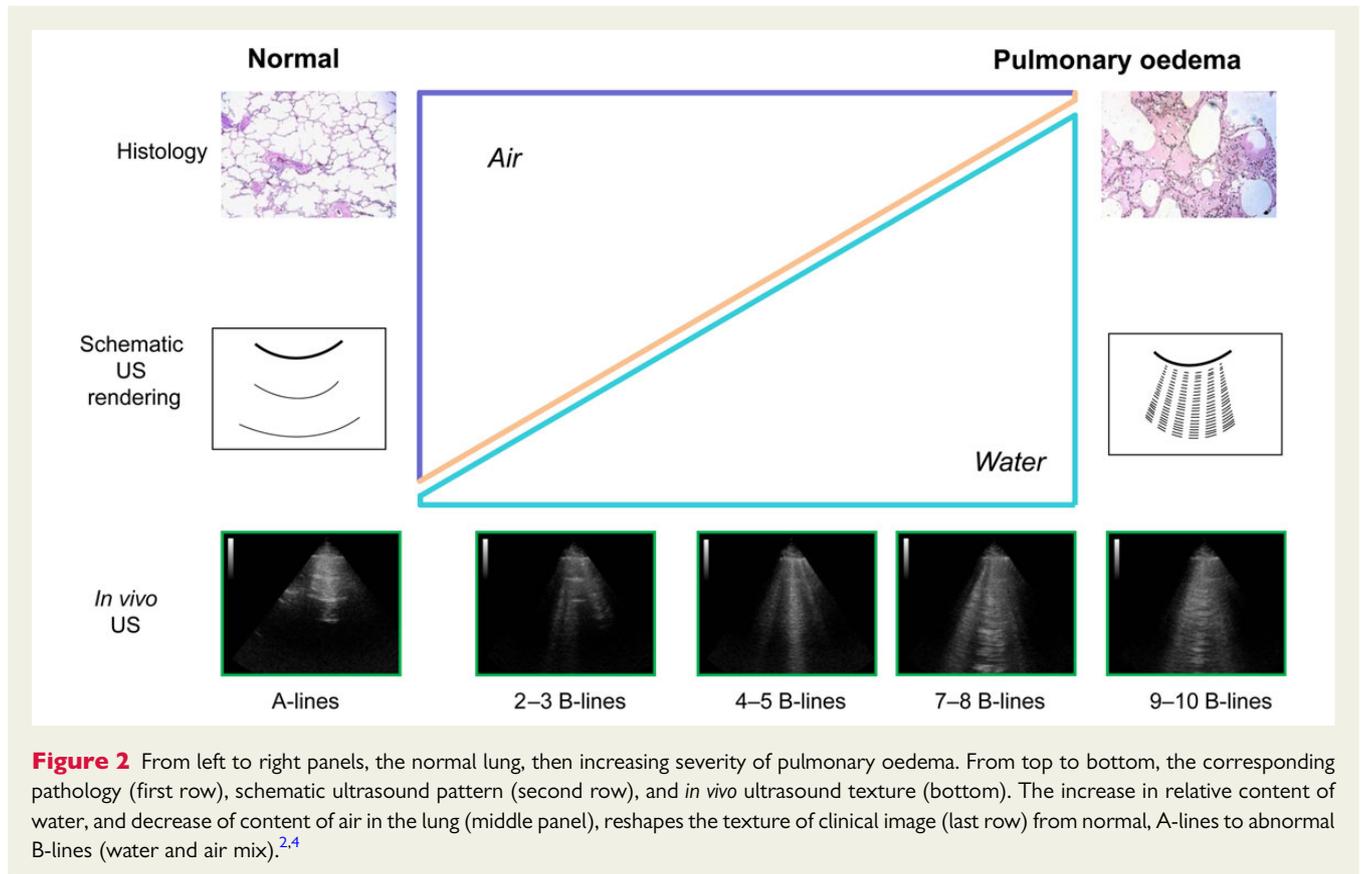


Figure 2 From left to right panels, the normal lung, then increasing severity of pulmonary oedema. From top to bottom, the corresponding pathology (first row), schematic ultrasound pattern (second row), and *in vivo* ultrasound texture (bottom). The increase in relative content of water, and decrease of content of air in the lung (middle panel), reshapes the texture of clinical image (last row) from normal, A-lines to abnormal B-lines (water and air mix).^{2,4}

fluid-filled, and well-aerated alveoli.^{6,7} The appearance of B-lines corresponds to a progressive loss of air per volume of lung tissue with a corresponding increase in relative and absolute content of EVLW (from normal, <5% or <500 mL, to overt pulmonary oedema, >90% or >2000 mL) (Figure 2).

The B-lines are detectable with cardiac, convex, or linear probes, from 2.5 (cardiac) up to 7.5 MHz (vascular) transducers.⁵ With a linear probe, B-lines run in parallel over the screen, whereas with the curvilinear probe, B-lines spread from the same proximal point of convergence.

The depth should be adjusted according to the body habitus of the patient, with thin patients requiring less depth and obese patients needing greater depth to visualize the pleural line. Neither the width of the sector angle nor the use of harmonic (instead of fundamental) imaging are known to have an impact on the B-lines count, although no systematic data are available.^{4,5} Higher frequencies and macro probes are useful for the evaluation of pleural line and sub-pleural space and may allow a better image of B-lines, but the overall number does not change significantly by changing the transducer.^{4,5}

The experimental and clinical validation of B-lines for extravascular lung water

Lung ultrasound has been applied to dogs with spontaneous left-sided heart failure⁸ and to a pig model of oleic acid-induced lung injury, which mimics human acute respiratory distress syndrome.^{9,10}

In dogs and pigs, the same instrument, transducer, and chest scan technique as used in humans can be adopted, making the translational implications more straightforward. In the pig model, there was a tight, linear correlation between the number of B-lines and wet/dry ratio by gravimetric method post-mortem, which is the gold standard for EVLW⁹ (Figure 3, left panel). In man, the number of B-lines, even assessed with a limited four-region scan of the anterior chest, correlate closely with invasive evaluation of EVLW,^{11,12} matching the experimental data (Figure 3, right panel). In intensive care patients with invasive gold standard transpulmonary thermodilution measurements of EVLW, LUS performed markedly better than chest radiography ($r = 0.91$ vs. $r = 0.33$), with a 92.3% sensitivity and 91.7% specificity for detecting abnormal values of EVLW.¹²

The same pig model was used to address the equally clinically relevant question as to whether B-lines could detect increased EVLW before the appearance of functional impairment. B-lines showed accumulation of EVLW very early in the course of lung injury in pigs, at a stage when no changes in hemo-gas analytic parameters or chest X-ray findings could be observed¹⁰ (Figure 4).

In the clinical setting, several groups have shown how B-lines correlate reasonably well with the imperfect gold standards of chest X-ray^{4,13} and CT¹⁴ radiological score. The correlation is stronger when intra-patient variations are considered.⁴

B-lines weakly correlate with clinical congestion score, cardiac peptide levels,^{15–18} and pulmonary wedge pressures.^{11,19} This is not unexpected, as in everyday practice, a patient can show variable degrees of B-lines (from absent to severe) for any given level of pulmonary artery wedge pressure, depending on the duration of

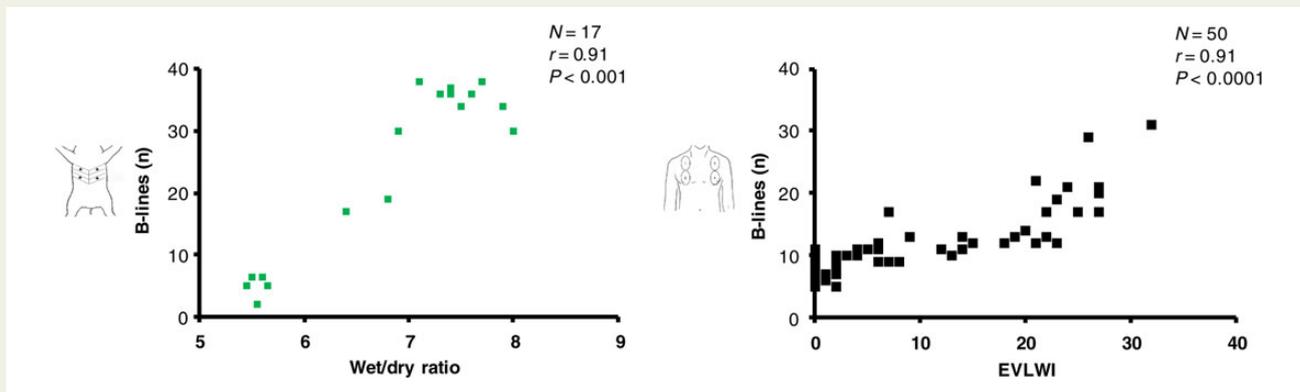


Figure 3 A very good correlation ($R = 0.91$ in both cases) is shown between B-lines and extravascular lung water evaluated experimentally by gravimetry in pigs with acute lung injury induced by oleic acid (left panel) and clinically by thermodilution in patients with acute lung injury-acute respiratory distress syndrome (right panel).^{9,12}

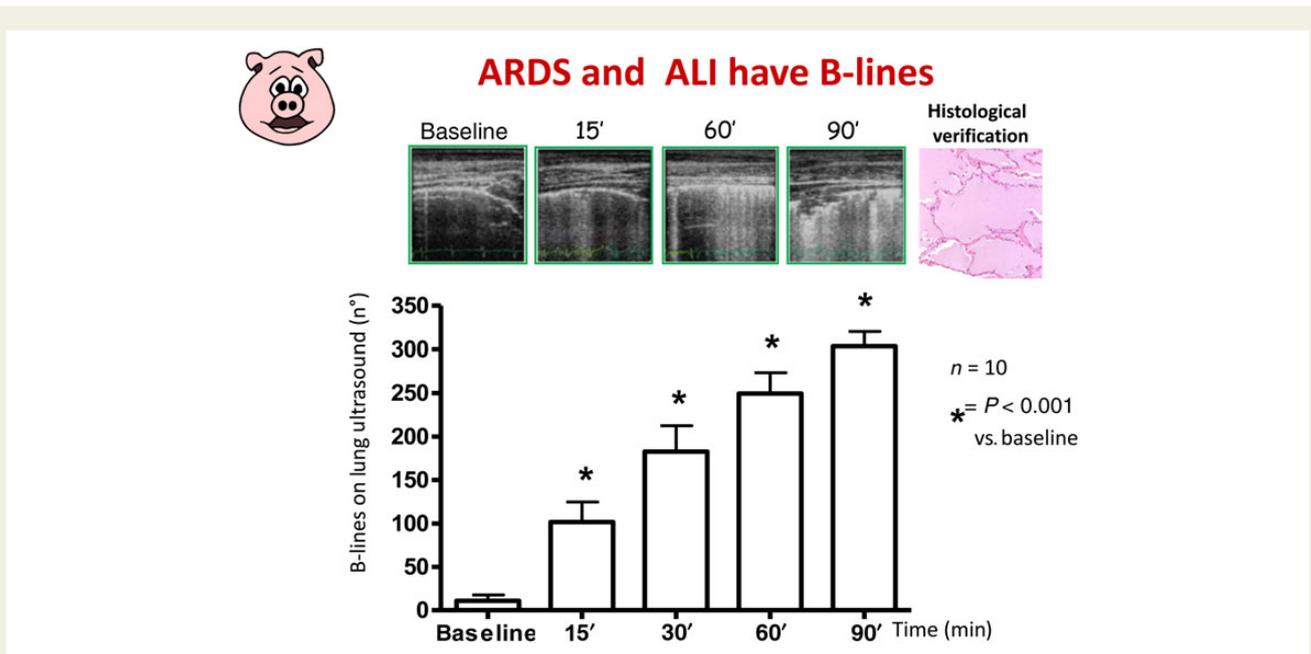


Figure 4 Sequence of events in a pig model of acute respiratory distress syndrome. B-lines occur early (already significantly increased at 15 min); only at a later stage (at 90 min) were changes in haemogasanalytic parameters significant.¹⁰ ALI, acute lung injury; ARDS, acute respiratory distress syndrome.

history of heart failure, speed of changes in pulmonary pressure, characteristics of the alveolar-capillary membrane, oncotic pressure, and lymphatic drainage capacity. B-lines without haemodynamic congestion are found in acute respiratory distress syndrome and environmental pulmonary oedema. B-lines are EVLW, not pulmonary wedge pressure.²⁰

Diagnostic and prognostic value in cardiology patients

B-lines are useful for the identification of cardiogenic origin of dyspnoea in the emergency room, with high sensitivity and excellent

specificity, yielding a 94% sensitivity and 92% specificity in differentiating acute heart failure syndrome from non-cardiac causes of acute dyspnoea as shown by a meta-analysis encompassing 1075 patients from seven different studies.²¹ These results were recently corroborated by a multicentre study which enrolled 1005 patients from seven Italian centres and showed that the LUS-based approach was more accurate than initial clinical work-up, chest X-ray, and natriuretic peptides.²²

B-lines have a limited specificity and can be found in the area surrounding isolated alveolar consolidations, from infectious, infiltrative, or traumatic lung disease. Oedematous (wet) B-lines cannot be readily distinguished from fibrotic (dry) B-lines associated with thickening of sub-pleural intralobular or interlobular septa, as found

for instance in systemic sclerosis.^{2,4,5} The consideration of the limited specificity is also important in assessing the diagnostic value and high sensitivity of LUS for detection of pulmonary congestion, which is strongly dependent on patient selection and comorbidities. In addition, it is not always possible with B-lines alone to separate EVLW accumulation due to heart failure or acute respiratory distress syndrome, although the latter may show a more inhomogeneous and irregular pattern, sub-pleural consolidation, highly fragmented pleural line, and multiple B-lines alternating with spared areas.^{5,20} Differentiation by LUS should include consideration of the clinical context and may be supported by other modalities such as echocardiography, which readily detects abnormal cardiac or valvular function and increased pulmonary artery pressure during acute heart failure syndrome.^{3,4}

B-lines also have a striking prognostic value, shown in patients with heart failure,^{23–25} acute coronary syndrome,²⁶ and dialysis.²⁷ Persistent B-lines at pre-discharge assessment are associated with a more malignant prognosis than B-lines on admission only.^{28,29} End-stage kidney disease patients with concomitant heart failure with very severe congestion (>60 B-lines) had a 4.2-fold increased risk of death, compared with patients having no or mild congestion (<15 B-lines).²⁷ The prognostic value is independent and additive over established clinical, imaging, and laboratory markers, such as NYHA class of dyspnoea, pulmonary congestion signs such as crackles, left ventricular ejection fraction, pulmonary artery systolic pressure, or cardiac natriuretic peptide levels.^{23–27}

Lung ultrasound also provides a useful biomarker to assess the time course of lung water changes following interventions, since within minutes or a few hours, B-lines in heart failure patients are substantially reduced after diuretics,^{3,30} or following dialysis.³¹

B-lines stress echocardiography

Exercise may result in the sudden appearance or increase of B-lines on the chest in heart failure patients (Figure 5), in whom an increase in left ventricular filling pressures may occur with or without inducible ischaemia.^{32,33} When B-lines develop or worsen during exercise, resting levels of cardiac peptides and pulmonary pressures are higher, as are the chances of an unfavourable outcome during short-term follow-up.³³

In addition, exercise-induced B-lines are detectable in patients with chronic mountain sickness during exercise performed at 3,600 m, but not in healthy high-altitude dwellers.³⁴ The rapid lung interstitial fluid accumulation can be prevented by oxygen inhalation.

Stress echo with B-lines can also be performed outdoors, with pocket size instruments, in an entirely different setting of ecological stress. The diagnostic target is the diagnosis, or early subclinical identification, of life-threatening pulmonary oedema. In this challenging but fascinating context, LUS detects B-lines in 20–50% of super-fit subjects in extreme physiology settings, such as high altitude^{35,36} or deep underwater apnoea diving^{37,38} (Figure 6).

Therefore, stress lung ultrasound may be useful to detect exercise-induced heart failure and also to appreciate lung interstitial fluid lung accumulation in the setting of extreme physiology (Table 3).

Lung ultrasound in extreme physiology setting is perhaps the best example of a new paradigm of 'ecologic' stress echocardiography, performed outside the controlled hospital setting, where some conditions—for instance, mental stress, psychological discomfort, environmental aggression, or extreme physiology states—cannot be reproduced.³⁹

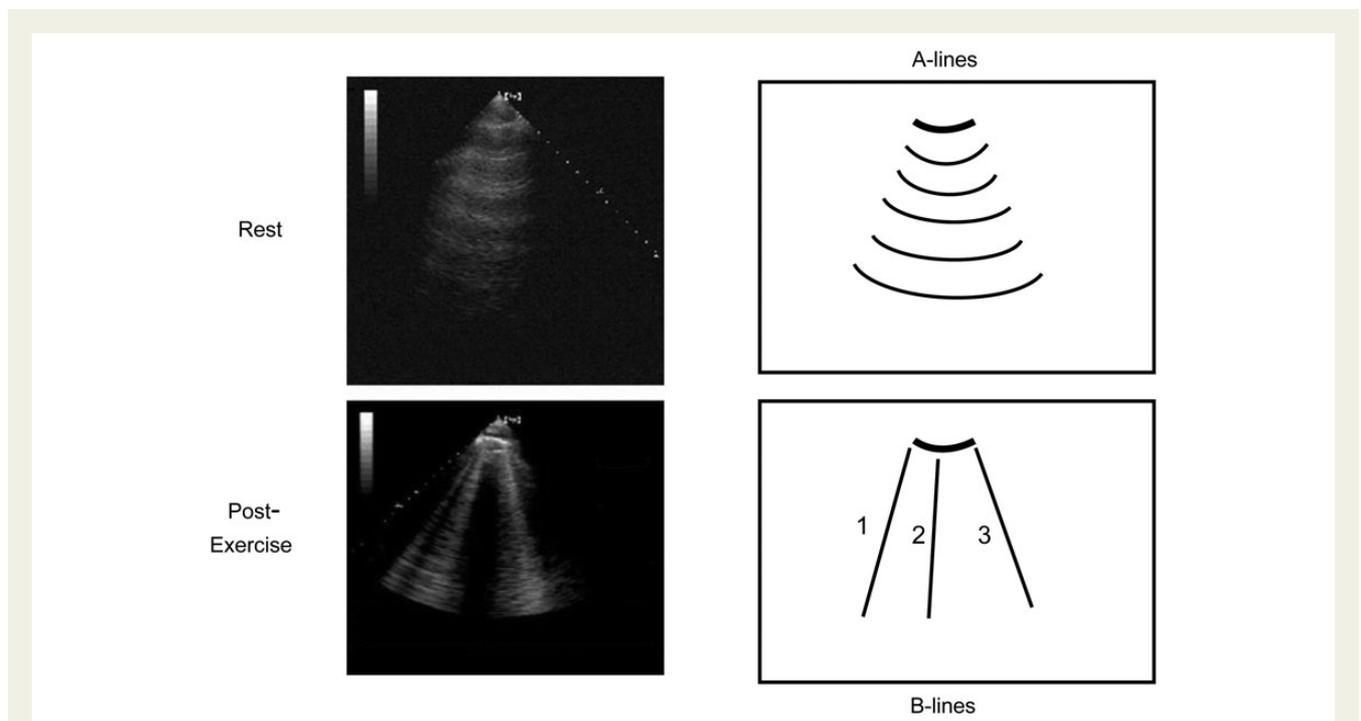


Figure 5 Lung ultrasound (third right intercostal space) at rest (upper panel) and immediately after exercise (lower panel). The exercise-induced appearance of B-lines eclipses the normal pattern of A-lines present at rest.³²

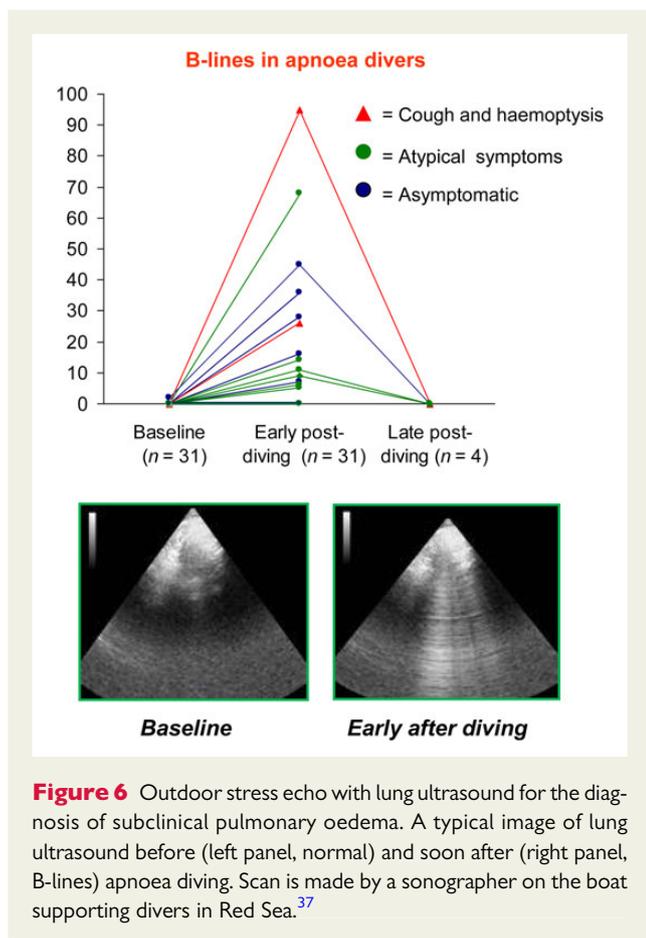


Figure 6 Outdoor stress echo with lung ultrasound for the diagnosis of subclinical pulmonary oedema. A typical image of lung ultrasound before (left panel, normal) and soon after (right panel, B-lines) apnoea diving. Scan is made by a sonographer on the boat supporting divers in Red Sea.³⁷

Table 3 B-lines stress echocardiography: from indoor to outdoor

Stress echo application	Indoors	Outdoors
Instrument	High cost, high weight	Low cost, light weight
Subjects	Patients with exertional dyspnoea or heart failure	Very fit normals
Stress	Semi-supine exercise	Extreme physical activity ^a
Environment	Echo laboratory	Ecological ^b
Scan anterior chest	28 regions (full information)	Four regions (to save time)
Stress physiology	Artificial	Real life
Management changes	Titrating diuretic therapy	Stopping exposure ^c

^aApnoea diving, marathon, triathlon, and trekking.
^bDesert, high-altitude, and deep sea.
^cAt a subclinical stage, preventing life-threatening pulmonary oedema.

Advantages

Lung ultrasound is radiation-free, which will reduce the need for chest-X rays in cardiology patients; such patients have commonly

Table 4 The dual nature of B-lines: wet or dry

B-lines nature	Wet	Dry
Dominant component	Water	Fibrosis
Underlying pathology	Heart Failure	Interstitial lung disease
Pleural line	Regular, smooth	Irregular, thickened
Effects of diuretics/dialysis	Acute decrease	No change
From sitting to supine	Acute increase	No change
Effects of volume loading	Acute increase	No change
Effects of exercise	Acute increase	No change

been subjected to increased levels of diagnostic radiation exposure.⁴⁰ Lung ultrasound requires an imaging time of a few minutes. Cardiac transducers work well for LUS, since they are designed with a small footprint, allowing easy scanning between rib interspaces.

The methodology and findings of B-lines are similar in pigs, dogs, and man.^{8–10}

In consecutive patients studied in a cardiology environment, such as echocardiography laboratory or intensive care unit, the feasibility of LUS approaches 100%, with intra- and inter-observer variability consistently <5% and <10%, respectively,^{3,11,18} and a mean difference of 0.3 B-lines between readers.²⁵ The reproducibility is excellent; thus, B-lines are ideally suited as a biomarker to assess intra-patient changes over time.

B-lines are appealingly simple to use, to learn, and to teach. A 1-h training session and a pocket size instrument are sufficient for a novice sonographer to reach the same accuracy in counting B-lines of a highly experienced cardiologist with top-level equipment.^{41,42} B-lines are readily obtainable; their assessment should be considered in the primary care of the dyspnoic patient.

Lung ultrasound study provides considerable information beyond assessing the presence of simple B-lines, from pleural effusion to consolidations and pneumothorax. As B-lines originate from the visceral pleura, their simple presence proves that the visceral pleura is opposing the parietal pleura, thus excluding pneumothorax at that point. The absence of any movement of the pleural line, either horizontal (sliding) or vertical (pulse), coupled with the absence of B-lines strongly supports a clinical suspicion of pneumothorax.^{5,20}

Limitations

For LUS, large wound dressings and subcutaneous emphysema may limit access in <1% of subjects. Soft tissue oedema or morbid obesity can degrade the quality of images. In general, LUS complements poor acoustic windows, and its feasibility is nearly 100%.²⁰

Lung ultrasound only evaluates the sub-pleural cortical area, extending for a depth of 2–4 cm.

The separation of wet, watery B-lines from fibrotic, dry, B-lines as can be found in systemic sclerosis can be difficult with an isolated LUS assessment: clinical context, integration with echocardiography and dynamic evaluation are recommended.⁴³ An accurate way to identify wet B-lines is to follow their acute variation within minutes, since they increase during exercise^{32,33} or volume loading²⁰ and decrease following diuretics^{3,30} or dialysis³¹ (Table 4). There are also

posture-dependent changes in lung water, with 25% more B-lines in the supine compared with the sitting position in patients with acute heart failure.⁴⁴

Future perspectives

The diagnosis will become more objective through simple soft computing algorithm.⁴⁶ Major scientific societies might clear the field from persisting terminology confusion and the lack of standardization and better tailor the LUS to the needs of the cardiologist imaging community. Large-scale prognostic validation in heart failure patients undergoing exercise stress echo is under way as a specific subproject of the 'Stress Echo 2020' study endorsed by the Italian Society of Echocardiography. Randomized multicentre studies are testing the hypothesis that B-line-guided therapy may improve clinical outcome in high-risk haemodialysis patients with cardiomyopathy. Therefore, the dissemination of the technique due to its obvious merits should go in parallel with an adequate assessment in outcome studies. The clinical use of the technique still is ancillary. Large-scale, randomized trials are needed to document to what extent its use would benefit the cardiac patient with a failing heart and to appreciate its limitations which could result in inappropriate therapy.

Current recommendations

Bedside LUS was recognized in a scientific statement of ESC since 2010 as a 'potentially useful way to assess pulmonary congestion',¹ and recommended in 2015 as a first-line test in the evaluation of suspected acute heart failure to assess pulmonary congestion,^{47,48} since 'in reasonably expert hands LUS maybe equally or more informative than chest X-ray allowing also an important time saving'.⁴⁸ The 2012 recommendations of an international committee on point-of-care LUS recognized LUS as ideally suited for 'monitoring pulmonary congestion changes in heart failure patients as they disappear or clear upon adequate medical treatment'.⁵

According to the 2016 EACVI recommendations, during exercise stress echo the acute increase in B-lines detected by LUS is a feasible way for demonstrating that the symptom 'dyspnoea when exercising' is related to pulmonary congestion due to backward heart failure.⁴⁹

EACVI recommendations for use of pocket size devices explicitly list 'semi-quantification of EVLW' among the top 8 indications for pocket size devices.⁵⁰

Conclusions

B-lines are a sign of interstitial syndrome of mixed origin (fibrosis, inflammation, and congestion), and in acute or chronic heart failure patients they mostly represent the direct, positive image of lung water, for a long time a forbidden fruit for the clinical cardiologist. Through the lung water teaser, the cardiologist will become familiar with the new diagnostic world of LUS, a friendly neighbour of transthoracic echocardiography, of critical help in many different and frequent clinical situations, from diagnosis and semi-quantification of pleural effusion to fluid management in cardiogenic shock to pneumothorax identification in differential diagnosis of dyspnoea.^{5,20,45} The rapidly dynamic nature of B-lines separates wet

B-lines made by water (decreased by diuretics) from dry B-lines made of connective tissue. B-lines can be used anywhere (even in extreme environmental conditions with pocket size devices), by anyone (including novice sonographer) on anybody (since the superficial acoustic window that is required usually is feasible even when echocardiography is not feasible). Rarely, in cardiac imaging, we have so much diagnostic gain with so little technological, training, and time pain. Lung ultrasound can quantify lung oedema noninvasively in real time, even at an early subclinical stage, with user-friendly, low cost, radiation-free, and direct imaging of EVLW.

Authors' contributions

E.P., P.A.P. performed statistical analysis, handled funding and supervision, acquired the data, conceived and designed the research, drafted the manuscript, and made critical revision of the manuscript for key intellectual content.

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