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Pulse Pressure, Mean Blood Pressure and Impaired Glucose Tolerance—A Study in Middle-aged Subjects

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ABSTRACT

In a study of 695 middle-aged subjects, without antihypertensive agents, and without more pronounced obesity, both pulse pressure (PP) and mean blood pressure (MBP) were strongly related to 2-h blood glucose in 75 g OGTTs ($p < 0.001$).

All hypertensives (DBP ≥ 90 mm Hg) were separated into 39 with higher PP (≥ 60 mm Hg) and 137 with lower PP (< 60 mm Hg). The high PP hypertensives, compared with the low PP hypertensives and all 519 normotensives, had higher frequency of impaired glucose tolerance (IGT; WHO-criteria), 33%, 6%, and 4%, respectively ($p < 0.001$), and also higher mean 2-h blood glucose, 5.9, 4.5, and 4,2 $mmol \cdot l^{-1}$, respectively ($p < 0.001$). These differences were independent of MBP levels.

Similarly, all 54 hypertensives with higher MBP (≥ 110 mm Hg) had more IGT and higher 2-h glucose than the 122 hypertensives with lower MBP (< 110 mm Hg) or the normotensives, 30%, 5% and 4%, respectively ($p < 0.001$), and 5.8, 4.4, 4.2 $mmol \cdot l^{-1}$, respectively ($p < 0.001$), independently of PP. Thus, both high PP and high MBP were related to IGT, independently of each other.

INTRODUCTION

Blood pressure can be divided into two components: a steady component, represented by mean blood pressure, and a pulsatile component, represented by pulse pressure (3,4,9). It was the aim of this study to analyse the independent relationships between blood glucose and these two components, in middle-aged untreated subjects.

MATERIAL AND METHODS

A sample of 695 subjects, 47-54-years-old, was obtained from a health survey in Uppsala, previously described, with a participation rate of 71% (1). All subjects in the health survey with more pronounced obesity or antihypertensive agents were excluded from the present study. The hypertensives, 176 subjects (45.5% males, 54.5% females), were the subjects with diastolic blood pressure (DBP) ≥ 90 mm Hg and no antihypertensive agents. The normotensives were 519 subjects (50.3% males, 49.7% females).

Body mass index (BMI) was computed as weight $\cdot$ height^{-2} (kg $\cdot$ m^{-2}) and expressed as relative BMI (RBMI, %), based on ideal BMI values.

Blood pressure (BP) was measured sitting after >15 min of rest and no previous smoking, using Korotkoff fifth phase sounds, with a mercury sphygmomanometer (cuff size 12.5 x 35 cm), by the same observer. Pulse pressure (PP) was the difference of systolic BP and diastolic BP. Mean blood pressure (MBP) was diastolic BP + one-third of PP. All subjects with RBMI >130% at the health survey were excluded from the present study, to avoid the problem of greater arm circumference in obese subjects.

Oral glucose tolerance tests (OGTT) were performed in the morning after 10 hours of fasting (11). Venous whole blood glucose was measured at 0-h and 2-h levels by a glucose oxidase method (YSI Model 23 AM). Impaired glucose tolerance (IGT) was diagnosed according to strict WHO-criteria, based on two subsequent OGTTs (11). Subjects with manifest diabetes mellitus were excluded from the present study.

A questionnaire was used to obtain information on smoking and physical activity during leisure time and at work, the latter evaluated with a 4-point scale as used in the Gothenburg studies.

Statistical analysis. Analyses were performed with the SAS program. A p value of $p < 0.05$ was considered statistically significant. Student's t-test, chi-square statistics and Pearson's correlations were used. Multiple regression analysis (PROC GLM) was used (Table 1) with t-values of the predictors and the coefficient of determination (R^2) given. Analysis of covariance (PROC GLM) yielded mean values (Table 3), after adjustment for confounding covariates.

N-way analysis of frequency distribution (PROC FREQ) yielded the odds ratio (Table 3), after adjustment for n confounding covariates, with Cochran - Mantel - Haenszel correlation and general association statistics.

Table 1. Multiple regressions, PP and MBP as dependent variables (n=695).

		Pulse pressure t-value	Mean blood pressure t-value
Predictors:	2-h glucose	4.8 ***	6.9 ***
	Body mass index	3.1 **	4.2 ***
	Age	5.2 ***	1.9
	R^2	0.10	0.12

*** p <0.001,** p <0.01. Sex, smoking and phys. act. included (ns).

RESULTS

In all 695 participants, the correlation coefficients (r) were: PP-SBP 0.84, PP-DBP 0.11, and MBP-SBP 0.89, MBP-DBP 0.91. Other correlations were: PP-MBP 0.52, SBP-DBP 0.62. All correlations were mainly similar in females and males.

Table 1 shows that 2-h glucose was independenly related to both PP and MBP (p <0.001).

Hypertensives with low or high PP levels. All hypertensives were divided in two groups, with the mean + 1 SD value of PP (60 mm Hg) as the dividing level (Table 2). Group 2 hypertensives (high PP level) had higher 2-h glucose than group 1 hypertensives (low PP level) or normotensives, also after adjustment for MBP levels (Table 3, left part). The frequency of IGT (Table 4, left part) was clearly increased in group 2 hypertensives, 33%, compared with group 1 hypertensives, 7%, and normotensives, 4%, also differing as odds ratios for IGT, adjusted for MBP levels (p <0.001).

Hypertensives with low or high MBP levels. All hypertensives were also divided in two groups, wih roughly the mean + 1 SD value of MBP (110 mm Hg) as the dividing level (Table 2). Group 4 hypertensives (high MBP) had higher mean 2-h glucose than group 3 hypertensives (low MBP) and normotensives, even when adjusted for PP levels (Table 3, right part), and the frequency of IGT was higher in group 4 hypertensives, 30 %, than in group 3 hypertensives, 5%, or normotensives, 4%, independently of PP according to adjusted odds ratios (p <0.001).

All differences of 2-h glucose and odds ratios above remained (p <0.01), when adjustment also was made for BMI, simultaneously with the other covariates above (not in the Table). Group 4 hypertensives included 16 IGT subjects, and 13 of them were also found among the group 2.

Table 2. Mean±SE of characteristics in normotensives and hypertensives.

	NT	Group1-HT	Group2-HT	Group 3-HT	Group4-HT
2-h glucose (mmol/l)	4.5±0.1	4.5±0.1[&]	5.9±0.4[§ $]	4.4±0.1[&]	5.8±0.3[§ $]
PP (mm Hg)	49±0.4	45±0.5[§]	64±1.0[§ $]	44±0.6[§]	60±1.2[§ $]
MBP (mm Hg)	96±0.2	106±0.3[§]	116±0.9[§ $]	105±0.2[§]	115±0.8[§ $]
Rel BMI (%)	113±0.5	113±1.0	123±1.8[§ $]	112±1.0[§]	122±1.5[§ $]
Age (years)	51±0.1	51±0.6	52±0.4	51±0.1	52±0.3
Sex (male%)	50	48	36	48	41
Numbers	519	137	39	122	54

Hypertensives (HT) versus normotensives (NT): [§] $p < 0.001$, [&] $p < 0.01$. SE = st err
Group2-HT vs Group1-HT or Group3-HT vs Group4-HT: [$] $p < 0.001$.

DISCUSSION

The main findings in this study was, that hypertensives with high PP levels or high MBP levels had increased prevalence of IGT (one-third), and that PP and MBP levels were, independent of each other, related to IGT and postload 2-h blood glucose.

Blood pressure has been divided in two components (3,9). The steady component, MBP, can be estimated as the product of cardiac output and vascular resistance (mainly in small arteries). The pulsatile component, PP, is determined by other mechanisms, and related to the ratio of ventricular ejection time (stroke volume) and vascular compliance (visco-elastic properties of mainly large arteries). The dominant factor causing high PP seems to vary greatly with age. Younger subjects with high PP have mainly increased velocity of ventricular ejection and stroke volume, with normal arterial compliance (9). Middle-aged may have both increased stroke volume and decreased arterial compliance (10), while old subjects have mainly decreased compliance (= increased arterial stiffness) (9).

PP was strongly correlated to SBP (r=0.85) and an obvious marker for systolic hypertension. On the contrary, PP is the variable least related to DBP, 'classical hypertension'.

PP was clearly related to postload glucose in Chicago (5), weakly in Paris (3). Small studies of hypertensives with high PP had increased rates of manifest diabetes (2,5). PP was also indepedently related to age in the present study, as in Paris and Chicago above the ages of 45-55 (3,4), since arteries stiffen with increasing age.

We found MBP independently related to 2-h blood glucose, as in the Paris study (3). Notably, our hypertensives with high MBP seemed to include many hypertensives with high PP. The corr coeff PP-MBP was 0.52 in the present study.

Table 3. Adjusted mean±SE, odds ratios in normo(NT)- and hypertensives(HT).

	Gr2-HT / Gr1-HT	Gr2-HT/NT	Gr4-HT/Gr3-HT	Gr4-HT/NT
2-h glucose	5.8/ 4.5[a§]	5.2/ 4.3[a§]	5.7/ 4.4[b§]	5.5/ 4.2[b§]
(mmol/l)	±0.3/+0.1	±0.3/+0.1	±0.3/+0.2	±0.2/+0.1
PP (mm Hg)	58±1.1/47±0.5[a§]	50±0.3/43±1.6[a§]	-	-
MBP (mm Hg)	-	-	113±0.6/106±0.3[b§]	112±0.6/96±0.2[b§]
Numbers	39/137	39/519	54/122	54/519
Freq. IGT (%)	33/6.6	33/4.1	30/4.9	30/4.1
Odds ratio IGT	5.2	4.6	5.2	6.4
(95% bounds)	(2.2-12.5)[a§]	(2.0-10.8)[a§]	(1.7-16.0)[b&]	(3.3-12.6)[b§]

[a]adjusted for MBP, age and sex (concerning group 2). [§] p <0.001. SE = st err
[b]adjusted for PP, age and sex (concerning Group 4). [&] p <0.01.

A possible bias was the single blood pressure measurement here, as in Paris (3) and partly Chicago (4), which might result in loss of power in the analysis. It has been shown, however, that a single blood pressure measurement can predict which individuals are more likely to develop cardiovascular diseases (4). Moreover in Chicago, relationships were similar with a single, the mean of 3, or the lowest of 3 measurements used (4). Furthermore, as our associations were strongly significant (p <0.001), we believe this bias was mitigated in the present study.

Hyperinsulinaemia in IGTs is related to hypertension, possibly due to increased sympathetic nervous activity (7), which might either increase the contractibility of the heart or increase smooth muscle tone and arterial stiffness (6,8). High PP has been related to left ventricular hypertrophy in hypertensives and to coronary heart disease above the age of 45 (4). Do hypertensives with IGT and high PP have changes in ventricular ejection, or do they have increased arterial stiffness due to atherosclerosis, microangiopathy or sympathetic activity? This could have therapeutical implications. ACE-inhibitors and calcium entry blockers, for example, seem useful in IGT, and might also improve PP and arterial compliance (9).

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