

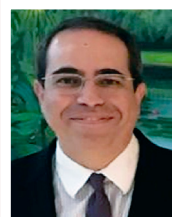
What Does the Cardiologist Expect from the Echocardiogram in Amyloidosis?

O que o Cardiologista Espera do Ecocardiograma na Amiloidose?

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Cardiac amyloidosis (CA), a disease considered rare, is actually underdiagnosed. Lousada et al. reported that more than half of the CA patients included in their study were diagnosed only six months after the onset of symptoms. They observed that these patients had previously been evaluated by more than three physicians of different specialties and that the first symptoms were still observed at the primary care level.¹ CA is commonly manifested as congestive heart failure, resulting in the request for an echocardiogram even before cardiac consultation. Here, the echocardiographer has an excellent opportunity to highlight this possible diagnosis² and the first step is to express a high degree of suspicion.

Electrocardiographic changes are practically the rule in more advanced cases of CA, in which an abundant amyloid fibril deposition in the myocardium causes disorders of the cardiac conduction system. The prevalence of atrial fibrillation (AF) in CA patients is approximately 36%, and that of atrioventricular block (AVB) is 25%.³ Such electrical changes are apparently irrelevant to the echocardiographer at first glance. However, when using two-dimensional speckle tracking echocardiography (2D-STE), diastolic function impairment and strain evaluation (which may result in an evasive report lacking diastolic classification and relative apical sparing) may be overlooked.

Approximately 50% of the patients clinically diagnosed with heart failure (HF) show a preserved or slightly reduced left ventricular ejection fraction (LVEF). CA should be considered a differential diagnosis in patients whose echocardiogram

scans reveal preserved ejection fraction HF and ventricular hypertrophy. Diastolic function is indirectly evaluated on echocardiography, by integrating the hemodynamic and structural variables (Figure 1). To assess the grade of diastolic dysfunction (grades I, II, and III or restrictive), the ratio between the peak velocities of the diastolic transmitral flow, i.e., the ratio between the E (corresponding to the rapid and passive filling after the mitral valve cusps open in early diastole) and A (corresponding to the peak velocity flow generated by atrial contraction in late diastole) waves must be analyzed.^{4,5}

These recommendations aim to establish consistency between the various parameters available when determining the presence or absence of elevated pressure in the left atrium of a patient in sinus rhythm and with an E/A wave ratio that can be analyzed.⁶

In the presence of AF and cardiac conduction blocks (first-degree AVB or left/right bundle branch block), an absence of the A wave secondary to the absence of atrial contraction and E- and A-wave fusion, occurs in these blocks (Figure 2). In practice, these are omitted in reports in which the diastolic function evaluation is limited to "Diastolic function analysis was not possible" or "Undetermined diastolic function". This lack of information is often misinterpreted by non-specialists as the absence of diastolic dysfunction, thereby impairing clinical reasoning and further delaying the correct diagnosis of a disease in which time is essential.

When the E/A is impaired and the diastolic function cannot be assessed, the echocardiographer should search for parameters applicable to this situation, and should attempt to provide as much clarity and explanation as possible (Box 1). The following sentences should be used to conclude the report: "The grade of diastolic function could not be classified; however, signs of diastolic dysfunction are observed" and "Signs of elevated left ventricular filling pressure and/or left atrial pressure are observed".

2D-STE is an essential tool in the diagnostic arsenal of restrictive cardiomyopathies. For example, the ratio between the LVEF value and the left ventricular global longitudinal strain (LVGLS) is the most accurate parameter in discriminating

Keywords

Diastole; Strain; Early diagnosis.

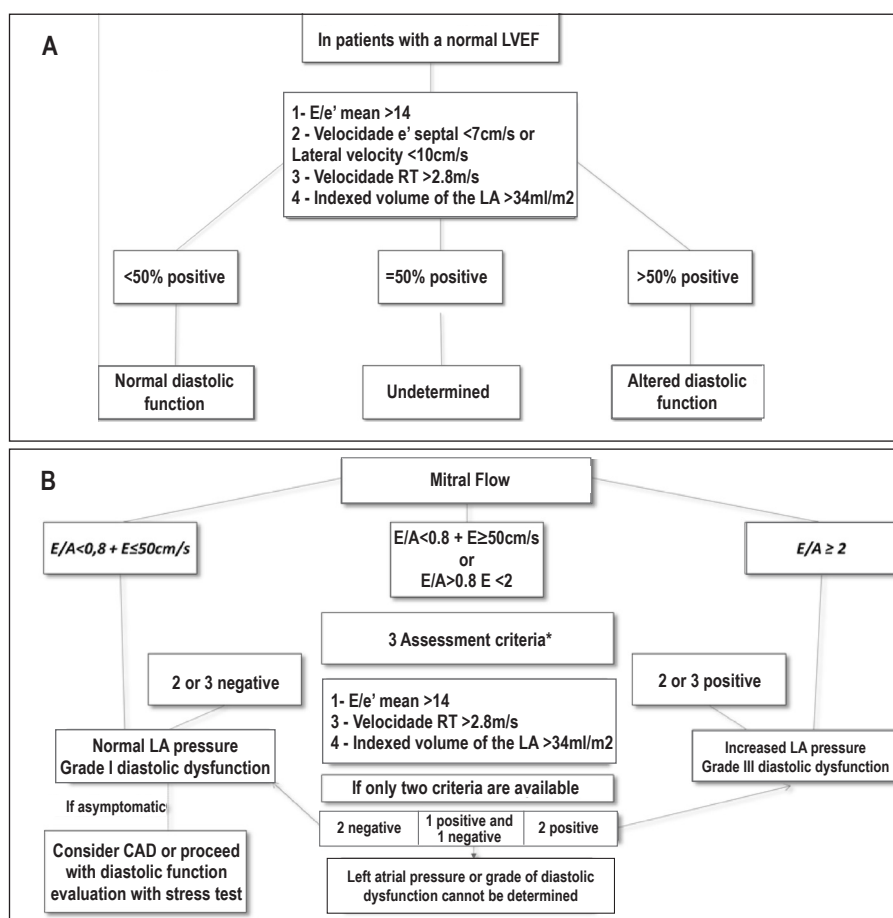
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*: LA pressure is undetermined if only one parameter is available. If the S/D wave ratio < 1 is equal to elevated LA pressure in reduced LVEF. LVEF: Left ventricular ejection fraction; LA: left atrium; CAD: coronary artery disease.

Figure 1 – Diagnostic approach to left ventricular diastolic function according to the American Society of Echocardiography (ASE) and the European Association of Cardiovascular Imaging (EACVI). (A) Algorithm for preserved left ventricular systolic function. (B) Algorithm for reduced left ventricular systolic function.

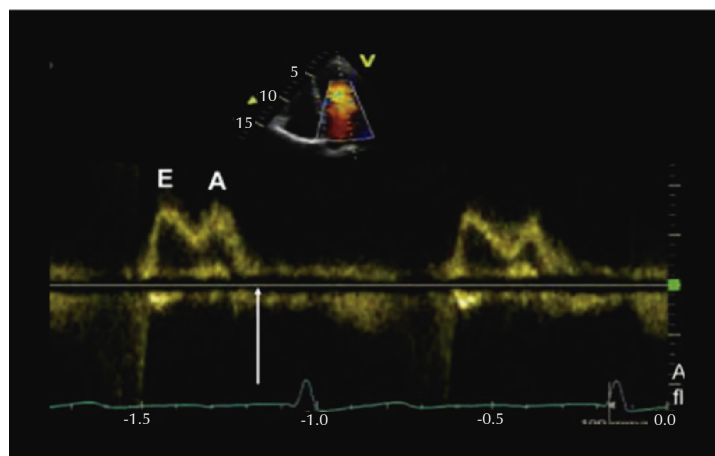


Figure 2 – Mitral flow in a patient with first-degree atrioventricular block showing E- and A-wave fusion and a shortened diastole (A wave ends before the end of the diastolic period).

amyloidosis from other causes of ventricular hypertrophy. Furthermore, the representation of the deformation of the 16 segments in a parametric graph, known as the Bull's eye plot or the polar map, highlights its key role in diagnostic investigation. Currently, the well-known apical preservation pattern (Figure 3), also known as apical sparing or "cherry on top", is one of the findings eagerly awaited by cardiologists to add data to their diagnostic reasoning. Strain evaluation by 2D-STE has an additional value, further increasing the suspicion of diagnosis in cases located in the gray area of the hypertrophic phenotype, i.e., when the interventricular septum is less than 16 mm and/or the LVEF is preserved.^{5,7}

Box 1. Red flags indicating cardiac amyloidosis.

HF with a preserved ejection fraction and without hypertension
Low-flow, low-gradient aortic stenosis
Bilateral carpal tunnel syndrome
Lumbar canal stenosis
Atraumatic biceps tendon rupture
Late-onset hypertrophic cardiomyopathy
Intolerance to standard therapy for HF (ACEI/ARB and beta blockers)
Low voltage or low voltage/hypertrophy ratio on electrocardiogram
Mild and persistent elevations of troponin without angina
Ventricular hypertrophy without etiology
Late MRI enhancement
Apical sparing on echocardiogram

HF: heart failure; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; MRI: magnetic resonance imaging.

As a final recommendation, despite the echocardiographers' hurried pace of life and limited time for each examination, if this diagnostic hypothesis is feasible, they should remember that in most cases, the patient is able to communicate and answer some questions. Before we are echocardiographers, we are all cardiologists; therefore, we should investigate the presence of the alarming signs of amyloidosis, i.e., the red flags. For example, if the patient reports a history of surgery for bilateral carpal tunnel syndrome, we would be closer to diagnosis because this information is an important diagnostic clue in this clinical context.

CA is increasingly becoming uncharacterized as a rare cause of HF. In parallel with the development of new and promising treatments, recent scientific advances have dramatically altered the diagnostic scenario, providing a variety of methods that offer a highly efficient and detailed characterization of cardiomyopathy. Due to this progress, early recognition of CA is critical because these new therapies have the potential of altering the course of a disease, which until recently, had little or no treatment.

An affirmation by the eighth United States Secretary of Defense, Robert S. McNamara (1916–2009), is relevant to the context of CA: "*Belief and seeing are both often wrong (...), we see what we want to believe*". In other words, to see the signs of CA during an echocardiogram, we must first believe that it is a possibility.

Conflict of interests

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

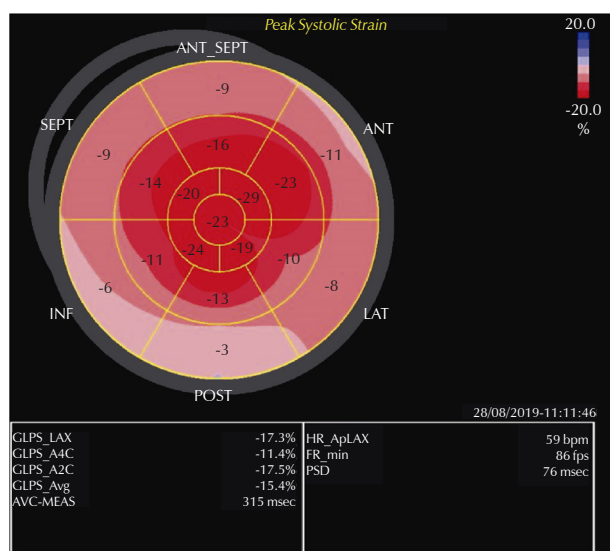


Figure 3 – Typical pattern of apical sparing in the 2D-STE polar map. The reddest segments with the highest modulus values are the segments with the highest longitudinal deformation.

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