Contribution of metabolic factors as effect modifiers to the relationships between blood pressure components and stroke in Chinese rural adults: the Henan Rural Cohort Study

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Abstract

Background Although previous studies have explored the relationship between blood pressure (BP) component and stroke, it remains uncertain which BP component is best marker to identify stroke, especially in rural China. Furthermore, the role of metabolic factors in this association has not been reported. The aim of the study was to evaluate the efficiency of BP components as markers for identifying stroke in Chinese rural adults. Simultaneously, we quantified how much of the effects of BP on stroke were mediated through metabolic factors. Methods Of 38880 eligible individuals aged 18 to 79 were derived from the Henan Rural Cohort study. The relationships between BP components and stroke were explored by restricted cubic splines and logistic regression models. Receiver-operating characteristic curve was conducted to evaluate the identifying performance of BP components. Mediation analysis by bootstrap was used to explore the contribution of metabolic factors to BP - related stroke. Results In the fully models, the odds ratios (ORs) and 95% confidence intervals (95% CIs) of systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure (PP) and mean arterial pressure (MAP) in the highest quartile with the risk of stroke were 1.81 (1.56-2.10), 1.72 (1.51-1.97), 1.55 (1.32-1.81) and 1.80 (1.57-2.06), respectively. The non-linear association tests demonstrated that the dose-response relationships were linear between SBP, DBP, PP and MAP with stroke (all p for non-linear > 0.05). In addition, PP had the largest area under curve value (0.655) for stroke in the crude model. However, MAP and SBP had the largest area under curve value (both 0.753) for identifying stroke after adjusting for potential confounders. We further reported that 3.51%–7.22% proportion explained risk of stroke was mediated through metabolic factors. Conclusions SBP and MAP might be better markers for identifying stroke than other BP components. In addition, BP -related stroke was mediated by some degree of metabolic factors.

Introduction

Stroke is the main cause of disability and the second-leading cause of death in the world [1,2]. Simultaneously, stroke is an emerging epidemic as economic conditions and lifestyles change in China, which is becoming a growing public health burden [3]. However rural populations are especially vulnerable receiving fewer preventive health screenings than their urban counterparts. Simultaneously, the majority of strokes are first events, primary prevention targeted at high-risk patients is a more effective strategy for reducing the burden of stroke in Chinese rural population.

Blood pressure (BP) components included systolic blood pressure (SBP), diastolic blood pressure(DBP), pulse pressure (PP) and mean arterial pressure (MAP). Previous studies have explored the relationship between single BP component and stroke [4-12]. In addition, some studies have shown that SBP showed the strongest association, and DBP and PP may be associated with different stroke types [5,10]. Studies have shown that MAP is a better predictor of stroke than PP [6,13], while result from other epidemiological study have indicated that PP is a better predictor of fatal stroke than MAP [14]. In summary, it remains uncertain which BP component is best marker to identify stroke. Simultaneously,

stroke can still occur even with normal BP [15].This indicates that other risk factors may play a role in the development of stroke.

Therefore, the present study were to compare the relationship between each BP component and stroke and evaluate the efficiency of BP components as markers for identifying stroke in Chinese rural adults. In addition, we also want to examine whether some degree of metabolic factors mediate BP-related stroke, because there is evidence to support the associations of metabolic dysfunctions with both BP [16] and stroke [17].

Methods

Study subjects

The study population was enrolled from the Henan Rural Cohort Study. The information of the Henan Rural Cohort Study has been described in detail in the previous article [18]. A total of 39,259 respondents aged 18-79 years old in rural areas completed the survey in this baseline data. Subjects were excluded if they did not have BP data (n=48), currently diagnosed with cancer (n = 331). Finally, 38880 eligible subjects were included for the further analysis. The present study was approved by the Zhengzhou University Life Science Ethics Committee (Code: [2015] MEC (S128)). In addition, this survey was also implemented in accordance with the guidelines of the Helsinki Declaration. And informed consent was signed by all study participants or their agents.

Assessment of BP components

On the basis of the America Heart Association's standardized protocol [19], the SBP and DBP of all participants was tested three times for each participant who was asked to sit at least 5 minutes by using electronic sphygmomanometer (Omron HEM-7071A, Japan). In order to receive more accurate data, subjects were required not to drink, smoke or excessive physical activity at least 30 minutes or more before the measurement. Average of the three readings was acquired for the analysis. If a difference more than 5 mmHg was observed, the closest two values were used for the average. PP was calculated by SBP subtracting DBP. MAP was calculated as one-third SBP plus two thirds DBP.

Assessment of potential covariates

Collected data included basic information such as social and demographic characteristic, details in health and lifestyle as described previously [20]. Briefly, anthropometric components were measured twice and the average readings were taken for statistical analysis. Weight and height (with light clothes and shoes off) were measured using standard measuring equipment to the nearest 0.1kg and 0.1cm, respectively. The body mass index (BMI) was calculated based on the height and weight measurements.

Waist circumference (WC) was measured at the mid-point between the lowest rib and the iliac crest to the nearest 0.1 cm.

Definition of mediator

Metabolic state was defined according to the updated ATPIII criteria by American heart association/American heart, lung and blood institute (AHA/NHLBI) in 2005 related metabolic indicators [21]. In brief, participants were diagnosed as metabolic dysfunctions if they had any of the following: (1) WC ≥ 90 cm for men and WC ≥ 80 cm for women; (2) raised triglycerides (TG) (≥1.7 mmol/L); (3) reduced high density lipoprotein cholesterol (HDL-C) (<1.04mmol/L); and (4) raised fasting plasma glucose (≥5.6 mmol/L). Since this study focuses on BP and stroke, the diagnostic criteria for metabolic status do not include BP indicators. Therefore, the metabolic dysfunctions in this study includes central obesity, abnormal triglyceride, abnormalities of high-density lipoprotein and abnormal fasting blood glucose. We used factor analysis to group these dichotomous variables into more basic underlying variables, which produced 1 continuous mediators for further analyses.

Definition of stroke

All respondents were covered by the New Rural Cooperative Medical System (NRCMS), and each participant had a unique medical insurance card number and ID, making it easy to track disease incidence and mortality. The stroke case from the epidemiological questionnaire was further identified and confirmed through the NRCMS medical records reviews by the outcome committee consisting of an internist, an endocrinologist, a cardiologist, and an epidemiologist based on well-accepted international standards. Only individuals of the nonfatal stroke was included and analyzed in this study based on the baseline database of the Henan Rural Cohort Study, and the ICD-10 code were I60, I61, I63 and I64, respectively.

Statistical analysis

Characteristics of the participants were described as mean ± standard deviation (SD) for continuous variables and numbers (percentages) for categorical variables. For continuous and categorical variables, t test and chi-square test were performed to identify the difference of characteristics, respectively. Besides, the age standardized prevalence of stroke was calculated according to the sixth census data in China. Pearson correlation coefficients were also computed among the components of BP.

Logistic regression models were used to explore the relationship of the BP quartiles and per SD increment of BP with the risk of stroke based on the odds ratios (*OR*s) and 95% confidence intervals (*CI*s). In addition, restricted cubic spline in logistic regression recommended by Loic Desquilbet and François Mariotti[22] was applied to explore the dose-response relationship between various levels of BP with the risk of stroke, using three knots located at 5th, 50th, and 95th percentiles of BP according to the

distribution, with the first knot as the reference group. According to the Pearson correlation test, seven main models were compared, including SBP only, DBP only, both SBP and DBP, PP only, both PP and DBP, MAP only, and both PP and MAP. Other joint models included SBP and PP, SBP and MAP, and DBP and MAP. The fully adjusted model included age, gender, smoking, drinking, physical activity, BMI, history of T2DM, family history of stroke and use of antihypertensive drugs. In addition, the area under the ROC curve (AUC) and 95% *CI*s were carried out to explore the performance of BP components as the marker for identifying stroke. And we applied the method of DeLong et al. (1988) to examine the statistical significance of differences among the components by using MedCalc v15.2.2 (MedCalc Software, Ostend, Belgium).

We used factor analysis to create continuous variables of metabolic dysfunctions to be examined as potential mediator of the association between BP and stroke. Finally, the contribution of metabolic dysfunctions to BP -related stroke was calculated by mediation analysis. Mediation analysis previously introduced elsewhere [23,24] was carried out running the PROCESS for SPSS. To guarantees the conduct of mediation analysis, the total effect must be significant.When statistical difference was found in indirect effect but not in direct effect, it was called a complete mediation.Partial mediation occurred when both indirect and direct effects were statistically significant.The proportion caused by the mediator was calculated by the formula (indirect effect/total effect).

The statistical analyses were performed using IBM SPSS Statistics for Windows software, Version 21.0 (IBM Corp, Armonk, NY, USA), MedCalc v15.2.2 (MedCalc Software, Ostend, Belgium), SAS 9.1(SAS Inst., Cary, NC) and R version 3.5.0 (The R Foundation for Statistical Computing; Vienna, Austria). Two-tailed *P* values <0.05 reported were considered statistically significant in this study.

Results

Demographic characteristics of the participants

The study sample composed of 38880 eligible subjects aged 18-79 years. There were a total of 2617 strokes (2353 ischemic, 282 hemorrhagic, and 8 unknown) and the crude and age-standardized prevalence of total, ischemic and hemorrhagic stroke were 6.73%, 6.05%, 0.73% and 2.98%, 2.62%, 0.38%, respectively.

Characteristics of BP components in subjects with and without stroke were shown in Table 1. Compared with the subjects without stroke, the stroke subjects had the following characteristics: older age, less heavy physical activity, positive family history of stroke ($P<0.05$ for each). The mean levels of WC, BMI, SBP, DBP, PP, MAP, total cholesterol (TC), TG, low-density lipoprotein cholesterol (LDL-C) and fasting plasma glucose (FPG) were significantly higher in subjects with stroke than in the non-stroke participants ($P<0.05$ for each).

Table 1. Comparison of characteristics between participants with and without stroke

Prevalence of stroke on BP components quartiles

As shown in Supplemental Figure 1, the crude prevalence of stroke was increased by quartiles of SBP (3.08%, 4.95%, 7.25% and 11.29%, respectively; P_{trend} <0.001), by quartiles of DBP (4.69%, 5.89%, 7.11% and 8.97%, respectively; P_{trend} <0.001), by quartiles of PP (2.85%, 4.69%, 7.40% and 11.43%, respectively; P_{trend} <0.001) and by quartiles of MAP (3.72%, 5.42%, 7.16% and 10.17%, respectively; P_{trend} <0.001). In addition, the age-standardized prevalence of stroke was also increased by quartiles of SBP (2.07%, 2.43%, 2.99% and 4.87%, respectively), by quartiles of DBP (2.03%, 2.60%, 2.99% and 4.27%, respectively), by quartiles of PP (2.29%, 2.61%, 3.24% and 3.71%, respectively) and by quartiles of MAP (1.99%, 2.49%, 3.07% and 4.45%, respectively).

Pearson correlation among the components of BP

Pearson correlation between SBP and DBP was 0.781(P <0.001). SBP and DBP were each highly correlated with MAP, with Pearson correlations of 0.934 and 0.952, respectively (both P <0.001). DBP was weakly correlated with PP, with Pearson correlation of 0.304 (P <0.001). SBP and MAP were each correlated with PP, with Pearson correlations of 0.832 and 0.580, respectively (both P <0.001).

Effects of BP components on stroke

The *OR*s (95% *CI*s) based on quartiles of each BP component for risk of stroke were shown in Figure 1. SBP, DBP, PP and MAP all had relationships with stroke. In the fully models, compared with the first quartile of SBP, DBP, PP and MAP, the *OR*s (95% *CI*s) of the highest quartile for the risk of stroke were 1.81 (1.56-2.10), 1.72 (1.51-1.97), 1.55 (1.32-1.81) and 1.80 (1.57-2.06) respectively. And increasing quartiles of SBP, DBP, PP and MAP were strongly associated with the risk of stroke.

In addition, dose-response analysis indicates that BP levels were associated with the prevalence of stroke (Supplemental Figure 2). In the fully models, the test for the overall association between SBP, DBP, PP and MAP with stroke was significant (all *p for overall* < 0.001).The non-linear association test demonstrated that this dose-response relationship was linear between SBP, DBP, PP and MAP with stroke (all *p for non-linear* > 0.05).

In logistic regression analyses (Table 2), after adjusted for confounders, increments of 1 SD in single measures of SBP and DBP and summary measures of PP and MAP were associated with similar and highly significant increases in the risk for stroke. When 2 BP components were entered into the models for the risk of stroke simultaneously (Table 2), SBP and MAP had the stronger association with stroke than either DBP or PP (for full details results see the Table 2).

Table 2. The *OR*s(95%*CI*s) for various levels of BP for the risk of Stroke

Evaluation of discriminating efficacy

In order to confirm which BP component is the best marker to identify stroke, we calculated AUC values for the components in terms of risk of stroke and *P* values for pairwise comparisons (Table 3). ROC curve analysis showed that among the 4 BP components, PP had the largest AUC value (0.655) for stroke in the crude model and the differences were statistically significant ($P<0.05$) except DBP. After adjustment for age (Model 2), MAP had the largest AUC values (0.733) and the differences were all statistically significant ($P<0.05$). MAP and SBP had the largest AUC value (both 0.753) for identifying stroke after adjusting for age, gender, education level, smoking, drinking, physical activity and BMI (Model 3), and the differences were statistically significant ($P<0.05$).

Table 3 Area under the ROC curve (AUC) values for BP components in relation to stroke

Stratified analyses for association of BP components with the risk of stroke

We subsequently conducted stratification analyses by metabolic state. The significant relationship between BP components and stroke was more evident in individuals with normal-weight and those without dyslipidemia or type 2 diabetes mellitus (Table 4). In addition, the significant interactions was found between SBP, DBP, PP and MAP and dyslipidemia (all *P* for interactions < 0.001).

Table 4. Associations of stroke risk with blood pressure parameters stratified by metabolic dysfunctions.

Discussion

The principal findings from study of the relationships of BP components with stroke in the large sample of a rural Chinese population are as follows: (1)the linear dose-response relationships all were found between BP components and stroke; (2) MAP and SBP might be better markers for identifying stroke than other BP components; (3) this relationships about BP - related stroke were mediated by some degree of metabolic factors.

Our findings are in line with and extend previous studies [5,8,25-29]. The present study indicated that an increased *OR* for with stroke as a function of SBP, DBP, PP, and MAP in quartiles or on a continuous scale, which was similar to other studies [5,8,24].Additionally, the linear dose-response relationships between SBP, DBP, PP and MAP and stroke in the large sample of a rural Chinese population were found first. The dose-response relationship was performed in previous studies [30,31], but not in the normal population.

Previous studies have shown that SBP and MAP were the strong predicting of stroke [26], which is in line with our study. A cohort study showed that the relationship of PP to mortality from total cardiovascular diseases was less strong than those of other BP components [27]. A previous study in the Chinese Han population, MAP and DBP may provide more information in predicting stroke mortality [28], and the

current study confirmed DBP and SBP had the stronger association with stroke than either PP or MAP when 2 BP components were entered into the models. Some evidence suggested PP might be an independent predictor of stroke, even independent of SBP [9], heng Liqiang et al reported that stroke prediction of PP depended on MAP, while in the REGARDS population, although PP did predict stroke risk, its association was not as strong and was not independent of the effect of SBP [11]. Simultaneously, Zr predicted ischemic stroke than PP did in diagnostic accuracy on a continuous scale [13].

Notably, the association between BP components and stroke risk was more obvious among persons with normal weight and those without comorbidities such as dyslipidemia, or T2DM. These findings were similar to previous studies, which found that the association was more pronounced for individuals without T2DM [29]. Additionally, the current study indicated a statistically significant interaction effect of BP components and dyslipidemia on stroke. Simultaneously, we further examined whether some degree of metabolic factors mediated BP-related stroke, and the results reported that 3.51%–7.22% of proportion explained risk of stroke was mediated through metabolic factors. Although the underlying pathophysiological mechanisms are unclear, the presence of metabolic factors may mask the effect of BP on the risk of stroke in high-risk populations and cause harmful effects in relatively healthy adults.

This is not a traditional epidemiological study looking for the cause of stroke. The focus of the study was to compare the relationships of each BP components with the stroke and to examine whether some degree of metabolic factors mediates BP-related stroke in Chinese rural population. In addition, another strength of this study was that using mediation analysis was performed to address whether BP -related stroke was explained by metabolic factors and calculated the proportion caused by mediator. However, several limitations should also be addressed in light of these results. First of all, the patients with stroke we observed were non-fatal strokes, not including fatal stroke, which may be a selection bias. Second, due to the nature of the cross section design, the relationship between cause and effect was not established. Third, the subjects came from only one province, which may not well represent the entire rural area of China. However, the rural population of Henan province accounted for 10% of China's rural population. Therefore, the results of this study could, to some extent, represent the relationship between BP components (SBP, DBP, PP, and MAP) and stroke.

Conclusion

In conclusion, the linear dose-response relationships all were found between BP components and stroke in Chinese rural adults. MAP and SBP might be better markers for identifying stroke than other BP components. In addition, BP -related stroke was mediated by some degree of metabolic factors. These results have important public health implications for rural area. BP components offer the prospect of a simple, effective, and non-invasive approach for first-level screening for stroke.

Abbreviations

BMI: Body mass index; BP: Blood pressure; *CI:* confidence interval; DBP: diastolic blood pressure;

FPG: fasting plasma glucose; HDL-C: high density lipoprotein cholesterol; MAP: mean arterial pressure; *OR*:odds ratio;PP: pulse pressure; SBP: systolic blood pressure; SD: standard deviation; TC: total cholesterol; TG: triglycerides; WC: Waist circumference.

Declarations

Ethics approval and consent to participate

The present study was approved by the Zhengzhou University Life Science Ethics Committee (Code: [2015] MEC (S128)).

Consent for publication

Not applicable.

Availability of data and materials

All relevant data are within the paper and its Supporting Information files. Contact to Dr. Chongjian Wang (tjwcj2005@126.com) for additional information regarding data access.

Competing interests

The authors declare no conflict of interest.

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Authors' contributions

CJW and GYZ conceived and designed the experiments. XZ,YQL , XYZ, ML, XTL, RQT, XLQ, HQZ, ZYT, DQ and ZXM performed and conducted the experiments. XZ,YQL , XYZ, ML, XTL and RQT analyzed the data

and take responsibility for the integrity and accuracy of the information.XLQ, HQZ, ZYT, DQ and ZXM contributed to the reagents/materials/analysis tools. XZ and YQL drafted and revised the manuscript. All authors have approved the final manuscript.

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Clinical Trial Registration

The Henan Rural Cohort study has been registered at Chinese Clinical Trial Register (Registration number: ChiCTR-OOC-15006699). Date of registration: 2015-07-06 http://www.chictr.org.cn/showproj.aspx?proj=11375

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Tables

Table 1. Comparison of characteristics between participants with and without stroke

Variables	Total (n=38880)	Non-Stroke (n=36263)	Stroke (n=2617)	*P*
Age (years), (mean±SD)	55.57±12.20	54.96±12.25	63.91±7.72	<0.001
Men, n (%)	15396 (39.60)	14177 (39.09)	1219 (46.58)	<0.001
Smoking, n (%)				<0.001
Nonsmoker	28266 (72.70)	26501 (73.08)	1765(67.44)	
Former smoker	3144(8.09)	2704(7.46)	440(16.81)	
Current smoker	7470 (19.21)	7058 (19.46)	412(15.75)	
Drinking, n (%)				<0.001
Nondrinker	30031(77.24)	28044 (77.34)	1987(75.93)	
Former drinker	1799 (4.63)	1466 (4.04)	333(12.72)	
Current drinker	7050 (18.13)	6753 (18.62)	297(11.35)	
Physical activity, n (%)				<0.001
Low	12573 (32.34)	11422 (31.50)	1151(43.98)	
Moderate	14653 (37.69)	13762 (37.95)	891(34.05)	
High	11654 (29.97)	11079 (30.55)	575(21.97)	
WC (cm) (mean±SD)	84.08±10.39	83.97±10.40	85.65±10.10	<0.001
BMI (kg/m^2) (mean±SD)	24.83±3.56	24.82±3.57	25.04±3.44	0.002
SBP (mm Hg) (mean±SD)	125.96±20.00	125.28±19.76	135.36±20.83	<0.001
DBP (mm Hg) (mean±SD)	77.70±11.64	77.50±11.60	80.42±11.81	<0.001
PP (mm Hg) (mean±SD)	48.27±13.10	47.78±12.88	54.94±14.31	<0.001
MAP (mm Hg) (mean±SD)	93.79±13.62	93.43±13.53	98.73±13.86	<0.001
FPG (mmol/l) (mean±SD)	5.54±1.51	5.52±1.50	5.81±1.68	<0.001
TC (mmol/l) (mean±SD)	4.76±0.99	4.76±0.98	4.79±1.08	<0.001
TG (mmol/l) (mean±SD)	1.68±1.12	1.67±1.13	1.77±1.10	<0.001
HDL cholesterol (mmol/l) (mean±SD)	1.32±0.33	1.33±0.33	1.28±0.33	<0.001
LDL cholesterol (mmol/l) (mean±SD)	2.87±0.82	2.87±0.82	2.90±0.91	<0.001
Family history of Stroke, n (%)	3322 (8.60)	2953 (8.20)	369 (14.13)	<0.001

Abbreviations: SD, standard deviation; min, minutes; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MAP, mean arterial pressure; BMI, body mass index; WC, waist circumference; TC, total cholesterol; TG, Triglyceride, HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FPG, fasting plasma glucose

Table 2. The *OR*s(95%*CI*s) for various levels of BP for the risk of Stroke

BP	1SD (mmHg)	*OR* (95%*CI*)[a]	*OR* (95%*CI*)[b]
Single measures			
SBP	20.00	1.52(1.47-1.57)	1.21(1.16-1.26)
DBP	11.64	1.25(1.21-1.3)	1.21(1.16-1.26)
Summary measures			
PP	13.10	1.54(1.49-1.59)	1.14(1.10-1.19)
MAP	13.62	1.40(1.35-1.45)	1.21(1.16-1.26)
2-Term models			
SBP		1.71(1.62-1.80)	1.12(1.05-1.19)
DBP		0.85(0.81-0.89)	1.11(1.05-1.18)
SBP		1.18(1.11-1.25)	1.23(1.15-1.31)
PP		1.36(1.28-1.44)	0.97(0.91-1.04)
SBP		1.75(1.63-1.88)	1.10(1.02-1.20)
MAP		0.85(0.78-0.91)	1.11(1.02-1.21)
DBP		1.1(1.06-1.15)	1.17(1.12-1.23)
PP		1.5(1.45-1.55)	1.09(1.04-1.14)
DBP		0.72(0.66-0.77)	1.10(1.01-1.20)
MAP		1.9(1.76-2.06)	1.12(1.02-1.22)
PP		1.45(1.39-1.51)	1.05(1.00-1.10)
MAP		1.12(1.07-1.17)	1.18(1.12-1.24)

[a] *OR* (95%*CI*) was unadjusted;

[b] *OR* (95%*CI*) was adjusted for age, gender, smoking, drinking, physical activity, BMI, history of T2DM, family history of stroke and use of antihypertensive drugs.

Table 3 Area under the ROC curve (AUC) values for BP components in relation to stroke

Model	BP	AUC(95% *CI*)	Sensitivity(%,95% *CI*)	Specificity (%,95% *CI*)
Model 1	SBP[a&]	0.645(0.640-0.649)	64.04(62.2-65.9)	58.06(57.5-58.6)
	DBP[&]	0.574(0.569-0.579)	58.08(56.2-60.0)	53.48(53.0-54.0)
	PP[* &]	0.655(0.650-0.660)	60.64(58.7-62.5)	62.67(62.2-63.2)
	MAP[*#a]	0.613(0.608-0.618)	54.18(52.3-56.1)	62.58(62.1-63.1)
Model 2	SBP[a&]	0.732(0.728-0.737)	80.89(79.3-82.4)	55.49(55.0-56.0)
	DBP[a&]	0.732(0.729-0.737)	84.22(82.8-85.6)	52.17(51.7-52.7)
	PP[*#&]	0.727(0.722-0.731)	82.35(80.8-83.8)	53.36(52.8-53.9)
	MAP[*#a]	0.733(0.729-0.737)	95.34(94.5-96.1)	34.25(33.8-34.7)
Model 3	SBP[#a]	0.753(0.748-0.757)	80.05(78.5-81.6)	57.63(57.1-58.1)
	DBP[a&]	0.752(0.748-0.756)	78.86(77.2-80.4)	58.36(57.9-58.9)
	PP[*#&]	0.750(0.745-0.754)	81.98(80.4-83.4)	54.41(54.9-55.9)
	MAP[#a]	0.753(0.749-0.757)	81.91(80.4-83.4)	55.81(55.6-56.3)

Model 1, unadjusted

Model 2, adjusted for age

Model 3, adjusted for age, gender, smoking, drinking, physical activity, BMI, history of T2DM, family history of stroke and use of antihypertensive drugs.

* significant differences with SBP ($p < 0.05$)

significant differences with DBP ($P< 0.05$)

[a] significant differences with PP ($P< 0.05$)

& significant differences with MAP ($P<0.05$)

Table 4. Associations of stroke risk with blood pressure parameters stratified by metabolic dysfunctions.

Metabolic dysfunctions		Q1	Q2	Q3	Q4	*P* for trend
Abdominal obesity						
No	SBP	reference	1.04(0.82-1.31)	1.12(0.89-1.40)	1.35(1.08-1.68)	<0.001
	DBP	reference	1.02(0.82-1.25)	1.02(0.84-1.24)	1.22(1.00-1.48)	<0.001
	PP	reference	1.05(0.84-1.32)	0.97(0.77-1.23)	1.08(0.85-1.37)	<0.001
	MAP	reference	1.15(0.92-1.43)	1.15(0.92-1.43)	1.40(1.13-1.74)	<0.001
Yes	SBP	reference	1.17(0.95-1.43)	1.27(1.04-1.55)	1.10(0.89-1.35)	<0.001
	DBP	reference	1.10(0.92-1.31)	1.13(0.94-1.35)	1.15(0.96-1.38)	<0.001
	PP	reference	1.38(1.11-1.71)	1.35(1.09-1.66)	1.17(0.94-1.45)	<0.001
	MAP	reference	1.26(1.04-1.52)	1.15(0.95-1.40)	1.18(0.98-1.43)	<0.001
Dyslipidemia						
No	SBP	reference	1.12(0.90-1.39)	1.11(0.89-1.37)	1.27(1.03-1.58)	<0.001
	DBP	reference	1.06(0.88-1.28)	1.00(0.83-1.21)	1.19(0.99-1.44)	<0.001
	PP	reference	1.15(0.91-1.46)	1.26(1.01-1.57)	1.22(0.98-1.52)	<0.001
	MAP	reference	1.21(0.98-1.49)	1.15(0.94-1.41)	1.30(1.06-1.60)	<0.001
Yes	SBP	reference	1.24(1.00-1.53)	1.41(1.14-1.73)	1.24(1.00-1.53)	<0.001
	DBP	reference	1.25(1.04-1.50)	1.25(1.04-1.51)	1.26(1.04-1.53)	<0.001
	PP	reference	1.11(0.90-1.38)	1.16(0.94-1.43)	1.10(0.89-1.36)	<0.001
	MAP	reference	1.34(1.10-1.62)	1.22(1.00-1.49)	1.30(1.06-1.58)	<0.001
T2DM						
No	SBP	reference	1.10(0.92-1.30)	1.20(1.02-1.41)	1.28(1.08-1.50)	<0.001
	DBP	reference	1.15(0.99-1.34)	1.19(1.03-1.38)	1.26(1.08-1.47)	<0.001
	PP	reference	1.15(0.96-1.38)	1.26(1.06-1.49)	1.18(0.99-1.40)	<0.001
	MAP	reference	1.18(1.00-1.39)	1.28(1.09-1.51)	1.34(1.14-1.58)	<0.001
Yes	SBP	reference	0.99(0.71-1.37)	1.14(0.83-1.58)	1.11(0.80-1.54)	0.013
	DBP	reference	1.36(1.00-1.83)	1.14(0.83-1.56)	1.07(0.77-1.50)	0.142
	PP	reference	1.11(0.79-1.57)	1.24(0.87-1.75)	1.17(0.82-1.67)	0.017
	MAP	reference	1.24(0.90-1.71)	1.22(0.89-1.69)	1.16(0.84-1.61)	0.100

Adjusted for age and gender, smoking, drinking, physical activity, BMI, history of T2DM, family history of stroke and use of antihypertensive drugs.

The quartiles of SBP, DBP, PP and MAP were calculated by metabolic dysfunctions respectively.

In individuals with abdominal obesity, the cut off of SBP, DBP, PP and MAP was 115, 127, 142; 72, 80, 88; 40, 47, 57 and 87, 96, 105.

In individuals with normal-weight, the cut off of SBP, DBP, PP and MAP was 108, 119, 133; 67, 73, 81; 38, 45, 54 and 81, 89, 98, respectively.

In individuals with dyslipidemia, the cut off of SBP, DBP, PP and MAP was 115, 127, 142; 72, 80, 88; 40, 47, 56; 87, 96, 105. In individuals without dyslipidemia, the cut off of SBP, DBP, PP and MAP was 109, 121, 135; 68, 75, 83; 39, 45, 54; 82, 90, 100.

In individuals with T2DM, the cut off of SBP, DBP, PP and MAP was 120, 132, 146; 73, 80, 88; 43, 52, 61; 89, 97, 106. In individuals without T2DM, the cut off of SBP, DBP, PP and MAP was 111, 122, 137; 69, 76, 85; 39, 45, 54; 83, 92, 102.

Figures

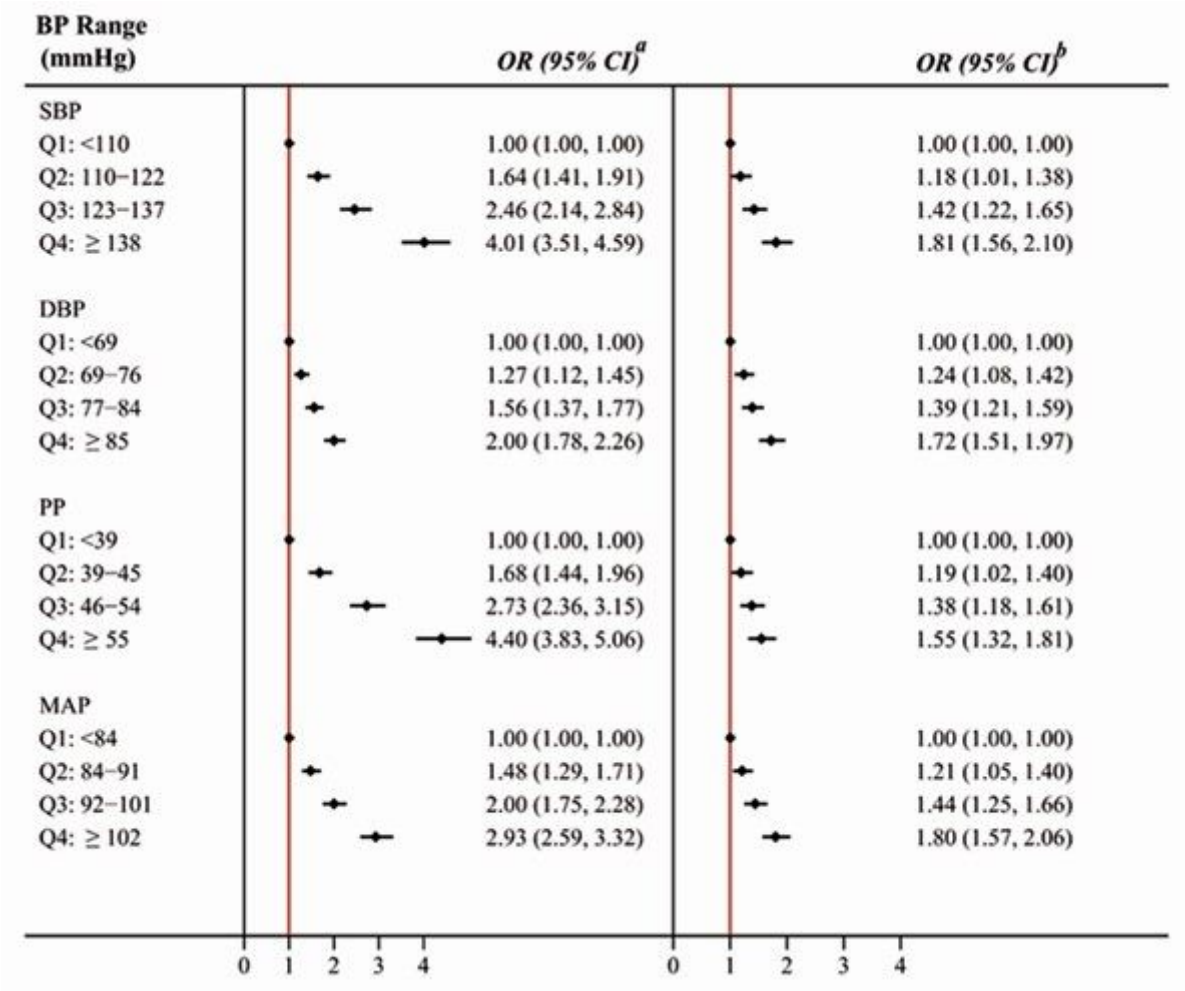

Figure 1

Analyses for the risk of stroke by quartiles of BP components a : Unadjusted; b : Adjusted for age, gender, smoking, drinking, physical activity, BMI, history of T2DM, family history of stroke and use of antihypertensive drugs.

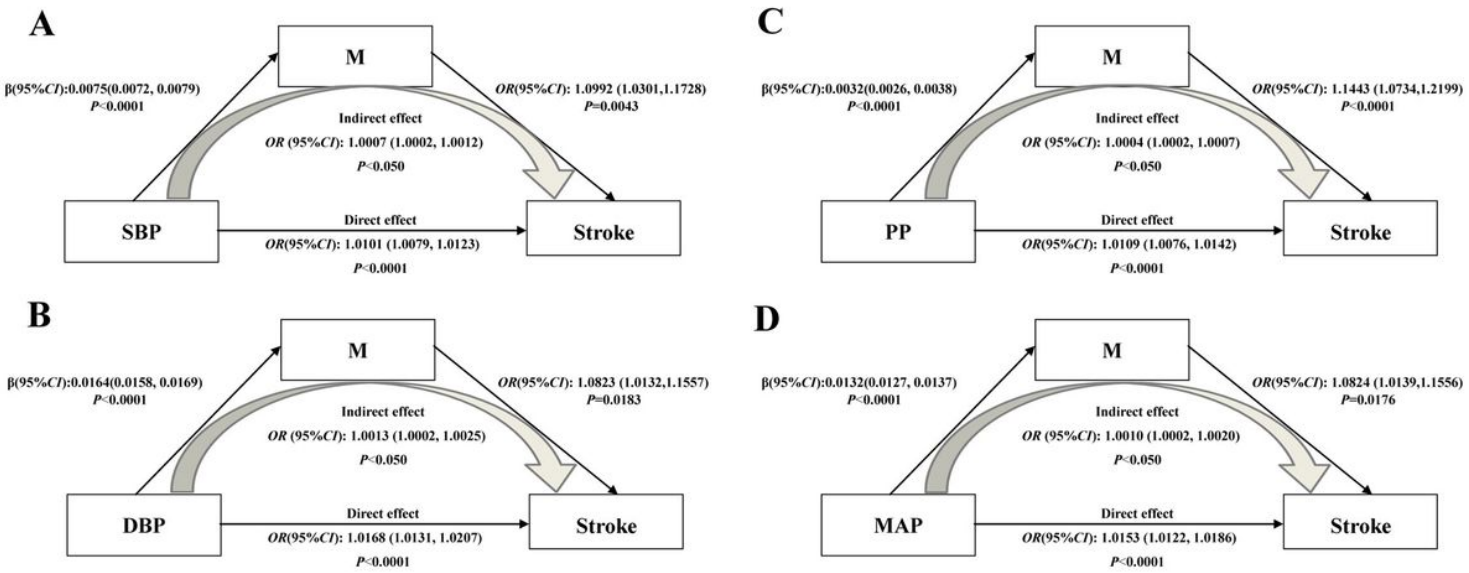

Figure 2

Mediation analysis to determine the relationship between SBP (A), DBP (B), PP (C), MAP (D) and stroke through metabolic factors. M, metabolic factors Odds ratio (OR; 95% CI) of total effect for SBP, DBP, PP and MAP on stroke was 1.0107 (1.0085-1.0128), 1.0180 (1.0142-1.0216), 1.0114 (1.0080-1.0147), 1.0162 (1.0131-1.0192), respectively. Adjusted for age, gender, smoking, drinking, physical activity, BMI, history of T2DM, family history of stroke and use of antihypertensive drugs.

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