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Original Article

# Serum uric acid to creatinine ratio is a useful predictor of renal dysfunction among diabetic persons

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ABSTRACT

*Background:* Serum uric acid (SUA) has been shown to be a predictor of renal disease progression in most but not all studies. This study aims to test whether renal function-normalized SUA {i.e, SUA/creatinine (Cr) ratio} is a predictor of decreased renal function among diabetic patients.
*Methods:* The subjects comprised 185 men aged 72 ± 11 (mean ± standard deviation) years and 175 women aged 77 ± 10 years from a rural hospital. We examined the relationship between SUA/creatinine (Cr) ratio and renal function evaluated by estimated glomerular filtration rate (eGFR) using the Modification of Diet in Renal Disease Study Group equation.
*Results:* Annual eGFR decline rate was significantly increased with increased tertile of baseline SUA/Cr ratio ($p = 0.011$), and prevalence of the rapid progression types (≥3.0 ml/min/1.73 $m^2$/year) was significantly higher in the second and third tertile (≥7,21) of baseline SUA/Cr ratio than the first tertile (<5.86) ($p = 0.032$). Pearson's correlation coefficient showed that baseline SUA/Cr ratio ($r = 0.136$, $p = 0.012$) as well as systolic blood pressure (SBP) and SUA were significantly correlated with annual eGFR decline rate. Multiple regression analysis using annual eGFR decline rate as an objective variable, adjusted for confounding factors as explanatory variables, showed that baseline SUA/Cr ratio ($\beta = 0.334$, $p < 0.001$) as well as gender and SBP were significantly and independently associated with annual eGFR decline rate. The multivariate-adjusted odds ratios (ORs) (95% confidence interval) of the baseline tertile of the SUA/Cr ratio for rapid progression of annual eGFR decline rate were 1.0, 3.15 (1.66–5.95) and 3.19 (1.57–6.51), respectively.
*Conclusion:* Our data demonstrated that baseline SUA/Cr ratio was independently and significantly associated with future renal function decline among diabetic patients.


## 1. Introduction

Diabetic kidney disease (DKD) is a common and morbid complication of diabetes (type 1 and 2) all over the world and among geriatric population [1] and the leading cause of chronic kidney disease (CKD). The serious complication occurs in 20%–40% of all diabetics [1]. Approximately 40% of persons with diabetes develop DKD, defined as albuminuria, impaired glomerular filtration rate (GFR), or both [2], and similar increases can be observed across many countries. There is now convincing corroborative evidence that patients with DKD have a high burden of cardiovascular morbidity [e.g., cardiovascular disease (CVD)] [3], mortality [4,5], progression to end-stage renal disease (ESRD) [5], and health-care services.

For decades high serum uric acid (SUA) levels were mainly considered a result rather than a cause of renal dysfunction [6]. However a number of experimental and epidemiological studies have demonstrated that increased SUA in humans is associated with systemic inflammation [7], hypertension [8], and progression to ESRD [9]. These studies provide direct evidence that SUA may be a true mediator of renal disease and progression. However, there are some studies showing conflicting results. The Cardiovascular Health Study on 5,808 patients reported no significant association

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between baseline SUA and incident CKD [10]. In patients with stages 3–4 CKD, hyperuricemia appears to be an independent risk factor for all-cause and CVD mortality, but not renal failure after a median follow-up of 10 years [11]. As renal dysfunction itself is an independently strong predictor of renal disease, progression and increased SUA often occurs as a consequence of renal dysfunction, those with lower estimated glomerular filtration ratio (eGFR) are more likely to have higher SUA levels and a higher risk of renal disease progression. Renal dysfunction is the major confounder in studies for the association between baseline SUA and CKD progression.

Thus, we developed new indices using renal function-normalized SUA {i.e., SUA/Creatinine (Cr) ratio} [12] and evaluated the relationship between baseline SUA/Cr ratio and potential risk factors such as hypertension, hyperglycemia, lipids, and renal dysfunction using cohort data from diabetic patients.

## 2. Subjects and methods

### 2.1. Subjects

Subjects for this investigation were continuously recruited from diabetic outpatients that visited the medical department of Seiyo Municipal Nomura Hospital from April to June 2017. We have found and compared patients who underwent a similar examination 6 months later to this study. For all these individuals, patients taking SUA lowering medication and with baseline SUA $\geq$8.6 mg/dL and eGFR <30 ml/min/1.73 $m^2$ were excluded. The study complies with the Declaration of Helsinki, and all procedures were approved by the Ethics Committee of Seiyo Municipal Nomura Hospital, and written informed consent was obtained from each subject.

### 2.2. Evaluation of confounding factors

Information on medical history, present conditions, smoking status, drinking habits, and medications (e.g., antihypertensives, antidyslipidemics, antidiabetics, and SUA lowering medications) were obtained using clinical files at baseline. Body mass index (BMI) was calculated as a person's weight in kilograms, divided by height in meters squared. Smoking status was calculated by multiplying the number of packs of cigarettes smoked per day by the number of years the person has smoked and the patients were categorized as never smokers, ex-smokers, light smokers (<20 pack-year) and heavy smokers ($\geq$20 pack-year). Daily alcohol consumption was obtained using the Japanese liquor unit of measurement, corresponding to 23 g ethanol, and the patients were categorized as never drinkers, occasional drinkers (<1 unit/day), daily light drinkers (1–2 units/day), and daily heavy drinkers (2–3 units/day). The systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured with an appropriate-sized cuff on the right upper arm of the subjects in a sedentary position using an automatic oscillometric blood pressure recorder while the patients were seated after having rested for at least 5 min. Triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), SUA, and hemoglobin A1c (HbA1c), and Cr (enzymatic method) were measured at the laboratory of the health examination center after overnight fasting. Renal function-normalized SUA was calculated using the SUA/Cr ratio. eGFR was calculated using a Japanese coefficient modified CKD equation: Male, $194 \times (Cr)^{-1.094} \times Age^{-0.287}$; Female, $194 \times (Cr)^{-1.094} \times Age^{-0.287}$ X 0.739 [13]. The annual eGFR decline rate was defined as (baseline eGFR -follow-up eGFR after 6-month)/0.5 years. We defined subjects with an annual eGFR decline rate over 3 ml/min/1.73 $m^2$ as rapid progression. Moreover, ischemic stroke, ischemic heart disease, and peripheral vascular disease were defined as cardiovascular diseases (CVD).

### 2.3. Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics Version 21 (Statistical Package for Social Science Japan, Inc., Tokyo, Japan). Data are presented as mean $\pm$ standard deviation (SD), unless otherwise specified, and in the cases of parameters with non-normal distribution (e.g., TG, and HbA1c), the data are shown as median (interquartile range) values. Parameters with non-normal distributions were used after log-transformation for analysis. Subjects were divided into three groups based on the tertile of baseline SUA/Cr ratio (first tertile, <5.86; second tertile, 5.86–7.20; third tertile, $\geq$7.21). Differences in means and prevalence among baseline findings were analyzed by ANOVA for continuous variables and $\chi^2$ test for categorical variables. Pearson's correlations were calculated in order to characterize the associations between baseline characteristics and annual eGFR decline rate. Multiple linear and logistic regression analysis was used to evaluate the contribution of each confounding factor to annual eGFR decline rate. When $p < 0.05$ the finding is considered statistically significant.

## 3. Results

### 3.1. Baseline characteristics of patients according to tertile of baseline SUA/Cr ratio

Baseline characteristics of the subjects according to tertile of baseline SUA/Cr ratio are illustrated in Table 1. The subjects comprised 176 men aged 72 $\pm$ 11 years and 168 women aged 77 $\pm$ 10 years. SUA, SUA/Cr ratio, and eGFR increased significantly with increase in tertile of the baseline SUA/Cr ratio, while presence of men, age, prevalence of CVD, and Cr decreased significantly. There was no inter-group difference regarding other baseline characteristics.

### 3.2. Annual eGFR decline rate of patients according to tertile of baseline SUA/Cr ratio

Table 2 shows annual eGFR decline rate and prevalence of three progression types of patients according to tertile of baseline SUA/Cr ratio. Annual eGFR decline rate was increased significantly with increase in tertile of the baseline SUA/Cr ratio, and prevalence of rapid progression type ($\geq$3.0 ml/min/1.73 $m^2$/year) were significantly higher in the second and third tertiles ($\geq$5.86) of the baseline SUA/Cr ratio than in the first tertile (<5.86).

### 3.3. Relationship between baseline characteristics including SUA/Cr ratio and annual eGFR decline rate

As shown in Fig. 1, baseline SUA/Cr ratio was significantly correlated with annual eGFR decline rate ($r = 0.136$, $p = 0.012$). Table 3 shows the relationship between baseline characteristics and annual eGFR decline rate. Pearson's correlation coefficient revealed that baseline SUA/Cr ratio as well as SBP and SUA were significantly correlated with annual eGFR decline rate. Multiple regression analysis using annual eGFR decline rate as an objective variable, adjusted for confounding factors as explanatory variables, showed that baseline SUA/Cr ratio as well as gender, SBP, and presence of antidiabetic medication, and SUA were significantly and independently associated with annual eGFR decline rate.

**Table 1**
Baseline characteristics according to tertiles of baseline SUA/Cr ratio.

| Baseline Characteristics N = 344 | Tertiles of baseline SUA/Cr ratio | | | *P*-value |
|---|---|---|---|---|
| | First tertile <5.86 N = 113 | Second tertile 5.86–7.20 N = 114 | Third tertile 7.21 ≤ N = 117 | |
| Men, N (%) | 75 (66.4) | 62 (54.4) | 39 (33.3) | **<0.001** |
| Age (years) | 77 ± 10 | 74 ± 11 | 73 ± 12 | **0.013** |
| Body mass index (kg/m$^2$) | 22.2 ± 3.5 | 24.3 ± 4.1 | 24.6 ± 3.7 | 0.732 |
| Diabetes duration (years) | 10 ± 7 | 13 ± 10 | 12 ± 10 | 0.157 |
| Smoking status † (%) | 57.5/34.5/4.4/3.5 | 60.5/29.8/2.6/7.0 | 70.9/19.7/2.6/6.8 | 0.180 |
| Drinking status ‡ (%) | 64.6/6.2/23.0/6.2 | 67.5/7.0/15.8/9.6 | 69.2/3.4/17.9/9.4 | 0.632 |
| Cardiovascular disease, N (%) | 50 (44.2) | 32 (28.1) | 26 (22.2) | **0.001** |
| Systolic blood pressure (mmHg) | 141 ± 20 | 146 ± 19 | 134 ± 21 | 0.274 |
| Diastolic blood pressure (mmHg) | 71 ± 11 | 73 ± 12 | 74 ± 12 | 0.181 |
| Antihypertensive medication, N (%) | 83 (73.5) | 82 (71.9) | 72 (61.5) | 0.103 |
| Triglycerides (mg/dL) | 103 (74–149) | 120 (76–171) | 121 (80–181) | 0.077 |
| HDL cholesterol (mg/dL) | 57 ± 16 | 61 ± 18 | 58 ± 15 | 0.169 |
| LDL cholesterol (mg/dL) | 101 ± 27 | 107 ± 28 | 108 ± 30 | 0.196 |
| Antilipidemic medication, N (%) | 41 (36.3) | 29 (25.4) | 43 (36.8) | 0.119 |
| Hemoglobin A1c (%) | 6.7 (6.1–7.2) | 6.7 (6.2–7.3) | 6.7 (6.2–7.4) | 0.695 |
| Antidiabeteic medication, N (%) | 97 (85.8) | 97 (85.1) | 99 (84.6) | 0.966 |
| Creatinine (mg/dL) | 0.97 ± 0.27 | 0.82 ± 0.18 | 0.68 ± 0.13 | **<0.001** |
| Serum uric acid (mg/dL) | 4.7 ± 1.2 | 5.3 ± 1.2 | 5.7 ± 1.1 | **<0.001** |
| Serum uric acid/Creatinine ratio | 4.9 ± 0.81 | 6.5 ± 0.38 | 8.5 ± 1.16 | **<0.001** |
| eGFR (ml/min/1.73 m$^2$/year) | 56.9 ± 16.9 | 65.1 ± 16.3 | 73.8 ± 14.6 | **<0.001** |

HDL, high-density lipoprotein; LDL, low-density lipoprotein; eGFR, estimated glomerular filtration rate. †Smoking status was defined as the number of cigarette packs per day multiplied by the number of years smoked (pack-year), and the participants were classified into never smokers, past smokers, light smokers (<20 pack-year), and heavy smokers (≥20 pack-year). ‡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 never drinkers, occasional drinkers (<1 unit/day), daily light drinkers (1–2 unit/day), and daily heavy drinkers (2–3 unit/day). Data presented are mean ± standard deviation. Data for triglycerides and hemoglobin A1c were skewed and presented as median (interquartile range) values, and were log-transformed for analysis. **P*-value: ANOVA for continuous variables or the $\chi^2$ -test for categorical variables. Bolded numbers indicate significance.

**Table 2**
Annual eGFR decline rate according to tertiles of baseline SUA/Cr ratio.

| Characteristics N = 344 | Tertiles of baseline SUA/Cr ratio | | | *P*-value |
|---|---|---|---|---|
| | First tertile <5.86 N = 113 | Second tertile 5.86–7.20 N = 114 | Third tertile 7.21 ≤ N = 117 | |
| Annual eGFR decline rate (ml/min/1.73 m$^2$/year) | 1.89 ± 12.7 | 5.89 ± 12.9 | 6.60 ± 12.4 | **0.011** |
| Progression type Non-progression: <0.0 ml/min/1.73 m$^2$/year | 41 (36.3) | 29 (25.4) | 27 (23.1) | 0.076 |
| Moderate progression: 0–3.0 ml/min/1.73 m$^2$/year | 18 (15.9) | 12 (10.5) | 18 (15.4) | 0.492* |
| Rapid progression: ≥3.0 ml/min/1.73 m$^2$/year | 54 (47.8) | 73 (64.0) | 72 (61.5) | **0.032*** |

Annual eGFR decline rate, (baseline eGFR -follow-up eGFR after 6-month)/0.5. * versus Non-progression.

### *3.4. Multivariate logistic regression analysis of tertile of baseline SUA/Cr ratio with annual eGFR decline rate*

As shown in Table 4, the multivariate-adjusted odds ratios (ORs) (95% confidence interval) of tertiles of baseline SUA/Cr ratio for rapid progression type of annual eGFR decline rate were 1.0, 3.15 (1.66–5.95), and 3.19 (1.57–6.51), respectively.

### *3.5. Standard coefficient of baseline SUA/Cr ratio for annual eGFR decline rate within selected subgroups*

In Table 5, to control potential confounding factors by baseline gender, age, prevalence of CVD, and eGFR, the data were further stratified based on gender (men, women), age (<65 years, ≥65 years), prevalence of CVD (absence, presence), SUA (<6.0 mg/dL, ≥6.0 mg/dL), and eGFR (≥60 ml/min/1.73 m$^2$, <60 ml/min/1.73 m$^2$). The Standard coefficient of baseline SUA/Cr ratio for annual eGFR decline rate were significant in patients with age ≥65 years and eGFR <60 ml/min/1.73 m$^2$, irrespectively of gender, prevalence of CVD, and SUA. However, there was no significant interaction between the two groups regarding those parameters.

## 4. Discussion

In this prospective follow-up cohort study of 344 diabetic persons, we set out to determine renal dysfunction, as assessed by annual eGFR decline rate, and examine potential confounding factors. Baseline SUA/Cr ratio was significantly and independently associated with annual eGFR decline rate among diabetic persons with preserved kidney function, and can help clinicians to predict the progression of CKD. To our knowledge, few studies have indicated that baseline SUA/Cr ratio as renal function-normalized SUA could be an important potential risk factor for renal function decline among diabetic patients [12].

In this study, we determined renal dysfunction by two markers of annual eGFR decline rate [14–17]. Annual decline rate of eGFR is a useful therapeutic marker to control CKD progression. According to previous studies, annual eGFR decline of <1 ml/min/1.73 m$^2$/year is thought as a normal aging process and annual eGFR decline rate of ≥3.0 ml/min/1.73 m$^2$/year is commonly associated with the risk of ESRD and mortality [14–18]. In our study, baseline SUA/Cr ratio was significantly associated with an increased risk of these outcomes as markers.

In subjects with normal renal function, an elevated SUA has been found to independently predict the development of CKD [9,19–21]. A recent meta-analysis found that elevated SUA levels were associated with incident CKD [22]. SUA has shown to be a predictor of kidney disease progression in most but not all studies [10,11,23]. A large cohort study of the Swedish Renal Registry showed that SUA is not associated with decline in renal function or

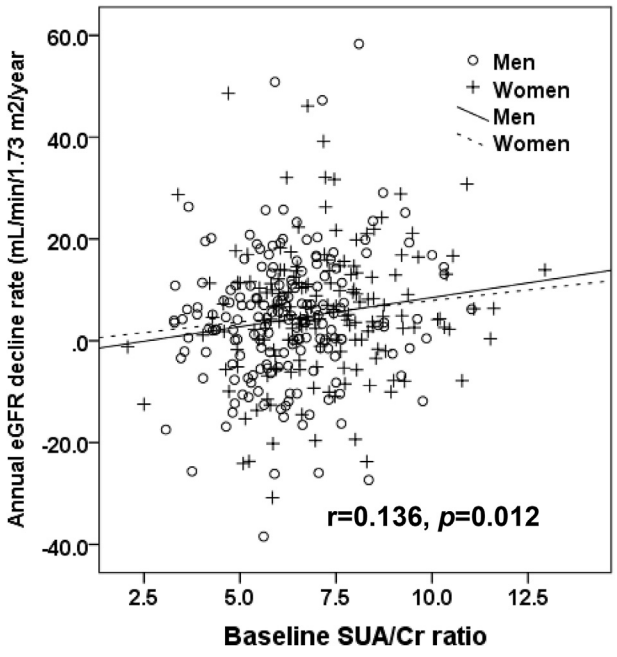


**Fig. 1.** Relationship between serum uric acid to creatinine ratio and rate of decline in annual estimated glomerular filtration (eGFR) decline rate. Serum uric acid to creatinine (SUA/Cr) ratio is significantly associated with the rate of decline in estimated glomerular filtration rate (eGFR) ($r = 0.136$, $p = 0.012$). The eGFR decline rate was defined as {(baseline eGFR -follow-up eGFR after 6-month)/0.5}.

time to renal replacement therapy initiation in patients with Stage 3, 4 and 5 CKD [23]. These results were probably due to the strong interaction between SUA and eGFR. In addition, these contradictory results may be attributed to the differences in baseline characteristics, adjustment of confounding factors, and sample size. In Taiwanese cohort study including 127,771 adults aged of ≥65 years, either SUA levels ≥ 8 or <4 mg/dL were significantly associated with higher all-cause and CVD mortality as compared with the reference strata of 4 to <5 mg/dL [11]. In our study, subjects with baseline SUA ≥8.6 mg/dL were excluded, thus, baseline SUA might show a negative association with eGFR decline rate.

UA is catalyzed by the enzyme xanthine oxidase, which is responsible for the production of UA and the destruction of free radicals, and it also possesses dual pro-oxidant and antioxidant properties. UA is the final oxidation product of purine metabolism in humans and is excreted renally [24]. Therefore, increased SUA levels are seen in patients with reduced GFR and are more likely to have higher risks of renal disease progression. Thus, if SUA is truly a risk factor of renal disease progression, baseline renal function-normalized SUA, which may reflect the net production of UA, will be more important as the predictor of incident CKD. Moreover, Al-Daghri et al. [25] reported that SUA/Cr ratio in type 2 diabetes is strongly and independently associated with higher risk of metabolic syndrome as well as central obesity, hypertriglyceridemia, low HDL-cholesterol, and hypertension. SUA/Cr ratio in type 2 diabetes was significantly associated with preserved β-cell function (i.e., insulin resistance), independently of potential confounders including sex, BMI, and renal function [26]. In fact, our study demonstrated that renal function-normalized SUA (e.g., SUA/Cr) ratio was independently associated with an increased risk of annual eGFR decline rate among diabetic patients.

Its main strengths are the 6-month follow-up, the control for potential confounding variables, and the inclusion of sensitivity analyses. However, there are limitations to this study as it is a 6-month cohort study. First, the causal relationship between hyperuricemia and renal function could not be explained by the study. Second, the estimation of renal function was based on a single creatinine measurement, which may result in a misclassification/information bias. Third, gold-standard techniques (e.g., inulin and radioscopic clearance) were not available for GFR measurement. Fourth, we have to consider the possible effects of underlying diseases and medications (e.g., antihypertensive, antidyslipidemic, and antidiabetic medication) on the present findings. Fifth, SUA/Cr ratio may cause a distortion when Cr is increased (e.g., men have a higher Cr than women), so that the ratio would be low even if SUA is high. Therefore, we cannot eliminate the possible effect of these confounders on the present findings.

In conclusions, this study showed that baseline SUA/Cr ratio contributed to annual eGFR decline rate, independent of baseline confounding factors. The underlying mechanism behind this relationship is unknown, and these factors seem to be independent of

**Table 3**
Relationship between baseline characteristics including SUA/Cr ratio and annual eGFR decline rate.

| Baseline Characteristics N = 344 | Annual eGFR decline rate | | |
|---|---|---|---|
| | Simple analysis | Multivariate analysis Forced entry Stepwise | |
| | r (*p*-value) | β (*p*-value) | β (*p*-value) |
| Gender (Men = 0, Women = 1) | 0.052 (0.340) | **−0.171 (0.038)** | …. … |
| Age | 0.044 (0.416) | 0.085 (0.212) | …. … |
| Body mass index | 0.020 (0.714) | 0.019 (0.752) | …. … |
| 病気期間 | −0.007 (0.898) | −0.071 (0.205) | …. … |
| Smoking status | −0.032 (0.554) | −0.062 (0.340) | …. … |
| Drinking status | −0.062 (0.249) | −0.066 (0.324) | …. … |
| Cardiovascular disease (No = 0, Yes = 1) | −0.032 (0.553) | −0.050 (0.382) | …. … |
| Systolic blood pressure | **0.135 (0.013)** | **0.137 (0.026)** | **0.127 (0.015)** |
| Diastolic blood pressure | 0.053 (0.329) | 0.003 (0.962) | …. … |
| Antihypertensive medication (No = 0, Yes = 1) | 0.014 (0.793) | 0.028 (0.630) | …. … |
| Triglycerides | −0.040 (0.460) | −0.066 (0.296) | …. … |
| HDL cholesterol | −0.041 (0.453) | **−0.127 (0.049)** | …. … |
| LDL cholesterol | −0.023 (0.665) | −0.019 (0.732) | …. … |
| Antilipidemic medication (No = 0, Yes = 1) | 0.042 (0.433) | 0.046 (0.409) | …. … |
| Hemoglobin A1c | −0.018 (0.746) | −0.103 (0.078) | …. … |
| Antidiabeteic medication (No = 0, Yes = 1) | 0.074 (0.168) | **0.154 (0.008)** | …. … |
| Serum uric acid | **−0.134 (0.013)** | **−0.314 (<0.001)** | **−0.237 (<0.001)** |
| Serum uric acid/Creatinine ratio | **0.136 (0.012)** | **0.334 (<0.001)** | **0.234 (<0.001)** |
| $R^2$ | ————— | **0.133 (<0.001)** | **0.081 (<0.001)** |

r, Pearson's correlation coefficient; β, standard coefficient; $R^2$, multiple coefficient of determination. Data for triglycerides and fasting blood glucose were skewed and log-transformed for analysis. ———— Not used in the final model by logistic regression analysis. Bolded numbers indicate significance.

**Table 4**
Prevalence and odds ratio for annual eGFR decline rate according to tertiles of baseline SUA/Cr ratio.

| Baseline SUA/Cr ratio N = 344 | Rapid progression type versus non-progression type Odds ratio (95% CI) | | | | *P*-value |
|---|---|---|---|---|---|
| | Total N = 344 | First tertile <5.86 N = 113 | Second tertile 5.86–7.20 N = 114 | Third tertile 7.21 ≤ N = 117 | |
| Prevalence Non-adjusted | 199 (57.8) | 54 (47.8) | 73 (64.0) | 72 (61.5) | **0.028** |
| | | 1.0 | 1.95 (1.14–3.31) | 1.75 (1.04–2.95) | **0.029** |
| Age and gender-adjusted | | 1.0 | 2.05 (1.19–3.53) | 1.87 (1.06–3.28) | **0.021** |
| Age, gender, and SUA-adjusted | | 1.0 | 2.38 (1.34–4.20) | 2.43 (1.29–4.59) | **0.005** |
| Multivariate-adjusted § | | 1.0 | 3.15 (1.66–5.95) | 3.19 (1.57–6.51) | **0.001** |

CI, confidence interval. § Adjusted for baseline all confounding factors in Table 3.

**Table 5**
Standard coefficient of baseline SUA/Cr ratio for annual eGFR decline rate within selected subgroups.

| Baseline characteristics N = 344 | N | Baseline SUA/Cr ratio | |
|---|---|---|---|
| | | β (*p*-value) | *P*-interaction* |
| Gender | | | |
| Men | 176 | **0.440 (<0.001)** | 0.144 |
| Women | 168 | **0.241 (0.012)** | |
| Age | | | |
| <65 years | 64 | 0.318 (0.066) | 0.216 |
| ≥65 years | 280 | **0.379 (<0.001)** | |
| Cardiovascular disease | | | |
| Absence | 236 | **0.270 (0.001)** | 0.102 |
| Presence | 108 | **0.492 (0.001)** | |
| eGFR | | | |
| ≥60 ml/min/1.73 $m^2$ | 212 | **0.407 (0.004)** | 0.178 |
| <60 ml/min/1.73 $m^2$ | 132 | 0.249 (0.060) | |
| Serum uric acid | | | |
| <6.0 mg/dL | 92 | **0.400 (0.002)** | 0.630 |
| ≥6.0 mg/dL | 252 | **0.345 (<0.001)** | |

§ Adjusted for baseline all confounding factors in Table 3. **P*-interaction was estimated using a general linear model. Significant values ($p < 0.05$) are presented in bold.

confounding factors, such as age, gender, drinking status, smoking status, hypertension, lipids, HbA1c, and medication. Our study provided new information for the understanding of the association between SUA, diabetes and renal dysfunction. Additional studies are needed to evaluate the reproducibility of our results and to further elucidate the association among these conditions.

## Author disclosure statement

No competing financial interests exist for any of the authors.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2019.04.023.

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