ORIGINAL RESEARCH

Age-Related Effect of Uric Acid on Contrast-Induced Acute Kidney Injury of Patients Undergoing Coronary Angiography

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Background: The association between uric acid (UA) and contrast-induced acute kidney injury (CI-AKI) following coronary angiography (CAG) has been established. However, whether the association would vary with age remained undetermined.

Methods: We performed the retrospective analysis based on the Cardio-renal Improvement II study, (ClinicalTrials.gov NCT05050877), which enrolled consecutive patients undergoing coronary angiography in 5 teaching hospitals in China from 2007 to 2020. The primary outcome was CI-AKI defined as the rise of serum creatinine (SCr) ≥ 0.5 mg/dL or 25% compared with the baseline value within 48 hours following CAG. The effect of age on the association between uric acid and CI-AKI was assessed by the logistic regression model.

Results: A total of 36,550 patients (mean age 63.08±5.6-year-old, 41.7% men) were included in the study. After adjusting for the confounders, the risk of CI-AKI between each quartile of uric acid was insignificant in the young group. In patients of the middle group, lower UA was associated with a lower risk of CI-AKI while higher UA was associated with a higher risk (Q1 OR: 0.853, 95% CI: 0.734–0.993; Q4 OR: 1.797, 95% CI: 1.547–2.09). In patients of the elder group, lower and higher UA were both associated with a higher risk of CI-AKI (Q1 OR: 1.247, 95% CI: 1.003–1.553; Q4 OR: 1.688, 95% CI: 1.344–2.124). The restricted cubic spline indicated a non-linear association between UA and CI-AKI in middle and elder age groups but a linear association in the young age group.

Conclusion: The association between uric acid and CI-AKI vary in patients of different age. Patients with elder age should maintain a middle level of uric acid while patients with middle age should consider a lower level of uric acid to reduce the risk of CI-AKI. The level of UA was an insignificant risk factor for CI-AKI in young patients.

Keywords: uric acid, coronary angiography, CI-AKI, age-related

Introduction

Contrast-induced acute kidney injury (CI-AKI) is one of the most common complications of coronary angiography (CAG), which is usually associated with adverse clinical outcomes.^{1,2} There is no generally proven measure to treat CI-AKI effectively and the best strategy for the guideline recommendation is prophylaxis for prevention.³ Therefore, the

Clinical Interventions in Aging 2023:18 2053-2061

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identification of high-risk patients with specific characteristics is essential for the purposes of preventive treatment before the procedure.

A broad spectrum of risk factors of CI-AKI has been reported previously, including impaired renal function, hypotension, congestive heart failure, age, anemia, diabetes, contrast medium volume and so on.⁴ As an increasing number of populations, especially young people, are undergoing CAG procedures, whether these risk factors affect the development of CI-AKI in patients irrespective of age has seldom been investigated. Serum uric acid (SUA), a degradation metabolite of purines, was also demonstrated to be associated with the development of CI-AKI as well.^{5,6} However, the level of uric acid is an age-related factor that their filtration and affection on kidney function may vary in patients of different ages.⁷ Limited research has yet been conducted to examine the potential impact of age on the relationship between uric acid level and CI-AKI.

In this study, we aim to evaluate the association between uric acid level and the risk of CI-AKI at different ages in patients undergoing coronary angiography, to further improve the risk assessment before the procedure and minimize the occurrence of complications.

Method

Study Population

145,256 consecutive patients undergoing CAG were included in the study based on the Cardiorenal Improvement II (CIN-II) study, which was a multi-center cohort study with patients enrolled from 5 teaching hospitals (Cardiorenal Improvement II, ClinicalTrials.gov NCT05050877). The exclusion criteria were as follows: the following: patients without laboratory results of serum uric acid, preoperative and postoperative serum creatinine (SCr) (n=107,282); patients with an estimated Glomerular Filtration Rate (eGFR) < 15 mL/min/1.73 m² or requiring dialysis (n=1,424). Eventually, 36,550 patients were included (Figure 1). All traceable personal identifiers were removed from the analytic dataset to protect patients' privacy. The study protocol and informed consent exemption were approved by the ethics committees of Guangdong Provincial People's Hospital and the participant centers. The study was performed according to the declaration of Helsinki.

Data Collection

Data were extracted from the electronic clinical management system (ECMS) of each participant hospital. We had access to all primary and secondary care records. The baseline information included demographic characteristics, coexisting



Figure I Patient flow diagram.

conditions, laboratory examinations and medications. Uric acid was measured at admission. When numerous results of preoperative and postoperative results of SCr existed, the first examination at admission and the highest value within 48h following coronary catheterization were adopted.

Endpoint and Clinical Definition

The primary endpoint was CI-AKI, which was defined as a rise in SCr of $\ge 0.5 \text{ mg/dL}$ or a 25% increase from the baseline value within 48 hours after contrast media administration in the procedure of coronary catheterization.⁸ The level of UA was quartered into four groups in each age group, respectively (young age group: <50 years, middle age group: 50-70 years, old age group: >70 years). The eGFR was calculated by the Modification of Diet in Renal Disease (MDRD) formula.⁹ Chronic kidney disease (CKD) was defined according to the kidney disease: Improving Global Outcomes Organization (KDIGO) clinical practice guideline, in which eGFR < 60 mL/min/1.73 m² was determined as CKD.¹⁰ Anemia was defined as a hematocrit $\le 39\%$ (male) or $\le 36\%$ (female) according to the World Health Organization criteria. Diabetes mellitus (DM) was defined using ICD-10 codes or hypoglycemic medication use. Acute myocardial infarction (AMI), hypertension, coronary artery disease (CAD), atrial fibrillation (AF) and stroke were defined using ICD-10 codes.

Statistical Analysis

The distribution of each variable was evaluated by the Kolmogorov–Smirnov test. Normally distributed variables are reported as mean \pm SDs, whereas variables with skewed distribution are reported as median (interquartile interval). Categorical data are reported as frequencies and percentages. Differences of groups in baseline characteristics were compared through the use of chi-square tests for categorical variables and Student's *t*-test and One-way ANOVA for continuous variables. Multinomial multiple logistic regression analyses were performed to examine between the UA and CI-AKI adjusted for age, gender,intra-aortic balloon pump (IABP), congestive heart failure (CHF), anemia, DM, pre-SCr, contrast medium volume, AMI and PCI, which were based on the classic Mehran CIN risk score⁴ and relevant literature.^{11,12} Furthermore, restricted cubic spline (RCS) was used to investigate the linear tendency of the association between UA value and the risk of CI-AKI. In this method, we selected four SUA values as knots based on UA percentiles, tested the linear and non-linear associations between knots using a cubic function, and presented the smoothly integrated graph. Presented tests were 2-tailed for all, and a p-value<0.05 was considered statistically significant. All statistical analyses were performed using R (ver. 4.0.3).

Result

Baseline Characteristics

The mean age of the study population was $63.08 (\pm 5.6)$ years, and 71.3% were men. The proportion of male patients was higher in the younger age group, who were more likely to have higher low-density lipoprotein cholesterol (LDL-C) levels. Elderly patients were characterized by a higher level of SCr, more likely to be complicated with DM, CKD, hypertension, CHF and CAD. Both the young and the old age group had higher levels of UA. Detailed data between patients in different age groups is shown in Table 1.

Compared with patients with contrast-associated acute kidney injury (CA-AKI), patients in the CA-AKI group were more likely to be female. Patients with CA-AKI had a higher proportion of CHF, anemia, and higher levels of UA and IABP usage. In contrast, the pre-operative SCr of patients with CA-AKI seemed to be lower than those without CA-AKI. Detailed data between patients in CA-AKI and non-CA-AKI groups is shown in Table 2.

Association of Uric Acid and CI-AKI in Different Age Groups

Multivariate logistic regression showed that in patients of the young-age group, both higher and lower uric acid levels did not correlate with a higher risk of CI-AKI compared with the quartile 2 level of uric acid (OR for Q1: 0.927, 95% CI: 0.648–1.329; Q3: 1.249, 95% CI: 0.875–1.787; Q4: 1.243, 95% CI: 0.841–1.833). In patients in the middle-age group, the lower level of uric acid was associated with a lower risk of CI-AKI while the higher level of uric acid was associated with a higher risk of CI-AKI (OR for Q1: 0.853, 95% CI: 0.935–1.273; Q3: 1.091, 95% CI: 0.935–1.273; Q4: 1.797.95%

Table I	Baseline	Characteristics	of the l	Patients	Undergoing	Coronary	Angiography	in Different /	Age Groups
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N	Overall 36,550	Young Age Group (<50 Years)	Middle-Age Group (50–70 Years)	Old Age Group (>70 Years)	P-value
		4459	21,887	10,204	
	De	emographic characteristi	cs		
Age, year, mean (SD)	63.08 (11.54)	43.12 (5.65)	60.79 (5.80)	76.69 (4.47)	<0.001
Female, n (%)	10,479 (28.7)	536 (12.0)	6164 (28.2)	3779 (37.0)	<0.001
		Laboratory tests			
ALB, g/L, mean (SD)	37.93 (4.92)	39.63 (4.82)	38.15 (4.86)	36.72 (4.79)	<0.001
TRIG, mmol/L, mean (SD)	1.66 (1.32)	2.00 (1.80)	1.70 (1.32)	1.43 (0.97)	<0.001
CHOL, mmol/L, mean (SD)	4.63 (1.24)	4.82 (1.37)	4.66 (1.23)	4.47 (1.17)	<0.001
HDL-C, mmol/L, mean (SD)	1.08 (0.33)	1.01 (0.30)	1.07 (0.32)	1.12 (0.34)	<0.001
LDL-C, mmol/L, mean (SD)	2.93 (1.06)	3.08 (1.16)	2.96 (1.05)	2.81 (1.02)	<0.001
HbAIc, %, mean (SD)	6.54 (1.47)	6.35 (1.58)	6.56 (1.48)	6.57 (1.38)	<0.001
Pre-SCr, mg/dL, mean (SD)	1.03 (0.43)	0.97 (0.38)	1.00 (0.41)	1.11 (0.47)	<0.001
eGFR, mL/min/1.73 m ² , median[IQR]	80.99 [64.07, 98.25]	94.19 [80.03, 111.48]	83.37 [68.03, 99.53]	69.54 [53.35, 85.88]	<0.001
NEUT, 10 ⁹ /L, mean (SD)	5.78 (3.17)	6.77 (3.70)	5.61 (3.05)	5.71 (3.11)	<0.001
LYMPH, 10 ⁹ /L, mean (SD)	1.83 (0.75)	2.07 (0.80)	1.88 (0.71)	1.62 (0.75)	<0.001
Uric acid, mmol/L, mean (SD)	393.46 (119.40)	400.57 (119.65)	388.61 (116.93)	400.75 (123.92)	<0.001
	L	Medical Complications		1	
DM, n (%)	12,144 (33.2)	1167 (26.2)	7362 (33.6)	3615 (35.4)	<0.001
CKD, n (%)	8537 (23.4)	364 (8.2)	3927 (17.9)	4246 (41.6)	<0.001
HT, n (%)	19,602 (54.0)	1618 (36.6)	11,306 (52.1)	6678 (65.7)	<0.001
CHF, n (%)	7183 (19.8)	684 (15.5)	3739 (17.2)	2760 (27.2)	<0.001
AF, n (%)	2832 (7.8)	141 (3.2)	1580 (7.3)	1111 (10.9)	<0.001
CAD, n (%)	27,921 (76.9)	3222 (72.8)	16,116 (74.2)	8583 (84.5)	<0.001
AMI, n (%)	10,555 (29.1)	1814 (41.0)	5863 (27.0)	2878 (28.3)	<0.001
PCI, n (%)	21,482 (58.8)	2646 (59.3)	12,433 (56.8)	6403 (62.7)	<0.001
Pre-stroke, n (%)	622 (1.7)	24 (0.5)	317 (1.5)	281 (2.8)	<0.001
Anemia, n (%)	11,521 (31.8)	628 (14.3)	6106 (28.1)	4787 (47.3)	<0.001
COPD, n (%)	1586 (4.4)	17 (0.4)	700 (3.2)	869 (8.6)	<0.001
IABP, n (%)	882 (2.4)	83 (1.9)	490 (2.2)	309 (3.0)	<0.001
	L	Medications		1 1	
Statins, n (%)	29,463 (86.6)	3534 (83.7)	17,404 (85.0)	8525 (91.5)	<0.001
ACEI, n (%)	13,349 (39.2)	1937 (45.9)	7991 (39.0)	3421 (36.7)	<0.001
ARB, n (%)	8939 (26.3)	763 (18.1)	5250 (25.6)	2926 (31.4)	<0.001
Aspirin, n (%)	26,924 (79.2)	3404 (80.6)	15,918 (77.7)	7602 (81.6)	<0.001
Beta-blocker, n (%)	25,058 (73.7)	3301 (78.2)	15,041 (73.5)	6716 (72.1)	<0.001
CCB, n (%)	9461 (27.8)	1298 (30.7)	5408 (26.4)	2755 (29.6)	<0.001
Diuretic, n (%)	7483 (22.0)	779 (18.4)	4210 (20.6)	2494 (26.8)	<0.001

Note: Values are, n (%) or mean ± SD.

Abbreviations: ALB, albumin; TRIG, triglyceride; CHOL, cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; HbA1c, glycosylated hemoglobin; Pre-SCr, pre-serum creatinine; eGFR, epidermal growth factor receptor; NEUT, neutrophil; LYMPH, lymph cell count; DM, diabetes mellitus; CKD, chronic kidney disease; HT, hypertension; CHF, congestive heart failure; AF, atrial fibrillation; CAD, coronary artery disease; AMI, acute myocardial infarction; PCI, percutaneous coronary intervention; COPD, chronic obstructive pulmonary disease; IABP, intra-aortic balloon pump; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blockers.

CI: 1.547-2.09). However, in patients of the old-age group, both higher or lower levels of uric acid were associated with high risks of CI-AKI (OR for Q1: 1.247, 95% CI: 1.003-1.553; Q3: 1.34, 95% CI: 1.074-1.675; Q4: 1.688, 95% CI: 1.00-2.88) (Figure 2).

Ν	Overall 36,550	Non-CI-AKI 32,897	CI-AKI 3653	P-value
	Demographi	c characteristics		
Age, year, mean (SD)	63.08 (11.54)	62.92 (11.51)	64.44 (11.64)	<0.001
Female, n (%)	10,479 (28.7)	9127 (27.7)	1352 (37.0)	<0.001
	Labora	atory tests	·	
ALB, g/L, mean (SD)	37.93 (4.92)	38.03 (4.88)	36.99 (5.20)	<0.001
TRIG, mmol/L, mean (SD)	1.66 (1.32)	1.67 (1.33)	1.57 (1.21)	<0.001
CHOL, mmol/L, mean (SD)	4.63 (1.24)	4.62 (1.23)	4.75 (1.31)	<0.001
HDL-C, mmol/L, mean (SD)	1.08 (0.33)	1.08 (0.33)	1.08 (0.34)	0.569
LDL-C, mmol/L, mean (SD)	2.93 (1.06)	2.92 (1.05)	3.03 (1.12)	<0.001
HbAIc, %, mean (SD)	6.54 (1.47)	6.53 (1.46)	6.57 (1.49)	0.235
Pre-SCr, mg/dL, mean (SD)	1.03 (0.43)	1.04 (0.41)	0.93 (0.53)	<0.001
eGFR, mL/min/1.73 m ² , median	80.99 [64.07, 98.25]	80.47 [63.97, 96.83]	88.77 [64.84, 115.56]	<0.001
[IQR]				
NEUT, 10 ⁹ /L, mean (SD)	5.78 (3.17)	5.72 (3.10)	6.29 (3.72)	<0.001
LYMPH, 10 ⁹ /L, mean (SD)	1.83 (0.75)	1.84 (0.75)	1.74 (0.74)	<0.001
Uric acid, mmol/L, mean (SD)	393.46 (119.40)	392.84 (118.28)	399.07 (128.87)	0.003
	Medical C	Complications		
DM, n (%)	12,144 (33.2)	10,834 (32.9)	1310 (35.9)	<0.001
CKD, n (%)	8537 (23.4)	7610 (23.1)	927 (25.4)	0.003
HT, n (%)	19,602 (54.0)	17,722 (54.2)	1880 (51.9)	0.009
CHF, n (%)	7183 (19.8)	6033 (18.5)	1150 (31.8)	<0.001
AF, n (%)	2832 (7.8)	2358 (7.2)	474 (13.1)	<0.001
CAD, n (%)	27,921 (76.9)	25,396 (77.7)	2525 (69.8)	<0.001
AMI, n (%)	10,555 (29.1)	9358 (28.6)	1197 (33.1)	<0.001
PCI, n (%)	21,482 (58.8)	19,576 (59.5)	1906 (52.2)	<0.001
Pre-stroke, n (%)	622 (1.7)	553 (1.7)	69 (1.9)	0.383
Anemia, n (%)	11,521 (31.8)	10,152 (31.1)	1369 (37.8)	<0.001
COPD, n (%)	1586 (4.4)	1442 (4.4)	144 (4.0)	0.242
IABP, n (%)	882 (2.4)	612 (1.9)	270 (7.4)	<0.001
	Mec	lications	I	
Statins, n (%)	29,463 (86.6)	27,107 (88.2)	2356 (71.9)	<0.001
ACEI, n (%)	13,349 (39.2)	12,313 (40.1)	1036 (31.6)	<0.001
ARB, n (%)	8939 (26.3)	8123 (26.4)	816 (24.9)	0.063
Aspirin, n (%)	26,924 (79.2)	24,756 (80.5)	2168 (66.2)	<0.001
Beta-blocker, n (%)	25,058 (73.7)	22,795 (74.2)	2263 (69.1)	<0.001
CCB, n (%)	9461 (27.8)	8623 (28.1)	838 (25.6)	0.003
Diuretic, n (%)	7483 (22.0)	6022 (19.6)	1461 (44.6)	<0.001

Abbreviations: CI-AKI, contrast-induced acute kidney injury; ALB, albumin; TRIG, triglyceride; CHOL, cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; HbA1c, glycosylated hemoglobin; Pre-SCr, pre-serum creatinine; eGFR, epidermal growth factor receptor; NEUT, neutrophil; LYMPH, lymph cell count; DM, diabetes mellitus; CKD, chronic kidney disease; HT, hypertension; CHF, congestive heart failure; AF, atrial fibrillation; CAD, coronary artery disease; AMI, acute myocardial infarction; PCI, percutaneous coronary intervention; COPD, chronic obstructive pulmonary disease; IABP, intra-aortic balloon pump; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blockers.

To further investigate the association between the continuous change of uric acid and risk of CI-AKI, restrict cubic spline showed that the risk of CI-AKI linearly increased as the uric acid level increased but without significance for the most part in the young-age group (P for non-linear=0.483). The risk of CI-AKI remained lower at the lower level of uric

Group	Event, n (%)	Adjusted	p-value
<50 year			
Quartile1	98(8.77)	0.927(0.648-1.329)	0.68
Quartile2	79(7.05)	ref	
Quartile3	86(7.76)	1.249(0.875-1.787)	0.222
Quartile4	64(5.76)	1.243(0.841-1.833)	0.273
50-70 year			
Quartile1	533(9.74)	0.853(0.734-0.993)	0.04
Quartile2	500(9.14)	ref	
Quartile3	485(8.84)	1.091(0.935-1.273)	0.269
Quartile4	654(11.99)	1.797(1.547-2.09)	< 0.001
>70 year			
Quartile1	314(12.23)	1.247(1.003-1.553)	0.047
Quartile2	250(9.86)	ref	
Quartile3	268(10.46)	1.340(1.074-1.675)	0.01
Quartile4	322(12.68)	1.688(1.344-2.124)	< 0.001

Figure 2 Multiple logistic regression analysis stratified by uric acid level in different age groups for CI-AKI.

Note: Adjusted by age, gender, IABP, CHF, anemia, DM, pre-SCr, contrast medium volume, AMI and PCI.

Abbreviations: IABP, intra-aortic balloon pump; CHF, congestive heart failure; DM, diabetes mellitus; Pre-SCr, pre-serum creatinine; AMI, acute myocardial infarction; PCI, percutaneous coronary intervention.



Figure 3 Uric acid associated risk of CI-AKI in different age groups.

acid but sharply increased as the uric acid increased at the higher level in the middle-age group (P for non-linear=0.002). The RCS of the old-age group was a "U" shape which demonstrated both higher or lower levels of uric acid significantly increased the risk of CI-AKI (P for non-linear<0.001) (Figure 3).

Discussion

In this study, our results showed that the association between uric acid level and CI-AKI varied with age. Uric acid did not significantly correlate with the risk of CI-AKI in younger patients. Both higher and lower uric acid levels increased the risk of CI-AKI in elderly patients. For middle-aged patients, only the high level of uric acid was correlated with a higher risk of CI-AKI, while the lower level of uric acid was associated with a lower risk of CI-AKI.

Previous studies have also revealed that increased uric acid levels played a role in the progression of CI-AKI. Wei Guo et al found higher level of uric acid is an independent predictor associated with a risk of CI-AKI in patients undergoing PCI.¹³ Murat Saritemur et al demonstrated uric acid level is a simple independent early predictor of CI-AKI in patients who underwent primary PCI.¹⁴ Although uric acid and renal function affect each other, clinical studies showed that hyperuricemia was significantly associated with the risk of contrast-induced acute kidney injury after adjusting preoperative renal function levels in patients undergoing percutaneous coronary interventions.^{14,15} Therefore, our study adjusted preoperative creatinine to reduce this aspect of the factor. The previous studies mainly focused on the impact of uric acid on the CI-AKI without considering the differences by age. While Maurice C. Gephardt found uric acid values as related to age.⁷ Eghlim Nemati et al showed that older patients have relatively higher levels of uric acid than younger.¹⁶ Herein, our study has shown that the effect of uric acid on CI-AKI may be age-related. A middle level of uric acid in old-aged patients and a lower level of uric acid in the middle age patients might be more beneficial for reducing the risk of CI-AKI following coronary catheterization.

Previous studies have also shown that excess uric acid is associated with the susceptibility of renal impairment on exposure to contrast medium,^{17,18} The underlying mechanism of this relationship may be attributed to, the increased oxidative stress and crystals-related inflammation of high-level uric acid, leading to tubular injury, endothelial dysfunction and caused kidney injury following CAG.^{19–22} However, young patients have been reported as not susceptible to oxidative stress induced than the elderly,²³ which may explain the insignificant association between uric acid and CI-AKI. Similarly, Victoria Zigmont has also reported that serum Vitamin D and glioma risk was weak positive associated with younger adults due to the risk alleles in telomerase-related genes being more common among older patients.²⁴ And Victoria Zigmont et al reported that central obesity was identified as an independent factor of renal function impairment for all groups except males under 45 years of age.²⁵ On the other hand, studies have reported that low uric acid levels may reflect inadequate protection against oxidant-mediated stress in elder patients;^{26–28} Moreover, low uric acid levels in elder patients may reflect malnutrition,^{27,28} which may lead to immunodeficiency and impaired renal function susceptibility. These may be the potential mechanisms leading to an increased risk of CI-AKI in elderly people with low levels of uric acid in our study. Nonetheless, further studies are needed to illustrate how age differences would affect the association of risk factors, such as uric acid, on CI-AKI.

At what target level of uric acid should be controlled to reduce kidney dysfunction in patients undergoing CAG remained inconsistent. Hyperuricemia, defined as a serum uric acid level of >7 mg/dL (417 mol/L) in males and >6 mg/dL (357 mol/L) in females, was related to the risk of CI-AKI in patients with normal renal function, according to Yong Liu et al.¹⁴ Sunil Pillai proposed that those with serum uric acid levels more than 4.05 mg/dL were more likely to develop postoperative AKI.²⁹ According to the result presented in our study, the influence of uric acid on CI-AKI should take age into account, and it is not feasible to establish a universal standard for patients at any age. Given the disparities in renal function and the differences in the ability of uric acid and contrast agent excretion between age groups,³⁰ we suggested that the uric acid management strategies for patients in different age groups should not be identical. In general, a stricter strategy may be considered to control uric acid for middle-aged patients and a modest strategy may be better for old patients to keep uric acid at a median level. As for young patients, intentional treatment of hyperuricemia may not help prevent CI-AKI following CAG.

In patients aged \geq 50 years, the mean glycemia was higher than among those aged < 50 years. TC was also higher among the patients aged \geq 50 years compared to those aged < 50 years.³¹ Hua-Fen Chen et al showed that very high relative hazards of coronary complications were observed in younger and female diabetic patients in Taiwan.³² Previous studies have shown age, estimated glomerular filtration rate and ejection fraction score can predict contrast-induced acute kidney injury in patients with diabetes and chronic kidney disease.³³ Based on the above studies, age plays a great role in the control of blood lipids, blood glucose and uric acid, and different thresholds for human metabolic indicators are formulated according to different ages. Previous studies have also revealed that increased uric acid levels played a role in the progression of CI-AKI; However, they seldom reported the effect of age and did not pay attention to the part of the young and middle-aged patients.^{13,34} Our study suggests that for patients before undergoing CAG, not only the level of preoperative renal function should be a concern, but also the risk of CI-AKI caused by age-related uric acid and blood glucose may be further considered, so as to make individualized treatment plans.

Therefore, we may suggest that age differences need to be considered for the risk of contrast nephropathy associated with relevant metabolic indicators besides uric acid.

Limitation

Firstly, due to the nature of the observational study, only associations can be drawn without the causal relationship being inferred. The effect of uric acid-lowering medication on the correlation between age and uric acid-associated risk for CI-AKI needs further prospective studies to validate. Secondly, although some data were missing for the retrospective reason, a fully adjusted analysis was performed in this study, and the sample size was large enough to give adequate power for correlation.

Conclusion

In conclusion, the association between uric acid and CI-AKI in patients undergoing CAG was affected by age. Preoperative assessment of uric acid levels should be taken into account in the context of age. Further research is warranted to determine the optimal target of uric acid for preventing CI-AKI in different age groups.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This research was sponsored by Longyan City Science and Technology Plan Project (Grant number: 2021LYF17040), Guangdong Provincial science and technology project (2020B1111170011, DFJH2020026, DFJH201919); Guangdong Provincial science and technology project (KJ022021049); Guangdong Provincial Key Laboratory of Coronary Heart Disease Prevention (No. Y0120220151). The funders had no role in the study design, data collection, and analysis, decision to publish, or preparation of the manuscript; the work was not funded by any industry sponsors.

Disclosure

The authors report no conflicts of interest in this work.

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