European Review for Medical and Pharmacological Sciences 2023; 27: 188-198

Relationship between body mass index and pulse pressure in a non-diabetic population: evidence from a multicenter, cross-sectional study

Y.-Y. WANG[1], S. YANG[2], S.-W. CHEN[1]

[1]Department of Cardiovascular Medicine, The Third Hospital of Nanchang, Jiangxi, China
[2]Department of Geriatrics, Zaozhuang Mental Health Center, Shandong, China

Abstract. – OBJECTIVE: Growing evidence shows that pulse pressure (PP) is a strong risk factor for cardiovascular disease and is closely associated with cardiovascular events, strokes, and mortality. However, currently, data on the relationship between body mass index (BMI) and PP are still limited.

SUBJECTS AND METHODS: Here, a cross-sectional study was conducted based on 211,809 non-diabetic adults in 11 cities in China from 2010 to 2016. Raw data were obtained from a public database (www.datadryad.org). According to the BMI level, they are classified into "underweight", "normal", "overweight", and "obesity" groups. Two groups of continuous variables were measured by the Mann-Whitney test, while the differences between multiple groups were tested by Kruskal-Wallis' One-Way ANOVA and Dunn's test. Besides, multiple linear regression analyses were performed to assess the linear relationship between BMI and PP. In addition, multivariate logistic regression was carried out to further confirm the relationship between different BMI levels and the prevalence of high PP.

RESULTS: In the total population, BMI was linearly positively related to PP regardless of gender and age, but it was not observed in the elevated blood pressure group. Multiple linear regression analysis showed that after fully adjusting for the maximum covariates, compared to the normal group, PP in the overall population decreased by 2.19 mmHg in the underweight group and increased by 1.426 and 2.919 mmHg in the overweight and obese groups, respectively. Similar results were observed in men, women, age <60 years, and normotensive groups. However, there was no significantly linear relationship between BMI and PP at the age of ≥60 years and elevated blood pressure groups. Besides, from multiple logistic regression analysis, the similar results were obtained, with no obvious association between BMI and high PP prevalence in those aged ≥60 years or with elevated blood pressure.

CONCLUSIONS: PP increased with rising BMI in the overall population. However, stratified analysis demonstrated no significant association between BMI and PP in individuals aged over 60 years or with elevated blood pressure.

Key Words:
Body mass index, Blood pressure, Pulse pressure, Cross-sectional study.

Introduction

Obesity, which plays a critical role in causing disability and serious health care costs, is widely considered to be the greatest public health challenge in the 21st century[1]. Several large observational studies[2-4] have previously demonstrated that there is a positive relationship between body mass index (BMI) and blood pressure levels, while Mendelian randomization studies[5,6] have further reinforced their causal relationship.

Hypertension is related to adverse cardiovascular outcomes and is manifested primarily as a chronic, multifactorial, asymptomatic and usually incurable disease[5]. Long-term poor control of blood pressure causes severe changes in multiple organs, including the heart, blood vessels, kidneys, eyes, and the brain, thereby increasing the risk of health complications[5]. Fortunately, BMI is an important variable determinant of blood pressure levels, and weight interventions would have a positive effect on the maintenance of normal blood pressure level[6,7].

It has been reported[8,9] that the pulsatile component of blood pressure captures cardiac risk better than the steady component. The former is usually measured as pulse pressure (PP), and according to the Windkessel model of arterial blood pressure, PP can be considered simply as a reflection of stroke volume and arterial wall compliance[10].

Corresponding Author: Siwei Chen, MD; e-mail: chen08030322@163.com

However, in actual clinical practice, most physicians take blood pressure control at desired levels as the primary goal, and PP is often treated secondarily or even ignored. A growing number of studies[11-13] have shown that PP is a strong risk factor for cardiovascular disease and is closely related to cardiovascular events, strokes, and mortality. Whereas, as data on the relationship between body mass index and PP are still limited currently, the purpose of this paper is to assess their relationship.

Subjects and Methods

Study Design and Data Extraction

This is a cross-sectional study, and a secondary analysis on the study by Chen et al[14]. The raw data were downloaded from a public database (www.datadryad.org). Specifically, 211,833 non-diabetic adults from 32 health screening centers in 11 cities (Shanghai, Beijing, Suzhou, Wuhan, Changzhou, Shenzhen, Nanjing, Guangzhou, Hefei, Nantong, and Chengdu) of China are involved in. At their first health screening center visit, a detailed questionnaire including demographics, lifestyle and family history of chronic disease was completed. Then, fasting venous blood was collected after a fast of at least 10 hours. Apart from that, lipid profiles, fasting plasma glucose (FPG), blood urea nitrogen (BUN), serum creatinine (Scr), aspartate, aminotransferase (AST), and alanine aminotransferase (ALT) were measured directly using a uniform automated analyzer (Beckman 5800, Brea, CA, USA). While height, weight and blood pressure were measured by trained staff, when the former two were measured the nearest to 0.1 cm and 0.1 kg, respectively.

In addition, the original study[14] was approved by the Rich Healthcare Group Review Board. As the study was observational, along with the retrieval of information being retrospective, and the data being anonymous and never violating the rights of the participants, the Rich Healthcare Group Review Board gave up the requirement for informed consent[15]. Beyond that, this study complies with the Declaration of Helsinki.

Study Population

Since this paper is a secondary analysis of the data provided by Chen Y et al[14], the inclusion criteria were consistent with that of the original study. To be specific, 211,833 non-diabetic adults aged between 20-99 years with at least two visits between 2010 and 2016 and with complete information on height, weight and FPG were selected. On this basis, an additional 24 participants were excluded from further analysis due to the absence of recorded systolic or diastolic blood pressure values, resulting in a total of 211,809 participants included in this study. The specific flow chart is shown in Figure 1.

Exposure of Interest and Outcome Measures

The exposure of interest was BMI, obtained by dividing weight (kg) by the square of height (m^2). According to the current Chinese BMI classification criteria, BMI fell into four categories. "<18.5 kg/m^2" is underweight; "18.5-23.99 kg/m^2" is normal weight; "24-27.99 kg/m^2" is overweight, and "≥ 28 kg/m^2" is obesity[16].

The study outcome was PP. All participants' blood pressure was obtained by trained staff using a standard mercury sphygmomanometer in a quiet environment. Then, PP was acquired by subtracting diastolic blood pressure (DBP) from systolic blood pressure (SBP). "High PP" was defined a >60 mmHg[17]. In addition, participants were classified into "normal blood pressure" and "elevated blood pressure" groups according to their baseline blood pressure levels. Here, it should be noted that the "normal blood pressure" was defined as SBP <140 mmHg and DBP <90 mmHg, while the "elevated blood pressure" was defined as SBP ≥ 140 mmHg or DBP ≥ 90 mmHg[18].

Statistical Analysis

All continuous variables were skewed and expressed as median (interquartile range, IQR), whereas categorical variables were denoted as percentages. In addition, two groups of continuous variables were analyzed using the Mann-Whitney test, and multiple comparisons were performed by conducting Kruskal-Wallis' One-Way ANOVA and Dunn's test. Other than that, categorical variables were assessed by the Chi-square test. In addition, multiple linear regression models were adopted to analyze the relationship between BMI levels and PP, and the results were expressed as β and standard error (SE). Meanwhile, the multivariate logistic regression model was used to analyze the relationship between BMI levels and the prevalence of high PP, and the results were indicated as odds ratios (ORs) with their corresponding 95% confidence intervals (CIs). All variables adjusted in the regression model include

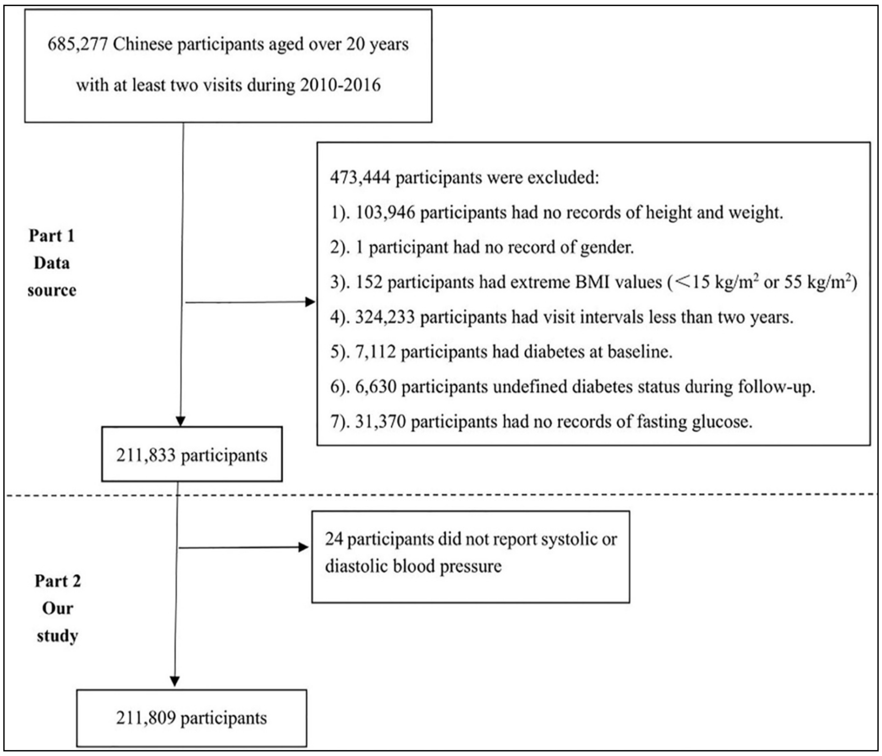

Figure 1. The flowchart of study. The first part is the flowchart of the original study, and the second part is the flowchart of the current study.

age, gender, BMI, ALT (U/L), AST (U/L), BUN, Scr (μmol/L), total cholesterol (TC) (mmol/l), triglycerides (TG) (mmol/l), low-density lipoprotein cholesterol (LDL-c) (mmol/l), high-density lipoprotein cholesterol (HDL-c) (mmol/l), smoking status (current smoker or not), drinking status (current drinker or not), and family history of diabetes (Yes or No).

Furthermore, all regression analyses were assessed stratified by gender (male and female), age (<60 years and ≥60 years), and blood pressure level (normal blood pressure and elevated blood pressure). Apart from that, the test for trend was performed with a polynomial contrast procedure. All statistical analyses were made using SPSS 26.0 (IBM Corp., Armonk, NY, USA) and GraphPad 9.0 (La Jolla, CA, USA). Besides, two-tailed *p*-values lower than 0.05 showed statistical differences.

Results

Table I displays the demographic data and baseline characteristics of the 211,809 participants, respectively. The total population was classified into four groups according to BMI: "underweight", "normal", "overweight" and "obesity", and their baseline characteristics were statistically different. Besides, the age of the overweight group was higher than that of the other groups, with a median age of 45 (IQR: 36-56) years. Moreover, in the underweight group, the largest proportion of women was 71.6% and had higher levels of HDL-c, while other characteristics were more obvious in the obesity group.

Relationship Between BMI and PP Stratified by Gender, Age, and Blood Pressure Levels

As shown in Table II, at the same BMI level, PP was higher in men than in women except for the obesity group (p <0.05); participants aged ≥60 years had higher PP than those aged <60 years (p <0.001); participants with high blood pressure had higher PP than those with normal blood pressure (p <0.001). Meanwhile, there was a trend of increasing PP as BMI level increased (p <0.001).

In the overall population, the increase in PP with increasing BMI showed a linear relationship, as displayed in Figure 2. Similarly, a linear relationship between BMI and PP was observed in

Table I. Baseline information of the overall population according to BMI levels

	Underweight (n=12,081)	Normal (n=116,802)	Overweight (n=64,762)	Obesity (n=18,164)	*p*
Age (years)	33 (30-40)	39 (33-50)	45 (36-56)	43 (35-55)	<0.001
Female (%)	8,652 (71.6)	64,067 (54.9)	18,607 (28.7)	4,371 (24.1)	<0.001
Current smoker (%)	352 (2.91)	5,138 (4.4)	4,959 (7.7)	1,625 (8.9)	<0.001
Current drinker (%)	23 (0.19)	528 (0.45)	587 (0.91)	213 (1.2)	<0.001
Family history of diabetes (%)	188 (1.56)	2,463 (2.1)	1,284 (1.98)	408 (2.2)	<0.001
SBP (mmHg)	108 (100-118)	114 (105-125)	123 (113-134)	129 (119-140)	<0.001
DBP (mmHg)	69 (63-75)	71 (65-78)	77 (70-84)	81 (73-88)	<0.001
PP (mmHg)	40 (33-46)	43 (36-50)	45 (38-53)	48 (40-56)	<0.001
FPG (mmol/L)	4.77 (4.44-5.10)	4.91 (4.57-5.26)	5.09 (4.71-5.48)	5.18 (4.8-5.61)	<0.001
ALT (U/L)	12.6 (10-16.15)	15.9 (12.0-22.0)	23 (16.3-33.85)	30.7 (20.9-47)	<0.001
AST (U/L)	19.8 (17-23)	21 (18-25)	23.8 (20-28.7)	26.0 (21.3-33.0)	<0.001
BUN (mmol/L)	4.23 (3.55-5.03)	4.47 (3.75-5.28)	4.74 (4.02-5.56)	4.8 (4.06-5.62)	<0.001
Scr (μmol/L)	61 (53.6-72)	68 (57.1-80.2)	76.6 (65-86)	77 (65.8-87)	<0.001
TC (mmol/L)	4.40 (3.90-4.97)	4.60 (4.07-5.20)	4.86 (4.29-5.48)	4.92 (4.36-5.55)	<0.001
TG (mmol/L)	0.72 (0.57-0.97)	0.93 (0.69-1.34)	1.40 (1.0-2.08)	1.70 (1.20-2.42)	<0.001
LDL (mmol/L)	2.44 (2.11-2.87)	2.63 (2.24-3.07)	2.81 (2.39-3.27)	2.86 (2.44-3.32)	<0.001
HDL-c (mmol/L)	1.51 (1.30-1.72)	1.38 (1.21-1.59)	1.29 (1.12-1.48)	1.25 (1.08-1.44)	<0.001

SBP, systolic blood pressure. DBP, diastolic blood pressure. PP, pulse pressure. FPG, fasting plasma glucose. TG, triglycerides. TC, total cholesterol. HDL-c, high-density lipoprotein cholesterol. LDL, low-density lipoprotein cholesterol. Scr, Serum creatinine. BUN, blood urea nitrogen. ALT, alanine aminotransferase. AST, aspartate aminotransferase. BMI, Body mass index.

the men, women, age ≥60 years, age <60 years, and normal blood pressure groups, as shown in Figure 3. However, in the elevated blood pressure group, PP was obviously higher in the normal BMI group than in other groups (p <0.05).

Multiple Linear Regression Models to Analyze the Association Between BMI and PP

Table III presents the results of the multiple linear regression analysis on the association between BMI and PP. Besides, stratified analyses of the overall population were made by gender, age, and blood pressure level. In a crude model of the overall population, PP was decreased by 3.165 mmHg in the underweight group and increased by 2.95 and 5.172 mmHg in the overweight and obesity groups, respectively, when compared to that of the normal group. Moreover, similar results persisted regardless of age and gender. However, in the elevated blood pressure group, PP was decreased by 4.257 mmHg, 0.831 mmHg, and

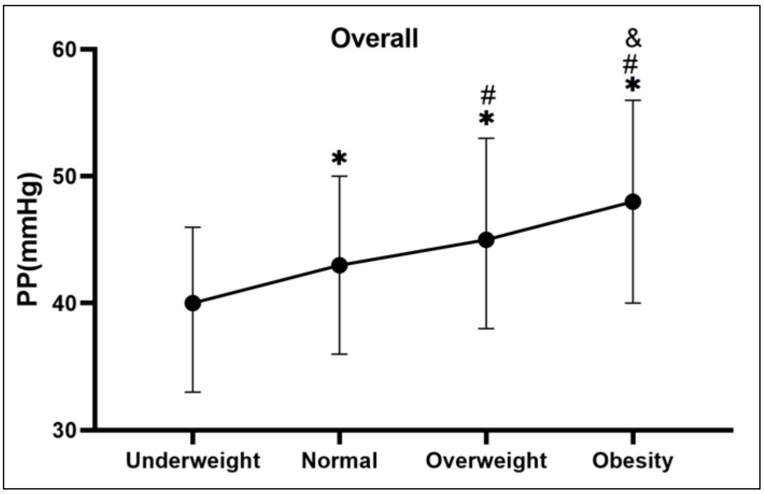

Figure 2. Between-group differences in PP at different BMI levels in the overall population. *indicates normal, overweight and obesity compared with underweight group with p <0.05. #indicates overweight and obesity compared with normal group with p <0.05. &indicates obesity compared with overweight group p <0.05.

Table II. Relationship between BMI and pulse pressure stratified by sex, age, and blood pressure levels.

	Gender			Age			Blood Pressure Levels		
	Men	Women	*p*	<60year	≥60 years	*p*	Normal	Elevated	*p*
BMI levels									
Underweight4	3 (36-50)	38 (33-45)	<0.001	39 (33-46)	50 (40-61)	<0.001	39 (33-46)	54 (36-66)	<0.001
Normal	45 (38-52)	41 (35-48)	<0.001	42 (36-49)	51 (42-62)	< 0.001	42 (36-49)	58 (43-68)	<0.001
Overweight	46 (39-53)	45 (38-54)	0.008	44 (38-52)	53 (44-63)	<0.001	44 (38-51)	55 (43-66)	<0.001
Obesity	48 (40-56)	48 (40-58)	<0.001	47 (40-55)	55 (45-66)	<0.001	46 (39-52)	55 (43-66)	<0.001
***p* for trend**	**<0.001**	**<0.001**		**<0.001**	**<0.001**		**<0.001**	**<0.001**	

SBP, systolic blood pressure. DBP, diastolic blood pressure. PP, pulse pressure. FPG, fasting plasma glucose. TG, triglycerides. TC, total cholesterol. HDL-c, high-density lipoprotein cholesterol. LDL, low-density lipoprotein cholesterol. Scr, Serum creatinine. BUN, blood urea nitrogen. ALT, alanine aminotransferase. AST, aspartate aminotransferase. BMI, Body mass index.

Table III. Multiple linear regression models to analyze the association between BMI and pulse pressure.

	Univariate Linear Regression analysis			Multivariate Linear Regression analysis		
	ß	SE	*p*	ß	SE	*p*
Overall						
Normal	0 (Ref)			0 (Ref)		
Underweight	-3.165	0.110	<0.001	-2.190	0.474	<0.001
Overweight	2.950	0.056	<0.001	1.426	0.231	<0.001
Obesity	5.172	0.092	<0.001	2.919	0.367	<0.001
Men						
Normal	0 (Ref)			0 (Ref)		
Underweight	-2.283	0.203	<0.001	-2.416	0.759	<0.001
Overweight	1.062	0.073	<0.001	1.221	0.271	<0.001
Obesity	2.971	0.110	<0.001	2.586	0.415	<0.001
Female						
Normal	0 (Ref)			0 (Ref)		
Underweight	-2.755	0.130	<0.001	-1.087	0.594	0.067
Overweight	4.687	0.094	<0.001	1.590	0.445	<0.001
Obesity	7.969	0.177	<0.001	4.187	0.811	<0.001
Age <60years						
Normal	0 (Ref)			0 (Ref)		
Underweight	-2.747	0.102	<0.001	-2.553	0.463	<0.001
Overweight	2.439	0.055	<0.001	1.413	0.234	<0.001
Obesity	4.786	0.090	<0.001	2.932	0.373	<0.001
Age ≥60years						
Normal	0 (Ref)			0 (Ref)		
Underweight	-1.514	0.658	0.021	1.519	2.744	0.580
Overweight	1.602	0.209	<0.001	1.124	0.849	0.186
Obesity	3.667	0.326	<0.001	2.679	1.303	0.040
Normal blood pressure						
Normal	0 (Ref)			0 (Ref)		
Underweight	-2.430	0.093	<0.001	-2.149	0.427	<0.001
Overweight	1.929	0.051	<0.001	1.121	0.220	<0.001
Obesity	3.387	0.091	<0.001	1.937	0.374	<0.001
Elevated blood pressure						
Normal	0 (Ref)			0 (Ref)		
Underweight	-4.257	0.802	<0.001	-6.681	3.246	0.04
Overweight	-0.831	0.220	<0.001	-0.934	0.867	0.282
Obesity	-1.291	0.271	<0.001	-0.465	1.082	0.668

Multivariate linear regression model adjusted age, gender, BMI, ALT (U/L), AST (U/L), BUN, Scr (μmol/L), total cholesterol (mmol/l), triglycerides (mmol/l), LDL cholesterol (mmol/l), HDL cholesterol (mmol/l), smoking status (current smoker or not), drinking status (current drinker or not), family history of diabetes (Yes or No). SE, standard error. BMI, Body mass index. Crude model no variable was adjusted. Model 1 adjusted age. Model 2 plus gender, BMI, ALT (U/L), AST (U/L), BUN, Scr (μmol/L), total cholesterol (mmol/l), triglycerides (mmol/l), LDL cholesterol (mmol/l), HDL cholesterol (mmol/l), smoking status (current smoker or not), drinking status (current drinker or not), family history of diabetes (Yes or No). PP, pulse pressure. BP, blood pressure. BMI, body mass index. OR, odds ratio. CI, confidence interval.

Table IV. Multivariate logistic regression of different BMI levels with the prevalence of high PP in the overall and subgroups..

	Crude Model		Model 1		Model 2	
	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
Overall						
Normal	Ref		Ref		Ref	
Underweight	0.557 (0.511-0.607)	<0.001	0.750 (0.687-0.819)	<0.001	0.666 (0.432-1.027)	0.066
Overweight	1.687 (1.636-1.740)	<0.001	1.319 (1.276-1.362)	<0.001	1.444 (1.246-1.674)	<0.001
Obesity	2.470 (2.366-2.578)	<0.001	2.050 (1.960-2.144)	<0.001	2.093 (1.704-2.571)	<0.001
Men						
Normal	Ref		Ref		Ref	
Underweight	0.715 (0.628-0.813)	<0.001	0.807 (0.708-0.919)	0.001	0.592 (0.318-1.104)	0.099
Overweight	1.223 (1.176-1.272)	<0.001	1.118 (1.074-1.164)	<0.001	1.315 (1.109-1.559)	0.002
Obesity	1.790 (1.699-1.887)	<0.001	1.719 (1.631-1.813)	<0.001	2.026 (1.607-2.554)	<0.001
Female						
Normal	Ref		Ref		Ref	
Underweight	0.539 (0.480-0.606)	<0.001	0.891 (0.788-1.007)	0.064	1.078 (0.577-2.013)	0.814
Overweight	2.577 (2.450-2.710)	<0.001	1.551 (1.468-1.638)	<0.001	1.664 (1.250-2.215)	<0.001
Obesity	3.955 (3.657-4.276)	<0.001	2.322 (2.130-2.532)	<0.001	1.991 (1.261-3.143)	0.003
Age <60years						
Normal	Ref		Ref		Ref	
Underweight	0.584 (0.528-0.646)	<0.001	0.633 (0.572-0.701)	<0.001	0.514 (0.307-0.858)	0.011
Overweight	1.619 (1.558-1.682)	<0.001	1.431 (1.375-1.490)	<0.001	1.550 (1.307-1.837)	<0.001
Obesity	2.611 (2.480-2.749)	<0.001	2.258 (2.141-2.381)	<0.001	2.350 (1.860-2.968)	<0.001
Age ≥60years						
Normal	Ref		Ref		Ref	
Underweight	0.943 (0.782-1.137)	0.537	0.718 (0.587-0.878)	0.001	0.963 (0.344-2.695)	0.942
Overweight	1.180 (1.114-1.250)	<0.001	1.306 (1.228-1.389)	<0.001	1.285 (0.930-1.774)	0.128
Obesity	1.579 (1.448-1.722)	<				
0.001	1.744 (1.590-1.912)	<0.001	1.499 (0.931-2.412)	0.096		
Normal BP						
Normal	Ref		Ref		Ref	
Underweight	0.715 (0.645-0.793)	<				
0.001	0.809 (0.729-0.898)	<0.001	0.652 (0.382-1.111)	0.115		
Overweight	1.292 (1.234-1.353)	<				
0.001	1.131 (1.078-1.186)	<0.001	1.352 (1.097-1.667)	0.005		
Obesity	1.735 (1.615-1.863)	<0.001	1.527 (1.420-1.642)	<0.001	1.665 (1.201-2.308)	0.002
Elevated BP						
Normal	Ref		Ref		Ref	
Underweight	0.785 (0.647-0.952)	0.014	0.825 (0.673-1.012)	0.065	0.727 (0.280-1.887)	0.512
Overweight	0.838 (0.795-0.883)	<0.001	0.855 (0.810-0.904)	<0.001	0.904 (0.704-1.160)	0.428
Obesity	0.754 (0.707-0.805)	<0.001	0.899 (0.840-0.963)	0.002	0.990 (0.723-1.355)	0.948

1.291 mmHg in the underweight, overweight, and obesity groups, respectively, compared to that of the normal weight group.

After fully adjusting for the maximum covariates, in the overall population, PP was reduced by 2.19 mmHg in the underweight group and increased by 1.426 and 2.919 mmHg in the overweight and obesity groups, accordingly, compared with that of the normal group. Similar results were obtained in the men, women, age <60 years and normal blood pressure groups. However, there was no significantly linear association between BMI and PP in the age ≥60 years and elevated blood pressure groups ($p > 0.05$).

Multivariate Logistic Regression Analysis of BMI and Prevalence of High PP

In the crude model, no variables were adjusted. In model 1, age was adjusted. In model 2, the maximum variables were adjusted. For example, model 1 plus sex, TC, TG, HDL-c, LDL-c, FPG, ALT, AST, BUN, Scr, smoking status, alcohol consumption status, and family history of diabetes was adjusted. The normal BMI group was considered as the reference group, as shown in Table IV.

In the overall population, as shown in the crude model, the prevalence of high PP decreased by 0.44 (OR: 0.557, 95% CI: 0.511-0.607) in the underweight group and increased 1.69-fold (OR: 1.687, 95% CI: 1.636-1.740) and 2.47-fold (OR: 2.470, 95% CI: 2.366-2.578) in the overweight and obesity groups, respectively, compared with that in the normal group. Similar results existed in other subgroups of the population. Moreover, these associations were maintained after adjusting for age in model 1. In model 2, after fully adjusting for covariates, there was still a trend towards a decrease in the prevalence of high PP in the underweight group compared to the normal group in the overall population (p =0.066). In contrast, the prevalence of high PP increased 1.44-fold (OR: 1.444, 95% CI: 1.246-1.674) and 2.09-fold (OR: 2.093, 95% CI: 1.704-2.571) in the overweight and obesity groups, separately.

Meanwhile, the prevalence of hypertension was dramatically increased in overweight and obesity

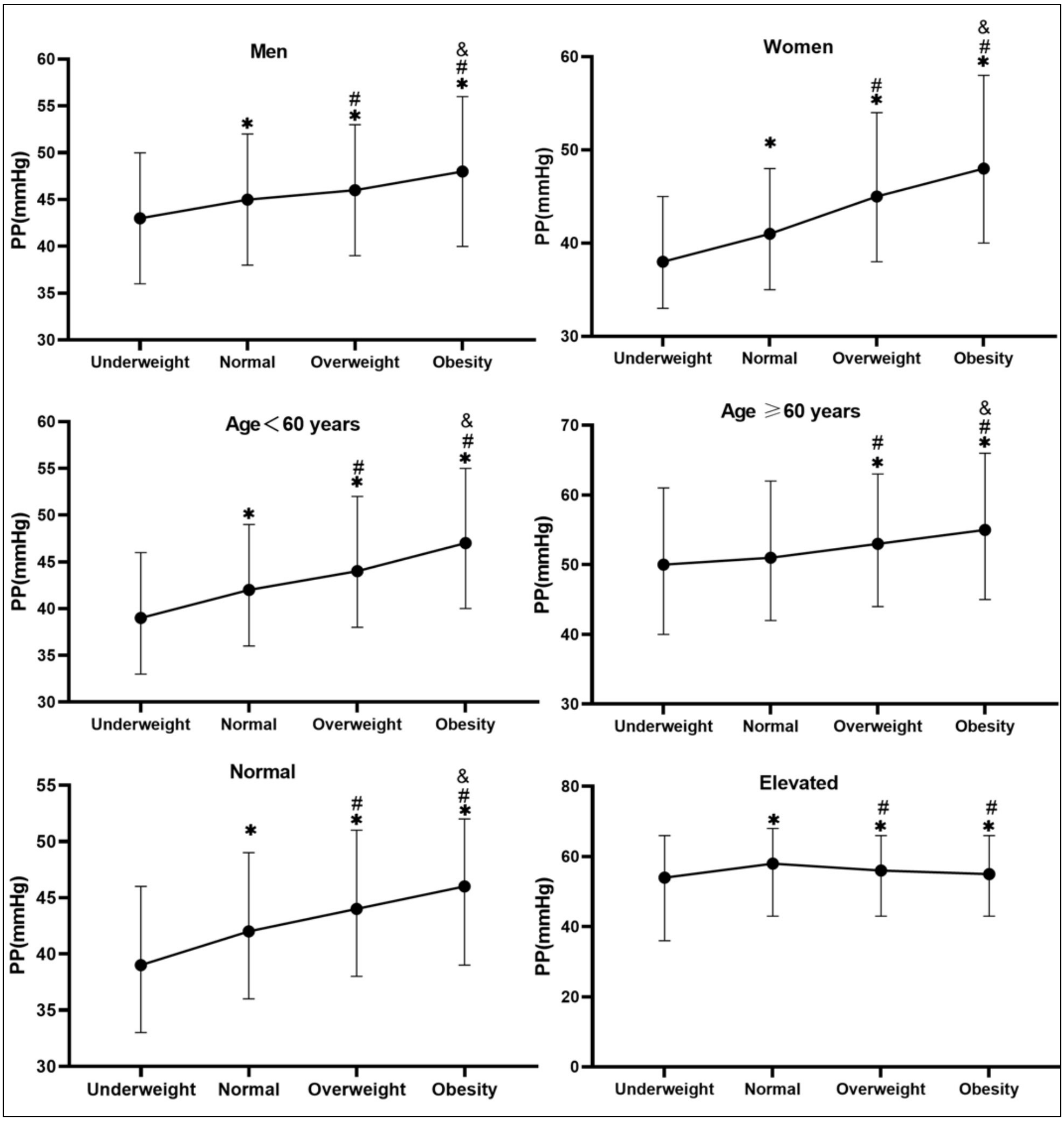

Figure 3. Between-group differences in PP at different BMI levels according to gender, age, and baseline blood pressure. *indicates normal, overweight and obesity compared with underweight group with p <0.05. #indicates overweight and obesity compared with normal group with p <0.05. &indicates obesity compared with overweight group with p <0.05.

individuals in the men, women, age <60 years and normal blood pressure groups (p <0.05). However, there were no significant differences in the prevalence of high PP between BMI levels in the age >60 years and elevated blood pressure groups (p >0.05).

Discussion

The present study is a large cross-sectional study based on a non-diabetic population in China. The main findings of this study can be summarized as follows. 1) Compared to the normal group, the underweight group was featured with lower PP, while the overweight and obesity groups had noticeably higher PP. Meanwhile, the obesity group tended to have abnormal biochemical parameters such as lipids and blood glucose, as well as unhealthy lifestyles such as smoking and alcohol consumption. 2) In the overall population, a linear positive correlation appeared between BMI and PP. Stratified analysis according to gender, age and blood pressure levels demonstrated that BMI remained linearly and positively correlated with PP in the men, women, age <60 years and normal blood pressure groups, while there was no linear association in the age >60 years and elevated blood pressure groups. 3) Similarly, in the groups of men, women, age <60 years and normal blood pressure, the prevalence of high PP was obviously higher in the overweight and obese groups than that in the normal group, whereas that did not differ to a great extent between BMI levels in the age >60 years or elevated blood pressure groups.

Hypertension is one of the most common risk factors for cardiovascular disease, and widely exists in the obese population[19]. BMI is associated with decreased functional capacity and increased risk of hypertension, which often leads directly to further decline in health status[20,21]. Considering that, this association has significant implications in China, where the prevalence of hypertension is high and that of obesity is on the rise. By 2025, the number of adults with hypertension is expected to increase by about 60% to 1.56 billion worldwide, and one-third of adults will suffer from hypertension in China[22]. In this case, improving unhealthy lifestyles and antihypertensive treatment is still recommended in the current guidelines for the prevention and treatment of hypertension[23], which however do not provide very clear treatment recommendations, which are mainly achieved by lowering the mean arterial blood pressure. Therefore, in clinical practice, most clinicians tend to focus on controlling blood pressure at the desired range as the main goal, and PP is frequently ignored.

An increasing number of evidence manifest that PP is a strong independent predictor of cardiovascular events, and increased PP is strongly connected with type 2 diabetes, strokes, myocardial infarction, coronary artery disease, heart failure and overall mortality[11,17,24]. Consistent with current guidelines for the management of hypertension, our study suggests that weight reduction may reduce PP in the overall population. Considering interindividual differences in blood pressure and weight, targeted weight loss interventions in the subgroups of the population may be more effective in preventing high PP than in the general population. Therefore, stratified analysis was made in the overall population by sex, age, and baseline blood pressure level. In addition, the relationship between BMI and PP as continuous or categorical variables in multiple linear and logistic regression models was explored. In both models, similar results were obtained.

Our study showed a significant difference in PP between men and women. In the non-obese population, PP was observably higher in men than in women, while in the obese population, it was higher in women than in men. Skurnick et al[25] pointed out that PP levels were lower in women than in men in early adulthood and higher in older age. In our study, women in the obesity group were significantly older than men (47, IQR 36-59 *vs.* 40, IQR 33-51 years), which is similar to the results of the meta-analysis by Skurnick et al[25]. Intriguingly, a nonsignificant association between BMI in those older than 60 years or with elevated blood pressure was observed. Aging and high blood pressure dramatically diminish arterial wall elasticity, leading to arterial stiffness. As the available "buffering" capacity of the arterial wall decreases, a decrease in compliance will increase PP[26]. Therefore, here, it is hypothesized that arterial stiffness is likely to occur in this population, and that once arterial stiffness develops, the effect of BMI on PP is significantly weakened.

Obesity and high PP may be involved with the following mechanisms. 1) Low-grade inflammation is a hallmark of obesity. Adipose tissue induces the expression of many inflammatory mediators, such as the cytokine IL-6[27]. Vascular endothelial dysfunction in the inflammatory state promotes the entry of low-density lipid cholesterol into the vessel wall and initiates the atherosclerotic process. Meanwhile, treatments that antagonize low-grade inflammation have been shown to prevent and treat obesity[28]. 2) Increased activity of the autonomic nervous system in obese people and the increased adrenergic activity lead to reduced vasodilation and decreased compliance[29]. 3) In the resting state, the heart rate of obese people does not increase to a great extent, but the stroke volume would increase the cardiac output to meet the greater metabolic demand due to the increased BMI, and the arterial vasculature is passively dilated[29].

This paper has the following strengths. Firstly, this study is a multicenter, large-sample study designed to investigate the relationship between BMI and PP, while previous studies were characterized with relatively small sample sizes. Secondly, in our study, the application value was extended by analyzing different subgroups. Meanwhile, the association between BMI and PP was analyzed by two regression models, and robust results were obtained.

Limitations

Inevitably, in this paper, the following limitations also exist. Firstly, the elevated blood pressure group in this study was classified according to baseline blood pressure levels. Since antihypertensive medication and previous chronic medical history were not included in the data provided by Chen et al[14], the impact of these aspects on the results of this paper still needs further clarification. In the future, designing our study or collaborating with other researchers to avoid this deficiency may be considered. Secondly, as the current study population was non-diabetic, the results of this study are only applicable among them. Thirdly, it was an observational study that provided inferences about the association between BMI and PP rather than a causality, which thus should be confirmed by further prospective studies in the future. Fourthly, considering the 11 cities included in this study are economically affluent areas, the results may be inapplicable to poor areas. Meanwhile, the results of this study may not be generalizable to other ethnic populations due to genetic reasons.

Conclusions

Overall, PP increased with rising BMI in the overall population. However, stratified analysis demonstrated no significant association between BMI and PP in individuals aged over 60 years or with elevated blood pressure. Therefore, weight interventions to reduce PP remain appropriate for most individuals. However, the association between weight and pulse pressure was weakened in individuals aged over 60 years or with elevated blood pressure.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Acknowledgements

Many thanks to Chen Ying et al[14] for their contributions to the original study (DOI: 10.1136/bmjopen-2018-021768).

Availability of Data and Materials

Raw data is publicly accessible (https://datadryad.org/stash/dataset/doi:10.5061%2Fdryad.ft8750v).

Funding

None.

Authors' Contributions

Y-Y Wang and S-W Chen drafted, analyzed, and interpreted this study. S.Yang provided some clinical advice. Y-Y Wang, S. Yang, and S-W Chen critically reviewed the study. All authors finally agreed and approved the submitted manuscript.

References

1) Wang YC, McPherson K, Marsh T, Gortmaker SL, Brown M. Health and economic burden of the projected obesity trends in the USA and the UK. Lancet 2011; 378: 815-825.
2) Prospective Studies Collaboration, Whitlock G, Lewington S, Sherliker P, Clarke R, Emberson J, Halsey J, Qizilbash N, Collins R, Peto R. Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. Lancet 2009; 373: 1083-1096.
3) Linderman GC, Lu J, Lu Y, Sun X, Xu W, Nasir K, Schulz W, Jiang L, Krumholz HM. Association of Body Mass Index With Blood Pressure Among 1.7 Million Chinese Adults. JAMA Netw Open 2018; 1: e181271.
4) Chen Z, Smith M, Du H, Guo Y, Clarke R, Bian Z, Collins R, Chen J, Qian Y, Wang X, Chen X, Tian

X, Wang X, Peto R, Li L; China Kadoorie Biobank Collaborative Group. Blood pressure in relation to general and central adiposity among 500 000 adult Chinese men and women. Int J Epidemiol 2015; 44: 1305-1319.

5) Moraes-Silva IC, Mostarda CT, Silva-Filho AC, Irigoyen MC. Hypertension and Exercise Training: Evidence from Clinical Studies. Adv Exp Med Biol 2017; 1000: 65-84.

6) Larsson SC, Bäck M, Rees JM, Mason AM, Burgess S. Body mass index and body composition in relation to 14 cardiovascular conditions in UK Biobank: a Mendelian randomization study. Eur Heart J 2020; 41: 221-226.

7) Dale CE, Fatemifar G, Palmer TM, White J, Prieto-Merino D, Zabaneh D, Engmann JEL, Shah T, Wong A, Warren HR, McLachlan S, Trompet S, Moldovan M, Morris RW, Sofat R, Kumari M, Hyppönen E, Jefferis BJ, Gaunt TR, Ben-Shlomo Y, Zhou A, Gentry-Maharaj A, Ryan A; UCLEB Consortium; METASTROKE Consortium, Mutsert R, Noordam R, Caulfield MJ, Jukema JW, Worrall BB, Munroe PB, Menon U, Power C, Kuh D, Lawlor DA, Humphries SE, Mook-Kanamori DO, Sattar N, Kivimaki M, Price JF, Davey Smith G, Dudbridge F, Hingorani AD, Holmes MV, Casas JP. Causal Associations of Adiposity and Body Fat Distribution With Coronary Heart Disease, Stroke Subtypes, and Type 2 Diabetes Mellitus: A Mendelian Randomization Analysis. Circulation 2017; 135: 2373-2388.

8) Domanski M, Norman J, Wolz M, Mitchell G, Pfeffer M. Cardiovascular risk assessment using pulse pressure in the first national health and nutrition examination survey (NHANES I). Hypertension 2001; 38: 793-797.

9) Safar ME, Blacher J, Jankowski P. Arterial stiffness, pulse pressure, and cardiovascular disease-is it possible to break the vicious circle? Atherosclerosis 2011; 218: 263-271.

10) Selvaraj S, Steg PG, Elbez Y, Sorbets E, Feldman LJ, Eagle KA, Ohman EM, Blacher J, Bhatt DL; REACH Registry Investigators. Pulse Pressure and Risk for Cardiovascular Events in Patients With Atherothrombosis: From the REACH Registry. J Am Coll Cardiol 2016; 67: 392-403.

11) Liu FD, Shen XL, Zhao R, Tao XX, Wang S, Zhou JJ, Zheng B, Zhang QT, Yao Q, Zhao Y, Zhang X, Wang XM, Liu HQ, Shu L, Liu JR. Pulse pressure as an independent predictor of stroke: a systematic review and a meta-analysis. Clin Res Cardiol 2016; 105: 677-686.

12) Verdecchia P, Schillaci G, Reboldi G, Franklin SS, Porcellati C. Different prognostic impact of 24-hour mean blood pressure and pulse pressure on stroke and coronary artery disease in essential hypertension. Circulation 2001; 103: 2579-2584.

13) Franklin SS, Khan SA, Wong ND, Larson MG, Levy D. Is pulse pressure useful in predicting risk for coronary heart Disease? The Framingham heart study. Circulation 1999; 100: 354-360.

14) Chen Y, Zhang XP, Yuan J, Cai B, Wang XL, Wu XL, Zhang YH, Zhang XY, Yin T, Zhu XH, Gu YJ, Cui SW, Lu ZQ, Li XY. Association of body mass index and age with incident diabetes in Chinese adults: a population-based cohort study. BMJ Open 2018; 8: e021768.

15) Wu Y, Hu H, Cai J, Chen R, Zuo X, Cheng H, Yan D. Association of hypertension and incident diabetes in Chinese adults: a retrospective cohort study using propensity-score matching. BMC Endocr Disord 2021; 21: 87.

16) Zhou BF. Predictive values of body mass index and waist circumference for risk factors of certain related diseases in Chinese adults--study on optimal cut-off points of body mass index and waist circumference in Chinese adults. Biomed Environ Sci 2002; 15: 83-96.

17) Zhang L, Wang B, Wang C, Li L, Ren Y, Zhang H, Yang X, Zhao Y, Han C, Zhou J, Luo X, Hu D. High pulse pressure is related to risk of type 2 diabetes mellitus in Chinese middle-aged females. Int J Cardiol 2016; 220: 467-471.

18) Guidelines for the Prevention and Treatment of Hypertension in China (2018 Revised Edition). Chin J Cardiovasc Med 2019; 24: 24-56.

19) Rocchini AP. Obesity hypertension. Am J Hypertens 2002; 15: 50S-52S.

20) Guh DP, Zhang W, Bansback N, Amarsi Z, Birmingham CL, Anis AH. The incidence of co-morbidities related to obesity and overweight: a systematic review and meta-analysis. BMC Public Health 2009; 9: 88.

21) Muennig P, Fiscella K, Tancredi D, Franks P. The relative health burden of selected social and behavioral risk factors in the United States: implications for policy. Am J Public Health 2010; 100: 1758-1764.

22) Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. Lancet 2005; 365: 217-223.

23) Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, Ramirez A, Schlaich M, Stergiou GS, Tomaszewski M, Wainford RD, Williams B, Schutte AE. 2020 International Society of Hypertension Global Hypertension Practice Guidelines. Hypertension 2020; 75: 1334-1357.

24) Kang MG, Kim KH, Koh JS, Park JR, Hwang SJ, Hwang JY, Ahn JH, Jang JY, Jeong YH, Kwak CH, Park HW. Association between pulse pressure and body mass index in hypertensive and normotensive populations in the Korea National Health and Nutrition Examination Survey V, 2010-2012. J Clin Hypertens (Greenwich) 2017; 19: 395-401.

25) Skurnick JH, Aladjem M, Aviv A. Sex differences in pulse pressure trends with age are cross-cultural. Hypertension 2010; 55: 40-47.

26) Dart AM, Kingwell BA. Pulse pressure--a review of mechanisms and clinical relevance. J Am Coll Cardiol 2001; 37: 975-984.

27) Fried SK, Bunkin DA, Greenberg AS. Omental and subcutaneous adipose tissues of obese subjects release interleukin-6: depot difference and regulation by glucocorticoid. J Clin Endocrinol Metab 1998; 83: 847-850.

28) Zhang QH, Cui XY, Wang D, Jin Y, Guan YX. Anti-obesity effect of escin: a study on high-fat diet-induced obese mice. Eur Rev Med Pharmacol Sci 2022; 26: 7797-7812.

29) Kwagyan J, Tabe CE, Xu S, Maqbool AR, Gordeuk VR, Randall OS. The impact of body mass index on pulse pressure in obesity. J Hypertens 2005; 23: 619-624.