Introduction

Uric acid (UA) is the end product of endogenous and dietary purine nucleotide metabolism in humans. Many previous studies have confirmed an independent association between hyperuricaemia and adverse cardiovascular outcomes, especially in high-risk individuals (1-3). However, the Framingham Heart Study (4) and the Atherosclerosis Risk in Communities Study (5) failed to link UA with atherosclerotic cardiovascular diseases (CVD). Thus, the specific role of serum UA in relation to atherosclerosis remains unclear.

Arterial stiffness occurs early in the atherosclerosis process and carries a poor prognosis for CVD (6). Pulse wave velocity (PWV) and pulse wave analysis are all noninvasive indices for early detection of arterial stiffness. PWV is an accepted gold-standard assessment of stiffness index and is measured at different sites of the arterial tree, such as carotid-femoral (PWVc-f), carotid-radial (PWVc-r) and carotid-ankle PWV (PWVc-a) (7,8). The augmentation index (AIx) measured by pulse wave analysis is a composite parameter reflecting both large and distal arterial properties. Accumulating studies have suggested of the relationship between the serum UA level and some of these surrogate markers for atherosclerotic...
sis. However, the results are far from sufficient and conclusive, while some even controversial (9-11). Most of the previous studies only analyzed in selected populations (11), including just one or two estimates of artery stiffness targeted (12) or in a relatively small sample. Whether higher UA contributes equally to central and peripheral arterial stiffness in the general subjects remains unclear. Because the differences in arterial stiffness among different ethnic groups have been documented (5), it is necessary to investigate the associations between UA concentration and indices of arterial stiffness in Chinese inhabitants. The present investigation was designed to explore their relationship in a community-based population participating in a health-screening programme.

Materials and Methods

Study Population
All participants were selected from a population-based cross-sectional investigation study that included 5116 Chinese inhabitants of Haidian or Daxing District, Beijing, China in 2007. Participants with CVD, chronic kidney disease, systemic inflammatory disease, gout, or under treatment which would affect UA levels were excluded. All measurements were obtained at the same time. The study was approved by the Ethics Committee of the Chinese People’s Liberation Army General Hospital, and each subject provided written informed consent prior to participation.

Questionnaire and anthropometric measurements
A questionnaire was filled out for each subject at inclusion using a face-to-face interview method. The survey assessed traditional cardiovascular risk factors, including age, family history of premature cardiovascular events, cigarette smoking, and history of hypertension, CVD and diabetes. Subjects were considered non-smokers if they had never smoked or if they had given up smoking for at least three consecutive years. The investigation was completed by physicians trained by the research team.

Physical examinations, including anthropometry and blood pressure (BP) measurements, were performed after an overnight fast in the morning for each patient in the supine position. Brachial BP was measured with a mercury sphygmomanometer (Yuyue, Armamentarium Limited Company, Jiangsu, China) after 15 minutes of recumbent rest. Phases I and V of the Korotkoff sounds were used as the systolic (SBP) and diastolic blood pressure (DBP), respectively. Two measurements at an interval of 3 minutes were averaged. Anthropometric measures (height, body weight, and waist and hip circumferences) were recorded by a standardized protocol. Body mass index (BMI) was calculated as weight (kg) / height (m²).

Laboratory measurements
All subjects were advised not to eat, smoke, or drink coffee before examination. A blood sample was collected by venipuncture after an overnight fast. The baseline plasma total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), fasting blood glucose (FBG), creatinine and UA were measured by a qualified technician using enzymatic assays (Roche Products Ltd., Switzerland) on a fully automatic biochemical autoanalyzer (COBAS c6000, Roche Products Ltd., Switzerland). The glycemic status of the participants was determined according to guidelines, with the use of an oral glucose tolerance test where appropriate. Hyperuricaemia was defined as a serum uric acid level of at least 420 µmol/L in men and at least 357 µmol/L in women (13).

Arterial stiffness and wave reflections evaluation
PWV was assessed by using the automatic waveform analyzers (Complior, Artech Medical, Pantin, France) as previously described (14, 15). All individuals were examined after resting in the supine position for at least 5 minutes. Different pressure waveforms were obtained simultaneously.
at four sites: the right carotid, radial, femoral and ankle arteries. Transit distances were assessed be-
tween each pulse-recording site. PWVc-f, PWVc-r and PWVc-a were then automatically calculated
from measurements of pulse transit time and the
distance between the 2 sites / from tonometry
waveforms and body surface measurements as
previously described. The mean PWV of at least
10 consecutive pressure waveforms was calculated
for further analysis.
AIx was measured by using a validated system
(SphygmnoCor; AtCor Medical, Sydney, Australia)
that employs the principle of applanation tonome-
try and appropriate software for noninvasive
recording and analysis of the arterial pulse, as pre-
viously described (7, 16). Peripheral pulse waves
were recorded from the radial artery and trans-
formed into the aortic pulse wave through pulse
wave analysis. From this aortic pressure waveform,
the augmentation pressure (AP) and AIx were
calculated. The AP is defined as the height of the
late systolic peak above the inflection point on the
waveform and may be positive or negative
depending on the relative heights of the two peaks.
AIx is defined as AP divided by central pulse
pressure and is expressed as a percentage. AIx was
averaged from 10 to 12 successive waves and was
corrected for a steady heart rate (HR) of 75
beats/min (17).
The same observer, unaware of the subjects’ clini-
cal and biochemical data, performed all the mea-
surements. The interclass correlation coefficients
between the first and second measurements were
0.95 for the AIx-75, 0.93 for PWVc-f, 0.91 for
PWVc-r and 0.89 for PWVc-a. The coefficients of
variation for the AIx-75 and PWV were less than
5%.

Statistical analyses
The data are presented as mean values ± standard
derivation or percentages, unless otherwise stated.
Student t test was used to compare groups for
continuous variables and the chi-square test to
compare categorical variables. In addition, differ-
ences in non-parametric variables were compared
using the Mann Whitney U-test. Pearson correla-
tion analyses between arterial stiffness and serum
UA, or other variables of interest were calculated
to examine potential relationships. Then, multiva-
riate stepwise regression analyses were performed
to look for independent associations between ar-
terial stiffness and the variables that were found to
have a significant association with arterial stiffness
in a univariate analysis. A P value of less than 0.05
(two-tailed) was considered statistically significant.
Statistical analyses were performed with SPSS 11.0
software (Statistical Package for the Social Science,
Inc., Chicago, IL, USA).

Results

Baseline characteristics
Table 1 shows the demographic, clinical, and
hemodynamic characteristics of the study
participants by gender. Of 2374 participants
included in the present analyses, there were
1138 men and 1236 women. Mean ages were
58.24 ± 12.38 years for all participants (range 35
to 96 years). The mean serum UA level was
found to be significantly higher in men (326.76
± 72.96 µmol/L) than in women (263.68 ± 64.4
µmol/L, P < 0.001). The mean PWVc-f, PWVc-
r and PWVc-a values were significantly higher,
while AIx-75 was much lower in men than in
women (P all < 0.05). Men, compared with
women, had higher brachial BP, higher
proportions of current smokers, higher UA and
TG, but lower serum TC, LDL-C and 2 h
postprandial blood glucose (2h BG) level.
Sub-group analyses showed that hyperuricemic
subjects, compared with those with normal
serum UA, had significantly higher PWVc-f in
women (P < 0.001), significantly higher PWVc-a
in both genders (P < 0.05) and marginally lower
log AIx-75 in men (P = 0.049). PWVc-r didn’t
differ in subjects with hyperuricaemia or normal
UA level in both genders (Fig. 1).
Table 1: Selected clinical, demographic and hemodynamic characteristics of the survey population according to gender

<table>
<thead>
<tr>
<th></th>
<th>Total (n = 2374)</th>
<th>Men (n = 1138)</th>
<th>Women (n = 1236)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>58.24 ± 12.38</td>
<td>56.74 ± 13.37</td>
<td>59.61 ± 11.22</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Current smoker, n/ %</td>
<td>620 (26.1%)</td>
<td>522 (45.9%)</td>
<td>98 (7.9%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hypertension, n/ %</td>
<td>798 (33.6%)</td>
<td>447 (39.3%)</td>
<td>351 (28.4%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>128.88 ± 17.87</td>
<td>130.59 ± 17.13</td>
<td>127.32 ± 18.39</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>76.8 ± 10.41</td>
<td>78.71 ± 10.34</td>
<td>75.04 ± 10.18</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>25.45 ± 3.4</td>
<td>25.5 ± 3.11</td>
<td>25.41 ± 3.65</td>
<td>0.539</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>76.03 ± 9.79</td>
<td>75.83 ± 9.98</td>
<td>76.16 ± 9.68</td>
<td>0.622</td>
</tr>
<tr>
<td>TC, mmol/L</td>
<td>5.04 ± 0.93</td>
<td>4.93 ± 0.91</td>
<td>5.14 ± 0.94</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>TG, mmol/L</td>
<td>1.81 ± 1.31</td>
<td>1.89 ± 1.52</td>
<td>1.73 ± 1.08</td>
<td>0.003</td>
</tr>
<tr>
<td>LDL-C, mmol/L</td>
<td>2.91 ± 0.74</td>
<td>2.79 ± 0.7</td>
<td>3.02 ± 0.75</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>UA, µmol/L</td>
<td>293.93 ± 75.52</td>
<td>326.76 ± 72.96</td>
<td>263.68 ± 64.4</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>FBG, mmol/L</td>
<td>5.39 ± 1.6</td>
<td>5.36 ± 1.4</td>
<td>5.42 ± 1.76</td>
<td>0.357</td>
</tr>
<tr>
<td>2 h BG, mmol/L</td>
<td>7.52 ± 3.94</td>
<td>7.16 ± 3.78</td>
<td>7.86 ± 4.06</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>PWVc-f, m/s</td>
<td>11.21 ± 2.89</td>
<td>11.34 ± 2.94</td>
<td>11.1 ± 2.84</td>
<td>0.044</td>
</tr>
<tr>
<td>PWVc-r, m/s</td>
<td>9.46 ± 1.46</td>
<td>10 ± 1.43</td>
<td>8.96 ± 1.31</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>PWVc-a, m/s</td>
<td>9.24 ± 2.18</td>
<td>9.35 ± 1.83</td>
<td>9.14 ± 2.45</td>
<td>0.019</td>
</tr>
<tr>
<td>Alx-75, %</td>
<td>25.24 ± 10.39</td>
<td>21.06 ± 10.25</td>
<td>29.09 ± 8.93</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Continuous variables are expressed as mean ± SD; dichotomous variables, as n (%)

Abbreviations: Alx-75, augmentation index at heart rate 75/min; 2 h BG, 2 h post blood glucose in OGTT; BMI, body mass index; DBP, diastolic blood pressure; FBG, fasting blood glucose; HR, heart rate; LDL-C, low density lipoprotein cholesterol; PWVc-a, carotid-ankle pulse wave velocity; PWVc-f, carotid-femoral pulse wave velocity; PWVc-r, carotid-radial pulse wave velocity; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; UA, uric acid

Fig. 1: Arterial stiffness changes according to hyperuricemia status and gender

Fig. 2: Scatter plot of arterial stiffness parameter against serum uric acid level

$r$ expresses the Pearson correlation coefficient.
Table 2: Pearson’s correlation coefficients between arterial stiffness, serum UA and other variables in male and female subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>PWVc-f (m/s)</th>
<th>PWVc-r (m/s)</th>
<th>PWVc-a (m/s)</th>
<th>AIx-75 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>UA</td>
<td>0.072*</td>
<td>0.209**</td>
<td>0.051</td>
<td>0.042</td>
</tr>
<tr>
<td>Age</td>
<td>0.517**</td>
<td>0.564**</td>
<td>-0.117**</td>
<td>0.089*</td>
</tr>
<tr>
<td>BMI</td>
<td>-0.061*</td>
<td>0.074*</td>
<td>-0.009</td>
<td>-0.012</td>
</tr>
<tr>
<td>SBP</td>
<td>0.33**</td>
<td>0.417**</td>
<td>0.075*</td>
<td>0.184**</td>
</tr>
<tr>
<td>DBP</td>
<td>-0.005</td>
<td>0.05</td>
<td>0.19**</td>
<td>0.196**</td>
</tr>
<tr>
<td>HR</td>
<td>0.106*</td>
<td>0.134*</td>
<td>0.137*</td>
<td>0.003</td>
</tr>
<tr>
<td>TC</td>
<td>-0.032</td>
<td>0.075*</td>
<td>0.048</td>
<td>0.051</td>
</tr>
<tr>
<td>TG</td>
<td>-0.025</td>
<td>0.156**</td>
<td>0.081*</td>
<td>0.018</td>
</tr>
<tr>
<td>LDL-C</td>
<td>0.062*</td>
<td>0.145</td>
<td>0.012</td>
<td>0.060*</td>
</tr>
<tr>
<td>FBG</td>
<td>0.084*</td>
<td>0.115**</td>
<td>0.051</td>
<td>0.029</td>
</tr>
<tr>
<td>2 h BG</td>
<td>0.168**</td>
<td>0.279**</td>
<td>0.046</td>
<td>0.060*</td>
</tr>
</tbody>
</table>

* $P$ value <0.05; ** $P$ value <0.001.

For other abbreviations, see table 1 footnote.

Relationship between serum UA, PWV and AIx-75

The associations of serum UA level with regional PWV and AIx-75 are presented in Table 2, Fig. 2 and Table 3. Figure 2 shows the relationship between serum UA, PWVc-f, PWVc-r, PWVc-a and AIx-75 in the entire population. These scatter charts clearly show that serum UA concentration positively correlates with PWVc-f, PWVc-r and PWVc-a, but negatively correlates with AIx-75 ($P$ all <0.001). Table 2 lists univariate correlation coefficients between arterial stiffness and various clinical parameters by gender. The results showed that PWVc-f and PWVc-a significantly correlated with UA concentration in both genders, while had no relationship with PWVc-r and AIx-75 in either gender. Parameters that represent cardiac risk factors, such as age, HR, SBP, BMI, serum UA, lipid profiles, blood glucose and eGFR, had different effects on arterial stiffness with gender difference. When these parameters were used as explanatory variables in the multivariate stepwise regression analysis for PWV and AIx-75, results showed that UA was a significant independent variable for PWVc-f in women though the contributions of age, SBP, FBG and BMI were large. On the contrary, UA level had no independent contribution to PWVc-f in men and to other regional arterial stiffness in both gender. All the explanatory variables included are listed in Table 3.

Discussion

In the present study, we explored the associations of UA levels and indices of arterial function in general Chinese population with gender specific analysis. Our findings here demonstrate that while serum UA concentration correlates positively with PWV measured at three different sites and negatively with AIx-75 in the entire population, only PWVc-f is independently associated with elevated UA after correcting for possible confounding factors in women, and no independent association is found between serum UA and PWVc-r, PWVc-a or AIx-75 both in both genders.
Table 3: Multivariate stepwise regression analysis showing independent contributions to arterial stiffness in men and women

<table>
<thead>
<tr>
<th>Independent variable</th>
<th>B</th>
<th>SE</th>
<th>β</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>PWVc-f men (R² = 0.333, SE = 1.873, F = 71, P &lt; 0.001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td>0.092</td>
<td>0.008</td>
<td>0.413</td>
<td>11.142</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>0.024</td>
<td>0.005</td>
<td>0.205</td>
<td>5.326</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>0.03</td>
<td>0.008</td>
<td>0.127</td>
<td>3.617</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>2h BG, mmol/L</td>
<td>0.064</td>
<td>0.02</td>
<td>0.118</td>
<td>3.24</td>
<td>0.001</td>
</tr>
<tr>
<td>PWVc-f women (R² = 0.286, SE = 2.143, F = 28.615, P &lt; 0.001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td>0.094</td>
<td>0.011</td>
<td>0.415</td>
<td>8.852</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>0.029</td>
<td>0.006</td>
<td>0.224</td>
<td>4.669</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>FBG, mmol/l</td>
<td>0.228</td>
<td>0.071</td>
<td>0.147</td>
<td>3.195</td>
<td>0.002</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>-0.11</td>
<td>0.038</td>
<td>-0.14</td>
<td>-2.917</td>
<td>0.004</td>
</tr>
<tr>
<td>UA, μmol/l</td>
<td>0.004</td>
<td>0.002</td>
<td>0.104</td>
<td>2.22</td>
<td>0.027</td>
</tr>
<tr>
<td>PWVc-r men (R² = 0.051, SE = 1.34, F = 7.195, P &lt; 0.001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>-0.062</td>
<td>0.022</td>
<td>-0.146</td>
<td>-2.757</td>
<td>0.006</td>
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<tr>
<td>HR, bpm</td>
<td>0.019</td>
<td>0.007</td>
<td>0.14</td>
<td>2.656</td>
<td>0.008</td>
</tr>
<tr>
<td>Current smoker</td>
<td>0.34</td>
<td>0.152</td>
<td>0.118</td>
<td>2.244</td>
<td>0.026</td>
</tr>
<tr>
<td>PWVc-r women (R² = 0.024, SE = 1.266, F = 7.959, P &lt; 0.001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TC, mmol/L</td>
<td>0.172</td>
<td>0.06</td>
<td>0.12</td>
<td>2.848</td>
<td>0.005</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>0.007</td>
<td>0.003</td>
<td>0.102</td>
<td>2.428</td>
<td>0.016</td>
</tr>
<tr>
<td>PWVc-a men (R² = 0.02, SE = 1.496, F = 4.44, P = 0.012)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR, bpm</td>
<td>0.018</td>
<td>0.008</td>
<td>0.12</td>
<td>2.222</td>
<td>0.027</td>
</tr>
<tr>
<td>Current smoker</td>
<td>0.34</td>
<td>0.17</td>
<td>0.108</td>
<td>2.001</td>
<td>0.046</td>
</tr>
<tr>
<td>PWVc-a women (R² = 0.062, SE = 2.897, F = 19.371, P &lt; 0.001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td>0.052</td>
<td>0.013</td>
<td>0.179</td>
<td>4.093</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>0.02</td>
<td>0.007</td>
<td>0.131</td>
<td>2.989</td>
<td>0.003</td>
</tr>
<tr>
<td>Aix-75 men (R² = 0.003, SE = 10.212, F = 4.503, P = 0.034)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>-1.348</td>
<td>0.635</td>
<td>-0.066</td>
<td>-2.122</td>
<td>0.034</td>
</tr>
<tr>
<td>Aix-75 women (R² = 0.038, SE = 8.6, F = 22.782, P &lt; 0.001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>0.063</td>
<td>0.015</td>
<td>0.132</td>
<td>4.185</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Age, yr</td>
<td>0.082</td>
<td>0.024</td>
<td>0.108</td>
<td>3.433</td>
<td>0.001</td>
</tr>
</tbody>
</table>

B, Unstandardized Coefficients; SE, standard error for B; β, Standardized Coefficients. For other abbreviations, see Table 1 footnote.

Higher serum UA might not have uniform effects along the arterial tree stiffness. Regarding serum UA on large arterial stiffening, our findings are in line and extend observations from selected diseases (11) or general population, (12, 18) which suggested a direct effect of serum UA on elastic arteries stiffness. However, only limited and inconclusive information exists about peripheral arterial changes. Tsai found that UA is an independent predictor of PWVc-r in hypertensive patients (11). On the contrary, in the present study, we found no association between the UA level and PWVc-r or PWVc-a in general residents at low risk for CVD. Differences in the baseline characteristics of a study population may explain the disparate result.

To date, scant data exist regarding the relationship of serum UA and wave reflections. Augmentation index (AIx) has been advocated as an indirect surrogate measure of arterial stiffness, and arterial stiffness is only one contributor to the observed AIx. Though arterial stiffness and wave reflection indices often change in parallel, this is not always the case. Our findings of a negative relationship between UA levels and wave reflections in the
presence of a positive association with arterial stiffness only in females are intriguing. Previous studies showed that though men have much higher serum UA concentration than women, their cardiovascular risks were relatively lower. Hoieggen (19) reviewed the epidemiological data and found an independent relationship between serum UA and cardiovascular risk, at least in women. The mechanisms that underline UA gender-specific effects were not clear but might involve gene discrepancies (20). However, gender-specific relationship between UA level and arterial stiffness, which is also considered as a cardiovascular risk factor, was inconclusively analyzed. In the study of Ishizaka (18) Pearson’s correlation coefficient between the UA level and brachial-ankle PWV is significant in females, but not in males. On the contrary, Lim (21) and Tomiyama (22) found that elevated UA level is not associated with heart-femoral PWV or brachial-ankle PWV in apparently healthy korean adult females or males. Vlachopoulos proved that (10) serum UA levels are independently associated with aortic stiffening (PWVc-f) in both genders while with wave reflections (AI) only in females in never-treated hypertensives. The inconsistency was probably due to different methods in measurement of arterial stiffness and also due to bias in the recruitment of patients.

To the best of our knowledge, this is the first study to explore gender-specific relationships between UA, regional arterial stiffness, and wave reflections in a sample of general Chinese residents. Our findings add to the general impression that UA does not have a uniform impact on both sexes, though we cannot yet explain the underlying mechanism. Our null finding in men could be attributable to the significantly different characteristics between men and women population of our study. In this cross-sectional study, though men had higher proportion of current smokers and hypertension, their mean age was much younger, serum TC, LDL-C and TG were much lower than those in women. These might serve as major underlying factors causing the divergence of the gender-specific associations in our study.

In both univariate correlation and multivariate stepwise regression analysis, we found that lower BMI is weakly but significantly associated with higher PWVc-f in women. This finding is contradictory to other studies (23) and not easy to explain in the present study. When BMI was replaced by waist to hip ratio, the results showed that waist to hip ratio was also an independent predictor for PWVc-f, though only in women (standardized coefficient β 0.084, \( P = 0.027 \), data not shown). Our results are in line with Tsai’s (11) findings of negatively correlated BMI and PWVc-f in hypertensive patients. This might indicate that central, but not general adiposity is an important determinant of aortic stiffness. However, our subjects were selected from middle to aged community based samples, which are not representative of the whole population, so the relationship between BMI and PWV should be further clarified.

It has been reported that hyperuricaemia is associated with oxidative stress, (24) endothelial dysfunction (25) and inflammation (26), all of the issues might contribute to arterial stiffening. However, the precise role that UA plays in arterial stiffening is not yet clear. Whether the relationship between serum UA and increased arterial stiffness is circumstantial or causal cannot be determined by this cross-sectional study.

In addition to its cross-sectional nature, our study had several other limitations. First, we ruled out the subjects who used UA-lowering agents or medications which might affect UA levels in our study. However, the relative homogeneity of the study subjects enhancing the internal validity of our findings by reducing confounding factors potentially affecting serum UA and PWV. Second, our study population consisted solely of Chinese subjects, thus the associations observed may not be applicable to other ethnic groups. However, the correlation between UA and PWV demonstrated in our study implied that PWV could be a surrogate marker for evaluation of UA-lowering agents in cardiovascular disease in the future. Taken together, our study suggests that serum UA preferentially increases central elastic (carotid) over peripheral muscular (femoral and brachial) arteries stiffness and positive association between
serum UA levels and large artery stiffness exists only in females. Though serum uric acid levels are much higher in men than those in women, null findings in men from multiple analyses remain to be elucidated. Further research, involving prospective and intervention studies, would be required to identify gender specific susceptible to vascular damage associated with hyperuricaemia or an elevated serum UA.

Ethical considerations

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc) have been completely observed by the authors

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References


