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ORIGINAL ARTICLE

# Peripheral arterial stiffness is associated with higher baseline plasma uric acid: A prospective cohort study

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Uric acid, risk factor;
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**Abstract** This prospective cohort study aimed at identifying association between uric acid (UA) and peripheral arterial stiffness. A prospective cohort longitudinal study was performed according to an average of 4.8 years' follow-up. The demographic data, anthropometric parameters, peripheral arterial stiffness (carotid-radial pulse-wave velocity, cr-PWV) and biomarker variables including UA were examined at both baseline and follow-up. Pearson's correlations were used to identify the associations between UA and peripheral arterial stiffness. Further logistic regressions were employed to determine the associations between UA and arterial stiffness. At the end of follow-up, 1447 subjects were included in the analyses. At baseline, cr-PWV ($r = 0.200$, $p < 0.001$) was closely associated with UA. Furthermore, the follow-up cr-PWV ($r = 0.145$, $p < 0.001$) was also strongly correlated to baseline UA in Pearson's correlation analysis. Multiple regressions also indicated the association between follow-up cr-PWV ($\beta = 0.493$, $p = 0.013$) and baseline UA level. Logistic regressions revealed that higher baseline UA level was an independent predictor of arterial stiffness severity assessed by cr-PWV at follow-up cross-section. Peripheral arterial stiffness is closely associated with higher baseline UA level. Furthermore, a higher baseline UA level is an independent risk factor and predictor for peripheral arterial stiffness.


## 1. Introduction

Hyperuricemia, a common clinical situation, has been demonstrated as an independent risk factor for cardiovascular diseases including arterial stiffening, atherosclerosis and hypertension (Chu et al., 2000; Iwashima et al., 2006; Katsiki et al., 2015). The abnormality of uric acid (UA) has also been

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indicated to be associated with regional arterial stiffness in patients with chronic kidney disease and diabetes mellitus (DM) (Iwashima et al., 2006; Alderman, 2007; Santos, 2012; Zhao et al., 2013). The relationship between normal serum UA and arterial stiffness has also been well documented previously (Lin et al., 2012; Shin et al., 2012). Regarding the mechanism underlying arterial stiffness in which UA participates in, it is involved in thickening vessel wall (intima-media) *via* proliferation and differentiation of smooth muscle cells as well as dysfunction of endothelial cells (Bian et al., 2012; Elsurer and Afsar, 2014; Ishizaka et al., 2007; Zhang et al., 2014).

It is also demonstrated that arterial stiffness is a risk factor for or pre-pathophysiological processes of various cardiovascular and cerebra-vascular diseases (Sun, 2015). Presently, the pulse wave velocity (PWV) has been used as a reproducible and valid non-invasive gold standard indicator in the assessments of arterial stiffness (Covic and Siriopol, 2015; Laurent and Boutouyrie, 2007; Liu, 2013). Nevertheless, PWVs from different arteries usually represent stiffness in distinct regions in vasculature system (Jadhav and Kadam, 2005; Weber et al., 2015), such as carotid-radial PWV (cr-PWV) which is applied to assess stiffness in arterioles (Hughes et al., 2004).

Inconsistent results on associations between serum UA level and arterial stiffness have been reported before (Elsurer and Afsar, 2014; Mallamaci et al., 2015; Zhao et al., 2013). However, majority of them were performed primarily based on a basic disease such as DM, hypertension and chronic kidney disease (Elsurer and Afsar, 2014; Zhang et al., 2014) among various ethnic groups (Ishizaka et al., 2007; Liang et al., 2012; Lim et al., 2010; Kristina and Gooyers, 2016). However, there were few follow-up studies that have been performed to identify the roles of baseline level of UA in peripheral arterial stiffness. Thus, we postulated that the higher UA level may also play a critical role in increasing peripheral arterial stiffness and performed this follow-up observational study aiming at identifying the associations between UA level and peripheral stiffness evaluated by cr-PWV, to provide novel index for stratification and risk management of arterial stiffness.

## 2. Material and methods

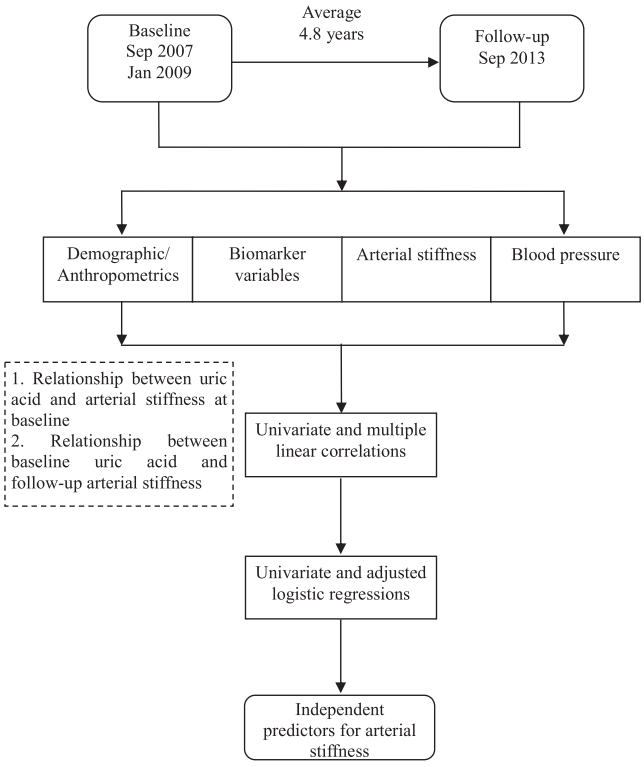
### 2.1. Participants and procedures

A total of 1680 health check participants were recruited between September 2007 and January 2009 from Pingguoyuan area, the Shijingshan district in this community-based follow-up cohort study according to the inclusion and exclusion criteria. The exclusion criteria were listed as following: endocrine and metabolic diseases (except DM), infection, neoplastic or severe liver or renal diseases. The inclusion criteria were as follows: residents who received a routine health examination in the community.

### 2.2. Follow-up and outcome assessment

Our study was reviewed and approved by the ethics committee at People's Liberation Army General Hospital. The study was thoroughly explained to all of the subjects who agreed to participate, and all of the subjects signed informed consent forms before their examinations.

The participants were followed up for cardiovascular diseases mortality, all-cause mortality, and the development of DM from the initial screening to September 30, 2013. After a median of 4.8 years' follow-up for 1680 subjects, 181 participants were lost for follow-up and excluded from analysis. Therefore, 1499 subjects (follow-up rate 89.2%) finished the follow-up and fifty-two of which were excluded because of death. In the final data analysis, 1447 participants were included.




### 2.3. Clinical data collection

The lifestyle factors, prevalent diseases, demographic information, anthropometrics, family history and medication use were recorded using a standardized self-reported questionnaire in our following-up study. Smoking status and alcohol use was categorized as current, former, or never drinking/smoking, respectively. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were also examined on the right arm in a sitting position after a rest of five minutes.

### 2.4. Biomarker variable determination

Between 8 am and 10 am after an overnight fast (at least 12 h), the venous blood samples were obtained from all participants. Plasma aliquots were obtained and stored at −80 °C for further study. Concentrations of plasma UA, total cholesterol (TC), triglyceride (TG), fasting blood glucose (FBG), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) concentrations were