Significantly Increased Visceral Adiposity Index in Prehypertension

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Abstract

Background

The prevalence of prehypertension has increased in China, and prehypertension frequently progress to hypertension over a short time period; both have become public health problems. Therefore, this study was conducted to determine the relationship between the Visceral Adiposity Index (VAI) and blood pressure (BP) in China.

Methods

A cross-sectional epidemiological survey was conducted in China using a stratified random cluster sampling method. Sex-specific VAI quartile cut-off points were used as follows: 0.88, 1.41, 2.45 in males and 0.85, 1.33, 2.22 in females. Prehypertension and hypertension were each defined according to The Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) guidelines. A multivariate logistic analysis was conducted to analyze the relationship among VAI, prehypertension and hypertension.

Results

The ORs for prehypertension and hypertension in the upper quartiles of the VAI were 1.514 (1.074-2.133), P=0.018 and 1.660 (1.084-2.542), P=0.020, in males, after adjusting for age, education, smoking habits, alcohol consumption, physical activity, serum creatinine, fasting glucose, and plasma insulin. Following further adjustments for the above confounders, chronic kidney disease, and diabetes, the ORs for prehypertension and hypertension in the upper quartile of the VAI were 1.660 1.533 (1.086-2.165), P=0.015, and 1.743 (1.133-2.680), P=0.011, in males. The ORs for prehypertension and hypertension in the upper quartile of the VAI were 1.691 (1.223-2.338), P=0.001, and 1.682 (1.162-2.435), P=0.006, in females, after adjusting for age, education, smoking habits, alcohol consumption, physical activity, serum creatinine, fasting glucose, and plasma insulin. Following further adjustments for the above confounders, chronic kidney disease, and diabetes, the ORs for prehypertension and
hypertension in the upper quartile of the VAI were 1.688 (1.220-2.334), P=0.002, and 1.657 (1.141-2.406), P=0.008, in females.

Conclusions
A higher VAI was positively associated with both prehypertension and hypertension in both males and females. It is both essential and urgent that clinicians take steps to control and prevent visceral adiposity.

Introduction
Many studies have shown that visceral fat dysfunction has a close relationship with cardiovascular disease as a result of increased adipokine production, proinflammatory activity, and decreased insulin sensitivity [1–3]. Waist circumference (WC) has been used to assess visceral adiposity; however, this parameter alone does not help in distinguishing between subcutaneous and visceral fat masses [4]. Therefore, the Visceral Adiposity Index (VAI), which is based on WC, body mass index (BMI), triacylglycerols (TG), and high density lipoprotein cholesterol (HDL-C) and was recently introduced by the AlkaMeSy Study Group [5], was used as a marker of both visceral fat dysfunction and an individual’s subsequent cardiometabolic risk.

Over the past several decades, various studies have indicated that hypertension represents a major health threat, as affected individuals carry an increased risk of cardiovascular disease, stroke, renal failure, and vision loss [6–10], and hypertension has become an important public-health problem worldwide [11]. Prehypertension frequently progresses to hypertension within a period of 4 years, particularly in older adults, as observed in an American population by the Framingham Heart Study [12], and in a Western European population by the Flemish Study on Environment, Genes and Health Outcomes [13]. Prehypertension is also associated with an increased risk of cardiovascular disease, with a risk-factor-adjusted hazard ratio of 2.5 in women and 1.6 in men, compared with individuals with optimal blood pressures [14].

However, only limited numbers of studies have examined the relationship between VAI and blood pressure (BP), therefore, we conducted an epidemiological survey to determine the relationship among VAI, prehypertension and hypertension in China.

Methods
Ethics Statement
Each of the participants provided written informed consent prior to data collection. Illiterate participants were read information about the study and provided a thumb impression. The Human Ethics Committee of The People’s Hospital of Zhengzhou, Affiliated with Southern Medical University, Zhengzhou, China, approved the study.

Participants
A community-based survey was conducted in Zhengzhou from October 2011 to October 2012 to investigate the prevalence of prehypertension. Participants were selected using a stratified random cluster sampling method. Three districts were first selected randomly; three additional communities were subsequently selected randomly from each district. Finally, each of the residents who had lived in Zhengzhou for at least 5 years and was a member of one of the chosen communities was selected and invited to participate our survey. A total of 4065 participants...
were selected from a pool of 4800 citizens who completed the entire survey, a response rate of 84.6%.

**Questionnaire**

All clinical doctors, technicians, medical students and nurses who participated in the project received intensive training regarding proper screening methods. All participants were asked to complete the questionnaire under the guidance of a well-trained investigator. The questionnaire consisted of questions regarding age, sex, a personal history of diabetes (yes vs. no), a personal history of hypertension (yes vs. no), a personal history of cardiovascular disease (yes vs. no), education (>10 years vs. 6–10 years vs. 1–5 years vs. no), >10 years equal to above high school in China, smoking habits (yes[current] vs. yes[former] vs. no), alcohol intake (yes[current] vs. yes[former] vs. no), and physical activity (>60 min/day vs. 30–60 min/day vs. <30 min/day vs. no), >60 min/day and 30–60 min/day were considered as active physical activity, and <30 min/day and no were considered as inactive physical activity; WC, height and BP were each measured manually. Prior to BP measurements, participants were seated quietly for 5 to 10 minutes in a chair with arm supported at heart level and the rotator cuff positioned 3 cm above the antecubital fossa, BP was measured using Omron (SEM 1 Model) automatic BP monitor (Omron Healthcare Co., Ltd., IL, USA) with an appropriate cuff size, and the same cuff was used for a participant’s subsequent visits [15, 16]. Study visits were approximately at the same time of day. Average BP was then calculated from three measurements. BMIs were calculated using the following equation: BMI = weight (kg)/height (m²). Previously diagnosed disease was determined based on a positive answer to the following question: “Has a doctor ever told you that you have hypertension?” Two-level variants of education status (above high school vs. below high school), physical activity (active physical activity vs. inactive physical activity), smoking (current smoking vs. non current smoking) and alcohol (current alcohol vs. non current alcohol) were analyzed.

**Blood and urine sample collection**

Appointments were scheduled for both urine and blood collection. Participants were asked to provide a sample of their first morning urine, as well as a midstream urine sample; no protease inhibitor was used. Menstrual periods were avoided among female participants. Fasting venous blood draws were performed either at local community clinics or at health stations. All urine and blood samples were sent to the central laboratory of The People’s Hospital of Zhengzhou, Affiliated with Southern Medical University. The blood and urine samples were either disposed of within 3 hours or stored at 4°C for as long as two days. The central laboratory successfully completed a standardization and certification program.

**Blood and urine measurements**

FPG (fasting plasma glucose, FPG) testing was performed, and fasting plasma insulin concentrations were measured via an electrochemical luminescence immunoassay. Serum total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triacylglycerols (TG), and low-density lipoprotein cholesterol (LDL-C) were each measured using an autoanalyzer (Toshiba, Japan). Serum creatinine (Scr) was measured using overnight fasting venous blood samples, via Jaffe’s kinetic method. Albuminuria was measured using immunoturbidimetric tests.
Evaluation criteria

VAI, a sex-specific index based on WC, BMI, TG and HDLC, was calculated as follows [5]:

Males : VAI = \( \frac{WC}{39.68 + (1.88 \times BMI)} \) \times \( \frac{TG}{1.03} \) \times \( \frac{1.31}{HDL} \)

Females : VAI = \( \frac{WC}{39.58 + (1.89 \times BMI)} \) \times \( \frac{TG}{0.81} \) \times \( \frac{1.52}{HDL} \)

The classifications of normotension, prehypertension and hypertension were each based on the classifications of BP as determined by the JNC-7 [17]. Normotension was defined as not requiring antihypertensive medication, and as having a systolic blood pressure (SBP) < 120 mm Hg and a diastolic blood pressure (DBP) < 80 mm Hg. Prehypertension was defined as not requiring antihypertensive medication, and as having an SBP of 120–139 mm Hg or a DBP of 80–89 mm Hg. Hypertension was defined as an SBP ≥ 140 mm Hg or a DBP ≥ 90 mm Hg, as well as the requirement of an antihypertensive medication. A family history of hypertension was defined as the diagnosis of hypertension in at least one parent.

The urinary albumin to creatinine ratio (ACR; mg/g creatinine) was calculated, and an ACR greater than 30 mg/g was defined as albuminuria. An eGFR (estimated glomerular filtration rate, eGFR) was calculated according to the equation developed by the Modification of Diet in Renal Disease (MDRD) Study [18, 19]. Reduced renal function was defined as an eGFR less than 60 ml/min/1.73 m². Chronic kidney disease (CKD) was defined as either reduced renal function or as albuminuria, according to KIDIGO [20]. The diagnosis of diabetes mellitus (DM) was based on the following criteria developed by the American Diabetes Association: an A1C ≥ 6.5%, an FPG ≥ 126 mg/dL or a 2-h plasma glucose level ≥ 200 mg/dL during an OGTT [21].

Statistical analysis

Acquired data were analyzed using SPSS 13.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were represented as means ± SDs, and categorical variables were represented as proportions of each subgroup.

Each of the participants was placed into one of the following two groups: men and women; each participant was subsequently placed into one of the following three subgroups: normotension, prehypertension and hypertension. The basic characteristics of the four VAI quartiles were examined in both the male and the female groups. Continuous variables were analyzed via one-way ANOVA, and categorical variables were analyzed via the Chi-square test or the Fisher’s exact test.

Logistic regression models were used to determine whether VAI is associated with both prehypertension and hypertension in both men and women. VAI was divided into four quartiles and considered a categorical variable. Model one was adjusted for lifestyle (smoking status, alcohol consumption, physical activity, and education), VAI, serum creatinine, fasting glucose, and plasma insulin. To determine whether CKD and DM affect the relationship between VAI and BP, each parameter was included in model two. The lower quartile was used as a reference category. Logistic regression was performed separately in men and women. P values less than 0.05 were considered statistically significant.

Results

Four-thousand-sixty-five participants completed the survey, and 115 participants were excluded due to either missing blood glucose data or missing anthropometric data. The 1688 men
(42.7%) and 2262 women (57.3%) were of Han Ethnic. The mean age of the subjects who participated in this study was 44.8 ± 13.0 years.

The basic characteristics of the male and female participants

As shown in Table 1, there were significant differences in smoking habits, alcohol consumption, physical activity, WC, BMI, DBP, serum glucose, plasma insulin, TG, HDLC, TC, and LDLC in males, as the upper VAI quartile participants exhibited higher DBP, serum glucose, plasma insulin, TG, TC, and LDLC, and lower HDLC, prevalence of smoking, and prevalence of alcohol consumption, compared with the lower VAI subjects, among the males enrolled in this study.

As shown in Table 2, there were significant differences in age, education, physical activity, prehypertension, hypertension, DM, WC, BMI, SBP, DBP, Scr, serum glucose, plasma insulin, TG, TC, and LDLC in females; the upper VAI quartile participants exhibited higher ages, prevalence of prehypertension, prevalence of hypertension, DM, SBP, DBP, Scr, serum glucose, plasma insulin, TG, TC, and LDLC, and lower HDLC and physical activity levels, compared with the lower VAI quartile subjects, among females.

Table 1. The basic characteristics of the male participants.

|                      | 1<sup>st</sup> Quartile (n = 422) | 2<sup>nd</sup> Quartile (n = 422) | 3<sup>rd</sup> Quartile (n = 422) | 4<sup>th</sup> Quartile (n = 422) | P       |
|----------------------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|---------|
| Age (years)          | 42.8±14.9                         | 43.6±13.7                        | 44.3±13.0                        | 44.3±11.9                        | 0.329   |
| Education status (>high school) (%) | 176(41.7)                         | 153(36.3)                        | 138(32.7)                        | 163(38.6)                        | 0.050   |
| Current Smoking (%)  | 277(65.6)                         | 264(62.6)                        | 242(57.3)                        | 216(51.2)                        | P<0.001 |
| Current Alcohol (%)  | 285(67.5)                         | 268(63.5)                        | 247(58.5)                        | 215(50.9)                        | P<0.001 |
| Inactive Physical Activity (%) | 134(31.8)                         | 143(33.9)                        | 157(37.2)                        | 174(41.2)                        | P<0.05  |
| Prehypertension (%)  | 143(33.9)                         | 147(34.8)                        | 146(34.6)                        | 175(41.5)                        | 0.076   |
| Hypertension (%)     | 89(21.1)                          | 113(26.8)                        | 100(23.7)                        | 118(28.0)                        | 0.089   |
| Chronic Kidney Disease (%) | 58(13.7)                          | 56(13.3)                         | 62(14.7)                         | 64(15.2)                         | 0.855   |
| Diabetes Mellitus (%)| 20(4.7)                           | 18(4.3)                          | 18(4.3)                          | 27(6.4)                          | 0.428   |
| Waist Circumference (cm) | 80.2±8.9                          | 84.3±8.3                         | 86.2±7.4                         | 89.6±7.7                         | P<0.001 |
| Body Mass Index (kg/m<sup>2</sup>) | 23.9±2.9                          | 23.6±2.4                         | 23.7±3.0                         | 24.8±2.8                         | P<0.001 |
| Systolic Blood Pressure (mmHg) | 121±19                            | 122±19                           | 122±18                           | 123±17                           | 0.167   |
| Diastolic Blood Pressure (mmHg) | 74±11                             | 76±11                            | 76±10                            | 78±10                            | P<0.001 |
| Serum Creatinine (μmol/L) | 80.9±48.8                         | 78.7±23.2                        | 78.2±19.4                        | 83.3±76.7                        | 0.386   |
| Serum glucose (mmol/L)  | 4.9±1.0                           | 5.0±1.1                          | 5.0±1.2                          | 5.4±1.9                          | P<0.001 |
| Plasma insulin (μU/mL) | 5.0±5.0                           | 5.8±5.5                          | 6.1±5.3                          | 7.6±6.3                          | P<0.001 |
| Total Cholesterol (mmol/L) | 4.5±0.9                           | 4.8±0.9                          | 4.9±1.0                          | 5.3±1.1                          | P<0.001 |
| High-Density Lipoprotein Cholesterol (mmol/L) | 1.7±0.5                           | 1.4±0.3                          | 1.2±0.3                          | 1.1±0.3                          | P<0.001 |
| Triacylglycerols (mmol/L) | 0.8±0.3                           | 1.2±0.3                          | 1.7±0.5                          | 3.7±2.2                          | P<0.001 |
| Low-Density Lipoprotein Cholesterol (mmol/L) | 2.4±0.8                           | 2.8±0.9                          | 2.9±0.8                          | 2.5±1.1                          | P<0.001 |

Means ± SDs represented the continuous variables, and proportions represented the categorical variables.

1<sup>st</sup> quartile of VAI: 0–0.88; 2<sup>nd</sup> quartile of VAI: 0.89–1.41; 3<sup>rd</sup> quartile of VAI: 1.42–2.45; 4<sup>th</sup> quartile of VAI: ≥2.46.

Continuous variables were analyzed via One-way ANOVA, categorical variables were analyzed via the Chi-square test or Fisher’s exact test, and P value less than 0.05 was considered statistical significant.

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The relationship between VAI and blood pressure in males and females

As shown in Table 3, the VAI was significantly associated with both prehypertension and hypertension in males, after adjusting for age, education, smoking habits, alcohol consumption, physical activity, serum creatinine, fasting glucose, and plasma insulin; the ORs for

| Table 2. The basic characteristics of the female participants. |
|---------------------------------------------------------------|
| VAI (female) | 1st Quartile (n = 565) | 2nd Quartile (n = 566) | 3rd Quartile (n = 566) | 4th Quartile (n = 565) | P |
|---------------------------------------------------------------|
| Age (years) | 40.8±11.8 | 43.2±12.5 | 48.0±12.3 | 50.7±11.5 | P<0.001 |
| Education status (≥ high school) (%) | 278(49.2) | 289(51.1) | 362(64.0) | 388(68.7) | P<0.001 |
| Current Smoking (%) | 71(12.6) | 73(12.9) | 76(13.4) | 80(14.2) | 0.870 |
| Current Alcohol (%) | 64(11.3) | 67(11.8) | 72(12.7) | 83(14.7) | 0.339 |
| Inactive Physical Activity (%) | 209(37.0) | 190(33.6) | 166(29.3) | 154(27.3) | P<0.05 |
| Prehypertension (%) | 113(20.0) | 144(25.4) | 167(29.5) | 168(29.7) | P<0.001 |
| Hypertension (%) | 80(14.2) | 99(17.5) | 148(26.1) | 203(35.9) | P<0.05 |
| Chronic Kidney Disease (%) | 93(16.5) | 89(15.7) | 86(15.2) | 84(14.9) | 0.891 |
| Diabetes Mellitus (%) | 20(3.5) | 33(5.8) | 39(6.9) | 84(14.9) | P<0.001 |
| Waist Circumference (cm) | 73.1±8.5 | 76.0±8.93 | 78.4±8.9 | 82.8±8.6 | P<0.001 |
| Body Mass Index (kg/m²) | 67.4±21.1 | 69.3±46.8 | 73.4±37.3 | 79.8±63.6 | P<0.001 |
| Systolic Blood Pressure (mmHg) | 4.6±1.0 | 4.7±1.0 | 5.1±1.1 | 5.4±1.2 | P<0.001 |
| Triacylglycerols (mmol/L) | 0.6±0.2 | 1.0±0.3 | 1.3±0.4 | 2.6±1.5 | P<0.001 |
| Low-Density Lipoprotein Cholesterol (mmol/L) | 2.3±0.9 | 2.5±0.8 | 2.8±0.8 | 2.8±1.0 | P<0.001 |

Means ± SDs represented the continuous variables, and proportions represented the categorical variables.

1st quartile of VAI: 0–0.85; 2nd quartile of VAI: 0.86–1.33; 3rd quartile of VAI: 1.34–2.22; 4th quartile of VAI: ≥2.23.

Continuous variables were analyzed via One-way ANOVA, categorical variables were analyzed via the Chi-square test or Fisher’s exact test, and P value less than 0.05 was considered statistical significant.

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The relationship between VAI and blood pressure levels in males.

As shown in Table 3, the VAI was significantly associated with both prehypertension and hypertension in males, after adjusting for age, education, smoking habits, alcohol consumption, physical activity, serum creatinine, fasting glucose, and plasma insulin; the ORs for

| Table 3. The relationship between visceral adiposity index and blood pressure levels in males. |
|---------------------------------------------------------------|
| VAI | Prehypertension (Male) | Hypertension (Male) |
|---------------------------------------------------------------|
| | Model one a | Model two b | Model one a | Model two b |
|---------------------------------------------------------------|
| 1st Quartile Reference | Reference | 1.130(0.815–1.568) | 0.464 | 1.134(0.816–1.576) | 0.453 | 1.046(0.688–1.589) | 0.835 | 1.069(0.701–1.630) | 0.758 |
| 2nd Quartile | 0.964(0.695–1.337) | 0.825 | 0.975(0.702–1.353) | 0.878 | 1.489(0.983–2.256) | 0.060 | 1.542(1.015–2.343) | 0.042 |
| 3rd Quartile | 1.151(1.074–2.133) | 0.018 | 1.533(1.086–2.165) | 0.015 | 1.660(1.084–2.542) | 0.020 | 1.743(1.133–2.680) | 0.011 |
| 4th Quartile | Reference | Reference | Reference | Reference |

a Adjusted for age, education, smoking habits, alcohol consumption, physical activity, serum creatinine, fasting glucose, and plasma insulin;

b Adjusted for the above + CKD and DM.

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prehypertension and hypertension in the upper quartile of the VAI were 1.514 (95% CI 1.074–2.133), P = 0.018, and 1.533 (95% CI 1.086–2.165), P = 0.015, in males. Following further adjustments for the above confounders, CKD, and DM, the ORs for prehypertension and hypertension in the upper quartile of the VAI were 1.660 (95% CI 1.084–2.542), P = 0.020, and 1.743 (95% CI 1.133–2.680), P = 0.011, in males.

As shown in Table 4, VAI was significantly associated with both prehypertension and hypertension in females following adjustments for age, education, smoking habits, alcohol consumption, physical activity, serum creatinine, fasting glucose, and plasma insulin; the ORs for prehypertension and hypertension in the upper quartile of the VAI were 1.691 (95% CI 1.223–2.338), P = 0.001, and 1.688 (95% CI 1.220–2.334), P = 0.002, in females. Following further adjustments for the above confounders, CKD, and DM, the ORs for prehypertension and hypertension in the upper quartile of the VAI were 1.682 (95% CI 1.162–2.435), P = 0.006, and 1.657 (95% CI 1.141–2.406), P = 0.008, in females.

### Discussion

Our research revealed that there was a significant relationship between the VAI and blood pressure in both men and women, a relationship independent of age, smoking habits, alcohol consumption, physical activity, education, Scr, serum glucose, plasma insulin, CKD and DM. Furthermore, the risk of prehypertension was higher in the upper quartile of the VAI compared with the lower quartile; the ORs were 1.533 (95% CI 1.086–2.165), P = 0.015, in males, and 1.688 (95% CI 1.220–2.334), P = 0.002, in females. Our pilot study also performed a multivariate logistic regression using VAI values as continuous variables, the result showed that VAI score was an independent risk factor of prehypertension, the ORs were 0.747 (95% CI 2.583–0.957), P = 0.021, in prehypertension, and 0.561 (95% CI 0.418–0.752), P = 0.000, in hypertension, in males; the ORs were 1.185 (95% CI 1.024–1.371), P = 0.023, in prehypertension, and 1.239 (95% CI 1.059–1.450), P = 0.008, in hypertension, in females. Our result was consistent with reports which revealed that VAI has significant correlation with hypertension [21, 22], and showed good predictive power regarding hypertension [23], however our current study revealed that VAI was also a good predictor regarding prehypertension.

There were reverse association between prevalence of current smoking as well as current alcohol consumption and VAI in males, and positive association between prevalence of inactive physical activity as well as chronic disease (CKD, DM and Hypertension) and VAI in males, according to Table 1, maybe it reflect the possible transition to healthy lifestyle in individuals who already have faced some chronic disease manifestations, however the underlying mechanism still need to be revealed in the future study. Generally speaking, well-educated middle
aged individuals involve in more social activities such as business dinner or banquet, consuming more high calorie and high fat foods, and have no time to participate in outdoor activities, this may help to explain the reason why well-educated ladies have less physical activities according to Table 2. However, there was no directly evidence of reverse association between well-educated individuals and inactive physical activity, since it was not the same in males. Age, as well as serum creatinine, have positive correlation with VAI in females. Maybe the possible reason is that there were sizeable number of postmenopause women included in the upper quartile VAI of females. It’s a well known fact that age is closely related with serum creatinine. However, the relationship between serum creatinine and VAI need to be revealed in the future study.

The VAI is a sex-specific scoring system based on WC, BMI, TG and HDLC and is capable of providing information regarding visceral adipose tissue function and insulin sensitivity; it has recently been suggested as a surrogate of visceral adiposity. However, there is no ideal cut-off point at which to diagnose visceral adiposity. Another researcher used VAI tertiles (mild visceral adipose dysfunction, moderate visceral adipose dysfunction, and severe visceral adipose dysfunction) to determine an appropriate stratified cut-off point [24]. We used quartiles to both evaluate visceral adipose dysfunction and undertake a detailed analysis of the relationship between VAI and blood pressure. We also found that the 3rd quartile of the VAI correlated positively with prehypertension in both model one and model two among women; the ORs were 1.517 (95% CI 1.114–2.066), P = 0.008, and 1.516 (95% CI 1.113–2.064), P = 0.008; the 3rd quartile of the VAI correlated positively with hypertension in model two among men; the OR was 1.542 (95% CI 1.015–2.343), P = 0.042. However, the upper quartile of the VAI correlated positively with both prehypertension and hypertension in both model one and model two. Therefore, the upper quartile of the VAI may be used as a criterion with which to evaluate visceral adipose dysfunction.

Visceral adiposity is almost well-validated for prediction of metabolic syndrome [25–29], however sparse data about VAI and metabolic syndrome reported. Therefore, a multivariate logistic regression was also performed in order to check the relationship between VAI and metabolic syndrome. According to the diagnostic criteria of metabolic syndrome recommended by American Heart Association 2009, elevated blood pressure was defined as systolic ≥130 and/or diastolic ≥85 mm Hg, or antihypertensive drug treatment in a patient with a history of hypertension [30]. Our results revealed that VAI score was independent risk factor of metabolic syndrome, the ORs were 6.279 (95%CI 2.813–14.018), P = 0.000, in males, and 1.854 (95%CI 1.314–2.663), P = 0.001, in females; if VAI values were used as continuous variables, the ORs were 1.771 (95CI 1.177–2.663), P = 0.006, in males, and 1.073 (95%CI 1.016–1.134), P = 0.011, in females. VAI, WC, and waist-height ratio (WHtR) were the best predictors of the individual components of the metabolic syndrome among Peruvian adults [31], more and more studies come to an agreement that VAI was a good marker of metabolic syndrome [32, 33].

VAI has a strong independent association with cardiovascular, OR = 2.45, 95%CI 1.52–3.95 [5]. VAI scores significantly increased in metabolically healthy obese individuals than metabolically healthy normal-weight individuals, and was an nontraditional risk factor of CVD [34]. VAI increase cardiometabolic risk in type 2 diabetes, and was significantly decreased after 12 month’s intervention with medicine [35]. VAI is predictive for cardiovascular events in prevalent hemodialysis patients [36] and polycystic ovary syndrome [21]. Increased adipokine production and proinflammatory activity caused by VAI, may served as accumulating evidence for identifying inflammation as a potential mechanism linking adipose tissue and cardiometabolic risk [37].

The VAI was significantly increased in prehypertension in our study, a scenario associated with an increased risk of CVD. Therefore, our study based on a cross-sectional epidemiological
survey, maybe suitable for managing risk factors of prehypertension, and prevent the progression of normalcy and prehypertension to hypertension.

**Limitations**

The VAI was established in Caucasian populations [5], its suitability for other populations needs to be further investigated, and each population and ethnic group should have their own VAI constants. However, one cross-sectional study have already validated its suitability in Chinese human [38], and our research revealed that the VAI correlates positively with BP. But there still remains much to develop a well-designed study to determine the mechanism underlying this relationship.

**Conclusions**

VAI was associated with blood pressure and significantly increased in prehypertension.

**Author Contributions**

Conceived and designed the experiments: QQ. Performed the experiments: QQ YD DG YZ WH HL. Analyzed the data: QQ YD DG YZ WH HL. Contributed reagents/materials/analysis tools: WH HL. Wrote the paper: YD DG. Performed statistical analysis: YZ. Read and approved the final manuscript: QQ YD DG YZ WH HL.

**References**

1. Despres JP, Lemieux I. Abdominal obesity and metabolic syndrome. Nature. 2006; 444(7121):881–7. Epub 2006/12/15. doi:10.1038/nature05488 PMID: 17167477.
2. DeNino WF, Tchernof A, Dionne IJ, Toth MJ, Ades PA, Sites CK, et al. Contribution of abdominal adiposity to age-related differences in insulin sensitivity and plasma lipids in healthy nonobese women. Diabetes care. 2001; 24(5):925–32. Epub 2001/05/12. PMID: 11347756.
3. Bruunsgaard H, Pedersen BK. Age-related inflammatory cytokines and disease. Immunology and allergy clinics of North America. 2003; 23(1):15–39. Epub 2003/03/21. PMID: 12645876.
4. Pouliot MC, Despres JP, Lemieux S, Moorjani S, Bouchard C, Tremblay A, et al. Waist circumference and abdominal sagittal diameter: best simple anthropometric indexes of abdominal visceral adipose tissue accumulation and related cardiovascular risk in men and women. The American journal of cardiology. 1994; 73(7):460–8. Epub 1994/03/01. PMID: 8141087.
5. Amato MC, Giordano C, Galia M, Criscimanna A, Vitabile S, Midiri M, et al. Visceral Adiposity Index: a reliable indicator of visceral fat function associated with cardiometabolic risk. Diabetes care. 2010; 33(4):920–2. Epub 2010/01/14. doi: 10.2337/dc09-1825 PMID: 20067971; PubMed Central PMCID: PMC2845052.
6. Chong EW, Lamoureux EL, Jenkins MA, Aung T, Saw SM, Wong TY. Sociodemographic, lifestyle, and medical risk factors for visual impairment in an urban asian population: the singapore malay eye study. Archives of ophthalmology. 2009; 127(12):1640–7. Epub 2009/12/17. doi: 10.1001/archophthalmol.2009.298 PMID: 2008720.
7. Lawes CM, Vander Hoorn S, Rodgers A. Global burden of blood-pressure-related disease, 2001. Lancet. 2008; 371(9623):1513–8. Epub 2008/05/06. doi: 10.1016/S0140-6736(08)60655-8 PMID: 18456100.
8. Mannisto T, Mendola P, Vaarasmaki M, Jarvelin MR, Hartikainen AL, Pouta A, et al. Elevated blood pressure in pregnancy and subsequent chronic disease risk. Circulation. 2013; 127(6):681–90. Epub 2013/02/13. doi: 10.1161/CIRCULATIONAHA.112.128751 PMID: 23401113.
9. Zoccali C, Mallamaci F, Tripepi G. Hypertension as a cardiovascular risk factor in end-stage renal failure. Current hypertension reports. 2002; 4(5):381–6. Epub 2002/09/10. PMID: 12217257.
10. Kim MJ, Lim NK, Park HY. Relationship between prehypertension and chronic kidney disease in middle-aged people in Korea: the Korean genome and epidemiology study. BMC public health. 2012; 12:960. Epub 2012/11/10. doi: 10.1186/1471-2458-12-960 PMID: 23137348; PubMed Central PMCID: PMC3549294.
11. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. Lancet. 2005; 365(9455):217–23. Epub 2005/01/18. doi: 10.1016/S0140-6736(05)17741-1 PMID: 15652604.

12. Vasan RS, Larson MG, Leip EP, Kannel WB, Levy D. Assessment of frequency of progression to hypertension in non-hypertensive participants in the Framingham Heart Study: a cohort study. Lancet. 2001; 358(9294):1682–6. Epub 2001/12/01. doi: 10.1016/S0140-6736(01)06710-1 PMID: 11728544.

13. Zhang H, Thijs L, Kuznetsova T, Fagard RH, Li X, Staessen JA. Progression to hypertension in the non-hypertensive participants in the Flemish Study on Environment, Genes and Health Outcomes. Journal of hypertension. 2006; 24(9):1719–27. Epub 2006/08/18. doi: 10.1097/01.hjh.0000242395.07473.92 PMID: 16915020.

14. Vasan RS, Larson MG, Leip EP, Evans JC, O’Donnell CJ, Kannel WB, et al. Impact of high-normal blood pressure on the risk of cardiovascular disease. The New England journal of medicine. 2001; 345(18):1291–7. Epub 2002/01/17. doi: 10.1056/NEJMoa003417 PMID: 11794147.

15. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics. 2004; 114(2 Suppl 4th Report):555–76. Epub 2004/08/03. PMID: 15286277.

16. Pickering TG, Hall JE, Appel LJ, Falkner BE, Graves JH, Hill MN, et al. Recommendations for blood pressure measurement in humans and experimental animals: Part 1: blood pressure measurement in humans: a statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. Hypertension. 2005; 45(1):142–61. Epub 2004/12/22. doi: 10.1161/01.HYP.0000150859.47929.8e PMID: 15611362.

17. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003; 42(6):1206–52. Epub 2003/12/06. doi: 10.1111/j.1525-152X.2003.00655.x PMID: 14656957.

18. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med. 1999; 130(6):461–70. Epub 1999/03/13. doi: 199903160-00002 [pii]. PMID: 10075613.

19. Eknoyan G, Levin N. NKF-K/DOQI Clinical Practice Guidelines: Update 2000. Foreword. Am J Kidney Dis. 2001; 37(1 Suppl 1):S5–6. Epub 2001/03/07. PMID: 11229966.

20. Eknoyan G, Laneire N, Barsoum R, Eckardt KJ, Levin A, Levin N, et al. The burden of kidney disease: improving global outcomes. Kidney Int. 2004; 66(4):1310–4. Epub 2004/10/02. doi: 10.1111/j.1523-1755.2004.00894.x KID894 [pii]. PMID: 15458424.

21. Amato MC, Verghi M, Galluzzo A, Giordano C. The oligomenorrhoic phenotypes of polycystic ovary syndrome are characterized by a high visceral adiposity index: a likely condition of cardiometabolic risk. Human reproduction (Oxford, England). 2011; 26(6):1486–94. Epub 2011/03/31. doi: 10.1093/humrep/der088 PMID: 21447694.

22. Chen C, Xu Y, Guo ZR, Yang J, Wu M, Hu XS. The application of visceral adiposity index in identifying type 2 diabetes risks based on a prospective cohort in China. Lipids in health and disease. 2011; 10:183. Epub 2011/10/21. doi:10.1186/1476-511x-10-183 PMID: 21447694.

23. Stepien M, Stepien A, Banach M, Wałęz RN, Paradowski M, Rizzo M, et al. New obesity indices and adipokines in normotensive patients and patients with hypertension: comparative pilot analysis. Angiology. 2014; 65(4):333–42. Epub 2013/05/03. doi: 10.1177/0003319713485807 PMID: 23636856.

24. Amato MC, Giordano C, Pitrone M, Galluzzo A. Cut-off points of the visceral adiposity index (VAI) identifying a visceral adipose dysfunction associated with cardiometabolic risk in a Caucasian Sicilian population. Lipids in health and disease. 2011; 10:183. Epub 2011/10/21. doi: 10.1186/1476-511x-10-183 PMID: 22011564; PubMed Central PMCID: PMC3224548.

25. Pickhardt PJ, Jee Y, O’Connor SD, del Rio AM. Visceral adiposity and hepatic steatosis at abdominal CT: association with the metabolic syndrome. AJR American journal of roentgenology. 2012; 199(5):1100–7. Epub 2012/04/25. doi: 10.2214/ajr.11.7361 PMID: 22528899.

26. Kishida K, Funahashi T, Matsuzawa Y, Shimomura I. Visceral adiposity as a target for the management of the metabolic syndrome. Annals of medicine. 2012; 44(3):233–41. Epub 2011/05/27. doi: 10.3109/07853890.2011.564202 PMID: 21612331.

27. Pierdomenico SD, Pierdomenico AM, Neri M, Cucurullo F. Epicardial adipose tissue and metabolic syndrome in hypertensive patients with normal body weight and waist circumference. American journal of hypertension. 2011; 24(11):1245–9. Epub 2011/08/05. doi: 10.1038/ajh.2011.134 PMID: 21814292.
28. Demerath EW, Reed D, Rogers N, Sun SS, Lee M, Choh AC, et al. Visceral adiposity and its anatomical distribution as predictors of the metabolic syndrome and cardiometabolic risk factor levels. The American journal of clinical nutrition. 2008; 88(5):1263–71. Epub 2008/11/11. PMID: 18996861; PubMed Central PMCID: PMC2801427.

29. Moller DE, Kaufman KD. Metabolic syndrome: a clinical and molecular perspective. Annual review of medicine. 2005; 56:45–62. Epub 2005/01/22. doi:10.1146/annurev.med.56.082103.104751 PMID: 15660501.

30. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation. 2009; 120(16):1640–5. Epub 2009/10/07. doi: 10.1161/CIRCULATIONAHA.109.192644 PMID: 19805654.

31. Knowles KM, Paiva LL, Sanchez SE, Revilla L, Lopez T, Yasuda MB, et al. Waist Circumference, Body Mass Index, and Other Measures of Adiposity in Predicting Cardiovascular Disease Risk Factors among Peruvian Adults. International journal of hypertension. 2011; 2011:931402. Epub 2011/02/19. doi: 10.4061/2011/931402 PMID: 21331161; PubMed Central PMCID: PMC3034939.

32. Elisha B, Messier V, Karelis A, Codere L, Bernard S, Prud'homme D, et al. The Visceral Adiposity Index: Relationship with cardiometabolic risk factors in obese and overweight postmenopausal women—A MONET group study. Applied physiology, nutrition, and metabolism = Physiologie appliquée, nutrition et métabolisme. 2013; 38(8):892–9. Epub 2013/07/17. doi: 10.1139/apnm-2012-0307 PMID: 23855278.

33. Mazzuca E, Battaglia S, Marrone O, Marotta AM, Castrogiovanni A, Esquinas C, et al. Gender-specific anthropometric markers of adiposity, metabolic syndrome and visceral adiposity index (VAI) in patients with obstructive sleep apnea. Journal of sleep research. 2014; 23(1):13–21. Epub 2013/10/15. doi: 10.1111/jsr.12088 PMID: 24118617.

34. Du T, Zhang J, Yuan G, Zhang M, Zhou X, Liu Z, et al. Nontraditional risk factors for cardiovascular disease and visceral adiposity index among different body size phenotypes. Nutrition, metabolism, and cardiovascular diseases: NMCD. 2014. Epub 2014/08/28. doi: 10.1016/j.numecd.2014.07.006 PMID: 25159728.

35. Russo GT, Labate AM, Giandalia A, Romeo EL, Villari P, Alibrandi A, et al. Twelve-month treatment with Liraglutide ameliorates Visceral Adiposity Index and common cardiovascular risk factors in type 2 diabetes outpatients. Journal of endocrinological investigation. 2014. Epub 2014/09/01. doi: 10.1007/s40618-014-0163-9 PMID: 25173876.

36. Chen HY, Chiu YL, Chuang YF, Hsu SP, Pai MF, Yang JY, et al. Visceral adiposity index and risks of cardiovascular events and mortality in prevalent hemodialysis patients. Cardiovascular diabetology. 2014; 13(1):136. Epub 2014/10/05. doi: 10.1186/s12933-014-0136-5 PMID: 25280960; PubMed Central PMCID: PMC4189758.

37. Hotamisligil GS. Inflammation and metabolic disorders. Nature. 2006; 444(7121):860–7. Epub 2006/12/15. doi: 10.1038/nature05485 PMID: 17167474.

38. Yang F, Wang G, Wang Z, Sun M, Cao M, Zhu Z, et al. Visceral adiposity index may be a surrogate marker for the assessment of the effects of obesity on arterial stiffness. PloS one. 2014; 9(8):e104365. Epub 2014/08/12. doi: 10.1371/journal.pone.0104365 PMID: 25105797; PubMed Central PMCID: PMC4126713.