Cardiac troponin T and I are differentially associated with myocardial fibrosis assessed by cardiac magnetic resonance imaging

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Background: Cardiac troponin T (cTnT) is more potently associated with non-cardiovascular (CV) mortality and cardiac troponin I (cTnI) is more specific for CV risk in the general population. Cardiovascular magnetic resonance imaging (CMR) measurement of extracellular volume (ECV) allows for assessment of diffuse myocardial fibrosis and is associated with adverse CV events. Focal myocardial scars are assessed by late gadolinium enhancement (LGE) and LGE scar presence is associated with unfavorable CV outcomes. The distinct clinical outcomes associated with cTnT and cTnI may be due to different subtypes and burden of myocardial fibrosis. Elevation of cTnT associates with increased ECV in a CMR referral base and with nonischemic myocardial scars in the general population. There is limited data comparing the associations of cTnT and cTnI with CMR indices of fibrosis in the general population.

Purpose: Perform head-to-head comparison of the associations of cTnT (Roche Elecsys) and cTnI (Abbott Alinity) with diffuse and focal myocardial fibrosis assessed by CMR.

Methods: Two hundred community-dwellers born in 1950 with approximately similar sex distribution were recruited. All participants were without contraindications to contrast-enhanced CMR, had normal kidney function and no known coronary artery disease. For the study a 1.5-T Philips MRI clinical scanner was used. Diffuse fibrosis was estimated by septal ECV and focal scars were quantified by LGE and classified as either ischemic or nonischemic. Complete MOLLI-sequence for assessment of ECV was present in 192 participants and 198 participants had complete LGE sequence. Logistic regression analysis was used to examine relationships between log transformed cardiac troponins and CMR indices of myocardial fibrosis, adjusting for a priori selected established cardiovascular risk factors. We analyzed ECV according to cut-off values based on the upper sex-specific quartile.

Results: The median age was 69 (68.6-69.3) and 52% were male (Table 1). The upper sex-specific quartile of ECV was 27% for men and 28% for women. cTnT was associated with ECV in the fully adjusted model (odds ratio [OR] 1.98, 95% CI 1.08-3.64), in contrast to cTnI which was not associated with ECV in any of the models (Table 2). cTnT (OR 3.71 95% CI 1.83-7.50) and cTnI (OR 1.69 95% CI 1.24-2.30) were associated with the presence of any LGE scar in the fully adjusted model, but the association was stronger for cTnT (p for comparison = 0.024). cTnT and cTnI were significantly associated with nonischemic scars in all models (Table 2), but stronger for cTnT (p for comparison = 0.018). In the fully adjusted model only cTnI was associated with the presence of ischemic scars (OR 1.66 95% CI 1.05-2.61).

Conclusion(s): In our cohort of community-dwellers, cTnT is the stronger marker of diffuse and nonischemic myocardial fibrosis, while cTnI seems to more strongly reflect the presence of ischemic scar as assessed by CMR.
Table 1. Participant characteristics according to concentrations of cardiac troponin T (cTnT) and cardiac troponin I (cTnI)

<table>
<thead>
<tr>
<th></th>
<th>Entire cohort</th>
<th>Concordant low concentrations</th>
<th>Discordant concentrations</th>
<th>Concordant high concentrations</th>
<th>p-value for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>200</td>
<td>131</td>
<td>36</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>200</td>
<td>103 (51.5%)</td>
<td>67 (51.1%)</td>
<td>20 (55.6%)</td>
<td>16 (48.5%)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>200</td>
<td>26.3 (23.5-28.7)</td>
<td>26.1 (23.1-27.7)</td>
<td>27.3 (23.7-29.7)</td>
<td>26.4 (24.0-29.8)</td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>200</td>
<td>13 (6.5%)</td>
<td>7 (5.5%)</td>
<td>3 (8.8%)</td>
<td>3 (9.1%)</td>
</tr>
<tr>
<td>Higher education, n (%)</td>
<td>200</td>
<td>105 (52.8%)</td>
<td>67 (51.1%)</td>
<td>21 (60%)</td>
<td>17 (51.5%)</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>200</td>
<td>136 (124.5-148)</td>
<td>134 (123-148)</td>
<td>141 (132-149)</td>
<td>136 (127-148)</td>
</tr>
<tr>
<td>Self-reported diabetes mellitus, n (%)</td>
<td>200</td>
<td>13 (6.5%)</td>
<td>6 (4.7%)</td>
<td>4 (11.4%)</td>
<td>3 (9.1%)</td>
</tr>
<tr>
<td>eGFR, ml/min/1.73 m²</td>
<td>200</td>
<td>76 (61.89)</td>
<td>78 (61.0-89)</td>
<td>78 (61.5-86.5)</td>
<td>61 (61.0-82)</td>
</tr>
<tr>
<td>LVMI, g/m²</td>
<td>199</td>
<td>46.6 (40.9-55.1)</td>
<td>45 (40.4-51.1)</td>
<td>48 (43.3-60.6)</td>
<td>56.1 (48.8-64.1)</td>
</tr>
<tr>
<td>ECV fraction, %</td>
<td>192</td>
<td>26 (25-28)</td>
<td>26 (24-28)</td>
<td>26 (25-28)</td>
<td>26 (24-29)</td>
</tr>
<tr>
<td>Ischemic scar type, n (%)</td>
<td>198</td>
<td>18 (9.1%)</td>
<td>6 (4.6%)</td>
<td>4 (11.3%)</td>
<td>8 (25%)</td>
</tr>
<tr>
<td>Nonischemic scar type, n (%)</td>
<td>198</td>
<td>27 (14%)</td>
<td>8 (6.2%)</td>
<td>8 (22.2%)</td>
<td>11 (34.4%)</td>
</tr>
</tbody>
</table>

Baseline data are presented as median (interquartile range) or number (percentage). Continuous variables were analyzed with the Mann-Whitney U test and categorical variables with the Pearson Chi-Squared test.

The cut-off value for elevated cTn represents the sex-specific upper quartile of each cTn. The participants were designated to groups according to elevated cTnT or cTnI, either concordant low concentrations (both cTnT and cTnI below the sex-specific upper quartile), discordant concentrations (either cTnT or cTnI concentration above the sex-specific upper quartile) or concordant high concentrations (both cTnT and cTnI concentrations above the sex-specific upper quartile).

Participant characteristics

Table 2. Associations of cTnT and cTnI with CMR variables

<table>
<thead>
<tr>
<th></th>
<th>Model 1 OR (95% CI)</th>
<th>Model 2 OR (95% CI)</th>
<th>Model 3 OR (95% CI)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septal ECV***</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cTnT</td>
<td>1.53 (0.95-2.46)</td>
<td>1.79 (1.04-3.09)</td>
<td>1.98 (1.08-3.66)</td>
<td>0.05</td>
</tr>
<tr>
<td>cTnI</td>
<td>1.10 (0.89-1.35)</td>
<td>1.15 (0.90-1.49)</td>
<td>1.17 (0.82-1.65)</td>
<td></td>
</tr>
<tr>
<td>LGE presence***</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>cTnT</td>
<td>5.44 (2.99-9.90)</td>
<td>4.74 (2.45-9.15)</td>
<td>4.71 (1.83-7.50)</td>
<td>0.024</td>
</tr>
<tr>
<td>cTnI</td>
<td>1.99 (1.51-2.63)</td>
<td>1.91 (1.43-2.57)</td>
<td>1.69 (1.24-2.30)</td>
<td></td>
</tr>
<tr>
<td>Ischemic scar</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cTnT</td>
<td>4.90 (2.20-10.91)</td>
<td>4.68 (1.69-11.87)</td>
<td>2.29 (0.80-7.19)</td>
<td>0.43</td>
</tr>
<tr>
<td>cTnI</td>
<td>1.94 (1.33-2.82)</td>
<td>1.96 (1.27-3.03)</td>
<td>1.66 (1.05-2.61)</td>
<td></td>
</tr>
<tr>
<td>Nonischemic scar</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cTnT</td>
<td>5.35 (2.66-10.74)</td>
<td>4.80 (2.24-10.29)</td>
<td>4.47 (1.99-10.05)</td>
<td>0.018</td>
</tr>
<tr>
<td>cTnI</td>
<td>1.86 (1.37-2.53)</td>
<td>1.81 (1.32-2.50)</td>
<td>1.73 (1.23-2.44)</td>
<td></td>
</tr>
</tbody>
</table>

Model 1, unadjusted; Model 2, adjusted for age, sex, BMI, eGFR, systolic blood pressure, self-reported current smoking status and self-reported diabetes mellitus; Model 3, adjusted for model 2 and LVMI OR, odds ratios; CI, confidence interval
*p-value for comparison represents results of generalized Hausman specification test comparing odds ratios of cTnT and cTnI in the fully adjusted models
***Septal extracellular volume (ECV) represents the upper sex-specific quartile of ECV (27% for men, 28% for women)
****Late gadolinium enhancement (LGE) presence represents the presence of any type of focal myocardial scar

Associations of cTnT and cTnI