COMMENTARY

Fitness, nighttime blood pressure and vascular ageing in type 2 diabetes

Vasilios Kotsis and Stella Stabouli

Hypertension Research (2011) 34, 799-800; doi:10.1038/hr.2011.48; published online 12 May 2011

 \mathbf{P} hysical inactivity is a cardiovascular risk factor, as it is associated with high blood pressure, overweight, obesity, insulin resistance, dyslipidemia and type 2 diabetes. In the study by Cardoso *et al.*,¹ type 2 diabetic patients with low fitness exhibited higher prevalence of obesity, hypertension, worse glycemic control and increased incidence of microvascular and macrovascular complications. Target organ damage including elevated serum creatinine, microalbuminuria, left ventricular hypertrophy and arterial stiffness were also more prevalent in low fitness diabetic patients than in those with higher grade of fitness.

The obesity epidemic has shared increasing interest during the last decades, as one of the major causal factors of type 2 diabetes, primary hypertension and early onset of cardiovascular disease. Obesity develops from the interaction between the genotype and the environment and involves social, behavioral, cultural, physiological, metabolic and genetic factors.² A large number of studies have shown that obesity has an important negative impact on health, leading to recommendations for the management of this condition and its associated comorbidities. Impaired glucose tolerance, high levels of circulating insulin and reduced sensitivity to the metabolic actions of insulin has been repeatedly demonstrated in obese individuals. The relationship between obesity and hypertension is well established in children and adults.3,4 Obese individuals exhibit higher levels of office and ambulatory blood pressure and non-dipping status.³ Low fitness is usually accompanied by higher body mass index, as overweight and obese subjects are usually inactive, despite the large amount of calories they consume. In extreme obese subjects, inactivity is more pronounced, as these patients have intolerance to minimal exercise due to cardiac systolic and diastolic dysfunction.⁵ Obesity, essential hypertension and type 2 diabetes are twisted in a syndrome highly affected from lifestyle.

A meta-analysis of endurance training on blood pressure⁶ reported that aerobic training reduced resting and daytime blood pressure. The possible mechanisms for blood pressure reduction after exercise include increase in cardiac output and stroke volume, with decreased resting heart rate and total peripheral vascular resistance. The blood pressurelowering effect has been associated with body weight reduction, especially in the body fat composition and distribution, decreased sympathetic nervous system activity, increased insulin sensitivity and improved endothelial function. Endothelium factors, such as nitric oxide or other relaxing factors produced during exercise, may contribute to lower inflammation and finally to reduced blood pressure in patients with regular physical activity and a better grade of fitness.

Non-dipping status and day to night blood pressure variation has been associated with cardiovascular complications and adverse outcomes. The prognostic value of non-dipping status on cardiovascular mortality has been reported in European⁷ and Japanese populations.⁸ The non-dipping pattern has been associated with severe hypertension, diabetic neuropathy, obesity, black race, salt sensitivity, ageing and less quality or quantity of sleep. Low activity during daytime that lead to lower daytime blood pressure may

relate to an erroneous decreased blood pressure fall during nighttime. Higher sympathetic nervous system activity and increased peripheral vascular resistance during nighttime, breath disorders during sleep and early renal abnormalities may contribute to the reduced nocturnal blood pressure fall. In the current study,1 patients with low fitness have been reported to have increased nighttime blood pressure and non-dipping pattern, adding a factor on top to their cardiovascular risk. The association of lower fitness with increased nighttime blood pressure could be explained by the increased number of obese patients in the low fitness group, which frequently suffer from obstructive sleep apnea disorders. Another hypothesis is that vascular relaxing factors produced in the endothelium during exercise may have a greater impact at nighttime. Moreover, autonomic nervous system abnormalities and peripheral neuropathy usually seen in type 2 diabetics with increased duration of the disease and poor glycemic control can contribute to the blunted nighttime blood pressure fall. These abnormalities may also associate with sleep breathing disorders and impaired nighttime peripheral vascular relaxation.

Vascular aging is described as a gradual process involving biochemical, enzymatic and cellular changes of the vasculature. Ageing represents a major determinant of arterial stiffness. As elastic arteries become stiffer, they can no longer absorb the energy released by heart ventricular ejection and recoil effectively. Systolic blood pressure increases as the reflected waves on the peripheral arteries arrive sooner to the central arteries, whereas diastolic blood pressure falls resulting in increased central pulse pressure. As a consequence, left ventricular afterload increases, forcing the heart to generate higher endsystolic pressures to sustain the constancy of

Professor V Kotsis is at the Hypertension-ABPM Center Papageorgiou Hospital of the 3rd Department of Medicine, Aristotle University of Thessaloniki, 3 Filippoupoleos, Thessaloniki S5132, Greece and Professor S Stabouli is at the Pediatric Intensive Care Unit, Hippokration Hospital, Thessaloniki, Greece. E-mail: bkotsis@med.uoa.gr or sstaboul@med.uoa.gr

blood flow in the stiffened arteries.⁹ In the current study, it is expected that the group of patients with low fitness have increased arterial stiffness, as they are more obese, present more severe hypertension and increased macrovascular and microvascular diabetes mellitus complications. Two adding factors may contribute to the increased stiffness of the low fitness patients. First, the older age of the low fitness group and second, the increased low grade inflammation reported in the same group of patients that may cause endothelial dysfunction and increased arterial damage.

Regular physical activity has a favorable effect on type 2 diabetic patients with cardiovascular risk factors.¹⁰ Exercise training has reported to improve insulin sensitivity and to decrease hyperglycemia-related medications in obese subjects with type 2 diabetes. The acute benefits of exercise on glycemic control can last up to 72 h and have a cumulative nature. Patients with type 2 diabetes should exercise a minimum of 3 days per week to ensure the glucose-lowering effect. Population studies also show reduced incidence of hypertension in proportion to the levels of physical activity. An immediate reduction in blood pressure occurs after an aerobic exercise course. Several studies using ambulatoryblood pressure monitoring showed that the blood pressure-lowering effects of exercise are most pronounced in people with hypertension, who engage in endurance exercise, after an acute isolated exercise session or following a regular aerobic exercise training.

In conclusion, lifestyle modification is an important step to reduce cardiovascular risk. We should suggest to our patients to increase their physical activity, which could lead to primary and secondary diabetes complications prevention. Higher physical activity, under proper supervision and guidance, can reduce blood pressure and obesity rates in diabetics and prevent from early vascular ageing and cardiovascular mortality and morbidity.

2 Kotsis V, Stabouli S, Papakatsika S, Rizos Z, Parati G. Mechanisms of obesity-induced hypertension. *Hypertens Res* 2010; **33**: 386–393.

- 3 Kotsis V, Stabouli S, Bouldin M, Low A, Toumanidis S, Zakopoulos N. Impact of obesity on 24-h ambulatory blood pressure and hypertension. *Hypertension* 2005; 45: 602–607.
- 4 Stabouli S, Kotsis V, Papamichael C, Constantopoulos A, Zakopoulos N. Adolescent obesity is associated with high ambulatory blood pressure and increased carotid intimalmedial thickness. J Pediatr 2005; 147: 651–656.
- 5 Kotsis V, Stabouli S, Toumanidis S, Tsivgoulis G, Rizos Z, Trakateli C, Zakopoulos N, Sion M. Obesity and daytime pulse pressure are predictors of left ventricular hypertrophy in true normotensive individuals. J Hypertens 2010; 28: 1065–1073.
- 6 Cornelissen VA, Fagard RH. Effects of endurance training on blood pressure, blood pressure-regulating mechanisms, and cardiovascular risk factors. *Hypertension* 2005; **46**: 667–675.
- 7 Staessen JA, Thijs L, Fagard R, O'Brien ET, Clement D, de Leeuw PW, Mancia G, Nachev C, Palatini P, Parati G, Tuomilehto J, Webster J. Predicting cardiovascular risk using conventional vs ambulatory blood pressure in older patients with systolic hypertension. Systolic Hypertension in Europe Trial Investigators. JAMA 1999; 282: 539–546.
- 8 Kario K, Schwartz JE, Davidson KW, Pickering TG. Stroke prognosis and abnormal nocturnal blood pressure falls in older hypertensives. *Hypertension* 2001; 38: 997–1002.
- 9 Kotsis V, Stabouli S. Arterial stiffness, vascular aging, and intracranial large artery disease. Am J Hypertens 2011; 24: 252.
- 10 Marwick TH, Hordern MD, Miller T, Chyun DA, Bertoni AG, Blumenthal RS, Philippides G, Rocchini A. Exercise training for type 2 diabetes mellitus: impact on cardiovascular risk: a scientific statement from the American Heart Association. *Circulation* 2009; **119**: 3244–3262.

Cardoso C, Maia M, Oliveira F, Leite N, Salles G. High fitness is associated with a better cardiovascular risk profile in patients with type 2 diabetes mellitus. *Hypertens Res* 2011; 34: 856–861.