Myocardial performance index improves prediction of major adverse cardiovascular events and heart failure in type 1 and type 2 diabetes without known heart disease: Thousand&1 and Thousand&2 study

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Background: Cardiovascular disease (CVD) is the leading cause of mortality and morbidity in type 1 (T1D) and type 2 diabetes (T2D). Despite myocardial involvement in diabetes, current risk prediction models do not include parameters of the myocardial function. Myocardial performance index (MPI) reflects left ventricular systolic and diastolic function. The prognostic value of MPI has not been evaluated in larger-scale diabetes populations.

Purpose: To assess the prognostic value of MPI in a larger-scale diabetes population.

Methods: We evaluated two prospective cohort studies: The Thousand&1 Study (1093 individuals with T1D) and The Thousand&2 Study (1030 individuals with T2D). Clinical data, including echocardiography, were collected at baseline. We excluded 480 individuals with heart disease. We collected follow-up data from national registries. We defined major adverse cardiovascular events (MACE) as the first incident of all-cause death, hospital admission for acute coronary syndrome, heart failure, or stroke.

Results: For included individuals (56% male, 54±15 years, MPI 0.51±0.1, 63% T1D), follow-up was 100% after a median of 5.3 years (interquartile range: 4.8 to 6.3). MPI was significantly associated with MACE (Hazard ratio 1.2, 95% confidence interval 1.0-1.3, p=0.012, per 0.10-unit increase) and heart failure (Hazard ratio 1.3, 95% confidence interval 1.1-1.6, p=0.005, per 0.10-unit increase) after adjusting for clinical and echocardiographic variables. MPI predicted MACE better in T1D than in T2D (p=0.031 for interaction). MPI added discriminatory power to the Steno T1D Risk Engine (1,2) in predicting heart failure, but not MACE.

Conclusions: MPI is an independent predictor of MACE and heart failure in T1D and T2D, with the strongest prediction in T1D. Echocardiographic assessment in diabetes may enhance risk prediction.

Association between myocardial performance index and major adverse cardiovascular events

<table>
<thead>
<tr>
<th>Models</th>
<th>Events/subjects</th>
<th>Estimate (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted</td>
<td>207/1643</td>
<td>1.40 (1.30 : 1.60)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age + gender + clinical variables(a)</td>
<td>200/1596</td>
<td>1.30 (1.10 : 1.40)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age + gender + clinical variables(a) + systolic indices(b)</td>
<td>194/1557</td>
<td>1.20 (1.00 : 1.30)</td>
<td>0.021</td>
</tr>
<tr>
<td>Age + gender + clinical variables(a) + systolic indices(b) + diastolic indices(c)</td>
<td>186/1534</td>
<td>1.20 (1.00 : 1.30)</td>
<td>0.012</td>
</tr>
</tbody>
</table>

Forest plot summarizing the crude and adjusted models’ effect size estimates and 95% confidence intervals.

a: Systolic blood pressure, duration of diabetes, HbA1c, estimated glomerular filtration rate, use of statins, albuminuria status, and smoking status.

b: Left ventricular ejection fraction < 50% and global longitudinal strain < [15].

c: The ratio between mitral early inflow velocity and mitral annular early diastolic velocity (E/e’) > 13.
<table>
<thead>
<tr>
<th>Echocardiographic characteristics of the study population stratified according to tertiles of myocardial performance index</th>
<th>All</th>
<th>1st tertile</th>
<th>2nd tertile</th>
<th>3rd tertile</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.20-1.15</td>
<td>&lt;0.46</td>
<td>0.46-0.54</td>
<td>&gt;0.54</td>
<td></td>
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<tr>
<td>(n=1643)</td>
<td>(n=548)</td>
<td>(n=548)</td>
<td>(n=547)</td>
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</tbody>
</table>

### Systolic function

- **Left ventricular ejection fraction >50%, %**
  - All: 1536 (94)
  - 1st tertile: 530 (97)
  - 2nd tertile: 519 (95)
  - 3rd tertile: 487 (89)
  - p-value: <0.001

- **Global longitudinal strain, %**
  - All: -17±3
  - 1st tertile: -18±3
  - 2nd tertile: -17±3
  - 3rd tertile: -16±3
  - p-value: <0.001

### Diastolic function

- **e' lateral, cm/s**
  - All: 10±4
  - 1st tertile: 12±4
  - 2nd tertile: 11±4
  - 3rd tertile: 10±4
  - p-value: <0.001

- **E/e' lateral**
  - All: 8±3
  - 1st tertile: 8±3
  - 2nd tertile: 8±3
  - 3rd tertile: 8±3
  - p-value: 0.583

- **Left atrial volume (index), ml/m²**
  - All: 28±8
  - 1st tertile: 29±7
  - 2nd tertile: 28±7
  - 3rd tertile: 28±8
  - p-value: 0.336

- **Maximal tricuspid regurgitation, mmHg**
  - All: 22±5
  - 1st tertile: 23±5
  - 2nd tertile: 22±5
  - 3rd tertile: 21±5
  - p-value: <0.001

- **Myocardial performance index**
  - All: 0.51±0.1
  - 1st tertile: 0.40±0.05
  - 2nd tertile: 0.50±0.02
  - 3rd tertile: 0.62±0.08
  - p-value: <0.001

- **Internal end-diastolic diameter (index), mm/m²**
  - All: 23±3
  - 1st tertile: 23±3
  - 2nd tertile: 24±3
  - 3rd tertile: 23±3
  - p-value: 0.002

- **Mass(C)d1, g/m²**
  - All: 76±18
  - 1st tertile: 75±17
  - 2nd tertile: 77±17
  - 3rd tertile: 76±18
  - p-value: 0.058

**Abbreviations:** E = Early wave; e' = Pulsed-wave tissue-Doppler-imaging derived mitral annular early diastolic peak velocity.