Ultrasonography in Heart Failure: A Story that Matters

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Abstract: Heart failure (HF) is a clinical syndrome caused by structural and/or functional cardiac abnormalities, resulting in a reduced cardiac output and/or elevated intracardiac pressures at rest or during stress. It is the leading cause of hospitalization in Internal Medicine departments. This article aims at reviewing evidence of the importance of ultrasound in HF both for hospitalized patients and in the follow-up. Ultrasound may be used as a recovery monitoring instrument at the bedside and also as a global cardiovascular assessment tool for these patients. HF represents an exciting opportunity to create an integrative ultrasound approach in Internal Medicine and/or Geriatric departments. The authors plan a five-step ultrasound examination to evaluate and monitor HF patients during hospitalization and follow-up. They call this examination: the "ABCDE" score. It includes the evaluations of A, the ankle-brachial index, B, the B-lines, C, the carotid intima media thickness, D, the diameter of the abdominal aorta and of the inferior cava vein and E, the echocardiographic assessment of the ejection fraction. This score may represent an integrative ultrasound approach in Internal Medicine and/or Geriatric departments. (Curr Probl Cardiol 2018;00:1–20.)

Abbreviations: HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; IMT, Carotid intima media thickness; LVEF, left ventricular ejection fraction; NASCET, North American Symptomatic, Carotid, Endarterectomy Trial.

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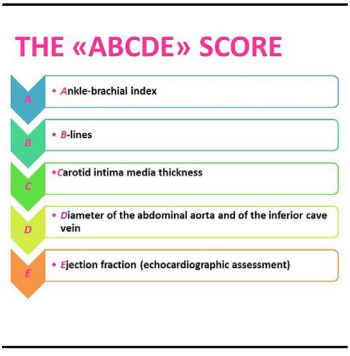
Background



Heart failure (HF) is a clinical syndrome characterized by typical symptoms and signs caused by structural or functional cardiac abnormalities, resulting in a reduced cardiac output or elevated intracardiac pressures at rest or during stress.[1] The prevalence of HF is approximately 1%-2% of the adult population in developed countries, rising to 10% among people >70 years of age, and it is the leading cause of hospitalization.[2]

The main terminology used to describe HF is historical and is based on the measurement of the left ventricular ejection fraction (LVEF).[1] HF comprises a wide range of patients, from those with normal LVEF (HF with preserved ejection fraction [EF], heart failure with preserved ejection fraction) to those with reduced LVEF (HF with reduced EF, heart failure with reduced ejection fraction). Patients with an LVEF in the range of 40%-49% represent a "grey area", which is now defined as heart failure with mid-range ejection fraction (HF with mid-range EF).

According to the current guidelines,[1] echocardiography is considered the most useful and widely available test in HF patients. It provides immediate information on chamber volumes, ventricular systolic, and diastolic function, wall thickness, valve function and pulmonary hypertension. This information is crucial in establishing the diagnosis and in determining appropriate treatment.

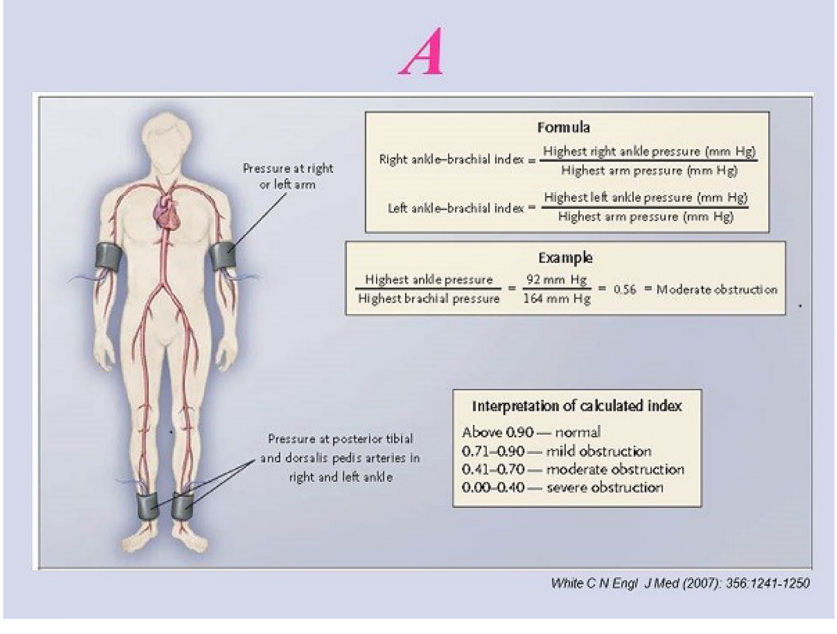
Nevertheless, ultrasound examinations other than echocardiography, give substantial information both during hospitalization and in the follow-up of HF patients. Over the last 2 decades, the concept of using sonography as a real-time bedside clinical tool (point of care) in the hands of the same physician who is treating the patient is obtaining a growing consensus.[3] Among them, lung ultrasound (LUS), with the quantification of the B-lines, is surely the most innovative and also the simplest to learn.

Congestion is an extremely complex condition in HF patients. Shifting of the fluids in the lungs causes pulmonary interstitial fluid and alveolar edema, which is the main cause of hospitalization. LUS and cava vein monitoring by the quantification of the collapsibility index, inferior cava vein collapsibility index (ICVCI), are considered efficient tools in monitoring the congestion recovery in HF patients.[4]

But the cardiovascular risk assessment of these patients may include also the peripheral vessels examination. In this perspective, carotid, abdominal aorta, and peripheral arteries evaluation may represent an integrative approach. So this article aims at reviewing evidence of the importance of ultrasound in HF both for hospitalized patients and in the follow-up. Ultrasound may be used as a recovery monitoring instrument at the bedside and also as a global cardiovascular assessment tool for these patients.

Focus on: Heart Failure and the Ankle Brachial Index

The ankle brachial index (ABI) is a marker of generalized atherosclerosis. It is predictive of future cardiovascular events.



It is a useful tool for specific, cost-effective, noninvasive diagnosis of peripheral artery disease.[5-7]

The ABI carries prognostic information related to all-cause mortality, cardiovascular death, and nonfatal cardiovascular events, including coronary heart disease and stroke.

The association between ABI and incident HF has been characterized. The Cardiovascular Health Study demonstrated that an ABI < 0.90 was independently associated with an increased risk of HF among participants without prevalent coronary heart disease.[8]

The Atherosclerosis Risk in Communities Study[9] described the relationship between ABI and the risk for HF. In a community cohort of middle-aged Americans, it has been found that a low ABI was associated with a 40% higher risk of HF than a normal ABI, and a borderline ABI was also associated with an increased risk of HF. Authors analyzed a middle-aged community cohort with ABI ≤ 1.00. It was significantly associated with an increased risk of HF independent of traditional HF risk factors, prevalent coronary artery disease, and carotid atherosclerosis. Authors hypothesized that an altered ABI may be a risk marker for HF. Mechanistically, a low ABI may be a marker for abnormal vascular stiffness and atherosclerotic microvascular dysfunction which may contribute to the pathogenesis of HF even in the absence of clinically apparent coronary artery disease.

It has been found[10] that greater aortic stiffness (reflected by higher carotid and/or femoral pulse wave velocity) was associated with increased risk of HF. Arterial stiffness has been recognized as a marker of cardiovascular disease and associated with long-term worse clinical outcomes in several populations. Arterial stiffness is increased in advancing age, and has been recognized as an independent risk factor for cardiovascular disease. Pulse wave velocity (PWV) is recognized as the gold standard measurement of arterial stiffness, thus a higher PWV is known as a significant predictor of cardiovascular morbidity and mortality in older subjects.

In a recent study[11] it was found that low and borderline ABIs were strongly associated with future HF in hospitalized cardiology patients. There are many factors, including arterial stiffness that can contribute to the onset of HF. Brachial ankle PWV was found increased with decreasing ABI. Thus, increasing PWV may be a key to explaining the association between decreasing ABI and the increased incidence of new-onset HF.

The relationship between ABI and incident HF in patients without previous HF has been assessed.[12] Authors found that low and borderline ABI were strong predictors for future incident HF in patients without previous HF. The cumulative incidence of HF was significantly higher in patients with low and borderline ABI than in those with normal ABI. In multivariate analysis, low ABI and borderline ABI were independent predictors of incident HF.

Furthermore, in the Multi Ethnic Study of Atherosclerosis,[13] authors observed that less compliant arteries were significantly associated with low ABI in cross-sectional analysis and with greater decline in ABI over time, using linear and logistic regression models on baseline data from 2803 female and 2558 male participants. A low ABI was associated with non−compliant small vessels, which in turn, has been associated with an increased risk for adverse cardiovascular events, including HF.

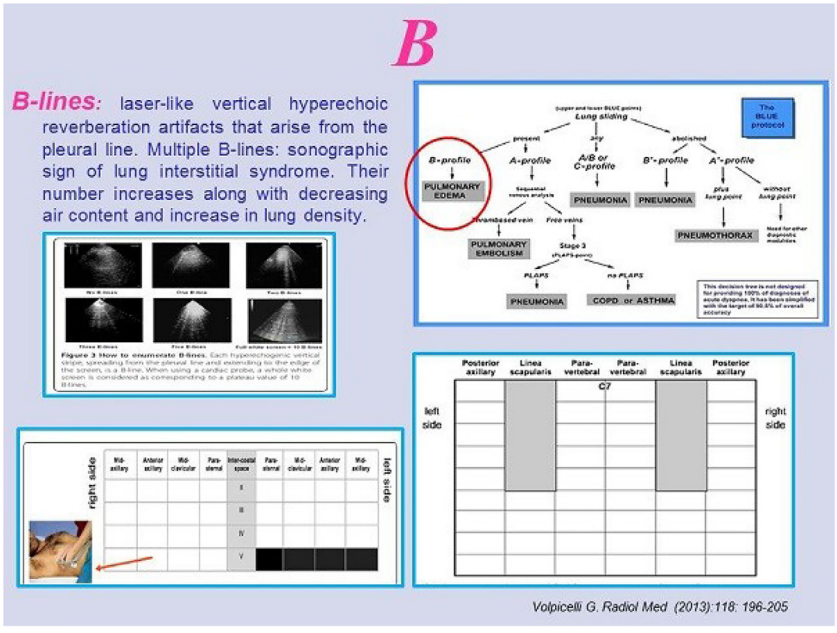
Focus on: Heart Failure and the B Lines in Lung Ultrasound

In recent years, LUS has been demonstrated to be a valid tool for the assessment of pulmonary congestion[14,15] through the quantification of the B-lines.

B-lines are laser-like vertical hyperechoic reverberation artefacts that appear from the pleural line (also defined as “comet tails” or better yet “ring-downs”). Multiple B-lines can be the sonographic sign of lung interstitial syndrome. Their number increases along with decreasing air content and increase in lung density.[3,16] Many authors report that clearing of B-lines significantly correlates with improved clinical symptoms and signs of HF.[3,14-16]

Their regular distribution allows the differentiation between cardiogenic pulmonary edema, acute respiratory distress syndrome, and pulmonary fibrosis.[3,16]

LUS is emerging as an important tool in critical care for the early diagnosis of acute respiratory failure.[17,18] The “decision tree” used to guide this diagnosis is the well-known bedside lung ultrasound evaluation protocol.[19] This protocol is based on rapidity. But LUS can be also used as a monitoring tool in HF patients.



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Recently[20] our group has confirmed the potential of LUS in tailoring diuretic therapy and speeding up the discharge time in HF hospitalization. In this study the reduction of the B-lines did not occur in accordance with the aminoterminal portion of B type natriuretic peptide levels, suggesting that serum aminoterminal portion of B type natriuretic peptide may not reliably indicate pulmonary congestion having been resolved. These results lead to consider this molecule as a useful marker for the discrimination of the possible origin of respiratory failure, but it is not so precise in monitoring HF recovery.

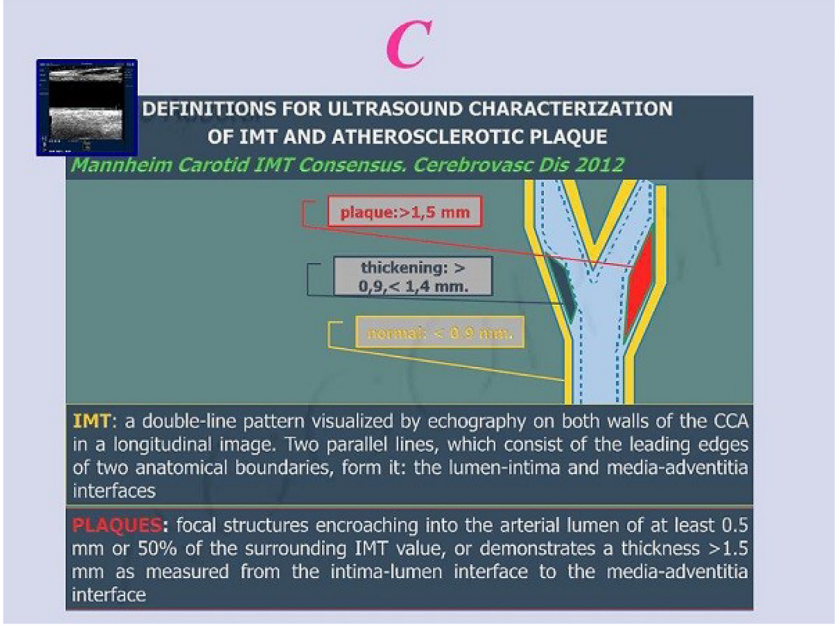
Different studies[21-23] have been designed in different settings other than Internal Medicine and Emergency.

The advantages of using LUS in the Internal Medicine department are well-established: the operator is not blinded to the patients' clinical situation, the examination could be performed at the bedside, it is cheap and safe. These studies have confirmed that the B-lines are prognostic markers for hospital re-admission or death in HF patients.

Focus on: Heart Failure and the Vascular Assessment, Carotid Ultrasonography and Intima Media Thickness, Inferior Cava Vein, and Abdominal Aorta Diameter

Carotid-wall intima-media thickness is a surrogate measure of atherosclerosis and it is associated

with cardiovascular risk factors and with cardiovascular outcomes.[24-27]



There is evidence of a direct relationship between increased carotid intima media thickness (IMT) and reduced left ventricular systolic and diastolic function assessed by myocardial strain in asymptomatic individuals without previous clinically evident cardiovascular disease.[28]

Previous cross-sectional analysis using data from the Atherosclerosis Risk in Communities Cohort showed that participants with HF

had a higher mean carotid IMT than participants without HF.[29] The Atherosclerosis Risk in Communities Study[30] used data from the Atherosclerosis Risk in Communities Cohort Study cohort to examine the hypothesis that subclinical atherosclerosis, assessed by mean carotid IMT, was associated with incident HF. Authors found that mean carotid IMT was significantly higher for subjects with HF. The association of carotid IMT with HF remained significant after adjustment for blood pressure, and other traditional cardiovascular risk factors.

Increasing carotid IMT leads to structural changes of the artery wall, which result in the deposition of collagen in the intracellular matrix and a decrease in arterial distensibility, causing increased pressure afterload, pressure wave propagation, and eventually diastolic dysfunction.[31-33]

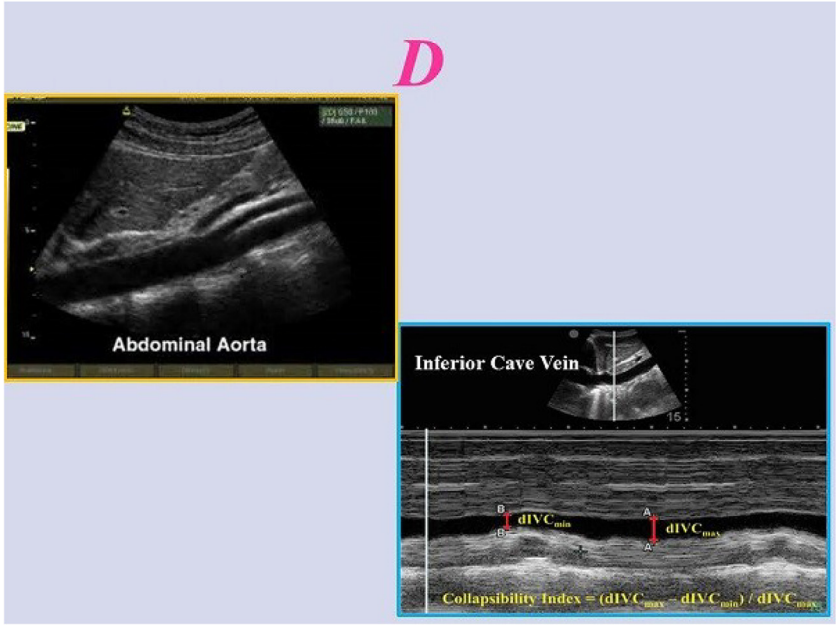
Some prospective and cross-sectional studies have established an association between increasing carotid IMT and regional left ventricular myocardial systolic and diastolic dysfunction.[34,35]

Aneurysmal aortic dilation may be associated with cardiovascular disease risk factors and may prognosticate an increased risk of adverse cardiovascular outcomes.[36]

The Framingham Heart Study[37] showed that enlarged infrarenal abdominal aortas are independent predictors of incident adverse cardiovascular events above traditional risk factors alone.

Similar results were found in the Tromsø study[38]: authors found that abdominal aorta aneurysm increases total and cardiovascular mortality.

The estimation of the right atrial pressure using echocardiographic measurement of inferior cava vein (IVC) size along with its respirophasic variation is commonly performed.[39] Cutoff values and measurement modalities have been established. Inferior cava vein (ICV) maximum and minimum diameter and its collapsibility index (ICVCI) are measured in subcostal view in M-mode, 2 cm from the right atrial junction. ICVCI is calculated according to the formula [(ICV max−ICV min)/ICV max] × 100. The ICVCI% cut-offs are: >75 (hypovolemia), ≥40, and ≤75 (euvolemia) and <40 (hypervolemia).[39]



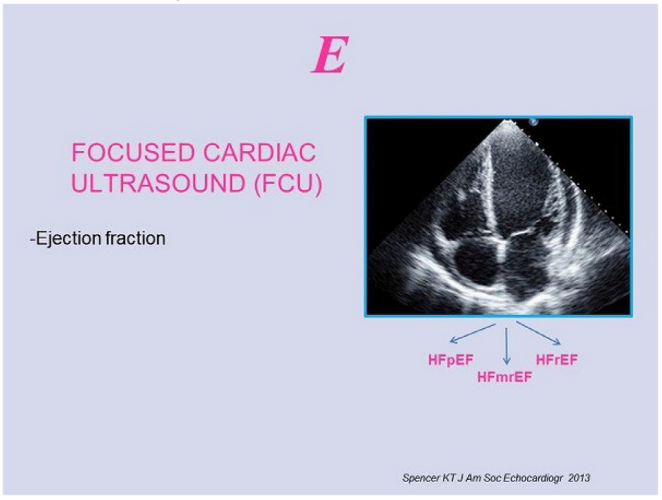
Nevertheless, reappraisal for its use has been suggested[40] in order to avoid the assessment of confounding factors that may affect the IVC size and the respirophasic changes.

Even so, ICVCI has been established as a helpful tool in monitoring HF patients' responses to diuretic therapy, checking the volume status. Different studies[4,20] propose ultrasonographic measurement of IVC parameters to guide HF therapy, incorporating it in the routine ultrasound assessment of the patient.

To summarize, caution is needed and the ICV evaluation *alone* is not recommended for assessing the volume status of the patient. In a simpler way a maximum diameter of the IVC greater than 2 cm and a collapsibility less than 40%-50% have good correlation with a central venous pressure > 10 mmHg.[40]

Focus on: Heart Failure and Echocardiography

Transthoracic echocardiography is the method of choice for the assessment of myocardial systolic and diastolic function of both left and right ventricles (RVs).[1]



LVEF remains the major phenotyping tool in HF, as underlined in the current guidelines.[1] This approach is based on the statement that LVEF is a surrogate marker for left ventricular systolic performance and, in turn, prognosis. LVEF has proved to be a good predictor of incident HF. In the CARE trial, with the exception of patient age, LVEF was the most relevant predictor of HF occurrence in 3860 long-term survivors of myocardial infarction without previous history of HF over a 5-year follow-up period.[41]

In the VALIANT echocardiography study (610 patients with HF, LV dysfunction, or both following myocardial infarction) LVEF and LV volumes at baseline were independently predictive of adverse clinical outcomes (total mortality, cardiovascular mortality, resuscitated sudden death, hospitalization for HF, and stroke).[42]

However, LVEF as a measure of LV function has some important limitations. LVEF is measured indirectly by most imaging techniques, including echocardiography, which calculate the ejection fraction from estimations of LV volume. As a volume-derived index, LVEF often relies on geometric assumptions (particularly in one- and two-dimensional echocardiography) and is extremely load-dependent. These limitations lead to substantial loss of reproducibility, and even repeated measures of ejection fraction in the same individual over a brief time period can result in a 5- to 7-point variability.

So that, the ESC 2016 Guidelines[1] specify that the assessment of RV structure and function, including RV and right atrial dimensions, an

estimation of RV systolic function and pulmonary arterial pressure are obligatory elements of echocardiography examination.

In fact, in case of initial evidence of heart failure with preserved ejection fraction and/or heart failure with mid-range ejection fraction, key structural and functional signs are shown by alterations in left atrial volume index, left ventricular mass index, E/e′ and mean septal and lateral wall.[43-45]

Also the correct timing for echocardiography has been determined.[1] Immediate echocardiography is required in patients with hemodynamic instability (and cardiogenic shock) and in patients having acute life-threatening structural or functional cardiac. Immediate echocardiography should be done in patients with de novo HF and in those with unidentified cardiac function.

The Guidelines underline that repeated echocardiography is usually not needed unless there is relevant deterioration in clinical status. Bedside thoracic ultrasound for signs of interstitial edema and/or pleural effusion may be convenient in identifying HF, if the expertise is available.

Advanced imaging technologies, as speckle-tracking echocardiography, can provide data on regional myocardial function and its specific components, in particular longitudinal myocardial function, which is often the earliest component to be affected by disease.

These methodologies are not commonly used in Internal Medicine and their explanation goes beyond the purpose of this review.

Compared to formal echocardiographic methods for the evaluation of LVEF, visual estimation (eyeballing) can be done faster, and is often easier to perform, even in studies with poor visual quality. Among the variety of terms that have been used to describe a focused ultrasound study of the heart, the American Society of Echocardiography[46] recommends the use of the term “focused cardiac ultrasound” to indicate a focused examination of the cardiovascular system by a physician using ultrasound as an adjunct to the physical examination to recognize specific ultrasonic signs that represent a narrow list of potential diagnoses in specific clinical settings. The estimation of the eyeballing EF is confirmed as a recommended method especially in contexts other from Cardiology.

Focus on: Ultrasound Limitations (Principally Concerning B-LUS) and Previous Attempts to Create Score Systems in Heart Failure

The main disappointment in the area of research of ultrasound in HF concerns B-LUS and, in particular, the role of the B-lines.

Table 1. The "ABCDE" score

A (Ankle-brachial index)
Normal (<90): points 0
Mild obstruction (0.71-0.90): points 1
Moderate obstruction (0.41-0.70): points 2
Severe obstruction 0-0.40): points 3
B (B-lines)
Number of B-lines for each space ≤5: points 0
Number of B-lines for each space ≥6 to ≤9: points 1
Number of B-lines for each space ≥ 10 ("Full white screen"): points 3
C (IMT or carotid plaque)
Normal: points 0
Altered IMT (>0.9 mm): points 1
Plaque presence (no significant stenosis, <70% following NASCET classification): points 2
Plaque presence (significant stenosis, >70% following NASCET classification): points 3
D (diameter of aorta and VCI collapsibility index)
Aorta
Normal (<25 mm): points 0
Normal diameter but with calcifications: points 1
Ectasia (25-30 mm): points 2
Aneurysm (>30 mm): points 3
Cava vein
Normal collapsibility index (40%-75%): points 0
Altered collapsibility index (if <40% or >75%): points 1
E (EF according to European Society of Cardiology guidelines 2016)
HFpEF (LVEF ≥50%): points 0
HFmrEF (LVEF in the range of 40%-49%):points 1
HFrEF (LVEF<40%): points 2

Abbreviations: EF, ejection fraction; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction; NASCET, North American Symptomatic Carotid Endarterectomy Trial; VCI, vein collapsibility index.

This issue is very demanding, so it is our duty to examine the problem in detail. This fact derives from the concept that B-lines are artefacts, so they are an expression of an error of the ultrasound machine.

Secondly, they are lacking in specificity.

It has to be recognized that the LUS technique in the B-lines identification and counting is not fully standardized and many issues against LUS in HF exist, in particular because of their low specificity in interpreting the acoustic interactions.[47,48]

B-lines due to cardiogenic pulmonary edema are usually bilateral, and usually spread or recover symmetrically.[3] Their regular distribution allows the differentiation between cardiogenic pulmonary edema, acute respiratory distress syndrome, and pulmonary fibrosis.[3]

B-lines are found in many other pulmonary pathologies, such as parenchymal and pleural diseases and chronic obstructive pulmonary disease.

Another source of possible pitfall in B-lines detection is the older age of the patient, as demonstrated.[49]

In addition, B-lines counting method is another source of possible errors, concerning both the ways of counting them and the used probe (type and frequency).

These essays have been largely addressed and caution is mandatory, principally for two reasons: (1) up to now not precise and largely accepted counting methods and preferred probe are available; (2) the patient with HF may be affected by different pulmonary conditions that confound the images.

Rea and Sperandeo have deeply analyzed these concepts.[47,48,50-53]

so that, a critical reappraisal of B-lines in HF is required. The overall clinical picture of the HF patient, conjuncted with biomarkers and other instrumental examinations are mandatory.

The other issue about HF is the continuous attempt to create scoring systems for risk stratification, prognosis, future re-admissions for HF.

In these studies[54-57] different items have been evaluated (principally electrocardiogram features, natriuretic peptide levels, serum creatinine levels, β blocker prescription at discharge, etc.).

In the elderly patient, also the nutrition status, the severity of dementia and medication adherence have been scored as single parameters,[58] also with different aims from cardiovascular outcome (eg a novel scoring system to predict delirium in HF patients).[59]

As far as we know, with regard to ultrasound, heart LVEF, B-lines counting and ICV diameter[20,60] are usually considered.

But up to now, no precise and integrated ultrasound score systems have been proposed, neither in hospitalized patient nor in the follow-up.

The Purpose of a Score (The "ABCDE" Score) as a Five-Step Vascular Ultrasound Examination in Heart Failure

In daily practice, HF patient management decisions are an integration of readily available clinical parameters and values obtained by various diagnostic techniques, proved to be of prognostic relevance.

In particular, during the last decade, there has been substantial progress in the use of biomarkers in the clinical management of HF. A broad range of clinical biomarkers have been rigorously tested in different

mechanistic domains. Several biomarkers have been proposed in the diagnosis, management, follow-up and therapy guidance in HF.

The natriuretic peptides and many markers of inflammation and oxidative stress have been deeply investigated, as reviewed.[61,62]

But for the ultrasound side of the matter, the author's purpose is the creation of a simple score system for assessing HF patients both at the bedside (during hospitalization) and for their global cardiovascular assessment.

Authors call this examination: the "ABCDE" score. In detail, it includes the evaluations of A, the ABI index, B, the B-lines, C, the carotid intima media thickness, D, the diameter of the abdominal aorta and of the inferior cava vein and E, the echocardiographic assessment of the ejection fraction.

Patients should undergo: A (calculated for each leg at admission), B-lines counting (calculated at admission, during hospital stay and at discharge with LUS, approach 72 spaces), C (at admission), D (at admission for the aorta and at admission, during hospital stay and at discharge for the ICV) and E (at admission and discharge).

Table 1 represents the ABCDE score, as suggested by the authors on the basis of the current literature data, as a five-step vascular ultrasound examination in HF patients.

How to Avoid Pitfalls and Misunderstandings and Create Consistent Endpoints

In order to avoid the detection of B-lines other than due to HF, because, as explained, B lines in HF are not an easy issue[63]; rigorous technical and study setting features should be performed.

Firstly, exclusion criteria must be strict: concomitant acute coronary syndrome, pneumonia, chronic obstructive pulmonary disease, lung cancer or metastases, lung fibrosis, acute respiratory distress syndrome previous pneumonectomy or lobectomy, breast prosthesis, and obesity. It has to be recognized that the LUS technique in the B-lines identification and counting is not fully standardized and many issues against LUS in HF exist, in particular because of the low specificity of the B-lines in interpreting the acoustic interactions. In fact, in this study, precise exclusion criteria have to be adopted in order to avoid the detection of B-lines other than due to HF.

These strict exclusion criteria are the strength of the study, especially to clarify the role of the clearing of the B-lines during HF recovery.

In addition, the measurements will be taken by two different physicians, in order to check the agreement of the results.

In addition, age ranges should be limited.

The same probe for all the patient should be used for B-LUS in order to avoid variability (cardiac probe or convex), due to the fact that no precise probe is commonly recommended and mandatory for LUS.

Anterior, lateral and basal-posterior chest (approach 72 spaces) should be scanned applying the well-established protocol,[3] that takes more time but that is feasible in a medical context other from Emergency. The authors will count the total number of the detectable B-lines in anterolateral and posterior scanning sites.

Going forward, according to Soldati and Zanforlin et al.[64,65] the description of extension (focal and/or bilateral), localization, involvement (homogeneous and/or dishomogeneous), and gradient of distribution (gravitational and/or irregular) of the B-lines, as well as features of the pleural line (rough/smooth/thickened) are pivotal in their better definition. This topic has been addressed and deeply discussed in the recent review by Soldati and Demi[65]: in particular the differences between the sonographic signs of interstitial syndrome related to lung diseases and that related to cardiogenic edema have been precisely described.

Finally, the authors can speculate that an interobserver variability could be limited by at least two different measurements performed by different Medical Doctors. So the proposed future study could be a milestone in the management of LUS in the setting of HF (in particular regarding the methodology).

To conclude, an integrated clinical and biochemical characterization of the patients should be completed.

Endpoints of the Study

The endpoints related to the ABCDE examination should be summarized as follows:

1) Related to the bedside evaluation of HF recovery:

   - test the association between each item of the ABCDE and the discharge time (days of hospitalization);
   - test the association between B, D (for cava vein) and E assessment and the number of diuretics shifts during hospitalization and recovery from HF;
   - test the association between B, D (for cava vein) and E assessment and natriuretic peptide variations and calculated ratio of arterial oxygen partial pressure to fractional inspired oxygen (PaO2/FiO2 ratio) at admission and discharge;

2) Related to the global cardiovascular assessment of the HF patient:

   - test the association between each item of the ABCDE and the number of "events" (death from any cause or re-admission for HF) in a follow up period (30 and 90 days from discharge);
   - test if A, C, and D (for aorta) assessment can better classify the global cardiovascular risk for the HF patient.

Conclusions

HF represents an exciting opportunity to create an integrative ultrasound approach in the Internal Medicine and/or Geriatric departments. The conception of a five-step ultrasound examination (the ABCDE score) to evaluate and monitor HF patients during hospitalization and follow-up may be the basis of a future study in these departments.

Authors' Contribution

CM, LC, AC, CS and MS conceived the study; CM wrote the manuscript.

Statement of human and animal rights

The study was conducted in accordance with the ethical standards laid down in the Helsinki Declaration of 1975 and its late amendments.

Informed consent

Not applicable (review article).

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