

- Luiz Clemente de Souza Pereira Rolim
- Paulo Henrique Rezende
- João Roberto Sá
- Fabio Nasri
- Romeu Meneghello
- Antonio Roberto Chacra
- Sérgio Atala Dib

## Coronary calcification score is higher in type 2 diabetic patients with cardiovascular autonomic neuropathy

*Diabetes Center, Department of Internal Medicine, Universidade Federal de São Paulo (Unifesp), São Paulo, Brazil*

An association between cardiovascular autonomic neuropathy (CAN) and mortality among individuals with diabetes is known.<sup>1,2</sup> However, the pathophysiology of this association is still under discussion. Silent myocardial ischemia is common in diabetics with CAN. Both parasympathetic and sympathetic pathways may be involved.<sup>3</sup> There are data suggesting that the extent of coronary calcification and the development of ischemic heart disease seem to be closely related to diabetic complications.<sup>4</sup> The present study was aimed at investigating the degree of coronary artery calcification in type 2 diabetes mellitus individuals (T2DMs) with CAN (WCAN; n = 9) and without CAN (WOCAN; n = 9).

A pilot study was conducted on 18 T2DMs, using the following inclusion criteria: diabetes diagnosed more than 10 years earlier (TDDM), normal resting electrocardiogram, non-smoking and being asymptomatic for coronary artery disease. The exclusion criteria were drug use for hyperlipidemia, glomerular filtration rate lower than 50 ml/min, congestive heart failure and history of stroke. Informed written consent was obtained from all patients and the Ethics Board of Universidade Federal de São Paulo had previously approved the protocol.

Fasting serum C-peptide (normal value): 0.36-3.4 ng/ml), HbA1c (A1c Hemoglobin; normal value: 3.4-6.8%), lipids and urinary albumin/creatinine ratio were measured by standard laboratory tests. Arterial hypertension and electrocardiogram (EKG) (Marquette MAC500) were also evaluated. Electron beam computed tomography imaging was performed using an ultrafast scanner (C-150 Imatron) and the coronary calcium score (CaS) was calculated using Agatston's method.<sup>5</sup> The CAN diagnosis was based on two or more abnormal cardiovascular autonomic tests on two different occasions. These tests were, firstly, the heart rate variability (HRV) at six deep breaths per minute (mean); secondly the 30:15 ratio appraised for the relationship between the longest RR interval of EKG around the thirtieth beat and the shortest interval around the fifteenth beat after the patient was standing; and finally, the orthostatic hypotension that was present when systolic blood pressure decreased by at least 20 mmHg in the third minute of standing.

The differences between WCAN and WOCAN were analyzed using the Mann-Whitney or Student t test. The significance level chosen was 0.05 for all statistical tests.

The two groups did not differ in relation to: sex (males: 44.4% versus 55.5%), age (54.7 ± 5.5 versus 59.2 ± 3.9 years), TDDM (14.4 ± 4.0 versus 13.7 ± 2.9 years), body mass index (28.2 ± 2.9 versus 27.6 ± 4.0 kg/m<sup>2</sup>), hypertension (88.9% versus 100%), albuminuria (55.6% versus 55.6%), high-density lipoprotein (1.36 ± 0.35 versus 1.06 ± 0.29 mmol/l), low-density lipoprotein (3.30 ± 0.81 versus 3.36 ± 1.14 mmol/l), triglyceride (1.65 ± 0.83 versus 2.11 ± 0.48 mmol/l), basal C-peptide (0.59 ± 0.33 versus 0.74 ± 0.73 nmol/l) and HbA1c (9.0 ± 1.3 versus 8.2 ± 1.5%). However, the coronary CaS in WCAN (565.0; 225.9 - 805.5) was significantly higher (p = 0.01) than in WOCAN (74.5; 6.6 - 221.8).

Therefore, despite the small number of individuals in this pilot study, the results suggest that even in T2DMs with similar clinical and metabolic characteristics, coronary calcification is more prevalent when CAN is present. Some points regarding this association had been shown in other studies.<sup>6,7</sup> However, greater numbers of subjects and long-term follow-up would help in determining the true association between CaS and CAN and its value in predicting coronary heart disease events in Type 2 diabetes.

### AUTHOR INFORMATION

**Luiz Clemente de Souza Pereira Rolim, MD.** Diabetes Center, Department of Internal Medicine, Universidade Federal de São Paulo (Unifesp), São Paulo, Brazil.

**Paulo Henrique Rezende, MD.** Diabetes Center, Department of Internal Medicine, Universidade Federal de São Paulo (Unifesp), São Paulo, Brazil.

**João Roberto Sá, MD, PhD.** Diabetes Center, Department of Internal Medicine, Universidade Federal de São Paulo (Unifesp), São Paulo, Brazil.

**Fabio Nasri, MD, MSc.** Check-up Unit, Albert Einstein Hospital, São Paulo, Brazil.

**Romeu Meneghello, MD, PhD.** Department of Radiology, Albert Einstein Hospital, São Paulo, Brazil.

**Antonio Roberto Chacra, MD, PhD.** Diabetes Center, Department of Internal Medicine, Universidade Federal de São Paulo (Unifesp), São Paulo, Brazil.

**Sérgio Atala Dib, MD, PhD.** Diabetes Center, Department of Internal Medicine, Universidade Federal de São Paulo (Unifesp), São Paulo, Brazil.

### Address for correspondence:

Luiz Clemente de Souza Pereira Rolim and Sergio Atala Dib

Rua Botucatu, 740 - 2º andar

Caixa Postal no 20.266

São Paulo (SP) - Brasil - CEP 04034-970

Tel. (+55 11) 5576-4229

Fax. (+55 11) 5579-6636

E-mail: rolim777@gmail.com

Copyright © 2007, Associação Paulista de Medicina

**REFERENCES**

1. Maser RE, Mitchell BD, Vinik AI, Freeman R. The association between cardiovascular autonomic neuropathy and mortality in individuals with diabetes: a meta-analysis. *Diabetes Care*. 2003;26(6):1895-901.
2. Vinik AI, Maser RE, Mitchell BD, Freeman R. Diabetic autonomic neuropathy. *Diabetes Care*. 2003;26(5):1553-79.
3. Baxter CG, Boon NA, Walker JD; DIAD study. Detection of silent myocardial ischemia in asymptomatic diabetic subjects: the DIAD study. *Diabetes Care*. 2005;28(3):756-7.
4. Yoshida M, Takamatsu J, Yoshida S, et al. Scores of coronary calcification determined by electron beam computed tomography are closely related to the extent of diabetes-specific complications. *Horm Metab Res*. 1999;31(10):558-63.
5. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. *J Am Coll Cardiol*. 1990;15(4):827-32.
6. Colhoun HM, Francis DP, Rubens MB, Underwood SR, Fuller JH. The association of heart-rate variability with cardiovascular risk factors and coronary artery calcification: a study in type 1 diabetic patients and the general population. *Diabetes Care*. 2001;24(6):1108-14.
7. Airaksinen KE. Silent coronary artery disease in diabetes—a feature of autonomic neuropathy or accelerated atherosclerosis? *Diabetologia*. 2001;44(2):259-66.

**Sources of funding:** None

**Conflict of interest:** None

**Date of first submission:** October 17, 2006

**Last received:** February 28, 2007

**Accepted:** February 28, 2007