

DECREASED BAROREFLEX GAIN MORE STRONGLY PREDICTS MICROALBUMINURIA AND INCREASED PULSATILE STRESS THAN DECREASED RR E/I RATIO IN PATIENTS WITH TYPE 1 DIABETES

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Background and Aims :

Long-lasting type 1 diabetes (T1DM) may be associated with cardiac autonomic neuropathy (CAN), increased pulse pressure (PP) or pulsatile stress, and microalbuminuria (μA), all cardiovascular risk factors. We compared the relationships of two markers of CAN, RR E/I (Expiratory/Inspiratory) ratio and baroreflex gain (BRG), with μA and pulsatile stress during an active orthostatic test in patients with T1DM.

Material and methods : 167 patients with T1DM (mean age 40 years, diabetes duration 20 years, body mass index 23.6 kg/m^2 , HbA1c 8.64%), who had a measurement of μA and of RR E/I ratio during a deep breathing test, were submitted to a postural squat-stand test with a continuous noninvasive arterial blood pressure (BP) monitoring (Finapres®). The mirror changes in heart rate and systolic BP during the squat-stand transition allows the calculation of a so-called BRG (msec.mm Hg^{-1}), by plotting the pulse intervals (RR) against systolic BP values, as classically assessed during a pharmacological test using the infusion of a vasodilator and a vasopressor agent. Pulsatile stress was defined as the product of PP and heart rate, both during the whole test and during the squatting position only. The T1DM cohort was separated in two subgroups according to the median value of RR E/I ratio (>1.25 vs <1.25) or of BRG (>2.20 vs $<2.20 \text{ bpm.mmHg}^{-1}$).

Results : Compared to T1DM patients with high BRG ($n = 82; 4.51 \pm 2.31$), patients with low BRG ($n = 85; 1.17 \pm 0.61 \text{ bpm.mm Hg}^{-1}$; $p < 0.00001$) tended to be slightly older (42 vs 38 years, NS), to have a slightly longer duration of diabetes (21 vs 18 years; NS), and to have lower RR E/I ratio (1.25 vs 1.31; NS), but had similar recent HbA1c levels (8.64 vs 8.64 %). However, T1DM patients with low BRG had an increased pulsatile stress index (5190 vs $4521 \text{ mmHg.min}^{-1}$; $p = 0.0019$), especially in squatting position (5408 vs $4396 \text{ mmHg.min}^{-1}$; $p < 0.0001$). Similarly, μA was higher in T1DM patients with low BRG, being expressed by the mean level (59 ± 133 vs $10 \pm 16 \text{ mg/l}$; $p = 0.0019$) or by its logarithm to adjust for a non Gaussian distribution (1.14 ± 0.67 vs 0.76 ± 0.42 ; $p = 0.0001$). There was an inverse correlation between BRG and $\log \mu\text{A}$ ($r = -0.28$; $p = 0.0006$), but not between RR E/I ratio and $\log \mu\text{A}$ ($r = 0.09$; $p = 0.12$). All together, 26.9 % of T1DM patients with low BRG had abnormal μA ($\geq 30 \text{ mg/l}$) versus only 5.3 % of patients with high BRG ($p < 0.001$). Similarly, the correlation between BRG and pulsatile stress ($r = -0.28$; $p = 0.0003$) was stronger than that between RR E/I ratio and pulsatile stress ($r = -0.19$; $p = 0.0153$).

Conclusion : The calculation of BRG during a squat-stand test in subjects with T1DM allows to better detect patients with increased pulsatile stress and even more strongly patients with μA than the classical RR E/I ratio CAN index. Decreased BRG may be used to detect T1DM patients at high risk of cardiorenal complications.

	T1DM cohort separated in two subgroups according to the median value of RR E/I ratio			T1DM cohort separated in two subgroups according to the median value of BRG (mmHg.min ⁻¹)		
	>1.25	<1.25	p	> 2.20	<2.20	p
N (F/M)	90 (42/48)	83 (45/38)		82 (41/41)	85 (45/40)	
Age(yrs)	36 ± 11	45 ± 9	0.0001	38 ± 12	42 ± 11	0.02
Diabetes duration (yrs)	16 ± 10	24 ± 11	0.0001	18 ± 12	21 ± 10	NS
μA (mg/l)	23 ± 79	48 ± 115	NS	10 ± 16	59 ± 133	0.019
HbA1c (%)	8.6 ± 1.7	8.7 ± 1.3	NS	8.6 ± 1.8	8.6 ± 1.2	NS
RR E/I ratio	1.41 ± 0.14	1.14 ± 0.07	0.0001	1.31 ± 0.16	1.25 ± 0.19	NS
BRG (msec.mm Hg ⁻¹)	3.19 ± 2.63	2.24 ± 1.84	0.0081	4.51 ± 2.31	1.17 ± 0.61	0.0001
Total pulsatile stress index (mmHg.min ⁻¹)	4666 ± 1299	5090 ± 1501	0.0545	4521 ± 1310	5190 ± 1428	0.0019
Squatting position pulsatile stress index (mmHg.min ⁻¹)	4533 ± 1389	5352 ± 1697	0.0009	4396 ± 1472	5408 ± 1543	0.0001