Metformin Improves Left Ventricular Size and Function in Adolescents with Type 1 Diabetes

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Introduction
- People with type 1 diabetes (T1D) have higher rates of cardiovascular disease (CVD) despite modern advances in glucose control.
- We previously demonstrated vascular and cardiac dysfunction in adolescents with T1D.
- In the EMERALD study, we showed that metformin improves BMI, body composition, insulin sensitivity, arterial stiffness, and carotid intimal media thickness in T1D adolescents.
- We hypothesized that metformin, with insulin-sparing effects, also improves cardiac function.

Methods
- 43 T1D youth ages 12-21 years in the EMERALD study underwent a comprehensive evaluation of cardiovascular health, insulin sensitivity, and body composition.
- After baseline assessments, participants were randomized 1:1 to 3 months of either 2000 mg of metformin daily or placebo with repeat evaluations performed after treatment.
- Standard echocardiographic exams using the EchoPac program (GE Healthcare) were completed to evaluate aortic and cardiac function.
- 2D speckle-tracking was used for cardiac strain and synchrony analysis.

Results
Baseline Participant characteristics (n=43)
- Age 16.8 ± 2.5 years
- Hba1c 8.6 ± 1.5%
- BMI 25.1 ± 4.3 kg/m²
- Diabetes duration 7.7 ± 4.2 years

<table>
<thead>
<tr>
<th></th>
<th>Metformin (n=23)</th>
<th>Placebo (n=20)</th>
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<tbody>
<tr>
<td></td>
<td>Month 0</td>
<td>Month 3</td>
</tr>
<tr>
<td>Ao Diam (cm)</td>
<td>2.57 ± 0.32</td>
<td>2.51 ± 0.39 *</td>
</tr>
<tr>
<td>IVSd (cm)</td>
<td>0.72 ± 0.11</td>
<td>0.76 ± 0.10</td>
</tr>
<tr>
<td>LVPWd (cm)</td>
<td>0.73 ± 0.09</td>
<td>0.76 ± 0.09</td>
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<tr>
<td>LVIDd (cm)</td>
<td>4.45 ± 0.47 *</td>
<td>4.26 ± 0.50 *</td>
</tr>
<tr>
<td>LVIDs (cm)</td>
<td>2.89 ± 0.39 *</td>
<td>2.69 ± 0.36 *</td>
</tr>
<tr>
<td>EF (%)</td>
<td>68.2 ± 4.1</td>
<td>68.0 ± 6.4</td>
</tr>
<tr>
<td>FS (%)</td>
<td>35.0 ± 6.3</td>
<td>36.8 ± 8.0</td>
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<tr>
<td>MV A wave (m/s)</td>
<td>0.56 ± 0.09</td>
<td>0.59 ± 0.16</td>
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<tr>
<td>MV E wave (m/s)</td>
<td>0.92 ± 0.17</td>
<td>0.87 ± 0.19</td>
</tr>
<tr>
<td>MV E/A Ratio</td>
<td>1.67 ± 0.44</td>
<td>1.55 ± 0.42</td>
</tr>
<tr>
<td>LV Dyssynchrony (ms)</td>
<td>98.0 ± 36.9 *</td>
<td>81.7 ± 27.5 *</td>
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<tr>
<td>GLS (%)</td>
<td>-17.4 ± 3.1</td>
<td>-17.3 ± 3.4</td>
</tr>
<tr>
<td>GCS (%)</td>
<td>-20.8 ± 4.6</td>
<td>-21.9 ± 4.6</td>
</tr>
</tbody>
</table>

Table 1. Echocardiography data by treatment arm

* p<0.05 for pre- vs. post-treatment
† p<0.05 for placebo vs. metformin

Conclusions
- Metformin improves multiple markers of cardiac and vascular function in T1D youth.
- Analysis of sex differences, and the impact of changes in blood pressure, BMI, % fat, insulin sensitivity, glycemic control, and other lab markers will be assessed in relation to the improved echocardiogram findings.
- The benefits of improving insulin action in T1D should be investigated longer-term.
- Echocardiography and/or other noninvasive biomarkers may provide helpful in screening T1D youth to identify those youth early-on in need of more intensive cardiovascular risk management.

Literature Cited
- Aurora, CO.

Acknowledgments
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