Chest pain, troponin rise and normal coronary arteries. Are they all myocarditis cases? Insights from Cardiovascular MRI in our population.

Poster No.: C-1126
Congress: ECR 2016
Type: Scientific Exhibit
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Keywords: Ischemia / Infarction, Inflammation, Acute, Diagnostic procedure, MR, Thorax, Cardiac
DOI: 10.1594/ecr2016/C-1126

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Aims and objectives

Current literature states that about 75% of patients with chest pain, electrocardiographic (EKG) alteration at admission, troponin (Tn) rise and normal coronary arteries (NCA: Coronary angiography with no or non significant lesions; stenosis <50%) are diagnosed of myocarditis in cardiovascular magnetic resonance scans (CMR).

CMR provides structural and functional information, and has the ability to detect regional differences in myocardial tissue characteristics after gadolinium infusion. In the case of myocarditis, late gadolinium enhancement (LGE) is localised in the epicardial or mid-wall layers or could also be patchy in distribution, where as in myocardial infarction the typical pattern is subendocardial or transmural. Additional information is provided in T2 weighted images, in which myocardial regions of increased signal indicate increases on water content, inferring myocardial inflammation. Together, LGE and T2 imaging may reliably differentiate between myocarditis and myocardial infarction.

The purpose of this review was to know the real final diagnosis of patients suffering from this condition in our centre.

Methods and materials

Inclusion criteria

A retrospective systematic review of our CMR data base was performed from January 2012 to October 2015. All patients referred to CMR that presented with prolonged chest pain at rest (at least 30 minutes), EKG alteration or Tn rise and had NCA were included.

Imaging protocol

CMR studies were performed within the first week of admission on a 1.5 T Philips Achieva (The Nederlands) scanner with a cardiac 32-channel phased array coil or a 3T Siemens Verio (Erlangen, Germany) scanner with a cardiac 16-channel phased array coil. Images were acquired during breath-holds with ECG gating. We used a segmented k-space steady-state free-precession sequence [RT 44·70 ms; echo time 1·26 ms; flip angle 50-78; matrix 272; spatial resolution (1·3-1·5)x(1·3-1·5)x8mm depending on the field of
view] for cine imaging in parallel short-axis (contiguous slices of 8-mm thickness covering from base to apex) and 3 long-axis views of the left ventricle. T2-weighted black-blood with fat saturation (TSE-STIR) images were performed at matching cine-image slice locations. Delayed enhancement images were acquired with a segmented gradient-echo inversion-recovery sequence [RT (600-800) ms depending on the cardiac heart rate; echo time 3-24ms; flip angle 25; matrix 256; spatial resolution 1·3x1·3x8mm] at matching cine-image slice locations 10 to 20 minutes after intravenous gadolinium-DTPA administration (0·15mmol/kg; Gadovist, Bayer Schering Pharma AG, Berlin, Germany).

All images were reviewed and analyzed off-line with a specialized post-processing software (Philips IntelliSpace Portal® software, Philips; The Netherlands). LV endocardial border (papillary muscles were excluded) were manually traced on all short-axis cine images at the end-diastolic and end-systolic frames to determine the LV end-diastolic and LV end-systolic volumes, respectively. LV mass was calculated by subtracting the endocardial volume from the epicardial volume at end diastole and then multiplying by the tissue density (1·05 g/mL).

Results

Over this period, 84 patients met the inclusion criteria. Medium age was 43 years old (range 16-83), and they were mainly males (71%). The most common EKG alterations were ST segment elevation (57%) and T wave inversion (24.7%). Mean peak TnI levels at 12h of admission was 9.4ng/ml [95% CI 5.5-13.1] (table 1).

Table 1. Clinical features

<table>
<thead>
<tr>
<th>Feature</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>84</td>
</tr>
<tr>
<td>Age, mean ± SD</td>
<td>43 ± 18.9</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>60 (71%)</td>
</tr>
<tr>
<td>Tn I, mean peak ± SD</td>
<td>9.4 ± 16.3</td>
</tr>
<tr>
<td>ECG, n (%)</td>
<td></td>
</tr>
<tr>
<td>ST elevation</td>
<td>44 (57%)</td>
</tr>
<tr>
<td>ST depression</td>
<td>4 (5.2%)</td>
</tr>
<tr>
<td>T wave inversion</td>
<td>19 (24.7%)</td>
</tr>
<tr>
<td>PR segment alteration</td>
<td>2 (2.6%)</td>
</tr>
</tbody>
</table>
AV Block 5 (6.5%)
Normal 3 (3.9%)

CMR diagnosis (Fig. 1) resulted in myocarditis in 40 patients (48% of cases) (Fig. 2 on page 6, Fig. 3 on page 7, Fig. 4 on page 8, Fig. 5 on page 9, Fig. 6 on page 10), myocardial infarct despite NCA in 15 (18%) (Fig. 7 on page 11, Fig. 8 on page 12, Fig. 9 on page 13), and Takotsubo in 11 (13%) (Fig. 10 on page 14, Fig. 11 on page 15, Fig. 12 on page 16, Fig. 13 on page 17, Fig. 14 on page 18, Fig. 15 on page 19). Dual pathology (myocarditis and infarct) was detected in 3 patients (3.6%). Dilated cardiomyopathy (DCM) was diagnosed in 3 cases (3.6%). Cardiac sarcoid and pericarditis were the less frequent results (1.2% each one). 8 cases had normal CMR scans (9.6%). MRI scan was not conclusive only in 1 case.

Fig. 1: CMR final diagnoses.

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Mean left ventricular ejection fraction (LVEF) was 56.7% (ranges 20 to 84%). Regional wall motion abnormalities (RWMA) were present in 56 cases (62.9%), and mean segmental score index (SCI) was 1.2 (ranges 1 to 3). High signal in T2 weighted images was detected in 65% of cases. Late gadolinium enhancement (LGE) was present in 60 cases (71.4%). Distribution of contrast is summarised in table 2.
Table 2. CMR findings

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with RWMA, n (%)</td>
<td>56 (62.9%)</td>
</tr>
<tr>
<td>Score Contractility Index (SCI), mean ± SD</td>
<td>1.22 ± 0.3</td>
</tr>
<tr>
<td>LVEF, mean ± SD</td>
<td>57.6% ± 12.3</td>
</tr>
<tr>
<td>Patients with high signal on T2w images, n (%)</td>
<td>55 (65%)</td>
</tr>
<tr>
<td>Segments with high signal on T2w images, mean ± SD</td>
<td>2.8 ± 3.2</td>
</tr>
<tr>
<td>Late gadolinium enhancement, n (%)</td>
<td>60 (71.4%)</td>
</tr>
<tr>
<td>Location of LGE</td>
<td></td>
</tr>
<tr>
<td>Subendocardial</td>
<td>15 (24%)</td>
</tr>
<tr>
<td>Epicardial</td>
<td>36 (58%)</td>
</tr>
<tr>
<td>Midwall</td>
<td>8 (12.9%)</td>
</tr>
<tr>
<td>Diffuse</td>
<td>2 (3.2%)</td>
</tr>
<tr>
<td>Pericardial</td>
<td>1 (1.6%)</td>
</tr>
</tbody>
</table>

Patients with final diagnosis of myocarditis had the highest peak TnI levels (15.5±21.5ng/ml vs 4.1±7.2ng/ml; p=0.02). ST segment elevation was more frequent in Takotsubo (100%), pericarditis (100%), myocarditis (54.3%) and IHD (35.7%) patients [p=0.032]. Interestingly, only 11.4% of patient with ST segment elevation at admission had a myocardial infarct, being other final diagnosis myocarditis (43.2%), Takotsubo (25%), DCM (4.5%) or normal (6.8%). The presence of edema was more frequent in myocarditis (80%) and Takotsubo (81%) cases as compared to the rest [p<0.01]. The extent of edema was more important in Takotsubo, myocarditis and IHD patients (segments affected: mean±SD 5.7±3.58, 3.2±3.1 and 1.53±1.84 respectively; p=0.02). Patients with myocarditis and pericarditis were significantly younger than the other (33yo vs 48yo; p<0.01). As expected, the 3 patients with DCM had larger ventricles (iLVEDV 154ml vs 80ml) and poorer LV EF (26% vs 61%) [p<0.01].

Images for this section:
**Fig. 1:** CMR final diagnoses.

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**Fig. 2:** 41 year-old-man, ex-smoker and with history of myopericarditiis in 1999 and 2005. Now back to the hospital with chest pain, Tn raise (TNI 37) and ECG with generalitized ST segment elevation anterior, lateral and inferior, and PR depression. Echocardiogram did not show segment alterations. Short axis STIR images (a) depict increase signal (edema) of septal and anterior mid and apical walls (arrows). Four-chamber (b) and two-chamber STIR images depict increase signal (edema) of septal and anterior mid and apical walls (arrows).

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Fig. 3: Myocarditis. Same patient as before. Short axis a), four-chamber (b) and two-chamber (c) delayed enhancement MR images show subepicardial enhancement of the inferior and lateral mid and apical walls (arrows).

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Fig. 4: 41 year-old-man with acute lung edema, fever and necrosis myocardial markers (TNI 7) raise. Four-chamber (a), three-chamber (b) and short-axis (c) STIR images depict increase signal (edema) in patchy distribution of mid septal wall and inferior and lateral segments (arrows).

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**Fig. 5:** Myocarditis. Same patient as before. Four-chamber (a), three-chamber (b) and short-axis (c) delayed enhancement MR images show patchy enhancement of inferior and lateral mid and apical walls (arrows), and more confluent enhancement in septal midwall (arrowheads).

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**Fig. 6:** Myocarditis. Same patient as before. Short axis delayed enhancement MR images show patchy enhancement of inferior and lateral mid and apical walls (arrows), and more confluent enhancement in septal midwall (arrowheads).

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Fig. 7: 40 year-old man with recent history of respiratory infection with chest pain and fever. EKG showed depressed ST segment at V4-V5 and myocardial necrosis markers were raised (TnI 29ng/mL). Short-axis STIR images depict increase signal (edema) of anterior and lateral mid and apical walls (arrows).

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**Fig. 8:** Myocardial Infarct. Same patient as before. Short axis delayed enhancement MR images show subendocardial enhancement of the anterior and lateral mid and apical walls (arrows).

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Fig. 9: 45 year-old-woman with chest pain, TNI raise and normal coronary arteries. STIR T2-weighted sequence planned four-chamber (a) and two-chamber (b) views show edema in inferior apical segment (arrow) Delayed enhancement sequence in the four-chamber (c) and two-chamber (d) views depict subendocardial enhancement in apical segments and apex

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Fig. 10: 68 year-old-woman with hypertension, diabetes and dyslipemia who presented prolonged chest pain. EKG did not show specific alterations, myocardial necrosis markers were high and echocardiography showed apical akinesia. Short axis cine images depict hypokinesia of anterior mid wall and apical segments.

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**Fig. 11:** Takotsubo. Same patient as before. STIR images in three-chamber (a), four-chamber (b), two-chamber (c) and short axis views (d) depict increase signal (edema) fully involving the mid and apical segments (arrows), and sparing of the basal segments.

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Fig. 12: Takotsubo. Same patient as before. Late gadolinium enhancement images (a-d) did not show myocardial enhancement.

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Fig. 13: Takotsubo. Different patient than previous. Three-chamber cine clip depict hypokinesia in the mid and apical segments, and sparing of the basal segments.

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Fig. 14: Takotsubo. Different patient than previous. Four-chamber cine clip depict hypokinesia in the mid and apical segments, and sparing of the basal segments.

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Fig. 15: Takotsubo. Different patient than previous. Four-chamber cine clip depict hypokinesia in the apical segments, and sparing of the mid and basal segments.

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Conclusion

- CMR is a useful technique for evaluating patients with chest pain, troponin rise or ECG alteration and normal coronary arteries.
- Less than half of patients (48%) of our cohort had final diagnosis for myocarditis; this proportion is much lower when compared to the reported in the literature.
- Interestingly, a not insignificant proportion of patients (18%) had myocardial infarcts despite NCA and dual pathology was depicted in 4%.
- More interestingly, when analysing those presenting with ST segment elevation at admission, only 11.4% corresponded to myocardial infarction.

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