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ORIGINAL ARTICLE

# Synergistic influence of age and serum uric acid on blood pressure among community-dwelling Japanese women

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**Serum uric acid (SUA) levels are strongly correlated with aging, gender, renal function, obesity, and metabolic abnormality; however, whether SUA has a causative role in elevated blood pressure (BP) is still a matter of debate. From a single community, we recruited 1177 eligible women (mean age, 61 ± 13 years) during their annual health examination. All subjects were divided into two groups according to their age (participants aged ⩾55 years and those aged <55 years). We investigated whether age and SUA are synergistically associated with BP, independent of confounding factors. Of these subjects, SUA significantly correlated with both systolic BP (SBP; $r=0.236$, $P<0.001$) and diastolic BP (DBP; $r=0.263$, $P<0.001$) in female participants aged <55 years but not in those aged ⩾55 years. The interaction between age and SUA on BP as well as age and body mass index, triglycerides, high-density lipoprotein cholesterol, fasting plasma glucose, prevalence of antidiabetic medication and SUA was a significant and independent determinant of both SBP ($\beta=-0.106$, $P=0.011$) and DBP ($\beta=-0.070$, $P=0.003$). In participants aged <55 years, the multivariate-adjusted odds ratio (95% confidence interval) for hypertension was 3.03 (1.13–8.11) for the highest tertile (4.8–10.8 mg dl$^{-1}$) of SUA compared with the lowest tertile (0.7–3.8 mg dl$^{-1}$) but was not significant in those aged ⩾55 years. These results suggested that age and SUA have a synergistic effect on BP status in community-dwelling women, independent of conventional cardiovascular risk factors.**
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**Keywords:** age; blood pressure; hypertension; interaction; uric acid

## INTRODUCTION

Hypertension or high blood pressure (BP) is likely the most common disease worldwide and is one of the risk factors for various cardiovascular diseases (CVDs). Moderate elevation of BP leads to shortened life expectancy, and it has been reported that an increased risk of CVD mortality is present in persons with BP levels as low as 115 mm Hg systolic BP (SBP) and 75 mm Hg diastolic BP (DBP). This risk increases steadily with a rise in BP.[1] In the guideline of the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High BP (JNC-7) in 2003, individuals with an SBP between 120 and 139 mm Hg and/or a DBP between 80 and 89 mm Hg were considered as having prehypertension.[2] Prehypertension frequently progresses to clinical hypertension over several years, especially in older adults,[3] and is associated with an increased risk of major CVD events, thus lifestyle changes and/or medical treatment are recommended for individuals with prehypertension.[1]

A number of experimental and epidemiological studies have demonstrated that increased serum uric acid (SUA) in humans is also associated with systemic inflammation,[4] endothelial dysfunction,[5] hypertension[6] and CVD morbidity and mortality,[2,7,8] although the results are not consistent.[9] SUA levels are strongly correlated with aging, gender, renal function, obesity and metabolic abnormality, and whether SUA has a causative role in elevated BP is still a matter of debate. SUA is more strongly associated with metabolic syndrome in women than in men.[10] However, there are few reports on the relationship between elevated BP and the combination of age and UA level in Japanese women.

The aim of this study was to determine whether aging and SUA are synergistically associated with BP by examining cross-sectional data from community-dwelling Japanese women.

## MATERIALS AND METHODS

### Subjects

Subjects were selected through a community-based annual check-up process in a rural town located in Ehime prefecture, Japan. Information on medical history, present conditions and drugs was obtained by interviewing the subjects. Other characteristics, such as smoking and alcohol habits, and

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medications, were investigated by individual interviews using a structured questionnaire. Subjects taking medications for hypertension and hyperuricemia were excluded. The final study sample consisted of 1177 eligible persons. The Ethics Committee of Ehime University School of Medicine approved all the procedures, and each subject gave informed consent to participate.

### Evaluation of risk factors

Information on demographic characteristics and risk factors was collected using clinical files. Body mass index (BMI) was calculated by dividing weight (in kilograms) by the square of the height (in meters). We measured BP in the right upper arm of participants in the sedentary position using an automatic oscillometric BP recorder (BP-103i; Colin, Aichi, Japan) while they were seated after having rested for at least 5 min. Appropriate cuff bladder size was determined at each visit based on arm circumference. Normotension was defined as SBP $<120$ mm Hg and DBP $<80$ mm Hg. Prehypertension was defined as SBP of 120–139 mm Hg and/or DBP of 80–89 mm Hg. Hypertension was defined as SBP $\geqslant 140$ mm Hg and/or DBP $\geqslant 90$ mm Hg.[2] Cigarette smoking was quantified based on daily consumption and the history of smoking: never-smoker, past-smoker, light smoker ($<30$ pack·year) and heavy smoker ($\geqslant 30$ pack·year). Daily alcohol consumption was measured using the Japanese liquor unit in which a unit corresponds to 22.9 g of ethanol, and the participants were classified into non-drinker, occasional drinkers ($<1$ unit day$^{-1}$) and daily drinkers ($\geqslant 1$ unit day$^{-1}$). Total cholesterol (T-C), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), fasting plasma glucose (FPG), creatinine (enzymatic method) and SUA were measured during fasting. The low-density lipoprotein cholesterol (LDL-C) concentration was calculated by the Friedewald formula.[11] Participants with TG levels $\geqslant 400$ mg dl$^{-1}$ were excluded. Estimated glomerular filtration rate (eGFR) was calculated using the following equation: $eGFR = 194 \times Cr^{-1.094} \times age^{-0.287} \times 0.739$ (if female).[12] Participants with an eGFR $<30$ ml min$^{-1}$ 1.73 m$^{-2}$ were excluded.

**Table 1 Characteristics of female participants categorized by age**

| *Characteristics* N = *1177* | *Age < 55 years* N = *351* | *Age ⩾ 55 years* N = *826* | P-*value*[a] |
|---|---|---|---|
| Age (years) | 45 ± 8 | 67 ± 7 | <0.001 |
| Body mass index (BMI; kg m$^{-2}$) | 22.7 ± 3.5 | 23.0 ± 3.1 | 0.093 |
| Obesity, BMI ⩾ 25 kg m$^{-2}$, *N* (%) | 75 (21.4) | 206 (24.9) | 0.204 |
| Smoking status (%) | 93.2/1.7/5.1/0 | 98.2/0.5/1.2/0.1 | <0.001 |
| Drinking status (%) | 41.9/47.9/10.3 | 70.7/24.9/4.4 | <0.001 |
| History of CVD, *N* (%) | 1 (0.3) | 54 (6.5) | <0.001 |
| SBP (mm Hg) | 121 ± 17 | 137 ± 21 | <0.001 |
| DBP (mm Hg) | 73 ± 11 | 79 ± 11 | <0.001 |
| Triglycerides (mg dl$^{-1}$) | 75 (55–105) | 94 (71–128) | <0.001 |
| HDL cholesterol (mg dl$^{-1}$) | 66 ± 15 | 63 ± 15 | 0.008 |
| LDL cholesterol (mg dl$^{-1}$) | 112 ± 30 | 127 ± 30 | <0.001 |
| Lipid-lowering medication, *N* (%) | 3 (0.9) | 60 (7.3) | <0.001 |
| Fasting plasma glucose (mg dl$^{-1}$) | 88 (83–94) | 93 (88–100) | <0.001 |
| Antidiabetic medication, *N* (%) | 5 (1.4) | 30 (3.6) | 0.040 |
| eGFR (ml min$^{-1}$ 1.73 m$^{-2}$) | 91.4 ± 17.0 | 78.5 ± 16.7 | <0.001 |
| Serum uric acid (mg dl$^{-1}$) | 4.2 ± 0.9 | 4.4 ± 1.1 | 0.003 |

Abbreviations: CVD, cardiovascular disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure.
Data presented as mean ± s.d. Body mass index was calculated using weight in kilograms divided by the square of the height in meters. Smoking status (never-smoker, past-smoker, light smoker ($<30$ pack·year) and heavy smoker ($\geqslant 30$ pack·year)). Drinking status (non-drinker, occasional drinker (1–6 days week$^{-1}$) and daily drinker ($\geqslant 7$ days week$^{-1}$)).
$eGFR = 194 \times Cr^{-1.094} \times Age^{-0.287} \times 0.739$ (if female). Data for triglycerides and fasting plasma glucose were skewed, and are presented as median (interquartile range), and log-transformed for analysis.
[a]*P*-value: Student's *t*-test for continuous variables or the $\chi^2$-test for categorical variables.

### Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics Version 20 (Statistical Package for Social Science Japan, Tokyo, Japan). All values are expressed as mean ± s.d., unless otherwise specified. Data for TG and FPG were skewed and log-transformed for analysis. In the present study, we divided the participants into two groups based on an age of 55 years, which is equivalent to $\geqslant 95\%$ of age distribution at menopause in a similar investigation.[13] Differences based on BP status were analyzed by Student's *t*-test for continuous variables or $\chi^2$-test for categorical variables. Correlations between SUA and BP were determined using Pearson's correlation test. Multiple linear regression analysis was used to evaluate the contribution of risk factors for SBP or DBP, and analysis of covariance was performed with the use of a general linear model approach to determine the association between age and SUA on BP status. Logistic regression analyses were used to test significant determinants of prehypertension or hypertension status serving as the dichotomous outcome variable. A value of $P<0.05$ was considered significant.

## RESULTS

The characteristics of the study participants categorized by age are illustrated in Table 1. The study sample was 1177 women, aged 61 ± 13 (range 19–88) years. SBP, DBP, TG, LDL-C, prevalence

**Table 2 Relationship between various characteristics and blood pressure status of female participants categorized by age**

| | *SBP* | | *DBP* | |
|---|---|---|---|---|
| | *Age < 55 years* N = *351* | *Age ⩾ 55 years* N = *826* | *Age < 55 years* N = *351* | *Age ⩾ 55 years* N = *826* |
| *Characteristics* N = *1177* | *r* (P-*value*) | | | |
| Age (years) | 0.317 (<0.001) | 0.284 (<0.001) | 0.367 (<0.001) | 0.107 (0.002) |
| Body mass index (BMI) (kg m$^{-2}$) | 0.403 (<0.001) | 0.137 (<0.001) | 0.381 (<0.001) | 0.176 (0.001) |
| Obesity, BMI ⩾ 25 kg m$^{-2}$ (%) | 0.284 (<0.001) | 0.123 (<0.001) | 0.295 (<0.001) | 0.163 (<0.001) |
| Smoking status (%) | −0.069 (0.198) | −0.053 (0.130) | −0.108 (0.044) | −0.009 (0.794) |
| Drinking status (%) | −0.025 (0.641) | −0.131 (<0.001) | −0.036 (0.505) | −0.042 (0.233) |
| History of CVD, *N* (%) | 0.032 (0.550) | 0.057 (0.099) | 0.037 (0.488) | 0.016 (0.637) |
| Triglycerides (mg dl$^{-1}$) | 0.306 (<0.001) | 0.142 (<0.001) | 0.303 (<0.001) | 0.136 (<0.001) |
| HDL cholesterol (mg dl$^{-1}$) | −0.095 (0.076) | 0.006 (0.865) | −0.070 (0.192) | 0.001 (0.977) |
| LDL cholesterol (mg dl$^{-1}$) | 0.259 (<0.001) | −0.030 (0.385) | 0.348 (<0.001) | 0.010 (0.770) |
| Lipid-lowering medication, % | 0.090 (0.091) | 0.039 (0.264) | 0.051 (0.345) | 0.029 (0.408) |
| Fasting plasma glucose (mg dl$^{-1}$) | 0.237 (<0.001) | 0.154 (<0.001) | 0.195 (<0.001) | 0.080 (0.022) |
| Antidiabetic medication, *N* (%) | 0.022 (0.686) | −0.033 (0.346) | 0.006 (0.914) | −0.067 (0.056) |
| eGFR | −0.112 (0.036) | −0.056 (0.106) | −0.196 (<0.001) | −0.047 (0.174) |
| Serum uric acid (mg dl$^{-1}$) | 0.236 (<0.001) | −0.014 (0.684) | 0.263 (<0.001) | 0.021 (0.554) |

Abbreviations: CVD, cardiovascular disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure.
*r*, Pearson's correlation coefficient.
Data for triglycerides and fasting plasma glucose were skewed and log-transformed for analysis.

of lipid-lowering medication, FPG, SUA and history of CVD were significantly higher in participants aged ⩾55 years than in those aged <55 years; however, prevalence of smoking and drinking, HDL-C and eGFR were lower. There was no inter-group difference in BMI and prevalence of obesity.

Table 2 shows the relationship between participant characteristics and BP status. Pearson's correlation coefficient showed that SUA as well as age, BMI, prevalence of obesity, TG, LDL-C, FPG and eGFR correlated with both SBP and DBP in participants aged <55 years but not in those aged ⩾55 years.

In addition to their direct associations, we observed a synergistic effect between age and SUA on BP status in Figure 1. In participants aged <55 years, SUA was significantly correlated with both SBP ($r=0.236$, $P<0.001$) and DBP ($r=0.263$, $P<0.001$); however, in those aged ⩾55 years, SUA was significantly correlated with neither SBP ($r=-0.014$, $P=0.684$) nor DBP ($r=0.021$, $P=0.554$). Analysis of covariance showed that the two regression lines in each graph were significantly different ($F=12.78$, $P<0.001$ and $F=16.92$, $P<0.001$, respectively).

In Table 3, we assessed the statistical significance of the synergistic relationship using a general linear model with the following confounding factors: age, BMI, smoking status, drinking status, history of CVD, TG, HDL-C, LDL-C, prevalence of lipid-lowering medication, FPG, prevalence of antidiabetic medication, eGFR, SUA and the interaction between age and SUA. The interaction between age and SUA was a significant and independent determinant of both SBP ($\beta=-0.106$, $P=0.011$) and DBP ($\beta=-0.070$, $P=0.003$).

Table 4 shows the odds ratios (ORs) (95% confidence intervals (CIs)) of prehypertension and hypertension with higher SUA categories in participants aged <55 years and ⩾55 years. In participants aged <55 years, higher SUA categories were positively associated with hypertension. Compared with the lowest tertile (0.7–3.8 mg dl$^{-1}$) of SUA, the multivariate-adjusted OR (95% CI) for hypertension was 3.03 (1.13–8.11) for the highest tertile (4.8–10.8 mg dl$^{-1}$) but not significant in those aged ⩾55 years.

## DISCUSSION

In this cross-sectional, population-based study, we have confirmed the prevalence of prehypertension and hypertension, as defined by the JNC-7 criteria,[2] and their relationship to the SUA levels of female participants categorized by age. This study showed that prehypertension and hypertension are extremely common, affecting more than 33% and 47%, respectively, of female participants, and higher SUA levels significantly increased with both elevated SBP and DBP in female participants aged <55 years but not in those aged ⩾55 years. Moreover, we observed a synergistic effect between age and SUA on BP status, independent of confounding factors.

The link between hyperuricemia and hypertension has been reported in several studies. Among 9104 participants (54.5% women, age: 45–64 years) in the Atherosclerosis Risk in Communities study who were free of hypertension at baseline, a higher SUA was associated with a greater risk of hypertension in the overall cohort (hazard ratio (95% CI) for each s.d. of higher SUA: 1.10 (1.04–1.15) and in the subgroup analyses (black men: 1.32 (1.14–1.54); black women: 1.16 (1.03–1.31); white men: 1.01 (0.94–1.09); white women: 1.04 (0.96–1.11)).[6] In 2520 hypertension-free individuals (56.3% women, age: 43–84 years, 98% Caucasian) at baseline, multivariable relative risk (95% CI) of incident hypertension was 1.65 (1.41–1.93) for the highest quartile of SUA (⩾6.56 mg dl$^{-1}$) compared with the lowest quartile (⩽4.37 mg dl$^{-1}$).[14] Among 6036 adolescents aged 12–17 years in the National Health and Nutrition Examination Survey, in the analyses adjusted for age, gender, race/ethnicity and BMI percentile, the OR (95% CI) of elevated BP, which was defined as a SBP or DBP ⩾95th percentile for age, sex and height, was 1.38 (1.16–1.65) for participants with SUA levels ⩾5.5 mg dl$^{-1}$ compared with <5.5 mg dl$^{-1}$.[15] In 3329 participants in the Framingham Study (55.6% women, age: 48.7 ± 13.7 years) who were free of hypertension,

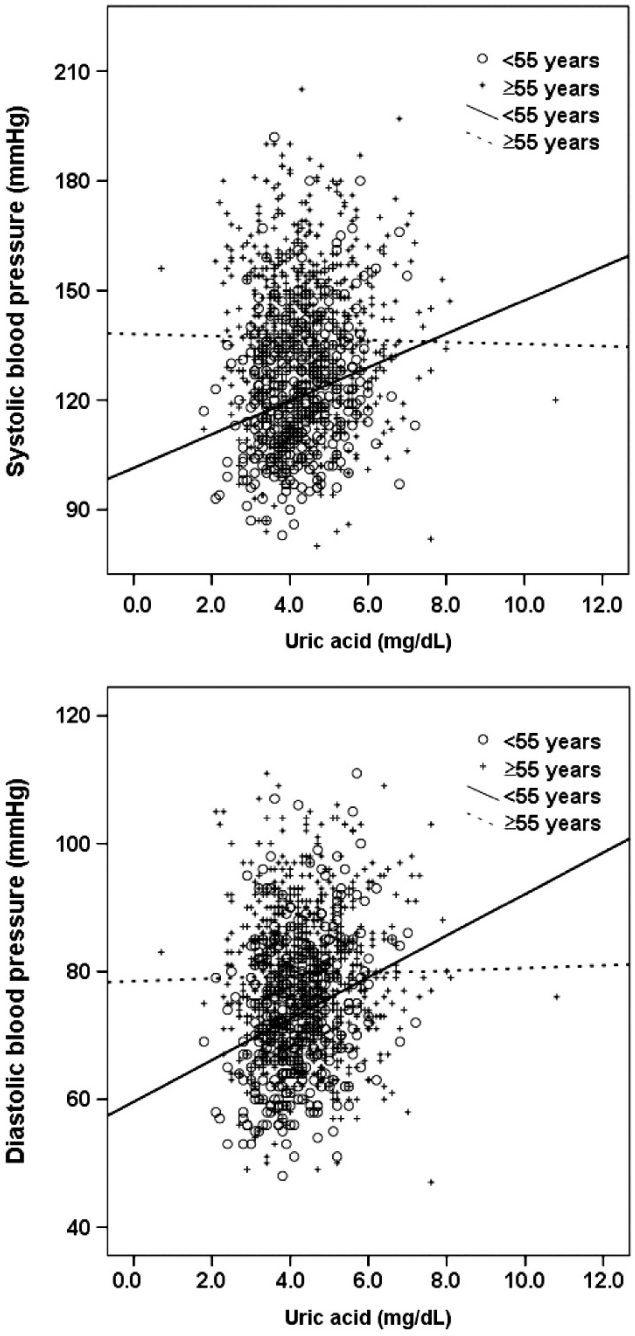


**Figure 1** Correlation between serum uric acid (SUA) and blood pressure status of female participants categorized by age. In participants aged <55 years, SUA was significantly correlated with both systolic blood pressure (SBP; $r=0.236$, $P<0.001$) and diastolic blood pressure (DBP; $r=0.263$, $P<0.001$) but not significantly correlated with SBP ($r=-0.014$, $P=0.684$) and DBP ($r=0.021$, $P=0.554$) in those aged ⩾55 years. Analysis of covariance showed that the two regression lines in each graph were significantly different ($F=12.78$, $P<0.001$ and $F=16.92$, $P<0.001$, respectively).

myocardial infarction, heart failure, renal failure or gout, each s.d. of SUA was associated with a multivariable-OR (95% CI) of 1.17 (1.02–1.33) for developing hypertension and 1.11 (1.01–1.23) for BP progression.[16] In the six-year follow-up of 3073 normotensive men (age: 35–57 years) with baseline hyperuricemia (SUA $>7.0\,mg\,dl^{-1}$) but without diabetes/glucose intolerance or metabolic syndrome from the Multiple Risk Factor Intervention Trial, normotensive men with baseline hyperuricemia had an 80% excess risk for incident hypertension (hazard ratio: 1.81; 95% CI: 1.59–2.07) compared with those without baseline hyperuricemia.[17] The magnitude of the risk, however, varied substantially because of the underlying heterogeneity in the study design, subject selection and the distribution of SUA.[17] Despite these and similar findings in cross-sectional and longitudinal studies, it was not clear whether the causative role of SUA can be inferred because of the possibility of the confounding factors (for example, age, drinking status, lipids, renal dysfunction, insulin resistance and diuretic use). As participants in these studies, as well as our study, were younger, the effect of hyperuricemia may be more pronounced in the younger subjects.[17]

The mechanisms that lead to elevated BP in individuals with hyperuricemia remains to be clarified. SUA reduces the levels of endothelial nitric oxide, which increases the blood flow to the skeletal muscles and enhances glucose uptake and is strongly associated with insulin action.[18] SUA alters the proliferation/migration and nitric oxide release of human vascular cells, mediated by the expression of C-reactive protein,[19] and it stimulates proliferation, angiotensin II production and oxidative stress in vascular smooth muscle cells through the tissue renin–angiotensin system.[20] Thus, hyperuricemia induces endothelial dysfunction; this may provide insight into a pathogenic mechanism by which SUA may induce hypertension and vascular disease.[21] We have previously demonstrated that SUA is also an independent determinant of insulin resistance, and combined assessment of SUA and high-sensitivity C-reactive protein levels provides incremental information for risk stratification of patients with metabolic syndrome in community-dwelling women.[22] Recent studies suggest that SUA levels are lower in premenopausal than in postmenopausal women because estrogenic compounds enhance the renal urate clearance[23] and are strongly associated with other cardiovascular risk factors such as age, gender, BMI, SBP, DBP, T-C, TG and FPG,[24,25] which have a causal role in the pathogenesis of CVD. In our study, the values of CVD risk factors in the younger participants aged $<55$ years were better than those in the older group (aged $\geqslant 55$ years), and the stronger association between SUA and BP among the younger group is consistent with previous cross-sectional studies.[26] A low prevalence of CVD risk factors, including renal dysfunction in younger participants, may explain the higher OR of increased SUA for hypertension in this group than among older participants.[26] Additionally, young adolescents with new-onset essential hypertension often have increased SUA levels,[27] and the strength of the relationship between SUA level and hypertension gradually decreases with increasing age and duration of hypertension,[28] suggesting that SUA may be more important in

**Table 3 Interaction between age and serum uric acid on blood pressure status**

| *Characteristics* | *SBP* | *DBP* |
|---|---|---|
| *N = 1177* | *β (P-value)* | |
| Age (years) | 1.078 (<0.001) | 0.506 (<0.001) |
| Body mass index ($kg\,m^{-2}$) | 1.248 (<0.001) | 0.731 (<0.001) |
| Smoking status (%) | −3.096 (0.340) | −2.679 (0.139) |
| Drinking status (%) | −1.912 (0.047) | −0.288 (0.592) |
| History of CVD, *N* (%) | 2.166 (0.402) | 0.450 (0.755) |
| Triglycerides ($mg\,dl^{-1}$) | 17.98 (<0.001) | 9.631 (<0.001) |
| HDL cholesterol ($mg\,dl^{-1}$) | 0.171 (<0.001) | 0.092 (<0.001) |
| LDL cholesterol ($mg\,dl^{-1}$) | −0.035 (0.059) | 0.008 (0.423) |
| Lipid-lowering medication, % | 0.052 (0.983) | −0.213 (0.874) |
| Fasting plasma glucose ($mg\,dl^{-1}$) | 36.19 (<0.001) | 12.05 (0.012) |
| Antidiabetic medication, *N* (%) | −9.359 (0.005) | −5.636 (0.003) |
| eGFR | 0.006 (0.860) | −0.018 (0.360) |
| Serum uric acid ($mg\,dl^{-1}$) | 6.058 (0.025) | 4.345 (0.004) |
| Age (years) × serum uric acid ($mg\,dl^{-1}$)[a] | −0.106 (0.011) | −0.070 (0.003) |
| $R^2$ | 0.278 (<0.001) | 0.194 (<0.001) |

Abbreviations: CVD, cardiovascular disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; β, standard coefficient.
Data for triglycerides and fasting plasma glucose were skewed and log-transformed for analysis.
[a]The net effect of each interaction was estimated using a general linear model.

**Table 4 Association between serum uric acid levels and blood pressure status of female participants categorized by age**

| *Characteristics* | *Age < 55 years* | | | *Age ⩾ 55 years* | | | |
|---|---|---|---|---|---|---|---|
| N = *1177* | N = *351* | *OR (95% CI)*[a] | P-*value*[b] | N = *826* | *OR (95% CI)*[a] | P-*value*[b] | *P-interaction* |
| Prehypertension vs normotension | 118/180 | | | 271/171 | | | |
| Tertile-1 (0.7–3.8 $mg\,dl^{-1}$) | 45/78 | 1 (referent) | | 90/57 | 1 (referent) | | 0.145 |
| Tertile-2 (3.9–4.7 $mg\,dl^{-1}$) | 39/71 | 0.94 (0.53–1.68) | 0.840 | 91/56 | 0.93 (0.57–1.54) | 0.786 | |
| Tertile-3 (4.8–10.8 $mg\,dl^{-1}$) | 34/31 | 1.48 (0.75–2.89) | 0.256 | 90/58 | 0.80 (0.48–1.35) | 0.407 | |
| Hypertension vs normotension | 53/180 | | | 384/171 | | | |
| Tertile-1 (0.7–3.8 $mg\,dl^{-1}$) | 13/78 | 1 (referent) | | 126/57 | 1 (referent) | | 0.009 |
| Tertile-2 (3.9–4.7 $mg\,dl^{-1}$) | 16/71 | 1.44 (0.56–3.68) | 0.451 | 137/56 | 1.08 (0.66–1.76) | 0.756 | |
| Tertile-3 (4.8–10.8 $mg\,dl^{-1}$) | 24/31 | 3.03 (1.13–8.11) | 0.028 | 121/58 | 0.75 (0.45–1.24) | 0.263 | |
| Hypertension vs prehypertension | 53/118 | | | 384/271 | | | |
| Tertile-1 (0.7–3.8 $mg\,dl^{-1}$) | 13/45 | 1 (referent) | | 126/90 | 1 (referent) | | 0.133 |
| Tertile-2 (3.9–4.7 $mg\,dl^{-1}$) | 16/39 | 1.41 (0.56–3.54) | 0.465 | 137/91 | 1.02 (0.69–1.52) | 0.909 | |
| Tertile-3 (4.8–10.8 $mg\,dl^{-1}$) | 24/34 | 1.96 (0.79–4.86) | 0.144 | 121/90 | 0.78 (0.51–1.20) | 0.265 | |

Abbreviations: CI, confidence interval; OR, odds ratio.
Data for triglycerides and fasting plasma glucose were skewed and log-transformed for analysis.
[a]Multivariate adjusted for age, obesity, drinking status, triglycerides, high-density lipoprotein cholesterol, fasting plasma glucose and antidiabetic medication, which were significant in Table 3.
[b]*P*-value versus Tertile-1.

younger participants with earlier stages of hypertension. Experimental evidence has demonstrated that increased SUA elevates BP in a manner that is initially reversible but leads to an irreversible salt-sensitive hypertension over time, regardless of the SUA levels,[29] and a randomized clinical trial has demonstrated that therapy that lowers SUA also lowers plasma renin activity and BP in this select population.[27]

Some limitations of this study must be considered. First, the cross-sectional study design is limited in its ability to eliminate the causal relationships between age, SUA and BP. Second, SBP and DBP are based on a single assessment of BP, which may introduce a misclassification bias. Third, we could not rule out one-time hypertension and white-coat hypertension. Fourth, formulas for eGFR tend to be less accurate in subjects with normal renal function than in those with chronic kidney disease, although ours is more accurate than that of serum creatinine[30] or blood urea nitrogen because these parameters are not raised to outside the normal range until 60% of total kidney function is lost. Therefore, the demographics and referral source may limit generalizability.

In conclusion, this study showed that SUA levels were significantly associated with elevated BP in a middle aged-female population. The mechanism underlying this relationship is not clear and seems to be independent of traditional confounding factors, such as age, BMI, smoking status, drinking status, TG, HDL-C, LDL-C, use of lipid-lowering and antidiabetic medication, FPG and eGFR. Further investigation of longitudinal data from our study will provide more definitive answers to this issue.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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*Author contributions:* RK, YT and KK participated in the design of the study, performed the statistical analysis and drafted the manuscript. YT and TK contributed to the acquisition of data and its interpretation. MA contributed to the conception and design of the statistical analysis. TM conceived of the study, participated in its design, coordination and helped to draft the manuscript. All authors read and approved the manuscript.

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