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RESEARCH ARTICLE

Plasma reactive carbonyl species: Potential risk factor for hypertension

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Abstract

To study the role of oxidative stress in hypertension and pre-hypertension, this study analysed plasma levels of reactive carbonyl species (RCS) in 1204 Chinese Han adults. Results showed a statistically significant positive correlation ($p < 0.001$) between blood pressure and plasma RCS levels with or without being adjusted for covariates. Multivariate-adjusted odds ratio (OR) illustrated that, compared with the lowest quartile of plasma RCS levels, the highest quartile subjects had a 59% and a 130% increase in the risk for developing pre-hypertension and hypertension, respectively. The multi-interaction analysis manifested that the underlying mechanism of the increase of hypertensive risk or pre-hypertensive risk by overweight and unhealthy lifestyles might, at least in part, be through oxidative stress. In conclusion, these findings suggest that oxidative stress, as indicated by plasma RCS levels, are not the necessary consequence of pre-hypertension or hypertension, but reliable risk factors for developing pre-hypertension or hypertension in Chinese Han adults.

Keywords: *Oxidative stress, reactive carbonyl species (RCS), hypertension, pre-hypertension*

Abbreviations: *ANOVA, analysis of variance; BMI, body mass index; BP, blood pressure; CAT, catalase; CI, confidence interval; EDTA, ethylene diamine tetra-acetic acid; LSD, least significant difference; MDA, malondialdehyde; OR, odds ratio; RCS, reactive carbonyl species; ROS, reactive oxygen species; SD, standard deviation; SOD, superoxide dismutase; TBA, thiobarbituric acid; TBARS, thiobarbituric acid reactive substance.*

Introduction

Essential hypertension accounts for 95% of hypertension. It can increase the risk for developing renal failure, cardiovascular disease and stroke [1]. According to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure [2], blood pressure can be classified as normotension, pre-hypertension and hypertension, and the pre-hypertension is at high risk for developing hypertension.

Hypertension is associated with increasing reactive oxygen species (ROS) and impairing endogenous antioxidant systems. Compared with normotensive subjects, higher levels of superoxide anion and hydrogen peroxide have been reported to produce in hypertensives [3], which mainly results from the activation of vascular NAD(P)H oxidase. Lower levels of plasma antioxidant capacity, plasma vitamin C, GSH/GSSG ratio and the expression and activity of various antioxidant enzymes have also been observed in hypertensive patients [4,5].

Although many factors such as age, stress [6], obesity [7,8] and unhealthy lifestyles (unhealthy dietary habit, cigarette smoking, alcohol intake and sedentary) [9–11] have been suggested to contribute to the elevation of blood pressure, the mainly initial mechanisms for hypertension are endothelial activation, oxidative stress and vascular smooth muscle

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dysfunction [12–15]. Considering that excessive oxidative stress is involved in impairing endothelium-dependent vasodilatation [16] and contributes to endothelial dysfunction and vascular hypertrophy in both animal models and human hypertension [12,14,15,17], it is reasonable to believe that oxidative stress may play a pivotal role in the pathogenesis of hypertension.

Results from the studies of genetic manipulation, gene polymorphism and anti-hypertensive drugs all confirm the above hypothesis. Microinjection of SOD1, SOD2 or CAT into spontaneously hypertensive rats have shown a long-lasting reduction in arterial pressure along with an increased SOD1, SOD2 or CAT enzyme activity and reduced superoxide anion and hydrogen peroxide levels [18]. Kidney androgen-regulated protein transgenic mice are demonstrated by hypertensive phenotype, diminished catalase and glutathione peroxidase activity and increased markers of oxidative stress [19]. Intriguingly, results from two separated groups have found that endothelial nitric oxide synthase gene haplotypes [20] or glutathione S-transferase M1 and T1 gene deletion homozygous [21] are potential genetic factors to predict the development of essential hypertension. Moreover, anti-hypertensive therapies can reduce oxidative stress and increase plasma antioxidant capacity [22].

However, the chronic antioxidants treatment fails to prevent or treat hypertension and hypertension-related cardiovascular diseases, which is contrary to the short-term treatment that exhibits some beneficial effects for hypertension [17,23]. Furthermore, the correlation of hypertension with oxidative stress biomarkers is not thoroughly consistent. Some reports indicate that the levels of ROS, malondialdehyde (MDA) or thiobarbituric acid reactive substances (TBARS) and 8-isoprostane do enhance in hypertensive patients compared with normotensives [24–26], while some reports display that the levels of urinary isoprostanes and plasma F_2-isoprostanes do not increase in hypertensives [27,28]. Therefore, some researchers surmise that oxidative stress, as indicated by lipid peroxidation products, may not be involved in the pathogenesis of human essential hypertension, at least in the early stages [28].

For these reasons, we test a hypothesis that the enhancement of oxidative stress is a direct risk factor for the pathogenesis of human pre-hypertension and hypertension under controlling for the potential effects of covariates, including age, gender and lifestyle factors. As a result, the blood pressure and oxidative stress, indicated by the levels of RCS in plasma, were measured from the volunteers and the questionnaire and physical examination were administered to know and suspect risk factors for pre-hypertension and/or hypertension.

Materials and methods

Chemicals

The chemicals 1,1,3,3-tetramethoxypropane and thiobarbituric acid (TBA) were purchased from Sigma-Aldrich (St. Louis, MO). Other chemicals (analytical grade) were from Sangon Biotech Co. Ltd., (Shanghai, China). Water was produced using a Milli-Q Plus purification system (Millipore, Bedford, MA).

Participants and questionnaire

The study was approved by the Institutional Review Board of Hunan Normal University. All study volunteers signed the informed consent forms before their inclusion in the project.

The total study subjects consisted of 1204 Chinese Han adults of both sex living in Changsha City and its surrounding areas in Central China. The basic characteristics of the participants are given in Table I.

The questionnaire included demographic information (age and gender), detailed medical history and lifestyle habits (dietary, smoking history, drinking history and physical activity).

Blood sampling

Blood samples (5 mL) were collected into vacutainer tubes containing ethylene diamine tetra-acetic acid (EDTA) from the median cubital vein on the inside of the elbow according to standard blood collection procedures [29,30] and stored at 0–4°C. All detections were carried out within 8 h of sampling.

Physical examination

Stature, body weight and body mass index (BMI) were detected by an ultrasonic body scale SK-CK (Sonka Electronic Technologies Co. Ltd., Shenzhen, China).

After the participants were at rest for 30 min, blood pressure was measured three times in sitting position, at the right arm relaxed and well supported by a table, with an angle of 45° from the trunk by an automatic electronic sphygmomanometer ken2-BPMSP-1 (Pengcheng Healthcare Products Co. Ltd., Shenzhen, China). According to the suggestion of the American Heart Association [2], subjects whose mean systolic/diastolic blood pressures were greater or equal to 140 mmHg/90 mmHg or under anti-hypertensive medication were classified as hypertensives, blood pressure within the range of 120–139 mmHg/80–89 mmHg who had never been told that they had high blood pressure were defined as pre-hypertensives and blood pressure within the range of 90–119 mmHg/60–79 mmHg were classified as normotensives.

Table I. Basic characteristics of participants.

Factor	All (n = 1204)	Normotensive (n = 526)	Pre-hypertensive (n = 444)	Hypertensive (n = 234)
Age, mean (SD), y	44.7 (14.3)	39.8 (11.7)	43.9 (13.8)	57.0 (13.4)
Gender, male, No (%)	830 (68.9)	297 (56.5)	361 (81.3)	172 (73.5)
BMI, mean (SD), kg/m^2	23.9 (3.2)	22.5 (2.9)	24.6 (3.0)	25.8 (3.1)
Blood pressure, mean (SD), mmHg				
Systolic	123.9 (15.2)	111.1 (6.8)	128.6 (6.0)	144.9 (13.7)
Diastolic	75.9 (10.9)	67.6 (5.3)	78.7 (6.2)	90.0 (10.9)
RCS, mean (SD), μmol/L	3.6 (1.0)	3.5 (1.0)	3.7 (0.9)	3.7 (1.0)
Cigarette smoking, No (%)	489 (40.6)	190 (36.1)	208 (46.8)	91 (38.9)
Current alcohol intake, No (%)	673 (55.9)	264 (50.2)	285 (64.2)	124 (53.0)
Healthy dietary habit, No (%)	645 (53.6)	291 (53.5)	237 (53.4)	117 (50.0)
Sleep quality, well, No (%)	604 (50.2)	256 (48.7)	227 (51.1)	121 (54.7)
Physical activity level, > 1 h/w, No (%)	359 (29.8)	123 (23.4)	130 (29.3)	106 (45.3)

RCS assay

A modified TBA method [31] was used to determine the concentration of RCS in plasma. The concentration of RCS was expressed as TBARS and determined by a LS-50B spectrofluorometer (Perkin-Elmer Corp., Norwalk, CT, USA). Data were presented as means.

Statistics

Results were expressed as mean ± standard deviation (SD). Statistical analysis of data was done using predictive analytics software (PASW) statistics18.0 (SPSS Inc., Chicago, IL). The outliers were expunged from the dataset based on Grubbs' test at $\alpha = 0.05$ [32]. As data showed a normal distribution, parametric statistical methods were used. For comparison of the groups, one-way analysis of variance (one-way ANOVA) was performed. To assess significant F-ratios obtained by analysis of variance, the least significant difference (LSD) post-hoc test was used. The associations between blood pressure and plasma RCS levels were analysed by Pearson partial correlation after adjusting for age and other factors. Quartiles of plasma RCS levels were created based on the distribution of RCS levels. The hypertension–, pre-hypertension–normotension differences were examined using multinomial logistic regression [33] adjusting for the potential confounding effects of age and other covariates. Other covariates that were considered as possible confounders include those that have been associated with hypertension and may also influence oxidative stress, including average physical activity levels, dietary habit, average lifetime alcohol intake, sleep quality, cigarette smoking and BMI. To examine effect modification on a multiplicative scale, the associations between hypertension and plasma RCS levels were stratified by sub-groups. To evaluate the effects of different covariates on plasma RCS levels, mean and SD were computed and independent-samples T-test was used to compare the levels of plasma RCS between sub-groups of gender, age, BMI, dietary habit, alcohol intake, cigarette smoking, sleep quality and average physical activity levels. A p-value less than 0.05 was considered statistically significant.

Results

Statistically significant corrections in systolic blood pressure or diastolic blood pressure with plasma RCS levels were observed ($p < 0.001$) (Table II), although there were some differences in the correlation coefficients between with and without adjusted for age and/or other covariates (Table II). The trend of pre-hypertensive risk was positively associated with increasing quartile of plasma RCS levels (multivariate-adjusted OR = 1.26, 95% CI = 0.86–1.84; OR = 1.75, 95% CI = 1.19–2.56; OR = 1.59, 95% CI = 1.08–2.34, for the 2nd, 3rd and 4th quartile vs the lowest quartile, respectively, p for trend = 0.019) and so do as the trend of hypertensive risk (multivariate-adjusted OR = 1.16, 95% CI = 0.68–1.99; OR = 2.14, 95% CI = 1.27–3.61; OR = 2.30, 95% CI = 1.37–3.84, for the 2nd, 3rd and 4th quartile vs the lowest quartile, respectively, p for trend < 0.001) (Table III). With or without adjusting for age, BMI, gender, dietary habit, alcohol intake, cigarette smoking, sleep quality and average physical activity levels results did not substantially change (Table III).

Table II. Pearson correlation coefficient between blood pressure and plasma RCS levels.

		RCS	RCS*	RCS**
BP	r	0.157	0.191	0.169
	p-value	0.000	0.000	0.000
	df	1191	1188	1181
DBP	r	0.178	0.197	0.176
	p-value	0.000	0.000	0.000
	df	1191	1188	1181

SBP, systolic blood pressure; DBP, diastolic blood pressure; RCS: Reactive carbonyl species.
*Adjusted for age.
**Adjusted for gender, age, BMI, dietary habit, alcohol intake, cigarette smoking, sleep quality, average physical activity levels, BMI.

Table III. The OR and adjusted OR for hypertension and pre-hypertension associated with plasma RCS levels.

	RCS (μmol/L)	OR (95% CI)	OR* (95% CI)	OR** (95% CI)
Pre-hypertension	< 3.04	1.00	1.00	1.00
	3.04–3.62	1.33 (0.93–1.90)	1.41 (0.98–2.03)	1.26 (0.86–1.84)
	> 3.62–4.23	1.75 (1.22–2.52)	1.93 (1.33–2.79)	1.75 (1.19–2.56)
	> 4.23	1.76 (1.22–2.54)	1.88 (1.30–2.73)	1.59 (1.08–2.34)
		$p = 0.003$	$p = 0.001$	$p = 0.019$
Hypertension	< 3.04	1.00	1.00	1.00
	3.04–3.62	0.91 (0.58–1.43)	1.29 (0.78–2.15)	1.16 (0.68–1.99)
	> 3.62–4.23	1.46 (0.95–2.26)	2.19 (1.33–3.60)	2.14 (1.27–3.61)
	> 4.23	1.75 (1.14–2.70)	2.44 (1.49–3.98)	2.30 (1.37–3.84)
		$p = 0.010$	$p = 0.000$	$p = 0.000$
	N$	526/444/234	526/444/234	526/444/234

*Adjusted for age.
**Adjusted for gender, age, BMI, dietary habit, alcohol intake, cigarette smoking, sleep quality, average physical activity levels.
OR: odds ratio; CI: confidence interval; N$ = normatensive/pre-hypertensive/hypertensive.

Tables IV and V show hypertension risk and pre-hypertension risk associated with plasma RCS levels stratified by different covariates, respectively. All values were adjusted for gender, age, BMI, dietary habit, alcohol intake, cigarette smoking, sleep quality and average physical activity levels. As for the ratio (N$) of hypertensives/normotensives or pre-hypertensives/normotensives, the trend across sub-groups was similar, there was an obvious risk increase in the sub-groups of male, age ≥ 50 years, BMI ≥ 25, unhealthy dietary habit, current alcohol intake, cigarette smoking, sleep not too well and higher physical activity levels as compared to the corresponding sub-group, respectively (Tables IV and V). As for the adjusted OR of hypertensive or pre-hypertensive risk across sub-group, significant hypertension risk increase only occurred in the sub-groups of female (4^{th} quartile vs lowest quartile OR = 2.78, 95% CI = 0.94–8.26), age ≥ 50 years (4^{th} quartile vs lowest quartile OR = 2.36, 95% CI = 1.07–5.20), overweight (4^{th} quartile vs lowest quartile OR = 2.19, 95% CI = 0.92–5.24), healthy dietary habit (4^{th} quartile vs lowest quartile OR = 2.83, 95% CI = 1.33-6.02), with lifetime cigarette smoking (4^{th} quartile vs lowest quartile OR = 3.22, 95% CI = 1.36–7.66) and higher physical activity levels (4^{th} quartile vs lowest quartile OR = 3.79, 95% CI = 1.64–8.77) (Table IV), while more evident pre-hypertensive risk just took place in the sub-groups of age ≥ 50 years (4^{th} quartile vs lowest quartile OR = 2.33, 95% CI = 1.06–5.15) and unhealthy dietary habit (4^{th} quartile vs lowest quartile OR = 2.44, 95% CI = 1.14–5.20) (Table V). Similarly, as for the adjusted OR of hypertensive or pre-hypertensive risk by quartile of plasma RCS levels, the overall trend was the risk of developing pre-hypertension and hypertension enhanced along with the increase of plasma RCS levels.

Table IV. Hypertensive risk associated with plasma RCS levels stratified by gender, age, BMI, dietary habit, alcohol intake, cigarette smoking, sleep quality and average physical activity levels.

				OR* (95% CI)			
	Factor	Sub-group	N$	< 3.04	3.04–3.62	> 3.62–4.23	> 4.23
Hypertension	Gender	male	172/297	1.00	1.16 (0.63–2.14)	1.84 (0.99–3.41)	1.96 (1.08–3.55)
		female	62/229	1.00	1.38 (0.41–4.60)	3.08 (1.05–9.02)	2.78 (0.94–8.26)
	Age (years)	< 50	65/429	1.00	0.97 (0.43–2.20)	1.82 (0.84–3.94)	2.00 (0.94–4.26)
		≥ 50	169/97	1.00	1.21 (0.55–2.64)	2.60 (1.17–5.77)	2.36 (1.07–5.20)
	BMI (kg/m^2)	< 25	92/430	1.00	1.06 (0.50–2.64)	1.89 (0.93–3.87)	1.66 (0.80–3.46)
		≥ 25	128/95	1.00	1.08 (0.44–2.69)	1.82 (0.74–4.44)	2.19 (0.92–5.24)
	Dietary habit	healthy diet	117/291	1.00	2.13 (0.99–4.59)	4.07 (1.89–8.79)	2.83 (1.33–6.02)
		unhealthy diet	97/152	1.00	0.49 (0.18–1.33)	0.61 (0.25–1.49)	1.45 (0.60–3.51)
	Alcohol intake	no	73/172	1.00	1.31 (0.45–3.82)	2.64 (0.92–7.55)	2.43 (0.95–6.23)
		yes	124/264	1.00	1.11 (0.53–2.31)	1.91 (0.95–3.87)	2.29 (1.14–4.61)
	Cigarette smoking	no	110/254	1.00	0.76 (0.31–1.84)	1.24 (0.55–2.80)	1.84 (0.82–4.14)
		yes	91/190	1.00	1.94 (0.81–4.66)	3.63 (1.51–8.73)	3.22 (1.36–7.66)
	Sleep quality	well	121/256	1.00	1.05 (0.48–2.29)	1.72 (0.82–3.65)	2.31 (1.10–4.83)
		not too well	94/194	1.00	1.10 (0.45–2.71)	2.00 (0.82–4.87)	2.03 (0.89–4.65)
	Physical activity level	≤ 1 h/w	103/321	1.00	0.66 (0.29–1.52)	1.38 (0.65–2.95)	1.13 (0.52–2.48)
		> 1 h/w	106/123	1.00	1.65 (0.66–4.10)	3.13 (1.25–7.85)	3.79 (1.64–8.77)

*Adjusted for gender, age, BMI, dietary habit, alcohol intake, cigarette smoking, sleep quality, average physical activity levels.
OR: odds ratio; CI: confidence interval; N$ = hypertensives/normotensives.

Table V. Pre-hypertension risk associated with plasma RCS levels stratified by gender, age, BMI, dietary habit, alcohol intake, cigarette smoking, sleep quality and average physical activity levels.

				OR* (95% CI)			
	Factor	Sub-group	N$	< 3.04	3.04–3.62	> 3.62–4.23	> 4.23
Prehypertension	Gender	male	361/297	1.00	1.28 (0.82–1.99)	1.62 (1.03–2.55)	1.50 (0.96–2.36)
		female	83/229	1.00	1.24 (0.57–2.68)	1.92 (0.91–4.03)	1.47 (0.65–3.30)
	Age (years)	< 50	308/429	1.00	1.23 (0.79–1.91)	1.49 (0.96–2.34)	1.33 (0.84–2.10)
		≥ 50	136/97	1.00	1.44 (0.67–3.07)	2.56 (1.16–5.67)	2.33 (1.06–5.15)
	BMI (kg/m^2)	< 25	250/430	1.00	1.22 (0.77–1.94)	1.78 (1.11–2.85)	1.53 (0.95–2.47)
		≥ 25	194/95	1.00	1.25 (0.59–2.62)	1.39 (0.66–2.93)	1.50 (0.70–3.18)
	Dietary habit	healthy diet	237/291	1.00	1.14 (0.69–1.89)	1.99 (1.17–3.38)	1.36 (0.81–2.28)
		unhealthy diet	155/152	1.00	1.62 (0.77–3.40)	1.60 (0.78–3.30)	2.44 (1.14–5.20)
	Alcohol intake	no	92/172	1.00	0.61 (0.25–1.44)	2.48 (1.13–5.45)	1.70 (0.80–3.60)
		yes	285/264	1.00	1.48 (0.90–2.43)	1.65 (1.00–2.73)	1.63 (0.97–2.73)
	Cigarette smoking	no	174/254	1.00	1.15 (0.62–2.13)	1.87 (1.03–3.41)	1.79 (0.97–3.31)
		yes	208/190	1.00	1.22 (0.68–2.20)	1.38 (0.75–2.56)	1.47 (0.81–2.69)
	Sleep quality	well	227/256	1.00	1.25 (0.72–2.18)	1.84 (1.06–3.18)	1.64 (0.93–2.88)
		not too well	163/194	1.00	1.22 (0.66–2.27)	1.40 (0.72–2.71)	1.63 (0.87–3.04)
	Physical activity level	≤ 1 h/w	258/321	1.00	1.22 (0.72–2.07)	1.37 (0.81–2.32)	1.51 (0.89–2.58)
		> 1 h/w	130/123	1.00	1.10 (0.55–2.23)	2.33 (1.10–4.99)	1.40 (0.69–2.83)

*Adjusted for gender, age, BMI, dietary habit, alcohol intake, cigarette smoking, sleep quality, average physical activity levels.
OR: odds ratio; CI: confidence interval; N$ = pre-hypertensives/normotensives.

To evaluate the effects of different covariates on oxidative stress biomarkers, the plasma RCS levels were compared within sub-groups of gender, age, BMI, dietary habit, alcohol intake, cigarette smoking, sleep quality and average physical activity levels. The increased trend of plasma RCS levels was obvious for overweight or unhealthy lifestyles, while only gender ($p = 0.002$), BMI ($p < 0.001$) and cigarette smoking ($p = 0.002$) resulted in statistically significant changes (Table VI).

Discussion

Plasma MDA levels are widely used as biomarkers of oxidative stress owing to the characteristics of being relative stable and easy to be detected [34,35]. As the TBA method is not specific for MDA [36], the TBARS levels rather than MDA levels have been suggested as an index of lipid peroxidation in some studies [37]. However, based on the chemical mechanism of TBA reaction, we believe that the RCS levels may serve as a more precise term.

The primary finding from this study is a significantly positive relation between the plasma RCS levels and change in blood pressures (Table II). Multivariate-adjusted OR illustrated that, compared with the lowest quartile of plasma RCS level, the highest quartile subjects had a 59% and 130% increased risk for developing pre-hypertension and hypertension, respectively (Table III). This finding seems logical and is in agreement with most results from hypertensive studies, but is not the results from isoprostanes which show that lipid peroxidation is not increased in hypertension [27,28], especially in the early stages of hypertension [28]. The discrepancy might be explained by several possibilities. First, the normotensive and pre-hypertensive were lumped into one category and the sample numbers were relatively small in the early studies [27,28]. Secondly, different methods used for the assessment of oxidative stress might have some influences. Finally, the underlying relationships between pre-hypertension or hypertension and RCS levels were overlooked by the relatively simple statistical methods used. As illustrated in Table I, there was no strong association between pre-hypertension or hypertension and RCS levels just from the mean ± SD of RCS levels. However, the data (Table I)

Table VI. Mean ± SD of plasma RCS levels within strata of gender, age, BMI, dietary habit, alcohol intake, cigarette smoking, sleep quality and average physical activity levels.

Factor	Sub-group	*n*	RCS (mean ± SD)	*p*-value*
Gender	male	830	3.71 ± 0.96	
	female	374	3.52 ± 0.96	0.002
Age (years)	< 50	802	3.66 ± 0.91	
	≥ 50	402	3.62 ± 1.06	0.519
BMI (kg/m^2)	< 25	772	3.58 ± 0.97	
	≥ 25	417	3.81 ± 0.94	0.000
Dietary habit	healthy	645	3.63 ± 0.94	
	unhealthy	404	3.73 ± 0.99	0.104
Alcohol intake	no	337	3.60 ± 1.02	
	yes	673	3.70 ± 0.92	0.130
Cigarette smoking	no	538	3.57 ± 0.95	
	yes	489	3.76 ± 0.96	0.002
Sleep quality	well	604	3.68 ± 0.92	
	not too well	451	3.66 ± 1.01	0.741
Average physical activity levels (h/week)	≤ 1 h/w	682	3.69 ± 0.91	
	> 1 h/w	359	3.63 ± 1.05	0.415

*Comparing differences between mean values by sub-group.

only indicated that higher blood pressure did not necessarily lead to dramatic increase of RCS levels, but did not prove that higher RCS levels had nothing to do with the risk of hypertension or pre-hypertension and further multinomial logistic regression had proven that higher RCS levels were hazardous risk for pre-hypertension or hypertension (Table III).

It has been reported that the increase in risk of developing higher blood pressure may be associated with many factors, including sedentary lifestyle [6], overweight or obesity [7,38], alcohol intake [11] and even ageing [39]. Inconsistent with these previous results, we found that overweight and unhealthy lifestyles (unhealthy dietary habit, alcohol intake and cigarette smoking) showed a similar increase in trend for pre-hypertensive risk (Table V), hypertensive risk (Table IV) and plasma RCS levels (Table VI). Together with the multivariate-adjusted OR of Table III, it is reasonable to consider that the underlying mechanism of the risk increase by overweight and unhealthy lifestyles may, at least in part, be through oxidative stress.

As for the gender difference, the risk of hypertension or pre-hypertension was significantly higher in males than in females. We thought that it might result from the higher levels of alcohol intake and cigarette smoking in men compared with women or result from the effects of oestrogen.

In summary, the most striking finding of our study is that higher levels of plasma RCS are not the necessary consequence of pre-hypertension or hypertension, but markers of risk factors for developing pre-hypertension or hypertension in Chinese Han adults.

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Declaration of interest

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