Abstract: 240

Symptomatic transthyretin cardiac amyloidosis is associated with chronic myocardial ischemia at rest and early death

Authors:
J Sorensen¹, HJ Harms², G Wikstrom³, B Pilebro⁴, O Vedin³, SO Granstam³, S Rosengren³, ¹Uppsala University, Surgical Sciences, Nuclear Medicine - Uppsala - Sweden, ²Aarhus University, Clinical Institute - Aarhus - Denmark, ³Uppsala University, Medical sciences - Uppsala - Sweden, ⁴Umea University Hospital, Cardiology - Umea - Sweden,

Topic(s):
Positron Emission Tomography (PET)

Citation:

Funding Acknowledgements:
Supported by Swedish Heart-Lung Foundation

Background: Cardiac amyloidosis (CA) is an infiltrative cardiomyopathy with poor outcome and appears to be underdiagnosed. A few reports using 13N-H3 and 11C-acetate PET in small samples indicated that resting MBF is severely lowered in CA, but it is not known if this is a partial volume effect or a true reduction. This question might be answered by kinetic modeling of 15O-water PET, which separates MBF (wash-out rate) and the partial volume effect PTF (=wash-in/wash-out).

Methods: we studied 44 subjects with 15O-water PET at rest between 2013-2017. Subjects included 27 verified CA (9 light chain (AL) and 8 transthyretin (ATTRwt) with typical echocardiography findings and heart failure; 10 asymptomatic hereditary TTR (ATTRm) with unspecific echocardiography findings), 8 LVH with heart failure in which CA was ruled out, and 9 healthy volunteers (HV). MBF (corrected for the rate-pressure product RPP) was measured using the aQuant software package, extended with a method for automated calculation of LV mass (LVM) and septal wall thickness (WT) by segmenting parametric PTF images. Minimal microvascular resistance (MMR) was defined by the ratio of peripheral diastolic blood pressure/MBF.

Results: Results are presented in Table 1. MBF in ATTRwt was lower and MMR in ATTRwt was higher than in all other groups (p=0.002 for all comparisons). MMR correlated with WT both in the transthyretin subjects (ATTRm+ATTRwt) (r=0.82, p<0.001) and the non-amyloid subjects (HV+LVH) (r=0.64, p<0.001), but the increase in MMR per mm was seven times higher in the transthyretin group (p<0.001). MMR and WT were not correlated in AL. There were 9 cardiac events (8 deaths) at median 26 months follow-up. MBF, MMR, PTF, WT and LVM index in CA predicted survival in univariate analysis (Log-rank p<0.05 for each). All events occurred in CA subjects with PET LVM index >104 g/m2, which was the only significant predictor in multivariate analysis (p<0.001).

Conclusion: Symptomatic transthyretin CA is characterized by dramatically lowered resting MBF, associated with a steep increase of microvascular resistance per unit wall thickness and early death. 15O-water PET at rest may be useful for risk prediction in CA.

<table>
<thead>
<tr>
<th></th>
<th>HV</th>
<th>LVH</th>
<th>ATTRm</th>
<th>ATTRwt</th>
<th>AL</th>
<th>ANOVA p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate-pressure product</td>
<td>8.2±0.7</td>
<td>9.0±0.7</td>
<td>8.2±0.7</td>
<td>8.1±0.7</td>
<td>8.9±0.7</td>
<td>0.85</td>
</tr>
<tr>
<td>Resting MBF corrected</td>
<td>1.1±0.1</td>
<td>0.8±0.2</td>
<td>1.0±0.2</td>
<td>0.6±0.1</td>
<td>0.8±0.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Microvascular resistance</td>
<td>86±15</td>
<td>105±14</td>
<td>87±15</td>
<td>175±33</td>
<td>101±0.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PET LV mass index (g/m2)</td>
<td>63±5</td>
<td>102±22</td>
<td>89±20</td>
<td>118±15</td>
<td>101±21</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Symptomatic transthyretin cardiac amyloidosis is associated with chronic myocardial ischemia at rest and early death.

Authors: J Sorensen, HJ Harms, G Wikstrom, B Pilebro, O Vedin, SO Granstam, S Rosengren.

1 Uppsala University, Surgical Sciences, Nuclear Medicine - Uppsala - Sweden, 2 Aarhus University, Clinical Institute - Aarhus - Denmark, 3 Uppsala University, Medical sciences - Uppsala - Sweden, 4 Umea University Hospital, Cardiology - Umea - Sweden.

Topic(s): Positron Emission Tomography (PET)

Citation: [details not provided]

Funding Acknowledgements: Supported by Swedish Heart-Lung Foundation.

Background: Cardiac amyloidos (CA) is an infiltrative cardiomyopathy with poor outcome and appears to be underdiagnosed. A few reports using 13N-H3 and 11C-acetate PET in small samples indicated that resting MBF is severely lowered in CA, but it is not known if this is a partial volume effect or a true reduction. This question might be answered by kinetic modeling of 15O-water PET, which separates MBF (wash-out rate) and the partial volume effect PTF (=wash-in/wash-out).

Methods: we studied 44 subjects with 15O-water PET at rest between 2013-2017. Subjects included 27 verified CA (9 light chain (AL) and 8 transthyretin (ATTRwt) with typical echocardiography findings and heart failure; 10 asymptomatic hereditary TTR (ATTRm) with unspecific echocardiography findings), 8 LVH with heart failure in which CA was ruled out, and 9 healthy volunteers (HV). MBF (corrected for the rate-pressure product RPP) was measured using the aQuant software package, extended with a method for automated calculation of LV mass (LVM) and septal wall thickness (WT) by segmenting parametric PTF images. Minimal microvascular resistance (MMR) was defined by the ratio of peripheral diastolic blood pressure/MBF.

Results: Results are presented in Table 1. MBF in ATTRwt was lower and MMR in ATTRwt was higher than in all other groups (p=0.002 for all comparisons). MMR correlated with WT both in the transthyretin subjects (ATTRm+ATTRwt) (r=0.82, p<0.001) and the non-amyloid subjects (HV+LVH) (r=0.64, p<0.001), but the increase in MMR per mm was seven times higher in the transthyretin group (p<0.001). MMR and WT were not correlated in AL. There were 9 cardiac events (8 deaths) at median 26 months follow-up. MBF, MMR, PTF, WT and LVM index in CA predicted survival in univariate analysis (Log-rank p<0.05 for each). All events occurred in CA subjects with PET LVM index >104 g/m2, which was the only significant predictor in multivariate analysis (p<0.001).

Conclusion: Symptomatic transthyretin CA is characterized by dramatically lowered resting MBF, associated with a steep increase of microvascular resistance per unit wall thickness and early death. 15O-water PET at rest may be useful for risk prediction in CA.

<table>
<thead>
<tr>
<th>PET Septal WT (mm)</th>
<th>10±2</th>
<th>17±4</th>
<th>14±2</th>
<th>19±2</th>
<th>15±5</th>
<th>&lt;0.001</th>
</tr>
</thead>
</table>

[Table continues with more comparisons and p-values]