Troponin-positive chest pain with unobstructed coronary arteries: incremental diagnostic value of cardiovascular magnetic resonance imaging

Bhupesh Pathik1†, Betty Raman1,2†, Nor Hanim Mohd Amin1, Devan Mahadavan2, Sharmalar Rajendran2, Andrew D. McGavigan1,3, Suchi Grover1, Emma Smith1, Jawad Mazhar1, Cameron Bridgman1, Anand N. Ganesan1, and Joseph B. Selvanayagam1,3,4*

1Department of Cardiovascular Medicine, Flinders Medical Centre, Flinders Drive, Bedford Park, SA 5042, Australia; 2Department of Cardiology, Queen Elizabeth Hospital, Woodville South, SA, Australia; 3School of Medicine, Faculty of Medicine, Nursing and Health Sciences, Flinders University, Bedford Park, SA, Australia; and 4South Australian Health and Medical Research Institute, Adelaide, Australia

Received 13 July 2015; accepted after revision 4 October 2015; online publish-ahead-of-print 20 November 2015

Aims
Troponin-positive chest pain patients with unobstructed coronaries represent a clinical dilemma. Cardiovascular magnetic resonance (CMR) imaging has an increasingly prominent role in the assessment of these patients; however, its utility in addition to expert clinical judgement is unclear. We sought to determine the incremental diagnostic value of CMR and the heterogeneity in diagnoses by experienced cardiologists when presented with blinded clinical and investigative data in this population.

Methods and results
A total of 125 consecutive patients presenting to a tertiary centre between 2010 and 2014 with cardiac chest pain, elevated troponin (>29 ng/L), and unobstructed coronaries were enrolled and underwent CMR. A panel of three experienced cardiologists unaware of the CMR diagnosis and blinded to each other’s assessment provided a diagnosis based on clinical and investigative findings. A consensus panel diagnosis was defined as two or more cardiologists sharing the same clinical diagnosis. Findings were classified into acute myocarditis, Takotsubo cardiomyopathy, acute myocardial infarction (AMI), or indeterminate. CMR provided a diagnosis in 87% of patients. Consensus panel diagnosis and CMR were concordant in 65/125 (52%) patients. There was an only moderate level of agreement between the three cardiologists (k = 0.47, P < 0.05) and a poor level of agreement between the consensus panel and CMR (k = 0.38, P < 0.05) with the most disagreement seen in patients with AMI diagnosed on CMR.

Conclusion
The clinical diagnosis of patients with non-obstructive coronaries and positive troponin remains a challenge. The concordance between CMR and clinical diagnosis is poor. CMR provides a diagnosis in majority of these patients.

Keywords
Cardiovascular magnetic resonance imaging • Troponin • Acute myocardial infarction • Myocarditis • Takotsubo cardiomyopathy

Introduction
Elevation of cardiac-specific troponin T (cTnT) in serum is highly sensitive and specific for myocardial injury. However, troponin elevation alone may not directly provide information on the mechanism of myocardial injury, which may be critically important to clinical management. In clinical practice, a cTnT greater than 99th percentile of the upper reference limit accompanied by acute ischaemic symptoms, ECG changes, and/or new regional wall motion (RWM) abnormality on imaging is usually investigated with a coronary angiogram to determine whether coronary vessel occlusion is the cause of the elevated cTnT.
In a significant subgroup of these patients, coronary angiography may, however, show either normal or patent coronary arteries with non-flow-limiting atheroma.\textsuperscript{4,5} Such patients represent a clinical dilemma as the cause of their symptoms and cTnT rise is not immediately clear. Clinicians are reliant on their clinical acumen to accurately diagnose and appropriately treat these patients. Moreover, there are no professional guidelines to assist clinicians in managing cTnT-positive chest pain patients with unobstructed coronaries. Determining the correct diagnosis is essential to tailor management and allow risk stratification of such patients.

Cardiovascular magnetic resonance (CMR) imaging is emerging as a potentially transformative imaging technique in these patients with elevated cTnT and angiographically unobstructed coronaries.\textsuperscript{6,7} In patients with myocardial infarction who had normal coronary arteries on angiogram, CMR has been shown to differentiate between acute myocarditis, myocardial infarction, and Takotsubo cardiomyopathy (TTC).\textsuperscript{8} Furthermore, in patients with suspected ST-segment elevation myocardial infarction and normal coronary arteries, those who had CMR were more likely to have a definitive diagnosis.\textsuperscript{9}

However, the additional diagnostic value of CMR to an experienced clinician's assessment, when presented with clinical history, ECG, echocardiography, and angiographic findings but without CMR results, is unclear. The variability in clinical diagnoses by physicians, in this subset of patients, although apparent, has not previously been established. We therefore sought to

(i) determine the incremental diagnostic value of CMR imaging in this cohort of patients and
(ii) demonstrate the heterogeneity in clinical diagnoses among patients with positive cTnT and normal coronaries.

### Methods

#### Patient population

The study protocol was approved by the Southern Adelaide Clinical Human Research Ethics Committee. All patients provided written informed consent. Consecutive patients presenting over a 4-year period to two institutions with cardiac chest pain and elevated cTnT were screened. The inclusion criteria were (i) acute chest pain considered to be cardiac in origin, lasting longer than 10 min and present at rest\textsuperscript{10} and (ii) an elevated high-sensitivity cTnT level greater than 29 ng/L based on the reference range of the locally available commercial assays (Roche Diagnostics). Patients with a history of chronic cTnT elevation defined as persistently raised cTnT for greater than 2 weeks were excluded.

All patients underwent coronary angiography to further evaluate their symptoms. Unobstructed coronary arteries were defined as <50% luminal stenosis angiographically. All coronary angiograms were reviewed by senior interventional cardiologists to exclude the presence of significant epicardial stenosis. Patients who had evidence of obstructive coronary artery disease were excluded. All patients underwent CMR following coronary angiography. A panel of three board-certified cardiologists, blinded to the CMR diagnosis, reviewed the clinical data independently. The data included clinical history; examination findings; blood investigations including full blood examination, renal function, liver function tests, C-reactive protein, and cTnT levels; serial ECGs; the coronary angiogram and left ventriculogram images; and transthoracic echocardiogram findings. Based on the clinical data, the cardiologists provided a diagnosis for the patient's symptoms blinded to the CMR diagnosis and to each other’s diagnosis. A consensus panel diagnosis was defined as two or more cardiologists sharing the same clinical diagnosis. Findings were classified into acute myocarditis, TTC, acute myocardial infarction (AMI), or indeterminate (for example, pulmonary embolism or cTnT elevation secondary to tachyarrhythmia).

AMI was defined according to the universal definition of myocardial infarction as a cTnT level greater than 99th percentile of the upper reference limit accompanied by ischaemic symptoms, electrocardiographic changes, or new RWM abnormality on imaging.\textsuperscript{3} TTC was defined using the Mayo Clinic Diagnostic Criteria of transient hypokinesis or akinesis of the left ventricular mid-segments with or without apical involvement in the absence of obstructive coronary artery disease in a patient with a possible stressful trigger with new ECG changes or elevation in cTnT.\textsuperscript{11} Acute myocarditis was defined according to the European Society of Cardiology diagnostic criteria for clinically suspected myocarditis by the presence of symptoms of chest pain and new onset dyspnoea at rest or with exercise in a patient with newly abnormal 12-lead ECG and/or Holter, elevated cTnT and new, otherwise unexplained left ventricular and/or right ventricular structure, and function abnormality.\textsuperscript{12}

Outcomes measured included all-cause mortality and cardiovascular readmissions using public hospital administrative datasets. Within these datasets, information regarding subsequent out-of-hospital mortality are routinely updated from the states registry of births, deaths, and marriages. Cardiovascular readmissions to any hospital were classified as hospital admissions as a result of either myocardial infarction, angina, heart failure, or stroke using administrative coding using the International Classification of Diseases 10th revision Australian modification (ICD10-AM) classifications supported by radiology and pathology results where available. Myocardial infarction was defined as a cTnT level greater than 99th percentile of the upper reference limit accompanied by ischaemic symptoms, electrocardiographic changes, or new RWM abnormality on imaging. New onset heart failure or worsening heart failure was defined by the presence of symptoms of dyspnoea either at rest or with exertion together with clinical signs of fluid retention and objective evidence either with chest X-ray or echocardiography leading to hospitalization. Stroke was classified as a sudden onset of a new neurological deficit, with symptoms resulting from intracranial vascular disturbance, usually lasting more than 24 h.

#### CMR protocol

The median time between CMR and admission was 6 days [interquartile range (IQR), 2 days]. CMR was performed with a 1.5 T scanner (Aera, Siemens, Erlangen, Germany). Transverse images were acquired with an inversion recovery prepared, dark blood half-Fourier acquisition single-shot turbo spin-echo (HASTE) sequence [repetition time 600 ms, echo time (TE) 26 ms, 6 mm slice thickness, 1.8 mm interslice gap, matrix 256 × 104]. A cine breath-hold balanced steady-state free precession sequence (temporal resolution 42 ms, TE 1.2 ms, flip angle of 70°, 7 mm slice thickness, image acquisition matrix 192 × 174) was used to acquire four long-axis views: a vertical long-axis view, a horizontal long-axis view, and two orthogonal views of the left ventricular outflow tract (LVOT). Subsequently, these images were used to plan the short-axis images that encompassed the entire left and right ventricle from base to apex in a stack of 10 contiguous short-axis slices (7 mm slice thickness and 3 mm slice gap). To evaluate myocardial oedema, T2-weighted short-tau inversion recovery (T2W STIR) sequence was used to obtain 3 long-axis views (horizontal long-axis, vertical long-axis, and one LVOT view) and 10 contiguous short-axis views that were performed identical to slice position of the cine short-axis stack (TE 61 ms, TR 1000 ms, inversion time 150 ms).
Late gadolinium enhancement (LGE) images were obtained after 6–8 min of 0.1 mmol/kg injection of gadolinium (Gd-DTPA, Gadovist, Bayer, Germany) with a T2-weighted segmented inversion recovery turbo fast low-angle shot FLASH sequence (TE 3.3 ms, TI 300–350 ms, flip angle of 20°, slice thickness 7 mm, and acquisition matrix 256 × 104). Images were acquired contiguously in the same short axis as cine and STIR imaging, followed by horizontal and vertical long-axis views and LVOT view. The inversion time was adjusted to achieve optimal nulling of non-infarcted myocardium.

**CMR post-processing analysis**

All analysis was performed off-line with the dedicated computer software (CMR42, Release 4.0.0, Circle Cardiovascular Imaging, Calgary, AB, Canada). Endocardial and epicardial tracings were drawn in the end-diastolic and end-systolic frame. The end-diastolic frame was defined as the frame showing the largest cavity area, and the end-systolic frame was defined as the frame showing the smallest cavity area in a mid-ventricular slice. Left ventricular volumes, mass, and left ventricular ejection fraction (LVEF) were calculated and indexed to body surface area.

The left ventricular cavity was divided into 17 segments according to a standardized model. RWM was graded as normal, mild, or moderate hypokinesia; severe hypokinesia or akinesia; and dyskinesia. Myocardial oedema was defined as a mean signal intensity of >2 SDs greater than that of remote myocardium by semiautomatic software detection on T2-weighted images and quantified as a percentage of total myocardium on matched slices. Where a discrete region of increased signal intensity was not appreciated, a relative myocardial to skeletal muscle was greater than 2:1 and the myocardial signal intensity relative to skeletal muscle. A ratio of ≥2 was considered significant.13

On LGE imaging, hyperenhancement was defined as hyperenhanced pixels with image intensities of 5 SD above the mean of image intensities in a remote myocardial region in the same image. For non-ischaemic pattern of hyperenhancement, a visual assessment of the hyperenhanced region was recorded. It was described as subepicardial, mid-wall, or transmural hyperenhancement.

An experienced CMR investigator blinded to the patient’s clinical, biochemical, and other imaging data, then classified the CMR result as (i) AMI, (ii) acute myocarditis, (iii) TTC, (iv) normal, or (v) other. Patients were placed in this last group if the CMR diagnosis could not be classified into the first four groups such as those diagnosed with hypertrophy cardiomyopathy or dilated non-ischaemic cardiomyopathy.

The diagnosis of AMI was made if LGE was present in vascular territory in a subendocardial or transmural pattern with a concurrent region of increased signal intensity on T2-weighted imaging in the peri-infarct territory to reflect the acuity of insult.14 Acute myocarditis was diagnosed based on the presence of myocardial inflammation detected as an increased signal intensity on T2-weighted images (where myocardial signal intensity relative to skeletal muscle was greater than 2:1) and there was presence of LGE in a pattern typical of myocarditis (i.e. subepicardial or mid-wall hyperenhancement, usually in the lateral and/or septal segments) in support of the diagnosis.15

The presence of characteristic wall motional abnormalities (apical and/or mid-ventricular akinesia) with or without increased STIR in those regions in the absence of LGE in patients was used to make the diagnosis of TTC.16 Scans with no T2 abnormalities or non-specific LGE with increased volumes or thickness with or without LV dysfunction were categorized as other.

**Statistical analysis**

Continuous variables are expressed as mean ± standard deviation and qualitative variables are expressed as percentages. Baseline characteristics were compared between subgroups using an independent sample t-test or Mann–Whitney test as appropriate. Fisher’s or χ2 tests were used for categorical variables. All tests were two-sided. Interobserver variability was assessed using Fleiss’s kappa statistic. The kappa statistic was also used to assess variability between physicians’ diagnosis and CMR diagnosis. Values of 0.75 or more indicate excellent agreement. A value of 0.40–0.75 suggests moderate agreement and a value of <0.40 refers to poor agreement. A P-value of <0.05 was deemed significant and SPSS v22 (Chicago, IL, USA) was used for all statistical analyses.

**Results**

**Study population**

A total of 125 consecutive patients with cTnT-positive chest pain with unobstructed coronary arteries were recruited. Baseline characteristics are presented in Table 1. The mean age was 50 ± 14 years (44% male) and 75% of patients had abnormal ECG with majority of them having T-wave inversion. The median concentration of peak cTnT was 40 (25, 75) ng/L.

**Table 1 Baseline characteristics of the study population**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Values (N = 125)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary ECG abnormality</strong></td>
<td></td>
</tr>
<tr>
<td>Normal, n (%)</td>
<td>34 (27)</td>
</tr>
<tr>
<td>T-wave inversion, n (%)</td>
<td>43 (35)</td>
</tr>
<tr>
<td>ST elevation, n (%)</td>
<td>28 (22)</td>
</tr>
<tr>
<td>ST depression, n (%)</td>
<td>11 (9)</td>
</tr>
<tr>
<td>LBBB, n (%)</td>
<td>3 (4)</td>
</tr>
<tr>
<td>Pathological Q-waves, n (%)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Left ventricular hypertrophy, n (%)</td>
<td>5 (4)</td>
</tr>
<tr>
<td><strong>CMR LV dimensions and function</strong></td>
<td></td>
</tr>
<tr>
<td>LVEDVI (mL/m2)a</td>
<td>81 ± 32</td>
</tr>
<tr>
<td>LVESVI (mL/m2)a</td>
<td>36 ± 30</td>
</tr>
<tr>
<td>LVEF (%)a</td>
<td>56 ± 16</td>
</tr>
<tr>
<td>LV mass index (g/m2)a</td>
<td>65 ± 18</td>
</tr>
</tbody>
</table>

**CMR**, cardiovascular magnetic resonance imaging; **ECG**, electrocardiogram; **LBBB**, left bundle branch block; **LV**, left ventricle; **LVEF**, left ventricular ejection fraction; **LVEDVI**, left ventricular end-diastolic volume index; **LVESVI**, left ventricular end-systolic volume index.

aPresented as mean ± standard deviation.

bPresented as median (25th, 75th percentiles).
cTnT was $485 \text{ ng/L (IQR 182, 840)}$. Out of 125 patients, 90 (72%) exhibited LGE on CMR, 25 (28%) in transmural pattern, 14 (15%) in the subendocardium, and 51 (57%) had subepicardial LGE. On CMR, the mean left ventricular end-diastolic volume index (LVEDVI) was $81 \pm 32 \text{ mL/m}^2$, mean LV end-systolic volume index was $36 \pm 30 \text{ mL/m}^2$, and the mean LVEF was $56 \pm 16\%$.

**CMR parameters and peak troponin**

There was a significant statistical difference in the median peak cTnT between the group with evidence of LGE on CMR compared with those without LGE [576 ng/L (IQR 306, 1284)] vs. $287 \text{ ng/L (IQR 123, 639)}, P < 0.05$.

**Diagnostic role of CMR**

CMR provided a specific diagnosis in 109 (87%) patients. A total of 46 patients (37%) were diagnosed with acute myocarditis. 34 (27%) were found to have TTC. 26 (21%) had findings consistent with AMI, 1 (1%) with apical hypertrophic cardiomyopathy, and 2 patients (2%) with dilated non-ischaemic cardiomyopathy.

**Normal CMR examinations**

Sixteen (13%) patients had normal CMR examinations. In these patients, 50% had normal electrocardiograms and 83% had a peak high-sensitivity cTnT $< 200 \text{ ng/L}$. All eight patients with a normal ECG and a peak cTnT $< 100 \text{ ng/L}$ had a normal CMR examination ($r = 0.484, P < 0.05$). Of the 16 patients with a normal CMR examination, 10 had a diagnosis of AMI based on consensus panel opinion.

**Heterogeneity in clinical diagnoses**

AMI was the most frequent diagnosis by each of the cardiologists. This is in contrast to the distribution of CMR diagnoses where myocarditis was the most common (37%). All three cardiologists had the same diagnosis as CMR in only 40 (32%) patients. Moreover, in a quarter of the patients, none of three cardiologists had a clinical diagnosis consistent with the CMR diagnosis. Overall, there was a moderate level of agreement among the three physicians ($k = 0.47)$. CMR findings and consensus panel (two or more cardiologists in agreement) diagnosis were concordant in 65 (52%) patients. The level of agreement between the consensus panel and CMR diagnosis was poor ($k = 0.39, P < 0.05$).

Of the diagnostic groups, in only 44% of patients diagnosed with TTC on CMR was the diagnosis of all three cardiologists concordant compared with 37 and 27% for myocarditis and AMI, respectively (Figures 1 and 2). There was a moderate level of agreement among the physicians in patients with TTC ($k = 0.45, P < 0.05$). However, for patients with a CMR diagnosis of myocarditis and AMI, there was only a fair level of agreement ($k = 0.36, P < 0.05; k = 0.20, P < 0.05$, respectively). When compared by diagnosis type, the consensus panel diagnosis was consistent with CMR in 67% of patients with TTC, 69% with AMI, and 62% for myocarditis (Figure 3). The level of agreement between the consensus panel and the CMR was generally poor in all diagnostic categories. The lowest level of agreement was seen in AMI as presented in Table 2.

**Outcomes**

The median follow-up was 24 months. Based on the CMR diagnosis, three patients with AMI, one with TTC, and one with normal CMR examination experienced stroke during follow-up (4.0%). Three (2%) patients were rehospitalized for heart failure. All of these patients had a diagnosis of TTC during the initial admission. Four patients with AMI, one patient with TTC, and one with myocarditis experienced an AMI during follow-up (5%). Four of these patients required revascularization and the other two were managed medically. One patient (1%) died during follow-up due to a non-cardiac cause. This patient’s CMR diagnosis was TTC. There were no cardiovascular deaths. In those patients who had a normal CMR examination, one patient experienced a stroke in the setting of temporary warfarin cessation. There were no other events in this group.

**Discussion**

The current study highlights the lack of agreement among clinicians in the diagnosis of cTnT-positive patients with unobstructed coronary arteries and the value of CMR in assisting clinicians to better diagnose such patients. The principal findings are as follows:

(i) Concordance between clinical and CMR diagnosis is poor in these patients.

(ii) In almost 50% of patients, CMR changed the consensus panel diagnosis.

(iii) CMR provided a diagnosis in 87% of patients, reinforcing the role of CMR in risk stratification in this population.

Our study has shown that clinicians struggle to correctly diagnose patients with cTnT-positive chest pain with unobstructed coronary arteries despite the availability of clinical details and investigations such as ECG, cTnT, coronary angiography, and echocardiography. For example, in only 32% of patients did all three cardiologists have the same diagnosis as CMR. Of concern, in 25% of patients, none of three cardiologists had a diagnosis consistent with the CMR diagnosis. Moreover, there was only a poor level of agreement between the diagnosis provided by the consensus panel and CMR diagnosis ($k = 0.39, P < 0.05$). These findings highlight the limitations of clinical acumen alone in correctly diagnosing patients in this population. CMR is an objective investigation, which can assist clinicians in managing such patients. Our study has shown that based on the consensus panel diagnosis, CMR changed the diagnosis in almost 50% of patients and, consequently, resulted in these patients being treated correctly.

Additionally, among the patients with a diagnosis of AMI on CMR, the consensus panel had an alternative diagnosis in a third of patients with at least one cardiologist missing the diagnosis in 75% of patients. This is also reflected by the lowest level of agreement between the consensus panel and CMR diagnosis among the diagnostic groups ($k = 0.09, P < 0.05$). A potential source of this difference could be explained by the impact of a ‘normal coronary angiogram’ on the clinician’s diagnosis. That is, since the angiogram in these patients shows normal coronary arteries, clinicians are influenced to believe that the diagnosis is not an AMI. Our findings thus highlight the potential risk of underdiagnosing and therefore undertreating patients. For example, if a patient received a clinical diagnosis of myocarditis but had evidence of AMI on CMR, this patient would not have received mortality benefit-proven secondary prevention AMI treatment if managed purely on clinical grounds. A correct diagnosis also has implications for providing appropriate
counselling, insurance, outpatient follow-up management, and future risk stratification.

To our knowledge, no previous study has used a blinded ‘expert clinical panel’ to assess the utility of clinician judgement vs. CMR findings. Only one study, to date, has reported a suspected clinical diagnosis with eventual CMR findings. The study by Gerbaud et al. found that the CMR diagnosis was different from the diagnosis suspected by the referring physician in 24.8% of cases. However, this differs significantly from our study, as there was only one clinician who was the patient’s treating physician and was not blinded to the CMR findings. We prospectively set up to use an ‘expert panel’ of board-certified cardiologists, who were not involved in the patient’s care and who were blinded to patient’s clinical details and CMR diagnosis. Furthermore, the study by Gerbaud et al. excluded patients with a history of ischaemic heart disease, clinically diagnosed myocarditis or heart failure. Hence, our findings likely reflect real-world practice and the difficulties that exist for a clinician in providing a diagnosis in this cohort of patients.

CMR has emerged as an important investigation in the assessment of cTnT-positive chest pain patients with unobstructed coronary arteries. Our study adds to the growing evidence that CMR provides a diagnosis in the majority of cases in this difficult-to-diagnose patient population. Large-scale registry data suggest that >80% of patients with cTnT-positive chest pain undergoing cardiac catheterization may have significant epicardial coronary stenosis. However, in up to 10% of these patients, coronary angiography does not reveal a flow-limiting stenosis and the diagnosis poses a clinical dilemma. This study demonstrates that CMR provided a definitive diagnosis in 87% of patients with cTnT-positive, non-obstructive coronary artery disease.

Our study has a relatively higher number of definitive CMR diagnoses when compared with earlier studies, in which 65–77% of patients had diagnostic CMR studies. Our more contemporary findings may be reflective of the improved CMR imaging techniques that allow better tissue characterization and subsequent diagnosis. As with earlier studies, acute myocarditis was the most commonly diagnosed pathology. In contrast to earlier work by Assomull et al. who only reported one case of TTC, we found that 27% of our patients had TTC. The higher prevalence of TTC in our cohort is likely due to the earlier use of CMR in our series, resulting in

Figure 1 An example of the discordance between consensus panel and CMR diagnosis. A 58-year-old male smoker with a history of hypertension presented with chest pain. Peak troponin was 2229 ng/L. ECG showed T-wave inversion in leads I and aVL (A). Coronary angiography revealed minor coronary disease. The consensus panel diagnosis was acute myocarditis. The CMR showed evidence of transmural LGE (white arrow) with microvascular obstruction (red arrow) in the basal to mid-anterolateral and inferolateral walls suggestive of an AMI (B).
timely detection of typical wall motion abnormalities and demonstrating the absence of LGE.19

As with any imaging modality, risk stratification is necessary to determine which patients would benefit most from the investigation. Although our study has shown a benefit of CMR in the troponin-positive patient with chest pain and unobstructed coronary arteries, there appears to be a subset of patients in whom CMR may not be helpful. We found that in all patients with a normal ECG and peak cTnT $<100$ ng/L, the CMR was normal. However, further studies are required to evaluate this subset of patients.

From a prognostic point of view, our study reinforces the growing evidence that troponin-positive patients with unobstructed coronaries should not be considered a low-risk population. Although there was only one death during follow-up due to a non-cardiac cause, $6$ (5%) patients experienced AMI during follow-up and the total event rate 12%. In large-scale registry data, major adverse cardiac events (defined as death, MI, and revascularization) was 7.8% in MI patients with near-normal coronaries.20 In a recent meta-analysis, 12-month all-cause mortality was 3.5% in this patient population.21 Troponin-positive chest pain patients with unobstructed coronaries should therefore receive close follow-up and the high rate of adverse cardiovascular events reinforces the importance of establishing a correct diagnosis from the outset.

**Study limitations**

The treating inpatient unit was not blinded to the CMR diagnosis and, therefore, would have managed the patients accordingly. This, however, does not influence the main finding of our study, which is the poor concordance between clinical and CMR diagnosis. There was no endomyocardial biopsy performed in the patients diagnosed with myocarditis on CMR. However, many studies have shown patterns seen on CMR to correlate with histological findings.22,23 A peak troponin rather than area under the curve of serial cTnT has been used which would limit comparisons between LGE and cTnT levels. In non-diagnostic CMR, non-cardiac causes of troponin elevation, such as pulmonary embolism, could not be ruled out. Furthermore, as we did not classify basal akinesis patients (with or without positive T2W images and no LGE) as TTC, we may have underestimated the true prevalence of TTC by possibly missing cases of atypical TTC. The assessment of myocardial oedema was undertaken by T2-weighted sequence (short-tau inversion recovery), and T1 or T2 mapping was not performed. Although the STIR sequence is a standard technique widely used in clinical practice for detection of acute myocardial oedema, it has several limitations.
including signal drop-out, long breath-holds, and blood pooling, resulting in artefactually high signal in subendocardium (particularly in the apical segments) and unreliable ‘normal’ reference region of interest due to signal inhomogeneity when using skeletal muscle as a reference.11,12,25 T1 and T2 mapping techniques are known to have superior diagnostic accuracy in comparison with STIR and may have been useful in providing a diagnosis in patient with non-diagnostic/normal CMR.26,27

**Conclusions**

Establishing the diagnosis in patients presenting with cTnT-positive chest pain with unobstructed coronary arteries represents a diagnostic dilemma. Our study reinforces the role of CMR in providing a diagnosis in such patients. Establishing a diagnosis on clinical grounds with the availability of investigations such as ECG, coronary angiography, and echocardiography in this group of patients remains a challenge, and CMR is an objective tool that can assist clinicians in better diagnosing these patients.

**Conflict of interest:** none declared.

**References**