Diabetes Mellitus Worsens Cardiac Remodeling in Aged Spontaneously Hypertensive Rats

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Introduction
The association of diabetes mellitus (DM) and systemic arterial hypertension induces greater structural and functional cardiac damage than either condition alone. However, few studies have examined this association, especially in aged rats.

Purpose
This study aimed to analyze the influence of DM on left ventricular and atrial remodeling in senescent hypertensive rats (SHR).

Methods
• DM induction: streptozotocin (40 mg/kg, i.p.)
• Nine weeks after DM induction: echocardiogram, myocardial functional study of left ventricular (LV) isolated papillary muscle, gene expression analysis and assessment of oxidative stress in serum
• Statistics: Student’s t test (p<0.05)

Echocardiographic Study
• Anesthesia: ketamine 50 mg/kg + xylazine 1 mg/kg
• Position: left lateral decubitus
• Echocardiography: Philips, HDI 5000, 12 MHz probe

Myocardial Functional Study
• Anesthesia and thoracotomy
• Dissection of the LV papillary muscles
• Variables analyzed: DT, +dT/dt, TPT, -dT/dt e RT
• Isometric contractions
• [Ca²⁺]c: 1.25 mM

Functional Study Apparatus

Gene Expression Analysis
• Real time RT-PCR
• Samples: left ventricular myocardium

Oxidative Stress Evaluation
• Serum was separated by centrifugation at 4000 rpm for 15 minutes
• Lipid hydroperoxide, superoxide dismutase, glutathione peroxidase

Echocardiographic Results

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<tr>
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<th>SHR-CTL</th>
<th>SHR-DM</th>
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<tbody>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>193 ± 34</td>
<td>201 ± 36</td>
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<tr>
<td>Body weight (BW, g)</td>
<td>347 ± 27</td>
<td>294 ± 42*</td>
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<tr>
<td>LV diastolic diameter (LVDD, mm)</td>
<td>8.36 ± 1.04</td>
<td>8.56 ± 0.72</td>
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<td>LVDD/BW (mm/kg)</td>
<td>24.1 ± 2.3</td>
<td>29.8 ± 5.6*</td>
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<td>Left atrium diameter (LAD, mm)</td>
<td>7.36 ± 1.13</td>
<td>7.09 ± 0.96</td>
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<tr>
<td>LAD/BW (mm/kg)</td>
<td>21.4 ± 3.7</td>
<td>24.5 ± 4.8*</td>
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<tr>
<td>LVPWT (mm)</td>
<td>1.91 ± 0.30</td>
<td>1.66 ± 0.09*</td>
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<tr>
<td>LV relative wall thickness</td>
<td>0.46 ± 0.07</td>
<td>0.39 ± 0.04*</td>
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<td>Endocardial FS (%)</td>
<td>48.6 ± 7.9</td>
<td>40.0 ± 8.6*</td>
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<tr>
<td>LVPW shortening velocity (mm/s)</td>
<td>31.8 ± 6.7</td>
<td>26.4 ± 5.93*</td>
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Values expressed as mean ± standard deviation; LV: left ventricle; LVPWT: LV posterior wall thickness; FS: fractional shortening; LVPW: LV posterior wall; *: p<0.05.

Conclusion
Diabetes mellitus causes dilation of the left cardiac chambers and impairs LV myocardial and ventricular function in aged spontaneously hypertensive rats. These alterations are associated with increased oxidative stress and higher ANP gene expression.

Acknowledgments