Clinical usefulness of baroreflex sensitivity test in the detection of cardiovascular autonomic neuropathy in patients with type 2 diabetes mellitus.

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 Doctoral Dissertation – abstract

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**Introduction** One of the neurological complications of diabetes is polyneuropathy – lesion of the peripheral nervous system, occurring in the course of this disease. Nowadays, the reference method for the detection of this complication are specialized and validated tests, called the “Ewing battery”. The complexity and time-consuming nature of this method contributed to seeking other diagnostic tools that would assess the function of the autonomic nervous system.

**Aim** The aim of the study was:

- to assess the clinical usefulness of baroreflex sensitivity tests (BRS) in detecting cardiovascular autonomic neuropathy in patients with type 2 diabetes mellitus

- to estimate the correlation between heart rate variability parameters (HRV) and a value of arterial baroreflex in patients with type 2 diabetes mellitus

- to appraise an impact of body weight, age and sex upon the value of arterial baroreflex in patients with type 2 diabetes mellitus.

**Material and methods** The study, which had been approved by the Bioethics Committee of the Medical University of Lodz, included 60 individuals. They were patients diagnosed as having type 2 diabetes mellitus, who had made themselves acquainted with the study protocol and had signed the informed consent form. The criteria of exclusion from the study was the occurrence of type 1 diabetes mellitus, acute coronary syndrome, heart failure, arrhythmias, liver or kidney failure, and polyneuropathies of different origin (infectious diseases, toxin-related ones, drug-induced ones, alcoholism, vitamin B12 deficiency, autoimmune diseases, paraneoplastic syndromes, paraproteinemias, hereditary diseases, etc.)

The neuropathy was diagnosed according to the Ewing tests and using the ProSciCard III system. The baroreflex sensitivity was assessed through plethysmography in the supine/lying (L-BRS) and standing position (S-BRS) after 10 minutes of verticalization by means of the Finometer (FMS Medical System BV) in each study participant. **In all patients, a time and frequency analysis of heart rate variability parameters also was performed by the use of a Holter monitor.**

**Results** Cardiovascular autonomic neuropathy was diagnosed, according to the Ewing tests, in 24 out of them (**the** **CAN group**) (mean age 58±8 years, BMI 33,6±5 kg\*m-2; HbA1c% 8,3±3; diabetes duration time 13,3±8 years; 54% of males). In 24 patients, despite detecting diabetes, there was no occurrence of cardiovascular autonomic neuropathy **(the non-CAN group**) (mean age 56±8 years; BMI 32,2±5 kg\*m-2; HbA1c% 9,1±2; diabetes duration time 9,3±9 years; 71% of males). **The control group** was comprised of 12 individuals without diabetes mellitus (mean age 59±8 years; BMI 27±7 kg\*m-2; 50% of males). The study groups were homogenous in terms of age and sex. They did not differ according to the incidence of traits such as: glycated haemoglobin level, smoking habit, hypertension, medication, and other basic laboratory test results. There were found significantly lower BRS readings in the CAN group (L-BRS 6,2±3,8; S-BRS 4,4±3,1 ms/mmHg) in comparison to the non-CAN group (L-BRS 9,6±4,4; S-BRS 6,9±3,9 ms/mmHg; p=0,009 for L-BRS, p=0,02 for S-BRS) and the control group (L-BRS 13±3,4; S-BRS 10,9±2,6 ms/mmHg; p<0,001). For the first time it was demonstrated the possibility to differentiate the patients with diabetic polyneuropathy from those without this complication based on the cut-off point of BRS ≤ 7 ms/mmHg. It was empirically established in this study that the area under the ROC curve (AUC) for L-BRS (AUC=0,714) and S-BRS (AUC=0,686) readings rendered possible the identification of identify patients with cardio-vascular neuropathy amongst individuals with type 2 diabetes mellitus. Significantly lower values of some HRV parameters in the patients with cardiovascular neuropathy versus the individuals with diabetes and without neuropathy were documented during the study (LF/HF ratio 0,4 vs 0,8, p=0,001; SDANN 15 vs 24, p=0,002). In patients with polyneuropathy and lower values of heart rate variability parameters, also lower L-BRS and S-BRS readings were found. Moreover, significant correlations regarding SDNN, SDNNI, SDANN and S-BRS values were established. There was observed a tendency for lower BRS values in patients with diabetes mellitus and high BMI values in comparison to thinner persons, whereas in the control group that dependency did not occur. In case of obese persons without diabetes mellitus – the BRS values tended to be higher.

**Conclusions**

 1. The BRS assessment constitutes a useful diagnostics method in detecting cardio-vascular neuropathy in patients with type 2 diabetes mellitus.

2. For the first time it was established a cut-off point of ≤ 7 ms/mmHg of arterial baroreflex that identified patients with cardiovascular autonomic neuropathy amongst individuals with type 2 diabetes mellitus altogether.

3. The value of BRS distinguished patients with cardiovascular autonomic neuropathy from individuals without this disorder.

4. The clinical usefulness of baroreflex sensitivity testing in the standing and supine position was equalized.

5. There were found correlations between baroreflex sensitivity results and some heart rate variability parameters.

6. In patients with diabetes mellitus and high BMI there was observed a tendency for lower values of BRS in comparison to thinner persons.