Original Paper

Metabolic Syndrome and the Iodine-Dose/ Creatinine Clearance Ratio as Determinants of Contrast-Induced Acute Kidney Injury

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Keywords

Metabolic syndrome · Contrast-induced nephropathy · Creatinine clearance

Abstract

Background: Finding patients at risk of developing contrast-induced acute kidney injury (CI-AKI) is important because of its associated complications. In the present study, the contribution of different variables, such as the presence of metabolic syndrome (MetS), the volume creatinine clearance (V/CrCl) ratio, the iodine-dose (I-dose)/CrCl ratio, or hypertension, to CI-AKI was evaluated. **Methods:** A total of 255 patients undergoing elective coronary angiography with or without intervention were enrolled and divided into a MetS and a control group. All patients were assessed for the development of CI-AKI after the procedures. **Results:** CI-AKI occurred in 39.23% (51 of 130) of the MetS patients and 14.4% (18 of 125) of the control group ($p < 0.001$). The multivariable regression model showed that male sex and the use of statins decreased the risk of CI-AKI, and high triglyceride levels, I-dose/CrCl > 0.52 , MetS, CrCl ≤ 60 mL/min, and age ≥ 70 years increased the risk of CI-AKI, independent of confounding factors. The difference in the mean V/CrCl ratio was statistically significant between patients who developed CI-AKI and those who did not show renal impairment (2.36 ± 1.35 vs. 1.43 ± 0.89 , respectively; $p < 0.001$). The ROC curve analysis of I-dose/CrCl determined the best cutoff value for patients with and those without MetS as 0.51 and 0.63, with a sensitivity value of 68 and 72% and a specificity value of 73 and 74%, respectively. **Conclusions:** We showed that MetS is a strong risk factor for CI-AKI in nondiabetic patients undergoing elective coronary interventions; and the I-dose/CrCl ratio is a strong predictor of CI-AKI in these patients. We suggest that clinicians identify MetS patients and calculate their I-dose/CrCl ratio before coronary interventions.

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Introduction

Intravascular injection of contrast agents is widely used in interventional and diagnostic cardiac procedures. Complications associated with contrast agents range from minor reactions, such as itching or discomfort, to life-threatening conditions, such as hypotension, anaphylaxis, renal dysfunction, and cardiovascular events [1, 2]. Contrast-induced acute kidney injury (CI-AKI) is a possible complication of any procedure involving the use of intravascular iodinated contrast agents (which are very harmful to the kidneys) [3]. While most common complications due to contrast agents are transient, CI-AKI can cause prolonged hospitalization, serious long-term renal impairment, morbidity, and mortality [1]. It is reported to be the third leading cause of in-hospital acute renal failure [4]. Although the incidence of CI-AKI in the general population undergoing coronary angiography is about 2%, it can be much more in high-risk patients (up to 80%) [5]. Furthermore, it is associated with 40% of the in-hospital mortality rate and 80% of the 2-year mortality rate in patients who require dialysis after coronary intervention [4].

CI-AKI is diagnosed as an absolute or relative increase in serum creatinine (SCr) to ≥ 0.5 mg/dL ($44 \mu\text{mol/L}$) or $\geq 25\%$ above baseline, respectively. This alteration in SCr level occurs within 24–48 h after contrast procedures without any other evidence of kidney damage [6]. Several risk factors have been identified for CI-AKI, such as pre-existing renal impairment, hypovolemia, diabetes mellitus (DM), advanced age, a high dose of contrast agent, and the concurrent use of nephrotoxic drugs. There are several reported prophylactic methods to prevent CI-AKI, including high-dose oral N-acetylcysteine consumption, sodium bicarbonate infusion, preprocedural hydration with saline, the use of statins, the cessation of nephrotoxic agents, the limitation of contrast agent volume, and iso-osmolar contrast agent replacement [4, 5, 7]. It has been proven that preprocedural hydration with saline is the most effective countermeasure [8].

Metabolic syndrome (MetS) is a debilitating health problem worldwide with several interrelated risk factors, including dyslipidemia, hypertension, central obesity, insulin resistance, and impaired glucose tolerance, which together increase the mortality and morbidity rates of diseases such as coronary heart disease, diabetes, stroke, and chronic kidney disease (CKD) [9]. Decreased physical activity, adopting a western lifestyle, and unhealthy food habits contribute to the development of MetS [10]. Individual components of MetS, such as insulin resistance, abdominal obesity, hypertension, and dyslipidemia, are associated with the incidence and development of different renal injuries [11]. The association between type 2 DM and CKD, obesity and CKD, and hypertension and CKD has been shown extensively [10].

Recently, the volume creatinine clearance (V/CrCl) ratio has been reported to be helpful in the prediction of an early abnormal increase in SCr [12, 13]. Laskey et al. [13] reported that a V/CrCl > 3.7 is a useful marker for predicting an increase in SCr after percutaneous coronary interventions. While the iodine concentration of different contrast agents ranges from 140 to 400 mg/mL, the iodine-dose (I-dose)/CrCl ratio has been proposed to solve this problem [12].

It is important to screen at-risk patients before the procedures and to use appropriate prophylactic measurement to reduce the risk of CI-AKI and its complications. Accordingly, we hypothesized that patients diagnosed with MetS would be at a higher risk of developing CI-AKI. Therefore, we examined the impact of MetS on the incidence rates of CI-AKI in patients who underwent elective coronary angiography with or without intervention. In these patients, we also evaluated the correlation between the incidence rate of CI-AKI and different variables such as hypertension, the use of statins, the V/CrCl ratio, or the I-dose/CrCl ratio.

Patients and Methods

We performed a prospective cohort study on patients who underwent nonemergent coronary angiography with or without intervention at Rasoul-e-Akram General Hospital, Tehran, Iran, between December 2016 and January 2017. Patients were excluded from the study if they met one of the following criteria: acute coronary events, DM (one of the MetS components is fasting serum glucose ≥ 110 mg/dL that includes both diabetics and non-diabetics subjects; therefore, we excluded all diabetics in order to examine the effect of MetS and fasting serum glucose on the development of CI-AKI), known acute renal failure (an increase in SCr by $\geq 1.5\times$ baseline within the prior 7 days), allergy against contrast agents, low left ventricular ejection fraction ($< 40\%$), end-stage renal failure requiring hemodialysis, exposure to nephrotoxic or contrast agents within 1 week before the procedure, pregnancy, and administration of protective drugs against CI-AKI (sodium bicarbonate, theophylline, prostaglandin E1, or N-acetylcysteine) within 3 days before angiography.

Written informed consent was provided by all patients. The study protocol complied with the 1964 Declaration of Helsinki and its later amendments and was approved by the Ethics Committee of the Rasoul-e-Akram Hospital Clinical Research Development Center.

A total of 255 patients were included. According to the National Cholesterol Education Program Expert Panel III guidelines (NCEP-ATP III), MetS was defined if ≥ 3 of the following components were present: high blood pressure (a systolic blood pressure ≥ 130 mm Hg, diastolic blood pressure ≥ 85 mm Hg, or under treatment for hypertension), high fasting glucose (fasting serum glucose ≥ 110 mg/dL), hypertriglyceridemia (serum triglycerides ≥ 150 mg/dL), low high-density lipoprotein (HDL) cholesterol (HDL < 40 mg/dL in men and < 50 mg/dL in women), and abdominal obesity (waist circumference > 102 cm in men and > 88 cm in women) [14]. Based on these criteria, the patients were divided into 2 groups: the MetS group ($n = 130$) and the control group ($n = 125$).

Blood samples were drawn before angiography to measure serum levels of glucose, creatinine, and lipids after a 8-h overnight fasting period. Follow-up SCr was measured 48 h after the procedure. Normal saline was given to patients at a rate of 2 mL/kg/h for 6 h before and after angiography; no further medication was given routinely unless CI-AKI was diagnosed. CI-AKI was defined as an absolute or relative increase in SCr to ≥ 0.5 mg/dL (44 $\mu\text{mol/L}$) or $\geq 25\%$ above baseline within 48 h after angiography, respectively. The Cockcroft-Gault formula ($140 - \text{age (in years)} \times \text{weight (in kg)} / 72 \times \text{SCr (in mg/dL)} \times 0.85$ for females) was used to estimate the baseline and postprocedural CrCl level.

According to standard clinical practice, coronary angiography was performed using 6-Fr or 5-Fr guiding catheters and a femoral or radial approach. A low osmolar non-ionic contrast agent (iodixanol, Visipaque 320; Opakim, Turkey) with a iodine concentration of 320 mg/mL was used in all patients.

Based on a previous study [4] with an incidence rate of CI-AKI of 3.6% in the control group (non-MetS) and of 14% in the MetS group, we found that a sample size of 236 patients would be required (118 patients per group) to detect a statistically significant difference with a power of 80% ($\alpha = 0.05$), which we increased to a useful study size ($n = 255$). SPSS software version 21.0 for Windows was used for the analysis of all data. Data are expressed as mean $\pm$ SD for continuous variables and as frequencies for discrete variables. The Student *t* test was used for comparison of normally distributed and the Mann-Whitney U test was used for non-normally distributed continuous variables between the different groups. The paired *t* test or the Wilcoxon signed-rank test was used for comparison of within-subject continuous variables (e.g., before and after angiography) in normally and non-normally distributed data, respectively. The χ^2 analysis or Fisher exact test was used for comparison of categorical variables. Univariate logistic regression was performed on the entire study population with CI-AKI as the dependent variable and the following factors as potential covariates: age, male sex, the use of statins, beta blockers, aspirin, and ARB/ACEI, a history of previous myocardial infarction, CrCl, I-dose/CrCl, MetS and its components including waist circumference, the presence of hypertension, fasting blood glucose, and plasma levels of HDL cholesterol and triglyceride. The statistically significant variables from the univariate analysis were included in the multiple logistic regression analysis to find predictors of CI-AKI. Receiver-operating characteristic (ROC) curves were calculated to determine the cutoff point for the I-dose/CrCl ratio and the prediction of CI-AKI development. All tests were two-sided, and the results were considered as statistically significant if the *p* value was < 0.05 .

Table 1. The baseline characteristics of the patients with and those without metabolic syndrome (MetS)

Characteristic	Patients with MetS (n = 130)	Patients without MetS (n = 125)	p value
Age, years	59.15±10.36	57.00±11.94	0.125
Triglyceride, mg/dL	143.72±51.23	118.20±27.58	<0.001
Fasting blood glucose, mg/dL	106.22±25.98	95.20±15.60	<0.001
HDL, mg/dL	30.29±8.15	37.99±16.86	<0.001
Cholesterol, mg/dL	156.67±31.84	152.97±32.11	0.356
LDL, mg/dL	83.97±34.14	91.36±37.42	0.100
Waist circumference, cm	101.38±10.45	95.06±9.91	<0.001
BMI	30.56±4.34	28.35±4.58	0.679
Male sex	63 (48.4)	96 (76.8)	<0.001
Hypertension	115 (88.4)	54 (43.2)	<0.001
Previous myocardial infarction	3 (2.3)	1 (0.8)	0.622
Previous cerebrovascular accident	2 (1.5)	0	0.498
Prior use of			
Diuretics	14 (10.7)	8 (6.4)	0.267
ARB/ACEI	34 (26.1)	16 (12.8)	0.008
Beta blockers	54 (41.5)	34 (27.2)	0.018
ASA	94 (72.3)	83 (66.4)	0.342
Statins	70 (53.8)	54 (43.2)	0.10
CCBs	10 (7.6)	6 (4.8)	0.441

Data are presented as mean ± SD or n (%).

HDL, high-density lipoprotein; LDL, low-density lipoprotein; BMI, body mass index; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ASA, acetylsalicylic acid; CCBs, calcium channel blockers.

Results

A total of 255 patients (159 men, 96 women; mean age 58.10 ± 11.19 years) met the inclusion criteria. No difference between pre- and postprocedural complications was seen, and all patients completed the study. 69 (27.1%) of all patients developed CI-AKI. The baseline characteristics of the patients with and those without MetS are shown in Table 1. In the patients with MetS, all components of MetS were significantly higher compared to those in patients without MetS: fasting blood glucose (difference: 11.1 mg/dL; 95% confidence interval (95% CI) 5.7–16.2; $p < 0.001$); blood pressure ($p < 0.001$); waist circumference (difference: 6.32 cm; 95% CI 3.8–8.8; $p < 0.001$); triglyceride (difference: 25.51 mg/dL; 95% CI 15.4–35.6; $p < 0.001$), and HDL cholesterol (difference: -7.7 mg/dL; 95% CI -10.9 to -4.4; $p < 0.001$). Before angiography, SCr and glomerular filtration rate were similar between both groups (Fig. 1). All subjects received an individual amount of contrast agent. After angiography, SCr increased ($p < 0.001$) and CrCl decreased ($p < 0.001$) significantly in both groups. Postprocedural SCr was significantly higher ($p = 0.002$) in the patients with MetS while postprocedural CrCl was higher (but not statistically significant) in the patients without MetS ($p = 0.09$). The renal parameters of all patients before and after angiography are shown in Table 2.

The rate of developing CI-AKI was 27.1% (69/255) in both groups. The patients with MetS had a significantly higher rate of developing CI-AKI compared to the control group (39.23 vs. 14.4%, respectively; $p < 0.001$). 14.5 and 85.5% of all patients underwent angioplasty and angiography, respectively. No statistically significant difference was observed between these groups of patients and CI-AKI development ($p = 0.23$). Renal failure requiring

Table 2. Serum creatinine (SCr) and creatinine clearance (CrCl) levels in the study patients

Parameter	Patients with MetS (n = 130)	Patients without MetS (n = 125)	p value
Volume of contrast agent, mL	134.62±84.64	123.20±78.17	0.26
SCr, mg/dL			
Baseline	1.10±0.21	1.11±0.19	0.56
Postprocedural	1.33±0.31	1.22±0.24	0.002
CrCl, mL/min			
Baseline	82.01±26.27	82.34±25.82	0.92
Postprocedural	70.45±29.51	76.31±25.47	0.09
CI-AKI	51 (39.2)	18 (14.4)	<0.001
SCr of patients with CI-AKI, mg/dL			
Baseline	1.07±0.24	1.04±0.22	0.62
Postprocedural	1.51±0.36	1.39±0.27	0.13

Data are presented as mean ± SD or n (%).

MetS, metabolic syndrome; CI-AKI, contrast-induced acute kidney injury.

Fig. 1. Bar graph of creatine clearance (CrCl) changes before and after angiography in patients with and in patients without metabolic syndrome (MetS).

dialysis was not observed in any patients, and none of the patients who developed CI-AKI presented with eosinophilia or livedo reticularis.

Univariate analysis showed that hypertension (odds ratio (OR) 2.48; 95% CI 1.28–4.78; $p = 0.007$), high triglyceride level (OR 2.75; 95% CI 1.50–5.01; $p < 0.001$), age ≥ 70 years (OR 7.89; 95% CI 3.81–16.36; $p < 0.001$), CrCl ≤ 60 mL/min (OR 11.93; 95% CI 5.80–24.53; $p < 0.001$), MetS (OR 3.83; 95% CI 2.08–7.06; $p < 0.001$), the use of statins (OR 0.49; 95% CI 0.28–0.88; $p = 0.017$), I-dose/CrCl > 0.52 (OR 5.17; 95% CI 2.83–9.42; $p < 0.001$), and male sex (OR 0.43; 95% CI 0.24–0.76; $p = 0.004$) were significant predictors of CI-AKI.

The multivariable regression model showed that while male sex and the use of statins were associated with a lower risk of developing CI-AKI, high triglyceride levels, I-dose/CrCl > 0.52 , MetS, CrCl ≤ 60 mL/min, and age ≥ 70 years were associated with a higher risk, independent of confounding factors (Table 3).

Comparing the patients who developed CI-AKI to those who did not develop CI-AKI (from the entire study population), the amount of contrast agent used was statistically different (152.9 ± 92.7 vs. 120.1 ± 75.4 mL, respectively; $p = 0.01$). The difference in the mean V/CrCl ratio was statistically significant between the patients who developed CI-AKI and those who did not show renal impairment (2.36 ± 1.35 vs. 1.43 ± 0.89 , respectively; $p < 0.001$).

Table 3. Risk factors for developing contrast-induced acute kidney injury

Variable	Univariate analysis			Multivariable analysis		
	OR	95% CI	p value	OR	95% CI	p value
Age 70 years	7.89	3.81–16.36	0.000	6.07	2.01–18.28	0.001
Male sex	0.43	0.24–0.76	0.004	0.41	0.19–0.91	0.028
CrCl 60 mL/min	11.93	5.80–24.53	0.000	5.98	2.17–16.50	0.001
MetS	3.83	2.08–7.06	0.000	3.76	1.38–10.23	0.009
Fasting blood glucose	1.35	0.72–2.52	0.33			
Hypertension	2.48	1.28–4.78	0.007	1.84	0.67–5.08	0.234
HDL	1.58	0.69–3.63	0.27			
Waist circumference	1.22	0.69–2.15	0.49			
Triglycerides	2.75	1.50–5.01	0.001	2.44	1.02–5.83	0.044
Prior use of						
ASA	0.70	0.39–1.25	0.23			
Statins	0.49	0.28–0.88	0.017	0.41	0.18–0.91	0.029
ARB/ACEI	1.90	0.98–3.65	0.054			
Beta blockers	0.79	0.43–1.43	0.44			
Previous myocardial infarction	2.74	0.37–19.88	0.31			
I-dose/CrCl >0.52	5.17	2.83–9.42	0.000	3.92	1.80–8.52	0.001

CrCl, creatinine clearance; MetS, metabolic syndrome; HDL, high-density lipoprotein; ASA, acetylsalicylic acid; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.

Furthermore, the mean I-dose/CrCl ratio was 0.75 ± 0.43 in the patients with CI-AKI and 0.45 ± 0.28 in the patients who did not develop CI-AKI (95% CI 0.18–0.41; $p < 0.001$).

Comparing the MetS and the control group, the ROC curve analysis of the I-dose/CrCl ratio determined the best cutoff value for the I-dose/CrCl ratio in patients with MetS as 0.51 with a 68% sensitivity and a 73% specificity (area under the curve (AUC) 0.738; 95% CI 0.649–0.826; $p < 0.001$). A higher cutoff value for the I-dose/CrCl ratio was found in the patients without MetS (cutoff value of 0.63, 72% sensitivity, 74% specificity, AUC 0.729, 95% CI 0.599–0.859; $p = 0.002$). Figure 2 shows the ROC curve analysis of the I-dose/CrCl ratio for the prediction of CI-AKI. Figure 3 shows the rates of developing CI-AKI in those with and those without MetS, stratified above and below the I-dose/CrCl ratio cutoff points for each group.

Discussion

CI-AKI versus MetS

The main new finding of the current study is that the risk of developing CI-AKI was significantly increased among the patients with MetS who underwent elective coronary angiography with or without intervention (OR 3.76; 95% CI 1.38–10.23; $p = 0.009$). In those with MetS, the incidence rate of CI-AKI was 39.23%. Current techniques, such as the Mehran risk score, are used to stratify the probability of developing CI-AKI after percutaneous coronary intervention. A higher Mehran risk score is associated with a higher risk of persistent renal impairment after CI-AKI [15, 16]. The prognosis of patients who developed CI-AKI after coronary angiography is worse than that of those without renal impairment. They are more prone to stroke, bleeding, electrolyte imbalance, sepsis, respiratory failure, and pulmonary embolus compared to patients without renal impairment [1, 17–19]. Hemodialysis and supportive measures are the available treatment options once CI-AKI has developed [11].

Fig. 2. Receiver-operating characteristic curve analysis of the iodine-dose(I-dose)/creatinine clearance (CrCl) ratio for the prediction of contrast-induced acute kidney injury. a Patients with metabolic syndrome (MetS). Cutoff value for the I-dose/CrCl ratio: 0.51. Sensitivity: 68%, specificity: 73%. Area under the curve (AUC): 0.738, 95% CI 0.649–0.826, $p < 0.001$. b Patients without MetS. Cutoff value for the I-dose/CrCl ratio: 0.63. Sensitivity: 72%, specificity: 74%. AUC: 0.729, 95% CI 0.599–0.859, $p = 0.002$.

Fig. 3. Bar graph of the probability of contrast-induced acute kidney injury (CI-AKI) stratified by the iodine-dose/creatinine clearance (CrCl) ratio cutoff points of 0.51 and 0.63 for patients with and patients without metabolic syndrome (MetS), respectively.

Several prophylactic methods, including high-dose oral N-acetylcysteine consumption, sodium bicarbonate infusion, preprocedural hydration with saline, the use of statins, the cessation of nephrotoxic agents, the limitation of contrast agent volume, and iso-osmolar contrast agent replacement, are recommended to be applied in patients with risk factors for CI-AKI and renal failure [4, 5, 7]. Therefore, it is an important matter to identify patients who are at high risk of developing CI-AKI. Thus, we examined the impact of MetS on the rates of developing CI-AKI in patients who underwent elective coronary angiography with or without intervention.

Several risk factors have been proposed as etiologic factors for the development of CI-AKI including nephrotoxic drugs, congestive heart failure, DM, anemia, baseline renal dysfunction,

volume depletion, hemodynamic instability, and hypoalbuminemia [20]. Previous studies stated that MetS has increased the incidence of CI-AKI [4, 11]. The present study confirmed the association of CI-AKI and MetS in the Iranian population with stable coronary artery disease.

Diabetes

Individual components of MetS including insulin resistance, abdominal obesity, hypertension, and dyslipidemia have been shown to be risk factors for renal injury [11]. Hypertension and DM are the main causes of CKD [21]. While DM is identified as a strong and independent predictor of CI-AKI, the relationship between CI-AKI and prehypertensive or prediabetic state (MetS characteristics) still remains unclear [17, 22, 23]. Toprak et al. [22] showed the incidence of CI-AKI in different groups – 20% in individuals with DM ($p = 0.001$), 11.4% in pre-DM ($p = 0.314$), and 5.5% in the normal fasting glucose group. In the present study on nondiabetic patients, no correlation between fasting blood glucose ≥ 110 mg/dL and CI-AKI was found ($p = 0.33$).

Hypertension

Some previous studies categorized hypertension (another component of MetS) as a minor risk factor for the development of CI-AKI [3, 23]. Iakovou et al. [24], in a study on 8,628 patients with percutaneous intervention, reported hypertension to be an independent risk factor of CI-AKI (OR 1.2; 95% CI 1.06–1.36; $p = 0.035$). In our study, we did not find a significant relationship between CI-AKI and hypertension as an independent predictor (OR 1.84; 95% CI 0.67–5.08; $p = 0.234$).

Dyslipidemia

It has been suggested that dyslipidemia is independently related with a reduction in kidney function. Moreover, excess cellular lipid, correlated with obesity and MetS, has been proposed to cause kidney injury [25]. Abdominal obesity, by inducing multiple mediators, may contribute to tubular cell injury, tubulointerstitial fibrosis, and focal and segmental glomerulosclerosis. Furthermore, it can lead to kidney injury by triggering atherosclerosis, hypertension, and DM [10]. Additionally, renin-angiotensin-aldosterone system activation affects the renal function of obese MetS patients via inflammatory cytokines, oxidative stress, and hypertension. Insulin resistance marks a pro-inflammatory state which is strongly related with obesity in patients with renal failure [10, 11].

Statins

Many studies have shown the efficacy of pretreatment with statins in decreasing the risk of developing CI-AKI in patients undergoing coronary interventions [26, 27]. In a meta-analysis of 15 controlled trials, Liang et al. [28] demonstrated the efficacy of pretreatment with rosuvastatin in reducing the incidence of CI-AKI in patients undergoing coronary interventions ($p < 0.05$). We found a significantly decreased rate of CI-AKI in those who were on chronic statin therapy before angiography, too (OR 0.41; 95% CI 0.18–0.91; $p = 0.029$). The reasons for the renoprotective effects of statins are believed to lie in their anti-inflammatory properties and positive effects on the function of endothelium at the level of glomerulus [17].

I-Dose/CrCl Ratio

In the present study, as we expected, a glomerular filtration rate ≤ 60 mL/min was reported to be another risk factor for CI-AKI development (OR 5.98; 95% CI 2.17–16.50; $p < 0.001$). Contrast agent volume, divided by a CrCl limit of 3.7, has been suggested as a way to predict CI-AKI development in unselected patients receiving contrast media [13]. While the

iodine concentration of different commercially available contrast agents ranges from 140 to 400 mg/mL, the I-dose/CrCl ratio has been proposed to solve this problem [12, 29]. In their systematic review and meta-analysis study, Nyman et al. [29] reported a linear correlation between the I-dose/CrCl ratio and CI-AKI development with a correlation coefficient of 0.91 ($p < 0.001$). In the present study, we revealed that the I-dose/CrCl ratio at >0.52 was a strong predictor of CI-AKI in nondiabetic patients undergoing elective coronary interventions. According to this index, the safety profile of contrast media could be more intently predicted, because the I-dose/CrCl ratio closely corresponds to the area under the blood iodine concentration versus time curve. Figure 3 indicates that I-dose/CrCl ratios >0.51 and >0.63 were related to a 2.9- and 5.3-times increase in the CI-AKI incidence in MetS and non-MetS patients, respectively. Patient's estimated CrCl, multiplied by these cutoff values, can be a useful tool to calculate the maximum safe amount of iodine, allowed to be used in MetS and non-MetS patients undergoing non-urgent coronary interventions. However, according to other risk factors, these cutoff values may be different.

Limitations

There are several limitations to the present study. A major one is that the sample size was small and consequently the number of CI-AKI events was limited. We measured the SCr levels and calculated the CrCl levels using the Cockcroft-Gault equation that both have been previously used to estimate renal function in large CI-AKI studies; however, more sensitive parameters of renal function such as neutrophil gelatinase-associated lipocalin, N-acetylglucosaminidase, inulin clearance, or cystatin C have not been measured. Levels of nitric oxide, insulin, oxidative stress parameters, and antioxidant status have not been measured either. Besides, this study is not representative for the general Iranian population because it is a single-center study.

Further studies on the utility of the I-dose/CrCl ratio in specific populations, e.g., in those with left ventricular dysfunction, CKD, emergency percutaneous coronary intervention, in addition to long-term clinical outcomes studies, could be useful and informative.

Conclusions

In summary, we have shown that MetS is a strong risk factor for the development of CI-AKI in patients without known predisposing factors such as DM, left ventricular dysfunction, acute renal failure, or acute coronary events, undergoing elective coronary interventions, and we have shown the I-dose/CrCl ratio as an independent and useful predictor of CI-AKI in MetS patients. We suggest that clinicians recognize high-risk patients prior to intervention and calculate the maximum safe amount of contrast agents which can be used without risking CI-AKI.

Statement of Ethics

Written informed consent was obtained from all participants, and the study protocol was approved by the Research and Ethics Committee of Rasoul-e-Akram General Hospital, Teheran, Iran.

Disclosure Statement

The authors declare that they have no potential conflicts of interests relevant to this article.

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