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Relationship of Uric Acid and Uric Acid to Creatinine Ratio with Reduced Glomerular Filtration Rate in Non-Alcoholic Fatty Liver Disease Among Apparently Healthy Adults

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Abstract **Objective:** The objective was to explore the potential existence and nature of the relationship between serum of uric acid (SUA) and serum uric acid to serum creatinine ratio (SUA/SCr) with reduced estimated glomerular filtration rate (eGFR) in patients with non-alcoholic fatty liver disease (NAFLD). **Methods:** A cross-sectional study was conducted among apparently healthy subjects with NAFLD (n=485). The association between tertiles of SUA and SUA/SCr with reduced eGFR (n=56) were investigated after adjustments for potentially relevant confounders. Also, the diagnostic performances of SUA and SUA/SCr were evaluated with the receiver operating characteristic (ROC) curve analysis. **Results:** In the adjusted models, SUA showed a significant positive association with reduced eGFR in the highest tertile (OR 5.65, 95% CI 2.48-12.86, p<0.001), and SUA/SCr, in the lowest tertile (4.21, 95% CI 1.76-10.07, p=0.001). The ROC curve analysis did not reveal any significant difference between the corresponding values of area under the curve for SUA and SUA/SCr (0.70 and 0.67, respectively; p=0.521). **Conclusions:** We revealed significant and independent associations of elevated SUA and reduced SUA/SCr with kidney function decline in NAFLD. However, the clinical utility of these two biomarkers seemed to be limited for the mentioned purpose and needs further investigations.

Key words: uric acid, uric acid to creatinine ratio, glomerular filtration rate, non-alcoholic fatty liver disease

Introduction

Non-alcoholic fatty liver disease (NAFLD), characterized by fatty liver deposition without significant alcohol consumption, is a prevalent condition linked to obesity, insulin resistance, hypertension, dyslipidemia, and type 2 diabetes.[1,2] Its global prevalence is estimated at around 25%, posing a rising health concern.[2] NAFLD, often undetected until late-stage disease, increases the risk of liver-specific, cardiovascular, and all-cause mortality.[3,4] Notably, it is closely associated with renal impairment, accelerating the development and progression of chronic kidney disease.[5] Existing literature suggests that NAFLD can accelerate the development and progression of chronic kidney disease characterized by impairment in kidney function (usually defined by a decline in the estimated glomerular filtration rate/eGFR), independent of traditional risk factors (Figure 1).[6] Such kidney impairment, marked by a decline in eGFR, presents substantial risks for morbidity and mortality, making it a significant public health concern worldwide.[7] Therefore, careful monitoring of NAFLD patients is crucial in order to prevent impaired kidney function and its progression. Identifying simple and effective biomarkers for early detection of impaired kidney function in NAFLD patients is paramount as it can profoundly impact morbidity, mortality, and overall quality of life for such individuals.

In humans, serum uric acid (SUA) is the final product of purine metabolism and its excretion is highly dependent on the function of the kidneys.[8] Impairment of kidney function can result in diminished uric acid excretion, leading to an elevated level of SUA.[9] Conversely, hyperuricemia itself can act as a causal risk factor for the development and progression of kidney diseases.[10] Due to this interactive relationship between SUA and the kidneys, relying solely on SUA may not offer a precise assessment of the relationship between uric acid and the state of kidney function. Since creatinine is a byproduct of muscle metabolism and is excreted by the kidneys, utilizing the SUA to serum creatinine ratio (SUA/SCr) helps to adjust for variations in creatinine levels based on the individual's renal performance. This normalized value for SUA level can provide a more accurate reflection of renal status and has been proposed as a superior predictor of kidney function. As documented in the existing literature, assessments of both SUA levels and SUA/SCr prove valuable in evaluating renal dysfunction.[8,11,12] Recent studies have further unveiled potential associations between SUA and SUA/SCr levels with NAFLD.[13,14]

As evident from the findings of the aforementioned studies, the measurements of SUA and SUA/SCr hold the potential to be valuable in detecting declines in kidney function among patients with NAFLD. However, published studies have explored the relationship of SUA and SUA/SCr among patients with kidney function decline and NAFLD separately. To the best of our knowledge, there is currently no study that has assessed the relationship of both SUA and SUA/SCr with kidney function decline among the same patient population diagnosed with NAFLD. Therefore, the usefulness of such tests remains uncertain for the purpose. On the other hand, a significantly higher level of SUA/SCr has been reported in patients with NAFLD compared to those without NAFLD.[15] Furthermore, separate studies indicate that a reduction in SUA/SCr is linked to a decline in renal function.[12] Yet, the crucial question remains unanswered in the existing literature: whether an increase or decrease in SUA/SCr is specifically associated with kidney function decline in individuals with NAFLD (Figure 1).

To address the above-mentioned gaps in

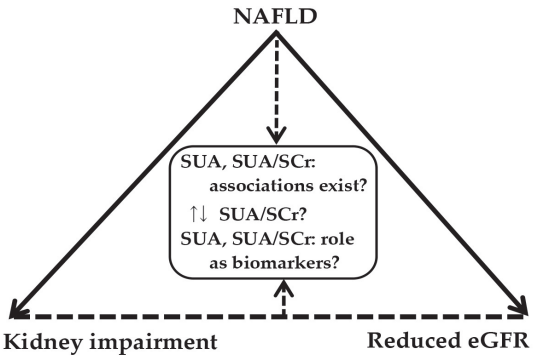

Fig. 1 Schematic illustration of the knowledge gap regarding SUA and SUA/SCr for kidney impairment/reduced eGFR in NAFLD.

the scientific literature, we aimed to explore and clarify the existence of the relationship between SUA and the SUA/SCr with reduced eGFR in NAFLD after adjustments for potentially relevant confounders. Additionally, we attempted to evaluate and compare the diagnostic performance of these two indicators in distinguishing individuals with reduced eGFR in NAFLD.

Materials and Methods

Ethical approval and informed consent:

The current study protocol, approved by the relevant institutional review board of Yamaguchi University, Japan (approval number 2022-096), was conducted in accordance with the Declaration of Helsinki. The existing Japanese law does not require the procurement of individual written informed consent from participants for research studies utilizing human biological specimens and not involving intervention. Therefore, for this study, we utilized an opt-out approach using the official website of Ube Kohsan Central Hospital, Yamaguchi Prefecture, Japan.

Study Design and Population

The flowchart of the study population recruited for this study has been depicted in Figure 2. For this single-center retrospective study, we considered the first visit of the adult subjects who attended the Health Checkup Center of Ube Kohsan Central Hospital, Yamaguchi Prefecture, Japan during April 2014 through March 2019, and underwent abdominal ultrasound examinations (n=5292). The health check-up consisted of physical examinations and clinical and laboratory tests. Also, the participants responded to a questionnaire on personal and medical history. Next, to analyze data from a seemingly healthy population, we selected subjects (n=1595) without a history of any diseases or major illnesses, except for fatty liver disease diagnosed by abdominal ultrasonography,

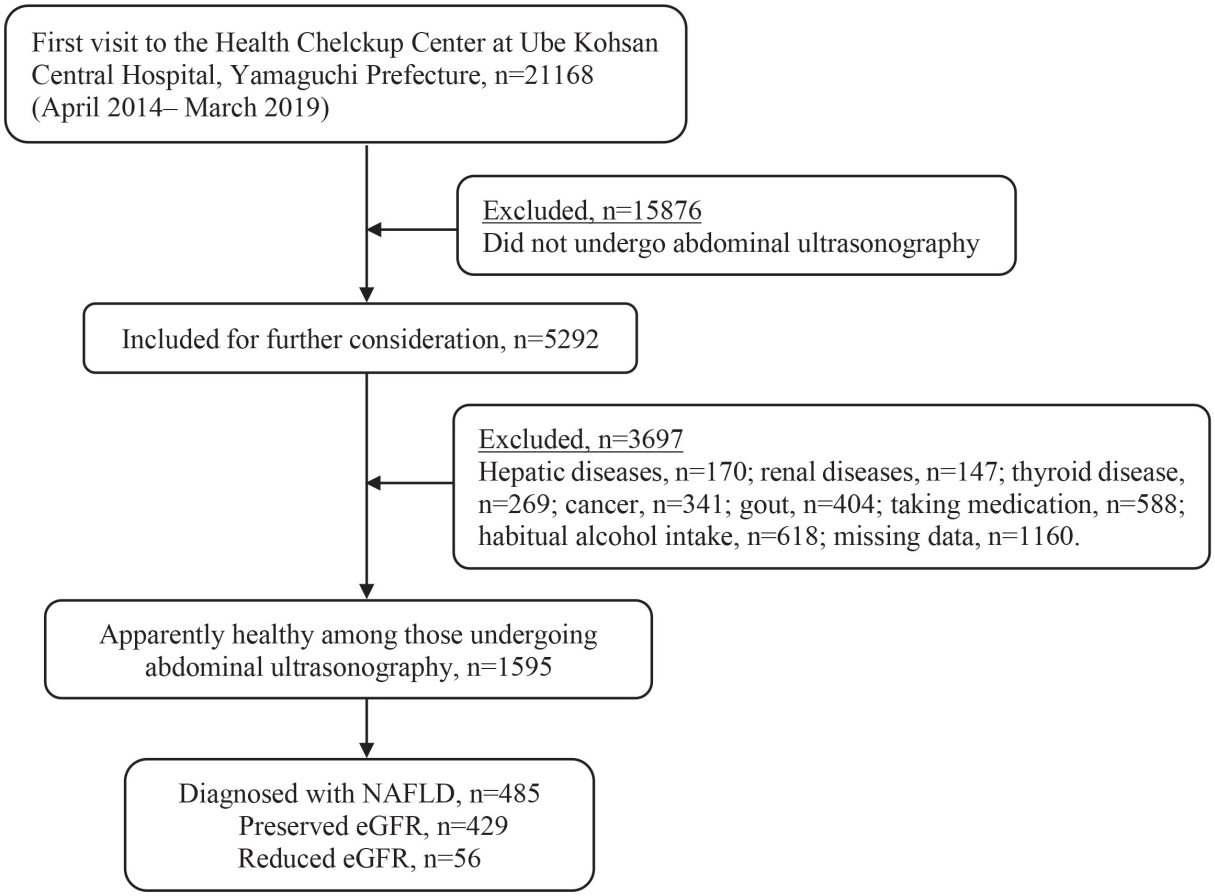

Fig. 2 Flowchart of current study population.

and who had no regular drinking habit. Consequently, we excluded individuals with known diagnoses or taking medications for conditions such as hypertension, diabetes mellitus, dyslipidemia, gout, cancer, hepatic diseases, thyroid disease, and cardiac diseases, leading to the exclusion of 3697 subjects from the initial study population considered for this research. Additionally, in line with our study's aim, we excluded subjects with a self-reported diagnosis of kidney disease.[16,17]

Data Collection

The medical data for all patients were anonymized and used for the analysis. The health checkup included physical examinations and clinical and other laboratory tests. Also, data on participants' personal and medical history were collected using a self-administered questionnaire. The drinking history within our study population was categorized into two groups: 'non-drinker' (comprising those who reported none or rare alcohol consumption) and 'drinker' (including those who reported occasional alcohol consumption).

Physical Examination

Height and body weight of each subject were measured to the nearest 0.1 cm and 0.1 kg, respectively and waist circumference, to the nearest 0.1 cm without shoes and in lightweight clothing. Body mass index (BMI) was calculated as individual subject's weight in kilograms divided by respective height in meters squared. Resting systolic (SBP) and diastolic (DBP) arm blood pressures were measured with automated noninvasive oscillometric arterial pressure measurement devices. The measurements were performed under a quiet environment by certified staffs, in sitting posture of the subjects and the arm supported at the heart level following the relevant standard guidelines.[18]

Measurement of Blood Samples

Blood samples were taken from the median cubital vein of a seated subject who were instructed to remain on an empty stomach. The laboratory measurements included alanine aminotransferase (ALT), aspartate aminotransferase (AST), fasting plasma glucose (FPG), gamma-glutamyl transpeptidase (GGT), high-density lipoprotein cholesterol (HDLC), low-density lipoprotein cholesterol (LDLC), total cholesterol (TC), and triglyceride (TG). The measurements of all laboratory variables were performed by HITACHI-7700 (Hitachi High-Technology Co., Tokyo, Japan), a commercially available automated biochemical analyzer, the broad application of which has been mentioned in the published research literature.[19-21] SUA and SCr were measured by the enzymatic method using the same autoanalyzer according to the protocols of the manufacturer.

Ultrasonographic Examination and Diagnosis of NAFLD

Abdominal ultrasonography was performed by a trained clinical laboratory technician with a commercially available device (ProSound α5 and α7, Aloka, Tokyo, Japan). The diagnosis of NAFLD was performed according to the guidelines for the assessment and management of it reported in the published literature.[22-24] Accordingly, NAFLD was diagnosed in the present study in the presence of following criteria: 1) imaging findings of fatty liver disease; 2) absence of excessive alcohol consumption; and 3) exclusion of diseases leading to steatoses, such as hepatitis, drug-induced liver disease, and alcohol-related liver disease. On the other hand, fatty liver disease was diagnosed in the presence of at least one of the four abnormal findings on abdominal ultrasonography that included bright liver, hepatorenal or hepatosplenic echo contrast, attenuation of the ultrasound signal, and vascular blurring. The ultrasonographic diagnosis was determined after a consensus was reached among at least two clinical laboratory technicians and one gastroenterologist.

Calculation and Assessment of eGFR

For this study, eGFR was calculated using the individual value of SCr and applying the following equation that has been recommended by the Japanese Society of Nephrology for the Japanese population: eGFR (mL/min/1.73 m^2) = 194 × SCr (-1.094) × age (-0.287) × 0.739 (if female).[25] Then the subjects were classified into two groups according to individual eGFR: (1) preserved eGFR

(eGFR≥60 ml/min/1.73 m^2) and (2) reduced eGFR (eGFR<60 ml/min/1.73 m^2).[26,27]

Statistical Analyses

The collected data did not follow a normal distribution and the continuous variables were analyzed using the Mann-Whitney U test for two-independent samples. Statistical analysis of the categorical variables was performed by the χ^2 test. Spearman's rank correlation analysis was performed between the concentrations of SUA and SUA/SCr. The patients with NAFLD were categorized into three groups according to the tertile cut-off values of SUA and SUA/SCr (tertile 1, lowest; tertile 2, middle; and tertile 3, highest), calculated separately for male and female subjects. For SUA, the tertile-specific cutoffs were <5.70 mg/dl, 5.70-6.83 mg/dl, and >6.83 mg/dl for males, and <4.30 mg/dl, 4.30-5.40 mg/dl and >5.40 mg/dl for females, respectively. For SUA/SCr, the tertile-specific cutoffs were <6.45, 6.45-7.53, and >7.53 for males, and <6.97, 6.97-8.14 and >8.14 for females, respectively.

At first, the crude association between SUA and SUA/SCr with the outcome variable (reduced eGFR) was investigated by applying the logistic regression analyses. Next, the models were adjusted for the demographic and clinical variables that differed significantly between the groups with and without reduced eGFR. From the logistic regression analyses, we obtained the odds ratios (OR) with corresponding 95% confidence intervals (CI) and p-values. The diagnostic performances of SUA and SUA/SCr were evaluated with the receiver operating characteristic (ROC) curve analysis and the area under the ROC curve (AUC) using non-parametric approach. The statistical analyses of the data were performed with the software packages SPSS version 22 for Windows (SPSS Inc., Chicago, IL, USA) and MedCalc version 22.009 (MedCalc Software Ltd, Ostend, Belgium). All statistical tests were considered as two-tailed; the significance level was set at a p-value less than 0.05.

Results

In the final analysis of this study, the data collected from a total of 485 patients with NAFLD (372 men, 113 women) and currently not taking any medications were considered for inclusion (Figure 2).

The demographic and clinical characteristics of the study population are presented in Table 1, according to the categories of preserved (n=429) and reduced eGFR (n=56). Compared to the subjects with preserved eGFR, those with reduced eGFR were predominantly older male subjects (χ^2 test, p<0.05), and with a higher BMI and waist circumference (Mann-Whitney U-test, p<0.05 to 0.001) (Table 1). However, smoking and drinking behaviors did not differ significantly between them (χ^2 test, p>0.05). On the other hand, in comparison with the subjects with preserved eGFR, subjects with reduced eGFR had significantly higher values of SBP, and elevated levels of AST and ALT and GGT (Mann-Whitney U-test, all p<0.05 to 0.005). Additionally, we observed significant differences in the levels of SUA, SCr, and SUA/SCr between the patients with preserved and reduced/declined eGFR (Mann-Whitney U-test, all p< 0.001). The serum concentrations of both SUA and SUA/SCr exhibited highly significant correlations in both the preserved eGFR group (r = 0.67; p < 0.001) and the reduced eGFR group (r = 0.76; p < 0.001).

We investigated the potential associations (both crude associations and associations with adjustments for potential confounders) between SUA and SUA/SCr with reduced eGFR (no versus yes) by logistic regression analyses (Table 2). For this purpose, we considered the corresponding lowest and highest tertile of SUA and SUA/SCr, respectively, as the reference category. For the observed associations with reduced eGFR, the trends of odds ratios (ORs) remained consistent across the tertiles of SUA and SUA/SCr in both crude and adjusted analyses. In the crude analysis, SUA showed a significant positive association with reduced eGFR in the highest tertile (OR 3.58, 95% CI 1.74-7.38, p=0.001). On the other hand, SUA/SCr demonstrated a significant positive association with reduced eGFR in the lowest tertile (OR 3.73, 95% CI 1.71-8.16, p<0.001). The adjusted models also demonstrated same trends, but stronger associations between SUA and SUA/SCr with

Table 1 Demographic and clinical characteristics of the study subjects. Values have been expressed as median and IQR values for the continuous variables, and as number (n) and percent (%) for the categorical variables.

	Preserved eGFR (n=429)		**Reduced eGFR** (n=56)		
Variables	Median or n	IQR or %	Median or n	IQR or %	p-value[§]
Age (Years)	50.0	14.0	58.0	10.0	<0.001
Sex					0.018
Male	322	66.4	50	10.3	
Female	107	22.1	6	1.2	
Smoking status					0.414
Non-smoker	346	71.3	44	9.1	
Smoker	83	17.1	12	2.5	
Alcohol					0.385
Non-drinker	264	54.4	31	6.4	
Drinker	165	34.0	25	5.2	
BMI (kg/m^2)	24.7	4.2	25.5	4.1	0.008
Waist (cm)	89.0	10.3	91.3	13.5	0.040
RBC ($10^4/\mu L$)	477.0	54.0	485.0	70.5	0.053
WBC ($/\mu L$)	5820.0	1930.0	5920.0	1805.0	0.201
Platelets[#] ($10^4/\mu L$)	24.5	6.0	23.7	7.5	0.068
SBP (mmHg)	126.0	18.0	128.0	24.0	0.024
DBP (mmHg)	80.0	13.0	82.0	15.0	0.062
ALT (U/L)	26.0	19.0	32.5	21.0	0.005
AST (U/L)	22.0	9.0	25.0	17.0	0.002
FPG (mg/dL)	102.0	15.0	105.0	24.0	0.223
GGT (U/L)	37.0	37.0	46.0	39.0	0.046
HDLC (mg/dL)	55.0	19.0	55.0	15.0	0.438
LDLC (mg/dL)	134.0	41.0	134.5	40.0	0.488
TC (mg/dL)	211.0	46.0	215.5	45.0	0.834
TG (mg/dL)	129.0	86.0	145.5	83.0	0.092
SUA (mg/dL)	5.8	1.8	7.0	1.5	<0.001
SCr (mg/dL)	0.8	0.2	1.1	0.1	<0.001
SUA/SCr	7.3	1.9	6.6	1.6	<0.001

BMI, body mass index; Waist: waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; ALT, Alanine aminotransferase; AST, aspartate aminotransferase; FPG, fasting plasma glucose; GGT, gamma-glutamyl transpeptidase; HDLC, high-density lipoprotein cholesterol; LDLC, low-density lipoprotein cholesterol; RBC, red blood cell; SUA, serum uric acid; SUA/SCr, SUA to serum creatinine ratio; TC, total cholesterol; TG, triglyceride; WBC, white blood cell. [#]n=403 and 49 for preserved eGFR and reduced eGFR groups, respectively (due to missing values). [§]Two-tailed p-values were obtained by the Mann-Whitney U-test for 2-independent samples or χ^2 test for categorical variables.

Table 2 Logistic regression analysis for association between reduced eGFR and tertiles of SUA and SUA/SCr with adjustment for relevant potential confounding demographic and clinical factors.

		Model I[a]				Model II[b]			
			95% CI				95% CI		
Variables	Categories	OR	Lower	Upper	P-value	OR	Lower	Upper	p-value
SUA	Tertile 1	Ref				Ref			
	Tertile 2	1.24	0.54	2.85	0.616	1.51	0.62	3.68	0.369
	Tertile 3	3.58	1.74	7.38	0.001	5.65	2.48	12.86	<0.001
SUA/SCr	Tertile 3	Ref				Ref			
	Tertile 2	2.17	0.94	4.98	0.068	2.09	0.85	5.12	0.106
	Tertile 1	3.73	1.71	8.16	<0.001	4.21	1.76	10.07	0.001

[a]Without adjustment.
[b]Adjusted for age, sex, BMI, SBP, ALT, AST, GGT, and waist.

reduced eGFR (OR 5.65, 95% CI 2.48-12.86, p<0.001 in the highest tertile category for SUA; and OR 4.21, 95% CI 1.76-10.07, p=0.001 in the lowest tertile category for SUA/SCr).

In Figure 3, the ROC curves demonstrate the effectiveness of SUA and SUA/SCr in distinguishing patients with reduced eGFR from those with preserved eGFR. The analysis could not reveal any significant difference between the corresponding values of AUC for SUA and SUA/SCr (AUC 0.70 with 95% CI 0.66 to 0.74 and AUC 0.67 with 95% CI 0.62 to 0.71, respectively; p=0.521).

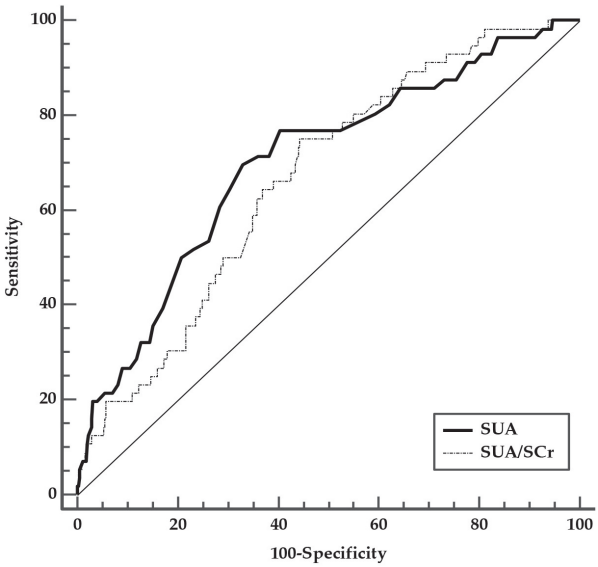

Fig. 3 ROC curves for SUA and SUA/SCr in discrimination of patients with reduced eGFR from those with preserved eGFR.

Discussion

Identification of useful biomarkers may play important roles in the prevention and/or early detection of impairments in kidney function among patients with NAFLD. This is the first study to report and characterize the nature of the association of SUA and SUA/SCr with decline in kidney function among NAFLD patients. As our results indicate, higher levels of SUA but lower SUA/SCr were closely associated with reduced eGFR among the patients with NAFLD.

In our study, NAFLD patients with reduced eGFR exhibited significantly higher values for age, BMI, waist circumference, and SBP.[28,29] This corresponds to the established link between aging and a heightened incidence of kidney damage, which is connected to an increased prevalence of conditions like hypertension and diabetes. On the other hand, elevated levels of ALT, AST, and GGT were observed in NAFLD patients with reduced eGFR, consistent with existing literature linking liver impairment to increased ALT and GGT levels in chronic kidney disease.[30,31] The simultaneous rise in ALT and AST, both markers of hepatocellular injury, suggests a potential association between kidney function decline and NAFLD in our study population.[32-34]

The intricate pathophysiologic mechanisms

underlying renal impairments in NAFLD remain incompletely understood. NAFLD-induced release of pro-inflammatory and oxidative stress mediators along with systemic and hepatic insulin resistance may lead to altered renin-angiotensin system activity, impaired antioxidant defense, and inflammatory responses. These factors could contribute to intrarenal immunologic inflammation, glomerulosclerosis, fibrosis, and tubular atrophy, culminating in chronic kidney disease.[35-37]

The documented independent association of high SUA with NAFLD development aligns with existing literature.[38] Additionally, the link between elevated SUA and kidney function decline and the role of the former as a potential biomarker for renal function is well-established.[10,39-41] Thus, our findings of a positive association between SUA and reduced kidney function in NAFLD patients are consistent with published literature.

In healthy humans, UA is mainly eliminated through the urine.[42] An increase in SUA generally occurs as a consequence of impaired UA clearance which is caused by a decline in kidney function.[43,44] Therefore, to indicate reduced kidney function while minimizing the confounding influence of renal function on increased level of UA, an indicator based on baseline renal function-normalized SUA has been suggested. The latter is expressed as SUA/SCr and considered to be a better biomarker than SUA.[11,12,43,45] In this study, we observed a close association between SUA/SCr and reduced eGFR among patients with NAFLD. Our findings corroborate with those of others reported previously.[12,46] In these studies, the investigators documented a positive correlation between SUA/SCr and eGFR. From their findings, it can be inferred that a reduction in SUA/SCr may be linked to a decline in eGFR. Consistent with this hypothesis, our study, following adjustments for potential confounders, demonstrated that a lower SUA/SCr was associated with reduced eGFR among individuals with NAFLD. It is noteworthy here that the current literature provides evidence either linking NAFLD to the development and progression of renal disease or on the relationship between SUA, and/or SUA/SCr with NAFLD or renal impairment.[5,6,11-14,36] Therefore, the direct comparison of our findings with such published literature is difficult as no previous studies are available that compared the relationship of SUA and SUA/SCr with reduced kidney function among patients with NAFLD. However, based on our current findings and those from previously published studies and the relevant mechanisms reported in the literature, it is obvious that close links exist between SUA, SUA/SCr, reduced kidney function, and NAFLD. Our findings also suggest that incorporating the calculation and reporting of the SUA/SCr ratio alongside individual measurements of SUA and SCr can potentially provide valuable insights. As mentioned under introduction, this ratio offers a more intricate assessment, reflecting the balance between uric acid and creatinine, which may enhance the sensitivity of kidney function assessment during routine screenings. Furthermore, utilizing SUA/SCr as an additional metric could contribute to a more comprehensive evaluation of renal health in apparently healthy individuals, particularly those with non-alcoholic fatty liver disease (NAFLD). Moreover, future longitudinal studies should properly establish the exact role (cause or consequence) of SUA and SUA/SCr in reduced kidney function among NAFLD patients.

In this study we explored the diagnostic performance of SUA and SUA/SCr in distinguishing individuals with kidney function decline among patients with NAFLD; with AUCs at or just below 0.7, their efficacy seemed to be limited for the purpose. For NAFLD patients, relevant information on these two biomarkers in distinguishing patients with reduced kidney function is not available in the existing literature. However, for the biomarkers SUA and SUA/SCr, previous studies tried to confirm whether one is superior to the other as the predictor of reduced kidney function in different disease states. But the relevant findings are conflicting. For example, in a study conducted among a group of hypertensive patients, the ROC curve analysis revealed that SUA was a better predictor of chronic kidney disease than SUA/SCr.[12] Also, in another study, SUA was found to be more accurate to assess the renal

dysfunction than SUA/SCr in patients with type 2 diabetes mellitus.[46] In contrast, SUA/SCr was suggested as a better predictor of incident chronic kidney disease among patients with type 2 diabetes mellitus.[43] On the other hand, we observed that the paired AUCs for the biomarkers SUA and SUA/SCr did not differ significantly, and hence, none of these can be considered as being superior to the other for the mentioned purpose.

Several potential limitations need to be considered while interpreting the findings of the current study. First, in this study, we excluded patients with known renal diseases, but included subjects with reduced eGFR. The underlying reason is that the purpose of this study was to investigate the relationship of SUA and the SUA/SCr with reduced eGFR in a group of patients diagnosed with NAFLD, but who were apparently healthy. Such a method of enrollment of apparently healthy subjects is a valid approach and completely in line with the published literature.[16,17,47-49] As we believe, the inclusion of a larger sample of patients with kidney impairment might lead to the revelation of stronger associations between the investigated biomarkers with reduced eGFR in NAFLD. Second, the unavailability of specific daily alcohol consumption data for the study population also poses a potential limitation. However, we addressed this by excluding individuals with regular drinking habits and focusing on none, rare, or occasional alcohol consumers. Additionally, among subjects with preserved eGFR, 34.0% (n=165) were identified as occasional drinkers, while only 5.2% (n=25) reported occasional alcohol consumption among those with reduced eGFR (Table 1). Thus, the lack of specific daily alcohol data should not bias our results. Conversely, a higher prevalence of occasional alcohol drinkers among those with reduced eGFR in NAFLD would suggest potential underestimation of our findings. Third, a question may arise on the confounding influence of age on eGFR as the subjects with reduced eGFR were older. In the current study, we adjusted our results for the variable age. Also, SCr-based equation utilized for the calculation of eGFR bears a multiplication factor for age which is about four times smaller than that for SCr level. Therefore, any potential impact of age on the study findings should be minimal. Fourth, in this study, we assessed kidney function by eGFR and did not investigate the urine samples for any relevant marker of kidney injury. However, we believe that it should not influence the reported outcome of this study as potential addition of more subjects with reduced eGFR detected by such tests would mean an underestimation of the current results. Lastly, in this retrospective study, NAFLD was determined by ultrasonography without any confirmation by histologic examination. However, in detection of NAFLD, ultrasonography (combined with the confirmed absence of excessive alcohol use or identifiable cause of secondary steatosis) is considered to be the most widely-used methodology and a valid, safe, easy-to-use, and commercially available, economical modality.[37,38,50]

Conclusions

We confirmed the significant and independent association of elevated SUA and reduced SUA/SCr with kidney function decline in NAFLD. The findings support the relevance and importance of these two indicators as potential biomarkers to detect kidney function decline among patients with NAFLD. However, the clinical utility of SUA and reduced SUA/SCr in distinguishing patients with reduced eGFR in NAFLD remains uncertain. The clinical usefulness of these two biomarkers for assessing the risk of decline in kidney function, early detection of the latter, and also identification of impaired kidney function in NAFLD needs to be confirmed in future prospective studies, including a relatively large cohort of such patients.

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Conflicts of Interest

The authors declare no conflict of interest.

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