# Cardiac Magnetic Resonance Imaging in Patients with Chest Pain, High Troponin Levels and Absence of Coronary Artery Obstruction

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## SUMMARY

The prevalence of myocardial infarction with angiographically normal coronary arteries is approximately 7-10%. The etiological diagnosis is sometimes difficult and is important in terms of clinical practice and prognosis. The goal of our study was to show a series of consecutive patients with an initial diagnosis of acute coronary syndrome with high troponin levels and absence of coronary artery obstruction in which cardiac magnetic resonance imaging (CMRI) gave a description of the myocardial lesion, orientating towards the etiological diagnosis.
From January 2005 to December 2009, 720 consecutive patients with an initial diagnosis of acute coronary syndrome and elevated troponins were included; 64 of these patients did not present angiographically significant coronary artery stenosis. Within 72 ± 24 h after coronary angiography, these patients underwent CMRI using b-SSFP sequences for cine imaging in short-axis, 2-, 3- and 4- chamber views for the evaluation of segmental wall motion, with T2-weighted and late enhancement (LE) images of the myocardium with an "inversion-recovery" sequence. The following diagnoses were made: myocarditis (39 patients); myocardial infarction (12 patients); Tako-Tsubo syndrome (8 patients); apical hypertrophic cardiomyopathy (2 patients); 3 patients remained without diagnosis.
These findings demonstrate the usefulness of CMRI in the clinical scenario of patients with chest pain, inconclusive ECG findings and high troponin levels with angiographically normal coronary arteries. The presence and distribution pattern of LE make it possible to define the etiological diagnosis and interpret the physiopathological process.

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**Key words >** Infarction - Magnetic Resonance Spectroscopy - Myocarditis

## BACKGROUND

The diagnosis of acute coronary syndrome (ACS) is based on clinical data, electrocardiographic (ECG) findings and biomarkers of myocardial damage. The use of troponins as markers of myocardial damage has allowed the detection of small areas of necrosis, which previously passed unnoticed. Despite this progress, the cause of myocardial damage is still a problem, as 7-10% of patients have angiographically normal coronary arteries.1 Different conditions are associated with chest pain, ECG changes and positive troponin levels in the absence of coronary artery stenosis: myocarditis, Tako-Tsubo cardiomyopathy or acute myocardial infarction (AMI) due to coronary artery thrombosis with spontaneous recanalization or secondary to prolonged vasospasm. This represents a diagnostic challenge, as the treatment and prognosis of these conditions are different. Cardiac magnetic resonance imaging (CMRI) with injection of contrast agent is particularly useful to recognize myocardial abnormalities and has great diagnostic value in this clinical scenario.2,3 The goal of this study was to evaluate the diagnostic usefulness of CMRI in a series of consecutive patients initially presenting with ACS and coronary angiography with absence of coronary artery obstruction.

## MATERIAL AND METHODS

### Population and study protocol

We conducted a descriptive observational study about the prevalence CMRI findings in patients with an initial diagnosis of ACS, high troponin levels and absence of significant stenosis in the coronary angiography.

From January 2005 to December 2009, 720 consecutive patients with an initial diagnosis of acute coronary syndrome and elevated troponins were prospectively included; all patients underwent coronary angiography. The patients were recruited from the Centro Cardiovascular Sant Jordi, in Barcelona (Spain) between 2005 and 2007 and from

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the Instituto Cardiovascular de Buenos Aires, Argentina from 2007 to 2009 (both institutions are single-specialty tertiary hospitals). Sixty-nine of these patients did not present significant lesions (stenosis < 50%) in the coronary angiography, representing 9.5% of the patients admitted with this syndrome. Patients with a history of previous myocardial infarction (n = 2), with chronic elevation of troponin levels (n = 1), with contraindications to undergo CMRI (1 patient with a definite pacemaker and 1 with claustrophobia) were excluded from the study. Finally, 64 patients were included.

All patients included in the study underwent serial ECG and determinations of markers of myocardial damage (total CK, CK-MB, troponin T), coronary angiography and CMRI. Coronary angiography and echocardiography were performed within 24 hours after admission. Cardiac MRI was carried out after coronary angiography and within 72 ± 24 from symptoms onset.

### Cardiac magnetic resonance imaging

Cardiac MRI was acquired on a General Electric Signa CVi-HDx 1.5T scanner with a dedicated cardiac coil and a Philips Achieva 1.5 Tesla scanner. The protocol included steady-state free-precession (b-SSFP) sequences for cine imaging, T2-weighted black-blood sequences (trueFISP technique, balanced fast field echo sequence) and late enhancement imaging in 2-, 3- and 4- chambers and short axis views, 10 minutes after gadolinium injection. Cine images were used to evaluate left ventricular (LV) systolic function. Two independent expert observers, unaware of the clinical case, performed the visual analysis of the areas of late gadolinium enhancement (LGE), high T2 signal intensity and wall motion in the 17 segments of the LV.4 The final diagnosis was based on the sequences of late enhancement, defining the presence and location of LGE (subendocardial, transmural, intramyocardial or subepicardial). The diagnosis of myocarditis was made in patients with subepicardial or intramyocardial LGE. Trasmural or subendocardial LGE corresponded to the diagnosis of myocardial infarction. The diagnosis of Tako-Tsubo syndrome was based in clinical criteria and reversible wall motion abnormalities of mid-ventricular and apical segments in the absence of both coronary artery obstructions (>50%) and late enhancement, or in the presence of mild late enhancement which normalized in the control study.5

### Statistical Analysis

Categorical variables are presented as percentages. Continuous variables are expressed as mean ± standard deviation. As this is a descriptive study without control group, we did not perform tests to determine statistical significance.

## RESULTS

### Clinical and echocardiographic findings

These findings are described in Table 1. Mean age was 49 ± 17 years and 78% were men. The electrocardiogram at admission showed ST-segment elevation in 21 patients, ST-segment depression in 10 patients, T-wave inversion in 28 and was normal in 5 patients. Twenty-five patients (39%) presented segmental wall motion abnormalities, particularly in the inferolateral segments. Mean left ventricular ejection fraction (LVEF) was 55 ± 13% and 14 cases (21.8%) presented mild pericardial effusion.

### Cardiac magnetic resonance imaging findings

Radiofrequency ablation is a therapeutic strategy Data are described in Tables 2A and 2B. Wall motion abnormalities were present in 35% of patients and average LVEF was 61± 12%.

A total of 58 patients (90.7%) presented LGE, with subendocardial, transmural, intramyocardial and subepicardial location in 8, 10, 9 and 33 patients, respectively. Late gadolinium enhancement in the subepicardium extended to involve the mid-myocardial regions in two patients who were included in the group with intramyocardial enhancement. The diagnosis of myocarditis was made in 29 patients with subepicardial and intramyocardial late enhancement. The most frequent locations of LGE were the inferolateral (33 cases) and anteroseptal (5 cases) regions; one patient had involvement of both regions. Twelve patients had diagnosis of AMI based of subendocardial (8 patients) and transmural (4 patients) LGE that correlated with specific coronary territories. Of these four patients, one presented a typical pattern of microvascular obstruction in the sequence of late enhancement and three had intense focal uptake suggestive of embolism. Patients with Tako-Tsubo syndrome undergoing CMRI within 72 hours from symptoms onset presented a mild transmural LGE without correlation with specific coronary territories. In these six patients, LGE was absent in the control CMRI performed between 60 and 90 days. One patient with intramyocardial enhancement had a diagnosis of apical hypertrophic cardiomyopathy. Inversion recovery sequences did not show LGE in 6 patients (9.3%); the diagnosis of these patients were a minor variant of apical hypertrophic cardiomyopathy in 1 patient, and typical Tako-Tsubo syndrome in 2. A final diagnosis was not established in 3 patients.

## DISCUSSION

The availability of CMRI is increasing in clinical practice. The accuracy of this method for the diagnosis or irreversible myocardial lesion using the late gadolinium enhancement (LGE) technique is high. The exceptional spatial resolution allows not only to make the precise diagnosis of small areas of necrosis but also to determine the type of LGE pattern, which gives the information about the etiological diagnosis that produced the myocardial lesion.

In our series, myocarditis was the most common final diagnosis (60.9%), similar to other series.2,3 This is the main differential diagnosis with ACS, as

**Table 1.**

| Clinical and echocardiographic findings | |
|---|---|
| N | 364 |
| Median age (years) | 49 ±17 |
| Men (n) | 50 (78%) |
| Trop T – ng/mL | 2.1 ± 0.9 |
| CK – IU/L | 905 ± 276 |
| Wall motion abnormalities (n) | 25 (39%) |
| LV ejection fraction (%) | 55 ± 13 |
| Pericardial effusion (n) | 14 (21.8 %) |

**Table 2A .**

| CMRI findings | |
|---|---|
| N | 64 |
| Wall motion abnormalities (n) | 23 (35.9) |
| LV ejection fraction (%) | 61 ± 12 |
| Negative late enhancement (n) | 6 (9.3%) |
| Subendocardial (n) | 8 (12.5%) |
| Transmural (n) | 10 (15.6%) |
| Intramyocardial (n) | 9 (14%) |
| Subpicardial (n) | 33 (51.5%) |

**Table 2B.**

| Final diagnosis | N |
|---|---|
| Acute myocarditis (n) | 39 (60.9 %) |
| Stress cardiomyopathy (n) | 8 (12.5%) |
| Myocardial infarction (n) | 12 (18.7%) |
| Possible spontaneous fibrinolysis (n) | 8 |
| Possible embolism (n) | 3 |
| Possible vasospasm (n) | 1 |
| Apical HCM (n) | 2 (3.2%) |
| No diagnosis (n) | 3 (4.6%) |

chest pain may also be oppressive and the presence of markers of myocardial damage have a pattern similar to that of myocardial infarction. In addition, the presence of coronary risk factors is frequent. On the other hand, only 20% of myocarditis mimicking ACS have evident symptoms of pericarditis and, in some cases, it is not possible to identify symptoms of airway or digestive disease preceding the event.6,7 In our patients, the typical patchy and multifocal pattern affecting the subepicardium and intramyocardium was most commonly seen in the inferolateral segments of the LV (Figure 1). When the study is performed early (acute phase) STIR and/or T2-weighted sequences are useful to put into evidence areas with high signal, corresponding to the presence of edema in the affected region. In our series, T2-weighted sequences supported the diagnosis in different situations, as the distribution of hyperintensity was different in myocarditis (absence of correlation with a coronary territory), Tako-Tsubo syndrome (LV mid-apical compromise) and myocardial infarction (correlation with a coronary territory). Yet, the evaluation of some patients included in the initial stages of this study was difficult due to the lack of artifact-free sequences. Therefore, we mostly based the diagnoses in the late enhancement sequences; the quality of these images was high in all the patients.

Our second diagnosis was AMI (18.8%). The LGE technique accurately identifies the area of LV necrosis and its extension in the LV wall.8,9 The technique may even identify the physiopathological process that produced the lesion. For example, patients with coronary artery spasm or thrombosis with spontaneous fibronolysis usually present lesions in the corresponding territory of the epicardial coronary artery, and the degree of trasmural involvement varies according to the duration of the obstruction, producing from minimal subendocardial lesions to transmural compromise. Conversely, patients with coronary embolism generated from thrombus in the coronary arteries, in the LV or secondary to interventional procedures, generally present a LGE pattern characterized by high-density focal lesions, which are generally transmural. In our series, we found eight patients with subendocardial uptake involving less than 25% of the wall and correlated with a cornary territory. The remaining four patients with a final diagnosis of AMI had trasmural LGE. The lesion was transmural and focal in three patients, suggestive of embolism (Figure 2), and the last patient had transmural lateral necrosis with microvascular obstruction. This type of lesion has been published in several studies and has been associated with an unfavorable LV remodelling.10

Finally, the Tako-Tsubo syndrome is an emerging clinical entity characterized by the presence of transient left ventricular dysfunction in the setting of a clinical picture mimicking a myocardial infarction, usually preceded by emotional or physical stress and without evidence of angiographically significant coronary artery lesions. 5,11 In our series, 25% of cases had this diagnosis, a percentage that is similar to that previously reported. In most of the studies, cardiac MRI has demonstrated the typical wall motion abnormalities associated with absence of LGE.2,3,12 However, Bruder et al. 13 have published a case of Tako-Tsubo syndrome with LGE when CMRI was performed early. In another recent study, Rolf A. et al. have demonstrated the association between increase of collagen-1 and late enhancement in the early stages of the disease, suggesting a relation with increased extracellular matrix.14 In our experience, the absence of LGE is related to the moment the CMRI is performed. In our series, early studies (< 72 hours) have systematically demonstrated a pattern of mild transmural late enhancement in the area with wall motion abnormalities which presents complete normalization in a few days. This might be due to edema/inflammation of the affected region (Figure 3).13-16

Finally, LGE was negative in six patients. Two patients with Tako-Tsubo syndrome had been transferred to our center and cardiac MRI was performed 3 days after symptoms onset.

In other patient, the diagnosis of apical hypertrophic cardiomyopathy was finally made and only three patients remained without etiological diagnosis. In these cases, the myocardial lesion might have been too small to be detected by CMRI despite the good spatial resolution.

## CONCLUSION

These findings demonstrate the usefulness of CMRI in the clinical scenario of patients with chest pain, inconclusive ECG findings and high troponin levels with angiographically normal coronary arteries. The presence and distribution pattern of LGE make it possible to define the etiological diagnosis and interpret the physiopathological process. Further studies with long-term follow-up are necessary to clarify the prognostic value of CMRI in these patients.

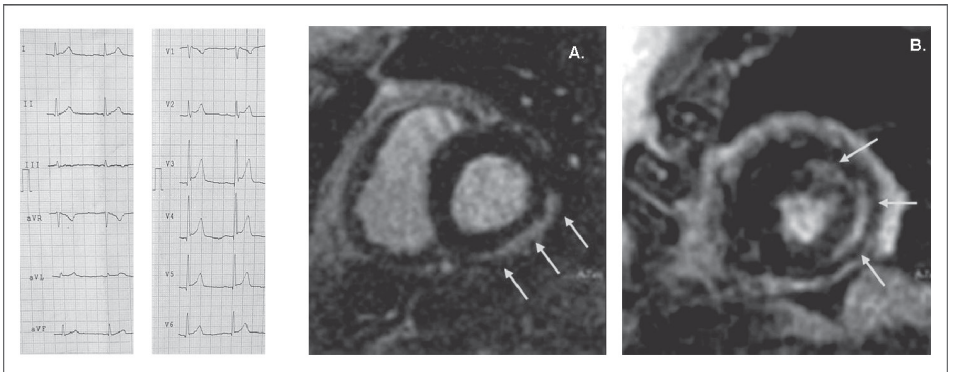


**Fig. 1.** Patient with a final diagnosis of myocarditis, with positive troponins and inconclusive ECG findings. CMRI: inversion recovery gradient echo sequence. Note the presence of subepicardical LME of the lateral wall in (**a**) extending to the mid-wall in an apical slice (**b**).

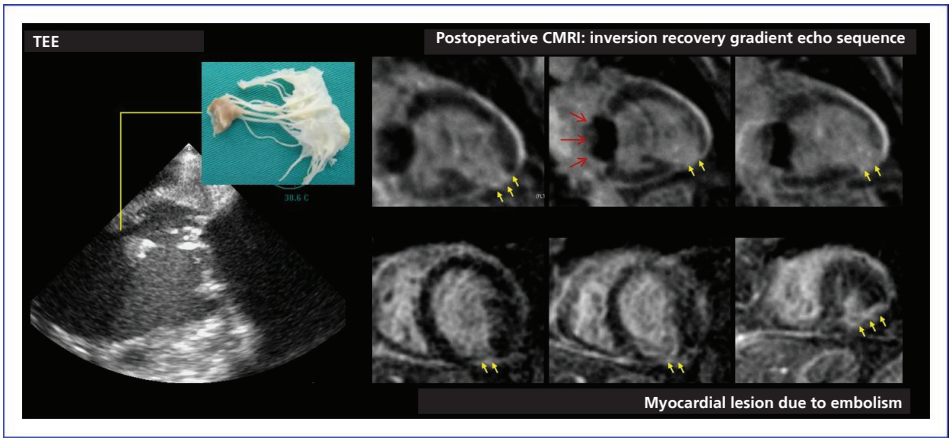


**Fig. 2.** A 72 year-old woman with essential thrombocythemia and severe thrombocytosis who discontinued treatment presented a lateral myocardial infarction with rupture of the head of a posteromedial papillary muscle and severe mitral regurgitation. The coronary angiography showed a 20% obstruction of the first obtuse marginal branch of the left circumflex artery with an image of a non-obstructive residual thrombus. **a** Transesophageal echocardiography showing the ruptured head of papillary muscle and its correlation with the surgical specimen. **b** CMRI: inversion recovery gradient echo sequence. Note focal, transmural late enhancement in the apical and inferolateral region suggestive of embolic lesion (yellow arrows). The low-intensity signal corresponds to the artifact generated by the mitral valve prosthesis (red arrows).

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## RESUMEN

### Utilidad de la resonancia magnética cardíaca en la valoración de los pacientes con dolor torácico, troponinas elevadas y ausencia de obstrucción arterial coronaria

El infarto de miocardio con coronarias angiográficamente normales tiene una prevalencia de aproximadamente el 7-10%. Muchas veces, el diagnóstico etiológico es dificultoso, y tiene importancia tanto en la clínica como en el pronóstico. El objetivo de nuestro estudio fue mostrar una serie consecutiva de pacientes con diagnóstico inicial de síndrome coronario agudo con elevación de troponina y ausencia de obstrucción arterial coronaria; en los cuales, la RM cardíaca (RMC) orientó al diagnóstico etiológico mediante la caracterización de la lesión miocárdica.

Desde enero de 2005 hasta diciembre de 2009 ingresaron 720 pacientes consecutivos, con diagnóstico inicial de síndrome coronario agudo y troponinas positivas, de los cuales, 64 no presentaron lesiones coronarias angiográficamente significativas. A estos pacientes, luego del cateterismo (dentro de las 72 ± 24 hs) se les practicó RMC, realizándose secuencias de cine (b-SSFP) en eje corto, con 2, 3 y 4 cámaras para valorar la motilidad segmentaria, en secuencias potenciadas en T2 e imágenes de realce tardío del miocardio (RTM) con secuencia "inversión-recuperación". De estos pacientes, 39 fueron diagnosticados de miocarditis; 12 con infartos, 8 con síndrome de Takotsubo, 2 con miocardiopatía hipertrófica apical y solo 3 casos quedaron sin diagnóstico.

Estos hallazgos ponen de manifiesto la gran utilidad de la RMC en el escenario clínico de síndromes de dolor

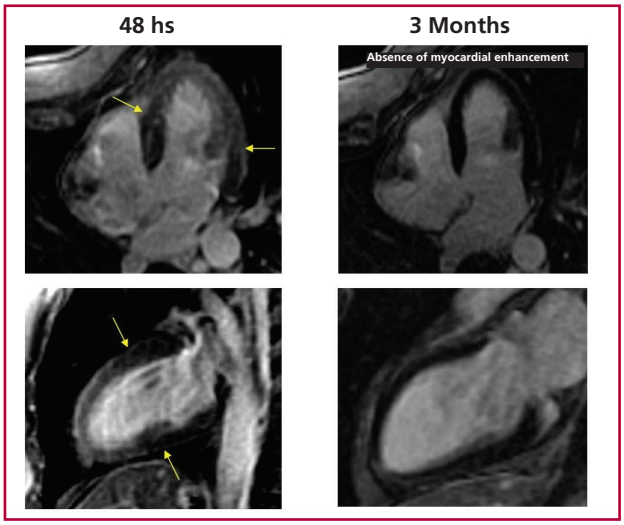


**Fig. 3.** Mid-apical Tako-Tsubo cardiomyopathy in a 51 year-old woman. CMRI performed 48 hours after symptoms onset. Left: inversion recovery gradient echo sequence showing mild transmural late enhancement in the segments with wall motion abnormalities. Right: CMRI 3 months later. Note that gadolium kynects has normalized with absence of late myocardium enhancement.

precordial, ECG no definitivos y troponinas elevadas con arterias angiográficamente normales. La presencia de RTM y su patrón de distribución permiten definir el diagnóstico etiológico y orientar a la interpretación del proceso fisiopatológico.

**Palabras clave >** Infarto - Resonancia magnética - Miocarditis

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