My Approach to the Echocardiographic Assessment of Anderson-Fabry Disease

Como Eu Faço Avaliação Ecocardiográfica da Doença de Fabry

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Echocardiographic assessment of anderson-fabry disease

Anderson-Fabry disease (AFD) is a rare lysosomal inborn metabolism error due to changes to the long arm of the X chromosome that result in deficiencies of the alpha-galactosidase enzyme, which is responsible for metabolizing glycosphingolipids. Systemic presentations result from the accumulation of these substances in the cells of organs such as the heart, central and peripheral nervous system, kidneys, eyes, skin, and others. This heart disease, which resembles a sarcomeric hypertrophic cardiomyopathy phenocopy, is a main cause of mortality due to heart failure, arrhythmia, and/or myocardial ischemia in this population in Brazil. The natural disease progression can be changed by an accurate and early diagnosis and the availability of specific intravenous enzyme replacement or oral chaperone therapy, thereby increasing quality of life and life expectancy. Thus, echocardiography plays an essential role as a diagnostic and risk stratification tool in the assessment of therapeutic efficacy and the investigation of cardiac complications.

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A quick anamnesis and precordium auscultation can aid the echocardiographic investigation prior to the test. A detailed history is not always possible, but complaints of intolerance to exertion, chest pain, and palpitations in a young person with no known pathologies should be highlighted. Adolescents and young adults with a history of physical exercise problems in childhood, hypohidrosis, neuropathic pain in the extremities, and/or the presence of reddish nodular lesions on the mucous membranes or in a swimsuit distribution pattern (angiokeratomas) may indicate carriers of the classic form of the disease. Some patients report a family history of AFD and heart disease, chronic kidney disease, and/or cerebral ischemia at an early age; these data are valuable. If an electrocardiogram is available, the presence of ventricular overload signs associated with a short PR interval, arrhythmias, and/or a QTc < 440 ms may help confirm the suspected diagnosis.

The flagship of AFD cardiomyopathy on conventional two-dimensional echocardiography is the presence of hypertrophy. However, it may not be present in the early stages of the disease or might assume unusual aspects. The increased wall thickness is typically concentric, and values greater than 11 mm in women and 12 mm in men are considered pathological by the main international guidelines. Such measures are valid for phenocopy situations and would not work for true hypertrophies such as those in sarcomeric heart diseases, whose values are considered diagnostic if greater than 15 mm in index cases and greater than 13 mm in family screening situations. Isolated asymmetric and apical forms are also described; in all cases, left ventricular (LV) outflow tract obstruction is not usually present. More severe cases of hypertrophy are observed concomitantly with chronic renal failure or other outflow tract obstructions, such as rheumatic disease. The right ventricle may be affected by deposits and present 50–70% increased parietal thickness, usually associated with LV hypertrophy.

Papillary muscle hypertrophy is visible even in the first ultrasound sections, but it is not a determinant of the onset of significant intraventricular gradients or severe valvular dysfunction. The latter is often discrete to moderate, and it usually does not progress to severe forms that require correction.

The binary sign, histological correspondent of glycosphingolipid deposits in the endocardium, is visible on two-dimensional images but not currently considered a pathognomonic finding of the disease. It is present in 20–30% of cases, being usually associated with increased ventricular thickness.

The presence of diastolic function changes is usually the earliest AFD cardiomyopathy finding. Cases of patients younger than 40 years of age without underlying diseases such as renal disorders, systemic arterial hypertension, or heart valve disease and presenting decreased tissue Doppler mitral annulus propagation velocities or transmitial flow should be highlighted even if the ventricle is not hypertrophic. Left atrial dilatation indicates advanced disease and is usually present in the final stages of the heart disease progression. This is also true for the development of diastolic dysfunction above grade II and for patterns with restrictive physiology.

Systolic function, on the other hand, remains normal over most of the disease course unless other comorbidities such as coronary artery disease, kidney disease, or uncontrolled...
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Figure 1 – Longitudinal parasternal image of the left ventricle showing increased wall thickness, a granulated myocardium (suggestive of deposit disease), increased mitral and aortic valve thickness, and increased endocardial refringence (binary sign).

Figure 2 – Five-chamber apical image of the left ventricle demonstrating increased papillary muscle thickness.

Figure 3 – Doppler images of the left ventricle of a patient with advanced fabry cardiomyopathy. A. transmitral flow pulsed wave doppler showing an increased e/a ratio. B. mitral ring tissue doppler in the septal position with a decreased propagation velocity and increased e/e’ ratio. both changes are compatible with a left ventricle diastolic dysfunction pattern.
hypothesis is very rare and usually associated with other pathologies. The progression to aneurysmal forms requiring specific treatment is determined by the deposits. However, the progression to aneurysmal forms requiring specific treatment is very rare and usually associated with other pathologies.  

The author declares no conflicts of interest.

**References**


