Comprehensive Echocardiogram: What is it? For which Patients?

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Amyloidosis occurs due to the gradual deposition of protein aggregates, which may infiltrate more than one organ, progressively evolving to organ dysfunction. Prognosis is determined by the organ involved and by the involvement of the heart; cardiac amyloidosis (CA) leads to the worst evolution. CA may be due to myocardial deposition of the protein transthyretin, which is derived from liver tissue; this condition is known as ATTR. The other form of myocardial deposition is secondary to immunoglobulin light chain proteins, which are derived from a clone of plasma cells; this is known as the systemic form or AL amyloidosis.¹ The ATTR and AL forms need to be differentiated, because they have different treatments.

CA is a common cause of restrictive cardiomyopathy, and it should always be considered in the context of patients with heart failure with preserved ejection fraction (HFpEF). Symptoms encompass reduced effort threshold, fatigue, and edema of the lower limbs. It is common for the conduction system to be involved, and reduced voltage of the QRS complex on electrocardiogram (ECG) is one of the diagnostic clues. Evolution with arrhythmias and atrioventricular block is also characteristic.²⁻⁴

The gold standard for diagnosis of CA is myocardial biopsy. This procedure, however, in addition to being invasive, can be inaccurate if we remove a fragment of tissue that is not affected by the disease. With the evolution of imaging methods, we are currently moving towards a non-invasive diagnostic algorithm. The use of nuclear medicine with pyrophosphate scintigraphy, combined with hematological tests for light chain immunoglobulins, makes it possible not only to diagnose but also, in many cases, to differentiate between the ATTR and AL forms.⁵ This algorithm is initiated following clinical suspicion, combining ECG with an imaging method, such as echocardiogram or magnetic resonance imaging.

And where does the importance of comprehensive echocardiogram come from? Due to the peculiar characteristics provided by each of the imaging methods in relation to the pathogenesis of CA, most patients will need more than one method for complete evaluation. Due to its wide availability and low cost, echocardiogram is usually the first diagnostic

tool in patients with clinical suspicion of heart failure, and it should always be performed in the investigation of CA.⁶ The initial alteration that should draw the attention of the echocardiographer is increased left ventricular (LV) wall thickness, usually above 12 mm. This finding, especially when it is associated with left atrial enlargement (or even biatrial enlargement) and preserved systolic function, raises the possibility of CA. Other associated findings that may be present include thickening of the atrioventricular valves and functional regurgitation (mitral and tricuspid valves without organic alterations). We may detect elevated pulmonary artery systolic pressure (a common finding in patients with HFpEF), and infiltration of the interatrial septum is also a very suggestive sign. The presence of pleural and/or pericardial effusion is very common. Although it is subjective in appearance, we can observe an image of granular infiltration of the ventricular walls (granular sparkling). The right ventricle may also be involved. These findings can be observed in Figure 1.

Nevertheless, typical alterations are more evident in the advanced stage of the disease, and they may go unnoticed at earlier stages, even when the patient is already in heart failure. Thus, a high degree of suspicion is necessary. It is through detailed study of diastole that we will be able to add information to our initial suspicion. As this is a muscular infiltration, reduced early diastolic filling velocities, detected by tissue Doppler (e' velocities in the septal and lateral mitral annulus), are very common. As the condition worsens, we will observe progressive diastolic dysfunction, with reduced atrial compliance and increased mean pressure of the left atrium. We will go from grade I diastolic dysfunction to a pseudonormal pattern and, subsequently, a restrictive pattern (e/a ratio > 2 on pulse Doppler and increased e/e' ratio), as exemplified in Figures 2 and 3.

CA is an example of a restrictive heart disease where LV ejection fraction may remain unchanged until the more advanced stages of the disease, but longitudinal contractile function is reduced in an early manner.⁷ With examination of myocardial deformation, known as global strain, we have yet another tool that can be explored via echocardiogram. In particular, LV longitudinal global strain is significantly altered in CA, in an early manner, before the drop in ejection fraction.⁸⁻¹⁰ Although it is a non-specific pattern, more than reduced global strain, the apical sparing pattern (colloquially known as “cherry on the cake,” visualized as a bull’s eye) is a characteristic that can be present in CA, as exemplified in Figure 4.

It is worth remembering other pathologies with which CA may be associated. A very common scenario, especially with greater population longevity, is the detection of aortic stenosis. LV hypertrophy secondary to valve restriction is very common, but valve stenosis is not always the only diagnosis. The association of these two pathologies, aortic stenosis and amyloidosis, has been described in

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Viewpoint

Figure 1 – Subcostal window. Important thickening of the left ventricular and right ventricular walls, the interatrial septum, and the mitral and tricuspid valves. Granular aspect of the left ventricular walls (granular sparkling). LA: left atrium; LV: left ventricle; RA: right atrium; RV: right ventricle. Source: personal archive.

Figure 2 – Mitral flow on pulse Doppler with e wave velocity = 1.33 m/s, low atrial contribution (a wave = 0.31 m/s), reduced acceleration time (115 ms), and e/a ratio = 4.29, denoting a restrictive pattern. Source: personal archive.

up to 13% of patients referred to the hemodynamic laboratory for percutaneous implantation of aortic prostheses.¹¹ Low-gradient aortic stenosis may be a form of presentation, with LV ejection fraction > 50%, indexed systolic volume < 35 ml/m², peak systolic velocity < 4 m/s, and mean LV-Ao gradient < 40 mmHg.

Amyloid deposits may also coexist among hypertrophic cardiomyopathies or even hypertensive

cardiomyopathies. In these cases, longitudinal global strain may be the only echocardiographic marker that is altered.¹² Only by conducting detailed examination, with the echocardiographer considering the possibility of amyloidosis, will we proceed with the appropriate diagnostic investigation.

In summary, CA is frequently underdiagnosed, and the echocardiographer's role is fundamental. More than

Figure 3 – Important reduction in e' wave velocity of the septal mitral annulus (0.04 m/s); e/e' ratio = 33.2 (1.33 m/s divided by 0.04 m/s), denoting a large increase in the mean pressure of the left atrium.
Source: personal archive.

Figure 4 – Important reduction in left ventricular global longitudinal strain (−11.1%), sparing the apical segments, which appear in red. Apical sparing, resembling a “cherry on the cake,” is demonstrated by the bull’s eye.
Source: personal archive.

using the name “comprehensive” echocardiogram, it is necessary to establish an examination routine, using all the tools that are available today. Think of all the situations in our daily routine where we find ventricular thickness > 12 mm! They are countless! It is through a good echocardiogram, combined with good interaction with the clinician, that suspicion will be more sharpened. The diagnostic algorithm will only be implemented if we raise the hypothesis. There is no point in using the exams in an isolated manner, given that the diagnostic sequence is only valid when used correctly.

Author contributions

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