

Role of Cardiac Magnetic Resonance Imaging in Acute Coronary Syndrome and Normal Coronary Arteries

Eva Larauogoitia Zaldumbide

Those patients who go to hospital with prolonged chest pain, elevation of cardiac enzymes and alterations in the electrocardiogram (ECG) are admitted with the initial diagnosis of acute coronary syndrome (ACS). About 7% and 10% of these patients do not show significant coronary lesions and in many occasions establishing an accurate diagnosis is difficult (1). Sometimes, it is an acute myocardial infarction with coronary arteries, with no lesions in the angiography at the moment of the study, but there are other non ischemic disorders that may have a clinical case similar to an ACS, as myocarditis or transient apical dyskinesia.(2) Establishing a correct diagnosis has important prognostic and therapeutic implications for the patient.

Cardiac magnetic resonance (CMR), specially with the use of those techniques of late enhancement of contrast with gadolinium, is a non invasive imaging with great sensitivity to detect myocardial abnormalities. One of the most known is the detection of areas of myocardial infarction, but it is also possible to see areas of fibrosis/necrosis in other diseases of non ischemic origin.^{2,3} As the prognostic and the therapeutic treatment would be different if it is an acute coronary episode or a non ischemic manifestation, it is really important to make an accurate diagnosis in these patients.

In this issue of the Argentine Journal of Cardiology, Avegliano et al.⁴ study the role of the CMR in patients with manifestations of ACS whose coronary angiography does not show significant coronary arteries stenosis.

Nowadays, the CMR late-enhancement is the most exact and better considered technique for the diagnosis of myocardial lesion. This simple method is based on the obtaining of inversion-recovery images of approximately 10 minutes after the intravenous administration of gadolinium contrast. When it is performed correctly, the normal myocardium appears in black or “disallowed”, while the non viable areas appear bright or “hyper-enhanced”.^{5,6} The mechanism of late-enhancement is not clear, but it seems to be based on the absence of viable myocytes, more than in a specific property of the acute necrosis, collagen scar or other ways of non viable myocardium.

There is ample evidence in the literature about the contribution of the T2-weighted sequences in the detection of myocardial oedema, although its additional value to late-enhancement is in controversy. The weighted MR in T2 seems good to assess acute, oedematous and inflammatory processes as AMI or myocarditis, and may

be useful to differentiate chronic myocardial lesions from new ones.⁷ However; T2- weighted MR did not improve significantly the diagnostic performance beyond the given by CMR-late enhancement and the images in film mode in this study.

Avegliano et al. did some examinations of CMR-late enhancement in 64 patients who were admitted due to chest pain and elevation of cardiac biomarkers, to whom a cardiac catheterism showing “absence of significant lesions” (<50%) in the following 24 hours of entering was performed. All the examinations of CMR were made in a period of 72±24 hours after the cardiac catheterism. A final diagnosis based on the detection of late enhancement of gadolinium was established. Based on hyper-enhancement, the final diagnosis was myocarditis in 39 patients (61%) and myocardial infarction in 12 patients (18%). A tako-tsubo cardiomyopathy was diagnosed in 8 patients (12%). Two patients were diagnosed with apical hypertrophic cardiomyopathy and there was no final diagnosis for 3 patients.

Myocarditis that seems acute coronary syndrome

In Avegliano et al. series,⁴ myocarditis was the most frequent cause of confusion, which coincides with the recently published data.

The explanation of the diagnostic mistakes in myocarditis is based on its diagnostic difficulty with standard methods. Clinical findings in myocarditis are limited to minor symptoms as dyspnoea, chest pain, or palpitations in the days following a febrile episode, but, frequently, the first clinical manifestation looks like an AMI, with alterations in ECG and elevation of myocardial damage markers.^{2,10} Due to the low specificity of its clinical symptoms, myocarditis is difficult to recognise in its initial episode and probably therefore, it is an underdiagnosed disease.

Endomyocardial biopsy has been considered the reference technique for myocarditis diagnosis,⁸ however, the sensitivity of this technique is low (<50%). Probably, myocarditis focal affection and mistakes in the samples determined its low sensitivity. ⁹ Apart from those limitations, the biopsy is a technique with complications, as several biventricular samples should be taken, which involves the performance of left and right catheterism. Nowadays it is only indicated if patients show poor clinical development and the obtained information may modify the treatment.

CMR is nowadays the elected technique for the diagnosis of myocarditis.^{10,11} The oedema and the inflammation produce an increase in the content of cellular and extracellular water, which alters T2

relaxation time, that are identified as areas of increased signal in T2-weighted sequences. In the sequences of late enhancement contrast, areas in early stages, usually with a patching and multifocal pattern, which are extended from the subepicardium to middle areas of the myocardium, which allows distinguishing it from myocardial enhancement in the acute myocardium infarction, which always affects the subendocardium, are seen. Mahrholdt et al.¹² demonstrated that these enhancement areas correspond to myocarditis focus. This demonstration was carried out from a study where CMR and endomyocardial biopsies were performed to all the patients, taking the samples of the areas in which the CMR showed enhancement. Subsequently, the same authors described different types of enhancement and related them to the clinical presentation and the causal agent.¹³ Those patients who consulted due to chest pain and elevation of enzymes, manifestation compatible with ACS, had subepicardium late enhancement which predominates in the LV lateral wall.

Acute myocardial infarction with normal coronary arteries

The usefulness of CMR for the study of myocardial infarction has been widely demonstrated in several studies. The area of late-enhancement shows the myocardial necrosis and its transmural shows the non viable area.^{5,6} In Avegliano et al. series,⁴ a total of 12 patients (15%) were diagnosed with myocardial infarction, number similar to the one found in previous studies.

The study coincides with other previous observations, relative to the presence of an AMI, despite the absence of coronary artery obstruction in a significant number of patients. The diagnosis is based on the subendocardium or transmural hyperenhancement patterns in areas of coronary arteries.

The elevated spatial resolution of CMR-late enhancement allows seeing, even, microinfarctions that affect only 1 g of tissue, which can be produced in a percutaneous coronary intervention, in other respects satisfactory.²³ The hyperenhancement pattern, and not only its presence or degree, is what gives important information regarding the aetiology of the myocardial lesion. For this, the concept that ischemic necrosis moves as a "wavefront"²⁷ from the subendocardium to the epicardium, as the time of coronary obstruction increases. Thus, hyperenhancement patterns that protect the subendocardium and are limited to the middle or epicardium area of the left ventricular wall (LV) are of non ischemic origin, given that the lesion that is produced in the context of a coronary disease usually affects the subendocardium.¹⁴

Tako-Tsubo syndrome as final diagnosis

In 11% of the cases in Avegliano et al series published in this issue of the journal, the final diagnosis was Tako-Tsubo syndrome. This result was based on the transient alterations of the segmental motility and the absence of coronary lesions. Of the 8 patients diagnosed with Tako-Tsubo, 6 of them showed "pale" transmural enhancement areas, which disappear in the following months, and 2 did not show late-enhancement of

contrast. In previous studies, it is pointed out that those patients with Tako-Tsubo do not show late-enhancement of contrast, which helps us discounting myocarditis or AMI.^{3,15} More recently, cases of Tako-Tsubo with pale transmural enhancement,¹⁶ were described and the authors, the same as in Avegliano et al. work's, attributed them to inflammation areas. The presence or absence of late-enhancement contrast is not conclusive in the diagnosis of Tako-Tsubo, but it may be based on: transient alterations of LV contractility, ECG alterations, modest elevation of cardiac enzymes, and coronary arteries with no significant lesions.

CONCLUSIONS

At the clinic, there are non ischemic diseases that can be presented as ACS. As a correct diagnosis has important prognostic and therapeutic implications for the patients, the performance of a study with CMR and specially the assessment of the presence, distribution and late-enhancement contrast pattern in the study of CMR, have an important role in the establishment of the diagnosis.

BIBLIOGRAPHY

1. Wang K, Asinger RW, Marriott HJ. ST-segment elevation in conditions other than acute myocardial infarction. *N Engl J Med* 2003; 349:2128-35.
2. Laradogoitia Zaldumbide E, Pérez-David E, Larena JA, Velasco del Castillo S, Rumoroso Cuevas JR, Onaindía JJ, et al. The value of cardiac magnetic resonance in patients with acute coronary syndrome and normal coronary arteries. *Rev Esp Cardiol* 2009; 62:976-83.
3. Isbell DC, Kramer CM. The evolving role of cardiovascular magnetic resonance imaging in nonischemic cardiomyopathy. *Semin Ultrasound CT MR* 2006; 27:20-31.
4. Avegliano GP, Huguet M, Costabel JP, Kuschnir P, Thierier J, Alves de Lima A, y col. Utilidad de la Resonancia Magnética Cardiovascular en la valoración de los pacientes con dolor torácico, troponinas elevadas y ausencia de obstrucción arterial coronaria. *Rev Argent Cardiol* 2011;79:XX-XX.
5. Kim RJ, Wu E, Rafael A, Chen EL, Parker MA, Simonetti O, et al. The use of contrast-enhanced magnetic resonance imaging to identify reversible myocardial dysfunction. *N Engl J Med* 2000; 343:1445-53.
6. Rehwald WG, Fieno DS, Chen EL, Kim RJ, Judd RM. Myocardial magnetic resonance imaging contrast agent concentrations after reversible and irreversible ischemic injury. *Circulation* 2002; 105:224-9.
7. Abdel-Aty H, Zagrosek A, Schulz-Menger J, Taylor AJ, Messroghli D, Kumar A, et al. Delayed enhancement and T2-weighted cardiovascular magnetic resonance imaging differentiate acute from chronic myocardial infarction. *Circulation* 2004;109: 2411-6.
8. Aretz HT, Billingham ME, Edwards WD, Factor SM, Fallon JT, Fenoglio JJ Jr, et al. Myocarditis. A histopathologic definition and classification. *Am J Cardiovasc Pathol* 1987; 1:3-14.
9. Shirani J, Freant LJ, Roberts WC. Gross and semiquantitative histologic findings in mononuclear cell myocarditis causing sudden death, and implications for endomyocardial biopsy. *Am J Cardiol* 1993; 72:952-7.
10. Abdel-Aty H, Boyé P, Zagrosek A, Wassmuth R, Kumar A, Messroghli D, et al. Diagnostic performance of cardiovascular magnetic resonance in patients with suspected acute myocarditis: comparison of different approaches. *J Am Coll Cardiol* 2005; 45:1815-22.
11. Laradogoitia E, Diez I. Miocarditis y Miocardiopatías. *Rev Esp Cardiol* 2006; 6 (Sup E):21-9.

- 12 Mahrholdt H, Goedeke C, Wagner A, Meinhardt G, Athanasiadis A, Vogelsberg H, et al. Cardiovascular magnetic resonance assessment of human myocarditis: A comparison to histology and molecular pathology. *Circulation* 2004;109:1250-8.
13. Mahrholdt H, Wagner A, Deluigi CC, Kispert E, Hager S, Meinhardt G, et al. Presentation, patterns of myocardial damage, and clinical course of viral myocarditis. *Circulation* 2006;114:1581-90.
14. Abdel-Aty H, Zagrosek A, Schulz-Menger J, Taylor AJ, Messroghli D, Kumar A, et al. Delayed enhancement and T2-weighted cardiovascular magnetic resonance imaging differentiate acute from chronic myocardial infarction. *Circulation* 2004;109: 2411-6.
15. Mitchell JH, Hadden TB, Wilson JM, Achari A, Muthupillai R, Flamm SD. Clinical features and usefulness of cardiac magnetic resonance imaging in assessing myocardial viability and prognosis in Takotsubo cardiomyopathy (transient left ventricular apical ballooning syndrome). *Am J Cardiol* 2007;100:296-301.
16. Rolf A, Nef HM, Möllmann H, Troidl C, Voss S, Conradi G, et al. Immunohistological basis of the late gadolinium enhancement phenomenon in tako-tsubo cardiomyopathy. *Eur Heart J* 2009;30:1635-42.