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Body mass index and serum uric acid level

Individual and combined effects on blood pressure in middle-aged and older individuals in China

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Abstract

Few studies on the individual and combined analysis between serum uric acid (SUA) and body mass index (BMI) and blood pressure (BP) were conducted in individuals aged ≥45 years. We aimed to assess the extent to which BMI and SUA and their interaction affect BP in Chinese middle-aged and older adults.

Data were selected from the China Health and Retirement Longitudinal Study (CHARLS). A total of 5888 individuals aged 45 to 96 was included. Differences between BMI, or between categories of blood pressure were evaluated by *t* test or chi-square test. The trend of related variables according to four BMI categories was also tested using contrast analysis. The adjusted associations between various characteristics and BP status were first compared using linear regression models, as appropriate. Then, general linear models adjusting for related potential confounders were used to examine the synergistic effect of SUA and BMI level on BP for middle-aged and elderly individuals in China.

Age-adjusted partial Pearson correlation coefficient showed that BMI was significantly and positively correlated with BP both in male and female, SUA positively correlated with both systolic blood pressure (SBP) and diastolic blood pressure (DBP) in males with BMI <24.0 kg/m^2 and females with BMI <24.0 kg/m^2. However, SUA level significantly and positively correlated with DBP, but not with SBP, in females with BMI ≥24.0 kg/m^2. Multiple linear regression analysis showed that BMI was independently associated with BP both in male and female, SUA significantly and positively associated with SBP in both males and females with BMI <24.0 kg/m^2, However, SUA level positively correlated with DBP in females with BMI <24.0 kg/m^2, but not with males with BMI <24.0 kg/m^2, independent of other confounding factors. A general linear model analysis adjusted for confounding factors did not reveal interaction between BMI, SUA levels and SBP (β=-1.404, P=.686 in males; β=-2.583, P=.575 in females) and DBP (β=-2.544, P=.263 in males; β=-2.619, P=.622 in females).

No interaction between BMI, SUA levels, and BP was observed in either males or females; However, BMI was independently associated with BP both in male and female, SUA independently associated with SBP both in males and females with BMI <24.0 kg/m^2, and SUA independently associated with DBP in females with BMI ≥24.0 kg/m^2.

Abbreviations: BMI = body mass index, CHARLS = China Health and Retirement Longitudinal Study, CRP = C-reactive protein, CVD = cardiovascular disease, DBP = diastolic blood pressure, eGFR = estimated glomerular filtration rate, HDL-C = high density lipoprotein cholesterol, LDL-C = low density lipoprotein cholesterol, SBP = systolic blood pressure, SD = standard deviation, SUA = serum uric acid, TG = triglycerides.

Keywords: blood pressure, body mass index, combined effect, serum uric acid

1. Introduction

As well known, according to the evidence of increasing risk[1–3] and incidence of cardiovascular disease (CVD),[4–6] the hypertension is defined as a systolic blood pressure (SBP) of >140 mm Hg and/or diastolic blood pressure (DBP) of >90 mm Hg. Hypertension is a cluster of risk factors[7–14] associated with aging, central obesity, overweight, poor lifestyle, family history of hypertension, diabetes and dyslipidemia, lack of physical

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activities, cigarette smoking, alcohol consumption, high levels of low-density lipoprotein cholesterol (LDL-C), low levels of high-density lipoprotein cholesterol (HDL - C), elevated fasting glucose levels, and elevated triglycerides (TG). Because hypertension is more complex and patients suffer from physical, psychosocial, and economical burden. Recently, it has become an important public health challenges worldwide.[15] The prevalence of hypertension has increased in the past few years in China.[16,17] Furthermore, as the aging population increases, the hypertension rate is disproportionately high among individuals aged ≥45 years in China.[18–20] Hypertension is a complex disease, and patients with hypertension suffer from economic, psychosocial, and physical burden. Recently, hypertension became most important public health challenges worldwide. Therefore, an effective strategy to prevent hypertension and determine its timely associated risks should be carefully implemented. Exploring the its timely associated risks and their interaction of hypertension may provide the insight in public health implications for prevention and management of hypertension in future.

Serum uric acid (SUA) is an endogenous end product and is involved in the production of reactive-oxygen species. It is important to evaluate their status in advance of chronic disease development.[21] In recent years, as a key mark, systemic measured by SUA has become an important marker for chronic disease development. Studies have conduct that SUA is associated with various diseases, such as CVD,[22–25] prehypertension,[26–29] metabolic syndrome,[30–32] and hypertension.[33–35] However, despite the association between SUA levels and these risk conditions, SUA levels may not be regarded as an independent risk factor. Since SUA level is highly associated with overweight, obesity and other risk factors,[36–38] which is in turn associated with risk of hypertension, a causal condition may exist between body mass index (BMI) and risk of hypertension. Therefore, the association between SUA levels and risk of hypertension and the effects BMI on this association are of considerable interest, and a modulating effect between BMI and SUA levels on blood pressure (BP) may also be fully considered.

To date, few studies on the association and interaction analysis between SUA and BMI level and blood pressure (BP) were conducted in individuals aged ≥45 years. Several studies[39,40] have explored the association and/or interaction analysis between BMI and SUA level and BP, but the relationships between SUA and BP of participants categorized by BMI level may be different, especially lack of related research in China culture background. The evidence on the association and interaction analysis between BMI and SUA level and BP in middle-aged and elderly individuals remains unclear.[40] Thus, the present study aimed to determine the prevalence of normotension and hypertension and their association with body mass index, SUA levels, and other confounding factors according to gender using cross-sectional data from community-dwelling individuals aged ≥45 years in China.

2. Methods

2.1. Participants

Data were extracted from the China Health and Retirement Longitudinal Study (CHARLS), Wave 1 (2011).[41] Samples of individuals with 45 years of age or older were selected by multistage probability sampling from 150 counties fell within 28 provinces between June 2011 and March 2012. CHARLS respondents are followed using a face-to-face computer-assisted personal interview (CAPI). The study was approved by the institutional ethical committees of Peking University. All participants enrolled for the study signed the consent, and the institutional review board of the Peking University approved the study protocol. The cross-section and observational design follow the STROBE guidelines.[42] The data is publicly available (http://charls.pku.edu.cn/zh-CN), and the research have no direct contact with the individual participants. At baseline, 17708 respondents in wave1 gave the consent to participate, and 7186 respondents were with full socio-demographic characteristics, health behaviors, medical history, and metabolic measures. Subjects who used anti-hypertensive drugs, had impaired kidney function (estimated glomerular filtration rate [eGfr]<60 mL/minute/1.73 m^2)[43] and diabetes were excluded from our study. Finally, 5888 subjects were included in our study. The CHARLS involved 5888 individuals aged 45 years or older, out of whom 46.91% were men [mean age=60.15 years, standard deviation (SD)=9.10, range: 45–93] and 53.09% were women (mean age=58.74 years, SD = 9.36, range: 45–96).

2.2. Self-reported factors

Variables like age, educational levels (1= Illiterate, 2= Less than elementary school, 3= High school, 4= Above vocational school), marital status (1= Single, 2= Married), place of residence (1= Rural, 2= Urban), cigarette smoking (1= No, 2= Former smoke,3= Current smoke), alcohol consumption (1= No, 2= Less than once a month, 3= More than once a month), eating habit (1= ≤2 meals per day, 2=3 meals per day, 3= ≥4 meals per day), social events (1= No, 2= Yes), history of accidental injury (1= No, 2= Yes), physical exercise (1= No physical exercise, 2= Less than regular physical exercises, 3= Regular physical exercises), hepatitis history (1= No, 2= Yes), history of CVD (0= No, 1= Yes), history of antilipidemic medication (1= No, 2= Yes) were obtained using a self-reported questionnaire, and most variables based on our previous studies.[44–47]

2.3. Measurements

BMI was defined as the body mass (kg) divided by the square of the body height (m).[48] C-reactive protein (CRP) was measured by immunoturbidimetric assay. Fasting plasma glucose (FPG), TG, LDL-C, and HDL-C were analyzed using the enzymatic colorimetric tests, SUA levels were analyzed using the urinalysis (UA) plus method. The average value of blood pressure was determined by mean of the 3 measurements. eGFR was measured by the chronic kidney disease epidemiology collaboration creatinine-cystatin equations.[49] BMI were divided into 4 categories:

(1) underweight (BMI <18.5 kg/m^2),
(2) normal (18.5–24 kg/m^2),
(3) overweight (24–28 kg/m^2), and
(4) obese (≥28 kg/m^2).[50]

Hyperuricemia (HUA) was defined as SUA concentration of >7 mg/dL in men and >6 mg/dL in women.[51] CRP were classified into 4 categories (1= ≤1.00 mg/l, 2= 1.01–3.00 mg/l, 3= 3.01–10.00 mg/l and 4=>10 mg/l).[43,52–54] The blood pressures were measured in quiet environment, and she or he should keep sitting, relaxing, and place the left arm on a flat surface, with the palm of the hand facing up, so that the upper arm was at the same height as the heart, then the tester would press the "start" button

in the Omron hem-7200 sphygmomanometer, and the cuff could automatically inflate and deflate. After three measurements, it would take the average of 3 measurements as the final blood pressures. Participants were divided into normotension (defined as not being on antihypertensive therapies with an SBP of <140 mm Hg and DBP of <90 mm Hg), and hypertension (defined as SBP of ≥140 mm Hg and/or DBP of ≥90 mm Hg) groups, the categorization has been widely used in previous studies.[40,46]

2.4. Statistical analysis

Data were analyzed by using SPSS17.0 software for Windows10 (IBM Corp., Armonk, NY) the mean SD or frequency, as appropriate. Differences between groups according to BMI (<18.5 kg/m^2, 18.5–24 kg/m^2, 24–28 kg/m^2, and ≥28 kg/m^2) and blood pressure (hypertension and normotension) were evaluated using the Student *t* test (continuous data) or the chi-square test (categorical data). The trends of the related variables according to the body mass index categories were also tested using contrast analysis. The adjusted associations between various characteristics and blood pressure status were first compared using linear regression models, as appropriate. Then, general linear models adjusting for related potential confounders[55] (socio-demographic characteristics [age, educational level, marital status, place of residence], health behaviors [cigarette smoking, alcohol consumption, eating habits, social events, history of accidental injury, physical activities], medical history [history of CVD, hepatitis history, history of antilipidemic medication], metabolic measures (CRP, low density lipoprotein, high density lipoprotein, TG) were used to examine the synergistic effect of SUA and body mass index level on blood pressure for middle-aged and elderly individuals in China. 2-tailed, and a value of *P* of .05 were considered significant.

3. Results

In the study, 5888 participants who effectively completed the questionnaires were included. Various baseline characteristics of participants categorized by BMI were shown in Table 1, and most variables based on our previous studies.[44–47] Overall, 2762 (46.91%) of the participants were male, and 3126 (53.09%) of the participants were female. The average ages of the male and female participants were 60.15 ± 9.10 and 58.74 ± 9.36 years old, respectively. The mean serum concentrations of SUA were 4.83 ± 1.18 mg/dL and 3.93 ± 1.00 mg/dL in males and females, respectively. In males, the mean SBP and DBP were 128.97 ± 20.18mm Hg and 76.44 ± 13.09 mm Hg, respectively, and, in females, the mean SBP and DBP were 130.39 ± 26.16 mm Hg and 76.15 ± 12.49 mm Hg, respectively. Considering the modified Chinese criteria for BMI,[50] the mean and SD of BMI were 22.79 ± 3.48 kg/m^2 in males, among whom 7.24% were underweight, 60.93% were normal, 24.44% were overweight, and 7.39% were obese, whereas the mean and SD of BMI were 23.89 ± 3.98 kg/m^2 in females, among whom 6.75% were underweight, 47.06% were normal, 32.41% were overweight, and 13.79% were obese.

In order to explore the direct associations, the effect between BMI category and SUA levels on BP was observed by the plot in Figure 1. SUA levels had a positive correlation with both DBP and SBP. Analysis of covariance showed that three regression lines in each graph were significantly different from the other groups (In male: SBP, F= 42.171, *P* = .000 and DBP, F = 57.628, *P* = .000; In female: SBP, F = 11.469, *P* = .000 and DBP, F = 42.034, *P* = .000; respectively).

Table 2 show the relationship between various characteristics of participants categorized by BMI and BP status in male and female.

(1) In male with BMI <24.0 kg/m^2, BMI, SUA, SBP, and DBP were significantly higher hypertension group than those in the normotension group.
(2) In male with BMI ≥24.0 kg/m^2, BMI, SBP, and DBP were significantly higher in hypertension group than those in the normotension group.
(3) In female with BMI <24.0 kg/m^2, SUA, SBP, and DBP were significantly higher in hypertension group than those in the normotension group.
(4) In female with BMI ≥24.0 kg/m^2, SUA, BMI, SBP, and DBP were significantly higher in hypertension group than those in the normotension group.

Table 3 show age-adjusted relationship between baseline of demographic variables and blood pressure status of participants categorized by gender. First, in male with BMI <24.0 kg/m^2, age-adjusted partial Pearson correlation coefficient showed that BMI and SUA were positively correlated with both SBP and DBP. Secondly, in male with BMI ≥24.0 kg/m^2, BMI were positively correlated with both SBP and DBP. Thirdly, in female with BMI <24.0 kg/m^2, BMI and SUA were positively correlated with both SBP and DBP; Lastly, in female with BMI ≥24.0 kg/m^2, BMI were positively correlated with both SBP and DBP; SUA were positively correlated with DBP.

Table 4 show multivariate-adjusted relationship between baseline of demographic variables and blood pressure in participants categorized by gender. The result showed that SUA level was significantly and positively associated with SBP in both men and women with BMI of <24.0 kg/m^2, and also significantly and positively associated with DBP in women with BMI of <24.0 kg/m^2 (males with BMI <24.0 kg/m^2: β=0.054, *P* = .021; females with BMI <24.0 kg/m^2: β=0.064, *P* = .009; females with BMI ≥24.0 kg/m^2: β=0.075, *P* = .003), independently of other confounding factors.

A general linear model adjusted for confounding factors (socio-demographic characteristics [age, educational level, marital status, place of residence], health behaviors [cigarette smoking, alcohol consumption, eating habits, social events, history of accidental injury, physical activities], medical history [history of CVD, hepatitis history, history of antilipidemic medication], metabolic measures [C-reactive protein, low density lipoprotein, high density lipoprotein, TG] was used to assessed the statistical significance of the synergistic relationship between BMI and SUA. Evidence of interaction between BMI and SUA level on SBP (β=-1.404, *P* = 0.686 in males; β=-2.583, *P* = .575 in females) and DBP (β=-2.544, *P* = .263 in males; β=-2.619, *P* = .622 in females) (Table 5).

4. Discussion

The individual and combined effects of BMI and SUA level and level with BP varied in middle-aged and elderly individuals. In our study, we attempted to explore the prevalence of hypertension and its association with BMI and SUA level. The results show that prevalence of hypertension was 28.13% in males and 30.07% in females, similar to those of the English individuals (men, 36.8%; women, 38.6%).[56] Moreover, SUA levels were positively

Table 1

Baseline of demographic variables of participants categorized by BMI in male (N = 2762) and female (N = 3126).

Variables	Male (N = 2762)						Female (N = 3126)					
	BMI ≤18.5 (n = 200)	BMI 18.5–24 (n = 1683)	BMI 24–28 (n = 675)	BMI ≥28 (n = 204)	t/χ^2	P	BMI≤18.5 (n = 211)	BMI 18.5–24 (n = 1471)	BMI 24–28 (n = 1013)	BMI ≥28 (n = 431)	t/χ^2	P
Age, yr	64.62 ± 9.27	60.54 ± 9.18	58.61 ± 8.61	57.68 ± 7.82	29.528	.000	64.41 ± 10.16	59.26 ± 9.42	57.70 ± 8.99	56.61 ± 8.29	40.344	.000
Educational levels												
Illiterate	37 (18.50)	263 (15.63)	55 (8.15)	21 (10.29)	46.525	.000	123 (58.29)	678 (46.09)	394 (38.89)	145 (33.64)	60.643	.000
Less than elementary school	139 (69.50)	1242 (73.80)	502 (74.37)	151 (74.02)			85 (40.28)	698 (47.45)	528 (52.12)	240 (55.68)		
High school	17 (8.50)	125 (7.43)	76 (11.26)	21 (10.29)			3 (1.42)	67 (4.55)	60 (5.92)	35 (8.12)		
Above vocational school	7 (3.50)	53 (3.15)	42 (6.22)	11 (5.39)			0 (0.00)	28 (1.90)	31 (3.06)	11 (2.55)		
Marital status												
Single	19 (9.50)	201 (11.94)	34 (5.04)	13 (6.37)	29.095	.000	55 (26.07)	248 (16.86)	132 (13.03)	43 (9.98)	35.100	.000
Married	181 (90.50)	1482 (88.06)	641 (94.96)	191 (93.63)			156 (73.93)	1223 (83.14)	881 (86.97)	388 (90.02)		
Place of residence												
Rural	150 (75.00)	1209 (71.84)	390 (57.78)	119 (58.33)	56.547	.000	163 (77.25)	978 (66.49)	625 (61.70)	239 (55.45)	36.057	.000
Urban	50 (25.00)	474 (28.16)	285 (42.22)	85 (41.67)			48 (22.75)	493 (33.51)	388 (38.30)	192 (44.55)		
Cigarette smoking												
NO	38 (19.00)	361 (21.45)	208 (30.81)	66 (32.35)	79.087	.000	182 (86.26)	1347 (91.57)	952 (93.98)	405 (93.97)	20.950	.002
Former smoke	28 (14.00)	230 (13.67)	142 (21.04)	46 (22.55)			5 (2.37)	37 (2.52)	15 (1.48)	6 (1.39)		
Current smoke	134 (67.00)	1092 (64.88)	325 (48.15)	92 (45.1)			24 (11.37)	87 (5.91)	46 (4.54)	20 (4.64)		
Alcohol consumption												
NO	101 (50.50)	709 (42.13)	298 (44.15)	91 (44.61)	7.047	.317	181 (85.78)	1285 (87.36)	886 (87.46)	389 (90.26)	8.320	.217
Less than once a mo	18 (9.00)	185 (10.99)	67 (9.93)	26 (12.75)			9 (4.27)	67 (4.55)	57 (5.63)	20 (4.64)		
More than once a mo	81 (40.50)	789 (46.88)	310 (45.93)	87 (42.65)			21 (9.95)	119 (8.09)	70 (6.91)	22 (5.10)		
Eating habit												
≤2 meals per d	29 (14.50)	254 (15.09)	76 (11.26)	23 (11.27)	13.240	.039	51 (24.17)	213 (14.48)	125 (12.34)	47 (10.9)	32.962	.000
3 meals per d	165 (82.50)	1402 (83.30)	592 (87.70)	180 (88.24)			158 (74.88)	1235 (83.96)	879 (86.77)	384 (89.10)		
≥4 meals per d	6 (3.00)	27 (1.60)	7 (1.04)	1 (0.49)			2 (0.95)	23 (1.56)	9 (0.89)	0 (0.00)		
Social events												
No	117 (58.50)	844 (50.15)	296 (43.85)	100 (49.02)	15.250	.002	131 (62.09)	795 (54.04)	468 (46.20)	185 (42.92)	36.116	.000
Yes	83 (41.50)	839 (49.85)	379 (56.15)	104 (50.98)			80 (37.91)	676 (45.96)	545 (53.80)	246 (57.08)		
History of accidental injury												
No	171 (85.50)	1460 (86.75)	588 (87.11)	179 (87.75)	0.514	.916	197 (93.36)	1375 (93.47)	943 (93.09)	403 (93.50)	0.163	.983
Yes	29 (14.50)	223 (13.25)	87 (12.89)	25 (12.25)			14 (6.64)	96 (6.53)	70 (6.91)	28 (6.50)		
Taking physical exercises												
No physical exercise	121 (60.50)	1054 (62.63)	395 (58.52)	136 (66.67)	9.434	.151	142 (67.30)	877 (59.62)	589 (58.14)	274 (63.57)	11.109	.085
Less than regular physical exercises	41 (20.50)	307 (18.24)	147 (21.78)	27 (13.24)			36 (17.06)	300 (20.39)	207 (20.43)	68 (15.78)		
Regular physical exercises	38 (19.00)	322 (19.13)	133 (19.70)	41 (20.10)			33 (15.64)	294 (19.99)	217 (21.42)	89 (20.65)		
History of cardiovascular disease												
No	184 (92.00)	1566 (93.05)	592 (87.70)	172 (84.31)	29.015	.000	179 (84.83)	1315 (89.39)	858 (84.70)	362 (83.99)	16.249	.001
Yes	16 (8.00)	117 (6.95)	83 (12.30)	32 (15.69)			32 (15.17)	156 (10.61)	155 (15.30)	69 (16.01)		
Hepatitis history												
No	193 (96.50)	1616 (96.02)	648 (96.00)	194 (95.10)	0.559	.906	206 (97.63)	1419 (96.46)	975 (96.25)	416 (96.52)	0.985	.805
Yes	7 (3.50)	67 (3.98)	27 (4.00)	10 (4.90)			5 (2.37)	52 (3.54)	38 (3.75)	15 (3.48)		
History of antilipidemic medication												
No	198 (99.00)	1651 (98.10)	636 (94.22)	173 (84.80)	101.461	.000	208 (98.58)	1431 (97.28)	950 (93.78)	391 (90.72)	43.612	.000
Yes	2 (1.00)	32 (1.90)	39 (5.78)	31 (15.20)			3 (1.42)	40 (2.72)	63 (6.22)	40 (9.28)		
CRP (mg/L)	3.62 ± 7.76	2.67 ± 6.98	2.64 ± 7.37	2.99 ± 4.97		.556*	2.04 ± 5.52	1.94 ± 5.59	2.30 ± 4.48	3.21 ± 6.11		.000*
LDL-C (mg/dL)	105.52 ± 32.73	110.76 ± 33.38	118.21 ± 35.08	117.09 ± 40.79		.000*	111.71 ± 29.84	119.67 ± 33.92	122.7 ± 36.00	123.43 ± 37.61		.000*
HDL-C (mg/dL)	57.89 ± 16.87	53.83 ± 16.41	45.73 ± 13.82	39.90 ± 11.92		.000*	60.90 ± 16.20	54.90 ± 14.45	48.62 ± 12.92	45.29 ± 11.17		.000*
TG (mg/dL)	90.78 ± 52.97	108.74 ± 79.61	147.69 ± 118.86	198.65 ± 183.51		.000*	101.62 ± 51.13	121.73 ± 81.68	147.24 ± 95.47	170.07 ± 123.70		.000*
BMI (kg/m^2)	17.35 ± 0.92	21.36 ± 1.50	25.68 ± 1.13	30.35 ± 3.15		.000*	17.30 ± 1.27	21.60 ± 1.48	25.75 ± 1.14	30.56 ± 3.42		.000*
SUA (mg/dL)	4.44 ± 1.05	4.75 ± 1.16	5.06 ± 1.21	5.20 ± 1.20		.000*	3.61 ± 0.92	3.80 ± 0.96	4.03 ± 0.98	4.32 ± 1.08		.000*
SBP (mm Hg)	122.97 ± 19.73	126.51 ± 19.53	133.74 ± 19.74	139.37 ± 20.76		.000*	126.67 ± 24.15	127.94 ± 24.8	131.89 ± 26.10	137.01 ± 30.12		.000*
DBP (mm Hg)	72.11 ± 11.55	74.62 ± 12.6	79.89 ± 13.18	84.27 ± 12.70		.000*	72.02 ± 12.56	74.16 ± 12.21	77.83 ± 12.07	81.00 ± 12.35		.000*

BMI = body mass index, CRP = C-reactive protein, DBP = diastolic blood pressure, SBP = systolic blood pressure, SUA = serum uric acid, TG = triglycerides.

* *P* for trend.

associated with SBP and DBP in both males and females with BMI <24 kg/m^2. In females with BMI ≥24.0 kg/m^2, SUA levels were positively correlated with DBP, but not with SBP.

Although previous studies[39,40,48] have explored the individual and combined analysis between BMI and SUA levels and BP, there are no consistent results. Lee et al[48] found that SUA levels were positively associated with SBP and DBP in males aged <40 years after adjustment for age, diabetes, dyslipidemia, BMI, and eGFR; however, no significant associations were found in males aged 60 years or older. Lyngdoh et al,[39] using 549 individuals aged 19 to 20 years, found that SUA levels tended to be positively associated with DBP and SBP in males, while the strength of the SUA-BP association was similar in females. Kawamoto et al[40] found that increased SUA levels were positively associated with SBP and DBP in participants with BMI <21.0 kg/m^2, while there was a negative association between SUA levels, SBP and DBP in those with BMI ≥ 21.0 kg/m^2, in whom the interaction between BMI and SUA levels was a significant and independent determinant for both SBP and DBP. However, since the sample size was relatively small, and individuals were not randomly selected, the analyses did not rely on gender (it was included the men). In our study, participants were divided into four categories according to the BMI. SUA levels positively correlated with both SBP and DBP in males with BMI <24.0 kg/m^2. Among females, the SUA levels significantly correlated with SBP and DBP in participants with BMI <24.0 kg/m^2 and positively correlated with DBP in those with BMI ≥24.0 kg/m^2. However, no correlation was found between SBP and SUA levels in females

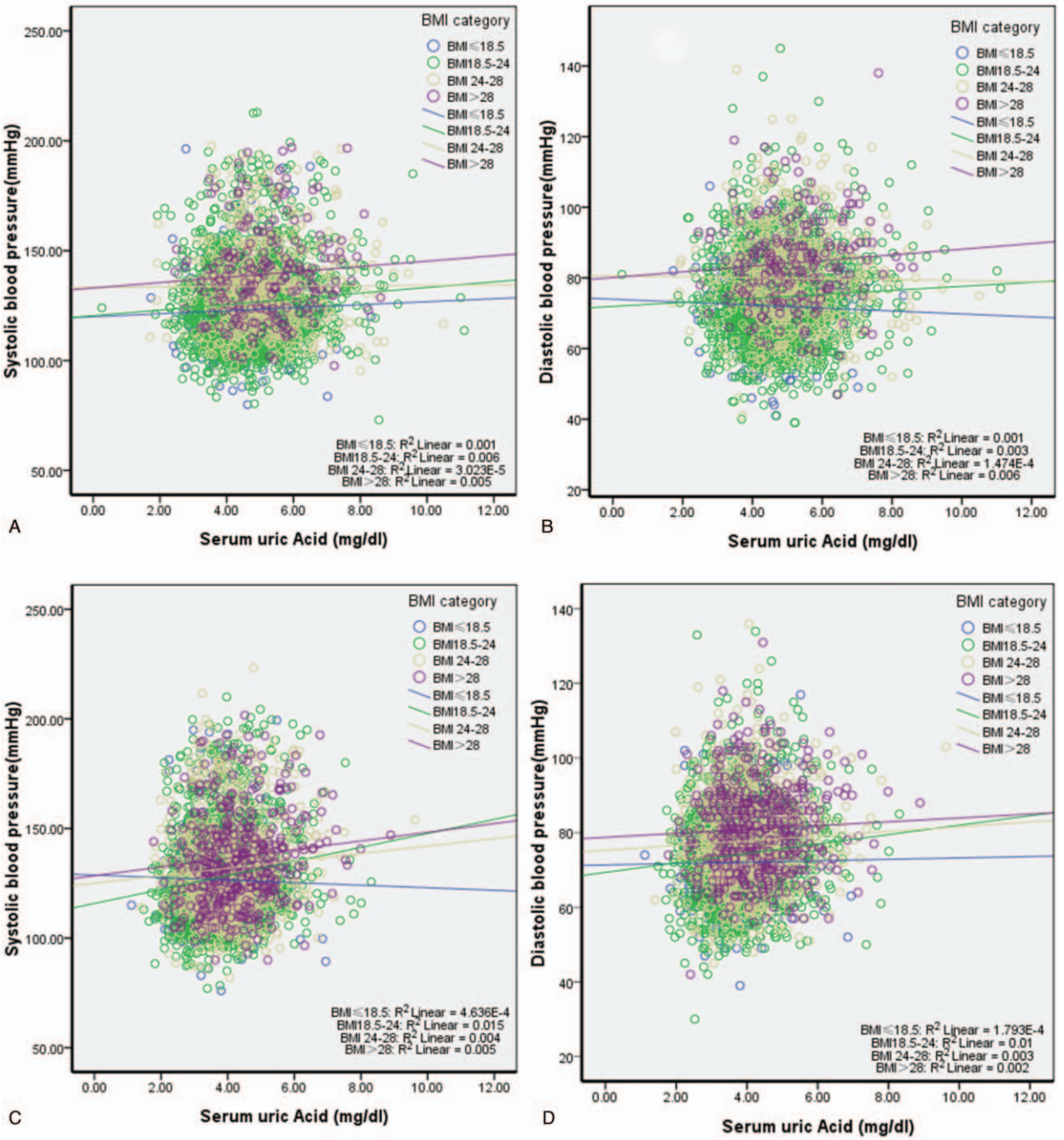

Figure 1. A, B, association between SUA and BP status of participants categorized by BMI in male. C, D, association between SUA and BP status of participants categorized by BMI in female. BMI = body mass index, BP = blood pressure, SUA = serum uric acid.

with BMI ≥24.0 kg/m^2. In addition, multiple linear regression analysis showed that the SUA levels were significantly and positively associated with SBP in both males and females with BMI <24.0 kg/m^2, and with DBP in females with BMI <24.0 kg/m^2, regardless of other confounding factors. In contrast, no effects of the interaction between BMI and SUA levels on BP were observed in both males and females, although their independent effects on BP were observed. The mechanisms that lead to hypertension in individuals with high BMI or SUA levels are not completely understood.[40] Choi et al[57] reported that high SUA levels induced endothelial dysfunction through vascular resistance in insulin-induced NO production, potentially leading to hypertension. Maxwell et al[58] suggested that the association of high SUA levels with CVD may be a consequence of impaired NO activity in the blood vessels. Papezikova et al[59] demonstrated that high SUA levels lead to a decreased NO bioavailability through multiple mechanisms. These studies may provide insights on the pathogenic mechanism by which SUA induces hypertension. Moreover, SUA is significantly associated with inflammation,[60–62] insulin resistance,[63–65] oxidative stress[66–68] and

Table 2

Baseline of demographic variables of participants categorized by BMI and BP in male (N = 2762) and female (N = 3126).

	Male (N = 2762)								Female (N = 3126)							
BMI<24 (n = 1883)					BMI≥24 (n = 879)				BMI<24 (n = 1682)				BMI ≥24 (n = 1444)			
Variables	Normotension	Hypertension	t/χ^2	*P*	Normotension	Hypertension	t/χ^2	*P*	Normotension	Hypertension	t/χ^2	*P*	Normotension	Hypertension	t/χ^2	*P*
Age, yr	60.12 ± 9.24	63.7 ± 8.83	−7.160	.000	57.73 ± 8.35	59.4 ± 8.43	−2.878	.004	58.31 ± 9.04	64.29 ± 9.89	−11.494	.000	55.83 ± 7.94	60.11 ± 9.58	−9.062	.000
Educational levels																
Illiterate	216 (14.93)	84 (19.27)	9.716	.021	47 (8.74)	29 (8.50)	1.667	.644	557 (44.35)	244 (57.28)	26.855	.000	311 (33.44)	228 (44.36)	20.219	.000
Less than elementary school	1065 (73.60)	316 (72.48)			403 (74.91)	250 (73.31)			612 (48.73)	171 (40.14)			517 (55.59)	251 (48.83)		
High school	121 (8.36)	21 (4.82)			60 (11.15)	37 (10.85)			61 (4.86)	9 (2.11)			73 (7.85)	22 (4.28)		
Above vocational school	45 (3.11)	15 (3.44)			28 (5.20)	25 (7.33)			26 (2.07)	2 (0.47)			29 (3.12)	13 (2.53)		
Marital status																
Single	142 (9.81)	78 (17.89)	21.181	.000	23 (4.28)	24 (7.04)	3.148	.076	184 (14.65)	119 (27.93)	38.011	.000	92 (9.89)	83 (16.15)	12.162	.000
Married	1305 (90.19)	358 (82.11)			515 (95.72)	317 (92.96)			1072 (85.35)	307 (72.07)			838 (90.11)	431 (83.85)		
Place of residence																
Rural	1057 (73.05)	302 (69.27)	2.386	.122	308 (57.25)	201 (58.94)	0.246	.620	850 (67.68)	291 (68.31)	0.059	.809	558 (60.00)	306 (59.53)	0.030	.862
Urban	390 (26.95)	134 (30.73)			230 (42.75)	140 (41.06)			406 (32.32)	135 (31.69)			372 (40.00)	208 (40.47)		
Cigarette smoking																
NO	313 (21.63)	86 (19.72)	0.991	.609	166 (30.86)	108 (31.67)	0.441	.802	1150 (91.56)	379 (88.97)	2.589	.274	878 (94.41)	479 (93.19)	0.951	.622
Former smoke	194 (13.41)	64 (14.68)			119 (22.12)	69 (20.23)			29 (2.31)	13 (3.05)			12 (1.29)	9 (1.75)		
Current smoke	940 (64.96)	286 (65.60)			253 (47.03)	164 (48.09)			77 (6.13)	34 (7.98)			40 (4.30)	26 (5.06)		
Alcohol consumption																
NO	631 (43.61)	179 (41.06)	0.904	.636	231 (42.94)	158 (46.33)	1.066	.587	1086 (86.46)	380 (89.20)	3.218	.200	810 (87.10)	465 (90.47)	3.686	.158
Less than once a mo	155 (10.71)	48 (11.01)			57 (10.59)	36 (10.56)			63 (5.02)	13 (3.05)			54 (5.81)	23 (4.47)		
More than once a mo	661 (45.68)	209 (47.94)			250 (46.47)	147 (43.11)			107 (8.52)	33 (7.75)			66 (7.10)	26 (5.06)		
Eating habit																
≤2 meals per d	205 (14.17)	78 (17.89)	4.090	.129	59 (10.97)	40 (11.73)	0.750	.687	181 (14.41)	83 (19.48)	6.382	.041	110 (11.83)	62 (12.06)	0.718	.698
3 meals per day	1218 (84.17)	349 (80.05)			473 (87.92)	299 (87.68)			1057 (84.16)	336 (78.87)			813 (87.42)	450 (87.55)		
≥4 meals per d	24 (1.66)	9 (2.06)			6 (1.12)	2 (0.59)			18 (1.43)	7 (1.64)			7 (0.75)	2 (0.39)		
Social events																
No	727 (50.24)	234 (53.67)	1.575	.209	232 (43.12)	164 (48.09)	2.084	.149	671 (53.42)	255 (59.86)	5.324	.021	425 (45.70)	228 (44.36)	0.240	.624
Yes	720 (49.76)	202 (46.33)			306 (56.88)	177 (51.91)			585 (46.58)	171 (40.14)			505 (54.30)	286 (55.64)		
History of accidental injury																
No	1244 (85.97)	387 (88.76)	2.251	.134	460 (85.50)	307 (90.03)	3.848	.050	1170 (93.15)	402 (94.37)	0.766	.381	858 (92.26)	488 (94.94)	3.768	.052
Yes	203 (14.03)	49 (11.24)			78 (14.50)	34 (9.97)			86 (6.85)	24 (5.63)			72 (7.74)	26 (5.06)		
Taking physical exercises																
No physical exercise	907 (62.68)	268 (61.47)	0.421	.810	316 (58.74)	215 (63.05)	2.378	.301	738 (58.76)	281 (65.96)	6.922	.031	551 (59.25)	312 (60.70)	2.410	.300
Less than regular physical exercises	268 (18.52)	80 (18.35)			115 (21.38)	59 (17.30)			263 (20.94)	73 (17.14)			171 (18.39)	104 (20.23)		
Regular physical exercises	272 (18.80)	88 (20.18)			107 (19.89)	67 (19.65)			255 (20.30)	72 (16.90)			208 (22.37)	98 (19.07)		
History of cardiovascular disease																
No	1354 (93.57)	396 (90.83)	3.852	.050	478 (88.85)	286 (83.87)	4.546	.033	1126 (89.65)	368 (86.38)	3.415	.065	799 (85.91)	421 (81.91)	4.056	.044
Yes	93 (6.43)	40 (9.17)			60 (11.15)	55 (16.13)			130 (10.35)	58 (13.62)			131 (14.09)	93 (18.09)		
Hepatitis history																
No	1386 (95.78)	423 (97.02)	1.351	.245	516 (95.91)	326 (95.60)	0.050	.824	1214 (96.66)	411 (96.48)	0.031	.861	891 (95.81)	500 (97.28)	2.023	.155
Yes	61 (4.22)	13 (2.98)			22 (4.09)	15 (4.40)			42 (3.34)	15 (3.52)			39 (4.19)	14 (2.72)		
History of antilipidemic medication																
No	1426 (98.55)	423 (97.02)	4.426	.035	498 (92.57)	311 (91.20)	0.529	.467	1227 (97.69)	412 (96.71)	1.220	.269	881 (94.73)	460 (89.49)	13.706	.000
Yes	21 (1.45)	13 (2.98)			40 (7.43)	30 (8.80)			29 (2.31)	14 (3.29)			49 (5.27)	54 (10.51)		
CRP (mg/L)	2.74 ± 7.19	2.86 ± 6.74	−0.299	.765	2.73 ± 7.82	2.71 ± 5.19	0.042	.966	1.69 ± 4.07	2.72 ± 8.60	−3.289	.001	2.27 ± 4.76	3.09 ± 5.51	−2.935	.003
LDL-C (mg/dL)	109.18 ± 32.99	113.7 ± 34.16	−2.482	.013	117.78 ± 35.70	118.17 ± 37.78	−0.155	.877	118.34 ± 32.24	119.62 ± 36.65	−0.680	.497	121.89 ± 34.20	125.02 ± 40.41	−1.552	.121
HDL-C (mg/dL)	54.02 ± 16.42	55.27 ± 16.84	−1.376	.169	44.46 ± 13.35	44.07 ± 13.94	0.412	.681	55.96 ± 14.62	54.69 ± 15.18	1.527	.127	47.87 ± 12.24	47.11 ± 12.85	1.109	.268
TG (mg/dL)	105.74 ± 80.01	109.79 ± 68.67	−0.955	.340	156.51 ± 129.6	165.08 ± 151.52	−0.891	.373	115.52 ± 74.79	129.98 ± 88.07	−3.283	.001	143.47 ± 85.67	172.10 ± 129.47	−5.021	.000
BMI (kg/m2)	20.88 ± 1.92	21.12 ± 1.85	−2.353	.019	26.57 ± 2.75	27.02 ± 2.39	−2.493	.013	21.06 ± 2.03	21.10 ± 2.03	−0.375	.708	26.96 ± 2.94	27.59 ± 3.19	−3.777	.000
SUA (mg/dL)	4.67 ± 1.14	4.84 ± 1.20	−2.594	.010	5.04 ± 1.20	5.15 ± 1.20	−1.348	.178	3.72 ± 0.96	3.91 ± 0.95	−3.461	.001	4.04 ± 0.94	4.25 ± 1.13	−3.717	.000
SBP (mm Hg)	117.96 ± 11.5	153.06 ± 16.28	−50.218	.000	122.73 ± 10.51	154.31 ± 15.98	−35.197	.000	117.19 ± 12.05	158.84 ± 26.12	−44.082	.000	120.05 ± 11.18	157.48 ± 31.38	−32.620	.000
DBP (mm Hg)	70.21 ± 9.25	87.97 ± 12.17	−32.469	.000	74.12 ± 8.94	91.49 ± 11.72	−24.741	.000	69.77 ± 9.05	85.95 ± 12.33	−28.843	.000	73.16 ± 8.70	88.8 ± 11.24	−29.318	.000

BMI = body mass index, CRP = C-reactive protein, DBP = diastolic blood pressure, SBP = systolic blood pressure, SUA = serum uric acid, TG = triglycerides.

Table 3

Age-adjusted association between baseline of demographic variables and BP of participants categorized by BMI in male (N = 2762) and female (N = 3126).

	Male (N = 2762)				Female (N = 3126)			
	BMI < 24 (n = 1883)		BMI ≥ 24 (n = 879)		BMI < 24 (n = 1682)		BMI ≥ 24 (n = 1444)	
Variables	SBP partial r (*P*-value)	DBP partial r (*P*-value)	SBP partial r (*P*-value)	DBP partial r (*P*-value)	SBP partial r (*P*-value)	DBP partial r (*P*-value)	SBP partial r (*P*-value)	DBP partial r (*P*-value)
Educational levels	−.026 (.259)	.018 (.437)	.003 (.931)	.017 (.616)	−.046 (.060)	−.034 (.170)	−.027 (.303)	−.030 (.254)
Marital status	−.102 (.000)	−.086 (.000)	−.080 (.018)	−.065 (.056)	−.054 (.029)	−.031 (.214)	−.058 (.030)	.003 (.908)
Place of residence	.030 (.195)	.060 (.010)	.009 (.801)	.029 (.402)	.019 (.441)	.011 (.661)	.004 (.891)	−.017 (.512)
Cigarette smoking	.042 (.074)	.021 (.364)	.011 (.754)	−.030 (.375)	.014 (.567)	.026 (.293)	−.004 (.882)	.015 (.574)
Alcohol consumption	.050 (.033)	.068 (.003)	−.021 (.544)	−.007 (.841)	−.053 (.032)	−.027 (.283)	−.062 (.021)	−.088 (.001)
Eating habit	−.050 (.031)	−.047 (.043)	−.084 (.013)	−.082 (.016)	−.013 (.586)	−.056 (.024)	−.014 (.597)	−.045 (.088)
Social events	−.019 (.407)	−.009 (.689)	−.102 (.003)	−.037 (.275)	−.046 (.065)	−.049 (.048)	.050 (.059)	.030 (.253)
History of accidental injury	−.015 (.523)	−.035 (.133)	−.092 (.007)	−.069 (.042)	−.032 (.200)	−.008 (.736)	−.017 (.514)	−.003 (.922)
Taking physical exercises	.020 (.400)	−.004 (.870)	−.008 (.812)	−.030 (.376)	−.014 (.575)	−.007 (.774)	−.028 (.285)	−.007 (.804)
History of cardiovascular disease	.041 (.079)	.024 (.294)	.052 (.126)	.079 (.021)	.022 (.365)	.018 (.466)	.008 (.767)	.036 (.172)
Hepatitis history	−.021 (.377)	−.028 (.226)	−.037 (.283)	−.005 (.872)	−.021 (.402)	−.019 (.451)	−.006 (.829)	−.057 (.033)
History of antilipidemic medication	.037 (.115)	.057 (.014)	.015 (.669)	.019 (.581)	.013 (.589)	.049 (.045)	.027 (.306)	.071 (.008)
CRP (mg/l)	−.006 (.789)	−.014 (.539)	.000 (.991)	−.003 (.928)	.037 (.134)	.019 (.446)	.011 (.682)	−.013 (.627)
LDL-C (mg/dl)	.069 (.003)	.058 (.012)	.028 (.406)	.017 (.625)	−.007 (.786)	.020 (.414)	.019 (.486)	.027 (.307)
HDL-C (mg/dl)	.013 (.580)	.004 (.862)	−.009 (.790)	.007 (.828)	−.055 (.026)	−.050 (.045)	−.020 (.447)	−.051 (.055)
TG (mg/dl)	.060 (.010)	.057 (.015)	.063 (.063)	.078 (.022)	.102 (.000)	.091 (.000)	.054 (.041)	.114 (.000)
BMI (kg/m^2)	.131 (.000)	.105 (.000)	.104 (.002)	.129 (.000)	.107 (.000)	.109 (.000)	.103 (.000)	.140 (.000)
SUA (mg/dl)	.079 (.001)	.051 (.030)	.022 (.519)	.016 (.629)	.096 (.000)	.096 (.000)	.041 (.125)	.064 (.016)

BMI = body mass index, CRP = C-reactive protein, DBP = diastolic blood pressure, SBP = systolic blood pressure, SUA = serum uric acid, TG = triglycerides.

Table 4

Multivariate-adjusted association between baseline of demographic variables and BP of participants categorized by BMI in male (N = 2762) and female (N = 3126).

	Male (N = 2762)				Female (N = 3126)			
	BMI < 24 (n = 1883)		BMI ≥ 24 (n = 879)		BMI < 24 (n = 1682)		BMI ≥ 24 (n = 1444)	
Variables	SBP β (*P*-value)	DBP β (*P*-value)	SBP β (*P*-value)	DBP β (*P*-value)	SBP β (*P*-value)	DBP β (*P*-value)	SBP β (*P*-value)	DBP β (*P*-value)
Age, yr	.204 (.000)	−.056 (.025)	.139 (.000)	−.142 (.000)	.238 (.000)	—	.224 (.000)	—
Educational levels	—	—	—	—	−.054 (.041)	—	—	—
Marital status	−.100 (.000)	−.091 (.000)	−.072 (.033)	—	−.064 (.014)	—	—	—
Place of residence	—	.060 (.011)	—	—	—	—	—	—
Cigarette smoking	.058 (.013)	—	—	—	—	—	—	—
Alcohol consumption	—	.056 (.021)	—	—	−.047 (.047)	—	−.054 (.037)	−.082 (.002)
Eating habit	—	—	−.083 (.013)	−.091 (.007)	—	−.057 (.022)	—	—
Social events	—	—	−.099 (.004)	—	−.056 (.018)	−.056 (.025)	—	—
History of accidental injury	—	—	−.077 (.021)	—	—	—	—	—
Taking physical exercises	—	—	—	—	—	—	—	—
History of cardiovascular disease	−.046 (.047)	—	—	—	—	—	—	—
Hepatitis history	—	—	—	—	—	—	—	−.065 (.014)
History of antilipidemic medication	—	.046 (.049)	—	—	—	—	—	—
CRP (mg/L)	—	—	.100 (.004)	—	—	—	—	—
LDL-C (mg/dL)	.065 (.004)	.056 (.017)	—	—	—	—	—	—
HDL-C (mg/dL)	.051 (.043)	—	—	.082 (.037)	—	—	—	—
TG (mg/dL)	.055 (.028)	—	—	.094 (.020)	.080 (.004)	.066 (.021)	—	.113 (.000)
BMI (kg/m^2)	.123 (.000)	.089 (.000)	.086 (.012)	.116 (.001)	.098 (.000)	.103 (.000)	.092 (.000)	.127 (.000)
SUA (mg/dL)	.054 (.021)	—	—	—	.064 (.009)	.075 (.003)	—	—
R^2	.080 (.000)	.035 (.025)	.064 (.000)	.048 (.000)	.104 (.000)	.026 (.000))	.080 (.000)	.031 (.000)

BMI = body mass index, CRP = C-reactive protein, DBP = diastolic blood pressure, HDL-C = high density lipoprotein cholesterol, LDL-C = low density lipoprotein cholesterol, SBP = systolic blood pressure, SUA = serum uric acid, TG = triglycerides.

Table 5

Interaction between BMI and SUA on BP in male and female (N = 5888).

Characteristics	Male (n = 2762)		Female (n = 3126)	
	SBP β (*P*-value)	DBP β (*P*-value)	SBP β (*P*-value)	DBP β (*P*-value)
Age, yr	.377 (0.000)	−.126 (.000)	.651 (.000)	
Educational levels	6.276 (0.000)		−1.466 (.037)	
Marital status		−3.647 (.000)	−4.273 (.002)	
Place of residence		1.588 (.002)		
Cigarette smoking	.778 (0.081)			
Alcohol consumption		.557 (.034)	−2.440 (.003)	−2.326 (.006)
Eating habit	−2.619 (0.009)	−1.935 (.003)		−1.429 (.263)
Social events	−1.759 (0.018)		−0.267 (.769)	−0.825 (.381)
History of accidental injury	−2.165 (0.046)			
History of cardiovascular disease	2.932 (0.025)			
Hepatitis history				−0.391 (.877)
History of antilipidemic medication		2.304 (.074)		
CRP (mg/L)		−0.012 (.720)		
LDL-C (mg/dL)	.040 (0.000)			
HDL-C (mg/dL)	.040 (0.116)	0.024 (.157)		
TG (mg/dL)	.017 (0.000)	0.009 (.001)	.021 (.000)	.025 (.000)
BMI (0= <24kg/m^2,1=≥24 kg/m^2)	−8.382 (0.013)	−3.481 (.117)	−9.548 (.057)	−7.243 (.167)
SUA (0= ≤7mg/dL in men and ≤6 mg/dL in women, 1= >7mg/dL in men and >6 mg/dL in women)	−1.381 (0.587)	0.077 (.963)	−5.832 (.063)	−7.485 (.023)
BMI* SUA	−1.404 (0.686)	−2.544 (.263)	2.853 (.575)	2.619 (.622)

BMI = body mass index, CRP = C-reactive protein, DBP = diastolic blood pressure, HDL-C = high density lipoprotein cholesterol, LDL-C = low density lipoprotein cholesterol, SBP = systolic blood pressure, SUA = serum uric acid, TG = triglycerides.

other risk factors for CVD, such as BMI, total cholesterol, HDL-C, blood pressure, TG, and fasting plasma glucose.[40] Risk factors associated with hypertension may lead to decreased vasomotor reactivity, endothelial dysfunction, and arterial stiffness,[40] ultimately causing hypertension. Our study suggests that SUA may play an important role in hypertension, and gender-specific factors may also be crucial. The SUA levels were higher in males than in females, which can partially explain the underlying mechanisms that possibly account for gender differences, such as alcohol consumption, whose prevalence is usually higher in males. Additionally, body fat and steroid hormones, and their interaction in middle-aged and older adults may also be associated with hypertension. Middle-aged and older females with higher BMI have higher concentrations of estrogen in blood, which may result in a strong protective effect against hypertension.

There are several strengths and limitations in our study. The individual and combined effects of BMI and SUA level and BP is unclear. In addition, we only considered the above mentioned confounders, and other unknown confounders are likely to exist. The relationship should be studied prospectively; however, this was a cross-sectional study including middle-aged and elderly participants. Follow-up was relatively short to comprehensively observe changes in the next phase. Our results contradict the results of a Japanese study that found an association between BMI and SUA in community-dwelling male individuals[40]; however, no interaction between BMI, SUA, and BP was observed either in males or females. In summary, our findings are unique, especially because we evaluated the association between SUA and BP in different BMI groups, where individuals were classified as obese, overweight, normal weight, and underweight, as defined by the Chinese criteria.[50] The BMI cut-off values of the Chinese population are lower than those of western populations, but higher than those of most Asian populations.[69]

5. Conclusions

No interaction between BMI, SUA levels, and BP was observed in either males or females; However, BMI was independently associated with BP both in male and female, SUA independently associated with SBP both in males and females with BMI <24.0 kg/m^2, and SUA independently associated with DBP in females with BMI ≥24.0 kg/m^2.

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Author contributions

Conceptualization: Lin Zhang.
Formal analysis: Lin Zhang.
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