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RAPID COMMUNICATION

Relationship Between Clinical, 24-Hour, Average Day-Time and Night-Time Blood Pressure and Measures of Arterial Stiffness in Essential Hypertension

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Summary

Arterial wall stiffness is considered an independent cardiovascular risk factor. Aim of this study was to evaluate relationship between clinical, 24-hour, average day-time and night-time blood pressure (BP) and measures of arterial stiffness assessed by pulse wave velocity (PWV) (using SphygmoCor applanation tonometer) in essential hypertension (severe-resistant (RH, n=29) and moderate hypertension (EH, n=35)) and in normotensive control subjects (n-29) (NCS) matched by age. After multiple regression analysis, PWV remains significantly correlated mainly with night-time pulse pressure and to a lesser extent with age. PWV was significantly higher in RH compared to moderate EH and NCS.

Key words

Essential hypertension • Arterial stiffness • 24 h blood pressure monitoring

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Hypertension is a major risk factor for the development of cardiovascular diseases and the benefits of reducing blood pressure (BP) are well established (MacMahon *et al.*1990). The role of large arteries in the pathogenesis and maintenance of hypertension has recently been widely studied. Their function is i) to conduct blood to distributing networks of smaller arteries and the microvasculature, and ii) to act as compliant elements buffering the changes in pressure arising during the cardiac cycle. Both these functions depend on the mechanical properties of the vessel wall. These properties can change in response to disease and, conversely, may also contribute to disease progression. Arteries become stiffer with increasing age and disease, e.g. hypertension, diabetes and atherosclerosis. Structural changes contributing to an increase in arterial stiffness include fragmentation of elastin, increased deposition of collagen fibers and cross-linking of collagen molecules by advanced glycation end-products (Hope and Hughes 2007). Although structural changes may be quantified pathologically, clinical evaluation of arterial stiffness properties is more complex and a complete description of the stress-strain relationship of arteries *in vivo* is not possible. Commonly applied methods include the measurement of transit times between different sites in the vasculature and calculation of arterial pulse wave velocity (PWV), and measurement of regional arterial stiffness (Van Bortel *et al.* 2002). A large variety of predictors of arterial stiffness can be found in the literature. PWV appears to be a reliable parameter of arterial stiffness which is influenced by several factors – age, heart rate (HR), diastolic blood pressure (DBP) (Nürnberger *et al.* 2003). Furthermore, arterial stiffness, determined by carotid-femoral PWV, may predict

cardiovascular and other causes of mortality besides classical risk factors in hypertensive, end-stage renal disease, diabetic patients and in the general population (Laurent *et al.* 2001).

We studied the determinants of arterial stiffness with special interest in the relationship between clinical BP, 24 h BP, average day-time and night-time BP and PWV. At the same time arterial stiffness assessed by carotid-femoral PWV in patients with severe-resistant hypertension (RH) was evaluated in comparison to patients with moderate essential hypertension (EH) and to normotensive control subjects (NCS).

We studied 29 patients with RH, 35 patients with moderate to severe EH and 29 normotensive controls. Patients with moderate to severe arterial hypertension were investigated during hospitalization. Subjects were recruited from patients recommended to our Hypertension center from other health care facilities, mostly from the central Czech region, in order to exclude secondary hypertension. Common forms of secondary hypertension (primary aldosteronism, pheochromocytoma, Cushing's syndrome, renal parenchymal disease or renovascular hypertension) were excluded in all patients. RH was defined before hospitalization as follows: 1) clinical arterial BP 140/90 mm Hg and higher when using three or more antihypertensive drugs including diuretics, or 2) home arterial BP 135/85 mm Hg or more when using three or more antihypertensive drugs including diuretics, or 3) 24 h mean BP 130/80 mm Hg or higher when using three or more antihypertensive drugs including diuretics (Mancia *et al.* 2007b). The diagnosis of EH was made by the exclusion of secondary or resistant hypertension. All patients discontinued their usual antihypertensive therapy and were switched to an alpha blocker (doxazosine) and slow releasing calcium channel blocker (verapamil) at least 14 days before the investigation to standardize the treatment not affecting rennin-angiotensin-aldosterone system and to minimize the influence of several drugs on arterial wall properties. Normotensive controls were recruited from subjects without history of hypertension or cardiovascular disease, mostly from hospital staff, who were free of antihypertensive medication.

The following parameters were measured in all studied objects: carotid-femoral PWV measurement was performed by using an applanation tonometer Sphygmocor (AtCor Medical, West Ryde, Australia). Clinical blood pressure values were obtained using an oscillometric sphygmomanometer (Dinamap, Critikon, Tampa, FL, USA). 24-h ambulatory blood pressure monitoring (ABPM) during hospitalization was performed using an oscillometric device (SpaceLabs 90207; SpaceLabs Medical, Redmond, WA, USA). All biochemical parameters were analyzed using multi-analyzers (Hitachi 717, Boehringer Mannheim, Germany) in the Institutional Central Laboratory.

Depending on the normal/non-normal distribution (Shapiro-Wilks W test) of particular variables, the data are shown either as means ± S.D. or median (interquartile range). Multiple-group comparisons were performed by one-way analysis of variance (ANOVA), followed by the Scheffe's *post hoc* test. Differences between both hypertensive groups were analyzed using a two-tailed t-test. Kruskal-Wallis test was used for non-normally distributed variables. Pearson's correlation analysis was applied to detect correlations of PWV to measured parameters and confounding factors in hypertensive patients. Multiple regression analysis, stepwise forward method, was applied to only those parameters which significantly correlated with PWV. $P<0.05$ value was considered to be significant. The statistical software Statistica (StatSoft, Inc. (2003), STATISTICA Cz, version 6) was used for the analysis.

The characteristics of the studied groups are shown in Table 1. There were no significant differences in most confounding factors like age, duration of hypertension, BMI, lipid profile, fasting glucose, creatinine levels between RH and EH groups. PWV was significantly higher in the RH group when compared to EH and to NCS, while clinical BP was comparable. Results of PWV might be influenced by the lowering effect of medication. This might be the cause of a relatively small difference in PWV between both hypertensive groups and NCS. However, 24-h ABPM values were significantly higher in the RH group than in the EH group. PWV correlated with age, clinical systolic blood pressure (SBP), brachial pulse pressure (PP), 24-h SBP and PP, day SBP and PP, night SBP and PP. After multiple regression analysis, PWV remains significantly correlated mainly with night PP and to a lesser extent with age. Results of simple and multiple regression analysis are shown in Table 2. Our findings are in agreement with other studies, where association of circadian variations of BP or night-time BP with target organ damage have been reported (Mancia *et al.* 2007a, Routledge *et al.* 2007).

Table 1. Characteristics of studied subjects.

	RH	EH	NCS	p-value
Number of subjects	29	35	29	-
Age [years]	51±10	49±10	44±15	0.989
Duration of hypertension [years]	16 (6-26)	11 (6-16)	-	0.204
Body mass index [kg/m^2]	29.2±4.9†††	28.8±4.3††	24.8±3.6	<0.001
Total plasma cholesterol [mmol/l]	5.3±1.2	5.2±1.1	5.1±1.2	0.870
Triacylglycerides [mmol/l]	1.8±0.9†	1.8±1.0†	1.2±0.5	<0.05
Fasting plasma glucose [mmol/l]	4.9 (4.5-5.4)	4.8 (4.4-5.2)	4.9 (4.5-5.5)	0.717
Creatinine [mmol/l]	82 (71-104)	83 (69-92)	81.5(69.5-93.5)	0.655
Clinical brachial BP [mm Hg]	173±22†††/94±11†††	169±18†††/93±12†††	120±14/70±9	<0.001
Brachial pulse pressure [mm Hg]	80±20†††	76±15†††	51±9	<0.001
Heart rate [bpm]	74±12††	70±12	63±10	<0.01
24-h BP [mm Hg]	160±16/98±11	141±15/89±12	-	<0.01
24-h pulse pressure [mm Hg]	62±13	52±10	-	<0.005
24-h heart rate [bpm]	76±10	74±10	-	0.386
Day BP [mm Hg]	161±17/100±12	145±16/92±13	-	<0.05
Day pulse pressure [mm Hg]	61±13	53±11	-	<0.01
Day heart rate [bpm]	79±10	77±12	-	0.558
Night BP [mm Hg]	154±16/91±10	132±15/82±11	-	<0.001
Night pulse pressure [mm Hg]	63±14	15±9	-	<0.001
Night heart rate [bpm]	67±9	65±9	-	0.267
Pulse wave velocity [m/s]	9.3±2.2***†††	7.2±1.0†	6.2±1.3	<0.001

Data are shown as means ± S.D. medians (interquartile range) or absolute numbers. Variables are compared by ANOVA followed by the Scheffe's post hoc test or Kruskal Wallis test or unpaired t-test where appropriate; * p<0.05. ** p<0.01. *** p<0.001 vs. EH; †p<0.05. ††p<0.01. †††p<0.001 vs. NCS.

Table 2. Simple regression analysis and multiple regression analysis using PWV as dependent variable.

	Simple regression		Multiple regression	
	r	p-value	β	p-value
Age	0.4870	<0.001	0.3471	<0.001
Clinical brachial SBP	0.3989	<0.01	-	-
Brachial pulse pressure	0.5057	<0.001	-	-
24-h SBP	0.5196	<0.001	-	-
24-h pulse pressure	0.5982	<0.001	-	-
Day SBP	0.4896	<0.001	0.2087	0.094
Day pulse pressure	0.5555	<0.001	-	-
Night SBP	0.5425	<0.001	-	-
Night pulse pressure	0.6396	<0.001	0.3919	<0.005

r = Pearson's correlation coefficient. β = multiple regression analysis coefficient.

Our data indicate that night-time BP appears to be a more accurate predictor of PWV in essential hypertension. It suggests the importance of 24-h ABPM in order to identify higher cardiovascular risk patients and the importance of whole-day hypertension control. Patients with RH have higher arterial stiffness (represented by carotid-femoral PWV) when compared to moderate EH patients. This difference appears to be independent of clinical blood pressure at the time of measurement.

Conflict of Interest

There is no conflict of interest.

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