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FULL PAPER

Cardiac MR enables diagnosis in 90% of patients with acute chest pain, elevated biomarkers and unobstructed coronary arteries

[1]T EMRICH, MD, [1]K EMRICH, MD, [2]N ABEGUNEWARDENE, MD, [1]K OBERHOLZER, MD, PhD, [1]C DUEBER, MD, PhD, [2]T MUENZEL, MD, PhD and [1]K-F KREITNER, MD, PhD

[1]Department of Diagnostic and Interventional Radiology, Universitätsmedizin, Johannes Gutenberg University of Mainz, Mainz, Germany
[2]Department of Cardiology, Universitätsmedizin, Johannes Gutenberg University of Mainz, Mainz, Germany

Address correspondence to: Mr Tilman Emrich
E-mail: *Tilman.Emrich@unimedizin-mainz.de*

Objective: To assess the diagnostic value of cardiac MRI (CMR) in patients with acute chest pain, elevated cardiac enzymes and a negative coronary angiogram.
Methods: This study included a total of 125 patients treated in the chest pain unit during a 39-month period. Each included patient underwent MRI within a median of 3 days after cardiac catheterization. The MRI protocol comprised cine, oedema-sensitive and late gadolinium-enhancement imaging. The standard of reference was a consensus diagnosis based on clinical follow-up and the synopsis of all clinical, laboratory and imaging data.
Results: MRI revealed a multitude of diagnoses, including ischaemic cardiomyopathy (CM), dilated CM, myocarditis, Takotsubo CM, hypertensive heart disease, hypertrophic CM, cardiac amyloidosis and non-compaction CM. MRI-based diagnoses were the same as the final reference diagnoses in 113/125 patients (90%), with the two diagnoses differing in only 12/125 patients. In two patients, no final diagnosis could be established.
Conclusion: CMR performed early after the onset of symptoms revealed a broad spectrum of diseases. CMR delivered a correct final diagnosis in 90% of patients with acute chest pain, elevated cardiac enzymes and a negative coronary angiogram.
Advances in knowledge: Diagnosing patients with acute coronary syndrome but unobstructed coronary arteries remains a challenge for cardiologists. CMR performed early after catheterization reveals a broad spectrum of diseases with only a simple and quick examination protocol, and there is a high concordance between MRI-based diagnoses and final reference diagnoses.

Acute coronary syndrome (ACS) is a common working diagnosis in emergency and chest pain units worldwide. Acute chest pain is the cardinal symptom of an ACS, but clinical findings vary among patients, ranging from mild discomfort to severe cardiac arrhythmias and sudden cardiac death. Among all patients admitted to a hospital with acute chest pain, only 30% receive a final diagnosis of ACS.[1] This is reasonable owing to the multitude of differential diagnoses for troponin-positive acute chest pain ranging from ST-elevation myocardial infarction to non-cardiac aetiologies, such as pulmonary embolism and sepsis.[2,3]

In addition to the examination of clinical signs and symptoms, electrocardiogram (ECG) diagnostics and troponin measurements are routinely used in ACS evaluation. Standard 12-lead ECG is a key diagnostic tool for determining which patients with suspected acute myocardial infarction should be directed to the angiography suite.[4] However, while ST elevations may indicate myocardial infarction, they can also be owing to other serious conditions, including pericarditis, myocarditis, cardiomyopathy (CM) and congestive heart failure. Moreover, ACS can be present even without ECG changes, for example, in cases of non-ST-elevation myocardial infarction (NSTEMI) or unstable angina pectoris.[3–5]

Cardiac troponin measurement, especially with implementation of highly sensitive assays, plays a central role in establishing a diagnosis and stratifying risk in patients with ACS.[6,7] However, aetiological diagnosis remains challenging in cases of troponin-positive acute chest pain with either normal coronary arteries or non-flow-limiting coronary artery disease. There are many possible responsible entities, such as clot lysis and recanalization of an acute thrombotic obstruction, coronary thromboembolism, acute myocarditis, apical ballooning syndrome, coronary vasospasm, inherited

thrombophilia, non-ischaemic cardiomyopathies and non-cardiac aetiologies.[3,8]

Cardiac MRI (CMR) does not yet have a well-established role in patients with suspected ACS and is not part of the routine clinical work-up described in the current guidelines of the European Society of Cardiology.[9] However, increasing evidence suggests that CMR may provide incremental diagnostic value in these patients.[10–13] We have adopted CMR in the diagnostic work-up of patients with suspected ACS.

The present study aimed to investigate the diagnostic value of CMR in patients with suspected ACS. As a standard of reference, we used a consensus-based final diagnosis established using clinical follow-up of up to 3 months after admission and the synopsis of all clinical, laboratory and imaging findings.

METHODS AND MATERIALS

Patient recruitment

We searched our data files for patients who presented with acute chest pain, elevated cardiac enzymes and non-obstructed coronary arteries at coronary angiography and who underwent CMR within a 39-month period between January 2007 and March 2010. Following current guidelines,[9] all patients underwent 12-lead ECG, determination of cardiac biomarkers and echocardiography within the first 20 min after admission to the chest pain unit. Coronary obstruction could not be ruled out in any case, even among patients without ST elevation. Therefore, all patients underwent coronary angiography within 12 h, which did not reveal relevant stenotic lesions in any case.

Subsequently, CMR was performed to exclude myocardial infarction and to provide an alternative diagnosis to explain the clinical presentation without reference to the previous results. Patients with a history of myocardial infarction and chronic troponin elevation were excluded, as were any patients with standard contraindications to CMR (*e.g.* claustrophobia or pacemaker). All patients gave their written informed consent to undergo CMR. Owing to the retrospective study design and the fact that CMR was performed as a routine part of the diagnostic work-up in these patients, the requirement for study approval by the local ethics committee was waived.

Cardiac MRI protocol

CMR was performed with a 1.5-T MAGNETOM® Sonata® MRI scanner (Maestro Class; Siemens Healthcare, Erlangen, Germany) using a six-channel phased-array cardiac coil and integrated spine array coil elements for signal detection. For imaging, all patients were positioned in the supine position.

Global and regional ventricular function was assessed via cine imaging using a segmented steady-state free precession pulse sequence. To cover the entire left ventricle, we acquired images in horizontal and vertical long-axis views as well as in multiple short-axis views every 10 mm. Typical inplane resolution was $2.0 \times 1.5\ mm^2$, with a section thickness of 6.0 mm, section gap of 4.0 mm, repetition time (TR)/echo time (TE) of 3.02/1.51 ms, flip angle of 60° and temporal resolution of 33.22 ms. Parallel imaging was performed using the GRAPPA (generalized autocalibrating partially parallel acquisition) algorithm, with an acceleration factor of 2, and 33 reference lines.

For oedema-sensitive imaging, we used a triple inversion recovery turbo spin echo sequence (TIRM) with acquisition in the same long- and short-axis planes [TE, 60 ms; TR, $2 \times$ RR interval; inversion time (TI), 170 ms; slice thickness, 10 mm; flip angle, 180° and pixel size, $2.3 \times 1.3\ mm^2$]. The integrated body coil was used for signal detection of this sequence.

Each CMR examination was enhanced with $0.2\ mmol\ kg^{-1}$ body weight of gadopentetate dimeglumine (Magnevist®; Bayer Vital, Leverkusen, Germany). 10 min after contrast application, late enhancement images were acquired using a segmented T_1 weighted inversion recovery turboFLASH sequence in identical long- and short-axis planes (TE, 4.38 ms; TR, $2 \times$ RR interval; flip angle, 25°; pixel size, $1.4 \times 1.8\ mm^2$; section thickness, 8 mm and section gap, 2 mm). After acquisition of a TI scout for each patient, TI was adjusted to optimize the nullification of normal myocardium. TI ranged between 260 and 320 ms and was increased by 10 ms approximately every minute during the acquisition to optimally "null" the normal myocardium.

Cardiac MRI analysis

Left ventricular (LV) ejection fraction, LV mass and ventricular volumes were measured with short-axis stack cine imaging, using semi-automated software (Argus v. 2.3; Siemens Medical Systems). All ventricular volumes were indexed for body surface area (BSA). Qualitative interpretation of CMR scans was performed based on the consensus between two experienced interpreters who were blinded to clinical details. Cine images were reviewed, including assessment of regional wall thickness and wall motion abnormalities. Fat-suppressed TIRM images were examined for areas of high signal intensity suggesting oedema and used for measuring the ratio of myocardial signal intensity to that of skeletal muscle. A ratio of >1.9 was considered to indicate a significant increase in signal intensity.[14] Finally, late-gadolinium-enhancement (LGE) images were assessed for the presence of areas of no-reflow (microvascular obstruction) and enhancing areas, as well as their locations within the myocardial tissue (*e.g.* subendocardial, subepicardial, midwall or transmural) and their segment-wise distribution. Segmental analysis of the left ventricle was performed using the 17-segment model of the American Heart Association.[15]

Acute myocardial infarction was diagnosed if image analysis revealed subendocardial or transmural late enhancement in the distribution of a coronary artery, accompanied by oedema and a regional wall motion abnormality (hypo- or akinesia) in that territory, which were larger than the LGE area.[12,16] Myocarditis was diagnosed in cases presenting with focal or diffuse areas of oedema not related to the territory of a coronary artery, along with LGE in at least one segment of the subepicardial or midventricular myocardial layers. In these cases, cine imaging revealed either a normal or only mildly reduced global systolic function and no apparent regional wall motion abnormalities.[14]

Takotsubo CM was diagnosed in patients showing dyskinetic myocardial segments that created a ballooning pattern on cine

images, mostly involving the left ventricle apex and not restricted to the territory of a coronary artery, along with slight-to-moderate reduction of global systolic LV function. These cases also showed myocardial oedema in the dysfunctional segments and an absence of substantial necrosis/fibrosis on LGE images.[17]

Dilated CM (DCM) was diagnosed in patients showing increased normalized volumes and reduced systolic function, without evidence of significant oedema on fat-suppressed images. When LGE was present, it showed a predominantly midwall distribution, mostly in the interventricular septum. LV non-compaction was diagnosed in the presence of prominent trabeculations, such that the trabeculated LV mass comprised >20% of the global LV mass, among patients with impaired systolic LV function and increased normalized volumes.[18,19]

Hypertensive heart disease was suspected in patients presenting with an end-diastolic wall thickness of the interventricular septum of ≤13 mm, a concentric hypertrophy of the LV myocardium and preserved or only mildly reduced global systolic LV function. These findings were sometimes accompanied by diffuse LV oedema and mild foci of midventricular or subepicardial enhancement on LGE images.[20–22] Hypertrophic CM was diagnosed in cases showing a focal or diffuse wall thickness of ≥18 mm and an increased normalized myocardial mass, along with the presence of areas of fibrosis within the thickened myocardium.[20,21,23] Cardiac amyloidosis was diagnosed in cases exhibiting concentric hypertrophy of the right and left myocardium and thickening of valve leaflets, atrial walls and septum, as well as LGE imaging results showing global or subendocardial enhancement of these structures.[21,24]

Arrhythmogenic right ventricular cardiomyopathy (ARVC) was diagnosed in cases that showed a right ventricular akinesia or dyskinesia or dyssynchronous right ventricular contraction. Other major criteria for ARVC diagnosis were as follows: a ratio of right ventricular end-diastolic volume to BSA of $\geq 110\,ml\,m^{-2}$ for males or of $\geq 100\,ml\,m^{-2}$ for females, or a right ventricular ejection fraction of ≤40%. Minor criteria for ARVC diagnosis included a right ventricular end-diastolic volume to BSA ratio of ≥100 and $<110\,ml\,m^{-2}$ for males and of ≥90 and $<100\,ml\,m^{-2}$ for females, or a right ventricular ejection fraction of >40% and ≤45%.[25]

Clinical data and final reference diagnosis

Clinical data included medical history, examination and ECG findings, troponin levels and the results of clinical follow-up with repeat echocardiographic examinations in the vast majority of patients. All coronary angiograms were reviewed by an experienced interpreter to verify that any stenosis of the epicardial vessels was <50%. The final reference diagnosis was made by the cardiologist based on the synopsis of all clinical, laboratory and imaging data combined with the findings of patient follow-up for up to 3 months. This diagnosis was compared with the diagnosis made based on only the results of MRI.

Statistics

Normally distributed continuous data are expressed as mean ± standard deviation, while continuous data with a non-normal distribution are shown as median and interquartile range. Categorical data are displayed as an absolute value and the percentage. Between-group comparisons were performed using either the nonparametric Wilcoxon rank-sum test for non-normally distributed continuous data or Fisher's exact test for categorical variables. All tests were two sided. A p-value of <0.05 indicated a significant difference on a local level. All computations were performed using SPSS® software v. 19.0 for Windows® (SPSS Inc., Chicago, IL).

RESULTS

This study included a total of 125 patients: 83 males and 42 females, with a mean age of 53.5 ± 15.1 years (range, 20–81 years). The median time interval between coronary angiography and CMR imaging was 3 days (interquartile range, 1–5 days). Table 1 lists the baseline characteristics of the patients with regard to clinical findings, biomarker elevation and MRI findings.

In 100/125 patients (80%), the diagnoses based on clinical, laboratory and echocardiographic data were in agreement with the diagnoses based on only MR data. Review of the 25 differing cases resulted in changes of the final reference diagnosis in 13 patients, such that the CMR diagnoses corresponded with the final reference diagnosis in 113/125 (90.4%) patients. Table 2 displays the CMR-based and final reference diagnoses. The most frequent diagnoses were myocarditis, followed by DCM, acute myocardial infarction, Takotsubo CM and hypertensive heart disease.

Among the final diagnoses, discrepancies occurred in 12 patients. CMR results failed to show tachycardia-induced CM in all five such cases. Three of these patients were diagnosed as having DCM, one as having hypertensive heart disease and another as having myocarditis. Two patients diagnosed with hypertensive heart disease based on CMR were given final reference diagnoses of myocarditis and DCM, respectively. Among four patients diagnosed with myocarditis based on CMR, two had final reference diagnoses of hypertensive heart disease; one of arrhythmias; and in one patient no final diagnosis could be made. One patient was suspected to have ARVC based on CMR but was found to have no structural heart disease. Considering the main diagnoses, CMR correctly identified all patients with acute myocardial infarctions and Takotsubo CM.

Table 3 summarizes the clinical, laboratory and functional CMR parameters of the five main cardiac diagnoses. Patients with final diagnoses of myocarditis showed median troponin and creatine kinase elevations of $4.03\,ng\,dl^{-1}$ and $470\,U\,l^{-1}$, respectively. Their functional parameters revealed an overall slight reduction in global systolic function of the left ventricle. Compared with patients with other diagnoses, those suffering from myocarditis were significantly younger ($p < 0.001$) and more often males ($p = 0.002$). Patients with DCM showed only moderately elevated cardiac enzymes ($p < 0.001$) but severe impairment of LV function and significantly increased LV-end-diastolic volume index ($p < 0.001$ for both).

Patients with acute myocardial infarction showed the highest elevation of cardiac enzymes ($p < 0.001$) and only slightly reduced global LV function. Patients with Takotsubo CM were significantly older ($p < 0.001$) and more often females ($p = 0.003$). Overall, the

Table 1. Baseline characteristics of 125 study patients

Characteristics		Range	Normal value
Clinical			
Age (years)	53.5 ± 15.1	20–81	
Males	83/125 (66.4%)		
Females	42/125 (33.6%)		
Biological			
Peak serum concentration			
Troponin ($ng\,dl^{-1}$)	1.78 (0.39–8.14)	0.02–293.0	<0.1
Creatine kinase ($U\,l^{-1}$)	462 (263–908)	178–8429	30–200
Cardiac MRI characteristics			
Cine imaging			
LV ejection fraction (%)	44.8 ± 17.8	5.0–80.0	56–78
LV end-diastolic volume index ($ml\,m^{-2}$)	74.6 (64.1–107.4)	6.0–315.9	47–92
LV end-systolic volume index ($ml\,m^{-2}$)	35.3 (27.6–63.1)	5.7–263.2	12.8–30.0
LV stroke volume index ($ml\,m^{-2}$)	35.8 ± 12.6	0.3–81.5	32.0–62.0
Cardiac index ($l\,min^{-1}\,m^{2}$)	2.6 ± 0.9	0.03–5.7	1.7–4.2
Oedema	91/125 (72.8%)		
Presence of late gadolinium enhancement	120/125 (96%)		

LV, left ventricular.
Normally distributed continuous data are expressed as mean ± standard deviation, while non-normally distributed continuous data are shown as median and interquartile range. Categorical data are displayed as an absolute value (percentage).

Takotsubo CM group showed moderate-to-severe impairment of the LV function at the time of CMR.

DISCUSSION

Patients with acute chest pain, elevated cardiac enzymes and unobstructed coronary arteries continue to present a diagnostic and therapeutic challenge for cardiologists.[3,26] This patient group reportedly represents between 1.9% and 15% of the patients in cohorts undergoing cardiac catheterization, depending on the definitions of biomarkers levels and ECG changes.[13,27–31] Receiving a correct final diagnosis is important in these cases, as this diagnosis will influence prescriptions for

Table 2. Cardiac MRI (CMR)-based diagnoses and final reference diagnoses

Diagnoses by CMR, *n* (%)		Final consensus diagnoses, *n* (%)	
Myocarditis	52 (41.6)	Myocarditis	48 (38.4)
DCM	25 (20.0)	DCM	23 (18.4)
AMI	20 (16.0)	AMI	20 (16.0)
Takotsubo CM	12 (9.6)	Takotsubo CM	12 (9.6)
HHD	10 (8.0)	HHD	9 (7.2)
HCM	2 (1.6)	HCM	2 (1.6)
ARVC	2 (1.6)	ARVC	1 (0.8)
Cardiac amyloidosis	1 (0.8)	Cardiac amyloidosis	1 (0.8)
LVNC-CM	1 (0.8)	LVNC-CM	1 (0.8)
		Tachycardia induced CM	5 (4.0)
		Arrhythmias	1 (0.8)
		No structural heart disease	2 (1.6)

AMI, acute myocardial infarction; ARVC, arrhythmogenic right ventricular cardiomyopathy; CM, cardiomyopathy; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; HHD, hypertensive heart disease; LVNC, left ventricular non-compaction.

Table 3. Biomarker and cardiac MRI characteristics of the five main diagnoses

Characteristics	Myocarditis	Dilated cardiomyopathy	Acute myocardial infarction	Takotsubo cardiomyopathy	Hypertensive heart disease
n	48	23	20	12	9
Age (years)	45.5 ± 14.5	56.1 ± 9.9	54.7 ± 14.4	74.5 (64.8/77.8)	60.9 ± 16.7
Male (sex)	40 (83.3%)	14 (60.9%)	8 (40%)	3 (25%)	7 (77.8%)
Troponin (ng dl^{-1})	4.04 (1.08/11.86)	0.19 (0.13/0.36)	12.0 (7.8/32.1)	1.78 (0.50/2.97)	1.34 (0.67/1.80)
Creatine kinase (U l^{-1})	470 (291.8/822.8)	341 (201.0/1008.0)	763.5 (525.0/2057.5)	238 (227.5/334.5)	466 (286.3/816.8)
LV ejection fraction (%)	55.6 ± 9.9	16.7 (14.9/23.4)	50.8 (39.7/59.1)	42.4 ± 14.3	54.9 (42.0/64.5)
LV end-diastolic volume index (ml m^{-2})	72.7 (66.5/80.8)	155.3 ± 65.9	77.1 ± 28.9	76.3 (58.7/89.1)	65.2 ± 18.8
LV end-systolic volume index (ml m^{-2})	31.2 (27.7/39.2)	125.8 ± 58.7	40.7 ± 23.0	42.6 ± 18.4	26.0 (22.9/32.5)
Stroke volume index (ml m^{-2})	42.7 ± 11.9	39.6 ± 12.5	36.3 ± 8.1	29.5 ± 11.1	32.6 ± 11.6
Cardiac index (l min^{-1} m^{2})	2.9 ± 0.9	2.3 ± 1.0	2.9 ± 0.7	2.0 ± 0.6	2.3 (1.6/2.9)
Oedema	48/48 (100%)	3/23 (13.0%)	19/20 (95.0%)	12/12 (100%)	6/9 (66.7%)
Late gadolinium enhancement	45/48 (93.8%)	23/23 (100%)	20/20 (100%)	12/12 (100%)	9/9 (100%)

LV, left ventricular.
Normally distributed continuous data are expressed as mean ± standard deviation, while non-normally distributed data are shown as median and interquartile range. Categorical data are displayed as an absolute value (percentage).

treatment and determination of fitness for permissible activities, occupation and medical insurance.[32] Recent evidence suggests that CMR may play an important role in patients presenting with acute chest pain, elevated biomarkers and unobstructed coronary arteries.[10,11,13,30,31,33–35] Here, we found that CMR-based diagnoses in 90% of patients were identical to the final reference diagnoses made by a cardiologist based on a synopsis of all clinical, laboratory and imaging data (coronary angiography, echocardiography and CMR) combined with a clinical follow-up of up to 3 months.

The present study showed a multitude of different cardiac diagnosis, ranging from myocarditis to LV non-compaction CM (Table 2). Compared with previous publications, the present number of patients without any diagnosis was very low (2/125 patients, 1.6%). This may be because CMR was performed within 3 days after cardiac catheterization in the vast majority of patients,[30,32] which would substantially lower the risk of missing transitory imaging findings.

Our patient cohort also showed a high prevalence of oedema and LGE of >90%, which is not typical for patients with DCM or hypertensive heart disease. However, all patients presented with acute clinical symptoms and showed biomarker release indicating myocardial cell damage irrespective of the underlying disease. Most of the patients with hypertensive heart disease presented with a hypertensive crisis at the chest pain unit. We can speculate that this may have led to disturbance of the microvasculature of the myocardial tissue, consequently resulting in oedema and/or a positive LGE imaging finding.

The five main diagnoses in the present study were myocarditis, DCM, acute myocardial infarction, Takotsubo CM and hypertensive heart disease. The prevalence of myocarditis, acute myocardial infarction and Takotsubo CM corresponded to the ranges reported in other recent studies.[11,13,30–35] Myocarditis occurred with the highest prevalence in our cohort. This can be explained by the difficulty of interpreting the clinical signs of myocarditis, as they vary from mild discomfort, fever and mild chest pain to severe clinical conditions, such as arrhythmias and cardiogenic shock. Furthermore, initial clinical test results (*e.g.* ECG changes and cardiac enzyme elevation) can often be similar to those seen in acute myocardial infarction.[36]

CMR led to the correct diagnosis of acute myocardial infarction and Takotsubo CM in all such cases. In cases of Takotsubo CM, it is essential to perform imaging as early as possible because the regional wall motion abnormalities may be rapidly reversible.[17,35] Although areas of LGE are often lacking in patients with Takotsubo CM, all patients with Takotsubo CM in our present series demonstrated faint areas of LGE, which is in line with other recent reports.[17,37,38] Acute myocardial infarction, even in the absence of a relevant stenosis of the epicardial vessels during coronary angiography, is an important differential diagnosis that can be easily detected with CMR. Potential mechanisms of myocardial infarction without relevant stenosis of the epicardial arteries include coronary vasospasm and embolism as well as thrombosis with spontaneous recanalization of the affected vessel.[27,28]

Compared with the reference standard in our study, the CMR-based diagnoses were incorrect in 12 patients. In five patients, CMR results failed to indicate a diagnosis of tachycardia-induced CM. Tachycardia-induced CM is considered a DCM mimicking and potentially reversible form of congestive heart failure.[39] Of these five patients, three were primarily diagnosed as having DCM by CMR. In these three patients, 3 months of follow-up revealed that the LV size and function returned to normal values after successful treatment of tachycardia.[39,40]

In four cases, CMR could not differentiate between myocarditis, hypertensive heart disease and DCM. This was partly owing to an overlap of imaging features that may exist in patients with myocarditis and hypertensive heart disease, especially when only conventional imaging techniques are used. Arrhythmias were regarded as the source of one patient's acute chest-pain syndrome. Finally, in two patients lacking any structural heart disease, the cause of the chest pain and elevated biomarkers remained unclear. It is possible that the clinical presentation in these cases involved a false-positive troponin test and/or the presence of non-cardiac disease.

Since only two patients were not given a final explanation for their clinical presentation, CMR correctly assigned a final diagnosis in 113/123 patients (92%). This demonstrates the diagnostic power and usefulness of CMR in an emergency setting.[2,12] The MRI protocol used in our study was kept as simple as possible, consisting of only three imaging techniques: cine, oedema-sensitive and late-enhancement imaging. All patients underwent a coronary catheterization that excluded substantial stenosis of the coronary arteries before CMR; therefore, we did not perform perfusion imaging, in contrast with previous studies.[31,33,35] A very recent multicentre study of 120 patients also achieved a high diagnostic yield by using only conventional imaging techniques with a similar imaging protocol.[32] Analogous to our present study, this previous study performed CMR early after cardiac catheterization within a median of 3 days (interquartile range, 1–6 days). The use of novel tissue characterization techniques (T_1 mapping) improved the detection rate of myocardial injury from 95% with use of conventional imaging techniques to 98%.

These results strengthen the evidence for a useful role of CMR in patients with suspected ACS in an emergency setting. However, it remains unclear whether it is possible to identify those patients who should primarily undergo CMR instead of cardiac catheterization. It may be prudent to use CMR in younger patients who have a low probability of acute myocardial infarction. A potential time frame for implementation of the CMR examination could be easily established for mid- and low-risk NSTEMI cases, as current guidelines suggest a time to catheterization of 24–72 h.[9] Further research in larger patient cohorts is needed to develop a general recommendation.

Furthermore, there remains a paucity of knowledge concerning the prognostic implications of CMR abnormalities. Gerbaud et al[33] recently investigated 130 patients with acute chest pain, elevated troponin and unobstructed coronary arteries, with a mean follow-up of more than 34 months in 124 patients. They reported that CMR provided a formal diagnosis (acute myocardial infarction, myocarditis and Takotsubo CM) in 100/130 patients (77%). They found no statistical differences in the occurrence of major adverse cardiac event between patients with and without a CMR diagnosis. On the other hand, Chopard et al[41] investigated 87 patients and found that CMR provided a final diagnosis in only 55 (63%) patients. They observed adverse events within a 1-year follow-up period in 14/55 patients (25%), whereas no adverse events occurred in patients with a normal CMR study ($n = 32$).

Limitations

The present study has several limitations. One limitation is that the final reference diagnosis was based on the synopsis of all clinical, laboratory and imaging findings—including findings of CMR imaging and during a follow-up of up to 3 months. Data from follow-up enabled the diagnosis of tachycardia-induced CM, as the normalization of LV function documented by repeat echocardiography was paralleled by the normalization of tachycardia. However, the correctness of the CMR-based diagnosis can at least partly be explained by an imaging bias, as the cardiological diagnosis was influenced by the results of CMR in this clinical setting. Despite this bias, the fact that one test enabled a correct diagnosis in 90% of patients clearly demonstrates the value of CMR in the acute setting.

Another limitation is that we did not routinely perform endomyocardial biopsy in our patients and thus histopathological confirmation was available in only a few patients with myocarditis.[30] However, EMB carries a risk of reduced sensitivity owing to sample errors. Furthermore, current recommendations[42] state that EMB has a Class I recommendation with a B level of evidence only among the following patients: those with new-onset heart failure with a duration of less than 2 weeks with a normal-sized or dilated LV and haemodynamic compromise; and in patients with new-onset heart failure with a duration of 2 weeks–3 months with a dilated LV and with new ventricular arrhythmias, second- or third-degree heart block, or failure to respond to usual care within 1–2 weeks.

Moreover, it should be noted that the retrospective study design and the limited number of patients limit the statistical power and hamper the possibility to generalize the present findings to larger populations. Additionally, the presently utilized CMR protocol was unable to rule out non-cardiac differential diagnoses of troponin elevation and acute chest pain, such as pulmonary embolism and sepsis. Finally, we must point out that our study period ended almost 5 years ago. Over the past 5 years, there have been several improvements in sequence design (for example T_1 and T_2 mapping), which improve the diagnostic precision of CMR imaging. However, these techniques are not yet used routinely as they are not available in all institutions worldwide.

CONCLUSIONS

CMR is a useful tool with a high diagnostic yield among patients with acute chest pain, elevated biomarkers and unobstructed coronary arteries. When performed early after cardiac catheterization, CMR with a conventional protocol enabled a definitive diagnosis in 90% of such patients and is thus useful in the further diagnostic work-up and management of these patients. Further studies are required to determine the prognostic implications of CMR in this patient cohort.

REFERENCES

1. Post F, Münzel T. Acute coronary syndrome. A diffuse diagnosis. [In German.] *Internist (Berl)* 2010; **51**: 953–62. doi: 10.1007/s00108-009-2536-2
2. Budge LP, Salerno M. The role of cardiac magnetic resonance in the evaluation of patients presenting with suspected or confirmed acute coronary syndrome. *Cardiol Res Pract* 2011; **2011**: 605785. doi: 10.4061/2011/605785
3. Jeremias A, Gibson CM. Narrative review: alternative causes for elevated cardiac troponin levels when acute coronary syndromes are excluded. *Ann Intern Med* 2005; **142**: 786–91.
4. Zimetbaum PF, Josephson ME. Use of the electrocardiogram in acute myocardial infarction. *N Engl J Med* 2003; **348**: 933–40.
5. Wang K, Asinger RW, Marriott HJ. ST-segment elevation in conditions other than acute myocardial infarction. *N Engl J Med* 2003; **349**: 2128–35.
6. Heidenreich PA, Alloggiamento T, Melsop K, McDonald KM, Go AS, Hlatky MA. The prognostic value of troponin in patients with non-ST elevation acute coronary syndromes: a meta-analysis. *J Am Coll Cardiol* 2001; **38**: 478–85.
7. Keller T, Zeller T, Peetz D, Tzikas S, Roth A, Czyz E, et al. Sensitive troponin I assay in early diagnosis of acute myocardial infarction. *N Engl J Med* 2009; **361**: 868–77. doi: 10.1056/NEJMoa0903515
8. Dokainish H, Pillai M, Murphy SA, DiBattiste PM, Schwaiger MJ, Lotfi A, et al. Prognostic implications of elevated troponin in patients with suspected acute coronary syndrome but no critical epicardial coronary disease: a TACTICS-TIMI-18 substudy. *J Am Coll Cardiol* 2005; **45**: 19–24.
9. Hamm CW, Bassand JP, Agewall S, Bax J, Boersma E, Bueno H, et al; ESC Committee for Practice Guidelines. ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J* 2011; **32**: 2999–3054. doi: 10.1093/eurheartj/ehr236
10. Codreanu A, Djaballah W, Angioi M, Ethevenot G, Moulin F, Felblinger J, et al. Detection of myocarditis by contrast-enhanced MRI in patients presenting with acute coronary syndrome but no coronary stenosis. *J Mag Reson Imaging* 2007; **25**: 957–64.
11. Assomull RG, Lyne J, Keenan N, Gulati A, Bunce NH, Davies SW, 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.
12. Mather AN, Fairbairn TA, Artis NJ, Greenwood JP, Plein S. Diagnostic value of CMR in patients with biomarker-positive acute chest pain and unobstructed coronary arteries. *JACC Cardiovasc Imaging* 2010; **3**: 661–4. doi: 10.1016/j.jcmg.2010.03.006
13. Stensaeth KH, Fossum E, Hoffmann P, Mangschau A, Klow NE. Clinical characteristics and role of early cardiac magnetic resonance imaging in patients with suspected ST-elevation myocardial infarction and normal coronary arteries. *Int J Cardiovasc Imaging* 2011; **27**: 355–65. doi: 10.1007/s10554-010-9671-7
14. Friedrich MG, Sechtem U, Schulz-Menger J, Holmvang G, Alakija P, Cooper LT, et al. Cardiovascular magnetic resonance in myocarditis: a JACC white paper. *J Am Coll Cardiol* 2009; **53**: 1475–87. doi: 10.1016/j.jacc.2009.02.007
15. Cerqueira MD, Weissman NJ, Dilsizian V, Jacobs AK, Kaul S, Laskey WK, et al; American Heart Association Writing Group on Myocardial Segmentation and Registration for Cardiac Imaging. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart. A statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. *Circulation* 2002; **105**: 539–42.
16. Bogaert J, Kalantzi M, Rademakers FE, Dymarkowski S, Janssens S. Determinants and impact of microvascular obstruction in successfully reperfused ST-segment elevation myocardial infarction. Assessment by magnetic resonance imaging. *Eur Radiol* 2007; **17**: 2572–80.
17. Eitel I, von Knobelsdorff-Brenkenhoff F, Bernhardt P, Carbone I, Muellerleile K, Aldrovandi A, et al. Clinical characteristics and cardiovascular magnetic resonance findings in stress (takotsubo) cardiomyopathy. *JAMA* 2011; **306**: 277–86. doi: 10.1001/jama.2011.992
18. Jacquier A, Thuny F, Jop B, Giorgi R, Cohen F, Gaubert JY, et al. Measurement of trabeculated left ventricular mass using cardiac magnetic resonance imaging in the diagnosis of left ventricular non-compaction. *Eur Heart J* 2010; **31**: 1098–104. doi: 10.1093/eurheartj/ehp595
19. Grothoff M, Pachowsky M, Hoffmann J, Posch M, Klaassen S, Lehmkuhl L, et al. Value of cardiovascular MR in diagnosing left ventricular non-compaction cardiomyopathy and in discriminating between other cardiomyopathies. *Eur Radiol* 2012; **22**: 2699–709. doi: 10.1007/s00330-012-2554-7
20. Maron MS. Clinical utility of cardiovascular magnetic resonance in hypertrophic cardiomyopathy. *J Cardiovasc Magn Reson* 2012; **14**: 13. doi: 10.1186/1532-429X-14-13
21. Bogaert J, Olivotto I. MR imaging in hypertrophic cardiomyopathy: from magnet to bedside. *Radiology* 2014; **273**: 329–48. doi: 10.1148/radiol.14131626
22. Andersen K, Hennersdorf M, Cohnen M, Blondin D, Mödder U, Poll LW. Myocardial delayed contrast enhancement in patients with arterial hypertension: initial results of cardiac MRI. *Eur J Radiol* 2009; **71**: 75–81. doi: 10.1016/j.ejrad.2008.03.009
23. Hansen MW, Merchant N. MRI of hypertrophic cardiomyopathy: part 1, MRI appearances. *AJR Am J Roentgenol* 2007; **189**: 1335–43.
24. Hansen MW, Merchant N. MRI of hypertrophic cardiomyopathy: part 2, differential diagnosis, risk stratification, and posttreatment MRI appearances. *AJR Am J Roentgenol* 2007; **189**: 1344–52.
25. Marcus FI, McKenna WJ, Sherrill D, Basso C, Bauce B, Bluemke DA, et al. Diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia: proposed modification of the task force criteria. *Circulation* 2010; **121**: 1533–41. doi: 10.1161/CIRCULATIONAHA.108.840827
26. Roongsritong C, Warraich I, Bradley C. Common causes of troponin elevations in the absence of acute myocardial infarction: incidence and clinical significance. *Chest* 2004; **125**: 1877–84.
27. Roe MT, Harrington RA, Prosper DM, Pieper KS, Bhatt DL, Lincoff AM, 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) trail investigators. *Circulation* 2000; **102**: 1101–6.
28. Germing A, Lindstaedt M, Ulrich S, Grewe P, Bojara W, Lawo T, et al. Normal angiogram in acute coronary syndrome—preangiographic risk stratification, angiographic findings and follow-up. *Int J Cardiol* 2005; **99**: 19–23.

29. Larson DM, Menssen KM, Sharkey SV, Duval S, Schwartz RS, Harris J, et al. "False-positive" cardiac catheterization laboratory activation among patients with suspected ST-segment elevation myocardial infarction. *JAMA* 2007; **298**: 2754–60. doi: 10.1001/jama.298.23.2754
30. Baccouche H, Mahrholdt H, Meinhardt G, Merher R, Voehringer M, Hill S, et al. Diagnostic synergy of non-invasive cardiovascular magnetic resonance and invasive endomyocardial biopsy in troponin-positive patients without coronary artery disease. *Eur Heart J* 2009; **30**: 2869–79. doi: 10.1093/eurheartj/ehp328
31. Leurent G, Langella B, Fougerou C, Lentz PA, Larralde A, Bedossa M, et al. Diagnostic contributions of cardiac magnetic resonance imaging in patients presenting with elevated troponin, acute chest pain syndrome and unobstructed coronary arteries. *Arch Cardiovasc Dis* 2011; **104**: 161–70. doi: 10.1016/j.acvd.2011.01.005
32. Ferreira V, Dall'Armellina E, Piechnik S, Karamitsos T, Francis J, Choudhury R, et al. High diagnostic yield in patients presenting with acute chest pain, positive troponins but non-obstructive coronaries by cardiovascular magnetic resonance imaging with conventional and novel T1 mapping techniques. *Heart* 2014; **100**(Suppl. 3): A69–70. doi: 10.1136/heartjnl-2014-306118.121
33. Gerbaud E, Harcaut E, Coste P, Erickson M, Lederlin M, Labèque JM, et al. Cardiac magnetic resonance imaging for the diagnosis of patients presenting with chest pain, raised troponin, and unobstructed coronary arteries. *Int J Cardiovasc Imaging* 2012; **28**: 783–94. doi: 10.1007/s10554-011-9879-1
34. Christiansen JP, Edwards C, Sinclair T, Armstrong G, Scott A, Patel H, 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.
35. Laraudogoitia Zaldumbide E, Perez-David E, Larena JA, Velasco del Castillo S, Rumoroso Cuevas JR, Onaindía JJ, et al. The value cardiac magnetic resonance patients acute coronary syndrome normal coronary arteries. [In Spanish.] *Rev Esp Cardiol* 2009; **62**: 976–83.
36. Monney PA, Sekhri N, Burchell T, Knight C, Davies C, Deaner A, et al. Acute myocarditis presenting as acute coronary syndrome: role of early cardiac magnetic resonance in its diagnosis. *Heart* 2011; **97**: 1312–18. doi: 10.1136/hrt.2010.204818
37. Avegliano G, Huguet M, Costabel JP, Ronderos R, Bijnens B, Kuschnir P, et al. Morphologic pattern of late gadolinium enhancement in Takotsubo cardiomyopathy detected by early cardiovascular magnetic resonance. *Clin Cardiol* 2011; **34**: 178–82. doi: 10.1002/clc.20877
38. Kohan AA, Yeyati EL, De Stefano L, Dragonetti L, Pietrani M, Perez de Arenaza D, et al. Usefulness of MRI in takotsubo cardiomyopathy: a review of the literature. *Cardiovasc Diagn Ther* 2014; **4**: 138–46. doi: 10.3978/j.issn.2223-3652.2013.10.03
39. Umana E, Solares CA, Alpert MA. Tachycardia-induced cardiomyopathy. *Am J Med* 2003; **114**: 51–5.
40. Ben Morrison T, Jared Bunch T, Gersh BJ. Pathophysiology of concomitant atrial fibrillation and heart failure: implications for management. *Nat Clin Pract Cardiovasc Med* 2009; **6**: 46–56. doi: 10.1038/ncpcardio1414
41. Chopard R, Jehl J, Dutheil J, Genon VD, Seronde MF, Kastler B, et al. Evolution of acute coronary syndrome with normal coronary arteries and normal cardiac magnetic resonance imaging. *Arch Cardiovasc Dis* 2011; **104**: 509–17. doi: 10.1016/j.acvd.2011.05.004
42. Cooper LT, Baughman KL, Feldman AM, Frustaci A, Jessup M, Kuhl U, et al; American Heart Association; American College of Cardiology; European Society of Cardiology. The role of endomyocardial biopsy in the management of cardiovascular disease: a scientific statement from the American Heart Association, the American College of Cardiology, and the European Society of Cardiology. *Circulation* 2007; **116**: 2216–33.