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Running Title: C-reactive protein, uric acid, glomerular filtration and arterial stiffness

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Abstract

The relationships between C-reactive protein (CRP), uric acid (UA), glomerular filtration rate (GFR), and arterial stiffness have not been fully investigated. The aim of this study to clarify whether CRP, UA, and estimated GFR are related to arterial stiffness estimated using brachial-ankle pulse wave velocity (baPWV). The subjects were local government employees (3412 men and 854 women). baPWV, CRP, UA, GFR and conventional risk factors were evaluated. Multiple linear regression analyses revealed that CRP and UA were significantly related to an elevation of PWV in male and female subjects, and that the estimated GFR was significantly related to an elevation of PWV in male subjects. Significant progressive increases in baPWV were observed across the quartiles of CRP in male subjects and for UA in male and female subjects. In female subjects, the relationship of quartile CRP to baPWV had marginal significance (p=0.055). But, in male and female subjects, quartile of estimated GFR had no significant association with PWV. These results suggest that CRP and UA are associated with an increase of arterial stiffness in males and females, and that estimated GFR is possibly related to arterial stiffness in males.

Key Words; C-reactive protein; uric acid; glomerular filtration rate; pulse wave velocity; arterial stiffness

Introduction

Pulse wave velocity (PWV) in known to be an indicator of arterial stiffness,[1, 2] and there have been many reports on PWV and the development of atherosclerotic diseases.[3-5] A simple noninvasive automatic measurement of brachial-ankle PWV (baPWV) has recently been developed. The technical simplicity and short sampling time of the new method make it more feasible for screening a large population than previous methods such as carotid-femoral PWV.

Atherosclerosis is now generally accepted to be an inflammatory disorder in the arterial wall,[6] and C-reactive protein (CRP) level is a strong predictor of cardiovascular events.[7-10] The influence of CRP on arterial stiffness is therefore important. There have been several studies on the relationship between CRP and arterial stiffness, but the association is controversial. Several studies indicated a significant relationship between CRP and PWV,[11-14] but one large-sample-size study found no significant association.[15]

Many epidemiological studies have shown that an increased serum uric acid level is a risk factor for cardiovascular disease.[16-19] Meanwhile, the recent Framingham Heart Study and Atherosclerosis Risk in Communities (ARIC) Study failed to link uric acid with cardiovascular diseases,[20, 21] and the ARIC Study reported that the association of uric acid with carotid artery intima-media thickness was negligible. Thus, the specific role of serum uric acid in relation to atherosclerosis remains unclear and the relationship between uric acid and arterial stiffness has

not been fully investigated.

It is well documented that patients with kidney disease have a high burden of cardio-vascular diseases. The end-stage renal disease (ESRD) population has increased arterial stiffness, and the PWV level is a strong independent predictor.[22] In one study of 1290 untreated subjects who entered a hospital for cardiovascular checkup, the subjects were divided into three tertiles based on their estimated glomerular filtration rates (GFR). Only in the lower tertile was elevated PWV significantly associated with reduced GFR.[23] But there have been few reports of the relationship between GFR and arterial stiffness in the general population.

In this study, we have investigated the association between CRP, UA, GFR, and arterial stiffness to clarify whether CRP, UA and GFR are related to early-stage atherosclerosis.

Methods

Subjects

The subjects were local government employees (8229 men and 2194 women) aged 35 years or more who had their annual health checkup during the period from April 2003 through March 2004. We used a self-administered questionnaire including clinical history, family history, smoking, alcohol consumption, frequency of exercise, menopausal status, and hormone-replacement therapy. The questionnaires were distributed to the subjects in advance of their annual health checkup, and were collected at the checkup. Answers to the questionnaire and written consent to view health checkup data were obtained from 3907 men and 1044 women (response rate: men 47.5%, women 47.6%). A total of 685 subjects (495 men, 190 women) were excluded for the following reasons: past history of coronary disease or stroke (n=136; 124 men, 12 women), low ankle/brachial pressure index (<0.9, n= 12; 11 men, 1 woman), not measured PWV (n= 600; 416 men, 184 women), or not measured blood samples (n=3; 3 women). The final study group thus consisted of 3412 male and 854 female subjects.

This study was conducted with all the subjects' written informed consent and approved by the institutional ethical board for epidemiological studies of Hokkaido University Graduate School of Medicine.

Data collection

The smoking statuses of included subjects were classified as either 'nonsmokers', which included subjects who either had never smoked or were ex-smokers and 'current smokers'. Drinkers were defined as those who drank alcohol at least once per week. Subjects were also grouped according to their answer to the question, ‘Do you normally exercise (with perspiration) other than work?’ Those who exercised one or more times per week were placed in a “>1 per week” group, and those who exercised less than one time per week were placed in a “rarely or never” group.

Anthropometric measures (height, body weight, and waist and hip circumferences) were recorded by a standardized protocol. The body mass index (BMI) was calculated as weight (kg)/height (m^2).

Blood samples were drawn from the antecubital vein of the seated subject with minimal tourniquet use after a 12-hour fast. Total cholesterol (TC) levels and the triglyceride (TG) level was measured by an enzymatic method. The high density lipoprotein cholesterol (HDL-C) level was measured by a direct method. Blood glucose was measured using an amperometric method. Uric acid (UA) by an enzymatic method (Daiichi Pure Chemicals) and creatinine by an enzymatic method (KANTO KAGAKU, Tokyo, Japan).

The CRP level was measured by nephelometry, with a latex particle-enhanced immunoassay (N Latex CRP II, Dade Behring, Tokyo, Japan). The assay could detect 0.004mg/dL of CRP.

Undetectable CRP values were recorded as 0.002mg/dL.

All blood variables except for CRP were measured at DAIICHI CLINICAL LABORATORIES, INC. (Sapporo, Japan), a commercial hematology laboratory, where the measurements of TC and HDL cholesterol were all standardized by the Lipid Standardized Program, Centers for the Disease Control and Prevention, Atlanta, Georgia. CRP was measured at Mitsubishi Kagaku Bio-Clinical Laboratories, Inc. (Tokyo, Japan), a commercial hematology laboratory.

Estimated GFR was calculated using the Cockcroft-Gault formula[24] adjusted for body surface area (BSA) as follow:

Cockcroft-Gault = (140 – age)/Scr * weight/72 * 1.73/BSA

where Scr is the serum creatinine concentration (mg/dL) and weight is measured in kilograms. In females, a correlation factor (0.85) was used. BSA was estimated using the DuBois formula.[25]

baPWV was measured using a volume-plethysmographic apparatus (Form PWV/AVI; model BP-203RPEII, Colin Co., Komaki, Japan).[26, 27] This device records the phonocardiogram, electrocardiogram, and volume pulse form and arterial blood pressure at both the left and right brachia and ankles. baPWV was calculated by time-phase analysis between right brachial and volume waveforms at both ankles. Blood pressure, heart rate (HR), and the ankle brachial index (ABI) were measured using the pulse-wave velocimeter at the same time as measuring the PWV.

ABI was the ratio of ankle systolic blood pressure to brachial systolic blood pressure, and right and left ABIs were measured simultaneously. In all the studies, baPWV was obtained after an at least 5-min rest.

Statistical analysis

All analyses were performed separately for males and females. The data of the subjects are presented as mean ± SD, median (and interquartile range) for variables with a skewed distribution, or percentages. Linear regression analysis was performed to evaluate the association between baPWV and other variables. Then multiple linear regression analysis was used to clarify the contributions of CRP, UA, and estimated GFR to baPWV after adjusting for age, BMI, systolic blood pressure, HR, TC, HDL, FBS, log TG, WBC, smoking status (smoker/nonsmoker), alcohol consumption (drinker/rarely or never), frequency of exercise (≥1/week/ rarely or never), hypertension, hyperlipidemia, and diabetes for men; and of these all variables and menopausal status for women.

The adjusted mean of baPWV was compared among the quartiles of CRP, UA, and estimated GFR, with analysis of covariance (ANCOVA) where age, BMI, systolic blood pressure, HR, TC, HDL, fasting glucose, log TG, UA (except for analysis of the quartile UA), estimated GFR (except for analysis of the quartile estimated GFR), log CRP (except for analysis of the quartile

CRP), smoking status (smoker/nonsmoker), alcohol consumption (drinker/rarely or never), frequency of exercise (≥1/week/ rarely or never), hypertension, hyperlipidemia, and diabetes for men; and of these all variables and menopausal status for women.

P-values <0.05 were considered to be statistically significant. All analyses were conducted using the SPSS software package Version 12 for Windows (SPSS Inc., Chicago, U.S.A.).

Results

Characteristics of the male and female subjects are presented in Table 1. The mean ages of male and female subjects were 48.4 (SD 6.8) and 46.8 (SD 7.2) years, respectively. The medians of CRP for male and female subjects were 0.045 (interquartile range: 0.023-0.089) and 0.025 (interquartile range: 0.012-0.052) mg/dL, respectively. The means of UA in male and female subjects were 5.9 (SD 4.2) and 4.5 (SD 1.0) mg/dL, respectively. The means of estimated GFR for male and female subjects were 105.8 (SD 18.2) and 116.6 (SD 21.6) mL/min per 1.73m^2, respectively.

Table 2 depicts the coefficient of correlation in linear regression analysis between baPWV and other variables in male and female subjects. In male subjects, age, BMI, hemodynamic variables, parameters reflecting either atherosclerotic risk factors or metabolic disorders (except for HDL cholesterol), estimated GFR, drinking habit, frequency of exercise, hypertension, hyperlipidemia, and diabetes were significantly associated with baPWV. In female subjects, age, BMI, hemodynamic variables, parameters reflecting either atherosclerotic risk factors or metabolic disorder (except for HDL cholesterol), hypertension, hyperlipidemia, diabetes, and menopausal status were significantly associated with baPWV.

Table 3 shows the results of multiple regression analysis between baPWV and other variables in male and female subjects. In male subjects, age, BMI, SBP, heart rate, log triglycerides, fasting

glucose, UA, log CRP, estimated GFR, exercise and hypertension were significantly associated with baPWV. In female subjects, age, BMI, SBP, heart rate, TC, fasting glucose, UA, log CRP, and drinking habit were significantly associated with baPWV.

Next we visualized the relationships among CRP, UA, estimated GFR, and baPWV. The adjusted means of baPWV were compared with the quartiles of CRP, UA, and estimated GFR (Figure 1 for males, and Figure 2 for females). Significant progressive increases in baPWV were observed across the quartiles of CRP in male subjects and UA in both genders. In female subjects, the relationship of quartile CRP to baPWV had marginal significance (p =0.055). But, in male and female subjects, quartiles of estimated GFR had no significant association with baPWV.

Discussion

In males and females, CRP and UA were consistently associated with an increase of baPWV. And, in males, estimated GFR was related to baPWV in multiple regression analysis.

Several studies indicated a significant relationship between CRP and PWV,[11-14] but one large-sample-size study found no significant association.[15] Yasmin *et al.*[11] reported that log CRP was significantly related to aortic PWV and brachial PWV in stepwise regression analysis. However, the sample size was rather small (n=427) and, in stepwise analysis, BMI, heart rate, TC and fasting glucose were not selected in the model. Thus, the result was not adjusted for such potential confounders. Okamura *et al.*[12] found a significant relationship between log CRP and baPWV in middle-aged male workers in multiple regressions analysis and that the quartile of CRP had a positive graded relation with baPWV in multivariate-adjusted analysis of means of baPWV, but the sample size was also rather small (n=178) and the subjects were only male. Tomiyama *et al*.[13] reported that elevated CRP was significantly related to elevated baPWV in a large number of Japanese subjects (n=7283). In the logistic regression analysis, adjustment was made by age, hypertension, diabetes, dyslipidemia, obesity, and smoking status, but the result was not fully adjusted for other potential confounders of continuous variables such as blood pressure, heart rate, TC, HDL-C, TG, fasting glucose, etc. Nagano *et al.*[14] reported that multiple liner regression analysis demonstrated that CRP was significantly related to baPWV in 870 Japanese subjects, but

the result was not fully adjusted for other potential confounders of continuous variables such as TC, HDL-C, TG, fasting glucose, etc. Another report of Tomiyama *et al*.[15] described that multiple linear regression analysis demonstrated that CRP was not significantly related to baPWV in Japanese male subjects. The sample size was relatively large (n=2668), but the result for the relationship between CRP and PWV was different from the former three studies and our data. In the negative study, linear repression analysis showed a significant correlation between baPWV and log CRP, but beta and *P*-values of log CRP were not shown in multiple regression analysis and not adjusted for TG and heart rate. Since we found a significant relationship between log CRP and baPWV in multiple linear regression analysis and significant progressive increases in baPWV were observed across the quartiles of CRP in fully adjusted analyses, we believe that CRP is actually related to PWV in male subjects. In female subjects, the relationship between log CRP and baPWV in multiple linear regression analysis was significant, but the relationships of quartiles of CRP to baPWV had marginal significance of trend. The smaller sample size (a quarter of that of male subjects) could have reduced the statistical power. Also, it is well known that menopause aggravates the progression of atherosclerosis,[28] and the CRP level of females is lower than that of males.[29] The baPWV of females was significantly lower than that of males in subjects $\leq$55 years old, [27] so CRP in younger females might have a limited effect on arterial stiffness.

Torzewski *et al.*[30] have reported that CRP deposited in the arterial wall in early atherosclerosis

activates a complement protein, which might cause vascular remodeling and stiffen the artery. Wang *et al.*[31] showed that CRP upregulated angiotensin type 1 receptor on vascular smooth muscle cells and promoted vascular smooth muscle cell migration and proliferation, reactive oxygen species production, and increased collagen and elastin contents, which might cause arterial stiffness, too.

One large-sample-size study (n=12517) showed that UA was significantly related to baPWV in stepwise regression analysis in males and females, but the subjects were recruited at a number of institutes, and the method of UA measurement and whether UA was measured at one laboratory or more were not reported.[27] In addition, a study of 194 type 2 diabetes patients reported that UA was significantly related to aortic PWV in stepwise regression analysis.[32] Because we found a significant relationship between UA and baPWV in multiple linear regression analysis and significant progressive increases in baPWV were observed across the quartiles of UA, the measurement of UA was performed at one laboratory, and the subjects were a large number of the general working population, we believe that UA is actually related to PWV in males and females.

Uric acid directly stimulates VSM proliferation in vitro, and studies in rats have shown that elevated UA levels produce primary arteriopathy independent of blood pressure.[33] These effects, possibly mediated via activation of the renin-angiotensin system and down regulation of nitric oxide synthase,[34] might cause arterial stiffness.

In male subjects, the relationship between estimated GFR and baPWV in multiple linear regression analysis was significant, but the relationships of quartile-estimated GFR to baPWV had no significance of trend. As previously mentioned, 1290 untreated subjects were divided into three tertiles based on their GFR, and only in the lower tertile was elevated PWV significantly associated with reduced GFR.[23] In that study, the Cockcroft-Gault formula was used for GFR estimation, and the parameters of multiple repression analysis included "obesity (yes/no)", not BMI. Since both the formula of estimated GFR and BMI involve body weight, BMI adjustment for estimated GFR analysis is probably unsuitable. When we used obesity ($\geq$25kg/m^2 or not) instead of BMI for multiple repression analysis, the beta of estimated GFR was reduced (male: -0.050, P<0.001, female: -0.037, P=0.12). Since the direct assessment of GFR is rather complicated, we believe that estimated GFR is sufficient for a large population study.

In a review, Safar *et al*.[35] reported that arterial stiffness and renal dysfunction were related via endothelial dysfunction, oxidative stress, the calcium-phosphate mechanism, and activation of the renin-angiotensin-aldosterone system. But the relationship between reduced GFR and arterial stiffness remains incompletely understood. And the roles of CRP and UA in arterial stiffness have not been fully investigated. Further studies are required to elucidate the roles of CRP, UA, and GFR in arterial stiffness.

The present study has several limitations. First, this study could not identify a causal role for

CRP, UA and GFR in the pathogenesis of arterial stiffness. Second, we measured only estimated GFR, using the Cockcroft-Gault formula. Since the direct assessment of GFR is rather complicated, we believe that estimated GFR is sufficient for a large population study. Third, we could not obtain the subjects' income data, but the subjects worked for one local government. We therefore believe that the subjects were socioeconomicaly similar, so it was considered that the influence of socioeconomic status on the adjusted analysis was practically nil. Fourth, Significance of baPWV for the prediction of cardiovascular events has not been published. However, the validity and reliability of baPWV were reported.[36] Yamashita *et al.*[26] reported that baPWV significantly correlated with aortic PWV measured directly by catheter pressure transducer ($n=41$, $r=0.87$, $P<0.01$) and that the coefficient of variation of interobserver reproducibility was 8.4% and that of intraobserver reproducibility was 10.0%. The path length was estimated from the height of each subject based on the superficial measurements in Japanese population, suggesting possible errors. However, use of the equation should not seriously biased the reliability of PWV measurements because Pearson' correlation coefficient between the estimated length and the actual surface measurement was higher than 0.9.[37] Finally, the number of female subjects was rather small. A further study with a large number of female subjects is thus required.

In summary, our results suggest that CRP and UA are associated with an increase of arterial

stiffness in males and females, and estimated GFR is probably related to arterial stiffness in males. Because there are many interventional methods to improve these factors, further studies are needed to clarify whether anti-inflammatory strategies, UA lowering strategies, and protection of renal function prevent the progression of arterial stiffness.

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Figure legends

FIGURE 1 Adjusted means of baPWV compared among quartiles of C-reactive protein, uric acid, and estimated GFR in male subjects.

(a) adjusted[a] means of baPWV compared among quartiles of C-reactive protein, (b) adjusted[a] means of baPWV compared among quartiles of uric acid, (c) adjusted[a] means of baPWV compared among quartiles of estimated GFR in male subjects.

[a]adjusted for age, BMI, systolic blood pressure, HR, TC, HDL, FBS, log TG, UA (except for analysis of the quartile UA), estimated GFR (except for analysis of the quartile estimated GFR), log CRP (except for analysis of the quartile CRP), smoking status, alcohol consumption, frequency of exercise, hyperlipidemia, and diabetes.

FIGURE 2 Adjusted means of baPWV compared among quartiles of C-reactive protein, uric acid, and estimated GFR in female subjects.

(a) adjusted[a] means of baPWV compared among quartiles of C-reactive protein, (b) adjusted [a]means of baPWV compared among quartiles of uric acid, (c) adjusted[a] means of baPWV compared among quartiles of estimated GFR in male subjects.

[a]adjusted for age, BMI, systolic blood pressure, HR, TC, HDL, FBS, log TG, UA (except for analysis of the quartile UA), estimated GFR (except for analysis of the quartile estimated GFR),

log CRP (except for analysis of the quartile CRP), smoking status, alcohol consumption, frequency of exercise, hyperlipidemia, diabetes and menopausal status.

TABLE 1 Characteristics of male and female subjects

	Male (n=3412)	Female (n=854)
Age (y)	48.4 ± 6.8	46.8 ± 7.2
BMI (kg/m^2)	23.8 ± 2.9	21.8 ± 3.4
SBP (mmHg)	122.8 ± 15.3	114.6 ± 15.7
DBP (mmHg)	77.9 ± 10.9	69.3 ± 10.3
Heart rate (bpm)	60.6 ± 9.5	59.6 ± 8.2
Total cholesterol (mg/dL)	207.3 ± 33.4	208.3 ± 32.2
Triglyceride (mg/dL)	105 (75-152)	67 (50-91)
HDL cholesterol (mg/dL)	56.7 ± 14.4	69.7 ± 15.0
Fasting glucose (mg/dL)	95.8 ± 21.0	88.8 ± 14.8
Uric acid (mg/dL)	5.9 ± 1.2	4.5 ± 1.0
WBC(/μL)	5921 ± 1663	5087 ± 1396
CRP (mg/dL)	0.045 (0.023-0.089)	0.025 (0.012-0.052)
Estimated GFR (mL/min per 1.73m^2)	105.8 ± 18.2	116.6 ± 21.6
Current smoker (%)	59.7	24.3
Drinker (%)	72.9	52.8
Frequency of exercise (%)		
Rarely or never	54.5	67.3
≥1week	45.5	32.7
Hypertension (%)	9.3	7.8
Hyperlipidemia (%)	5.0	4.7
Diabetes (%)	2.3	2.0
Menopausal Status (%)		39.3
Postmenopausal		

Current use of hormone-replacement therpy (%)		2.0
PWV (cm/s)	1369 ± 200	1250 ± 181

Variables are presented as mean±SD, median (interguartile range) for skewed variables, or percentage.

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cell; CRP, C-reactive protein; GFR, glomerular filtration rate; PWV, pulse wave velocity.

TABLE 2 Coefficents of correlation from linear regression analysis between baPWV and variables in male and female subjects.

Variables	Male (n=3412)		Female (n=854)	
Age (y)	0.39	**	0.43	**
BMI (kg/m^2)	0.10	**	0.19	**
SBP (mmHg)	0.69	**	0.63	**
DBP (mmHg)	0.64	**	0.59	**
Heart rate (bpm)	0.33	**	0.21	**
Total cholesterol (mg/dl)	0.05	**	0.27	**
Log Triglycerides (mg/dl)	0.18	**	0.33	**
HDL cholesterol (mg/dl)	0.01		-0.10	**
Fasting glucose (mg/dl)	0.31	**	0.30	**
Uric acid (mg/dl)	0.10	**	0.25	**
WBC (/μl)	0.11	**	0.10	**
Log CRP (mg/dl)	0.15	**	0.19	**
Estimated GFR (ml/min per $1.73m^2$)	-0.12	**	-0.06	
Current smoker (vs. ex- or non-smoker)	-0.01		-0.03	
Drinker (vs. non-drinker)	0.08	**	-0.02	
Exercise ($\geq$1/week vs. rarely or never)	-0.05	**	0.05	
Hypertension	0.30	**	0.26	**
Hyperlipidemia	0.10	**	0.19	**
Diabetes	0.13	**	0.13	**
Postmenopausal (vs.premenopausal)			0.33	**
Current use of HRT (vs. not use of HRT)			-0.02	

** $P<0.01$. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cell; CRP, C-reactive protein; GFR, glomerular filtration rate.

TABLE 3 Multiple linear regression analysis with baPWV as the dependent variable in male and female subjects

	Male (n=3412)			Female (n=854)		
Variables	Beta	95% CI	P value	Beta	95%CI	P value
Age (y)	0.214	0.188 , 0.241	<0.0001	0.152	0.086 , 0.217	<0.0001
BMI (kg/m^2)	-0.121	-0.148 , -0.094	<0.0001	-0.149	-0.206 , -0.092	<0.0001
SBP (mmHg)	0.567	0.541 , 0.593	<0.0001	0.621	0.570 , 0.672	<0.0001
Heart rate (bpm)	0.162	0.138 , 0.185	<0.0001	0.095	0.050 , 0.140	<0.0001
Total cholesterol (mg/dl)	-0.006	-0.031 , 0.018	0.61	0.070	0.017 , 0.124	<0.05
Log Triglycerides (mg/dl)	0.051	0.022 , 0.080	<0.001	0.011	-0.045 , 0.067	0.70
HDL cholesterol (mg/dl)	0.016	-0.012 , 0.044	0.27	-0.016	-0.068 , 0.037	0.56
Fasting glucose (mg/dl)	0.100	0.073 , 0.126	<0.0001	0.104	0.055 , 0.154	<0.0001
Uric acid (mg/dl)	0.043	0.020 , 0.067	<0.001	0.057	0.009 , 0.105	<0.05
WBC (/μl)	0.014	-0.012 , 0.040	0.29	0.018	-0.029 , 0.064	0.45
Log CRP (mg/dl)	0.036	0.011 , 0.060	<0.01	0.038	-0.010 , 0.085	0.12
Estimated GFR (ml/min per 1.73m^2)	-0.029	-0.056 , -0.001	<0.05	0.003	-0.050 , 0.056	0.90
Current smoker (vs. ex- or non-smoker)	0.017	-0.008 , 0.041	0.18	0.032	-0.013 , 0.078	0.16
Drinker (vs. non-drinker)	-0.009	-0.032 , 0.014	0.43	-0.056	-0.099 , -0.012	<0.05

Exercise (≥1/week vs. rarely or never)	-0.043	-0.065 ,	-0.021	<0.001	0.001	-0.042 ,	0.043	0.98
Hypertension	0.049	0.025 ,	0.072	<0.0001	0.032	-0.013 ,	0.077	0.16
Hyperlipidemia	0.009	-0.013 ,	0.031	0.42	0.029	-0.015 ,	0.073	0.20
Diabetes	0.020	-0.005 ,	0.045	0.11	-0.028	-0.074 ,	0.018	0.23
Postmenopausal (vs.premenopausal)					0.025	-0.033 ,	0.083	0.40

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cell; CRP, C-reactive protein; GFR, glomerular filtration rate.

TABLE 4

(a) What is known about this topic.

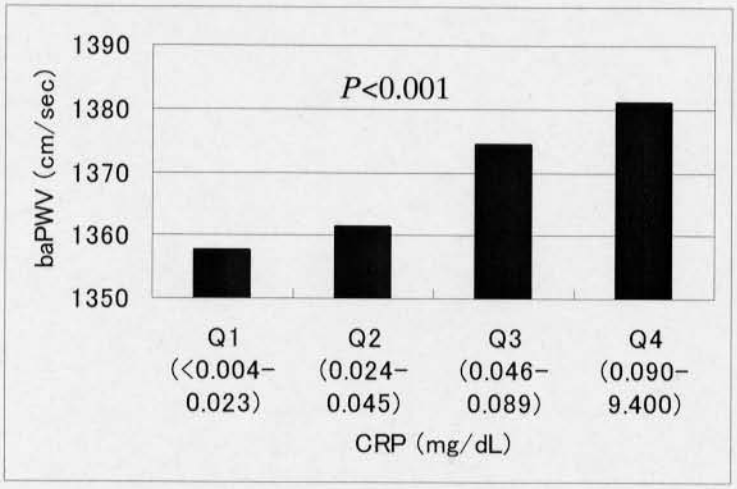
- CRP, UA, and ESRD are risk factors of cardiovascular diseases.
- But the relationships of CRP, UA, and GFR to arterial stiffness have not been fully investigated.

(b) What this study adds.

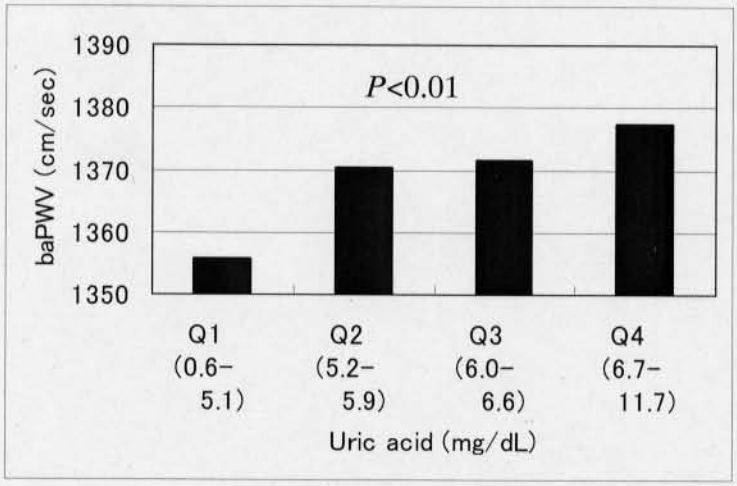
- CRP and UA are associated with an increase of arterial stiffness in males and females.
- GFR is possibly related to arterial stiffness in males.

FIGURE 1 Adjusted means of baPWV compared among quartiles of C-reactive protein, uric acid, and estimated GFR in male subjects.

a



b



c

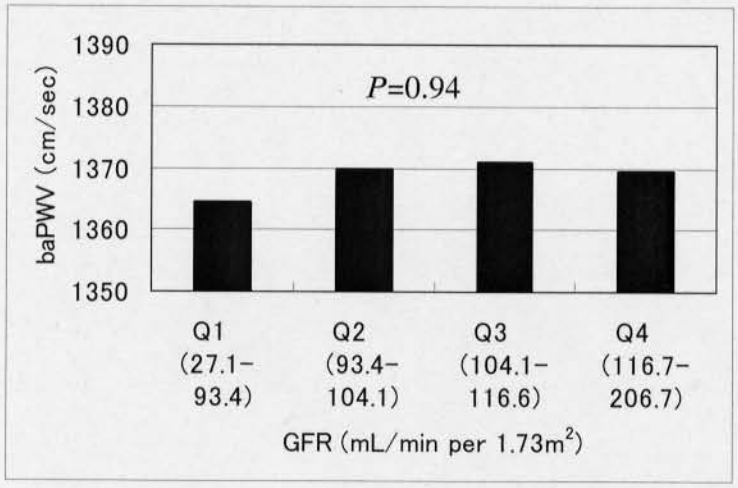


FIGURE 2 Adjusted means of baPWV compared among quartiles of C-reactive protein, uric acid, and estimated GFR in female subjects.