ISSN: 0976-3031

Available Online at http://www.recentscientific.com

CODEN: IJRSFP (USA)

International Journal of Recent Scientific Research
Vol. 10, Issue, 06(E), pp. 32985-32990, June, 2019

International Journal of Recent Scientific Research

DOI: 10.24327/IJRSR

Research Article

THE ROLE OF CARDIOVASCULAR MAGNETIC RESONANCE IN PATIENTS PRESENTING MYOCARDIAL INFARCTS WITH NON OBSTRUCTED CORONARY ARTERIES

Kettani Y*, Arbaoui Z, Oukerraj L, Doghmi N and Cherti M

Cardiovascular Magnetic Resonance Unit, Department of Cardiology,
Ibn Sina Hospital, Rabat, Morocco

DOI: http://dx.doi.org/10.24327/ijrsr.2019.1006.3582

ARTICLE INFO

Article History:
Received 6th March, 2019
Received in revised form 15th April, 2019
Accepted 12th May, 2019
Published online 28th June, 2019

Key Words:

Magnetic resonance; acute coronary syndromes; troponin; Myocarditis;Coronaryangiography

ABSTRACT

Aims: Troponin measurement is used in the assessment and risk stratification of patients presenting acutely with chest pain when the main cause of elevation is coronary artery disease. However, some patients have no coronary obstruction on angiography, leading to diagnostic uncertainty. We evaluated the incremental diagnostic value of cardiovascular magnetic resonance (CMR) in these patients.

Methods and results: one hundred consecutive patients (mean age50 years,70% male)with a troponin-positive episode of chest pain and unobstructed coronary arteries were recruited within 3 months of initial presentation. All patients underwent CMR with cine imaging,T2-weighted imaging for detection of inflammation, and late gadolinium enhancement imaging for detection of infarct and fibrosis. An identifiable basis for troponin elevation was established in80%of patients. The commonest underlying cause was cardiomyopathy (37%) myocarditis (13%), followed by myocardial infarction (12%) and In the38%of patients where no clear diagnosis was identified by CMR, significant myocardial infarct and fibrosis was excluded.

Conclusion: CMR is a valuable adjunct to conventional investigations in a diagnostically challenging and important group of patients with troponin-positive chest pain and unobstructed coronary arteries.

INTRODUCTION

Troponin measurement is used routinely in the assessment and risk stratification of patients presenting acutely with chest pain. It can accurately predict the presence of acute coronary syndromes (ACS) in coronary artery disease (CAD).1,2 The magnitude of troponin elevation reflects the complexity of the atherosclerotic lesions and guides risk stratification for death and re-infarction.3–6 However, in a small but important subgroup of patients presenting with chest pain and an elevated troponin, subsequent coronary angiography reveals normal or non-flow-limiting CAD.7,8 These patients present a difficult diagnostic dilemma.9,10 There are a number of potential causes of this scenario, including non-cardiac etiologies, myocardial infarction with a recanalized coronary artery, and acute myocarditis. 7,11 In patients with ACS, antithrombotic, antiplatelet, and interventional therapies are important, but no data support the role of these therapies in the management of patients with a non-thrombotic syndrome. For this reason, defining the underlying cause of the clinical presentation is important and further investigation is justified, as lack of an accurate diagnosis is likely to result in patients not receiving appropriate treatment and/or follow-up. The current lack of diagnostic certainty may in turn explain why this cohort of patients has been shown to have a poorer prognosis.12,13 In order to establish the underlying cause for the troponin elevation, cardiovascular magnetic resonance (CMR) offers a potential opportunity due to its ability to non-invasively identify areas of in vivo inflammation and replacement fibrosis with a high spatial resolution. Using a combination of available sequences, CMR is able to distinguish between different causative etiologies including acute infarction, myocarditis, and other cardiomyopathies.14–18 We therefore hypothesized that CMR would offer incremental value in determining the underlying etiology.

METHODS

Patient population one hundred and ten consecutive patients presenting with new-onset chest pain (present at rest, lasting for longer than 30 min), an elevated troponin, and unobstructed coronary arteries on X-ray angiography were prospectively recruited between January 2016 and December 2018.

Corresponding author:* **Kettani Y
Cardiovascular Magnetic Resonance Unit, Department of Cardiology,Ibn Sina Hospital, Rabat, Morocco

All CMR scans were performed during the inpatient admission or within 3 months of initial presentation. Coronary angiograms were performed in all patients prior to enrolment and subsequent CMR scanning. Patients with a history of chronic troponin elevation were excluded, as were any patients with standard contraindications to CMR (one patient excluded due to severe claustrophobia).

The final cohort comprised 100 patients. Written consent was obtained from all patients.

Cardiovascular Magnetic Resonance

CMR (Siemens Sonata 1.5T, Erlangen, Germany) was performed using steady-state, free precession breath-hold cines echo time (TE)/ repetition time (TR) (1.6/3.2 ms, flip angle 608) in long-axis planes and sequential 7 mm short-axis slices (3 mm gap) from the atrioventricular ring to the apex. T2-weighted images (triple inversion recovery; TE: 60 ms, TR: 2_ R–R interval, TI: 170 ms, slice thickness 7–15 mm, flip angle: 1808, pixel size 2.3 _ 1.3 mm) were acquired in the same long- and short-axis planes. Finally, late gadolinium enhancement (LGE) images were acquired 10 min after intravenous gadolinium-DTPA (Schering; 0.1 mmol/kg) in identical short-axis planes using an inversion-recovery gradient echo sequence. Inversion times were adjusted to null normal myocardium (typically 320– 440 ms; pixel size 1.7 _ 1.4 mm). LGE images were phase-swapped to exclude artefact. Ventricular volumes and function were measured for both ventricles using standard techniques19–21 and analyzed using semi-automated software (CMRtools, Cardiovascular Imaging Solutions, London, UK). All volumes and masses were Indexed for age, gender, and body surface area (BSA).22

Cardiovascular Magnetic Resonance Analysis

CMR scans were analyzed independently by two experienced interpreters who were blinded to clinical details. Scans were reviewed with assessment of ventricular volumes and function, review of T2-weighted images for areas of high signal suggesting myocardial inflammation, and by measuring the ratio of myocardial signal intensity to skeletal muscle.23 Finally, the LGE images were assessed for subendocardial enhancement in the distribution of a coronary artery compatible with myocardial infarction18 or for midwall/subepicardial enhancement which was compatible with myocarditis in this cohort. The myocarditis group was further subclassified into acute (T2 raised) or non-acute (T2 not raised) based on the corresponding T2-weighted signal in that territory or increased global ratio. Scans with increased normalized volumes and reduced systolic function but without evidence of LGE/T2 abnormalities were categorized as dilated cardiomyopathy (DCM). Scans with completely normal range volumes and function with no LGE/T2 abnormalities were considered non-diagnostic for cause by CMR. The incremental value of CMR was expressed as the proportion of cases where LGE-CMR scans yielded a new diagnosis.

Clinical Data

Clinical data including history, examination findings, troponin levels, ECG recordings, transthoracic echocardiography, and coronary angiography were reviewed by a single experienced observer prior to enrolment into the study. The primary ECG abnormality was assigned using the Minnesota code.24 ST-segment elevation was defined as the elevation of the ST-segment .1 mm in leads II, III, aVF; I, aVL, V5, and V6 or .2 mm in leads V1–V4. Readings were taken 60 ms after the J point. In addition, details of investigations for pulmonary emboli and serum electrolytes were recorded. Renal disease was defined as a reduced GFR (90 mL/min/ 1.73 m2).25 Troponin assays differed between referring centers, and the recorded level was cross-checked with the upper limit of normal for the appropriate referring centre (typically 10–20% in excess of the 99th percentile value for a reference control group) to ensure they were elevated at a level to suggest significant myocardial injury. For each patient, the results of all troponin assays performed during the index admission were recorded. The peak troponin results for patients were also subdivided into categories depending on the extent of their elevation (2 upper limit of normal (ULN), 5 ULN, 10 and 10 ULN). A 'false positive' troponin was considered a possibility in patients with a single troponin elevation, which was not repeated during the admission or if a single elevated troponin was followed by a second normal troponin level within 24 h. Coronary angiograms were reviewed to ensure there were no epicardial stenoses (defined as .50% stenosis in the main- and side branch arteries). The subsequent progress of patients was assessed by telephone contact with their primary care physician to establish whether subsequent investigations had uncovered any alternative diagnoses that were not evident on CMR.

Statistical Analysis

Continuous data are expressed as a mean+SD. Baseline characteristics were compared between subgroups using an independent sample t-test or Mann–Whitney test as appropriate. Fisher's or x2 tests were used for categorical variables. All tests were two-sided. A P-value of 0.05 was deemed significant and SPSS v12 (Chicago, USA) was used for all statistical analyses.

RESULTS

Baseline Characteristics

Group baseline characteristics are summarized in Table 1.2.3.
The mean age of the cohort was 50+13years (54% male). 20 of the patients had a prior history of cardiac disease before presenting with acute chest pain. They had not required electrical cardioversion or undergone invasive cardiovascular investigations/treatment other than angiography.

Table 1 Epidemiology characteristics

Epidemiology Characteristics	Value (n=100) A ± DS or %
Mean Age (SD), years	50 ± 13
Male sex (%)	54
Diabetes(%)	29
Hypertension(%)	37
History of smoking(%)	33
History of alcohol excess(%)	4
Dyslipidaemia(%)	25
History of Coronary Artery Disease (%)	20

A± DS = Average ± Standard Deviation, n=effectif

Table 2 Clinical parameters at the admission

Clinical parameters at the admission	Value (n=100) A ± SD
Systolic arterial pressure	121,25 ± 21,892
Diastolic arterial pressure	72,79 ± 11,530
Heart Rate	94,58 ± 30,934
Pulmonary Frequency	14,67 ± 3,533

A± DS = Average ± Standard Deviation, n=effectif

In addition, none of the recruited cohort had pre-existing renal impairment, prior exposure to cardiotoxic drugs, or prior chemotherapy/radiotherapy. At the time of the recorded troponin elevation, none of the patients had been treated for a prolonged episode of septicemia. There was a low prevalence of cardiac risk factors. 94 (94%) of the cohort had an abnormal ECG on presentation, with ST-segment elevation being the most commonly detected abnormality (32%). The median interval from presentation of chest pain to CMR was 20 days (range 10 to 50 days). (Table 4)

Table 3 Biological parameters at the admission

Biological parameters at the admission	Min	Max	A ± SD
Hemoglobin	9,50	15,00	13,0375 ± 1,25
White Blood cell	3720	11000	7091 ± 2025
Platelette	128000	400000	269083 ± 80498
Natremia	131,00	141,00	136,6250 ± 2,45
Serum potassium	3,10	5,00	4,1971 ± 0,49
Urea	0,22	0,69	0,3605 ± 0,10
Creatinin	6,00	17,20	8,9957 ± 2,35
Thyroid stimulating hormone	0,50	4,00	1,9405 ± 0,91
T3 thyroid hormone	0,46	4,00	2,0568 ± 0,99
T4 thyroid hormone	1,00	2,65	1,4016 ± 0,5
Low Density Lipoproteine	0,61	1,64	1,1836 ± 0,3
High Density Lipoproteine	0,27	0,50	0,4076 ± 0,06
First Troponin	0,00	50,00	4,5673 ± 11
Second Troponin	0,00	25,00	4,2663 ± 6,6
Triglyceride	0,70	2,64	1,4462 ± 0,5

A± DS = Average ± Standard Deviation, n=effectif

Table 4 Primary ECG abnormality

Primary ECG abnormality	Pourcentage (%)
Normal	6
T wave changes	24
ST Elevation	32
ST depression	26
LBBB	26
Q waves	26
rhythm disorder	18
hypertrophy of the left ventricle	16

A± DS = Average ± Standard Deviation, n=effectif

Incremental Value of Cardiovascular Magnetic Resonance

The range of diagnoses determined by CMR is summarized in Table 5; CMR provided a new diagnosis in 50 patients (50% of cohort). In the remaining patients, there was no detectable CMR in troponin-positive chest pain and unobstructed coronary arteries infarction or inflammation and no additional new diagnosis was made. There was 100% concordance of diagnosis between the two observers. Myocarditis was the most common diagnosis, which was present in 50% of the patients. Myocardial infarction was found in seven (12%) patients. In 8 female patient with a history of recent stress, CMR revealed apical ballooning with preserved basal LV function and no LGE or T2 abnormalities.

A diagnosis of Takotsubo cardiomyopathy was made, and repeat CMR 3 months later showed complete normalization of LV function. In 25 patient, CMR revealed LV dilatation with moderate impairment of systolic function, with no evidence of detectable inflammation or fibrosis, and a diagnosis of DCM was made. Finally, 4 patients who presented with ECG evidence of inferior myocardial infarction had a CMR which revealed an hypertrophique cardiomyopathy.

Table 5 diagnoses determined by CMR

CMR Findings	N(%)
Primitive Dilated Cardiomyopathy	25(25)
Myocarditis	13(13)
Myocardial infarction	12(12)
TakoTsubo cardiomyopathy	8(8)
Hypertrophique cardiomyopathy	4(4)
Normal	38(38)

A± DS = Average ± Standard Deviation, n=effectif

Diagnostic vs. non-Diagnostic group

Patients with a non-diagnostic CMR were defined as patients in whom CMR did not reveal any structural or myocardial tissue abnormalities. None of these scans were suboptimal in the quality of images obtained. There was no significant difference in baseline LV parameters between the groups with and without a new CMR diagnosis, except for the baseline LVEF which was lower in the new diagnosis group (50 ± 15 vs. 55 ± 5%, P< 0.007). A higher proportion of patients with a non-diagnostic CMR had a potential false-positive troponin (as defined previously) than those with a diagnosis confirmed by CMR (57 vs 8%, P < 0.001).

ECG findings are presented in Table 4. As can be seen, only tachyarrhythmia (SVT/VT) appeared to correlate with CMR findings. A significantly higher proportion of patients with a non diagnostic CMR had a tachyarrhythmia at presentation (24 vs. 5%, P< 0.045).

On follow-up of both groups at a median of 398 (range160–736) days, no new or alternative cardiac diagnosis has been made in any patient.

Diagnosis of Inflammation in acute Myocarditis

Of the 13 patients diagnosed with myocarditis by CMR, 7 had evidence of acute inflammation (7 % of total cohort) with increased midwall/epicardial T2 signal and corresponding enhancement on LGE images. 6 patients (6 %) were ascribed a diagnosis of non-acute myocarditis without detectable active inflammation based on the presence of midwall/epicardial LGE abnormalities and normal intensity T2 images (Table 4). However, the median interval between troponin-positive chest pain and CMR scanning was significantly shorter in the acute myocarditis group [8 days (range1–88 days) vs 41 days (range 6–83 days), P< 0.005]. In addition, patients with a diagnosis of acute myocarditis were significantly younger than those diagnosed with non acute myocarditis (35.2+14.9 vs. 48.5+19.3 years, P <0.04). No patients in the cohort had increased T2 signal intensity in the absence of midwall/epicardial LGE.

Validation of Cardiovascular Magnetic Resonance Findings

On the basis of improving clinical scenario, no patients required or underwent myocardial tissue biopsy. We rescanned four patients with a CMR diagnosis of active inflammatory

myocarditis [median interscan time of 111 days (range 56–313 days)]. Repeat scans in all patients showed persistent fibrosis but diminished signal on T2 imaging, correlating with their clinical improvement.

Other Clinical Investigations

Depending on the clinical presentation and blood-gas profile, a small proportion of patients were additionally further investigated for pulmonary thromboembolism.

CT pulmonary angiography was performed in three patients, all of whom did not show evidence of embolism.

One patient was diagnosed with pulmonary embolism on the basis of a ventilation perfusion isotope scan.

DISCUSSION

Raised troponin levels reflect myocardial necrosis. The vast majority of patients presenting with acute chest pain, troponin elevation, and abnormal ECGs are correctly diagnosed and treated for ACS. Subsequent coronary angiography usually reveals flow-limiting epicardial stenoses.27

However, patients presenting with chest pain, an elevated troponin, and normal coronary angiography present a clinical dilemma. Further evaluation is required to establish a diagnosis and to direct treatment strategies. There are a large number of other causes of an elevated troponin in the absence of obstructive CAD, which include infarction, myocarditis, cardiomyopathy, cardiac contusion, congestive heart failure, and non-cardiac causes including pulmonary embolism, sepsis, and renal failure. CMR is able to provide detailed information on myocardial tissue characteristics. It therefore has a potential role in evaluating the cause of troponin elevation. LGE-CMR has become the gold standard for in vivo detection of scarring associated with myocardial infarction and other non ischemic conditions.11, 14,15,28,29 the high spatial resolution and contrast of CMR allows very small areas of infarction to be identified, which are missed by SPECT.30 Black-blood T2-weighted imaging delineates areas of myocardial edema based on a water-excitation pulse. This sequence has been clinically used to detect edema in acute infarction, sarcoid, myocarditis, and acute rejection following cardiac transplantation.31–33 The application of excellent tissue characterization that is validated, non-invasive, and free from non-ionizing radiation makes LGE-CMR a safe and powerful tool. Our study demonstrates that CMR can identify the basis for troponin elevation in 70% of patients presenting with ACS type symptoms but unobstructed coronary angiography.

In this group, the commonest cause was myocarditis (50%), followed by myocardial infarction (12%). This finding is in keeping with studies using nuclear techniques identifying high rates of myocarditis in patients with troponin-positive chest pain and normal coronary arteries.9 also importantly; significant infarction, fibrosis, or active inflammation was excluded in the remaining 35% of patients. Several studies have confirmed that the elevation of troponin in patients with ACS correlates with evidence of infarction by LGE-CMR and furthermore that the extent of elevation predicts the size of infarct.34,35 Unlike the present study, however, these studies excluded patients with normal coronaries and did not include patients with possible/suspected myocarditis.

In the subset with myocarditis, 63% of this group showed evidence of acute active inflammation as indicated by T2 imaging. These patients were scanned significantly sooner than those diagnosed with non-acute myocarditis. Previous work has demonstrated that the acute changes of edema and fibrosis as detected by LGE-CMR correlate well with biopsy findings and increase the diagnostic yield of biopsies by guiding the site of tissue sampling.17 More ever, serial studies in such patients also demonstrate regression of these pathological changes over time in a proportion of patients.36 In the present study, four patients who consented to a follow-up scan showed complete or partial resolution of myocardial inflammation on the repeat scanning using T2 after a period of 111 days. Therefore, if the extent of myocardial inflammation at baseline was limited, these changes may resolve following the acute period of inflammation. Failure to ensure early CMR scanning in these patients may miss any subtle changes that were present on acute admission. Myocardial infarction was detected in 11.6% of patients, despite the presence of unobstructed coronary arteries. The mechanism of infarction in these patients may be explained by arterial recanalization, embolism, or coronary spasm. Five of these seven patients received thrombolytic therapy, which may have resulted in recanalization of the occluded vessel. In one patient, a clear source of potential embolism was identified in the form of a PFO which resulted in both systemic and pulmonary emboli highlighting the limitations of luminography. The example of Takotsubo cardiomyopathy demonstrates the additional role of CMR in characterizing a disease entity that is being increasingly recognized and where management based on the ECG and angiography alone may have resulted in the interpretation of recanalization rather than this reversible cardiomyopathy.37

CMR did not provide a clear diagnosis in 35% of patients. Patients with non-diagnostic CMR scans in this study were more likely to have a modest elevation of troponin (5ULN) when compared with patients with a diagnostic CMR scan. Moreover, we hypothesize that a proportion of these troponin elevations may also be biochemical false positives. Evidence for this is also provided by the fact that patients with a non-diagnostic CMR were more likely to have had a tachyarrhythmia at presentation, which had subsequently resulted in a troponin elevation which was (in retrospect) unlikely to be clinically significant.

In addition, a proportion of cases may be due to an underlying non-cardiac etiology such as pulmonary embolism, although the confirmed incidence of this in our cohort was low. The delayed presentation for CMR scanning in part of our cohort may lead to a failure to diagnose mild inflammation without development of fibrosis in myocarditis, which was present on initial admission but subsequently resolved. Alternative explanations for troponin elevation, which do not involve tissue necrosis, have also been recently suggested.38

Limitations

Identical troponin assays were not used in this cohort. There was no histo-pathological correlation of the CMR diagnosis with biopsy findings for the diagnosis of myocarditis, which is

not a typical practice in the Morocco. However, several studies have already established the patterns of CMR findings with histology.39,40 Finally, in patients with normal CMR scans, other important causes of a troponin elevation need to be considered, most importantly the diagnosis of pulmonary embolism, but our CMR scanning protocol was not designed for this possibility. This also has relevance in terms of potential referral bias for the CMR scan.

CONCLUSION

This study reveals a role for CMR as an adjunct to conventional investigations in patients with troponin-positive chest pain and unobstructed coronary arteries. In our cohort, LGE-CMR provided a new diagnosis in 65% of cases and excluded significant pathology in the remainder. Further studies are required to evaluate the prognostic implications of CMR abnormalities in this cohort of patients.

Acknowledgements

Conflict of interest: the authors declare that there is no conflict of interest

References

1. Adams JE III, Bodor GS, Davila-Roman VG, Delmez JA, Apple FS, Ladenson JH, Jaffe AS. Cardiac troponin I. A marker with high specificity for cardiac injury. Circulation 1993;88:101–106.
2. Hamm CW, Goldmann BU, Heeschen C, Kreymann G, Berger J, Meinertz T. Emergency room triage of patients with acute chest pain by means of rapid testing for cardiac troponin T or troponin I. N Engl J Med 1997; 337:1648–1653.
3. Heeschen C, van Den Brand MJ, Hamm CW, Simoons ML. Angiographic findings in patients with refractory unstable angina according to troponin T status. Circulation 1999;100:1509–1514.
4. Benamer H, Steg PG, Benessiano J, Vicaut E, Gaultier CJ, Aubry P, Boudvillain O, Sarfati L, Brochet E, Feldman LJ, Himbert D, Juliard JM, Assayag P. Elevated cardiac troponin I predicts a high-risk angiographic anatomy of the culprit lesion in unstable angina. Am Heart J 1999;137: 815–820.
5. 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;38:478–485.
6. Antman EM, Tanasijevic MJ, Thompson B, Schactman M, McCabe CH, Cannon CP, Fischer GA, Fung AY, Thompson C, Wybenga D, Braunwald E. Cardiac-specific troponin I levels to predict the risk of mortality in patients with acute coronary syndromes. N Engl J Med 1996;335: 1342–1349.
7. Bakshi TK, Choo MK, Edwards CC, Scott AG, Hart HH, Armstrong GP. Causes of elevated troponin I with a normal coronary angiogram. Intern Med J 2002;32:520–525.
8. Mahajan N, Mehta Y, Rose M, Shani J, Lichstein E. Elevated troponin level is not synonymous with myocardial infarction. Int J Cardiol. Published online ahead of print November 9, 2005.
9. Sarda L, Colin P, Boccara F, Daou D, Lebtahi R, Faraggi M, Nguyen C, Cohen A, Slama MS, Steg PG, Le Guludec D. Myocarditis in patients with clinical presentation of myocardial infarction and normal coronary angiograms. J Am Coll Cardiol 2001;37:786–792.
10. Roongsritong C, Warraich I, Bradley C. Common causes of troponin elevations in the absence of acute myocardial infarction: incidence and
11. clinical significance. Chest 2004;125:1877–1884.
12. McCrohon JA, Moon JC, Prasad SK, McKenna WJ, Lorenz CH, Coats AJ, Pennell DJ. Differentiation of heart failure related to dilated cardiomyopathy and coronary artery disease using gadolinium-enhanced cardiovascular magnetic resonance. Circulation 2003;108:54–59.
13. Dokainish H, Pillai M, Murphy SA, DiBattiste PM, Schweiger MJ, Lotfi A, Morrow DA, Cannon CP, Braunwald E, Lakkis N, TACTICS-TIMI-18 Investigators. 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.
14. Jeremias A, Gibson CM. Narrative review: alternative causes for elevated cardiac troponin levels when acute coronary syndromes are excluded. Ann Intern Med 2005;142:786–791.
15. Abdel-Aty H, Zagrosek A, Schulz-Menger J, Taylor AJ, Messroghli D, Kumar A, Gross M, Dietz R, Friedrich MG. Delayed enhancement and
16. T2-weighted cardiovascular magnetic resonance imaging differentiate acute from chronic myocardial infarction. Circulation 2004;109: 2411–2416.
17. Mahrholdt H, Wagner A, Deluigi CC, Kispert E, Hager S, Meinhardt G, Vogelsberg H, Fritz P, Dippon J, Bock CT, Klingel K, Kandolf R, Sechtem U. Presentation, patterns of myocardial damage, and clinical course of viral myocarditis. Circulation 2006;114:1581–1590.
18. De Cobelli F, Pieroni M, Esposito A, Chimenti C, Belloni E, Mellone R,Canu T, Perseghin G, Gaudio C, Maseri A, Frustaci A, Del Maschio A.Delayed gadolinium-enhanced cardiac magnetic resonance in patients with chronic myocarditis presenting with heart failure or recurrent arrhythmias. J Am Coll Cardiol 2006;47:1649–1654.
19. Mahrholdt H, Goedecke C, Wagner A, Meinhardt G, Athanasiadis A, Vogelsberg H, Fritz P, Klingel K, Kandolf R, Sechtem U. Cardiovascular magnetic resonance assessment of human myocarditis: a comparison to histology and molecular pathology. Circulation 2004;109:1250–1258.
20. Kim RJ, Fieno DS, Parrish TB, Harris K, Chen EL, Simonetti O, Bundy J, Finn JP, Klocke FJ, Judd RM. Relationship of MRI delayed contrast enhancement to irreversible injury, infarct age, and contractile function. Circulation 1999;100:1992–2002.
21. Bellenger NG, Pennell DJ. Ventricular function. In: Manning WJ, Pennell DJ, eds. Cardiovascular Magnetic Resonance. New York: Churchill Livingstone; 2002. 99–111.

22. Grothues F, Smith GC, Moon JC, Bellenger NG, Collins P, Klein HU, Pennell DJ. Comparison of interstudy reproducibility of cardiovascular magnetic resonance with two-dimensional echocardiography in normal subjects and in patients with heart failure or left ventricular hypertrophy. Am J Cardiol 2002;90:29–34.
23. Grothues F, Moon JC, Bellenger NG, Smith GS, Klein HU, Pennell DJ. Interstudy reproducibility of right ventricular volumes, function and mass with cardiovascular magnetic resonance. Am Heart J 2004;147:218–223.
24. Maceira AM, Prasad SK, Khan M, Pennell DJ. Normalized left ventricular systolic and diastolic function by steady state free precession cardiovascular magnetic resonance. J Cardiovasc Magn Reson 2006;8:417–426.
25. Abdel-Aty H, Boye P, Zagrosek A, Wassmuth R, Kumar A, Messroghli D, Bock P, Dietz R, Friedrich MG, Schulz-Menger J. Diagnostic performance of cardiovascular magnetic resonance in patients with suspected acute myocarditis: comparison of different approaches. J Am Coll Cardiol 2005;45:1815–1822.
26. Prineas RJ, Crow RS, Blackburn H. The Minnesota Code Manual of Electrocardiographic Findings: Standards and Procedures for Measurement and Classification. Boston: John Wright, PSG Inc.; 1982.
27. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification.
28. Am J Kidney Dis 2002;39(2 Suppl. 1):S1–S266.
29. Akashi YJ, Musha H, Kida K, Itoh K, Inoue K, Kawasaki K, Hashimoto N, Miyake F. Reversible ventricular dysfunction takotsubo cardiomyopathy. Eur J Heart Fail 2005;7:1171–1176.
30. Braunwald E, Antman EM, Beasley JW, Califf RM, Cheitlin MD, Hochman JS, Jones RH, Kereiakes D, Kupersmith J, Levin TN, Pepine CJ, Schaeffer JW, Smith EE 3rd, Steward DE, Theroux P, Gibbons RJ, Alpert JS, Faxon DP, Fuster V, Gregoratos G, Hiratzka LF, Jacobs AK, Smith SC Jr. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction—summary article: a report of the American College of Cardiology/American Heart Association task force on practice guidelines (Committee on the Management of Patients With Unstable Angina). J Am Coll Cardiol 2002;40:1366–1374.
31. Simonetti OP, Kim RJ, Fieno DS, Hillenbrand HB, Wu E, Bundy JM, Finn JP, Judd RM. An improved MR imaging technique for the visualization of myocardial infarction. Radiology 2001;218:215–223. 1248 R.G. Assomull *et al*.
32. Moon JC, Reed E, Sheppard MN, Elkington AG, Ho SY, Burke M, Petrou M, Pennell DJ. The histologic basis of late gadolinium enhancement cardiovascular magnetic resonance in hypertrophic cardiomyopathy. J Am Coll Cardiol 2004;43:2260–2264.
33. Wagner A, Mahrholdt H, Holly TA, Elliott MD, Regenfus M, Parker M, Klocke FJ, Bonow RO, Kim RJ, Judd RM. Contrast-enhanced MRI androutine single photon emission computed tomography (SPECT) perfusion imaging for detection of subendocardial myocardial infarcts: an imaging study. Lancet 2003;361:374–379.
34. Aletras AH, Tilak GS, Natanzon A, Hsu LY, Gonzalez FM, Hoyt RF Jr, Arai AE. Retrospective Determination of the Area at Risk for Reperfused Acute Myocardial Infarction With T2-Weighted Cardiac Magnetic Resonance Imaging: Histopathological and Displacement Encoding With Stimulated Echoes (DENSE) Functional Validations. Circulation 2006;113:1865–1870.
35. Vignaux O, Dhote R, Duboc D, Blanche P, Dusser D, Weber S, Legmann P. Clinical significance of myocardial magnetic resonance abnormalities in patients with sarcoidosis: a 1-year follow-up study. Chest 2002;122: 1895–1901.
36. Marie PY, Angioi M, Carteaux JP, Escanye JM, Mattei S, Tzvetanov K, Claudon O, Hassan N, Danchin N, Karcher G, Bertrand A, Walker PM, Villemot JP. Detection and prediction of acute heart transplant rejection with the myocardial T2 determination provided by a black-blood magnetic resonance imaging sequence. J Am Coll Cardiol 2001;37:825–831.
37. Ingkanisorn WP, Rhoads KL, Aletras AH, Kellman P, Arai AE. Gadolinium delayed enhancement cardiovascular magnetic resonance correlates with clinical measures of myocardial infarction. J Am Coll Cardiol 2004;43:2253–2259.
38. Christiansen JP, Edwards C, Sinclair T, Armstrong G, Scott A, Patel H, Hart H. 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: 768–771.
39. Friedrich MG, Strohm O, Schulz-Menger J, Marciniak H, Luft FC, Dietz R. Contrast media-enhanced magnetic resonance imaging visualizes myocardial changes in the course of viral myocarditis. Circulation 1998;97:1802–1809.
40. Sharkey SW, Lesser JR, Zenovich AG, Maron MS, Lindberg J, Longe TF, Maron BJ. Acute and reversible cardiomyopathy provoked by stress in women from the United States. Circulation 2005;111:472–479.
41. Jeremias A, Gibson CM. Narrative review: alternative causes for elevated cardiac troponin levels when acute coronary syndromes are excluded.Ann Intern Med 2005;142:786–791.
42. Deckers JW, Hare JM, Baughman KL. Complications of transvenous right ventricular endomyocardial biopsy in adult patients with cardiomyopathy: a seven-year survey of 546 consecutive diagnostic procedures in a tertiary referral center. J Am Coll Cardiol 1992;19:43–47.
43. Chow LH, Radio SJ, Sears TD, McManus BM. Insensitivity of right ventricular endomyocardial biopsy in the diagnosis of myocarditis. J Am Coll Cardiol 1989;14:915–920. CMR in troponin-positive chest pain and unobstructed coronary arteries 1249