ORIGINAL ARTICLE

Does sodium intake affect the relationship between blood pressure and vascular damage?

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KEY WORDS

blood pressure, central pulse pressure, cardiovascular risk, intima-media thickness, sodium

ABSTRACT

INTRODUCTION Although the differences between central and peripheral blood pressure (BP) values have been known for decades, the consequences of decision making based on peripheral rather than central BP have only recently been recognized. Recently, a U-shaped relation between sodium intake and cardiovascular risk has been suggested.

OBJECTIVES The aim of the study was to evaluate the relationship between intima-media thickness (IMT) and central and peripheral BP as well as the effect of 24-hour urinary sodium excretion on this relationship.

PATIENTS AND METHODS The study included 182 subjects (mean age, 37.3 ±14.0 years, 92 men and 90 women) who were members of families randomly selected from one of the *gminas* (administrative regions) in southern Poland. In all patients, peripheral and central BP (using applanation tonometry), IMT, and 24-hour sodium excretion were measured.

RESULTS Hypertension was observed in 44.5% of the participants. The mean urinary sodium excretion was 243 ±81 mmol/d. IMT was significantly more correlated with central pulse pressure (PP) compared with peripheral PP ($r = 0.54$ vs $r = 0.27$; $P < 0.01$). After multivariate adjustments, IMT remained significantly related to central systolic BP and central and peripheral PP. When the study group was divided according to the tertiles of sodium excretion, central PP was related to IMT only in the second and third tertiles. When the study group was divided according to sex and sex-specific median values of sodium excretion, IMT was associated with central PP only in subjects with sodium excretion exceeding the median values (both in men and women).

CONCLUSIONS IMT is more correlated with central than with peripheral BP. The association between IMT and central PP may be modulated by sodium intake. This hypothesis should be tested in larger studies.

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Received: February 24, 2015.
Revision accepted: March 30, 2015.
Published online: March 31, 2015.
Conflict of interest: none declared.
Pol Arch Med Wewn. 2015; 125 (5): 347-357

INTRODUCTION Although the differences between central and peripheral blood pressure (BP) have been known for decades, the consequences of decision making based on peripheral rather than central BP have only recently been recognized.[1,2] As central BP directly affects the heart as well as coronary and carotid arteries and is potentially directly related to the incidence of major cardiovascular complications, more and more attention has been given to central BP measurements in recent years.[1,2] However, although some studies showed a higher predictive value of central BP,[3,4] other studies failed to confirm this.[5] The intima-media thickness (IMT) of extracranial carotid arteries is a marker of advanced vascular disease in coronary and peripheral circulation and a predictor of cardiovascular events.[6,7] High BP plays a direct pathogenic role in the initiation and progression of carotid artery wall hypertrophy and atherosclerosis.[6,8] Indeed, IMT correlates with brachial BP.[9] Subsequently published data have shown that IMT correlates closely with central systolic BP and pulse pressure (PP) when compared with peripheral pressures, although the adjusted coefficients were not compared in these analyses.[3,4] Moreover, some other studies did not show significant differences even in a univariate analysis.[10,11]

Observational and experimental data support an independent positive relationship between BP and sodium intake.[12] However, prospective studies on the association between the risk of cardiovascular events and salt intake have provided conflicting data. A number of studies have shown that sodium intake predicts the risk of cardiovascular complications[13,14]; however, there are also studies that showed the lack of such an association[15,16] or even a higher risk in subjects with low sodium intake.[17-21] Although the latter studies have been criticized for using 24-hour dietary recall,[12,22] it seems that mean sodium intake in the investigated populations could also contribute to these conflicting results. Indeed, positive results were found in populations with high sodium intake,[13,14] while negative—in populations with relatively low salt consumption (just about 100 mmol).[15-20] It appears that the relationship between sodium intake and risk of cardiovascular events may not be linear, being steeper in subjects with high salt intake. Indeed, recently, a U-shaped relation between sodium intake and cardiovascular risk has been suggested.[23]

Considering all the above data, the present study was designed to compare the relations between IMT and central and peripheral BP and to evaluate the effect of urinary sodium excretion on the relationship between IMT and BP.

PATIENTS AND METHODS

Study population

The European Project On Genes in Hypertension (EPOGH) was conducted according to the principles outlined in the Helsinki declaration for investigations in human subjects. The study protocol has been approved by the local Ethics Committee. All participants provided written informed consent to participate in the study.

Data from 1 EPOGH center were included in the present analysis. Participants of the EPOGH project were members of families randomly selected from a population living in one of the *gminas* (administrative region) in southern Poland (Niepołomice, n = 358). Out of the invited patients, 195 agreed to participate in the study. Data of 13 subjects were excluded from the analysis because of incomplete information on important covariates or insufficient quality of the recorded pulse wave. Thus, the overall number of participants included in a statistical analysis was 182 (92 men and 90 women).

Clinical and biochemical measurements

Participants were asked to refrain from smoking, heavy exercise, and drinking alcohol or caffeine-containing beverages for at least 3 hours before the examination. Trained nurses measured the subjects' anthropometric characteristics, heart rate, and BP. They administered a questionnaire to collect information about each participant's medical history, smoking status, and use of medications. Body mass index (BMI) was measured as weight in kilograms divided by the square of height in meters. The levels of creatinine, cholesterol, and blood glucose were measured after overnight fasting by automated methods. Participants collected a 24-hour urine sample in a wide-neck plastic container for the measurement of sodium and potassium excretion.

Measurements of blood pressure

Trained staff visited participants at home. BP was measured on the nondominant arm, after exclusion of a significant difference between both arms. Each subject's BP was the average of 3 consecutive readings after the subjects had rested in the sitting position for at least 5 minutes. The cuff size was adjusted to the circumference of the arm. Hypertension was defined as systolic BP of at least 140 mmHg or diastolic BP of at least 90 mmHg or the use of antihypertensive drugs.

Central BP was measured using applanation tonometry. After subjects had rested for at least 15 minutes, we recorded, during an 8-second period, the radial arterial waveform at the dominant arm. We used a high-fidelity SPC-301 micromanometer (Millar Instruments, Inc., Houston, Texas, United States) interfaced with a computer running the SphygmoCor software, version 6.31 (AtCor Medical Pty. Ltd., West Ryde, New South Wales, Australia). We discarded recordings when the systolic or diastolic variability of consecutive waveforms exceeded 5% or when the amplitude of the pulse wave signal was less than 80 mV. We calibrated the pulse wave by measuring BP at the contralateral arm immediately before the recordings. Each subject's BP was the average of 3 consecutive readings after the subjects had rested in the sitting position for at least 5 minutes. The cuff size was adjusted to the circumference of the upper arm. From this BP reading, we calculated mean arterial pressure as diastolic pressure plus one-third of PP. From the radial signal, the SphygmoCor software calculates the aortic pulse wave by means of a validated and population-based generalized transfer function.

Home examinations, clinical examinations, and blood and urine sampling were performed within 3 weeks.

Measurements of carotid intima-media thickness

The carotid IMT was measured using the Vivid 7 scanner (General Electric Vingmed Ultrasound, Horten, Norway) equipped with a 7.0 MHz transducer. The IMT of the right and left common carotid artery 1 cm proximal of the bulb was recorded. The automated IMT package from Vivid 7 was used. The mean of the IMT of the right and left common carotid arteries was used in the analysis.

Statistical analyses

For database management and statistical analysis, we used the Statistica software (StatSoft Inc, Tulsa, Oklahoma, United States). Categorical variables were reported as percentages and continuous variables as means ± standard deviation. Departure from normality was evaluated by the Shapiro–Wilk test. Normally distributed continuous variables were compared

TABLE 1 Characteristics of the study participants

Variable		Sodium excretion		*P* value	All patients (n = 182)
		≤232.55 mmol/d (n = 91)	>232.55 mmol/d (n = 91)		
age, y		37.3 ±14.4	37.3 ±13.7	NS	37.3 ±14.0
sex	women	68.1	30.8	<0.001	49.5
	men	31.9	69.2		50.5
smoking		20.9	27.5	NS	24.2
hypertension		40.7	48.4	NS	44.5
antihypertensive treatment		23.1	27.5	NS	25.3
diuretic		15.4	9.9	NS	12.6
β-blocker		15.4	12.1	NS	13.7
ACEI or sartan		13.2	17.6	NS	15.4
calcium antagonist		6.6	8.8	NS	7.7
diabetes		2.2	1.1	NS	1.6
alcohol consumption		7.7	30.8	<0.001	19.2
body mass index, kg/m^2		24.9 ±5.2	26.1 ±4.5	NS	25.5 ±4.9
blood biochemistry					
LDL cholesterol, mmol/l		2.87 ±1.05	2.84 ±1.05	NS	2.85 ±1.05
glucose, mmol/l		4.63 ±1.00	4.57 ±0.94	NS	4.60 ±0.98
creatinine, mmol/l		78.6 ±17.5	84.0 ±14.7	<0.01	81.3 ±16.4
eGFR, ml/min/1.73 m^2		90.2 ±23.7	91.8 ±20.3	NS	91.0 ±22.0
urinary excretion					
volume, l/d		1.33 ±0.51	1.58 ±0.55	<0.001	1.46 ±0.54
sodium, mmol/d		180 ±33	307 ±64	<0.001	243 ±81
potassium, mmol/d		56 ±18	78 ±27	<0.001	67 ±25

Data are presented as mean ± standard deviation or percentage of subjects.

Conversion factors: to convert millimoles of sodium to grams, multiply by 0.02299; to convert millimoles of potassium to grams, multiply by 0.039098.

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; eGFR, estimated glomerular filtration rate; LDL, high--density lipoprotein; NS, nonsignificant

using the *t* test for independent samples. The Mann–Whitney *U* test was used for variables without normal distribution. The correlation coefficients were compared using the r-to-Fisher-z transformation. Our statistical methods also included multiple linear regression. To identify covariables of IMT, in addition to BP, we applied a stepwise selection procedure with a *P* value for independent variables to enter and stay in the model set at 0.1. The baseline covariables considered for entry into the model were sex (male 0, female 1), age, smoking (0, 1), hypertension (0, 1), antihypertensive treatment (0, 1), alcohol consumption (0, 1), BMI, blood glucose level, low-density lipoprotein (LDL) cholesterol, serum creatinine level, and heart rate to obtain a model in which all remaining variables had *P* values of less than 0.05 (basic model). We repeated multiple regression analyses with the model containing all the above potential confounders (full model). Finally, we forced mean arterial pressure to each statistical model. In sensitivity analyses, we divided the study population according to urinary sodium excretion and sex. Statistical significance was set at a 2-sided α-level of 0.05 or less.

RESULTS **Characteristics of participants** The study population consisted of 92 men and 90 women. The mean age was 37.3 ±14.0 years (TABLE 1). Overall, 24.2% of the participants were smokers, 44.5% had hypertension, and 17.6% had obesity (BMI, ≥30 kg/m^2). The mean urinary sodium excretion was 243 ±81 mmol/d (median, 232.55 mmol/l) and mean potassium excretion—67 ±25 mmol/d (median, 62.83 mmol/l). Proportions of study participants according to the value of urinary sodium excretion are presented in FIGURE 1. A urinary sodium excretion of 100 mmol/d or less was observed in 2.5% of the patients with hypertension, but none of the patients without hypertension had urinary sodium excretion lower than that. Overall, 1.1% of male participants had a urinary sodium excretion of 100 mmol/d or less; 3.3%, of 100–150 mmol/d; 16.3%, of 150–200 mmol/d; 19.6%, of 200–250 mmol/d; 26.1%, of 250–300 mmol/d; 16.3%, of 300–350 mmol/d; 15.2%, of 350–400 mmol/d; and 2.2%, of more than 400 mmol/d. The corresponding proportions in women were 1.1%, 14.4%, 32.2%, 23.3%, 15.6%, 11.1%, 2.2%, and 0.0%. Participants with sodium excretion above

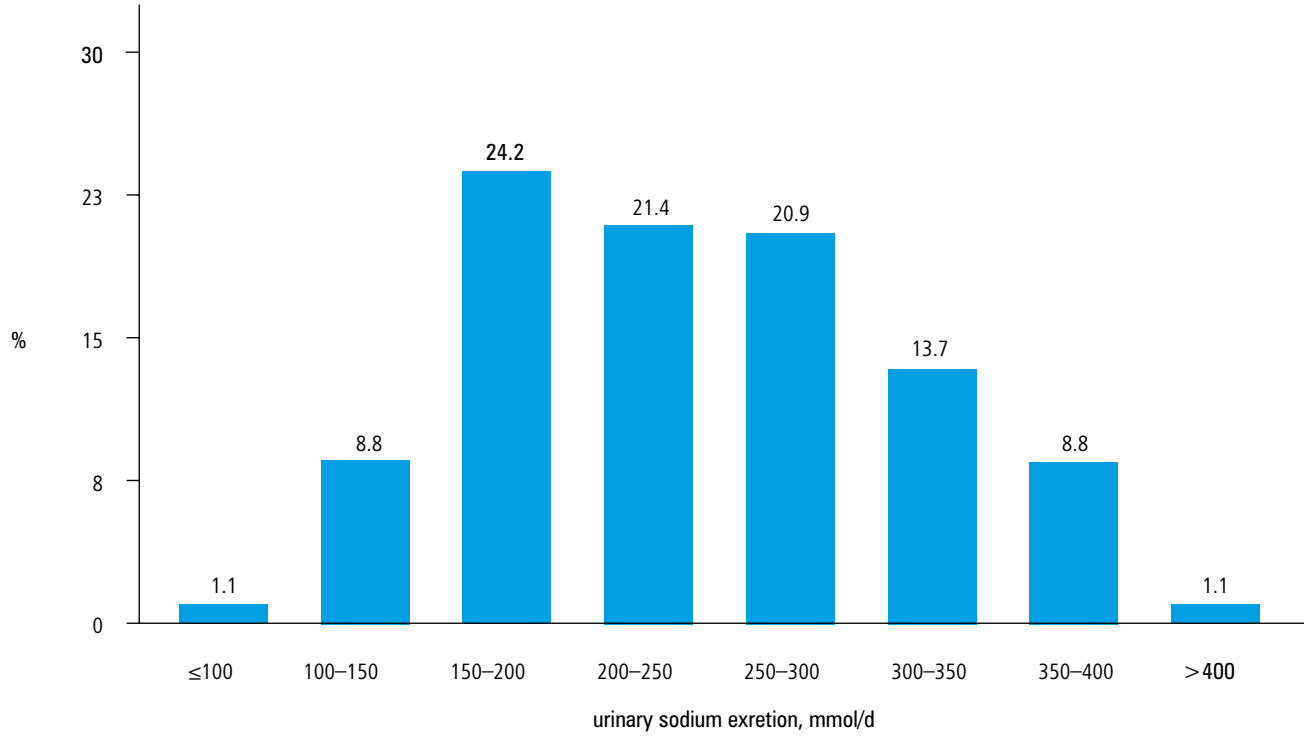

FIGURE 1 Proportions of study participants according to urinary sodium excretion; for conversion factors, see TABLE 1

the median value more often were men compared with those with lower sodium excretion (TABLE 1). Blood pressure, heart rate, and IMT did not differ between patients with sodium excretion lower and higher than the median value (TABLE 2).

Univariate analysis IMT was significantly correlated with both central and peripheral BP (FIGURE 2). It was significantly more closely correlated with central PP compared with peripheral PP. The other significant correlates of IMT in the univariate analysis were age (r = 0.70; P <0.001), BMI (r = 0.49; P <0.001), LDL cholesterol (r = 0.35; P <0.001), and fasting blood glucose level (r = 0.21; P <0.01). Urinary sodium and potassium excretion, heart rate, and serum creatinine levels were not significantly correlated with IMT in the study population.

Multivariate analysis The stepwise multivariate regression analysis revealed that IMT was independently related to age (β ± standard error, 0.579 ±0.063; P <0.001), sex (–0.173 ±0.055; P <0.01), BMI (0.145 ±0.062; P <0.05), creatinine levels (0.156 ±0.062; P <0.01), and antihypertensive treatment (–0.202 ±0.053; P <0.001). When BP was added to the model containing all these variables, IMT was independently related only to systolic BP and PP (TABLE 3). In a model containing all potential confounders, IMT again was independently related only to systolic BP and PP (TABLE 3). Further adjustment for mean arterial pressure did not change the results significantly. IMT was not associated with mean arterial pressure when adjusted for PP.

Sensitivity analysis When adjusted for age, sex, creatinine levels, and BMI, IMT was related to central PP in hypertensive patients (β ± standard error, 0.340 ±0.102; P <0.01), but not in patients with normal BP (0.100 ±0.075; P = 0.19). Similarly, IMT was related to brachial PP in hypertensive patients (0.250 ±0.089; P <0.01) but not in those with normal BP (0.045 ±0.070; P = 0.52). IMT was not related to central systolic pressure (hypertensive patients, 0.194 ±0.104; P = 0.07; normotensive patients 0.025 ±0.093; P = 0.79), brachial systolic BP (hypertensive patients, 0.167 ±0.093, P = 0.08; normotensive patients, –0.018 ±0.082, P = 0.82), central diastolic BP (hypertensive patients, –0.046 ±0.100, P = 0.65; normotensive patients, –0.063 ±0.081, P = 0.44), brachial diastolic BP (hypertensive patients, –0.071 ±0.102, P = 0.49; normotensive patients, –0.079 ±0.079, P = 0.32).

When the study population was divided according to the median value of urinary sodium excretion (232.55 mmol/d), IMT was independently related to central systolic BP and PP in patients with high urinary sodium excretion, while in those with low urinary sodium excretion, IMT was related only to central PP (TABLE 4). IMT was not significantly related to peripheral BP in participants with low urinary sodium excretion but was associated with central systolic BP in those with high sodium excretion. We also divided the analyzed population according to the tertiles of urinary sodium excretion showing increasing slopes of the IMT—central PP association with the increasing tertiles of urinary sodium excretion (FIGURE 3). Central PP was not related to IMT in participants with urinary sodium excretion of

TABLE 2 Hemodynamic characteristics of the study participants

Variable	Sodium excretion		*P* value	All patients (n = 182)
	≤232.55 mmol/d (n = 91)	>232.55 mmol/d (n = 91)		
central BP				
systolic, mmHg	114.5 ±21.0	118.2 ±17.2	NS	116.4 ±19.2
diastolic, mmHg	80.0 ±13.3	83.2 ±12.5	NS	81.6 ±13.0
pulse pressure, mmHg	35.4 ±11.3	36.1 ±9.7	NS	34.7 ±10.7
peripheral BP				
systolic, mmHg	127.1 ±18.3	131.6 ±15.9	NS	129.4 ±17.2
diastolic, mmHg	79.1 ±12.8	81.5 ±11.9	NS	80.3 ±12.4
mean, mmHg	95.1 ±14.0	98.2 ±12.1	NS	96.7 ±13.1
pulse pressure, mmHg	48.1 ±10.6	50.1 ±12.2	NS	49.1 ±11.4
heart rate, bpm	73.4 ±9.8	70.8 ±12.1	NS	72.1 ±11.1
carotid intima-media thickness, µm	610 ±130	609 ±118	NS	610 ±124

Data are presented as mean ± standard deviation.

For conversion factors, see TABLE 1.

Abbreviations: BP, blood pressure

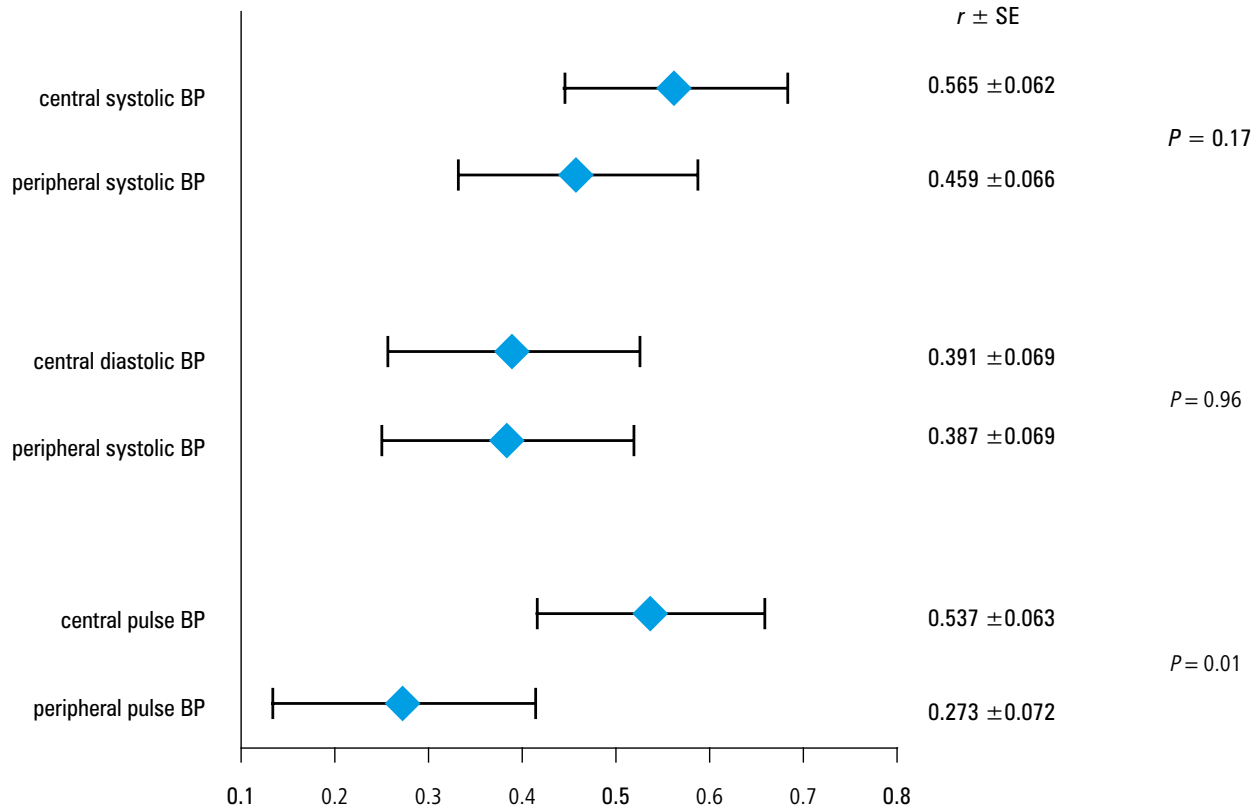

FIGURE 2 Correlation coefficients between intima-media thickness and central and peripheral blood pressure in the study group; all correlation coefficients are significant (all $P < 0.001$); rhomboids denote correlation coefficients; horizontal lines denote 95% confidence intervals
Abbreviations: SE, standard error; others, see TABLE 2

less than 199.48 mmol/d, while the association was significant in the other tertiles. We also divided the analyzed population according to the quartiles of urinary sodium excretion (data not shown). Central PP was not related to the IMT in participants with urinary sodium excretion below 185.8 mmol/d, while the association was significant in all other quartiles. When we divided the study population according to sex and used sex-specific median values of urinary sodium excretion, we were able to show the significant association in men and women with high urinary sodium excretion, but the association was not significant in those with low sodium excretion (FIGURE 4). Finally, we modeled the regression coefficient of the association between central PP and IMT as

TABLE 3 Regression coefficients of intima-media thickness with blood pressure

Variable		β ± SE	*P* value
basic model[a]			
systolic BP	central	0.143 ±0.068	0.04
	peripheral	0.111 ±0.060	0.07
diastolic BP	central	–0.010 ±0.062	0.87
	peripheral	–0.030 ±0.063	0.64
mean BP		0.034 ±0.064	0.59
pulse BP	central	0.217 ±0.059	<0.0001
	peripheral	0.144 ±0.051	<0.01
full model[b]			
systolic BP	central	0.198 ±0.079	0.01
	peripheral	0.167 ±0.071	0.02
diastolic BP	central	0.010 ±0.072	0.89
	peripheral	–0.016 ±0.073	0.82
mean BP		0.073 ±0.077	0.34
pulse BP	central	0.239 ±0.064	<0.001
	peripheral	0.153 ±0.053	<0.01

a age, sex, body mass index, creatinine level, and antihypertensive treatment were included in the basic model
b additionally adjusted for heart rate, smoking, alcohol consumption, hypertension, blood glucose, and LDL cholesterol level

Abbreviations: β, standardized regression coefficient; others, see **TABLE 2** and **FIGURE 2**

TABLE 4 Regression coefficients of blood pressure parameters with intima-media thickness as a dependent variable according to the urinary sodium excretion; age, sex, body mass index, heart rate, smoking, alcohol consumption, hypertension, antihypertensive treatment, blood glucose, low-density lipoprotein cholesterol, and creatinine level were included in the model

Variable	Sodium excretion ≤232.55 mmol/d (n = 91)		Sodium excretion >232.55 mmol/d (n = 91)	
	β ± SE	*P* value	β ± SE	*P* value
central BP				
systolic BP	0.154 ±0.113	0.18	0.273 ±0.114	0.02
diastolic BP	0.00 ±0.105	1.00	0.058 ±0.108	0.59
pulse pressure	0.190 ±0.090	0.04	0.282 ±0.096	<0.01
peripheral BP				
systolic BP	0.114 ±0.100	0.26	0.218 ±0.103	0.04
diastolic BP	-0.040 ±0.106	0.71	0.056 ±0.109	0.61
mean arterial pressure	0.034 ±0.111	0.76	0.157 ±0.114	0.17
pulse pressure	0.124 ±0.712	0.09	0.150 ±0.083	0.07
additional adjustment for mean arterial pressure				
central pulse pressure	0.199 ±0.101	0.052	0.260 ±0.100	0.01
peripheral pulse pressure	0.129 ±0.075	0.09	0.137 ±0.084	0.10

Mean sodium excretion in the low sodium excretion group was 180.1 ±33.1 mmol/d and in high sodium excretion group—306.7 ±64.0 mmol/d.

For conversion factors, see **TABLE 1**.

Abbreviations: see **TABLES 2** and **FIGURE 2**

the function of urinary sodium excretion showing a steep reduction of the coefficient with decreasing urinary sodium excretion below the value of 190 mmol/d (**FIGURE 5**). Urinary potassium excretion did not affect the association between BP and IMT (data not shown).

DISCUSSION Recent studies have provided conflicting results: while some showed that central pressure predicts risk of cardiovascular events in subjects with risk factors and in those with overt coronary artery disease,[3,4,24] others did not show such an association.[5] Central pressure was also proved to correlate with the extent of coronary atherosclerosis and with carotid IMT.[3,4,25] Our present results are in line with the previous findings suggesting that central pressure correlates strongly with carotid IMT when compared with brachial pressure.[3,4] This phenomenon is caused by a considerable difference between central and peripheral pressure values.[1,2] In addition, we showed the advantage of central PP even after multivariate adjustment. Moreover, our results are in line with the paper by Boutouyrie et al.[26] who showed that IMT is correlated with PP but not with mean arterial pressure when both indices are included in the statistical model. This is probably caused by the predominant role of pulsatile cyclic stress of the artery wall in arterial remodeling and the development and progression of atherosclerosis.[8] This finding is consistent with studies showing better prediction of cardiovascular complication rate using central PP instead of mean arterial pressure.[24]

The present study showed that urinary sodium excretion may influence the association between IMT and BP. Although we found no significant relationship between carotid IMT and central or peripheral BP in subjects with low urinary sodium excretion, it is still possible that the results may have differed if a larger group was analyzed. On the other hand, this finding is consistent with previous data from epidemiological and experimental studies. Indeed, in all studied populations (with one exception)[27] with a mean sodium intake around 100 mmol/l, no significant association between cardiovascular risk and sodium intake[15-16] or even higher risk[17-20] in those with low salt intake was found. In the analysis published by He at al.,[27] prognosis was related to sodium intake in overweight subjects but not in those with normal weight. In a population with average urinary sodium excretion (median value, 158 mmol/d) studied by Cook et al.,[28] the relation between cardiovascular risk and sodium excretion was not significant when all potential confounders were taken into account. On the other hand, the sodium-to-potassium excretion ratio predicted cardiovascular risk in this population. Tuomilehto et al.[13] and Nagata et al.[14] showed a positive correlation between cardiovascular risk and sodium excretion in populations with high sodium intake, whereas in the group studied by Umesawa et al.,[29] cardiovascular risk was significantly increased only in those with a daily sodium intake exceeding 160 mmol. This threshold is consistent with our results. Recently published results of the PURE study suggest an even higher threshold.[23]

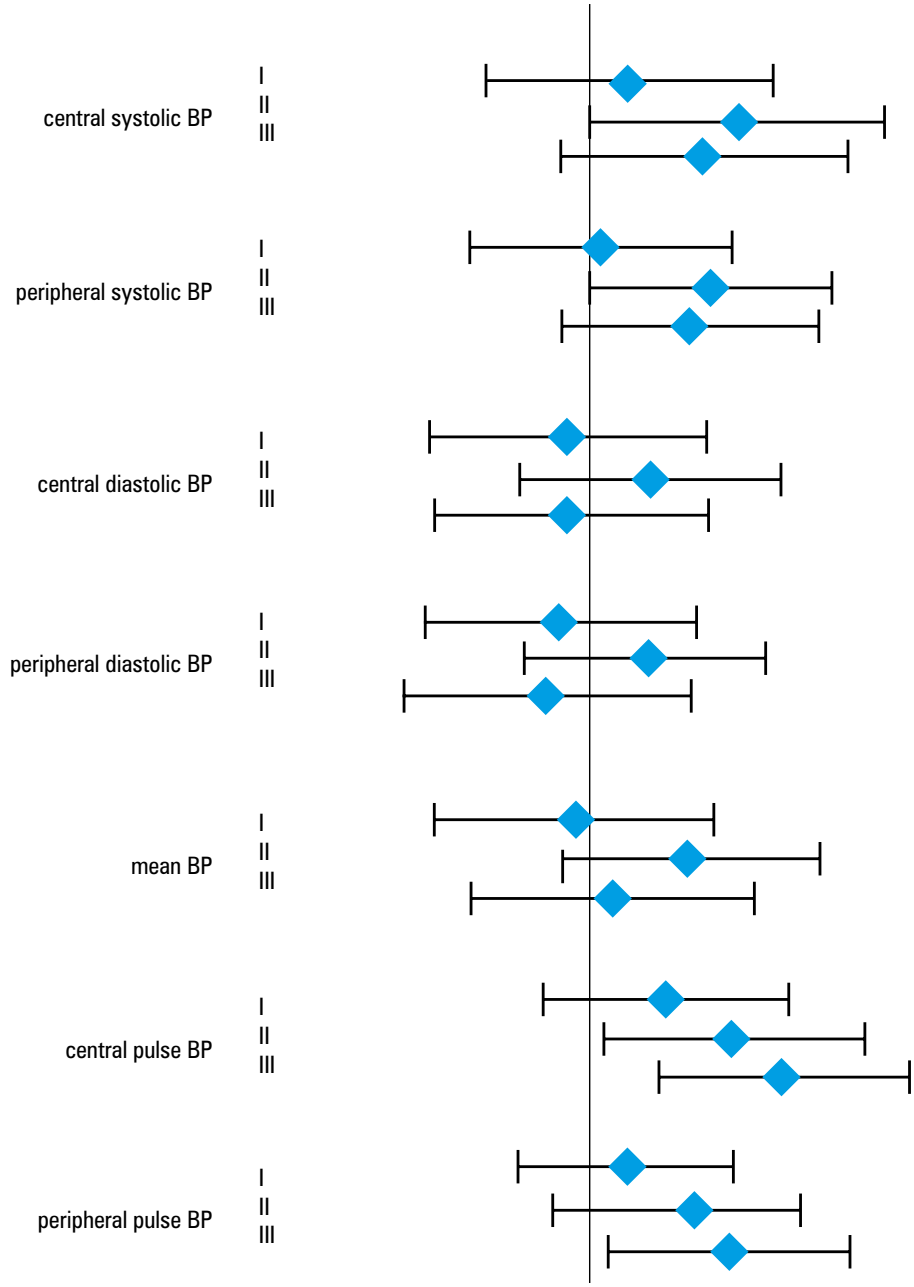

FIGURE 3 Regression coefficients of blood pressure with intima-media thickness as a dependent variable according to tertiles of urinary sodium excretion; age, sex, and body mass index are included in the multivariate models; rhomboids denote standardized regression coefficients; whiskers denote 95% confidence intervals
Abbreviations: see **TABLE 2**

It was suggested that the conflicting results of the above epidemiological studies are induced by differences in the methods used to estimate salt intake.[12,22] However, positive results were found using urinary sodium excretion[13] and food frequency questionnaire,[14] while among studies showing no or negative correlation, there are studies using urinary sodium excretion[17,21] along with studies using 24-hour dietary recall.[16,19,20] Moreover, among 2 studies showing the association between cardiovascular risk and salt in a subgroup of the analyzed population, one used urinary sodium excretion[30] and the other—24-hour dietary recall.[27] Indeed, it seems that one of the most important differences between studies with positive and negative results is the population's average salt intake. This issue was addressed in a meta-analysis published by O'Donnell et al.[31] suggesting a U-shaped relationship between sodium intake and cardiovascular risk.

Our hypothesis that salt intake may differentially affect the rate of complications is further supported by data from INTERSALT study. In an analysis of populations from 17 countries, the correlation coefficient between stroke mortality and urinary sodium excretion was –0.04 in men aged from 45 to 54 years with sodium excretion of less than 160 mmol/d and 0.82 in those with sodium excretion of 160 mmol/d or higher.[32] Similarly, the correlation coefficient in women aged from 45 to

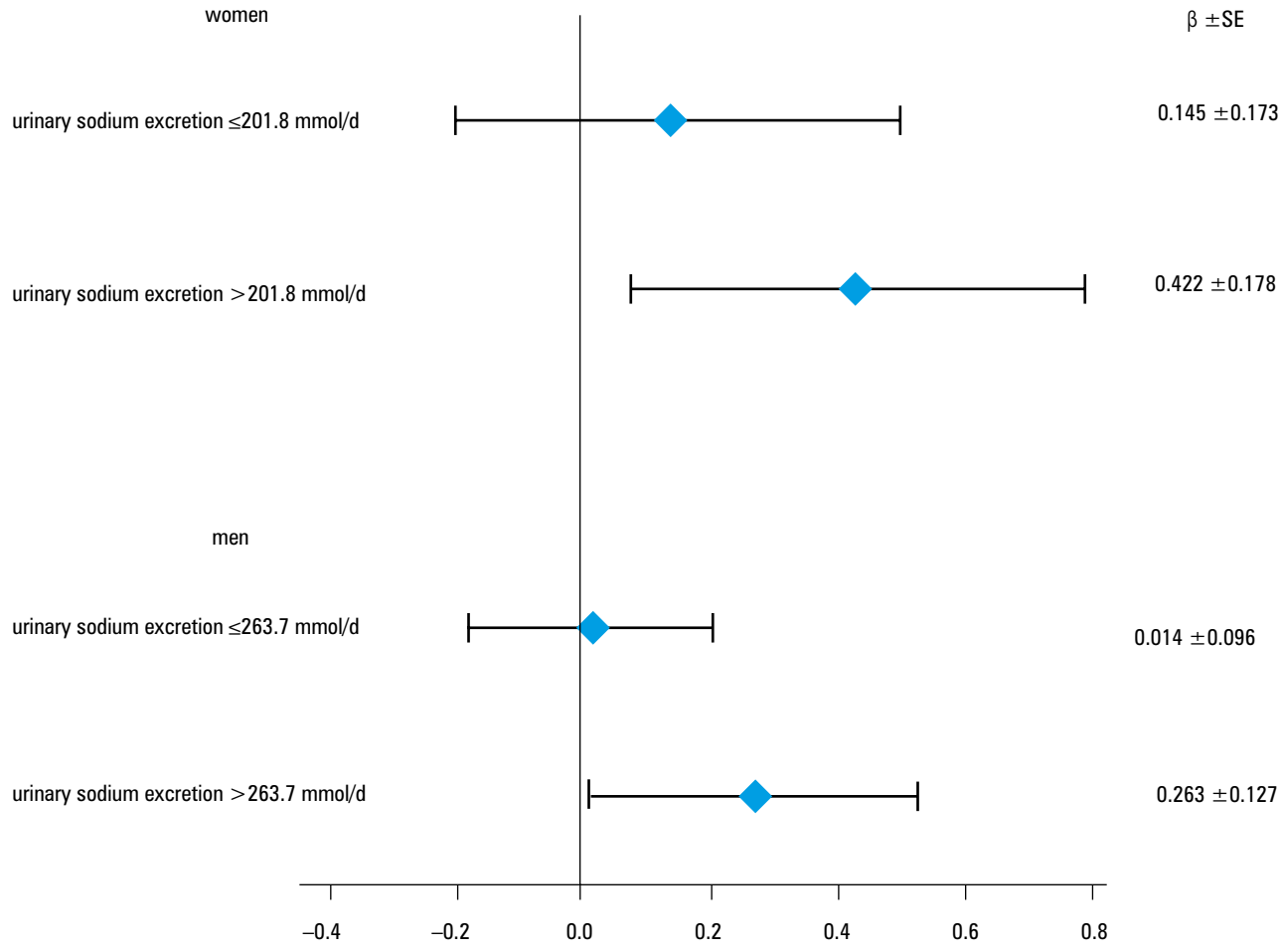

FIGURE 4 Regression coefficients of central pulse pressure with intima-media thickness as a dependent variable according to sex and sex-specific median value of urinary sodium excretion; age, sex, body mass index, heart rate, smoking, alcohol consumption, hypertension, antihypertensive treatment, blood glucose, low-density lipoprotein cholesterol, and creatinine levels were included in multivariable models; rhomboids denote standardized regression coefficients; whiskers denote 95% confidence intervals
Abbreviations: see **FIGURE 2**

54 years with sodium excretion of less than 160 mmol/d was 0.29 and in those with sodium excretion of 160 mmol/d or higher—0.79.[32] Another analysis of the INTERSALT study included data from 12 European countries.[33] On the basis of these data, it can be calculated that an increase in urinary sodium excretion by 10 mmol/d is related to an increase in stroke mortality by 17/100 000 in populations with the median value of sodium excretion below 160 mmol/d and 99/100 000 in populations with the median value of sodium excretion over 160 mmol/d.[33]

Similarly to other studies, we did not find a significant relation between sodium excretion and IMT.[34] BP-independent harmful effects of long-term dietary salt loading may contribute to the interaction between sodium excretion and the relation between BP and IMT. Indeed, salt-loading results in increased cardiac, aortic, and renal mass even before an increase in pressure, severe ventricular fibrosis associated with ventricular diastolic dysfunction, arterial remodeling, and reduced aortic distensibility in proportion to the extent of salt intake.[35,36] Moreover, high sodium intake is related to increased vascular reactivity and growth.[37] High sodium levels can stimulate vascular growth by enhancing trophic responses to angiotensin II, vasopressin, and various growth factors, whose actions involve sodium influx. Thus, carotid intima-media thickening in the presence of a high-sodium diet may occur as a combination of a compensatory response to increased BP and a response of vascular wall cells to their high sodium environment.[37] It can be also speculated that high sodium intake may predispose to atherosclerosis in response to high BP by enhancing the response of mechanoreceptors.

Carotid IMT is related to vascular endothelial function.[38] Tzemos et al.[39] showed impaired endothelial function in subjects with oral salt overload. Importantly, urinary sodium excretion in the group with salt overload was 225 mmol/d as compared with 76 mmol/d in the control group. These values are consistent with our findings. It should be underlined that our results do not deny harmful effects of moderately increased salt consumption. Rather, they suggest that increased BP may be particularly dangerous in the case of high salt consumption.

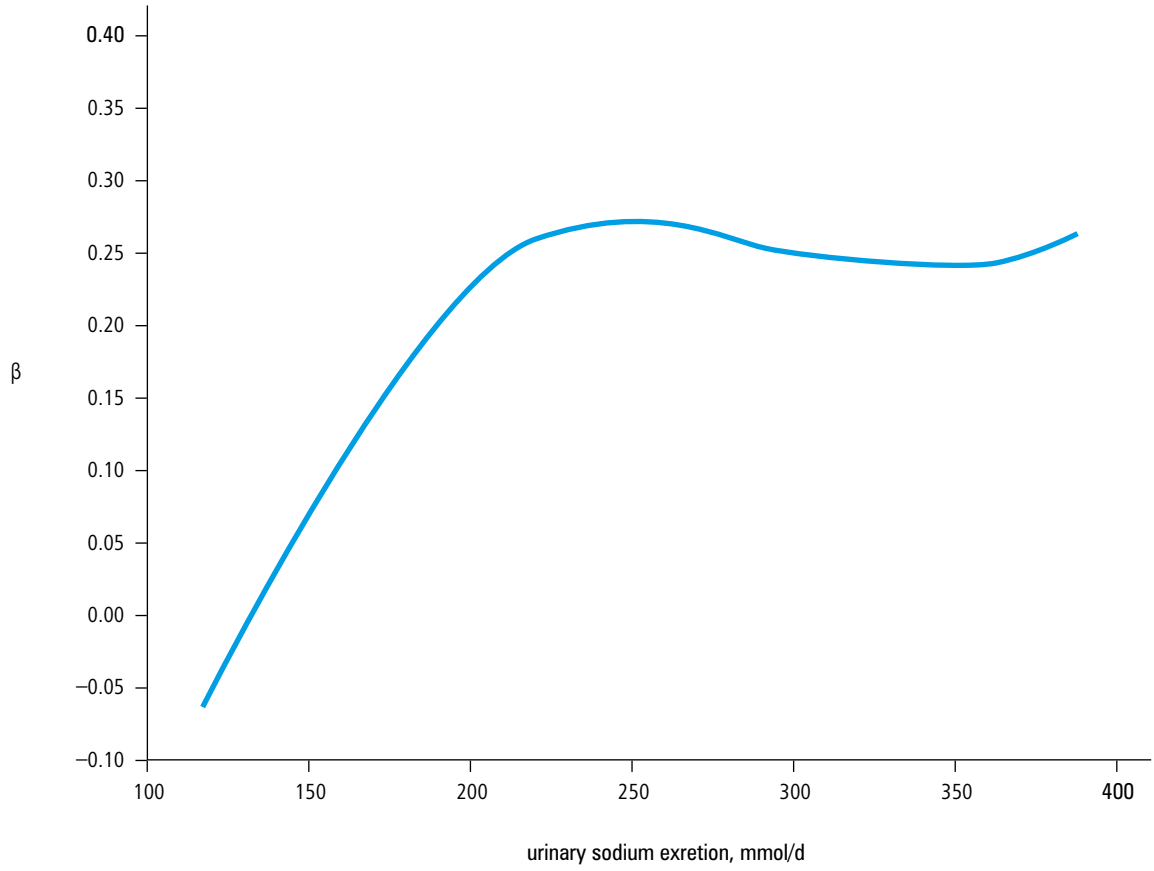

FIGURE 5 Regression coefficient of the association between central pulse pressure and intima-media thickness as the function of urinary sodium excretion; age, sex, and body mass index were included in the statistical model; β denotes standardized regression coefficient; for conversion factors, see **TABLE 1**

Our study was observational and not designed to reveal causality; therefore, it should be considered as hypothesis generating. Nevertheless, if confirmed by experimental studies and other epidemiological observations, our findings may have important implications for the management of hypertension, prevention of cardiovascular diseases, and future research. Indeed, our findings may have a deep influence on the understanding of the association between vascular wall changes and BP wave. We showed that among all studied BP indices, central PP is the most important index independently correlated with IMT and that urinary sodium excretion may influence the association between IMT and BP. Our results underline that central pressure rather than brachial pressure should be used in future research. Our results also provide evidence that high salt intake in addition to increasing prevalence of hypertension may accelerate the development of vascular changes in response to increased BP. This hypothesis should be tested in future studies.

The present study has several limitations. Its major limitation is the cross-sectional design. We did not follow up our study population so we cannot conclude that salt intake affects the association between BP and event-free survival. Nevertheless, carotid IMT may be considered as a surrogate for cardiovascular events.[6,40,41] We used a noninvasive assessment of central BP instead of invasive measurements, which are considered as the gold standard. However, it is unlikely that the use of an invasive technique could significantly change our results. Third, BP was measured by the trained staff during only 1 visit at each participant's home. The proportion of the study participants considered as hypertensive would be probably significantly lower if we had performed 24-hour ambulatory BP monitoring or measured BP during at least 2 visits. It is also possible that the participation rate among hypertensive patients was higher compared with subjects without hypertension artificially increasing the prevalence of hypertension in the study group.

Conclusions IMT is more closely related to central than to peripheral BP. The association between BP and IMT may be modulated by sodium intake. This hypothesis should be tested in larger studies.

Contribution statement PJ conceived the idea for the analysis. PJ and KS-S contributed to the design of the analysis. KS-S, WW, AO, and MC were involved in data collection. PJ analyzed the data. All authors edited and approved the final version of the manuscript

Acknowledgements The research group was supported by the European Union (grant LSHM-CT-2006-037093).

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ARTYKUŁ ORYGINALNY

Czy spożycie sodu wpływa na związek między ciśnieniem centralnym a stopniem uszkodzenia naczyń?

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SŁOWA KLUCZOWE

ciśnienie tętnicze, centralne ciśnienie tętna, grubość błony środkowej i wewnętrznej, ryzyko sercowo-naczyniowe, sód

STRESZCZENIE

WPROWADZENIE Chociaż od kilkudziesięciu lat wiadomo, że ciśnienie tętnicze i kształt fali tętna istotnie się różnią w poszczególnych odcinkach drzewa tętniczego, to dopiero niedawno znacznie wzrosło zainteresowanie klinicznym znaczeniem tej różnicy. Niedawno zasugerowano, że związek między spożyciem sodu, a ryzykiem sercowo-naczyniowym może mieć kształt litery U.

CELE Celem badania było porównanie związku między grubością błony środkowej i wewnętrznej (*intima-media thickness* – IMT) z centralnym i obwodowym ciśnieniem tętniczym oraz ocena interakcji między dobowym wydalaniem sodu z moczem a związkiem między IMT i ciśnieniem tętniczym.

PACJENCI I METODY W badaniu wzięły udział 182 osoby (średnia wieku: 37,3 ± 14,0 lat, 92 mężczyzn oraz 90 kobiet) będące członkami rodzin, które zostały losowo wybrane spośród rodzin zamieszkałych w jednej z gmin w południowej Polsce. U wszystkich uczestników badania zmierzono obwodowe i centralne (przy zastosowaniu tonometrii aplanacyjnej) ciśnienie tętnicze, IMT oraz dobowe wydalanie sodu z moczem.

WYNIKI Wśród uczestników badania 44,5% osób miało nadciśnienie tętnicze. Średnia dobowego wydalania sodu z moczem wyniosła 243 ±81 mmol/dobę. Współczynnik korelacji IMT z centralnym ciśnieniem tętna był wyższy niż współczynnik korelacji IMT z obwodowym ciśnieniem tętna ($r = 0,54$ *vs* $r = 0,27$; $p < 0,01$). Po uwzględnieniu zmiennych zakłócających IMT pozostał istotnie związany z centralnym ciśnieniem skurczowym oraz centralnym i obwodowym ciśnieniem tętna. Analiza w tertylach dobowego wydalania sodu z moczem wykazała, iż centralne ciśnienie tętna było istotnie związane z IMT tylko u osób z drugiego i trzeciego tertyla. Kiedy grupa została podzielona w zależności od płci i zależne od płci mediany dobowego wydzielania sodu z moczem IMT było związane z centralnym ciśnieniem tętna tylko u osób z wydalaniem sodu powyżej mediany (zarówno w grupie mężczyzn, jak i kobiet).

WNIOSKI IMT jest silniej związane z centralnym ciśnieniem tętniczym niż z ciśnieniem obwodowym. Spożycie sodu może wpływać na związek między IMT a ciśnieniem tętniczym. Hipoteza ta powinna być poddana ocenie w badaniach z większą liczbą uczestników.

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Praca wpłynęła: 24.02.2015
Przyjęta do druku: 30.03.2015
Publikacja *online*: 31.03.2015
Nie zgłoszono sprzeczności interesów.
Pol Arch Med Wewn. 2015; 125 (5): 347-357