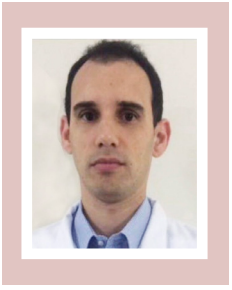
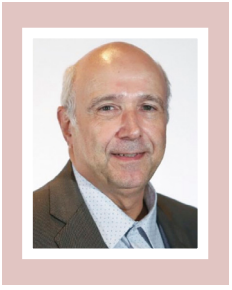
My Approach to Analyze Diastolic Function in Indeterminate Cases by the 2016 American Society of Echocardiography Guideline?

Como Eu Faço Análise da Função Diastólica nos Casos Indeterminados pela Diretriz da American Society of Echocardiography 2016?

[1]Department of Echocardiography, A Beneficência Portuguesa de São Paulo Hospital, São Paulo, SP; [2]Dante Pazzanese Cardiology Institute, São Paulo, SP, Brazil.



Renato Hortegal[1,2]



Henry Abensur[1]

Introduction

The current assessment of diastolic dysfunction has two main tasks: the assessment/categorization of diastolic dysfunction, and the recognition of signs of increased left ventricular filling pressure.[1,2]

The 2016 guideline of the American Society of Echocardiography (ASE) presents some areas of uncertainty regarding diagnosis.[3] There are situations in which two of the following parameters are inconsistent: e' septal and lateral, E/e', indexed volume of the left atrium, and speed of the tricuspid reflux. In these cases, the current algorithm could be insufficient for classifying such patients (indeterminate cases); thus, additional assessment parameters are required.

The following scenarios are not considered in this review: mitral annulus calcification, left bundle branch block, atrial fibrillation, regional wall motion abnormality, significant pulmonary arterial hypertension, left ventricular ejection fraction (LVEF) < 50%, and left ventricular hypertrophy.

Premises of the suggested approach

From a certain point of view, the limitations of the currently available technology seem to dissociate clinically relevant findings from interest accessing the intrinsic properties of the myocardium (e.g. stiffness). Therefore, the current evaluation of indeterminate diastolic dysfunction cases, as well as the entire ASE guideline, is guided by a much more inferential approach than the direct measurement of the diastolic properties of the heart. For this reason, the supplementary assessment should also be addressed according to the clinical context. This study focuses on echocardiographic findings that may explain a particular clinical status presenting with anomalous ventricular filling as the pathophysiological basis. Furthermore, we assumed that: 1) the blood´s hydrostatic pressure plays a major role in the central venous pressure as well as all pressures of the cardiovascular system since it is a communicating vessel system and 2) there is no extrinsic compression over the chambers/vessels.

An increased left ventricular end-diastolic pressure (LVEDP) leads to sequential retrograde pressure transmission from the left ventricle to the left atrium and, from there, to the pulmonary veins until it reaches the pulmonary capillary level. Thus, the target parameters can be systematically organized according to the topography of the liquid/blood column of the cardiovascular system from the highest level, i.e. the pulmonary capillary, to the lowest, the left ventricle.

Pulmonary capillary level

Pulmonary ultrasound: Looking for the "B pattern"

Evidence of hydrostatic violation of the alveolar-capillary barrier, which leads to pulmonary congestion, can be assessed by ultrasonography of this organ through the number and extension of B lines. The International Liaison Committee on Lung Ultrasound document[4] defines B lines as hyperechoic reverberation artifacts that arise from the pleural line (previously described as a comet tail) that extend to the bottom of the screen without fading, and move synchronously with lung sliding. Although the presence of B lines has low specificity, the B pattern of the Blue protocol[5] (combination

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Mailing Address: Renato Hortegal •
R. Maestro Cardim- 769, São Paulo, SP, Brazil. CEP 01323-001
E-mail: eletrocardio2009@gmail.com
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of multiple B lines, regular pleural line, and preserved pleural sliding) may suggest a cardiogenic cause of pulmonary congestion[6] (Figure 1).

The combination of B lines with other clinical and echocardiographic data can optimize the diagnosis. The recognition of a B pattern can be useful as residual evidence of a transient and resolved episode of exercise-induced increased pulmonary capillary pressure or myocardial ischemia, for example.[6]

Pulmonary vein level: accessing the retrograde pressure transmission flow point

The pulmonary venous flow has a three-phase pattern, including the systolic wave, with two components (S1 and S2), a diastolic wave (D), and the atrial reversal wave (Ar) (Figure 2). Understanding the physiology and pathophysiology of each component is crucial to interpreting these signs.

The early systolic component (S1) is caused by decreased atrial

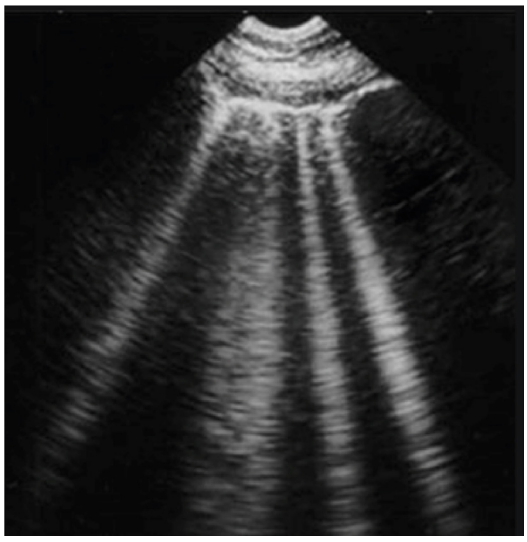
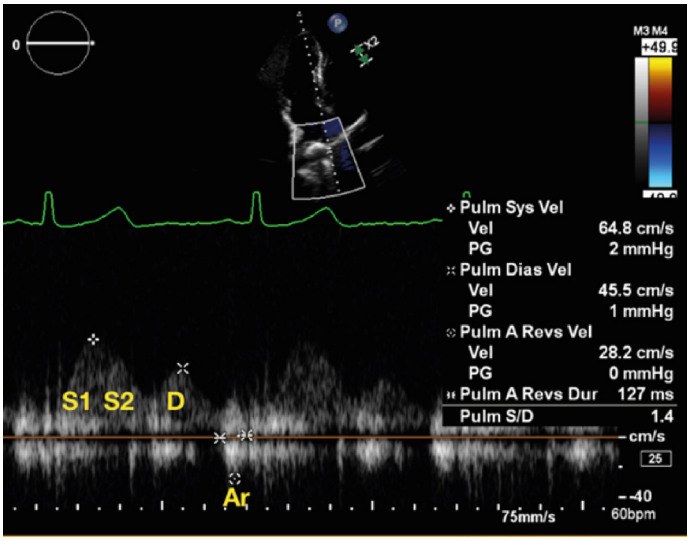


Figure 1 – *B pattern. B lines with a regular pleural line and a preserved lung sliding.*



S1: systolic component 1; S2: systolic component 2; D: diastolic wave; Ar: atrial reversal wave.

Figure 2 – *The three components of pulmonary vein flow.*

pressure, while the middle-late systolic component (S2) is caused mainly by pressure variations in the right ventricle added to the significant contribution of the descent of the atrioventricular ring.[7]

The D wave is equivalent to the mitral E wave and represents the rapid filling phase. Under normal conditions, the S wave is larger than the D wave (Figure 3). The opposite pattern (S < D) suggests grade II or III diastolic dysfunction, excluding other causes like mitral regurgitation, for instance.

The normal Ar wave represents the physiologic flow backward the pulmonary veins during the atrial contraction: during atrial systole, the LA reaches its peak pressure in order to pull volume into a partially filled LV. At this moment, some amount of blood is expelled from LV to pulmonary veins generating a physiologic reversal flow (A reversal wave). This avoids the excessive stress over the LA wall (Figure 3).

Under normal conditions, the atrial reversal flow should not last more than 110–120 ms in addition to being short than the atrial A wave measured at the level of the mitral annulus. The duration of the A reversal wave exceeding the duration of the A wave measured at the level of the mitral annulus suggests diastolic dysfunction with increased LVEDP in the left atrium. A difference ≥ 30 ms indicates a very high LVEDP.

Obviously, the use of this index presumes normal atrial contraction. Therefore, in patients with clinical evidence of stunned atrial myocardium (pos-electric cardioversion, for instance) or an interatrial block(IAB) in ECG (for P-wave duration is ≥ 120ms and the morphology of the P-wave in the inferior leads is biphasic or "positive-negative"- grade 1 IAB), the performance of this parameter might be jeopardized.

Left atrium level

Left atrium strain: Rational use of the reservoir phase

The left atrium function is divided into three phases: reservoir, conduit, and contraction. It is possible to access the deformation curves of each phase using the speckle tracking technique (Figure 4).

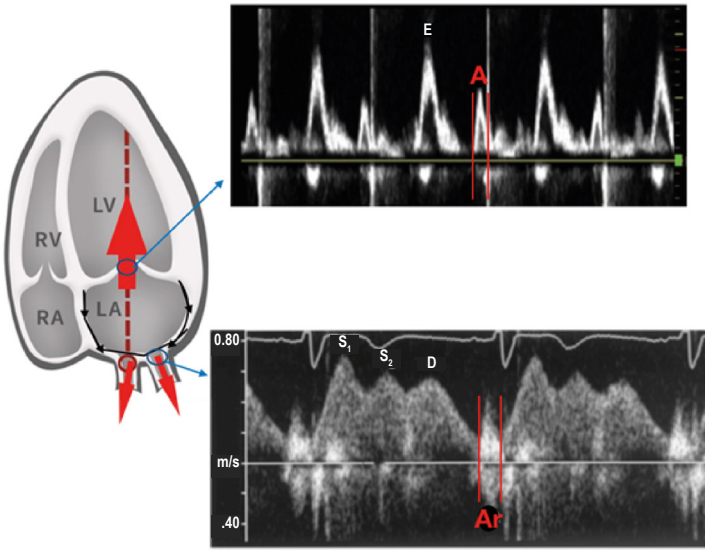
A recent consensus of the European Association of Cardiovascular Imaging (EACVI)/ASE/Industry Task Force[8] provides specific information on all technical requirements to measure the left atrial strain.

In the past 10 years, a solid evidence base has been built showing the clinical utility of left atrial deformation curves.[8] However, current evidence supports use of the reservoir phase only.

Before using left atrium strain to study diastolic function, it is crucial to reinforce that atrial deformation reflects not only its intrinsic properties (e.g. stiffness), but rather it merges to these data components from the LV GLS, MAPSE, LV and LA volumes.

In fact, Barbier et al.[9] revealed that there are two reservoir phases: an early one, which reflects the relaxation that occurs after atrial contraction; and a late one, which reflects the descent of the heart base and the stiffness of the left atrial chamber.

Singh et al.[10] described the behavior of the reservoir phase at different diastolic dysfunction levels. From this study it is possible to have some clues about the level of



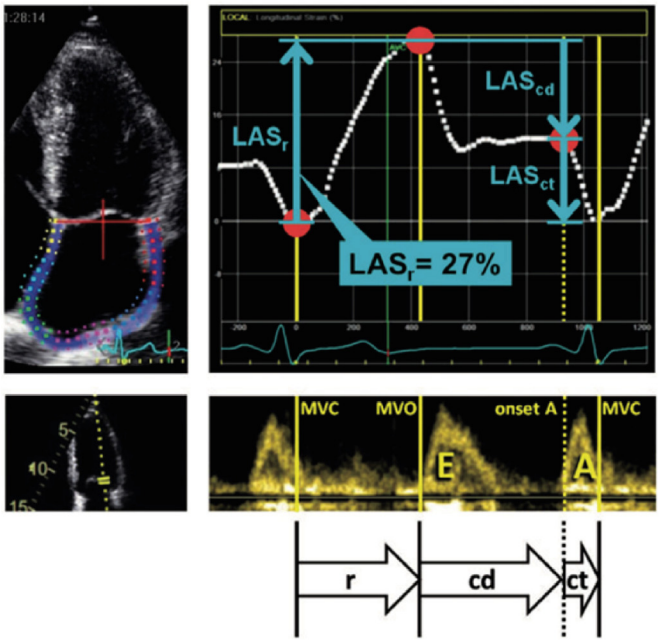
A, atrial wave; Ar, atrial reversal wave; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

Figure 3 – *Assessment of A and aR waves durations for the inference of left ventricular filling pressures.*

diastolic dysfunctions according to LA strain value (Figure 5).

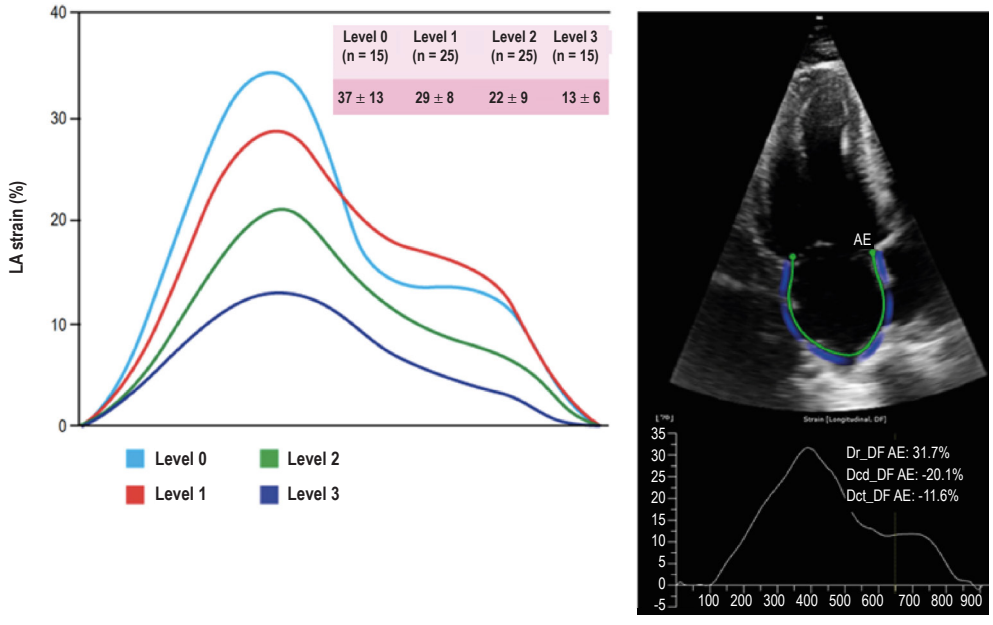
Lundberg et al.[11] showed that the left atrial strain better estimated left ventricular filling pressure than the current ASE/EACVI algorithm (Figure 6).

The proposed cutoff value for the atrial reservoir phase (LAr) strain (<20%) was based on studies using invasive measures in which the left atrium strain showed superior performance compared to the current ASE algorithm.[11]



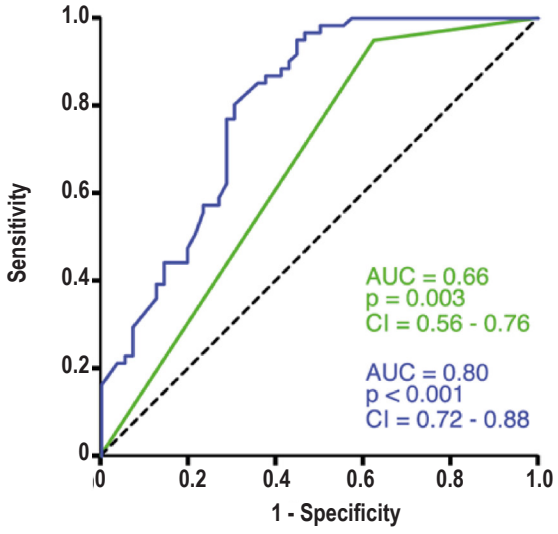
LASr, left atrium reservoir; LAScd, left atrium conduit; LASct, left atrium contraction; MVC, mitral valve closing; MVO, mitral valve opening.

Figure 4 – *Left atrial strain phases (reservoir, conduit, and contraction) according to the European Association of Cardiovascular Imaging/American Society of Echocardiography/Industry Task Force.*



Source: Adapted from Singh et al.[11]

Figure 5 – *Categorization of diastolic dysfunction using left atrium strain. (B) Example of grade I diastolic dysfunction.*



Source: Adapted from Lundberg et al.[11]. AUC, area under the curve; CI, confidence interval

Figure 6 – *Comparison of left artery strain and American Society of Echocardiography algorithm for predicting left ventricular filling pressures. The green ROC curve represents the ASE 2016 guideline,while the blue ROC curve represents the left atrium reservoir phase.*

Mitral valve level

Doppler transmitral input flow: Searching the L wave and exploring the input flow pattern under different load conditions

The presence of a mid-diastolic mitral flow (L wave) with velocity > 20 cm/s suggests abnormal active relaxation with increased filling pressures, although a small L wave with velocity < 20 cm/s may occur in normal bradycardic hearts (Figure 7).

On the other hand, the use of provocative maneuvers to change load conditions can unmask abnormal states in several situations in clinical cardiological practice.

The behavior of the mitral Doppler pattern when exposed to these variations provides valuable information on how the left chambers fill. Keeping the Valsalva maneuver effective for 10 s reduces the preload. The expected physiological response is a concordant decrease in the E and A waves, with a decreased E/A ratio < 50% (Figure 8A).

The pathological response is the discordant movement, with decreased E wave and increased A wave, together with an overall decreased E/A ratio > 50%. This behavior has high specificity for diastolic dysfunction, with increased filling pressures (Figure 8B). However, E/A ratio changes below 50% do not necessarily indicate normal diastolic function.

The same rationale suggests that the opposite effect should be expected with maneuvers that increase the preload, such as passive leg raise for 3 min at 45°. This can be useful for patients with E/A < 1 who do not meet all of the criteria for diastolic dysfunction. However, it does not replace the diastolic stress test when indicated.

Mitral ring level

Protodiastolic tissue Doppler imaging mitral annular velocities

Reporting the septal and lateral protodiastolic velocities of the mitral annulus in echocardiographic reports provides valuable information to cardiologists: values of <7 cm/s (septal) and <10 cm/s (lateral) suggest diastolic dysfunction, although reduced preload states can produce false-negative results.

Additionally, e', a', and s' velocities ≤ 5 cm/s are highly suggestive of myocardial disease (triple five sign).

Left ventricle level

GLS of the left ventricle: Combining the myocardial involvement degree and the hemodynamic evaluation

Throughout the cardiovascular system, the pressure within the different chambers is related to the two main factors: resistance and flow/volume. Thus, for a given scenario of increased LV filling pressures and preserved LVEF, we may have a restrictive cardiomyopathy (cardiac amyloidosis, for instance) as basic cause, but also a fluid overload condition (such as seen in acute renal failure) that produces a similar hemodynamic profile. Additionally, a mosaic of possibilities can be imagined between these two extreme conditions with different degrees of myocardial involvement. The assessment of how much myocardial involvement explains the hemodynamic profile is as important as or even more important than the characterization of left ventricular filling pressures.[12-14]

Recent data suggest that left ventricular deformation

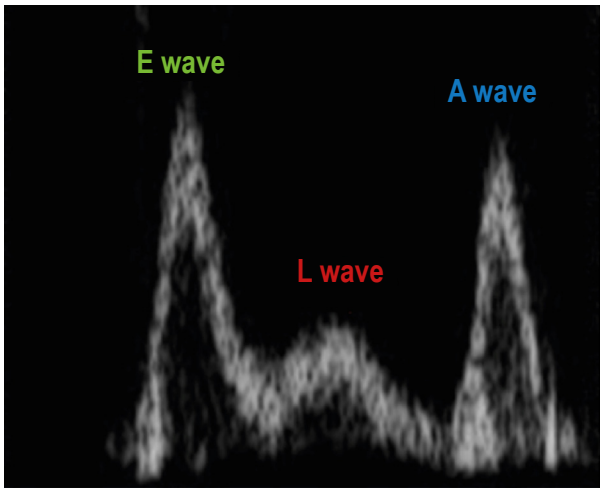


Figure 7 – *Pathological L wave.*

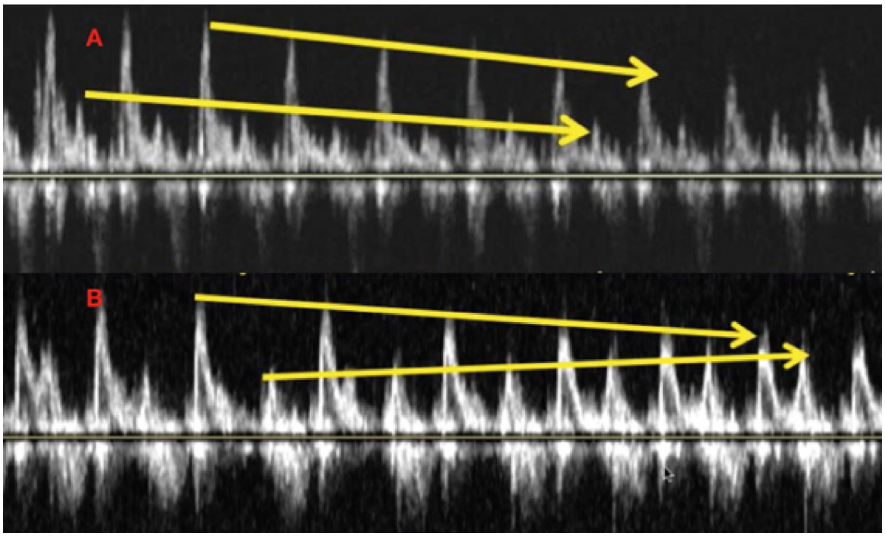


Figure 8 – *Strain phase of the Valsalva maneuver (10 s). (A) Physiological response; (B) Pathological response.*

accessed by speckle tracking may be useful for this purpose. This rationale was recently presented in an excellent article written by Shah et al.[15] For this reason, this proposed approach involves combining left ventricular global longitudinal strain (GLS) (how much myocardial involvement?) with other parameters that assess the aforementioned cardiovascular hemodynamics (are there signs of increased filling pressures?). Figure 9 summarizes these proposed parameters.

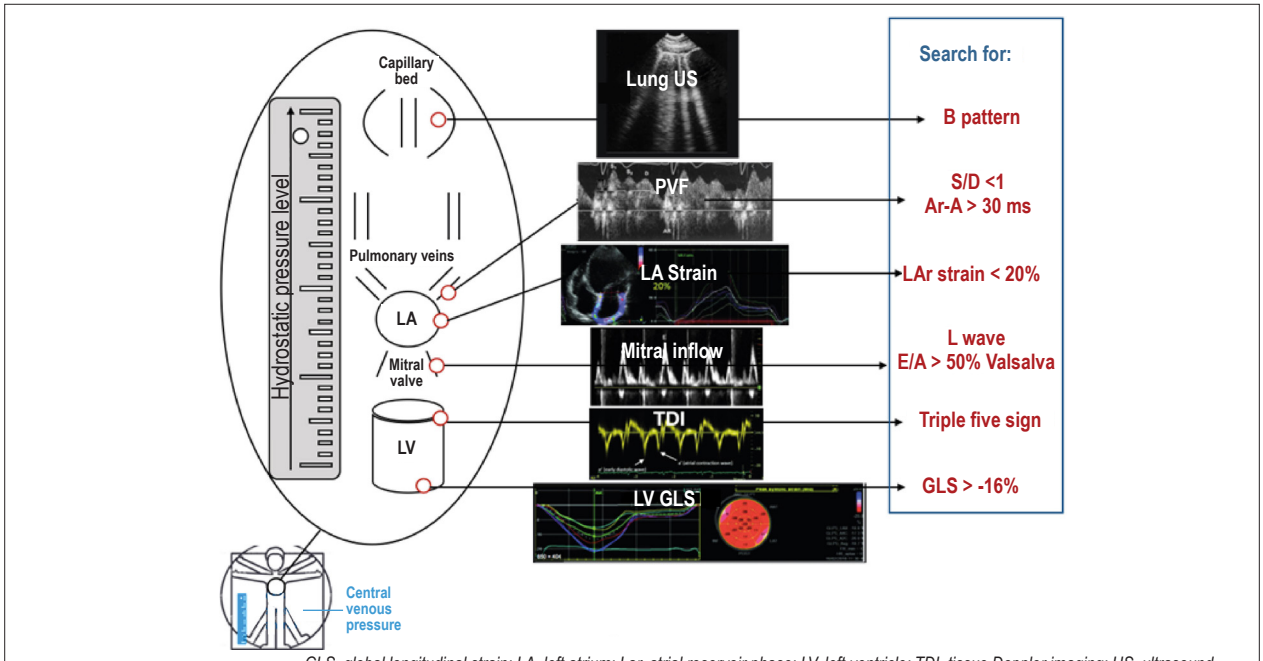
Limitations

The proposed assessment has many limitations and should be used only with initial support to organize all available parameters. Some pathophysiological scenarios, such as those related to anomalous ventricular–arterial coupling and right ventricular dysfunction, may not be assessed using this approach.

Finally, it can be predicted that more complex analyses will be possible in the near future guided by machine learning tools that process large numbers of variables and select the most relevant ones for each patient in an augmented intelligence scenario.

Conflict of interest

The authors have declared that they have no conflict of interest.



GLS, global longitudinal strain; LA, left atrium; Lar, atrial reservoir phase; LV, left ventricle; TDI, tissue Doppler imaging; US, ultrasound.

Figure 9 – *Topographic configuration of access parameters for diastolic dysfunction cases not determined in the 2016 American Society of Echocardiography criteria.*

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