Cardiac MRI study in a patient with amyloidosis: our experience

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Abstract

Amyloidosis are a group of diseases characterized by altered protein conformation, leading to the formation of fibrils that aggregate with non-protein substances and deposit extracellularly. These accumulations, called amyloids, can affect multiple organs simultaneously or only one organ.
Cardiac MRI is capable of providing a comprehensive evaluation of organ functionality by defining ejection volumes, perfusion, potential pericardial issues, and offering quantitative and qualitative data with high reproducibility, plays an important role in both the diagnosis and follow-up of patients with cardiac amyloidosis.

MRI PROTOCOLS

Before discussing the execution of cardiac MRI for suspected amyloidosis, let's briefly define the pathology. Amyloidosis are a group of diseases characterized by altered protein conformation, leading to the formation of fibrils that aggregate with non-protein substances and deposit extracellularly. These accumulations, called amyloids, can affect multiple organs simultaneously or only one organ. Initially, amyloidosis were classified into two groups: Systemic, where amyloids concentrated in multiple organs, and Localized, characterized by accumulation in a single organ. However, this classification did not consider the biochemical and etiopathogenic heterogeneity of the disease. In 2010, amyloidosis was divided into 30 types based on the protein that generates the amyloid fibril, as shown in the table on the left. Among these, only 5 types can accumulate in the myocardial wall, with the two most common being AL amyloidosis, associated with immune dysregulation, almost always systemic, and affecting the heart in 45% of cases with a rapid progressive course, leading to the principal cause of death in amyloidosis and being the most common form in the Western world.
AttrTransthyretin amyloidosis, on the other hand, arises from a genetic mutation with autosomal dominant transmission but has a slower progression and milder clinical manifestations, with cardiac involvement depending on the type of mutation. In both cases, their accumulation in the myocardial wall causes thickening, reduced muscular motility, and potential occlusion of coronary arteries and arterioles. Cardiac MRI, capable of providing a comprehensive evaluation of organ functionality by defining ejection volumes, perfusion, potential pericardial issues, and offering quantitative and qualitative data with high reproducibility, plays an important role in both the diagnosis and follow-up of patients with cardiac amyloidosis. For the reproducibility of the examination, it has been necessary to standardize the study protocol, as published by the European Association of Cardiovascular Imaging, which is also followed by our operating unit. The protocol consists of the following steps performed in chronological order:

- Pilot stack images (3D plane, Figure 1).
- Creation of standard cardiac planes (2-chamber, 3-chamber, 4-chamber, and short axis) using FIESTA CINE sequences with 30 reconstruction views (Figure 2).
- Black blood FSE fat saturation on 2-chamber and 4-chamber planes
- Cine FIESTA with 30 views on short-axis plane and, if necessary, 4-chamber plane
- Native T1 mapping on short-axis plane
- Fast gradient echo inversion recovery T1 on mid-ventricular short-axis plane, repeated 8- 10 times every minute after contrast administration
- Fast gradient echo inversion recovery T1 on short-axis plane, 10 minutes after contrast administration
- Post-contrast T1 mapping on short-axis plane

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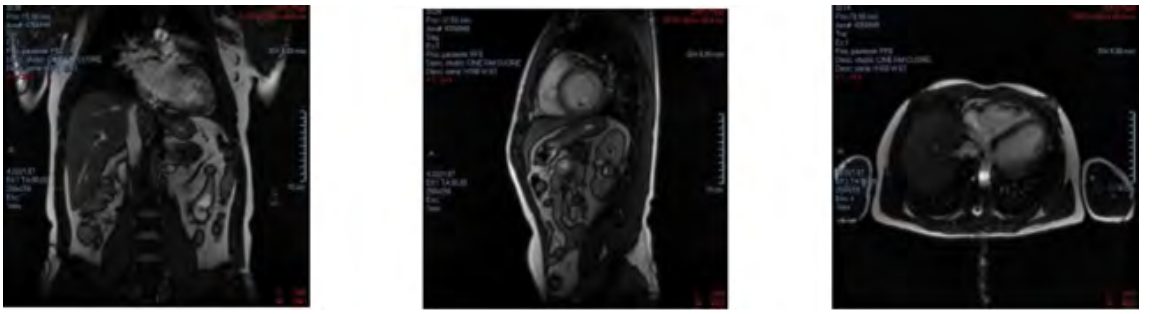

Figure 1. *3D plane Localizer*

The 3D plane is an SSFSE sequence commonly known as a scout in the three standard planes: axial, sagittal, and coronal. These images should include the entire thoracic cage, using a wide field of view to exclude any mediastinal masses or congenital abnormalities. Once acquired, these images serve as our starting point for setting up according to the standard cardiac protocols, specifically, we will acquire a 2-chamber long-axis view, a 2-chamber short-axis view, and a 4-chamber view, each with thirty images to include all cardiac phases from systole to diastole, as seen in the images on the side. On the left, we have systole in various cardiac projections, and on the right, we have diastole.

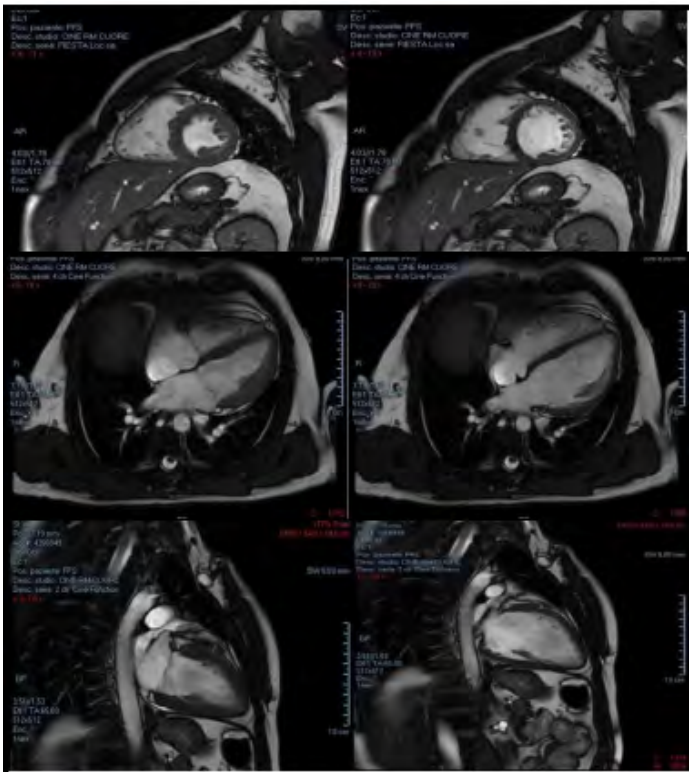

Figure 2. *FIESTA Cine short axis, 4 chambers long axis, 2 chambers*

We continue the investigation with a black blood fast spin echo sequence with fat suppression (BLACK BLOOD FSE FAT SAT). Starting from the short-axis plane, from the valve plane to the true apex of the heart, this sequence allows us to visualize blood as completely signal-free, or black, thanks to the double inversion pulse. It provides a good representation of the myocardial walls, which should appear isointense if healthy, as seen in the upper images. This sequence helps to differentiate areas of necrosis, fibrosis, and pathological thickening. If there are areas of altered signal intensity, either hypo- or hyperintense, in multiple slices of the acquired short-axis view, it is necessary to complement the examination with the same sequence but in a different plane, namely the 4-chamber view, as shown in the images on the left. This provides a better representation of the extent of the pathology within the entire myocardium (Figure 3).

However, if the signal alteration is present in only one image of the shortaxis view, there may be doubts about whether it is caused by chordal flipping, areas outside the field of view, or an artifact. In such cases, it is possible to repeat that particular slice with the caution of modifying only the phase direction from the menu, as indicated by the red circle in the image on the right, to demonstrate the origin of the signal alteration in the myocardium. If the alteration remains unchanged, it confirms a pathological area; otherwise, it will disappear or be projected to another point in the image.

Subsequently, we acquire a cine fiesta sequence on the short-axis plane, again from the valve plane to the true apex of the heart, with thirty images per slice, including the entire cardiac activity to document organ motility. This sequence is essential for calculating heart volume, ejection fraction, etc., using dedicated programs.

The study continues on the short-axis plane with a native T1 mapping sequence comprising only three slices: basal, mid, and apical cardiac slices, represented in red, blue, and green, respectively, on the left (Figure 4).

T1 mapping is a quantitative study based on the different longitudinal relaxation times characteristic of each tissue. The myocardium will have a different T1 value compared to blood and adipose tissue, and it may vary based on pathological conditions. For example, it will increase in the case of edema, fibrosis, or amyloidosis, with a coloration tending toward red on the color scale. Conversely, it will decrease, with a coloration toward blue, in cases of hemochromatosis or Fabry's disease. This allows us to identify the pathology but not to differentiate between intracellular and extracellular involvement. To

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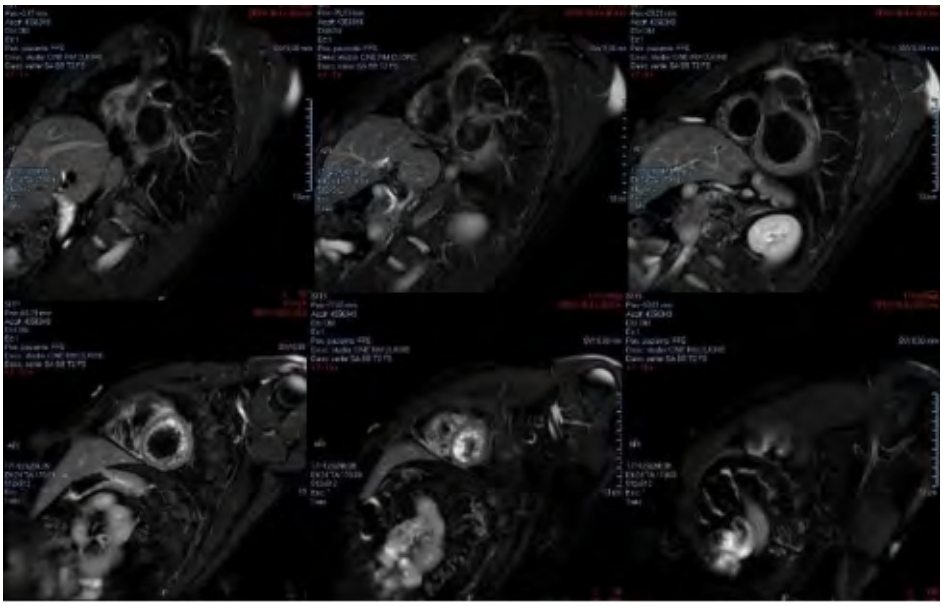

Figure 3. *Black blood FSE fat sat*

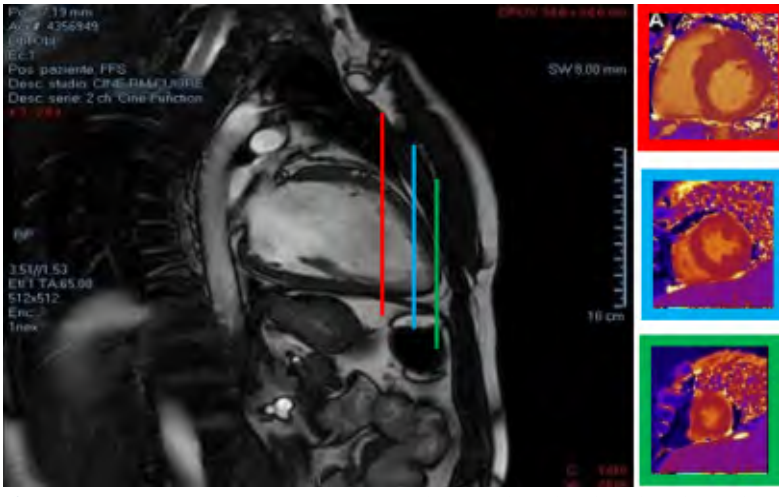

Figure 4. *native T1 mapping sequence with only three slices: basal, mid, and apical cardiac slices, represented in red, blue, and green.*

achieve that, the T1 mapping sequence needs to be repeated 20 minutes after the administration of intravenous contrast medium, and by comparing both sets of images, the extracellular volume (ECV) cine maps can be generated, as seen in the image on the side. In the first row, we have the pre-contrast T1 mapping, also known as native mapping; in the second row, the post-contrast T1 mapping as described earlier, and in the last row, the ECV reconstruction for the same basal, mid, and apical slices. But before performing the post-contrast T1 mapping, which will actually conclude the examination, we need to run another sequence twice but in different ways and for different purposes, which we will now analyze. The sequence in question is the fast gradient echo inversion recovery T1. The first time we set it up, as seen in the image on the side, we insert only one mid-ventricular slice along the short axis with an inversion time of 250 ms, which will nullify the signal from the healthy myocardium. It will be repeated 6-10 consecutive times, spaced one minute apart, starting one minute after the administration of the intravenous contrast agent, namely Gadolinium, with a dosage of 0.2 mmol/kg. This sequence aims to document the changes in longitudinal relaxation time undergone by the myocardial wall upon the arrival of the contrast agent, as depicted in the images below. It will be able to confirm or exclude the presence of amyloidosis by encoding, in positive cases, a heterogeneous signal of the cardiac wall with areas of hyperintensity alternating with markedly hypointense regions where the null point of healthy muscular tissue occurs. The second time, 10 minutes after the contrast administration, we will perform the sequence again, acquiring the entire cardiac mass along the short axis, from the valvular plane to the true apex (Figure 5).

In this case as well, we will set an inversion time of 250 msec to nullify the signal from the healthy myocardium and enhance the areas of hyperintensity generated by the pathological accumulation of gadolinium, which is known as late gadolinium enhancement. This phenomenon is based on two fundamental concepts:

1. The contrast agent's kinetics show delayed washout in pathological areas compared to healthy

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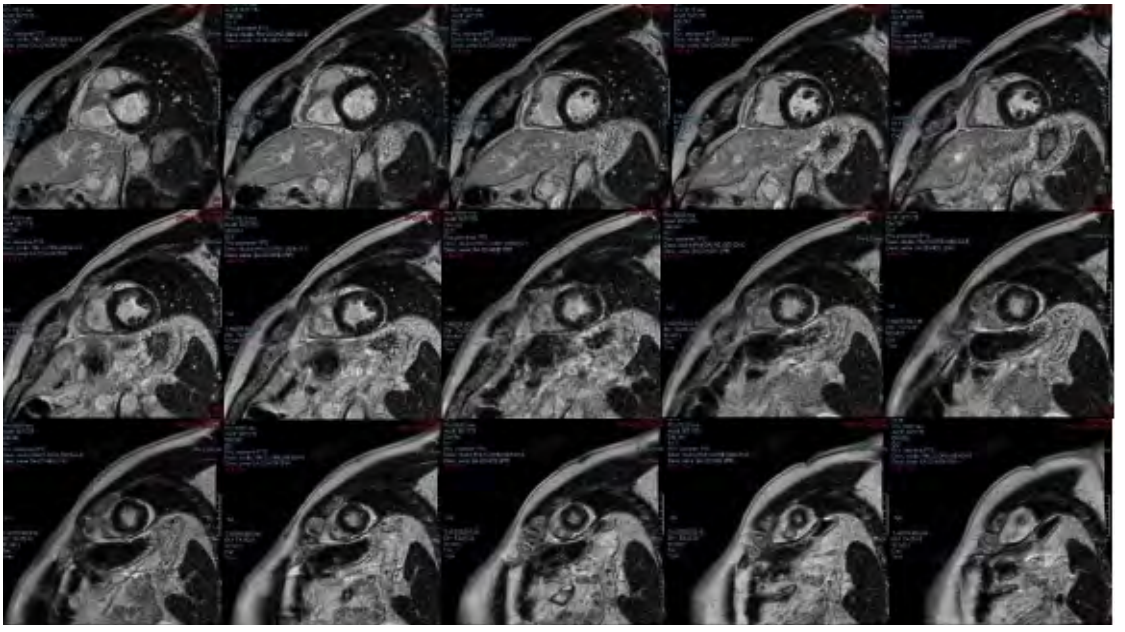

Figure 5. *Fast gradient echo inversion recovery t*1.

tissue.

2. The paramagnetic contrast agent is extracellular and cannot cross the sarcolemma of the tightly packed myocardial cells in a healthy heart, thereby preventing its penetration. However, in the presence of pathological areas, the extracellular space increases and the contrast agent accumulates.

There are several pathologies besides amyloidosis that can cause this phenomenon, such as ischemia and myocarditis. So, how do our radiologist colleagues determine the cause of hyperenhancement? Based on the extension and localization of late gadolinium enhancement, as seen in the representative image above, in the case of amyloidosis, it will always be diffused, with possible involvement of the atria or sub-endocardium, or with patchy hyperintensity in thickened walls (*Carreño-Morán et Al.*2013-Figure 6).

In conclusion, there are numerous cardiac MRI studies for amyloidosis that demonstrate high sensitivity and specificity, with excellent diagnostic values. Therefore, cardiac MRI is destined to play an increasingly important role in the study of such pathologies.

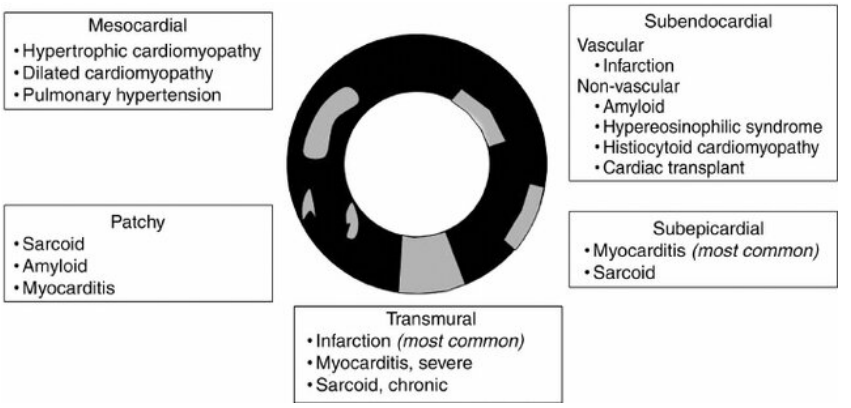

Figure 6. *Scheme of post contrast enhancement in several pathological conditions.*

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