The Role of Cardiac Magnetic Resonance in patients with Amyloidosis and Aortic Stenosis

O Papel da Ressonância Magnética Cardíaca em Pacientes com Amiloidose e Estenose Aórtica

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Abstract

Cardiac magnetic resonance imaging (CMR) plays an important role in the diagnosis and prognosis of various heart diseases. The incidence of cardiac amyloidosis and aortic stenosis has been increasing in recent years, especially with the aging population, and their possible coexistence has created frequent diagnostic challenges in clinical practice. CMR assumes an important value in this context due to its unique capacity for multiparametric assessment evaluations that include anatomical, functional, and histopathological aspects. The present review aimed to increase our knowledge of the diagnosis and prognosis of amyloidosis in the presence of aortic stenosis and highlighted the importance of CMR in this scenario.

Introduction

The coexistence of cardiac amyloidosis (CA) and aortic stenosis (AS) has increasing relevance in clinical practice due to its high prevalence, diagnostic difficulty, and therapeutic management challenges. Primary CA forms feature amyloid light chain amyloidosis (AL) and transthyretin amyloidosis (ATTR) as the main presentations affecting up to 25% of octogenarians,1 especially the latter. On the other hand, AS has a prevalence of up to 4% among individuals over 70 years,2 with calcific degeneration as its main etiological landmark. CA affects an estimated 5–16% of patients with major AS, reaching 30% in cases of low-flow low-gradient AS.2

The correlation between the two diseases can be explained by several factors, with the common prevalent age group being the most important. The second factor is related to the histological analysis of valves removed in valve replacement surgeries, demonstrating amyloid deposits in 74% of stenotic aortic valves, involving the possibility of AS and CA having a similar pathophysiological pathway.1 Another possible factor is mediated by increased AS afterload, which would potentially trigger amyloid protein accumulation in the ventricular myocardium.4

Keywords

Magnetic resonance imaging; Heart; Amyloidosis; Aortic valve stenosis.

CMRI diagnosis

Cardiac adaptations to increased afterload by AS are similar to those that occur in CA (e.g., concentric left ventricle remodeling). In addition, the presence of other diseases, such as coronary insufficiency and systemic arterial hypertension, interferes with the accuracy of several methods in the diagnosis of AS-associated CA. In this context, CMRI performs well (sensitivity, 85%; specificity, 92%) for diagnosing CA.8 Due to its multiparameter analysis, it is also fundamental in the diagnosis of AS-associated CA (Figure 2) or AS alone.
Anatomical functional parameters

Left ventricular (LV) myocardial mass thickening and increases, atrial dilatation, and LV diastolic and systolic dysfunction are common in ATTR and AS but more severe when coexistent.

Patients with ATTR + AS versus AS alone have a higher LV mass index (105 ± 21 vs. 73 ± 21 g/m²) as well as a lower LV ejection fraction and stroke volume (43 ± 17 vs. 52 ± 18% and 33 ± 10 vs. 44 ± 13 mL/m², respectively). Myocardial thickening tends to be septally asymmetrical in the presence of ATTR, with a prevalence of 79%, versus concentrically thickened in AL.

Characteristics that are common in CA but uncommon in
AS are pericardial effusion, interatrial septal thickening, biatrial dilatation (Figure 3), atrioventricular valve thickening, and RV thickening (with or without isolated systolic RV dysfunction). Atrial wall thickening occurs in up to 70% of patients with ATTR + AS.

**Histological parameters**

Noninvasive myocardial histological analysis by CMRI is based on the proton relaxation properties of each tissue used to identify the presence of localized or diffuse fibrosis. Different techniques (late enhancement, native myocardial T1 mapping, myocardial extracellular space volume calculations, myocardial-blood inversion time rate analysis, and myocardial edema investigation) can be used for cardiac tissue characterizations with quantitative measurements that assess the extent of damaged induced by amyloid substance deposits.

**Native myocardial T1 mapping**

Native myocardial T1 mapping, which analyzes the magnetic characteristic of tissue proton relaxation, is performed without a gadolinium injection. Its primary advantage involves the early identification of myocardial fibrosis, especially that with diffuse distribution, which may not be identified by late enhancement, making the diagnostic evaluation more sensitive. Normal myocardial T1 values may vary according to the machine used and are usually between 950 and 1,050 ms. Patients with isolated CA, CA + AS, or isolated AS may present with a prolonged T1, being significantly higher in patients with CA. Patients with ATTR + AS have higher native T1 values than those with isolated AS (native T1: 1,125 ± 49 vs. 1,035 ± 60 ms; p = 0.002).

**Myocardial edema research**

Myocardial edema may be present in CA but is uncommon in isolated AS. It is diagnosed through T2 time mapping or specific T2-weighted sequences without the need for a gadolinium injection. The presence of myocardial edema with AS should prompt the investigation of other concomitant heart diseases.

**Late myocardial enhancement**

Late enhancement, which is based on preferential gadolinium uptake in tissues rich in extracellular matrix, aids in the contrast of healthy and pathological myocardium minutes after its administration. The enhancement pattern changes according to etiology. In ATTR, there is a basal-apical enhancement distribution that can spare the apical segments (Figure 4). AL has its own characteristics with circumferential subendocardial involvement. The presence of late enhancement in the atrial myocardium (Figure 5) or the RV is frequent in CA, with a prevalence of atrial enhancement of up to 90% and of RV enhancement of 37–97% of ATTR + AS cases. Late enhancement occurs in up to 40% of isolated AS cases, being mainly present in the LV with a focal mesocardial pattern.

Extracellular volume (ECV) analysis is estimated based on native myocardial T1 time, post-contrast T1 time, and patient hematocrit at the time of the examination (normal ECV values are <25 to 27%). Both CA and AS can increase myocardial ECV, but greater increases are seen in the presence of CA, particularly the ATTR type. Patients with ATTR + AS have higher ECV values than those with isolated AS (41.2 ± 16.7 vs. 27.9 ± 4.1%; p < 0.001). ECV values > 40% are rare in diseases other than CA. In advanced CA stages, ECV can be more important for the diagnosis than T1 mapping.

**Prognosis by CMRI**

Patients with CA + AS lack formal therapeutic recommendations regarding the approach to AS, which makes its treatment challenging. A prognostic evaluation before valve replacement is essential, and CMRI can aid the decision, especially through late enhancement analysis and

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**Figure 3** – Cine-resonance image taken of a patient with ATTR amyloidosis showing biatrial dilatation, increased myocardial thickness, and a mild pericardial effusion.

Source: collection Dr. Pedro Macedo. ATTR, transthyretin amyloidosis; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.
ECV. Late enhancement is a poor independent prognostic factor for all heart diseases. Moderate to severe AS carries an eight-fold increased risk of mortality regardless of stenosis severity. An increased relative risk of major cardiovascular events after aortic valve replacement in the presence of late enhancement has also been documented, as has the possibility of left ventricular dysfunction maintenance post-aortic valve replacement in the presence of late enhancement.\(^{10}\)

ECV has excellent prognostic value in patients with ATTR + AS since it is correlated with mortality (Figure 6). An ECV < 25% is protective regardless of exclusive clinical treatment or valve replacement, with no reports of cardiovascular death within 1 year.\(^1\) Increased native myocardial T1 mapping interpreted in isolation showed only a tendency to be correlated with prognosis in patients with ATTR + AS, but the difference was not statistically significant (Figure 6).\(^1\) Further studies with a greater number of patients may provide additional information about the use of native myocardial T1 mapping in the prognostic definition of this patient group.

**Conclusion**

CA and AS are increasingly encountered in clinical practice, mainly due to an increased number of diagnoses and continued population aging. The diagnosis of CA
A

B

Figure 6 – Mean survival of patients with CA + AS by ECV (A) or T1 time (B).

should be considered in cases of suspicious signs or when phenotypic cardiac changes are noted beyond those expected according to AS severity. CMRI, which plays an important role in the diagnosis and prognosis of patients with CA + AS, is a fundamental test that enables more assertive therapeutic decisions.

Authors’ contributions
Research conception and design: Barbosa PME, Magalhães TA; data collection: Barbosa PME, Magalhães TA; data analysis and interpretation: Barbosa PME, Magalhães TA; statistical analysis: Barbosa PME, Magalhães TA; funding: Barbosa PME, Magalhães TA; manuscript writing: Barbosa PME, Magalhães TA; critical review of the manuscript for important intellectual content: Barbosa PME, Magalhães TA.

Conflict of interest
The author declares that he has no conflict of interest

References


