Gender-Related Association of Serum Uric Acid Levels with Premature Ventricular Contraction

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Summary

In this study, we aim to investigate the association of serum uric acid (SUA) with the prevalence of premature ventricular contraction (PVC). The relationship between SUA and the prevalence of PVC in 98,965 subjects (79,034 male subjects, mean age: 51.9 ± 12.6 years old) in the Kailuan cohort study ($n = 101,510$, age range: 18-98 years) from June 2006 to October 2007 was investigated. These subjects were divided into five groups on the basis of their SUA levels. A multivariate logistic regression model was constructed to evaluate the association between SUA and the prevalence of PVC. The prevalence of PVC was 1.1% in all subjects, 1.1% in male subjects, and 1.0% in female subjects. Compared with the first quintile of SUA, the odds ratio (OR) and 95% confidence interval (95% CI) of other quintiles were 1.33 (1.05-1.69), 1.14 (0.90-1.46), 1.37 (1.08-1.74), and 1.63 (1.30-2.06) in male subjects; 1.12 (0.68-1.87), 1.27 (0.77-2.09), 1.45 (0.90-2.36), and 1.33 (0.81-2.18) in female subjects; and 1.30 (1.04-1.61), 1.20 (0.96-1.50), 1.33 (1.07-1.66), and 1.57 (1.26-1.95) for all subjects. The correlation between SUA and the prevalence of PVC was significant in all subjects and in male subjects, but not in female subjects. We demonstrated that SUA was apparently associated with the prevalence of PVC. The significant relationship between SUA and PVC identified in male subjects suggests the potential involvement of a gender-specific mechanism. Prospective studies are needed to further corroborate our results.

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Key words: Kailuan Study, Cross-sectional, Population-based

In healthy populations, the incidence and frequency of premature ventricular contractions (PVCs) are approximately 1% and 10%, respectively, which increase with advanced age.^{1,2} Several epidemiological studies have shown that PVC is associated with a higher risk of cardiovascular events in different clinical settings.^{3,4} For instance, the high frequency of PVCs has been linked to a decrease in the left ventricular ejection fraction (LVEF), an increase in congestive heart failure (CHF), and an elevated mortality.^{5,6} More recent studies have suggested that PVC detected on 12-lead electrocardiography was a significant predictor of frequent PVCs.^{3,7}

Serum uric acid (SUA) is the final product of purine metabolism catalyzed by xanthine oxidase,⁸ which has been demonstrated to be an independent risk factor for various cardiovascular diseases including hypertension, chronic heart failure, metabolic syndrome, and coronary artery disease.⁹⁻¹³ Nevertheless, it remains to be determined whether any correlation between SUA and PVC occurrence exists in the general population. In the present

study, we aimed to evaluate the relationship between SUA and the incidence of PVC in China. In addition, we also analyzed the effects of gender on the independent correlation between SUA and PVC.

Methods

Study design and population: In the present study, health examination data were collected from the employees and retirees of Kailuan (Group) Co. Ltd., which is a large coal mining enterprise located in Tangshan, Hebei Province, China. As of 2006, Tangshan city has approximately 7.2 million inhabitants, is situated 150 km southeast of Beijing, and is the center of the coal mining industry in China. From June 2006 to October 2007, 101,510 subjects (81,110 males and 20,400 females) participated in the health examination. Subjects with missing electrocardiography or SUA data ($n = 1,889$) and a history of atrial fibrillation/flutter or Wolff-Parkinson-White (WPW) syndrome at baseline ($n = 656$) under which the prevalence

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of PVC was higher than that in the general population were excluded from the study.¹⁴⁻¹⁶⁾ Finally, a total of 98,965 employees (79,034 male subjects, mean age: 51.9 ± 12.6 years old) were enrolled in the present study.

Structured interviews with a standardized questionnaire were administered face-to-face by trained investigators. The questionnaire included information on demographic and socioeconomic background, educational level, self-reported income, alcohol use, smoking habits, physical activity, and major medical history such as hypertension, diabetes, myocardial infarction, and stroke. Standard protocols were used in all measurements, as previously described.^{17,18)} These were performed by specially trained doctors and nurses. All experiments in the present study were performed according to the Declaration of Helsinki. This study was approved by the Ethics Committee of the Kailuan General Hospital. Written informed consent was obtained from each participant prior to enrollment.

Electrocardiography measurements: Each participant underwent 12-lead electrocardiography at rest for 5 minutes. All subjects were prohibited from drinking alcohol and tea before the examination. Each electrocardiography rhythm strip was read back-to-back by two researchers. If the outcomes differed, the electrocardiographs were further reviewed by an experienced cardiologist. The primary exposure was the prevalence of at least one PVC on 12-lead electrocardiography.

Clinical measurements: The heights and weights of the subjects were measured while wearing light clothing without shoes and hats. Heights were measured to the nearest 0.1 cm using a portable stadiometer, and weights were measured to the nearest 0.1 kg using calibrated platform scales. Blood pressure (BP) was measured to the nearest 1 mmHg using mercury sphygmomanometers following standard recommended procedures. Two independent readings of systolic and diastolic BP were recorded at 5 minutes intervals. The average of these two readings was used in the data analysis. If these two measurements differed by more than 5 mmHg, an additional reading was taken.

Laboratory tests: Blood samples were collected from each subject in the morning at a fasting state through the antecubital vein. They were then stored in vacuum tubes containing ethylenediaminetetraacetic acid (EDTA). All blood tests were carried out at the Central Laboratory of Kailuan Hospital. SUA, creatinine, fasting blood glucose (FBG), total cholesterol (TC), triglycerides (TGs), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) levels were assessed using an autoanalyzer (Hitachi 747; Hitachi, Tokyo, Japan). SUA was determined using the uricase-peroxidase method.

SUA quintile thresholds: In the present study, subjects were divided into five groups on the basis of SUA concentrations. Thresholds when dividing the first and second, second, third, fourth and fourth, and fourth and fifth SUA quintiles were 3.70, 4.40, 5.08, and 5.97 mg/dL, respectively, in the whole population. Similarly, thresholds when dividing the SUA quintiles were 3.90, 4.61, 5.28, and 6.14 mg/dL, respectively, in male subjects and 3.18, 3.72, 4.25, and 4.98 mg/dL, respectively, in female subjects. The standard deviations (SDs) of these

SUA concentrations were 1.42, 1.40, and 1.20 mg/dL, respectively.

Definition of clinical variables: Hypertension was defined as the presence of a history of hypertension, the use of antihypertensive medications, systolic BP of ≥ 140 mmHg, or diastolic BP of ≥ 90 mmHg. Diabetes mellitus was defined as a self-reported history, the use of insulin or oral hypoglycemic agents, or FBG ≥ 7 mmol/L. Body weight (accurate up to 0.1 kg) and height (accurate up to 0.1 cm) were measured, and the body mass index (BMI) was calculated. The estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease (MDRD) formula as follows: $186 \times (\text{serum creatinine}^{-1.154}) \times (\text{age}^{-0.203}) \times (0.742 \text{ if female})$, with serum creatinine concentration expressed in milligrams per deciliter (mg/dL).¹⁹⁾

Statistical analysis: Statistical analyses were performed using SAS software version 9.1 (SAS Institute, Cary, NC, USA) and SPSS 13.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were described as mean $\pm$ SD and compared using one-way ANOVA. Categorical variables were described as percentages and compared using chi-squared tests. Linear regression was applied for analyzing the association between mean SUA concentration and PVC prevalence. Multivariable logistic regression was used to evaluate the relationship between different SUA concentrations and PVC occurrence by calculating the crude and adjusted odds ratios (ORs) and 95% confidence intervals (95% CIs). Furthermore, the association between the 1-SD increment of SUA and PVC was also analyzed using logistic regression models. A *P*-value < 0.05 (two-tailed) was considered statistically significant.

Results

Comparison of the Demographic and Basic Clinical Characteristics of Subjects: A total of 98,965 subjects (79,034 male subjects, 79.9%) with a mean age of 51.87 ± 12.62 years old were included in the survey. Among these subjects, 1,090 (1.1%) with a mean serum SUA concentration of 5.14 ± 1.48 mg/dL were diagnosed with PVC by 12-lead electrocardiography. Among these 1,090 subjects, 895 (1.1%) were male and 195 (1.0%) were female. Table I illustrates the demographic and basic clinical characteristics of subjects based on the presence/absence of PVC. Hypertension, myocardial infarction, diabetes mellitus, stroke, calcium channel blockers use, and β -R inhibitor use were more prevalent in subjects with PVC (all *P* < 0.05). Compared to subjects without PVC, subjects with PVC were significantly older and had significantly higher FBG, creatinine, and uric acid levels (all *P* < 0.05). However, there were no significant differences between these two groups in terms of BMI, smoking, TC, HDL-C, diuretic use, angiotensin-converting enzyme inhibitor use, and angiotensin receptor blocker use. Clinical characteristics based on gender are also summarized in Table II.

Correlation between SUA and PVC: From the first to the fifth SUA quintile, PVC prevalence was 0.80%, 1.10%, 1.02%, 1.19%, and 1.47% in all subjects; 0.81%, 1.15%, 1.00%, 1.21%, and 1.56% in male subjects; and

Table I. Comparison of Demographic and Clinical Characteristics of Participants Based on the Presence/Absence of PVC

Characteristics	Total	PVC	Non-PVC	P-value
Subjects	98,965	1,090	97,875	
Males, <i>n</i> (%)	79,034 (79.9)	895 (82.1)	78,139 (79.8)	0.063
Age (years)	51.87 ± 12.62	59.80 ± 13.70	51.78 ± 12.58	< 0.001
BMI	25.05 ± 3.49	25.06 ± 3.59	25.05 ± 3.49	0.880
Smoking, <i>n</i> (%)	33,232 (34.4)	335 (32.1)	32,897 (34.5)	0.117
History of DM	9,355 (9.5)	148 (13.6)	9,207 (9.4)	< 0.001
History of HTN	43,861 (44.3)	619 (56.8)	43,242 (44.2)	< 0.001
History of MI	1,281 (1.3)	44 (4.3)	1,237 (1.3)	< 0.001
History of stroke	2,483 (2.5)	55 (5.0)	2,428 (2.5)	< 0.001
Systolic BP (mmHg)	131.09 ± 21.07	137.77 ± 22.62	131.01 ± 21.04	< 0.001
Diastolic BP (mmHg)	83.51 ± 11.78	84.67 ± 12.33	83.49 ± 11.78	0.001
FBG (mmol/L)	5.48 ± 1.69	5.66 ± 2.06	5.48 ± 1.68	< 0.001
Total cholesterol (mmol/L)	4.95 ± 1.15	4.89 ± 1.09	4.95 ± 1.15	0.067
HDL cholesterol (mmol/dL)	1.55 ± 0.40	1.56 ± 0.39	1.55 ± 0.40	0.283
Creatinine (μmol/L)	91.91 ± 30.40	94.28 ± 28.31	91.89 ± 30.42	0.010
eGFR (mL/min*1.73 m ²)	83.45 ± 26.13	77.12 ± 20.43	83.52 ± 26.18	< 0.001
Medications, <i>n</i> (%)				
Diuretic	1,143 (1.2)	15 (1.5)	1,128 (1.2)	0.422
ACEI	674 (0.7)	11 (1.1)	663 (0.7)	0.154
ARB	197 (0.2)	1 (0.1)	196 (0.2)	0.443
CCB	1,159 (1.2)	25 (2.4)	1,134 (1.2)	< 0.001
β-R inhibitor	381 (0.4)	9 (0.9)	372 (0.4)	0.014
Uric acid (mg/dL)	4.88 ± 1.41	5.14 ± 1.48	4.88 ± 1.41	< 0.001

BMI indicates body mass index; HIN, hypertension; MI, myocardial infarction; DM, diabetes mellitus; BP, blood pressure; FBG, fasting blood glucose; HDL, high-density lipoprotein; eGFR, estimated glomerular filtration rate; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; and PVC, premature ventricular contraction.

Table II. Comparison of the Demographic and Basic Clinical Characteristics of Subjects Based on Gender

Characteristics	Total	Males	Females	P-value
Subjects	98,965	79,034 (79.9)	19,931 (20.1)	
Age (years)	51.87 ± 12.62	52.60 ± 12.77	48.95 ± 11.53	< 0.001
BMI	25.05 ± 3.49	25.14 ± 3.40	24.68 ± 3.80	< 0.001
Smoking, <i>n</i> (%)	33,232 (34.4)	32,866 (42.7)	366 (1.9)	< 0.001
History of DM	9,355 (9.5)	7,718 (9.8)	1,637 (8.2)	< 0.001
History of HTN	43,861 (44.3)	37,327 (47.2)	6,534 (32.8)	< 0.001
History of MI	1,281 (1.3)	1,115 (1.5)	166 (0.9)	< 0.001
History of stroke	2,483 (2.5)	2,213 (2.8)	270 (1.4)	< 0.001
Systolic BP (mmHg)	131.09 ± 21.07	132.66 ± 20.75	124.83 ± 21.14	< 0.001
Diastolic BP (mmHg)	83.51 ± 11.78	84.51 ± 11.75	79.51 ± 11.05	< 0.001
FBG (mmol/L)	5.48 ± 1.69	5.52 ± 1.69	5.32 ± 1.65	< 0.001
Total cholesterol (mmol/L)	4.95 ± 1.15	4.94 ± 1.16	4.99 ± 1.09	< 0.001
HDL cholesterol (mmol/dL)	1.55 ± 0.40	1.54 ± 0.40	1.59 ± 0.40	< 0.001
Creatinine (μmol/L)	91.91 ± 30.40	94.99 ± 31.03	79.73 ± 24.16	< 0.001
eGFR (mL/minute*1.73 m ²)	83.45 ± 26.13	84.43 ± 26.90	79.54 ± 22.41	< 0.001
Medications, <i>n</i> (%)				
Diuretic	1,143 (1.2)	911 (1.2)	232 (1.2)	0.991
ACEI	674 (0.7)	533 (0.7)	141 (0.7)	0.693
ARB	197 (0.2)	169 (0.2)	28 (0.1)	0.033
CCB	1,159 (1.2)	831 (1.1)	328 (1.6)	< 0.001
β-R inhibitor	381 (0.4)	268 (0.3)	113 (0.6)	< 0.001
Uric acid (mg/dL)	4.88 ± 1.41	5.07 ± 1.40	4.11 ± 1.20	< 0.001
PVC, <i>n</i> (%)	1,090 (1.1)	895 (1.1)	195 (1.0)	0.063

BMI indicates body mass index; HIN, hypertension; MI, myocardial infarction; DM, diabetes mellitus; BP, blood pressure; FBG, fasting blood glucose; HDL, high-density lipoprotein; eGFR, estimated glomerular filtration rate; ACEI, angiotensin-converting enzyme inhibitor; ARB, Angiotensin receptor blocker; CCB, calcium channel blocker; and PVC, premature ventricular contraction.

Table III. ORs (95% CI) for Uric Acid Associated with PVC

	Quintile 1	Quintile 2	SUA levels Quintile 3	Quintile 4	Quintile 5	P-trend	Increase per SD	P-value
Male								
Quintiles of uric acid (mg/dL)	< 3.90	3.90-4.61	4.61-5.28	5.28-6.14	> 6.14			
Subjects	15,741	15,626	15,927	15,298	15,547			
PVC, <i>n</i> (%)	128 (0.81)	180 (1.15)	160 (1.00)	185 (1.21)	242 (1.56)			
Model 1	1 (ref.)	1.41 (1.13-1.78)	1.24 (0.98-1.56)	1.49 (1.19-1.87)	1.91 (1.54-2.37)	< 0.001	1.19 (1.12-1.27)	< 0.001
Model 2	1 (ref.)	1.39 (1.11-1.74)	1.19 (0.94-1.50)	1.39 (1.11-1.75)	1.63 (1.31-2.02)	< 0.001	1.12 (1.06-1.19)	< 0.001
Model 3	1 (ref.)	1.33 (1.05-1.69)	1.14 (0.90-1.46)	1.37 (1.08-1.74)	1.63 (1.30-2.06)	< 0.001	1.13 (1.06-1.21)	< 0.001
Sensitivity analysis								
Model 4	1 (ref.)	1.40 (1.09-1.78)	1.18 (0.92-1.51)	1.43 (1.12-1.83)	1.68 (1.33-2.14)	< 0.001	1.13 (1.06-1.21)	< 0.001
Model 5	1 (ref.)	1.45 (1.13-1.85)	1.20 (0.93-1.56)	1.46 (1.14-1.88)	1.74 (1.36-2.22)	< 0.001	1.14 (1.07-1.23)	< 0.001
Female								
Quintiles of uric acid (mg/dL)	< 3.18	3.18-3.72	3.72-4.25	4.25-4.98	> 4.98			
Subjects	3,999	3,999	3,872	3,976	3,890			
PVC, <i>n</i> (%)	35 (0.88)	32 (0.80)	39 (1.01)	44 (1.11)	45 (1.16)			
Model 1	1 (ref.)	0.91 (0.57-1.48)	1.15 (0.73-1.82)	1.26 (0.81-1.98)	1.32 (0.85-2.06)	0.076	1.13 (0.99-1.29)	0.076
Model 2	1 (ref.)	0.92 (0.57-1.49)	1.13 (0.72-1.79)	1.21 (0.77-1.89)	1.15 (0.73-1.80)	0.352	1.07 (0.93-1.22)	0.352
Model 3	1 (ref.)	1.12 (0.68-1.87)	1.27 (0.77-2.09)	1.45 (0.90-2.36)	1.33 (0.81-2.18)	0.200	1.10 (0.95-1.27)	0.200
Sensitivity analysis								
Model 4	1 (ref.)	1.13 (0.68-1.90)	1.29 (0.78-2.12)	1.42 (0.87-2.31)	1.34 (0.81-2.21)	0.208	1.01 (0.99-1.04)	0.208
Model 5	1 (ref.)	1.13 (0.68-1.88)	1.26 (0.76-2.07)	1.43 (0.88-2.32)	1.33 (0.81-2.21)	0.297	1.08 (0.93-1.26)	0.297
Total								
Quintiles of uric acid (mg/dL)	< 3.70	3.70-4.40	4.40-5.08	5.08-5.97	> 5.97			
Subjects	19,864	19,381	19,848	19,418	19,364			
PVC, <i>n</i> (%)	159 (0.80)	213 (1.10)	202 (1.02)	232 (1.19)	284 (1.47)			
Model 1	1 (ref.)	1.37 (1.12-1.69)	1.27 (1.03-1.57)	1.49 (1.22-1.83)	1.83 (1.51-2.23)	< 0.001	1.19 (1.13-1.26)	< 0.001
Model 2	1 (ref.)	1.31 (1.07-1.62)	1.19 (0.96-1.47)	1.33 (1.08-1.64)	1.50 (1.23-1.84)	< 0.001	1.11 (1.05-1.18)	< 0.001
Model 3	1 (ref.)	1.30 (1.04-1.61)	1.20 (0.96-1.50)	1.33 (1.07-1.66)	1.57 (1.26-1.95)	< 0.001	1.13 (1.06-1.21)	< 0.001
Sensitivity analysis								
Model 4	1 (ref.)	1.36 (1.09-1.69)	1.22 (0.97-1.53)	1.38 (1.10-1.73)	1.62 (1.29-2.12)	< 0.001	1.13 (1.06-1.21)	< 0.001
Model 5	1 (ref.)	1.32 (1.06-1.65)	1.20 (0.96-1.51)	1.40 (1.11-1.75)	1.60 (1.28-2.01)	< 0.001	1.14 (1.07-1.22)	< 0.001

Model 1 indicates unadjusted; Model 2, adjusted for age (total + gender); Model 3, adjusted for Model 2 and smoking, BMI, SBP, FBG, TC, eGFR, MI, stroke, diuretics, and β -R inhibitor; Model 4, adjusted for Model 3 and further excluded MI; Model 5, adjusted for Model 3 and further excluded MI and stroke. PVC: premature ventricular contraction; BMI: body mass index; MI: myocardial infarction; SBP: systolic blood pressure; FBG: fasting blood glucose; TC: total cholesterol; eGFR: estimated glomerular filtration rate.

0.88%, 0.80%, 1.01%, 1.11%, and 1.16% in female subjects, respectively. Linear regression analysis revealed that the mean SUA concentration was positively correlated with the prevalence of PVC in all subjects ($PVC\% = 0.34 \times SUA + 0.16$, $P = 0.011$) and in male subjects ($PVC\% = 0.17 \times SUA + 0.26$, $P = 0.021$), but not in female subjects ($PVC\% = 0.10 \times SUA + 0.55$, $P = 0.056$) (Table III and Figures 1 and 2).

Evaluation of the association between SUA and PVC prevalence: The association between SUA and PVC occurrence was evaluated by multivariable logistic regression after the adjustment for various clinical covariates (Table III). Compared with the first quintile of SUA, the ORs and 95% CIs of the other quintiles were 1.30 (1.04-1.61), 1.20 (0.96-1.50), 1.33 (1.07-1.66), and 1.57 (1.26-1.95) for all subjects; 1.33 (1.05-1.69), 1.14 (0.90-1.46), 1.37 (1.08-1.74), and 1.63 (1.30-2.06) for male subjects; and 1.12 (0.68-1.87), 1.27 (0.77-2.09), 1.45 (0.90-2.36), and 1.33 (0.81-2.18) for female subjects, respectively. Furthermore, the relationship between the 1-SD increment in SUA and PVC was also evaluated, and it was found that

the OR and 95% CI were 1.13 (1.06-1.21) for all subjects, 1.13 (1.06-1.21) for male subjects, and 1.10 (0.95-1.27) for female subjects, respectively. The correlation between SUA and the prevalence of PVC was significant in all subjects and in male subjects, but not in female subjects. In the sensitivity analysis, a nearly identical result was found in subjects who had no history of myocardial infarction or stroke (Table III).

Discussion

A study was carried out on a large sample obtained from the general population. It was demonstrated that higher levels of SUA were significantly correlated with PVC prevalence after adjustment for multiple clinical factors. Elevated SUA was an independent risk factor of PVC in the whole population and in male subjects, but not in female subjects. Through the sensitivity analysis, it was also found that the relationship between SUA and PVC remained significant in participants without myocardial infarction or stroke.

Figure 1. PVC prevalence according to the quintiles of SUA. SUA indicates serum uric acid; and PVC: premature ventricular contraction.

Figure 2. Linear regression of the mean SUA concentration and PVC prevalence. SUA indicates serum uric acid; and PVC: premature ventricular contraction.

SUA is a common parameter in the clinic, which may be obtained by routine laboratory testing. Elevated SUA has been considered to be correlated to cardiovascular diseases, including hypertension,²⁰⁾ stroke,²¹⁾ chronic heart failure,^{22,23)} myocardial infarction,²⁴⁾ atrial fibrillation,²⁵⁾ and left ventricular hypertrophy.²⁶⁾ The present results were in agreement with the finding reported by Yamada, *et al.*,²⁷⁾ which revealed that the SUA level is an independent predictor of ventricular arrhythmia in patients with left ventricular hypertrophy. In addition, in the present study, gender-specific analyses were performed, and a significant correlation between elevated SUA levels and PVC prevalence in males, but not in females, was found. This was consistent with one previous report, which suggested the positive association of SUA with cardiovascular morbidity and mortality in a large population of males, and not in females, in Japan.²⁸⁾ In addition, Sun, *et al.*²⁹⁾

also revealed that the independent association between SUA and AF was significant in males. In contrast, two prior studies demonstrated that hyperuricemia was a risk factor for cardiovascular events in females, but not in males.^{30,31)} Thus, it is highly likely that a gender-specific mechanism may underlie the link between SUA and cardiovascular diseases. The discrepancy between findings from different studies might be potentially attributed to ethnic and territorial specificity.

In the present study, we uncovered the relationship between SUA and PVC. However, the pathophysiological mechanism underlying this relationship remains obscure. SUA was found to inhibit the generation of nitric oxide and to activate inflammatory mediators such as tumor necrosis factor- α and mitogen-activated protein kinases, further impairing endothelial function and smooth muscle cell proliferation.³²⁻³⁴⁾ SUA was also involved in an-

giotensin II-mediated hypertrophy and the hyperplasia of myocytes and vascular smooth muscle cells.³⁵⁾ Higher production of angiotensin II would influence the expression of fibrogenic cytokine and promote perivascular and interstitial fibrosis, which would thereby promote myocardial fibrosis.^{36,37)} This is well known to be implicated in the pathogenesis to electrophysiological and structural abnormalities in a diseased atrial and ventricular myocardium.³⁸⁻⁴⁰⁾ Radovanovic, *et al.*⁴¹⁾ recently reported that SUA was associated with left ventricular remodeling in patients with chronic ischemic heart failure, and Chen, *et al.*⁴²⁾ also revealed a similar correlation between SUA and ventricular remodeling in infarcted rats with experimental hyperuricemia. Therefore, it is highly likely that the incidence of PVC might be linked to SUA-related unfavorable ventricular remodeling. However, the exact mechanism underpinning the association of SUA with PVC remains to be determined. In addition, our interesting findings suggest that if elevated SUA levels are causally involved in PVC occurrence, then lowering SUA may be one of the upstream therapies for reducing PVC occurrence.

Recent studies have revealed the association between frequent PVCs and the increased risk of adverse cardiovascular mortality and morbidity in different clinical settings.^{3,7,43,44)} However, long-term electrocardiography monitoring is expensive and not suitable for all clinical settings. Instead, 12-lead electrocardiography may be a convenient and viable measurement option for PVC. Sajadieh, *et al.*³⁾ reported that the detection of a single PVC on 12-lead electrocardiography was associated with a 70% risk of frequent PVCs. Yang, *et al.*⁷⁾ also demonstrated that the C-statistic for the number of PVCs on 12-lead electrocardiography, as a predictor of high-burden PVCs, was 0.7949. Hence, it should be recommended that physicians monitor PVC using 12-lead electrocardiography.

Limitations and strengths: The limitations of the present study need to be acknowledged. For example, the present study had a cross-sectional design. In addition, the prognosis of subjects with PVC and elevated SUA was not investigated in the present study. Furthermore, it was not further explored whether the application of SUA-lowering drugs could reduce PVC occurrence. In addition, in the present study, we were not able to further investigate the relationship between SUA and the severity of PVCs, or the association of PVC with other electrocardiography parameters. Notwithstanding these limitations, the present survey had important strengths, including its large sample size and population-based research.

Conclusion

In this paper, we demonstrated that the level of SUA is apparently associated with the prevalence of PVC. Therefore, we believe that SUA can be used as an indicator to clinically screen and identify subjects with a high risk of PVC. The relationship between SUA and PVC in males suggests the potential involvement of gender-specific mechanisms.

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Disclosures

Conflicts of interest: None.

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