

Original Article

Incidence of Contrast-Induced Nephropathy after Coronary Procedures in the United Arab Emirates: A Single-Center Study

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ABSTRACT. Contrast-induced nephropathy (CIN) is a major cause of morbidity and mortality in patients undergoing coronary procedures. The reported incidence of CIN ranges from ~3% to 30%. The profile of patients undergoing coronary procedures in the United Arab Emirates (UAE) differs from those included in published reports of CIN, and the incidence of CIN after coronary procedures in the UAE remains unknown. We conducted a retrospective analysis of all adult patients who underwent coronary procedures at a large tertiary care facility in the UAE in 2013–2014. Patients on dialysis or missing creatinine values were excluded. CIN was defined as an increase of creatinine of ≥ 44 $\mu\text{mol/L}$ within 48–72 h after coronary procedures. Most patients (84.8%) underwent coronary procedures for urgent/emergent indications. The incidence of CIN was 44 out of 1010 (4.35%), with 17 out of 44 (38%) of CIN patients requiring dialysis. After adjusting for baseline differences, older patients, use of angiotensin-converting enzyme inhibitors, and oxygen use during the procedure were associated with a 20.6% increased risk of development of CIN. The risk of in-hospital mortality was significantly higher in the CIN group (29.5% vs. 1.8%).

Introduction

The incidence and prevalence of cardiovascular diseases and chronic kidney disease (CKD) are rising in the Middle East, and they often are present concurrently.^{1,2} This is likely

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due to the prevalence of coexisting risk factors for developing both CKD and cardiovascular disease such as diabetes, hypertension, obesity and dyslipidemia at much higher rates than in the western world.³⁻⁵

Contrast-induced nephropathy (CIN) is a common cause of acute kidney injury in hospitalized patients and is associated with higher morbidity, mortality and increased healthcare costs.⁶⁻⁹ CIN is defined by a rise of creatinine of either a 25% from baseline or 44 $\mu\text{mol/L}$ within 48–72 h after administration of a contrast agent in the absence of alternate

explanation.^{10,11} The reported rate of CIN after coronary procedures varies between populations, but can be as high as 50% in high-risk populations.^{7,12-14} Little is known about the incidence and predictors of CIN in patients with cardiovascular disease in the Gulf region. Whilst the relatively young age of patients with coronary artery disease in this region might be expected to be associated with lower rates of CIN, the higher prevalence of diabetes mellitus (DM) may increase this risk.^{2,3,5} We conducted a retrospective case-control study of patients undergoing coronary procedures in a large public hospital in Abu Dhabi to estimate the incidence of CIN and identify factors associated with its development.

Methods

Study population and definition of contrast-induced nephropathy

We performed a retrospective electronic health record review of all adult patients (age >18 years) who underwent a coronary procedure at Sheikh Khalifa Medical City (SKMC) from January 1, 2013, to December 31, 2014. SKMC is a 586-bed public sector hospital in Abu Dhabi with 24/7 cardiac catheterization service. The study was approved by the Human Research Protection Office/Institutional Review Board of SKMC.

Variables

The following variables were collected on each subject: age, sex, body mass index (BMI), ethnicity, history of DM, hypertension, CKD, history of previous percutaneous coronary intervention (PCI), peripheral vascular disease, smoking, left ventricular ejection fraction (LVEF) during admission or within three months prior admission, medications history, serum creatinine measurements on admission, within 24 h during the procedure, 24, 48 and 72 h postprocedure, glycated hemoglobin (HbA1c), hemoglobin and hematocrit levels, type of procedure (diagnostic vs. interventional coronary angiography, elective vs. urgent procedure) with number of lesions treated, type and volume of contrast used,

duration of procedure, vascular access used for procedure, preprocedure intravenous (IV) hydration and N-acetylcysteine use, the need of inotropes and intraaortic balloon pump during the procedure, need for dialysis, in-hospital mortality, re-admission and length of stay (LOS). One small study suggested that oxygen use before angiography¹⁵ may improve outcomes, so we studied this variable also.

The CIN prevention protocol implemented prophylactically at our institution included IV hydration with normal saline 50–100 mL/h, commencing 2–6 h prior the procedure and 6 h post the procedure.¹⁶ The rate of IV hydration depended on the volume status of the patient and left ventricular function and was decided by the treating physician. N-acetylcysteine was given by the nephrology team to those they considered high-risk, usually those with known CKD. It was not routine in our practice to stop angiotensin-converting enzyme inhibitors (ACE-I) or angiotensin-receptor blocker (ARB's) prior coronary angiography as most of our patients presented as emergencies.

Statistical Analysis

Data are presented as the mean \pm standard deviation for continuous variables and percentages for categorical variables. The continuous variables of many groups were compared with the Mann–Whitney test. Categorical variables were compared with the Chi-square test. A multiple logistic regression was used to determine independent significant predictors of outcome. Incidence, odds ratio and relative risk (RR) with 95% confidence intervals (CIs) was expressed relative to a reference baseline category. $P < 0.05$ were used to establish the significance level. Data were analyzed using the IBM SPSS Statistics version 23.0 (IBM Corp., Armonk, NY, USA).

Results

Baseline characteristics

A total of 1010 patients were included, 46 patients were excluded from the study (38 patients were on dialysis at baseline, and 8

patients had missing data). 44/1010 developed CIN (4%, 95% CI 3% to 6%) with 17/44 (39%) requiring dialysis. Twelve patients in the non-CIN group required dialysis during the hospital stay and this was attributed to other causes of AKI, including sepsis, or cardiogenic shock, etc.

Demographics, comorbidities, laboratory values, procedure characteristics, and outcome data of 1010 patients are presented in Table 1. The mean age of the study was 56 ± 12 years and were predominantly males (83%). 21% of the patients were United Arab Emirates (UAE) nationals, and the majority of patients were

Table 1. Baseline characteristics of the study population.

	All (n=1010)	Non-CIN group (n=966)	CIN group (n=44)	P
Demographics				
Age in years (\pmSD)	56 \pm 12	55 \pm 12	63 \pm 12	<0.001
Male	834 (83)	800 (96)	34 (4)	0.218
Nationality				
United Arab Emirates	212 (21)	204 (21)	8 (18)	0.250
Other Arab nationalities	384 (38)	361 (37)	23 (52)	
Indian subcontinent	347 (34)	336 (35)	11 (5)	
Others	67 (7)	65 (7)	2 (5)	
Comorbidities				
Body mass index (kg/m²)	29 \pm 7	29 \pm 7	29 \pm 4	0.358
Left ventricular ejection fraction	49 \pm 12	47 \pm 12	43 \pm 13	0.013
Diabetes	450 (59)	418 (45)	32 (73)	<0.001
NYHA III/IV	90 (9)	79 (8)	11 (25)	0.001
Hypertension	597 (59)	564 (58)	33 (75)	0.019
PVD	25 (3)	21 (2)	4 (9)	0.02
Smoking	325 (32)	316 (33)	9 (21)	0.058
Laboratory data				
HbA1c (%)	7 \pm 2	7 \pm 2	8 \pm 2	0.054
Hemoglobin	140 \pm 22	138 \pm 21	123 \pm 27	0.001
Heart rate (beats/min)	78 \pm 16	76 \pm 17	79 \pm 25	0.783
Creatinine on admission	100 \pm 51	99 \pm 51	123 \pm 53	<0.001
Creatinine after 72 h	104 \pm 72	-6 \pm 26	97 \pm 96	<0.001
Procedure characteristics				
Volume of contrast (mL)	170 \pm 74	144 \pm 87	144 \pm 93	0.896
Duration of procedure (min)	44 \pm 21	39 \pm 29	46 \pm 34	0.188
Number of lesions treated	2 \pm 1	2 \pm 1	1 \pm 1	0.555
Oxygen during procedure	655 (65)	617 (64)	38 (86)	0.001
Type of Procedure				
Elective	154 (15)	151 (16)	3 (7)	0.076
Urgent/E	856 (85)	815 (84)	41 (93)	
Medication				
NSAIDs	11 (1.1)	10 (1)	1 (2)	0.389
Metformin	71 (7)	68 (7)	3 (7)	0.626
ARB	256 (25)	246 (25)	10 (23)	0.419
ACEI	454 (45)	446 (46)	8 (18)	<0.001
Outcomes				
Length of stay (days)	8 \pm 8	7 \pm 8	19 \pm 17	<0.001

CIN: Contrast-induced nephropathy, NYHA: New York Heart Association, HbA1c: Glycated hemoglobin, NSAIDs: Nonsteroidal anti-inflammatory drugs, ARB: Angiotensin-receptor blocker, ACEI: Angiotensin-converting enzyme inhibitor.

from other Arab countries and the Indian subcontinent. More than half of the patients were diabetic and hypertensive (59%). The mean BMI was 29 ± 7 kg/m² and the mean LVEF was $49\% \pm 12\%$. The mean creatinine was 100 ± 51 μ mol/L and 104 ± 72 μ mol/L at baseline and 72 h postprocedure, respectively. The average of the volume of contrast used was 170 ± 74 mL and the average duration of the procedure was 44 ± 21 min. The LOS on average was 8 ± 8 days. N-acetylcysteine was given to 114 patients as a prophylactic measure to prevent CIN.

The group who developed CIN were significant older (63 ± 12 years) than those who did not (56 ± 12 years, $P < 0.001$). The sex distribution was equal between CIN and non-CIN groups (Table 1). This reflects the general resident population of UAE, which is 70% male, and mostly expatriates who make up a large migrant workforce in the country.¹⁷ The population was heterogeneous, with most non-UAE nationals hailing from the wider Arab world and the Indian subcontinent (Table 1).

Patients with CIN were more likely to be diabetic (73 vs. 45%; $P < 0.001$), hypertensive (75 vs. 58%; $P < 0.02$), with lower LVEF (43 ± 13 vs. $47 \pm 12\%$; $P < 0.02$), hemoglobin (123 ± 27 vs. 138 ± 21 g/L; $P = 0.001$) and higher baseline creatinine (122 ± 53 vs. 99 ± 51 μ mol/L; $P < 0.001$). The CIN group had a

longer LOS (19 ± 17 days vs. 7 ± 8 days; $P < 0.001$) and a higher mortality (13 (30%) vs. 18 (2%), $P < 0.001$). Figure 1 shows the rate of change in creatinine post coronary procedure in both the groups, as expected, those who develop CIN, the creatinine started rising two days postprocedure and peaks at day 3.

There was no statistical difference in the volumes of the contrast in the CIN and non-CIN groups (144 ± 87 vs 143 ± 93 mL, $P = NS$) or the duration of the coronary procedures between groups (46 ± 34 vs. 39 ± 29 min; $P = NS$).

A higher proportion of patients in the CIN group 41/44 (93%) underwent their coronary procedure for an urgent indication (i.e, acute coronary syndrome or out-of-hospital cardiac arrest), compared with the non-CIN group 815/967 (84%).

Diabetics were 3.5 times more likely to develop CIN ($P < 0.001$) (Table 2). Hypertension was twice as prevalent in the CIN group ($P < 0.002$). Subjects with CKD or peripheral vascular disease were over four times more likely to develop CIN ($P < 0.001$ and 0.02, respectively). Smoking history, previous PCI, or obesity were not associated with increased risks in our study (Table 2). There was no association found between CIN and the use of ARB, metformin, or nonsteroidal antiinflammatory agents (NSAIDs) (Table 3). However,

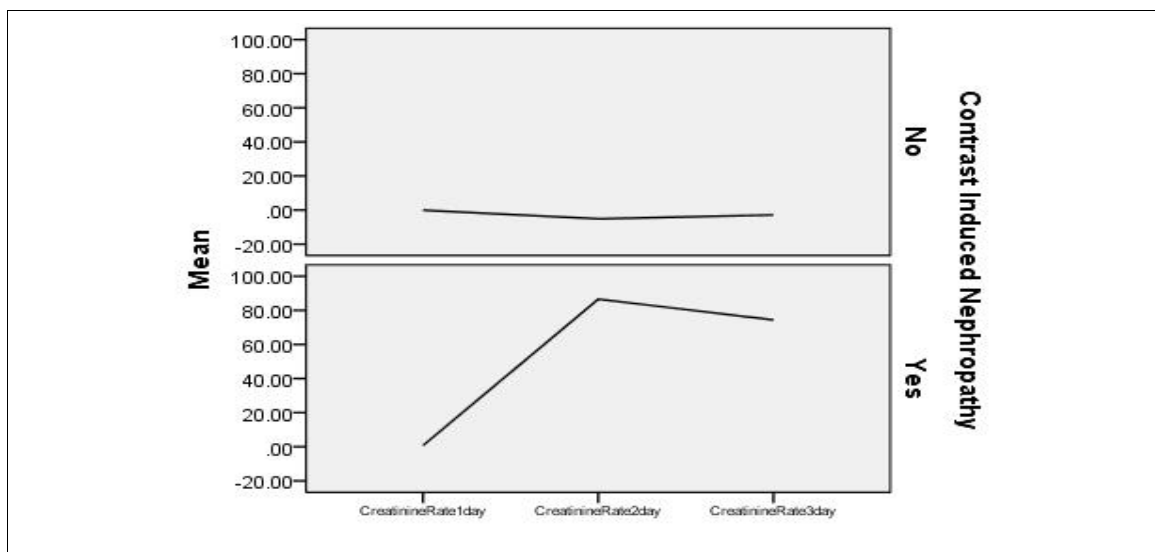


Figure 1. Tendency of rate of change over three days from the day of admission.

Table 2. Association between contrast-induced nephropathy and different variables.

Variables	Development of CIN		OR (95% CI)	P
	Non-CIN group Number (%)	CIN group Number (%)		
Diabetes	418 (43)	32 (73)	3.496 (1.779–6.870)	<0.001
Hypertension	564 (58)	33 (75)	2.138 (1.068–4.281)	0.019
Smoking	316 (33)	9 (20)	0.529 (0.251–1.114)	0.058
NYHA III/IV	79 (8)	11 (25)	3.743 (1.821–7.690)	0.001
Presence of chronic kidney disease	110 (11)	16 (36)	4.447 (2.332–8.480)	<0.001
Pervious percutaneous cardiac intervention	230 (24)	9 (20)	0.823 (0.390–1.737)	0.381
Peripheral vascular disease	21 (2)	4 (9)	4.5 (1.476–13.724)	0.02
Obesity	724 (75)	36 (82)	1.461 (0.670–3.187)	0.222

CIN: Contrast-induced nephropathy, OR: Odds ratio, CI: Confidence interval, NYHA: New York Heart Association, *P*-value <0.5: Significant.

the use of ACEI was associated with a nearly four-fold increased risk of CIN more compared with subjects who were not on an ACEI (RR 3.86, *P* <0.001). Subjects taking insulin were more likely to develop CIN (*P* <0.001) (Table 3), but blood sugar, HbA1c were not significant.

In contradistinction to previous studies, the volume of contrast was not associated with

increased risk.^{12,18} In addition, duration of procedure and number of stents treated were also not associated with increased risk of CIN (Table 1).

The risks of in-hospital mortality were significantly higher (RR = 22, *P* <0.001) in those who developed CIN (Table 3).

In a logistic regression analysis, it revealed that in our study population older patients, use

Table 3. Association between contrast-induced nephropathy and management/outcomes.

Variables	Development of CIN		OR (95% CI)	P
	Non-CIN group Number (%)	CIN group Number (%)		
ARB	246 (25)	10 (23)	0.861 (0.419–1.768)	0.419
ACEI	446 (46)	8 (18)	0.259 (0.119–0.563)	<0.001
Metformin	68 (7)	3 (7)	0.966 (0.292–3.201)	0.626
NSAIDs	10 (1)	1 (2)	2.223 (0.278–17.764)	0.389
Insulin	362 (37)	31 (70)	3.979 (2.055–7.703)	<0.001
Access				
Femoral	646 (67)	32 (73)	0.763 (0.388–1.501)	0.271
Radial	318 (33)	12 (27)		
Indication procedure				
Elective	151 (16)	3 (7)	2.532 (0.774–8.282)	0.074
Urgent	815 (84)	41 (93)		
Type of contrast				
Omnipaque (iohexol)	952(99)	44 (4)		
Visipaque (iodixanol)	14 (2)	0 (0)		0.534
Balloon Pump	32 (3)	8 (18)	6.49 (2.791–15.073)	0.001
Need of dialysis	12 (1)	17 (39)	49.37 CI (46.37–52.37)	<0.001
In hospital Mortality				
No	18 (2)	13 (30)	22.09 (9.943–49.058)	<0.001

CIN: Contrast-induced nephropathy, OR: Odds ratio, CI: Confidence interval, ARB: Angiotensin-receptor blocker, ACEI: Angiotensin-converting enzyme inhibitors, NSAIDs: Nonsteroidal anti-inflammatory drugs, *P*<0.5: Significant.

Table 4. Logistic regression for dependent variable contrast-induced nephropathy.

	Coefficient	P	OR	95% CI OR	
				Lower	Upper
Diabetes	0.194	0.709	1.214	0.439	3.353
Hypertension	0.1	0.805	1.106	0.498	2.455
NYHA Functional Classification III and IV	0.383	0.36	1.467	0.645	3.332
Presence of CKD	0.419	0.323	1.521	0.662	3.496
Peripheral vascular disease	0.492	0.45	1.635	0.456	5.862
Use of Insulin	0.714	0.147	2.042	0.779	5.353
Oxygen use during procedure	1.263	0.006	3.537	1.433	8.733
Age	0.04	0.013	1.041	1.008	1.074
Ejection fraction	-0.022	0.093	0.978	0.954	1.004
Hemoglobin	-0.009	0.255	0.991	0.977	1.006
Angiotensin-converting enzyme inhibitors	-0.973	0.02	0.378	0.167	0.856
Constant	-4.751	0.008	0.009		

OR: Odds ratio, CI: Confidence interval, NYHA: New York Heart Association, CKD: Chronic kidney disease, $P < 0.05$: Significant.

of ACE-I and use of oxygen procedure were associated with increased risks of development of CIN adjusted over diabetes, hypertension, ejection fraction, ACEI, insulin and New York Heart Association III and IV functional classifications, $P < 0.001$ (Table 4).

Discussion

We conducted a large retrospective review of patients who underwent coronary procedures in a large tertiary hospital in the UAE to identify the incidence of CIN and its risk factors. We found the incidence of CIN to be 4%. Factors associated with CIN were older age, diabetes, hypertension, preexisting CKD, PVD, use of ACEI and insulin and use of oxygen during the procedure.

There are limited data in the Middle East on the incidence and outcomes of CIN. The majority of the studies were from Saudi Arabia. Balghith reported a similar incidence of CIN (4.9%).¹⁹ This lower incidence of CIN could be attributable to the use of IV hydration in most of the patients.^{6,20,21} The major risk factors were the presence of diabetes and hypertension. On the contrary, AlDeeri et al reported an incidence of 31.3% among patients in the Saudi tertiary care center who underwent cardiac catheterization and renal

denervation.²² Their higher incidence of CIN might be related to measuring creatinine up to 96 h post-contrast exposure.^{6,20,21} Hypertension and baseline estimated GFR were the major predictors for CIN in their study. However, compared to our results, the short-term prognosis of the study was favorable without dialysis. In our study, the population treated is fairly heterogeneous reflecting the population of UAE, which are mostly expatriates. The overall rate of CIN in this group was also low compared to historical data.^{6,20,21}

Though a significant number of the study population was diabetic and hypertensive, the patient's risk of development of CIN was lower to previous studies. This may be related to the recognition of CIN as a complication of contrast procedure and adequate preparation with IV hydration, which is considered the best available strategy to lower the risk of CIN.¹⁹ In this study, low osmolar contrast agent was not associated with increased risk of CIN compared to other studies might be related to the fact the study population mostly had patients with mild to moderate CKD and the volume of contrast use was also low.²³⁻²⁵

In this study, patients who were diabetic, especially those who were insulin dependent, those with CKD, those with LV dysfunction, and those who needed an intra-aortic balloon

pump during their coronary procedure were more likely to develop CIN.

In addition, patients who were on ACE-I were more likely to be diabetic, hypertensive and those with heart failure, just reflecting the trend off ACE-I being the first-line medications. In our opinion, this is the reason in our study, patients on ACE-I versus those on ARB were more likely to develop CIN.

Development of CIN especially need for dialysis, led to increase LOS and conferred increased risk of mortality. This study highlights the continued need for vigilance and optimizing the fluid status peri-procedure if possible.

Its previously been reported that using oxygen pre-coronary angiography could reduce the incidence of CIN in patients with normal and impaired renal function.²⁶ Our study found the opposite effect, which may be attributed to the fact that most of our patients underwent urgent/emergent coronary angiography. This suggests that they may have been cardiovascularly more compromised than those undergoing elective procedures, and oxygen use here was merely a marker of more unstable pathology. The possible mechanisms whereby oxygen use may be helpful may be in trying to deliver more oxygen to renal tissue beds, but equally oxygen use may enhance free radical injury and a number of recent publications discourage the use of oxygen in sick patients.²⁷

The limitations of this study are that it is a single-center retrospective study with indication bias. Further, we cannot be completely confident that the renal dysfunction we saw after the contrast study was related to contrast media and not simply part of the pathology for which they were undergoing the study. Nevertheless, our study had a large sample size and reflecting real-world data from a complete electronic record from a large tertiary hospital in the Middle East. This is the first such study from UAE comparing renal dysfunction rates post coronary procedures. This may help health-care providers benchmark renal dysfunction and guidance patients and quality teams.

Conclusion

The incidence of CIN post coronary procedures may improve with increased recognition of risk factors and modifying risk factors such as adequate hydration and streamlining care protocols. In high-risk groups, there is a need for heightened vigilance as the development of CIN is still a harbinger of poor prognosis in patients undergoing coronary procedure. Our data will help develop a CIN risk calculator in middle eastern population and help physicians estimate risks of CIN pre-contrast procedures.

Conflict of interest: None declared.

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