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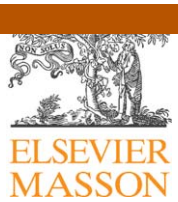

CLINICAL RESEARCH

Diagnostic contributions of cardiac magnetic resonance imaging in patients presenting with elevated troponin, acute chest pain syndrome and unobstructed coronary arteries

Apport diagnostique de l'IRM cardiaque dans la prise en charge des patients présentant un syndrome douloureux thoracique avec élévations des troponines et absence de lésion coronaire significative

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KEYWORDS
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Acute coronary syndrome;
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Myocardial infarction;
Takotsubo syndrome

Summary
Aims. — Myocardial infarction with unobstructed coronary artery disease represents a serious diagnostic challenge. The role of cardiac magnetic resonance in the management of cardiomyopathies is increasing. We examined the diagnostic contributions of cardiac magnetic resonance in patients presenting with acute chest pain syndrome, elevated serum cardiac troponin concentrations and no significant coronary artery stenoses.
Methods. — Over a 3-year period, 107 consecutive patients (mean age 43.5 years; 62% men) presented to our institution with acute onset of chest pain, elevated serum troponin concentration and unobstructed coronary arteries, and underwent 3-tesla cardiac magnetic resonance at a

Abbreviations: CMR, Cardiac magnetic resonance; cTn, Troponin concentration; FOV, Field of view; LVEF, Left ventricular ejection fraction; TTE, Transthoracic echocardiography.

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mean delay of 6.9 days. A diagnosis was made based on: wall motion abnormalities and pericardial effusion on cine mode; myocardial oedema on T2-weighted imaging; abnormalities on first-pass perfusion imaging; and late gadolinium enhancement on T1-weighted imaging.
Results. — Cardiac magnetic resonance was normal in 10.3% of patients and contributed a diagnosis in 89.7%, including myocarditis in 59.9%, stress cardiomyopathy (takotsubo syndrome) in 14% and myocardial infarction in 15.8%. Patients with normal cardiac magnetic resonance had a significantly lower mean peak troponin concentration (2.6 ng/mL) than patients with diagnostic cardiac magnetic resonance (9.7 ng/mL; $P = 0.01$).
Conclusion. — Cardiac magnetic resonance contributed a diagnosis in nearly 90% of patients presenting with acute chest pain, elevated serum troponin and unobstructed coronary arteries.

MOTS CLÉS
IRM cardiaque ;
Syndrome coronaire aigu ;
Myocardite ;
Infarctus du myocarde ;
Syndrome de takotsubo

Résumé
Objectif. — Les infarctus du myocarde sans lésion coronaire significative constituent une difficulté diagnostique importante. Le rôle de l'IRM cardiaque dans la prise en charge des cardiopathies est croissante. Nous avons étudié l'apport diagnostique de l'IRM cardiaque chez les patients présentant un syndrome douloureux thoracique avec élévations des troponines et absence de lésion coronaire significative.
Méthode et résultats. — Sur une période de trois ans, 107 patients consécutifs (âge moyen : 43,5 ; hommes : 62 %) ont été hospitalisés dans notre service pour syndrome douloureux thoracique, troponine sérique élevée, absence de lésion coronaire significative et ont bénéficié d'une IRM cardiaque 3 tesla dans un délai moyen de 6,9 jours. Le diagnostic était basé sur : (a) la présence d'anomalies de la cinétique segmentaire ou d'un épanchement péricardique sur les séquences « ciné » ; (b) d'un œdème myocardique sur les séquences pondérées T2 ; (c) les anomalies de la perfusion de premier passage ; (d) le rehaussement tardif sur les séquences pondérées T1. L'IRM était normal chez 10,3 % et a apporté un diagnostic chez 89,7 % des patients, dont 59,9 % de myocardite, 14 % de cardiopathie de stress (syndrome de takotsubo) et 15,8 % d'infarctus du myocarde. Les patients avec une IRM normale avaient un pic de troponine significativement plus bas (2,6 ng/ml) que les patients avec une IRM contributive (9,7 ng/ml ; $p = 0,01$).
Conclusion. — L'IRM cardiaque apporte un diagnostic étiologique chez près de 90 % des patients présentant un syndrome douloureux thoracique avec élévations des troponines et absence de lésion coronaire significative.

Introduction

Cardiac magnetic resonance (CMR) is a safe, non-invasive and reliable diagnostic test [1]. Chest pain syndrome with elevated troponin concentration (cTn) occurring in the absence of significant coronary artery stenosis represents a serious diagnostic challenge [2,3]. Studies have recently been published describing the usefulness of CMR in the diagnosis of myocardial infarction [4—7], myocarditis [8—13] and apical ballooning or ''takotsubo syndrome'' [14—17]. Consequently, its role is increasing in the initial diagnosis and management of various heart diseases [18]. In this study, we sought to define the prevalence of the different aetiological diagnoses in patients presenting with acute chest pain syndrome, elevated serum cTn and unobstructed coronary arteries, because few studies have been published regarding the systematic use of CMR in this situation.

Methods

This single-centre, prospective study enrolled consecutive patients between November 2006 and November 2009 who presented with: acute onset of chest pain; serum cTn >0.1 ng/mL in two separate assays; and unobstructed coronary arteries (stenosis <50% of the diameter of the vessel) on angiography, computed tomography or both. Initial management, including left ventriculography or transthoracic echocardiography (TTE), was carried out according to the usual local practice. Patients with a history of myocardial infarction, significant valvular disease or hypertrophic cardiomyopathy were excluded.

Cardiac magnetic resonance study

All CMR examinations were performed with a 3-tesla Achieva® clinical imager (Philips Medical Systems, Best, The Netherlands). A six-element, phased-array, cardiac synergy coil was used for signal detection. Cardiac synchronization was performed using a four-electrode vectorcardiogram. CMR imaging associated cine and morphological sequences for each patient, as described below.

The typical protocol (see details below) involved three stages, after surveys (scout views) to determine cardiac axis locations. First, cine-mode sequences were acquired in the short-axis view (left ventricular function) and T2-weighted black-blood spin echo was carried out in the three

Table 1 Cardiac magnetic resonance criteria used to identify the specific clinical diagnoses.

Diagnosis	Wall-motion abnormalities	Pericardial effusion	Oedema	Microvascular obstruction on first-pass perfusion imaging	Late gadolinium enhancement		
					Present	Distribution	Extent
Myocarditis	1/0	1/0	1/0	0	1	No coronary artery distribution	Subepicardial; mid-wall
Myocardial infarction	1/0	1/0	1/0	1/0	1	Coronary artery distribution	Subendocardial; transmural
Stress cardiomyopathy	1/0[a]	1/0	1/0	0	0	–	–
No specific diagnosis	0	0	0	0	0	–	–

1: present; 0: absent.
[a] Wall-motion abnormalities could be absent if cardiac magnetic resonance was delayed.

typical planes before gadolinium-chelate injection. Second, first-pass perfusion images were acquired in the short-axis view during a first infusion of gadolinium-chelate; immediately after a second gadolinium injection, cine sequences in four chambers and left ventricular long-axis views were acquired. Third, about 8 to 10 minutes after the second injection, inversion-time scouting was carried out and then late gadolinium enhancement sequences were done in the three cardiac planes.

Cine mode

Steady-state, free precession sequences (balanced fast field echo) were acquired in three cardiac conventional planes with these typical settings: 30 phases/R-R; breath-hold acquisition/each slice; slice thickness, 7 mm without or with minimal ($\leq$1 mm) gap; shortest TR/TE, typically 3.7/1.9 ms; flip angle, 45°; field of view (FOV), 320—400 mm; temporal resolution, 30—50 ms; in-plane resolution, 2 $\times$ 1.6 mm; matrix, 200 $\times$ 256. In the short-axis view, 10—12 slices were acquired with complete coverage of the left ventricle from base to apex, before injection of gadolinium-chelate (Dotarem®; Guerbet, Roissy, France). Left ventricular long-axis (three slices) and four-chamber (four to five slices) views were acquired after the injection of gadolinium-chelate. In some difficult cases, these views enabled complementary study of myocardial enhancement.

T2-weighted black-blood spin echo

Multislice, monophase, single-shot, turbo, spin-echo sequences with inversion recovery and fat suppression (T2 BB SPAIR-SSH—T2 Black Blood spectral presaturation attenuated inversion-recovery single shot) were acquired. The following settings were used in three planes covering the entire left ventricle: 10 slices in short-axis view, seven slices in left ventricular long-axis view, eight slices in four-chamber view; breath-hold acquisition in mid-diastole; slice thickness/gap, 7/0.7 mm; TR, 2 $\times$ R-R intervals; TE, 45 ms; inversion time, 100 ms; FOV, 370; matrix, 216 $\times$ 86; flip angle, 90°.

First-pass perfusion imaging

A single-shot, spoiled, gradient-echo sequence with saturation prepulse (dynamics turbo field gradient-echo) was used with these typical settings: five to six non-contiguous slices in short-axis view placed to cover the left ventricular basal to apical planes and recorded continuously for each cardiac cycle; slice thickness/gap, 8/8 mm; shortest TR/TE, typically 3.8/1/9 ms; flip angle, 20°; matrix, 128 $\times$ 77; in-plane resolution, 3 $\times$ 5 mm; FOV, 390; total duration, 1 minute with partial breath-hold during initial myocardial enhancement. The acquisition was synchronized to the intravenous injection of 0.1 mmol/kg of gadolinium-chelate at a rate of 4 mL/second, followed by a flush infusion at the same rate.

Late gadolinium enhancement imaging

Two-dimensional, multislice, T1-weighted, inversion-recovery, spoiled, turbo-field, gradient-echo sequences (Spoiled inversion recuperation turbo field echo 3D [SIRTFE 3D]) were acquired 10 minutes after a second injection of 0.1 mmol/kg gadolinium-chelate in three

Table 2 Baseline characteristics of 107 study patients.

Characteristics	
Clinical	
Age (years)	43.5 ± 19
Men	67 (62.6)
Recent infection/inflammation	46 (42.9)
Recent stress	13 (12.1)
Biological	
Peak serum concentration of	
Troponin (ng/mL)	9.0 ± 11
C-reactive protein (mg/L)	49.2 ± 77
Electrocardiographic	
Repolarization abnormalities	76 (71.0)
ST-segment elevation	14 (13.1)
Others	62 (57.9)
Transthoracic echocardiogram	
LVEF at admission (%)	48.2 ± 13
LVEF ≤40%	32 (29.9)
Pericardial effusion	15 (14.0)

LVEF: left ventricular ejection fraction.
Values are means ± standard deviations or numbers (%) of observations.

Table 3 Baseline cardiac magnetic resonance characteristics of 107 study patients.

CMR characteristics	
Cine mode	
LVEF (%)	53.4 ± 9
LVEF ≤40%	11 (10.3)
LV end-diastolic volume index (mL/m^2)	72.6 ± 5
Pericardial effusion	11 (10.3)
T2-weighted spin-echo sequences	
Oedema	53 (49.5)
First-pass perfusion imaging	
Microvascular obstruction	4 (4.6)
Presence of late gadolinium enhancement	78 (72.9)

CMR: cardiac magnetic resonance; LV: left ventricular; LVEF: left ventricular ejection fraction.
Values are means ± standard deviations or numbers (%) of observations.

planes, with breath-holding for each stack. The inversion time was chosen to null healthy myocardium, with a previous inversion-time scouting scan sequence. These settings were typically used: stack of 14–18 contiguous slices in the short-axis view; mean duration of apnoea, 18–20 seconds; 10–12 slices in left ventricular long-axis and four-chamber views; mean duration of apnoea, 12 seconds. Typical variables were: slice thickness, 10 mm; TR/TE, 4/1.25 ms; flip angle, 15°; FOV, 350–400; in-plane resolution, 1.5 × 2.4 mm; matrix, 224 × 142.

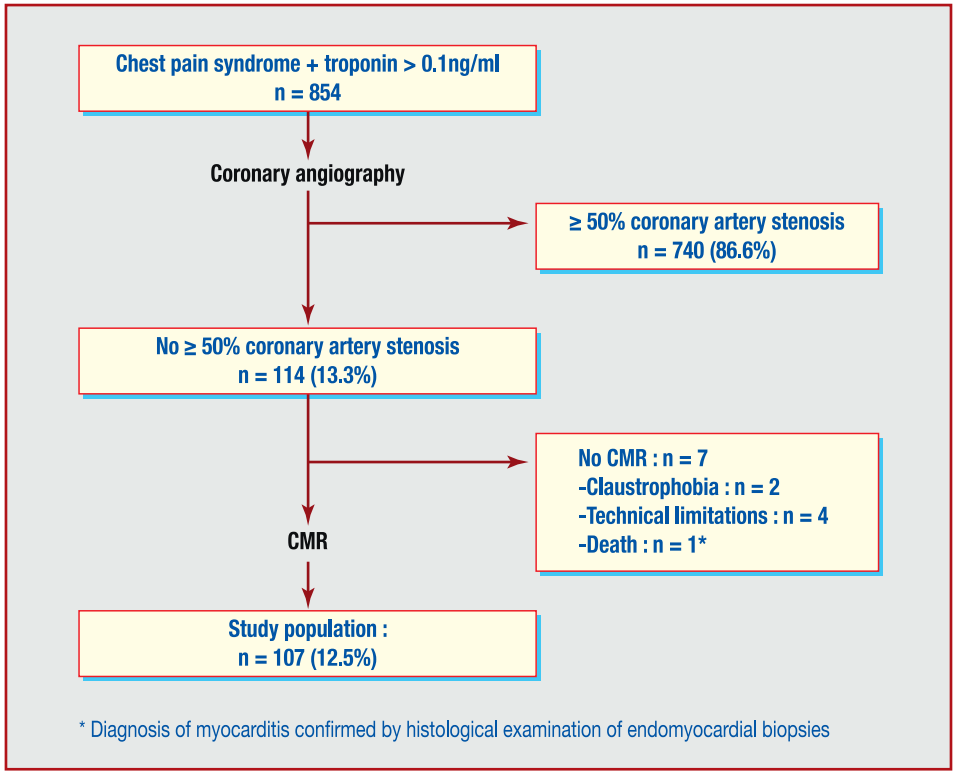

Figure 1. Flow of patients from screening to final selection for entry into the study. CMR: cardiac magnetic resonance.

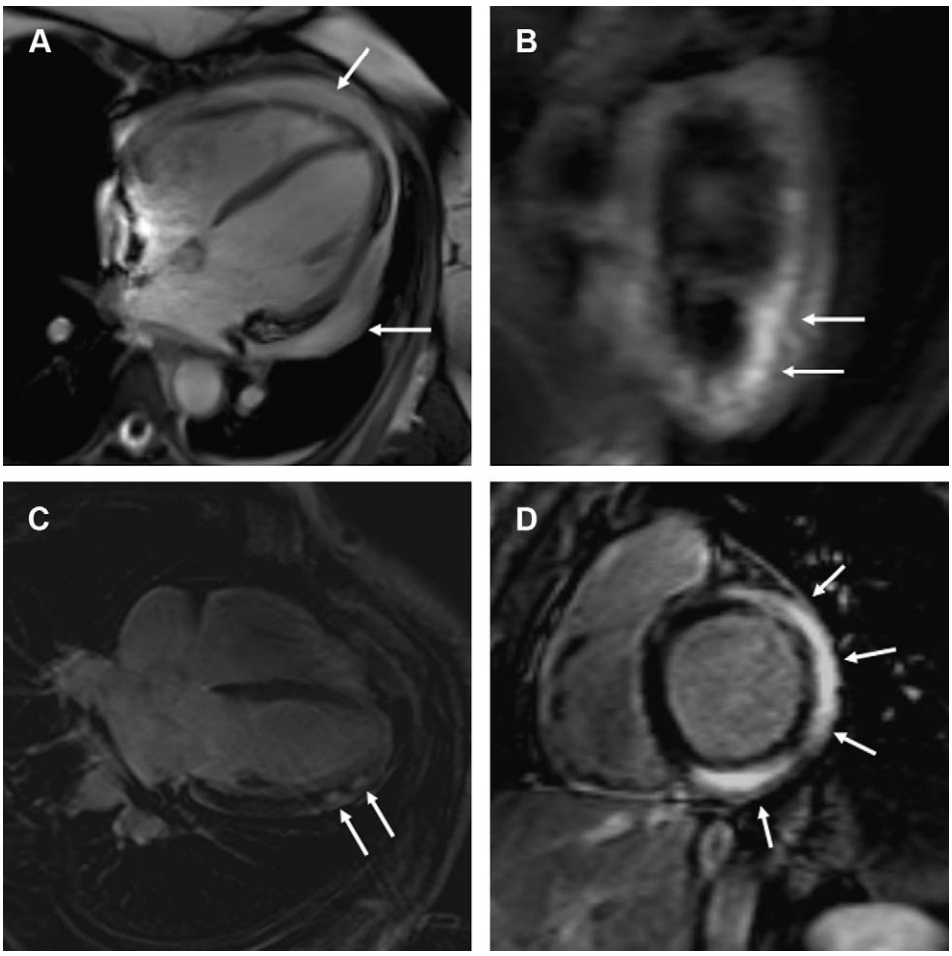

Figure 2. Various cardiac magnetic resonance patterns of myocarditis observed in this study. A. Circumferential pericardial effusion on the cine sequence. B. Hypersignal on the lateral wall on the T2-weighted sequence, corresponding to oedema. C. Subepicardial lateral nodular late gadolinium enhancement. D. Extensive late gadolinium enhancement.

Cardiac magnetic resonance analysis

The CRM scans were analysed by an experienced cardiologist and an experienced radiologist. Left ventricular ejection fraction (LVEF) and volumes were measured on short-axis stack cine imaging, using the dedicated software of a separate ViewForum™ workstation (Philips). LVEF and volumes, and the presence of myocardial abnormalities and pericardial effusion, were ascertained using standard techniques on cine mode [19]. T2-weighted sequences were visually reviewed for high-signal-intensity areas, consistent with myocardial oedema. The presence of microvascular obstruction was visually ascertained on first-pass perfusion images. Finally, the late gadolinium enhancement images were also visually reviewed for the presence, anatomical distribution and extent of subendocardial, subepicardial, mid-wall, and transmural contrast enhancement. A final CMR diagnosis was made according to the criteria listed in Table 1. CMR imaging was repeated if the images were interpreted as equivocal by the experienced observers.

Statistical analysis

The clinical, biological, electrocardiographic, TTE and CMR characteristics of patients with diagnostic versus normal CMR were compared. Quantitative data are expressed as means ± standard deviations. Between-group comparisons were made using Wilcoxon's test. Qualitative data are expressed as percentages and were compared using the Chi^2 or Fisher's test, as appropriate. All analyses were performed using SAS® statistical package version 9.1 (SAS Institute Inc., Cary, NC, USA). A P value <0.05 was considered statistically significant.

Results

Study population

The flow of patients between screening and entry into the study is shown in Fig. 1. Among 854 patients referred to our institution for acute chest pain with cTn elevation, 114 (13.3%) presented with an unobstructed coronary angiogram and 107 (12.5%) ultimately underwent CMR during the period of study enrolment. The baseline characteristics of the study population are presented in Table 2. No patient had a history of cardiomyopathy before enrolment. Coronary computed angiotomography was performed in eight patients (7.4%). LVEF at admission was 48.2 ± 13%. An LVEF ≤40% was found in 32 patients (29.9%) during the initial hospitalization and

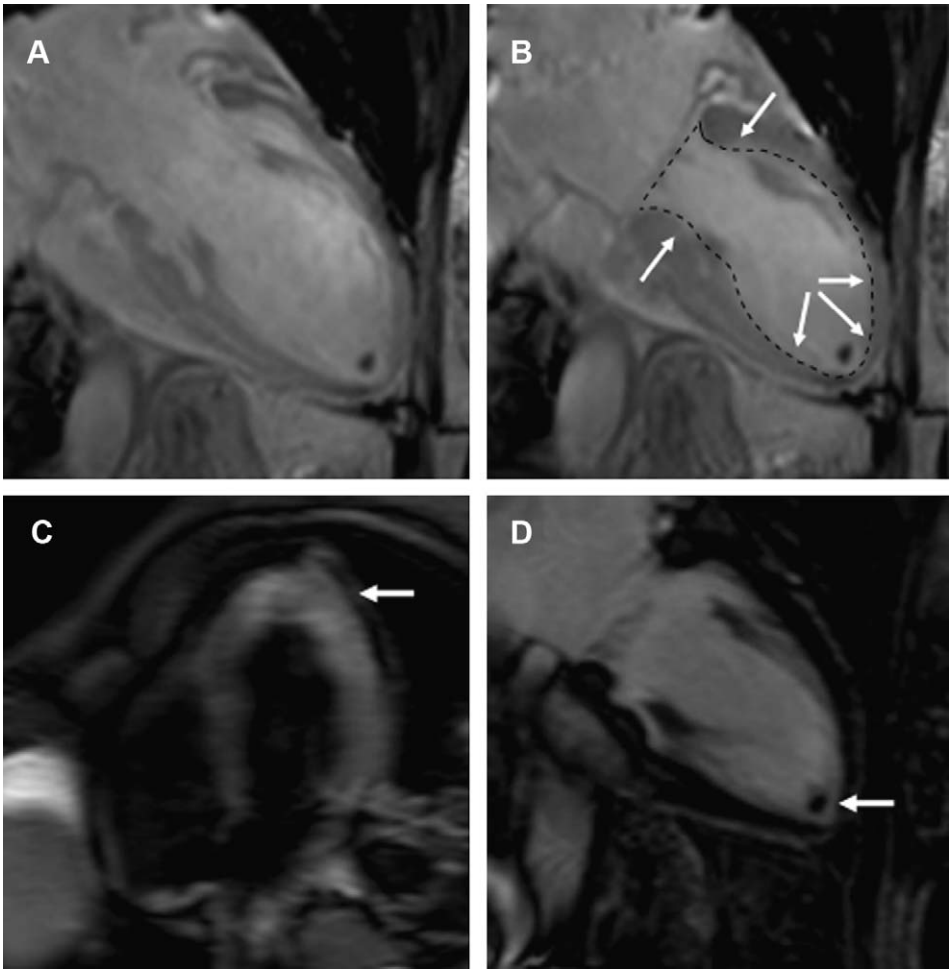

Figure 3. Cardiac magnetic resonance pattern of stress cardiomyopathy. A and B. Typical apical wall motion abnormalities in the cine sequences (Panel A, end-diastolic cine sequence; Panel B, end-systolic cine sequence). C. T2-weighted sequence showing the presence of apical oedema. D. Absence of late gadolinium enhancement, confirming the diagnosis of takotsubo syndrome. Cardiac magnetic resonance also reveals the presence of apical thrombus.

two patients (1.8%) required extracorporeal life support for 5 and 22 days, before undergoing CMR.

Cardiac magnetic resonance analysis

CMR imaging was completed in all patients without adverse events (Figs. 2—4). The median delay between the onset of symptoms and CMR was 5 days (mean 6.9 ± 9). A second image was obtained in nine patients (8.4%) because of equivocal initial images. The baseline CMR characteristics of the 107 study patients are presented in Table 3. A CMR diagnosis was made in 96 patients (89.7%), including myocarditis ($n = 64$, 59.9%), stress cardiomyopathy (takotsubo syndrome) ($n = 15$, 14.0%) and myocardial infarction ($n = 17$, 15.8%). CMR was normal in 11 patients (10.3%). No hypertrophic cardiomyopathy was found in this setting. The main clinical, biological, electrocardiographic, TTE and CMR observations made in the various final diagnostic subgroups are summarized in Table 4 and patients with diagnostic versus normal CMR are compared in Table 5.

The median age of the 64 patients with a final CMR diagnosis of myocarditis was 37 years, 71.8% were men and 62.5% had a recent history of viral infection or non-specific inflammation. Two patients (1.8%) had been previously hospitalized for management of myocarditis. Four of these 64 patients (3.7%) had inflammatory diseases, including scleroderma, Wegener's granulomatosis [20], rheumatoid arthritis and Crohn's disease. Fifteen patients (14.0%) presented with heart failure during the initial hospitalization; two of these patients needed circulatory mechanical assistance. The median delay between the onset of chest pain and the CMR scan was 4 days.

The median age of the 15 patients presenting with stress cardiomyopathy (or takotsubo syndrome) was 64 years, 86.6% were post-menopausal women and 86.6% had recent stress distinctly identified, including mourning ($n = 2$), disease or medical examinations ($n = 5$), travel ($n = 3$), family conflicts ($n = 2$) and a house fire ($n = 1$). A history of acute apical ballooning syndrome was elicited in three patients (20.0%), without CMR scan obtained 3, 5 and 10 years earlier. Despite only mild elevation of the cardiac enzymes, left ventricular dysfunction was severe, with 80.0% of these 15 patients presenting with an LVEF $\leq$40% during hospitalization. At the time of CMR scan, obtained after a median delay of 4 days, mean LVEF was 49.5%. An apical thrombus was detected by CMR in one patient (6.6%). Two patients (13.3%)

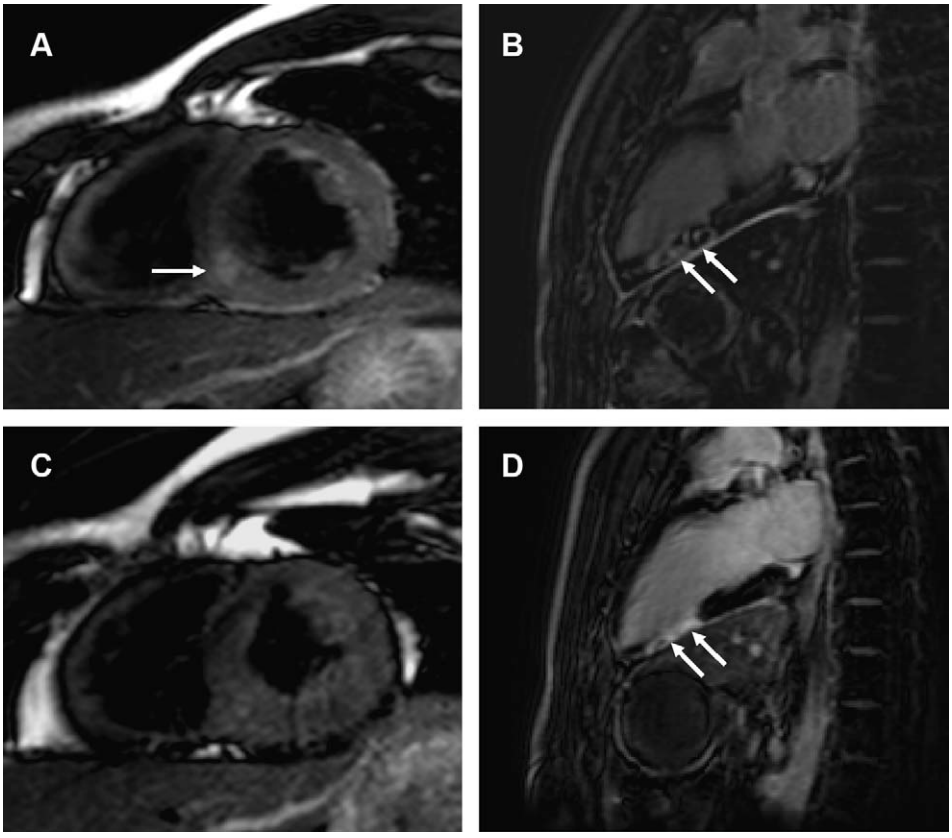

Figure 4. Cardiac magnetic resonance pattern of myocardial infarction. A and B (initial scan). T2-weighted sequence (Panel A) showing the presence of inferoseptal oedema with concordant but equivocal presence of late gadolinium enhancement (Panel B). C and D (follow-up scan, 4 months later). T2-weighted sequence showing the disappearance of oedema (Panel C) but the presence of transmural late gadolinium enhancement in a thinned segment is consistent with an ischaemic aetiology for the initial chest pain syndrome (Panel D).

developed life-threatening ventricular tachyarrhythmias, including ventricular fibrillation in one patient and ventricular tachycardia causing syncope in the other patient.

The 17 patients with a CMR diagnosis of myocardial infarction, despite the absence of obstructed coronary artery disease, represented a less homogeneous group, whose median age was 44 years. These 10 men and seven women presented without clinically contributory factors, such as recent inflammation, infection or stress. Despite a median delay of 5 days between TTE and CMR, the two tests yielded similar mean measurements of LVEF ($51.3 \pm 8\%$ and $49.6 \pm 7\%$, respectively). Complications were observed during the initial hospitalization in four patients (23.5%) including apical thrombi in two patients (one of whom had a reversible stroke) and sustained ventricular tachyarrhythmias in two patients. Finally, this initial ischaemic event disclosed the presence of sarcoidosis ($n = 1$), lupus erythematosus ($n = 1$) and paroxysmal atrial fibrillation ($n = 1$).

In the 11 patients with normal CMR, the median delay between onset of chest pain and imaging was 6 days. No particular clinical characteristic was identified in this group of patients. The main significant differences between patients with normal versus diagnostic CMR were a lower mean peak cTn (2.6 vs 9.7 ng/mL, $P = 0.01$), a better left ventricular systolic function (lowest LVEF 59.7 vs 46.8%, $P < 0.001$) and fewer patients with LVEF $\leq$40% (0 vs 33.3%, $P = 0.019$) in the ''normal'' CMR group. This group remained free of complications and, except for one patient with pheochromocytoma, had no concomitant illness diagnosed during hospitalization.

Discussion

This is the first report on the systematic application of 3-tesla CMR in a population of patients presenting with acute chest pain, elevated serum cTn and no angiographically significant coronary artery disease.

Diagnostic contributions of cardiac magnetic resonance

In this study, CMR provided a diagnosis in nearly 90% of patients. In a previous study by Assomull et al., who used a 1.5-tesla magnet in a similar but smaller patient population, the overall diagnostic contribution of CMR was 65%, including myocarditis in 50% of patients, myocardial infarction in 11.6% of patients and cardiomyopathy (including takotsubo syndrome) in 3.4% of patients [21]. The higher diagnostic yield of CMR in our study can be explained by: the higher field strength, higher signal-to-noise ratio and higher sensitivity of 3-tesla compared with 1.5-tesla CMR (although few

Table 4 Main observations according to the final cardiac magnetic resonance diagnosis.

Observations	Myocarditis ($n=64$)	Takotsubo syndrome ($n=15$)	Myocardial infarction ($n=17$)	Normal CMR ($n=11$)
Clinical				
Age (years)	36.8 ± 15	64.4 ± 17	44.5 ± 19	52.7 ± 16
Men	46 (71.8)	2 (13.3)	10 (58.8)	4 (36.3)
Recent infection/inflammation	40 (62.5)	0	3 (17.6)	3 (27.2)
Recent stress	0	13 (86.6)	0	0
Biological				
Peak serum concentration of				
Troponin (ng/mL)	10.5 ± 11	3.4 ± 3	12.4 ± 14	2.6 ± 3
C-reactive protein (mg/L)	59.9 ± 88	30.0 ± 36	12.4 ± 16	61.4 ± 76
Electrocardiographic				
Repolarization abnormalities	39 (60.9)	15 (100)	15 (88.2)	7 (63.3)
Transthoracic echocardiography				
LVEF at admission (%)	48.3 ± 13	35.8 ± 11	51.3 ± 8	59.7 ± 5
LVEF ≤40%	17 (26.5)	12 (80.0)	3 (17.6)	0
Pericardial effusion	13 (20.3)	0	2 (11.7)	0
Thrombus	0	0	1 (5.9)	0
Cardiac magnetic resonance				
LVEF (%)	54.4 ± 9	49.5 ± 12	49.6 ± 7	59.9 ± 4
LVEF ≤40%	4 (6.2)	4 (26.6)	3 (17.6)	0
LV end-diastolic volume index (mL/m^2)	70.6 ± 8	78.2 ± 16	74.1 ± 7	68.0 ± 6
Pericardial effusion	9 (14.0)	0	2 (11.7)	0
Thrombus	0	1 (6.6)	2 (11.7)	0
Oedema	37 (57.8)	6 (40.0)	10 (58.8)	0
Microvascular obstruction	0	0	4 (23.5)	0
Presence of late gadolinium enhancement	61 (95.3)	0	17 (100)	0

CMR: cardiac magnetic resonance; LV: left ventricular; LVEF: left ventricular ejection fraction.
Values are means ± standard deviations or numbers (%) of observations.

studies have compared the performances of these two types of magnets in the cardiovascular medicine setting [22]); and the shorter delay between onset of chest pain and CMR imaging. In the study by Assomull et al., the median interval between rise in serum cTn and CMR was 14.5 days compared with a median delay between onset of symptoms and CMR of 5 days in our study. During this interval of 9.5 days, several transient abnormalities that are detectable by CMR (such as dyskinetic wall motion, pericardial effusion and myocardial oedema), might have resolved. A more recent study from Spain, in 80 patients presenting with acute coronary syndrome and normal coronary arteries, reported results with 1.5-tesla CMR imaging that were similar to ours [23]. In that study, CMR provided a diagnosis in 95% of patients, including myocarditis in 63% of patients, myocardial infarction in 15% of patients and takotsubo cardiomyopathy in 11% of patients. Finally, in a population of only 23 patients, Christiansen et al. observed a 30% prevalence of myocardial scar [24]. This low prevalence can be explained by the exclusion from the study of patients presenting with changes consistent with myocarditis, limiting the population to patients with myocardial infarction in the absence of occlusive coronary artery disease. A similar patient selection in our study would have yielded a 39.5% prevalence of myocardial scar.

CMR for patients with elevated cTn, acute chest pain syndrome and unobstructed coronary arteries has a great impact on patient management, as knowledge of the diagnosis allows a better management of the disease. For instance, secondary prevention (statin, platelet aggregation inhibitors) may be necessary in case of myocardial infarction.

Disease prevalence

In our study, nearly 15% of patients presenting to our institution with acute chest pain and serum cTn >0.1 ng/mL had angiographically unobstructed coronary arteries. This proportion is concordant with those previously reported. In the FRISC II (Fragmin and fast revascularisation during instability in coronary artery disease II) study, 14% of the 2457 patients presenting with acute chest pain and elevated serum cTn or electrocardiographic changes had unobstructed coronary arteries [25]. Similar observations were made in the Platelet glycoprotein IIb/IIIa in unstable angina: receptor suppression using integrilin therapy (PURSUIT) study, with 12% of the 5767 patients presenting with unstable angina free from significant lesion on coronary angiograms [26]. Finally, in a meta-analysis of three separate Thrombolysis in myocardial

Table 5 Main observations made in patients with diagnostic versus normal cardiac magnetic resonance.

Observations	CMR		*p*
	Diagnostic (*n* = 96)	Normal (*n* = 11)	
Clinical			
Age (years)	42.4 ± 19	52.7 ± 16	0.059
Men	63 (65.6)	4 (36.3)	0.057
Recent infection/inflammation	43 (44.7)	3 (27.2)	0.26
Recent stress	13 (13.5)	0	0.19
Biological			
Peak serum concentration of			
Troponin (ng/mL)	9.7 ± 11	2.6 ± 3	0.01
C-reactive protein (mg/L)	48.2 ± 78	61.4 ± 67	0.43
Electrocardiographic			
Repolarization abnormalities	69 (71.8)	7 (63.3)	0.56
Transthoracic echocardiography			
LVEF at admission (%)	46.8 ± 12	59.7 ± 5	<0.01
LVEF ≤40%	32 (33.3)	0	0.019
Pericardial effusion	15 (15.6)	0	0.15
Cardiac magnetic resonance			
LVEF (%)	52.6 ± 9	59.9 ± 4	0.008
LVEF ≤40%	11 (11.4)	0	0.23
LV end-diastolic volume index (mL/m^2)	72.4 ± 12	68.0 ± 6	0.1
Pericardial effusion	11 (11.4)	0	0.23
Oedema	53 (55.2)	0	<0.001
Microvascular obstruction	4 (4.1)	0	0.49
Presence of late gadolinium enhancement	78 (81.2)	0	<0.001

CMR: cardiac magnetic resonance; LV: left ventricular; LVEF: left ventricular ejection fraction.
Values are means ± standard deviations or numbers (%) of observations.

infarction (TIMI) trials, 710 of 7656 patients (9.1%) had no angiographically visible coronary artery stenosis [27].

Normal cardiac magnetic resonance

Approximately 10% of patients presenting with acute chest pain syndrome and elevated serum cTn had normal CMR imaging studies. This may be partially explained by a longer median delay of 6 days between the onset of chest pain and CMR in this subgroup of patients versus 5 days in patients with contributory studies. We do not believe that the hypothesis of a false-positive elevation of cTn is plausible, as: repolarization abnormalities were present on the electrocardiogram in >60% of patients who had normal CMR images; in this group, the mean peak serum cTn was 2.6 ng/mL, far higher than 0.01 ng/mL (the upper limit of normal concentrations); and the mean peak serum concentration of C-reactive protein was 61 mg/L, also markedly above the upper limit of normal concentrations of 5 mg/L. These abnormalities were the manifestations of an unidentified underlying disorder. A modest yet unequivocal increase in cTn above the normal range is a sign of minimal myocardial necrosis. As the size of late gadolinium enhancement reflects the amount of necrosis [28,29], the size of the necrosis may have been insufficient to be detectable by CMR. Finally, it is noteworthy that all TTEs in this group were normal, suggesting that diagnostic tests that explore the cardiac structures are not helpful in these patients.

Study limitations

In this study, the final diagnosis was not systematically confirmed by histological analyses, in compliance with our institutional guidelines for the management of these patients, which do not include endomyocardial biopsies. Second, few patients underwent computed coronary angiotomography instead of coronary angiography. This is explained by the initial clinical presentation, often suggesting the presence of a myocardial infarction with ST-segment elevation, the management of which, in our institution, includes the direct admission of the patient to the catheterization laboratory. Third, we did not examine the early myocardial gadolinium enhancement, which might have highlighted myocardial hyperaemia in myocarditis [9] and reduced the number of normal CMR images. Fourth, the patients were not followed long term, which might have yielded prognostic information, particularly in the group with normal CMR images. Finally, despite being the largest study published thus far, the sample size in this single centre was small. Therefore, we believe that a multicentre registry needs to be organized.

Conclusions

CMR now plays a key role in the initial diagnosis and management of patients presenting with elevated serum cTn, acute onset of chest pain and unobstructed coronary arteries. CMR safely allowed the non-invasive identification of an aetiology without irradiation in approximately 90% of patients. The role of CMR needs to be emphasized, and a multicentre registry organized with a view to gathering further data on this common clinical presentation.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References

[1] Woodard PK, Bluemke DA, Cascade PN, et al. ACR practice guideline for the performance and interpretation of cardiac magnetic resonance imaging (MRI). J Am Coll Radiol 2006;3:665—76.

[2] Arai AE. False positive or true positive troponin in patients presenting with chest pain but ''normal'' coronary arteries: lessons from cardiac MRI. Eur Heart J 2007;28:1175—7.

[3] Mahajan N, Mehta Y, Rose M, et al. Elevated troponin level is not synonymous with myocardial infarction. Int J Cardiol 2006;111:442—9.

[4] Casolo G, Minneci S, Manta R, et al. Identification of the ischemic etiology of heart failure by cardiovascular magnetic resonance imaging: diagnostic accuracy of late gadolinium enhancement. Am Heart J 2006;151:101—8.

[5] Hillenbrand HB, Kim RJ, Parker MA, et al. Early assessment of myocardial salvage by contrast-enhanced magnetic resonance imaging. Circulation 2000;102:1678—83.

[6] Kim RJ, Fieno DS, Parrish TB, et al. Relationship of MRI delayed contrast enhancement to irreversible injury, infarct age, and contractile function. Circulation 1999;100:1992—2002.

[7] Laissy JP, Hyafil F, Feldman LJ, et al. Differentiating acute myocardial infarction from myocarditis: diagnostic value of early- and delayed-perfusion cardiac MR imaging. Radiology 2005;237:75—82.

[8] Abdel-Aty H, Boye P, Zagrosek A, 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.

[9] Friedrich MG, Sechtem U, Schulz-Menger J, et al. Cardiovascular magnetic resonance in myocarditis: a JACC White Paper. J Am Coll Cardiol 2009;53:1475—87.

[10] Mahrholdt H, Goedecke C, Wagner A, et al. Cardiovascular magnetic resonance assessment of human myocarditis: a comparison to histology and molecular pathology. Circulation 2004;109:1250—8.

[11] Mahrholdt H, Wagner A, Deluigi CC, et al. Presentation, patterns of myocardial damage, and clinical course of viral myocarditis. Circulation 2006;114:1581—90.

[12] Roditi GH, Hartnell GG, Cohen MC. MRI changes in myocarditis — evaluation with spin echo, cine MR angiography and contrast enhanced spin echo imaging. Clin Radiol 2000;55:752—8.

[13] Yelgec NS, Dymarkowski S, Ganame J, et al. Value of MRI in patients with a clinical suspicion of acute myocarditis. Eur Radiol 2007;17:2211—7.

[14] Abe Y, Kondo M, Matsuoka R, et al. Assessment of clinical features in transient left ventricular apical ballooning. J Am Coll Cardiol 2003;41:737—42.

[15] Eitel I, Behrendt F, Schindler K, et al. Takotsubo cardiomyopathy or myocardial infarction? Answers from delayed enhancement magnetic resonance imaging. Int J Cardiol 2009;135:e9—12.

[16] Leurent G, Larralde A, Boulmier D, et al. Cardiac MRI studies of transient left ventricular apical ballooning syndrome (takotsubo cardiomyopathy): a systematic review. Int J Cardiol 2009;135:146—9.

[17] Mitchell JH, Hadden TB, Wilson JM, et al. 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.

[18] Bruder O, Schneider S, Nothnagel D, et al. EuroCMR (European cardiovascular magnetic resonance) registry: results of the German pilot phase. J Am Coll Cardiol 2009;54:1457—66.

[19] Bellenger NG, Pennel DJ. Ventricular function. In: Manning WJ, Pennel DJ, editors. Cardiovascular magnetic resonance. New York: Churchill Livingstone; 2002. p. 99—111.

[20] Leurent G, Lentz PA, Henno S. A multimodal assessment of a multivisceral affect of a Wegener granulomatosis. Eur Heart J 2010;31:463.

[21] Assomull RG, Lyne JC, Keenan N, et al. The role of cardiovascular magnetic resonance in patients presenting with chest pain, raised troponin, and unobstructed coronary arteries. Eur Heart J 2007;28:1242—9.

[22] Wieben O, Francois C, Reeder SB. Cardiac MRI of ischemic heart disease at 3 T: potential and challenges. Eur J Radiol 2008;65:15—28.

[23] Laraudogoitia Zaldumbide E, Perez-David E, Larena JA, 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.

[24] Christiansen JP, Edwards C, Sinclair T, et al. Detection of myocardial scar by contrast-enhanced cardiac magnetic resonance imaging in patients with troponin-positive chest pain and minimal angiographic coronary artery disease. Am J Cardiol 2006;97:768—71.

[25] FRagmin and fast revascularisation during instability in coronary artery disease investigators. Invasive compared with non invasive treatment in unstable coronary-artery disease: FRISC II prospective randomised multicentre study. Lancet 1999;354:708—15.

[26] Roe MT, Harrington RA, Prosper DM, et al. Clinical and therapeutic profile of patients presenting with acute coronary syndromes who do not have significant coronary artery disease.The platelet glycoprotein IIb/IIIa in unstable angina: receptor suppression using integrilin therapy (PURSUIT) trial investigators. Circulation 2000;102:1101—6.

[27] Bugiardini R, Manfrini O, De Ferrari GM. Unanswered questions for management of acute coronary syndrome: risk stratification of patients with minimal disease or normal findings on coronary angiography. Arch Intern Med 2006;166:1391—5.

[28] Lin D, Kramer CM. Late gadolinium-enhanced cardiac magnetic resonance. Curr Cardiol Rep 2008;10:72—8.

[29] Vohringer M, Mahrholdt H, Yilmaz A, et al. Significance of late gadolinium enhancement in cardiovascular magnetic resonance imaging (CMR). Herz 2007;32:129—37.