ORIGINAL ARTICLE

Does metabolic syndrome increase contrast-induced nephropathy in patients with normal renal function?

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Background: Contrast-induced nephropathy (CIN) is associated with increased mortality and morbidity in patients undergoing coronary angiography (CAG) and percutaneous coronary intervention. This study aimed to compare the incidence of CIN in two groups of patients with and without metabolic syndrome (Mets) with baseline normal renal function. **Materials and Methods:** In this case – control study, 260 patient candidates for CAG, 130 patients with Mets and 130 patients without Mets participated, and their serum creatinine (Cr) level before and the 48 and 72 h after the angiography was measured. The incidence of CIN was compared in two groups. Two-way analysis of variance with repeated measures and univariate and multivariate logistic regression models. **Results:** The results showed a higher chance of being Mets with raising in triglyceride (adjusted odds ratio = 1.05, 95% confidence interval = (1.03–1.06), $P < 0.001$), Fasting blood glucose (1.010 [1.001–1.019], $P = 0.025$), and diastolic blood pressure (1.07 [1.07–1.20], $P < 0.001$), but declining in high-density lipoprotein-cholesterol (HDL-C) (0.91 [0.85–0.98], $P = 0.008$). Furthermore, blood urea nitrogen (BUN) and Cr level was raised in 48 and 72 h after contrast injection in both groups (All $P < 0.001$). Furthermore, in 48 h (3.11 [1.12–9.93], $P = 0.016$) and 72 h (2.82 [1.07–8.28], $P = 0.021$) after injection, a total of 25 patients had an increased Cr level and a significant difference between Mets and without Mets groups. The developing Mets had a significant association with the increased risk of AKI, which increased the chance of developing nephropathy (7.14 [2.27–22.5], $P = 0.001$). **Conclusion:** Mets, together with other risk factors, increased the overall risk of CIN development. Therefore, the incidence of CIN in patients Mets is significantly higher than that of patients without Mets, indicating a more important CIN risk factor.

Key words: Angiography, contrast-induced nephropathy, metabolic syndrome

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INTRODUCTION

Contrast-induced nephropathy (CIN) or contrast-induced acute kidney injury (CI-AKI) is an acute deterioration of renal function after the contrast medium administration. It is associated with increased mortality, hospital stay, prehospitalization, hemodialysis, and longtime mortality in patients undergoing coronary angiography (CAG) and percutaneous coronary intervention (PCI). There is no consensus on CIN definition, prevention, and treatment. Data are contradictory depending on the definition utilized on the biomarkers used to evaluate renal function and the timing of measurements. Consequently, the reported incidence of the condition varies among studies. CI-AKI was defined using either CI-AKI Network (serum creatinine [Scr] ≥0.3 mg/dL or 50%) or traditional (Scr ≥0.5 mg/dL or 25%) criteria in patients with baseline Scr levels <1.5 mg/dL (in about 90% of all patients).[1]

CIN is defined as an increase of the serum creatinine (Cr) level ≥0.5 mg/dl (44.2 mmol/L) or >25% of the baseline

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value 48–72 h after contrast media (CM) administration by the European Society of Urogenital Radiology.[2] The incidence of CIN ranges from 3% to 14% in patients undergoing PCI, and the incidence was even higher in those with impaired renal function, and most of the studies defined moderate-high risk as patients with estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m^2.[3-5] It also seems clear that patients with eGFRs <30 mL/min/1.73 m^2 are at greatest risk for CIN following intravenous CM exposure, despite mixed findings of the propensity score studies.[6]

CM may exert a direct cytotoxic effect on the proximal tubular renal cells characterized by vacuolization, interstitial inflammation, and apoptosis due to the production of reactive oxygen species and increase outflow resistance.[2] Another mechanism is related to the ability of CM to increase renal vasoconstriction. Angiography is the most commonly used diagnostic method for coronary artery disease, which can be used to accurately detect cardiovascular events by administering of contrast agent into the coronary artery by arterial catheter and recording the effects of X-rays, as well as assessing the performance and anatomy of the vascular and cavity heart. CIN is the third cause of hospital AKI only next to hypoperfusion and drug toxicity. According to Mehran's risk scale, a previous renal impairment is the most important risk factor, placing the patients in a high-risk cluster.[7-9] Because contrast agents are one of the most important causes of damage to renal tubules and the development of acute tubular necrosis and, on the other hand; diabetes, chronic renal failure, severe cardiac insufficiency, high age, fluid loss, hypotension, and volume of contrast agent are important common factors in this regard.[7-9]

Some of the risk factors associated with the underlying causes of contrast nephropathy seem to play a role, including metabolic syndrome (Mets') presence. The Mets, according to The National Education and Cholesterol Program (NCEP ATP III), is de criteria fined as blood pressure above 135/85 mmHg, an additional accumulated fat around the abdomen (waist circumference more than 102 and 88 cmin male and female, respectively), triglycerides (TG) above 150 mg/dL, high-density lipoprotein (HDL) levels <50 mg/dL in female and <40 mg/dL in male, fasting blood sugar above 100 mg/dl that the presence of three signs of the five mentioned signs is known as Mets.[10,11] The Mets can play an important role in developing contrast agent complications such as the kidneys' reduced function, immediate effect on the cardiovascular system, modifications, and changes in the patient's use of the drugs.

On the other hand, some patients, based on their initial angiogram, are candidates for coronary angioplasty, and the patient is again exposed to the contrast agent. Perhaps, in the case of nephropathy, the treatment of angioplasty is postponed.[12] The most important risk factor for CIN is baseline renal dysfunction.[13] In a prior study, Mets have increased CIN's risk among nondiabetic elderly patients with mild to moderate kidney insufficiency.[11] These studies with baseline renal impairment can induce biases. Therefore, this case-control study was designed to assess Mets' association with CIN in two groups of patients with and without Mets with baseline normal renal function.

MATERIALS AND METHODS

Study design and setting

This case-control study was conducted in Shahid Chamran hospital, Isfahan University of Medical Sciences, Isfahan, Iran, in 2019. The target population of the study was candidates for angiography referred to the center. The eligible patients were selected based on a convenience sampling procedure.

Ethics approval and consent to participate

The Institutional Review Board (IRB) of Isfahan University of Medical Sciences approved the study's protocol. Informed consent was obtained from all participants.

The inclusion and exclusion criteria

The inclusion criteria comprised the candidate for coronary artery angiography, age <75, no history previous of renal failure, baseline normal renal function, Mets (for case group), and patient consent to participate in the study. Besides: Anemia, heart failure, cr >1.5 mg/dL, hypotension, use of nephrotoxic drugs (nonsteroidal anti-inflammatory drugs, aminoglycosids), the impossibility of determining the degree of contrast nephropathy in 48–72 h after angiography for various causes and the patient that died within the 72 h of angiography that did not due to renal insufficiency were considered as exclusion criteria.

Study size

The sample size required for the study was calculated 98 patients per group. The sample size was estimated on the Incidence of contrast nephropathy, as the main outcome, using the formula for estimating the sample size for comparing the 2 ratios, taking into account the 95% confidence and the 80% power. However, we increased the sample size to 130 patients per group to increase the results' precision.

Study variables and measures

Before the angiography, echocardiography, demographic information, height (by SECA height measuring) and weight (by SECA scale), Cr (by jaffes method), urea (by conducting metric), cholesterol, TG, total cholesterol, low-density lipoprotein (LDL), HDL-cholesterol (HDL-C) (by calorimetric or CHOD-PAP methods), fasting glucose and hemoglobin A1C (by diazyme methods), and Mets

criteria (by ATP III criteria) were studied in patients and recorded in each patient's data collection form.

Procedure

This study was conducted after obtaining permission from the University's Medical Ethics Committee (IR.MUI.REC.1396.3.013).

One hundred thirty patients Mets according to ATP III CRT, and 130 without Mets were selected. Patients were followed for 48 and 72 h after angiography by assessing of cr daily. Their urea and Cr control and the Incidence of contrast nephropathy were assessed and recorded in two groups of patients with and without Mets. According to the ATP III criteria, patients with Mets must have at least 3 of the five signs.[10,11] Current preventive management includes adequate hydration, use of iso-osmolar or low–osmolar contrast agents, minimization of contrast load, withdrawal of nephrotoxic agent, and high statins dosage used.[1] Also, Intravenous volume expansion using isotonic fluids before CM administration is the intervention proven most effective. In our study, all patients received normal intravenous saline in the range of 500-300 ml begin 1 h before and continue 3-6 after receiving the contrast agent, and the kind of contrast agent was iso-osmolar. Contrast volume recorded by operator.

Statistical analysis

Numeric variables were reported as the mean (standard deviation) and categorical data using frequency (percent). The numeric variables' normality was evaluated and confirmed using the Kolmogorov–Smirnov test and distributions measures, the skewness (within ± 1.5) and kurtosis (within ± 2). Independent samples *t*-tests and Chi-squared tests were used to compare numeric variables and categorical variables between two groups. The univariate and multivariate logistic regression models were carried out to test the differences between case and control groups regarding the clinical and laboratory variables, especially blood urea nitrogen (BUN) and Cr before, 48 and 72 h after injection. In the multivariate models, the effect size of interest, odds ratios (ORs) have been adjusted for potential confounders, age, sex, and in the model for BUN and Cr, the ORs have adjusted baseline values of these measures either.

Furthermore, a two-way analysis of variances (ANOVAs) with repeated measures (RM-ANOVA) was used to test the time effect, group effect, and possible interactions. The Muchly test tested the underlying assumption of sphericity, and proper Greenhouse-Geiser correction was chosen when the assumption was not met. The RM ANOVA was followed by the Sidak *post hoc* test, where an effect was significant. All data were analyzed using the IBM SPSS Statistics, version 26 (IBM SPSS Statistics, Armonk, NY, USA), at a significance level of 0.05.

RESULTS

Participants' profile

In this study, 130 patients with Mets and 130 patients without Mets, who were candidates for diagnostic and therapeutic angiography, were recruited. There were no significant differences between the Mets and without Mets groups in terms of age, sex, the kind of patients that manage for underlying illness (included: HTN, DM, HLP, hypothyroidism and…) The causes of angiography (diagnostic or treatment by intervention), and the cause of angiography (all patiens evaluated for coronary artetry disease) in both univariate and multivariate analyses (All $P > 0.05$). However, significant differences were observed between Mets and without Mets group in terms of BMI Just in the univariate analysis ($P < 0.001$) but not in the multivariate analysis ($P > 0.05$) as well as waist circumference in both multivariate analyses (both $P < 0.001$) [Table 1].

Table 1: The distribution of the demographic and basal variables of the two nonmetabolic and metabolic syndrome groups and the results of logistic regression models

Variables	Metabolic syndrome		OR (95% CI), $P^{\#}$	OR (95% CI), $P^{\#\#}$
	No (*n*=130)	Yes (*n*=130)		
Age (year)	64.07±13.37	63.69±1.18	0.99 (0.98-1.02), 0.786	0.99 (0.98-1.02), 0.746
Sex, *n* (%)				
Male	96 (73.8)	92 (7.8)	0.99 (0.60-1.63), 0.974	0.96 (0.57-1.61), 0.876
Female	34 (26.2)	38 (29.2)	Referent	-
Management for underlying illness*, *n* (%)	125 (96.2)	123 (94.6)	1.05 (0.29-3.82), 0.936	0.89 (0.23-3.40), 0.863
The causes of angiography, *n* (%)				
Diagnostic	90 (68.7)	91 (7.5)	1.06 (0.64-1.75), 0.830	1.05 (0.63-1.74), 0.864
Treatment	41 (31.3)	38 (29.5)	Referent	-
Waist circumference (cm)	81.96±9.48	88.53 10.58	**1.09 (1.07-1.12), <0.001**	**1.10 (1.04-1.16), <0.001**
BMI (kg/m^2)	24.57±3.34	29.28±11.61	**1.25 (1.17-1.35), <0.001**	1.12 (0.96-1.29), 0.142

$^{\#}$Unadjusted OR, CIs, and *P* values are computed based on simple logistic regression; $^{\#\#}$Adjusted OR, CIs and *P* values are computed based on multiple logistic regression; age- and sex-adjusted OR and CIs for waist circumference and BMI. Significant relationships are shown in bold font. In multiple logistic regression model the Hosmer-Lemeshow test indicated the good fit of model (χ^2 [8]=14.34, *P*=0.058), models sensitivity=00.0%, specificity=100.0%, accuracy=58.6%. *HTN, DM, HLP, hypothyroidism and… Data are expressed by mean±SD or frequency (%). BMI=Body mass index; OR=Odds ratio; CIs=Confidence intervals; SD=Standard deviation

The distribution of the clinical and laboratory

Table 2 presents the distribution of the clinical and laboratory findings of the two groups of patients. The results of both univariate and multivariate analyses showed a higher chance of being Mets with raising in TG (Both OR >1, and $P < 0.001$), Fasting blood glucose (Both OR >1, and $P < 0.05$), and diastolic blood pressure (Both OR >1, and $P < 0.001$), but declining in HDL-C (Both OR <1, and $P < 0.05$). Besides, the univariate analysis results showed a higher chance of being Mets when systolic blood pressure went up (OR = 1.02, confidence interval [CI] = 1.01–1.03, and $P = 0.006$). However, LDL-C, the mean EF index (measured before angiography), according to the findings of echocardiography, and the mean contrast volume consumption were not significantly different between Mets and without Mets groups (All $P > 0.05$) [Table 2].

Besides, the results showed no significant difference between Mets and without Mets groups who underwent angiography and angioplasty (91 [70.0%] vs. 90 [69.2%], OR = 1.04, CI = 0.59–1.82, and $P = 0.893$).

Nonetheless, the results showed a significant difference between Mets and without Mets groups in terms of being diabetic (71 [54.6%] vs. 54 [41.5%], OR = 1.69, CI = 1.01–2.85, and $P = 0.035$).

The trend of blood urea nitrogen and creatinine in metabolic syndrome and without metabolic syndrome groups

Figure 1 and Table 3 show the distribution of BUN and Cr in the before 48 and 72 h after contrast injection in Mets and without Mets groups. According to the Greenhouse-Geiser test, the

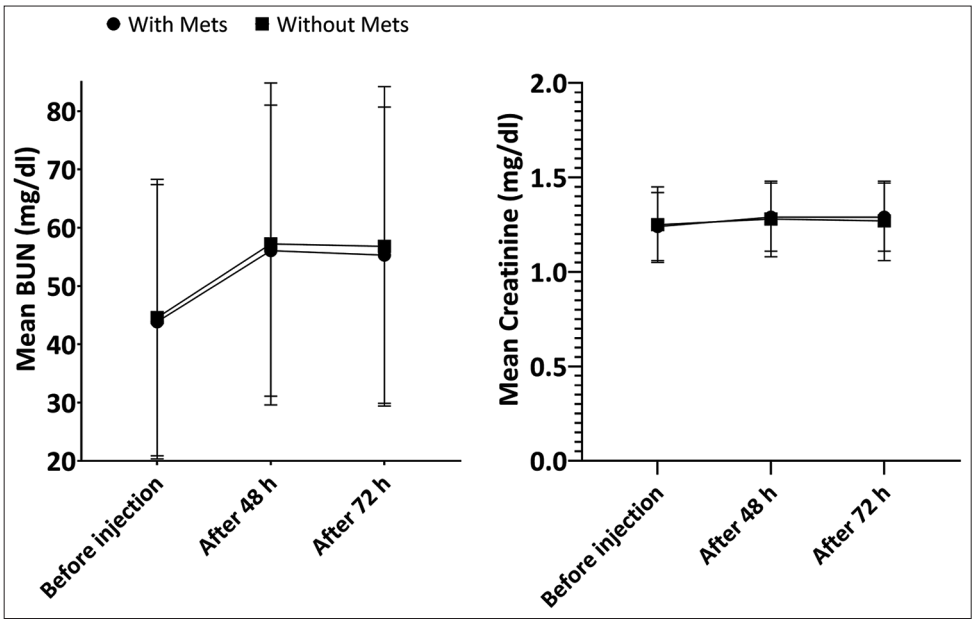

Figure 1: Changes of BUN (left) and creatinine (right) during study in metabolic and no metabolic syndrome. BUN = Blood urea nitrogen; Mets = Metabolic syndrome

Table 2: The distribution of clinical and laboratory findings across the nonmetabolic and metabolic syndrome groups and the results of logistic regression models

Variables	Metabolic syndrome		OR (95% CI), $P^{\#}$	OR (95% CI), $P^{\#\#}$
	Yes (n=130)	No (n=130)		
TG (mg/dl)	180.25±93.34	101.53±31.05	**1.03 (1.02–1.04), <0.001**	**1.05 (1.03–1.06), <0.001**
Cholesterol (mg/dl)	168.29±48.59	156.73±40.04	**1.006 (1.001–1.011), 0.024**	0.99 (0.98–1.01), 0.063
LDL-C (mg/dl)	115.81±32.97	118.17±30.68	0.99 (0.98–1.01), 0.517	1.01 (0.99–1.02), 0.424
HDL-C (mg/dl)	41.24±4.99	45.21±9.24	**0.93 (0.89–0.96), <0.001**	**0.91 (0.85–0.98), 0.008**
Fasting blood glucose (mg/dl)	157.09±63.29	134.80±52.79	**1.007 (1.003–1.011), 0.001**	**1.010 (1.001–1.019), 0.025**
HbA1C (mmol/mol)	7.31±1.77	7.00±1.43	1.13 (0.98–1.30), 0.100	1.02 (0.78–1.34), 0.889
Systolic blood pressure (mmHg)	119.80±17.42	114.54±15.32	**1.02 (1.01–1.03), 0.006**	1.03 (0.99–1.06), 0.063
Diastolic blood pressure (mmHg)	80.24±8.86	76.72±5.36	**1.08 (1.04–1.11), <0.001**	**1.07 (1.07–1.20), <0.001**
Mean ejection fraction	43.47±10.61	40.96±13.16	1.02 (0.99–1.04), 0.092	1.02 (0.98–1.05), 0.314
Mean contrast volume consumption	167.75±84.95	166.30±86.89	1.00 (0.99–1.01), 0.887	1.00 (0.99–1.01), 0.541

$^{\#}$Unadjusted OR, CIs, and P values are computed based on simple logistic regression; $^{\#\#}$Adjusted OR, CIs and P values are computed based on multiple logistic regression adjusted for age and sex. Significant relationships are shown in bold font. In multiple logistic regression model, the Hosmer-Lemeshow test indicated the good fit of model (χ^2 [8]=3.33, P=0.912), models sensitivity=83.2%, specificity=89.0%, accuracy=86.6%. Data are expressed by mean±SD. OR=Odds ratio; CIs=Confidence intervals; LDL-C=Low-density lipoprotein-cholesterol; HDL-C=High-density lipoprotein- cholesterol; HbA1C=Hemoglobin A1C; SD=Standard deviation; TG=Triglyceride

interaction effect was not significant, so the changes were not significantly different across groups for BUN ($P = 0.705$), and Cr ($P = 0.879$) [Figure 1]. Also, according to the within group comparisons' tests, the level of BUN and Cr raised in 48 and 72 h after contrast injection in both groups when compared to the before injection (All $P < 0.001$), but there were no significant differences between 42 and 72 h after injection according to the Sidak *post hoc* test (All $P > 0.05$).

Besides, at the end of the study, according to both univariate and multivariate logistic regression models, levels of BUN and Cr were not significantly different between Mets and non-Mets groups when their baseline values, as well as the potential confounders (age, sex), were adjusted (All $P > 0.05$) [Table 3].

The distribution of contrast nephropathy

Besides, the evaluation of Cr level after 48 h showed that in total in 23 patients, the serum Cr level increased by more than 25%, with a significant difference between Mets and without Mets groups (17 (13.1%) vs. 6 (4.6%), OR = 3.11, CI = 1.12–9.93, and $P = 0.016$). Besides, in 72 h after injection, a total of 25 patients had an increased Cr level and a significant difference between Mets and without Mets groups (18 [13.9%] vs. 7 [5.4%], OR = 2.82, CI = 1.07–8.28, and $P = 0.021$) [Table 4]. Also, in follow-up, no patient required dialysis.

According to the results, the developing Mets had a significant association with the increased risk of AKI, which increased the chance of developing nephropathy by about 7 times (OR = 7.14, 95% CI: 2.27–22.5, $P = 0.001$) after adjusting for age and sex.

Considering the common prevalence of nephropathy and Mets, this study aimed to compare the Incidence of contrast nephropathy in two groups of 130 patients with and without Mets and showed a significant difference in metabolic rate, but no significant difference in terms of underlying diseases and the cause of angiography. On the other hand, the study of laboratory and clinical findings in both patients with and without Mets groups showed that most of the Mets criteria included waist circumference, TG levels, fasting blood glucose, and systolic diastolic blood pressure were significantly higher in patients with Mets. In contrast, HDL levels were lower in the Mets group.

DISCUSSION

In this study, it was found that patients with MetS, who underwent angiography and PCI, presented more than twice (2/64) risk for CIN as those without Mets (5.3% vs. 14%) despite normal renal function, hydration, and a significant difference was observed between the two groups. Several mechanisms have been suggested as etiologic factors for CIN. The main mechanism is kidney hypoperfusion and flows due to acute vasoconstriction induced by endothelin and adenosine release initiated by the contrast agent. Furthermore, the contrast agent concentration in the renal

Table 3: The distribution of blood urea nitrogen and creatinine in the before 48 and 72 h after contrast injection in nonmetabolic and metabolic syndrome groups and the results of logistic regression models

Variables	Time	Metabolic syndrome		OR (95% CI), $P^{\#}$	OR (95% CI), $P^{\#\#}$
		Yes (n=130)	No (n=130)		
BUN (mg/dl)	Before	43.86±23.53	44.59±23.71	0.999 (0.989-1.008), 0.790	1.001 (0.989-1.013), 0.904
	48 h after	56.07±24.96	57.22±27.60	0.998 (0.990-1.007), 0.710	0.994 (0.982-1.007), 0.390
	72 h after	55.33±25.41	56.81±27.40	0.998 (0.989-1.007), 0.631	0.999 (0.989-1.010), 0.886
	$P^{\#\#}$	<0.001	<0.001	-	-
Creatinine (mg/dl)	Before	1.24±0.85	1.25±0.89	0.995 (0.767-1.291), 0.972	0.980 (0.751-1.278), 0.881
	48 h after	1.29±0.18	1.28±0.20	1.392 (0.426-4.550), 0.584	1.016 (0.194-5.320), 0.985
	72 h after	1.29±0.18	1.27±0.21	1.416 (0.446-4.490), 0.555	1.208 (0.273-5.343), 0.803
	$P^{\#\#}$	<0.001	<0.001	-	-

$^{\#}$Unadjusted OR, CIs, and P values are computed based on simple logistic regression; $^{\#\#}$Adjusted OR, CIs and P values are computed based on multiple logistic regression adjusted for age and sex; Within-group changes of BUN and creatinine during the study based on repeated measures ANOVA. Data are expressed by mean±SD. Significant relationships are shown in bold font. In multiple logistic regression model the Hosmer-Lemeshow test indicated the good fit of model (χ^2 [8]=3.33, P=0.912), models sensitivity = 83.2%, specificity=89.0%, accuracy=86.6%. ANOVA=Analysis of variance; OR=Odds ratio; CIs=Confidence intervals; BUN=Blood urea nitrogen; SD = Standard deviation

Table 4: The distribution of contrast nephropathy until 48 and 72 h after injection in nonmetabolic and metabolic syndrome groups

Variables	Nephropathy	Metabolic syndrome		OR (95% CI), $P^{\#}$
		Yes (n=130)	No (n=130)	
Contrast nephropathy after 48 h from injection	No	113 (86.9)	124 (95.4)	**3.11 (1.12–9.93), 0.016**
	Yes	17 (13.1)	6 (4.6)	
Contrast nephropathy after 72 h from injection	No	112 (86.1)	124 (94.6)	**2.82 (1.07–8.28), 0.021**
	Yes	18 (13.9)	7 (5.4)	

$^{\#}$Unadjusted OR, CIs, and P values are computed based on simple logistic regression. Significant relationships are shown in bold font. OR=Odds ratio; CIs=Confidence intervals

tubules and collecting ducts causes direct cellular injury to the renal tubular cells.[3]

In the "Mets," a collection of glucose intolerance and hyperinsulinemia accompanied by hypertriglyceridemia, low HDL levels, hypofibrinolysis, hypertension, microalbuminuria, the predominance of small dense LDL particles, and central obesity.[14,15] A combination of risk factors incorporated in Mets' concept augments risk beyond the sum of the risk attributable to the individual components.[16-18]

In addition to systemic metabolic abnormalities, hyperglycemia causes an increase of advanced glycation end products associated with vascular damage. Diabetic patients have impaired endothelial vasodilator function and appear to have increased leukocyte adhesion to vascular endothelium, a critical early step in atherogenesis.[19-21] Abdominal Obesity is an important component of the Mets, leading to segmental glomerulosclerosis, intestinal fibrosis, and tubular damage caused by various mediators. Mets can also indirectly contribute to kidney damage by causing diabetes, hypertension, and atherosclerosis.[20,22] Also, during angiography and contrast adminisrtaion the renin-angiotensin-aldosterone system's activation can affect kidney function due to increased blood pressure, oxidative stress, and inflammation of the cytokines in obese people Mets.[17]

Insulin resistance is a key factor in the Mets' pathophysiology, which leads to inflammatory conditions in these individuals,[18,23] and increased inflammation has a definitive association with Obesity in patients with renal insufficiency.[19] On the other hand, diabetes and hypertension are also factors that contribute to the development of chronic kidney disease.[21] Also, diabetes mellitus is a strong and predictive factor in CIN.[23,24] In any case, the relationship between contrast nephropathy and high blood pressure in people with prediabetes is one issue that still exists in people Mets.[22] Dyslipidemia is also one of the known causes that indirectly affect renal function,[25] and cellular fat is thought to be involved in Mets and Obesity in renal injury.[26]

Also, numerous studies of patients undergoing CAG have demonstrated AKI rates of about 13%, which exceeds the average AKI rates of 5% to 6% associated with intravenous CM exposure.[27] Therefore patients Mets who undergo coronary artery angiography have more risk for AKI and CIN, representing a severe complication of CM.

Measurement of urea and Cr levels in patients showed no significant difference between the two groups before the contrast agent injection. However, at 48 and 72 h after injection, the patients Mets had higher Cr levels, and ultimately, the Incidence of contrast nephropathy was significantly higher in the Mets group (5.3% vs. 14% - $P = 0.019$). In a study by Toprak *et al*., 219 patients underwent angiography (107 patients Mets and 112 with the nonmetastatic syndrome). In 48 h after injection, the Incidence of contrast nephropathy was 14% in the affected group and 3/6% in the nonaffected group, and the difference between the two groups was significant. In this study, the chance of developing nephropathy in patients with Mets was 6.24,[28,29] while in our study, it was 7.14, perhaps because of longer time measurement urea and Cr levels to 72 h after CM administration, and in any case, the results of this study were consistent with our findings.

In another study by Ozcan *et al*., 599 patients candidate for coronary artery angiography with contrast agent (313 Mets and 286 without Mets) were evaluated for the incidence of contrast nephropathy after receiving the contrast agent. Comparison of the results showed that the incidence of nephropathy in the two groups of patients with and without Mets was 9.3% and 4.9%, respectively. The incidence of nephropathy was significantly higher in the Mets group. In this study, Mets have been introduced as a risk factor for nephropathy development due to CM.[30] In this study, patients with baseline abnormal renal function incorporated that may induce biases in estimated CIN, but our study baseline renal function was normal.

Study limitation

The results should be interpreted in light of the study limitations. First, the study population is restricted to one of the university hospitals of Isfahan city, limiting the generalizability of the findings; further studies in various districts are suggested. Second, the short time follow-up of patients (up to 72 h) limits the results' timing effect. Therefore, a longer monitoring period is recommended. There are many cases of our should be differentiation of AKI that are co-incidence with but casually unrelated to intravenous contrast media administration.

CONCLUSION

Although the occurrence of AKI following intravenous CM should not be automatically inferred as being due to CIN and American College of Radiology recommendation.[6] Our study results showed that the incidence of CIN in patients Mets is significantly higher than that of patients without Mets, indicating a more important risk factor for CIN, even with normal renal function.

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Conflicts of interest
There are no conflicts of interest.

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