Coronary microvascular dysfunction and Obesity in ED chest pain patients
A potential area for early prevention of coronary artery disease

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Background
- 8 million patients present with chest pain to emergency departments (ED) in the U.S each year.
- About 15-20% of these have ischemia from large vessel coronary artery disease (CAD).
- The distribution of chest pain from coronary microvascular dysfunction (CMD) in ED patients and its characteristics is unknown.
- Coronary flow reserve (CFR) is an indirect measure for CMD and CFR < 2 has been shown to have a linear relationship with adverse cardiac outcomes.

Objectives
- To identify CMD in ED patients with chest pain who are ruled out for myocardial infarction.
- To identify clinical factors associated with CMD in ED patients.

Methods
- Prospective observational cohort of consecutive patients admitted to Yale ED chest pain center (CPC), an observation unit.
- Patients who met clinically indicated 3D cardiac Rb-82 dynamic PET/CT imaging were enrolled.
- Exclusions: age ≤ 30 years, acute coronary syndrome, hemodynamic instability, heart failure or dialysis.
- Gated PET/CT images were evaluated for regional perfusion abnormalities, and coronary calcification.
- Quantitative coronary flow and flow reserve (CFR) were derived by kinetic modeling of dynamic PET/CT images, and corrected for rate pressure product.
- Coronary microvascular dysfunction (CMD) was defined as: no regional perfusion defect, no calcification and CFR < 2.
- CAD defined: new or old regional defect, prior MI, calcification or revascularization.

Results

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>N=2405</th>
<th>Overall (N=195)</th>
<th>Normal (N=43)</th>
<th>CMD (N=81)</th>
<th>CAD (N=71)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (SD)</td>
<td>56 (12)</td>
<td>55 (11)</td>
<td>51 (10)</td>
<td>51 (7)</td>
<td>61 (11)</td>
</tr>
<tr>
<td>% Female</td>
<td>54</td>
<td>70</td>
<td>58</td>
<td>81*</td>
<td>63</td>
</tr>
<tr>
<td>% White</td>
<td>58</td>
<td>64</td>
<td>65</td>
<td>63</td>
<td>63</td>
</tr>
<tr>
<td>% Hispanic</td>
<td>17</td>
<td>19</td>
<td>14</td>
<td>21</td>
<td>20</td>
</tr>
<tr>
<td>% Hypertension</td>
<td>53</td>
<td>73</td>
<td>67</td>
<td>64</td>
<td>87</td>
</tr>
<tr>
<td>% Diabetes</td>
<td>19</td>
<td>41</td>
<td>40</td>
<td>31</td>
<td>54</td>
</tr>
<tr>
<td>% Dyslipidemia</td>
<td>41</td>
<td>55</td>
<td>51</td>
<td>38</td>
<td>76</td>
</tr>
<tr>
<td>% Smoking</td>
<td>15</td>
<td>19</td>
<td>21</td>
<td>14</td>
<td>17</td>
</tr>
<tr>
<td>% Family HX</td>
<td>28</td>
<td>28</td>
<td>33</td>
<td>30</td>
<td>24</td>
</tr>
<tr>
<td>Mean BMI (SD)</td>
<td>30 (7)</td>
<td>38 (9)*</td>
<td>39 (9)</td>
<td>40 (10)</td>
<td>37 (8)</td>
</tr>
<tr>
<td>Mean CFR (SD)</td>
<td>N/A</td>
<td>2.6 (0.8)</td>
<td>1.6 (0.3)*</td>
<td>1.9 (0.6)*</td>
<td></td>
</tr>
</tbody>
</table>

*non-PET/CT imaging included exercise treadmill test, exercise SPECT, pharmacological SPECT, CT angiogram and stress echocardiogram.

Conclusions
- Cardiac microvascular dysfunction is common in ED chest pain patients in the absence of CAD.
- ED patients with CMD had severely depressed CFR, even lower than in the CAD group – suggesting an ‘at risk’ population that would benefit from early risk stratification and interventions.
- CMD diagnosed in obese ED patients could serve as an early correlate of CAD.

Future Implications
- CMD could explain up to a third of the cases of ED chest pain that are otherwise ruled out for acute myocardial infarction.
- These patients often have recurrent symptoms and remain undiagnosed with routine testing.
- Further work on measuring insulin resistance and sensitivity in these patients would help identify targets for early intervention.
- Longitudinal follow-up is needed to correlate the severely depressed CFR seen in obese ED with adverse outcomes.
- Quantitative PET/CT could improve identification and management of CMD in obese ED patients with recurrent chest pain.

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