## Differential Patterns of Impaired Cardiorespiratory Fitness and Cardiac Autonomic Dysfunction in Recently Diagnosed Type 1 and Type 2 Diabetes

Martin Röhling, MS<sup>1,2</sup>\*, Alexander Strom, PhD<sup>1,2</sup>\*, Gidon Bönhof, MD<sup>1</sup>, Sonja Püttgen, MD<sup>1</sup>, Kálmán Bódis, MD<sup>1,2</sup>, Karsten Müssig, MD<sup>1,2,3</sup>, Julia Szendrödi, MD<sup>1,2,3</sup>, Daniel Markgraf, PhD<sup>1,2</sup>, Stefan Lehr, PhD<sup>2,4</sup>, Michael Roden, MD<sup>1,2,3</sup>\*, Dan Ziegler, MD<sup>1,2,3</sup>\* for the GDS study group

\*Equal authorship

<sup>1</sup> Institute for Clinical Diabetology, German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich Heine University Düsseldorf, Düsseldorf, Germany

<sup>2</sup> German Center for Diabetes Research (DZD), München-Neuherberg, Germany

<sup>3</sup> Department of Endocrinology and Diabetology, Medical Faculty, Heinrich Heine University, Düsseldorf, Germany

<sup>4</sup> Institute of Clinical Biochemistry and Pathobiochemistry, German Diabetes Center at the Heinrich Heine University Düsseldorf, Düsseldorf, Germany

## Abstract

*Objective* Both impaired cardiorespiratory fitness (CRF) and heart rate variability (HRV) are predictors of mortality, but their relative roles in recent-onset diabetes are unknown. We determined to which extent CRF and HRV are reduced and interrelated in recent-onset diabetes.

*Research design and methods* Participants from the German Diabetes Study with type 1 (n=163) or type 2 diabetes (n=188) with known diabetes duration <1 year and two agematched glucose-tolerant control groups (n=40 each) underwent spiroergometry and HRV assessment during a hyperinsulinemic-euglycemic clamp.

*Results* Compared to controls, patients with type 2 diabetes showed reduced maximal oxidative capacity (median  $[1^{st}-3^{rd} \text{ quartiles}]$  VO<sub>2</sub>max: 19.3 [16.5-22.9] vs 25.6 [20.7-29.9] ml\*min<sup>-1</sup>\*kg<sup>-1</sup>; P<0.05), diminished maximal carbon dioxide production (VCO<sub>2</sub>max: 23.0 [19.1-26.8] vs 30.9 [24.5-34.4] ml\*min<sup>-1</sup> \*kg<sup>-1</sup>; P<0.05), blunted heart rate recovery after 2 min (-29.0 [-35.0 to -23.0] vs -36.0 [-42.8 to -28.0] bpm; P<0.05) as well as reduced HRV in 4 out of 9 indices, whereas type 1 diabetes individuals had unaltered CRF, but reduced HRV in 3 out of 9 indices (P<0.05) indicating both diminished vagal and sympathetic HRV modulation. HRV measures correlated with VO<sub>2</sub>max in patients with type 1 diabetes (r>0.34; P<0.05), but not those with type 2 diabetes.

*Conclusion* Cardiorespiratory fitness is reduced in recently diagnosed type 2 diabetes, but preserved in type 1 diabetes, while cardiac autonomic function is reduced in both diabetes types albeit strongly associated with cardiorespiratory fitness only in type 1 diabetes. These results support the therapeutic concept of promoting physical fitness in the early course of diabetes.