INCREASED PULSE PRESSURE AND SYSTOLIC x HEART RATE DOUBLE PRODUCT AND CARDIOVASCULAR AUTONOMIC NEUROPATHY IN TYPE 2 DIABETIC PATIENTS

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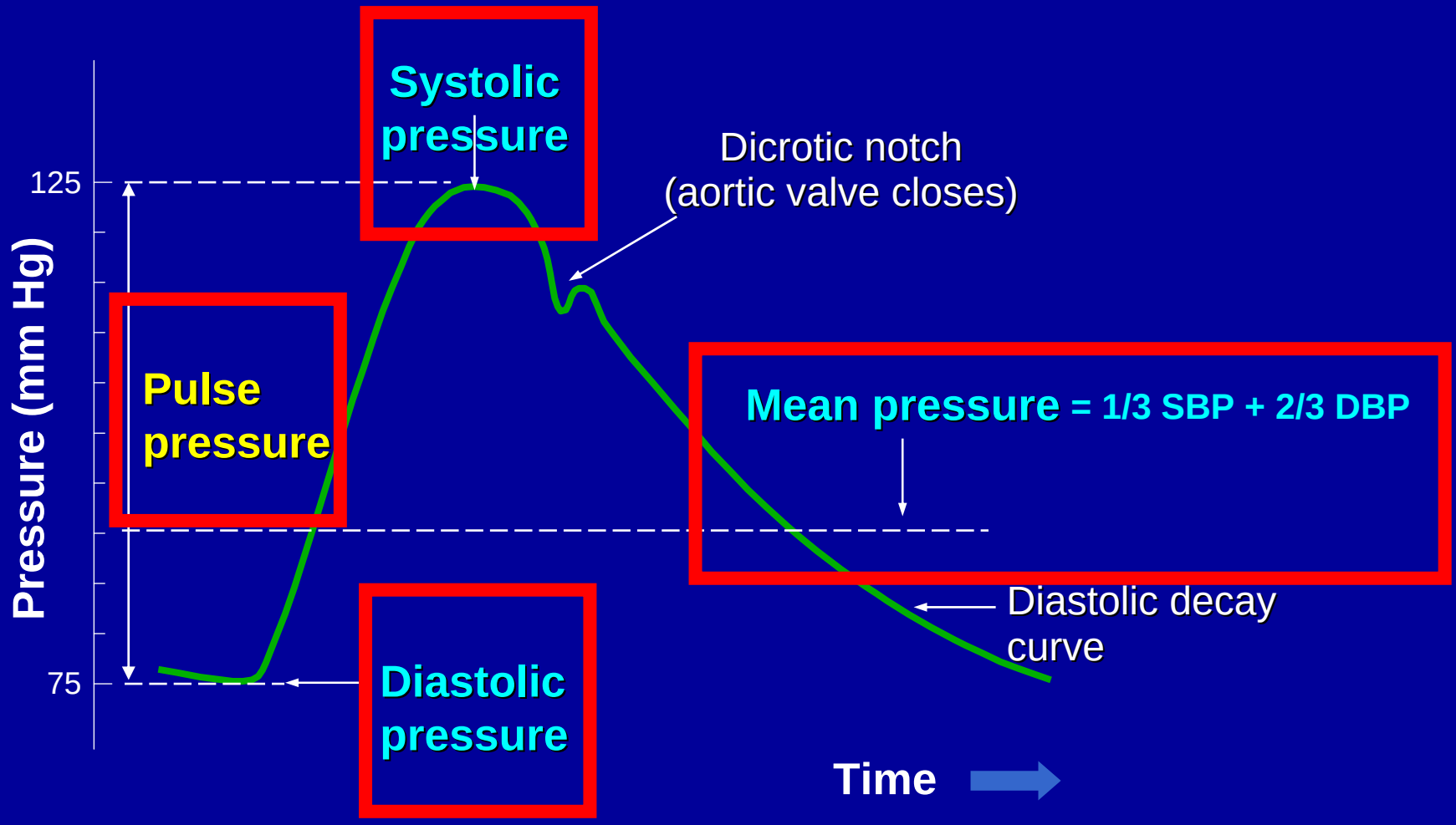
The BP Components of the Arterial Pulse Wave
"Pulsatile stress"



Background

Arterial pulse pressure (PP), a surrogate marker of large artery stiffness, was shown to be an independent cardiovascular disease (CVD) risk factor in several large longitudinal studies in patients with type 2 diabetes mellitus.

Schram MT et al. Diabetes, pulse pressure and cardiovascular mortality the Hoorn Study. J Hypertens 20: 1743–1751, 2002

Cockcroft JR et al. Pulse pressure predicts cardiovascular risk in patients with type 2 diabetes mellitus. Am J Hypertens 18: 1463-1467; discussion 1468-1469, 2005

Nilsson PM et al. Pulse pressure strongly predicts cardiovascular disease risk in patients with type 2 diabetes from the Swedish National Diabetes Register (NDR). Diabetes Metab 35: 439-446, 2009

Aims

- **To compare PP and systolic blood pressure (SBP) x heart rate (HR) double product during an active orthostatic test in patients with T2DM and in nondiabetic individuals matched for age (40-60 years), body mass index (BMI) and sex ratio (1/1).**

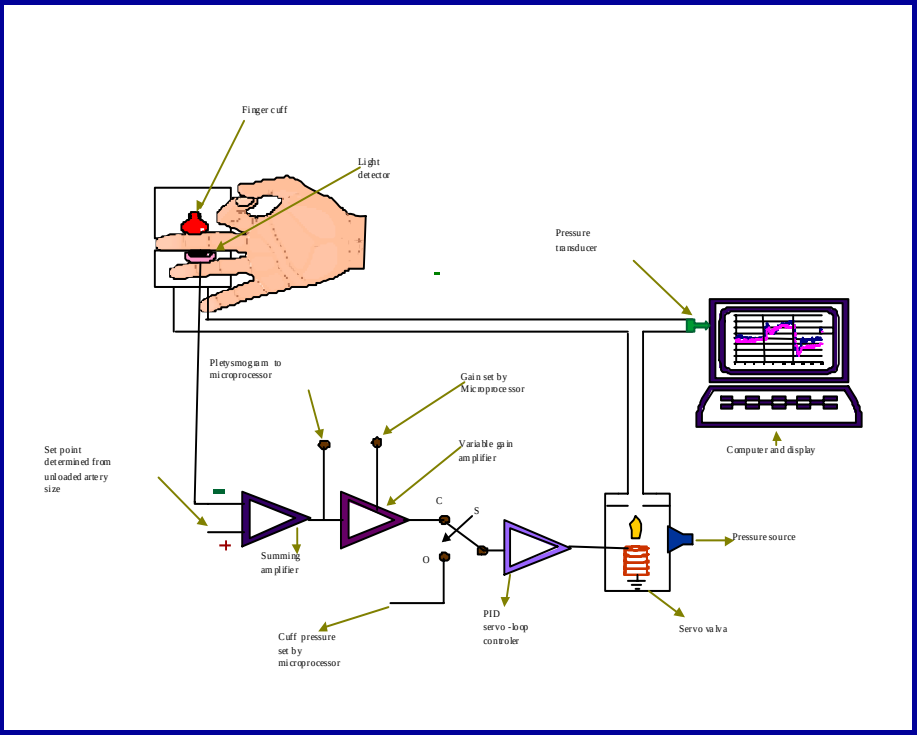
- **To analyze the relationships between pulsatile stress and cardiovascular autonomic neuropathy in patients with T2DM**

Methods : population

	Patients with type 2 diabetes (T2DM)	Nondiabetic overweight/obese subjects (OC)	P value
N (Male/Female)	20/20	20/20	
Age (yrs)	50 ± 6	50 ± 6	0.8971
Diabetes duration (yrs)	8 ± 7	-	NA
BMI (kg/m^2)	29.7 ± 3.7	28.6 ± 2.7	0.1288
HbA1c (%)	7.8 ± 1.6	-	NA

Patients with arterial hypertension, renal insufficiency or CVD or taking medications interfering with vascular reactivity (including any type of antihypertensive agents) were excluded from the study.

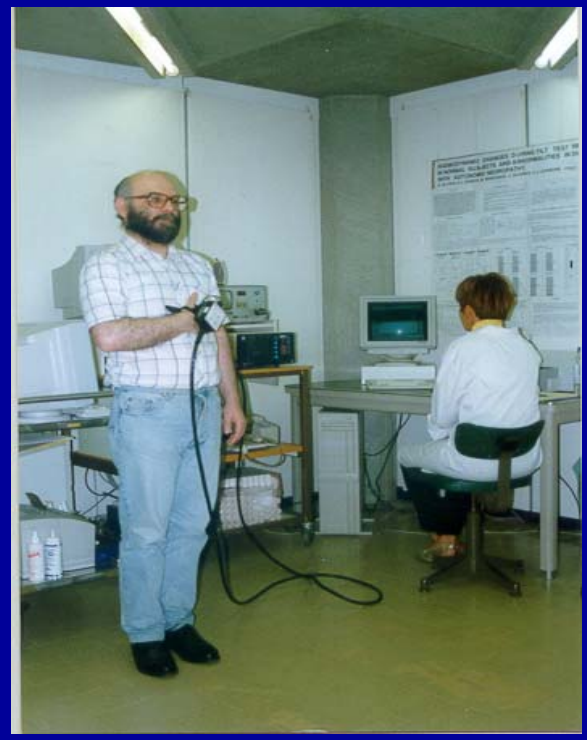
Methods : Finapres®



Non-invasive beat-to-beat monitoring of arterial blood pressure was obtained using a Finapres® device (Finger Arterial Pressure, Ohmeda, Louisville, CO, USA) and a photoelectric method. Several studies have demonstrated the accuracy of such indirect measurement with direct intra-arterial blood pressure and its reproducibility during various laboratory tests.

The Finapres® device provides a beat to beat set of 3 measured parameters : systolic (SBP), diastolic (DBP) and mean (MAP) arterial blood pressure. Heart rate (HR) was derived from pressure wave after having verified a perfect concordance with ECG recording, and pulse pressure (PP) was calculated as the difference between systolic and diastolic pressure values.

Methods : Squatting Test



All patients were evaluated with a continuous arterial blood pressure monitoring (Finapres®) in standing (1min), squatting (1min) and again standing position (1min).

Squatting and pulse pressure
Recent reports in type 1 diabetes

Philips JC, Marchand M, Scheen AJ

Squatting amplifies pulse pressure increase according to duration of type 1 diabetes.

Diabetes Care 2008; 31: 322-324.

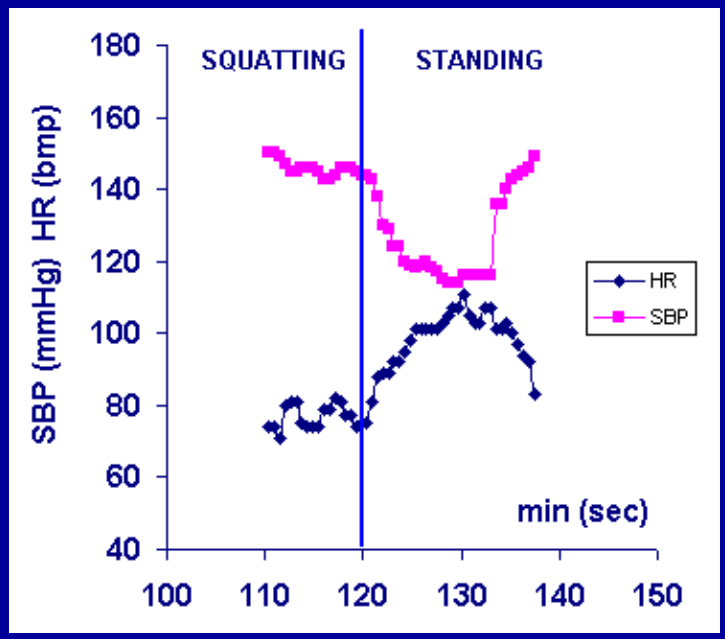
Pulse pressure and cardiovascular autonomic neuropathy according to duration of type 1 diabetes.

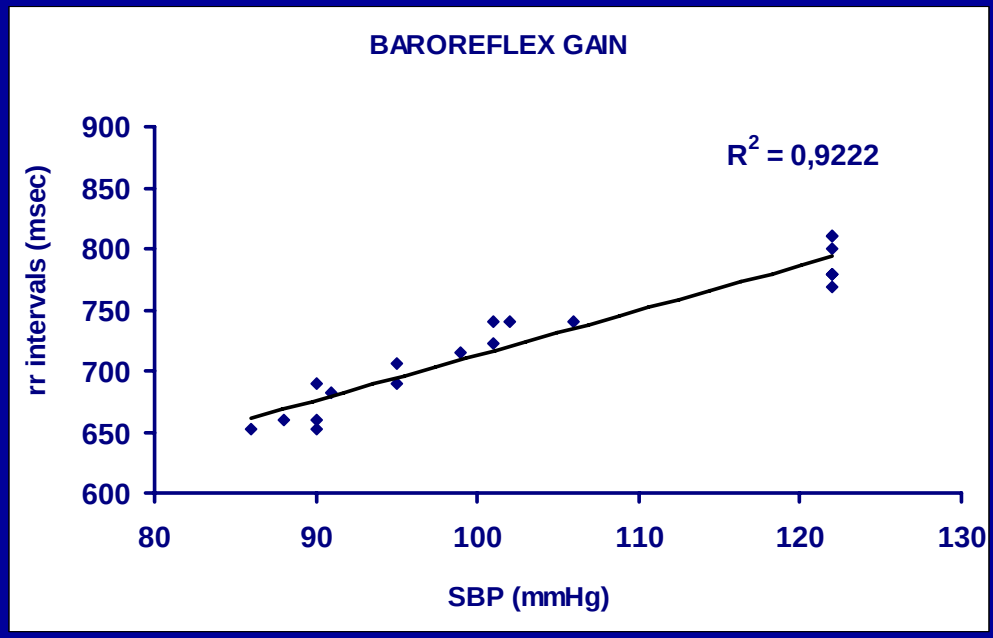
Diabetes Metab Res Rev 2009; 25: 442-451.

Changes in pulse pressure, heart rate, and the pulse pressure x heart rate product during squatting in Type 1 diabetes according to age.

Diabetic Medicine 2010; in press.

Methods : Baroreflex gain

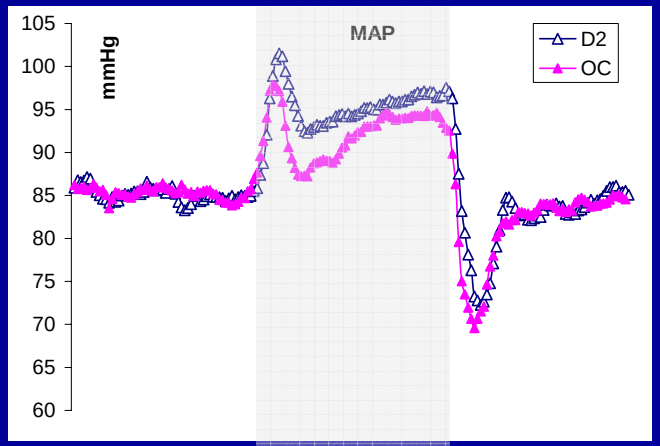




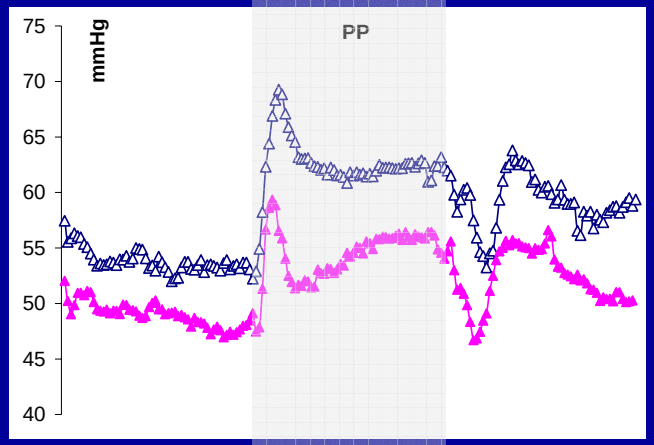
Cardiovascular autonomic neuropathy (CAN) was assessed by the baroreflex gain measured by comparing HR and SBP changes during the transition from squatting to standing.

Baroreflex gain : slope of the regression line relating R-R intervals to SBP changes (well correlated with other CAN indices).

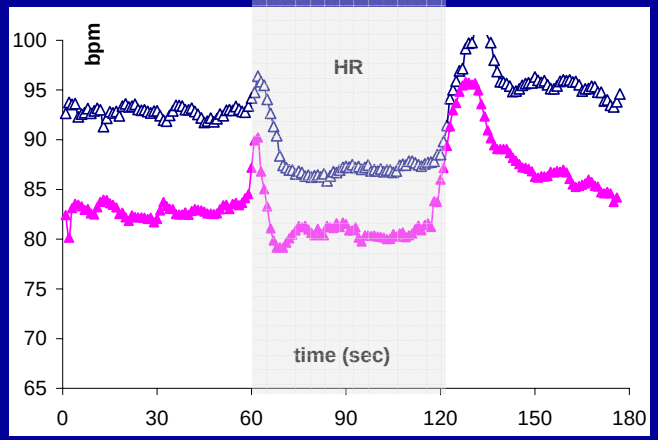
Results



Similar Mean Arterial Pressure (MAP) in selected T2DM patients and overweight/obese nondiabetic controls (exclusion of patients with hypertension)



Higher pulse pressure (PP) in T2DM patients than in overweight/obese nondiabetic controls (in relation to arterial stiffness)



Higher heart rate (HR) in T2DM patients than in overweight/obese nondiabetic controls (in relation to cardiovascular autonomic neuropathy or CAN)

Results

	Patients with type 2 diabetes (T2DM) (n = 40)	Nondiabetic overweight/obese subjects (OC) (n = 40)	P value
Mean BP (mm Hg)	**88 ± 13**	**86 ± 12**	**0.5991**
Systolic BP (mm Hg)	**128 ± 20**	**122 ± 18**	**0.1087**
Diastolic BP (mm Hg)	**70 ± 13**	**70 ± 10**	**0.1662**
PP (mm Hg)	**58 ± 16**	**52 ± 13**	**0.0451**
HR (bpm)	**91 ±10**	**84 ± 13**	**0.0029**
SBP x HR product ($mm\ Hg*min^{-1}$)	**12082 ± 2521**	**10195 ± 2291**	**0.0008**

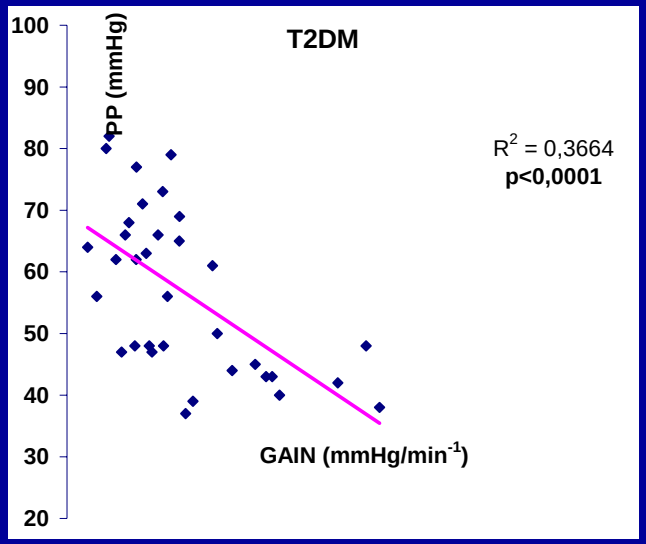
Significantly higher PP, HR and SBP x HR product in type 2 diabetes, despite similar BP

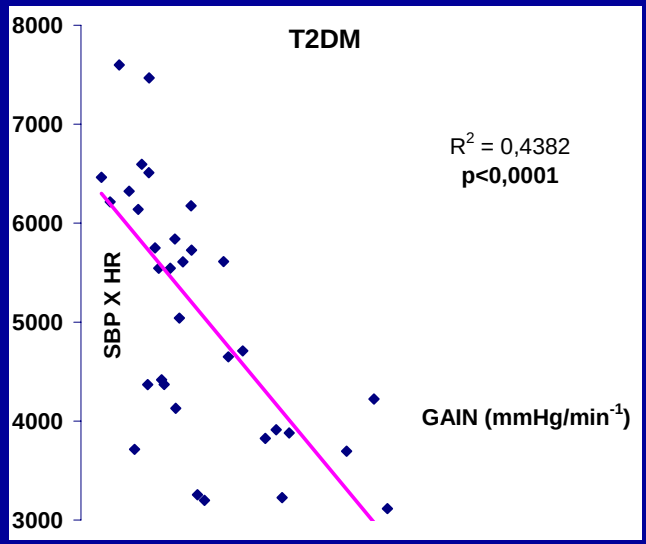
Results

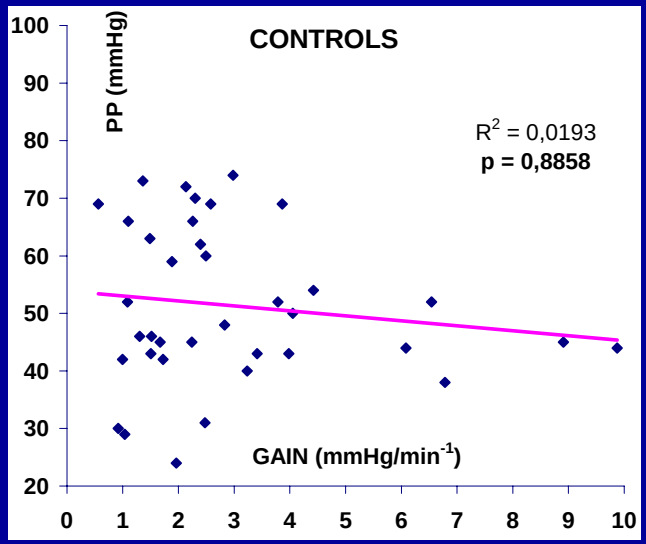
	Patients with type 2 diabetes (T2DM)	Nondiabetic overweight/obese subjects (OC)	P value
Baroreflex gain $mmHg/min^{-1}$	2.05 ± 1.31	2.97 ± 2.18	0.0256

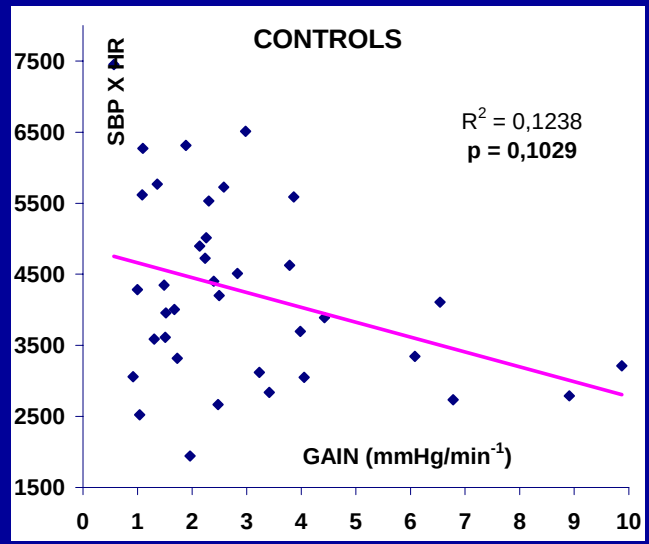
Patients with type 2 diabetes (8-year duration, HbA1c 7.8 %) have significantly reduced baroreflex gain when compared to nondiabetic individuals, demonstrating the presence of cardiovascular autonomic neuropathy (CAN)

Results : PP / NAC correlations









Highly significant negative correlations between PP or SBPxHR and baroreflex gain in patients with T2DM

No significant correlations between PP or SBPxHR and baroreflex gain in nondiabetic individuals

Discussion : Relationships between arterial stifness and autonomic nerve function

- **Ahlgren AR et al.**

  Increased aortic stiffness in women with type 1 diabetes mellitus is associated with diabetes duration and autonomic nerve function.

  Diabetic Med 1999; 16: 291-7.

- **Mattace-Raso FU et al.**

  Arterial stiffness, cardiovagal baroreflex sensitivity and postural blood pressure changes in older adults: the Rotterdam Study.

  J Hypertens 2007; 25:1421-6.

Conclusion

- Patients with T2DM have higher PP, an indirect marker of arterial stiffness, and higher SBP x HR double product, an index of cardiac workload, than nondiabetic patients with similar age and BMI, as well as markers of CAN, which all may contribute to the higher cardiovascular risk associated with T2DM.