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Risk Factors of Contrast-Induced Nephropathy after Percutaneous Coronary Interventions: An Observational Study

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ABSTRACT

Background: Contrast-induced nephropathy (CIN) refers to a temporary decline in kidney function after using iodinated contrast agents. Identifying high-risk patients and implementing suitable preventive measures are crucial for reducing CIN incidence.

Objective: This study aimed to investigate risks associated with CIN after percutaneous coronary interventions (PCI).

Patients and methods: This prospective observational study included 500 patients aged 18 years or older with a glomerular filtration rate (GFR) of 60 ml/min/1.73 m² or higher who underwent PCI at Al-Husain University Hospital between January 2022 and August 2023. **Results:** Hypertension significantly increased the risk of AKI after PCI [adjusted OR = 15.34 (4.77-60.36, p<0.001)]. Adjustment of hemoglobin level significantly decreased the risk of AKI [adjusted OR = 0.26 (0.12-0.53, p<0.001)] but an increased level of LDL increased the risk of AKI after PCI [adjusted OR = 1.05 (1.02-1.08, p=0.002)] and decrease of HDL level below normal significantly increased the level of AKI [adjusted OR = 1.21 (1.03-1.46, p=0.030)].

Conclusion: Hypertension, dyslipidemia, contrast volume, and impaired cardiac parameters significantly increased the risk of AKI following PCI, while higher hemoglobin levels were protective.

Keywords: Percutaneous coronary intervention, Contrast-induced nephropathy, Risk factors.

INTRODUCTION

Contrast-induced nephropathy (CIN) refers to a temporary decline in kidney function after using iodinated contrast agents. It is characterized by a rise in serum creatinine levels of 25% or more, or an absolute increase of 0.5 mg/dL or more, within 48 to 72 hours after exposure to the contrast media [1, 2]. The mechanism of CIN remains unclear. It may involve hemodynamic impacts, the generation of reactive oxygen species (ROS), and toxicity to renal tubules. Additionally, inflammation, immune reactions, and reduced endothelial progenitor cell count have been implicated in CIN onset [3]. Various risk factors, including age, glomerular filtration rate (GFR), pre-existing hyperglycemia, cholesterol levels upon admission, and elevated glycosylated hemoglobin, are associated with CIN development [4, 5].

Research indicates that individuals with diabetes are particularly vulnerable to CIN, with diabetic nephropathy being a significant independent risk factor. Both diabetes and the use of iodinated contrast agents can profoundly alter renal function, impacting factors such as GFR, renal hemodynamics, tubular transport, oxygen consumption, and ROS production [6]. Prolonged hyperglycemia induces various pathophysiological changes, including endothelial and microvascular dysfunction, heightened production of vascular inflammatory markers and ROS, and compromised immune responses [7].

Identifying high-risk patients and implementing suitable preventive measures are crucial for reducing CIN incidence. In this study, we aimed to investigate the potential laboratory, echocardiographic, and echocardiologic risk factors associated with the development of CIN in patients undergoing PCI.

PATIENTS AND METHODS

Study design: This study was a prospective observational study of consecutive cohort of patients who attended at Al-Husain University Hospital through the period from January 2022 to August 2023 and met the inclusion criteria.

Inclusion criteria: Adult individuals aged 18 years or older undergoing contrast angiography as a part of their PCI for non-ST-segment elevation myocardial infarction (NSTEMI), unstable angina (UA), ST-segment elevation myocardial infarction (STEMI), as well as asymptomatic individuals. Additionally, participants must exhibit a glomerular filtration rate (GFR) of 60 ml/min/1.73m^2 or higher.

Exclusion criteria: Cases with active malignancies, those currently participating in other intervention studies, and women who are pregnant or planning to become pregnant during the follow-up period. Additionally, patients with active urogenital infections and history of diabetic ketoacidosis, or cardiogenic shock. Furthermore, individuals with a GFR below 60 ml/min/1.73m^2.

Study outcomes: The main outcome of this study was the occurrence of AKI following contrast angiography. AKI was defined as either a rise in creatinine level of at least 0.3 mg/dL (26.5 μmol/L), or a minimum 1.5-fold increase in creatinine level compared to the baseline within 72 hours after the procedure.

Ethical considerations: The study was done after being accepted by the Research Ethics Committee, Faculty of Medicine, Al-Azhar University, Cairo,

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Egypt. All patients provided written informed consents prior to their enrolment. The consent form explicitly outlined their agreement to participate in the study and for the publication of data, ensuring protection of their confidentiality and privacy. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

All analysis was conducted using R version 4.3.2 and R-Studio (version 2023.12.1+402 for windows). We assessed the distribution of the continuous data using the Shapiro test. In the case of normally distributed data, we used mean and stander deviation (SD). In the case of non-normally distributed data, we used median and interquartile range. The categorical variables are described using numbers and percentages. To compare among the baseline characteristics, we used the Mann-Whitney U test to compare between non-normally distributed continuous data and fisher exact in case of categorical data. We used logistic regression analysis to identify the risk factors of AKI. We used AKI as outcome variable. We added the explanatory variables one by one to identify the suitable variables for the model. A two tailed p-value ≤ 0.05 was considered statistically significant.

RESULTS

Descriptive statistics: We included 500 patients in this study, only 27 (0.5%) developed AKI. There was a significant difference in age between the two groups (p = 0.047). The percentage of hypertensive patients was significantly higher in AKI group than in control [19 (70.4%), 143 (30.2%); p < 0.001; respectively]. The hemoglobin level was significantly higher in control group than in AKI group [12.6 (12.0 to 13.1), 11.8 (11.0 to 12.9); p = 0.002; respectively]. There were no differences in sex, diabetes, smoking, and BMI, (P = 0.234), (P = 0.834), (P = 0.096), and (P = 0.060) respectively. The platelet count (PLT) was significantly higher in AKI group [311.0 (270.5 to 335.0), 278.0 (234.0 to 321.0); p = 0.038; respectively]. High density lipoprotein (HDL) level was significantly lower in AKI group than in control group [51.2 (6.8), 55.0; p = 0.030 respectively]. Low density lipoprotein (LDL) and cholesterol levels were significantly higher in AKI group than in control group [119.1, 109; p = 0.002; respectively] and [187.0 (167.0 to 234.0), 171.0 (161.5 to 179.5), P=0.002 respectively] respectively. Baseline total leukocytic count (TLC), triacyl glyceride (TAG), low density lipoprotein (LDL), and glycosylated hemoglobin (HBA1C) were not statistically different between those who developed AKI and those who did not, (P=0.298), (P=0.150), (P=0.156), (P=0.566), respectively (Table 1).

Table (1): Baseline characteristics

		No AKI (n = 473)	AKI (n = 27)	P-value
Age		57.0 (52.0 to 63.0)	58.0 (55.0 to 67.5)	0.047
Sex	**Female**	204 (43.1)	15 (55.6)	0.234
	Male	269 (56.9)	12 (44.4)	
Diabetes	**No**	324 (68.5)	18 (66.7)	0.834
	Yes	149 (31.5)	9 (33.3)	
Hypertension	**No**	330 (69.8)	8 (29.6)	<0.001
	Yes	143 (30.2)	19 (70.4)	
Smoking	**No**	308 (65.1)	22 (81.5)	0.096
	Yes	165 (34.9)	5 (18.5)	
Dyslipidemia	**No**	339 (71.7)	24 (88.9)	0.073
	Yes	134 (28.3)	3 (11.1)	
BMI		28.7 (26.8 to 31.2)	26.7 (25.4 to 29.9)	0.06
HB		12.6 (12.0 to 13.1)	11.8 (11.0 to 12.9)	0.002
TLC		5.3 (4.7 to 6.0)	5.2 (4.8 to 5.3)	0.298
PLT		278.0 (234.0 to 321.0)	311.0 (270.5 to 335.0)	0.038
TAG		146.0 (132.0 to 177.0)	143.0 (130.5 to 152.5)	0.15
Cholesterol		187.0 (167.0 to 234.0)	171.0 (161.5 to 179.5)	0.002
LDL		111.0 (91.0 to 148.0)	98.0 (93.0 to 118.0)	0.156
HDL		53.0 (47.0 to 57.0)	57.0 (55.5 to 58.0)	0.001
HBA1c		5.7 (5.3 to 8.0)	5.6 (5.2 to 8.1)	0.566

AKI: acute kidney injury; **BMI:** body mass index; **HB:** hemoglobin; **TLC:** total leukocytic count; **PLT:** platelet count; **TAG:** triacyl glyceride; **LDL:** low-density lipoprotein; **HDL:** high-density lipoprotein; and **HbA1c:** glycosylated hemoglobin. Categorical data are presented as numbers and percentages, and continuous data are presented as median and interquartile range, P-value < 0.05 is statically significant.

ECG, ECHO and Coronary Angiography: Left ventricular ejection fraction was not different in the two groups (P = 0.2). Left ventricular end diastolic dimensions (LVEDD), left ventricular end-systolic diameter (LVESD), interventricular septum (IVS), and left ventricle posterior wall (LVPW) were significantly higher in AKI group (p values = 0.001, 0.036, 0.009, 0.002; respectively) (Table 2).

Table (2): Echocardiographic parameters

	No AKI (n = 473)	AKI (n = 27)	p-value
EF	53.0 (50.0 to 57.0)	52.0 (48.0 to 55.0)	0.217
LVEDD	5.4 (5.2 to 5.9)	6.0 (5.5 to 6.3)	0.001
LVESD	3.2 (2.8 to 3.6)	3.4 (3.2 to 3.8)	0.036
IVS	1.0 (0.9 to 1.2)	1.3 (0.9 to 1.4)	0.009
LVPW	1.0 (0.9 to 1.2)	1.3 (0.9 to 1.4)	0.002

AKI: acute kidney injury; **LVEF:** left ventricular ejection fraction; **LVEDD:** left ventricular end-diastolic dimensions; **LVESD:** left ventricular end-systolic diameter; **IVS:** interventricular septum; and **LVPW:** Left ventricle posterior wall. Data are presented as median and interquartile range, P-value < 0.05 is statically significant.

Risk factors for AKI: Hypertension significantly increased risk of AKI after PCI [adjusted OR = 15.34 (4.77-60.36, p<0.001)]. Adjustment of hemoglobin level significantly decreased the risk of AKI [adjusted OR = 0.26 (0.12-0.53, p<0.001)] but increased level of LDL significantly increase the risk of AKI after PCI [adjusted OR = 1.05 (1.02-1.08, p=0.002)] and decreased HDL level below normal significantly increased the level of AKI [adjusted OR = 1.21 (1.03-1.46, p=0.030)] (Table 3).

Table (3): Univariate and multivariate logistic regression analysis of baseline risk factors of AKI

		No AKI (n = 473)	AKI (n = 27)	OR (univariable)	OR (multivariable)
Age	Mean (SD)	57.4 (8.2)	60.9 (7.0)	1.06 (1.01-1.11, p=0.031)	1.06 (1.00-1.13, p=0.076)
sex.	Female	204 (93.2)	15 (6.8)	-	-
	Male	269 (95.7)	12 (4.3)	0.61 (0.27-1.32, p=0.210)	7.29 (0.98-62.00, p=0.058)
Diabetes	No	324 (94.7)	18 (5.3)	-	-
	Yes	149 (94.3)	9 (5.7)	1.09 (0.46-2.42, p=0.842)	13.67 (0.45-363.76, p=0.128)
Hypertension	No	330 (97.6)	8 (2.4)	-	-
	Yes	143 (88.3)	19 (11.7)	5.48 (2.42-13.56, p<0.001)	15.34 (4.77-60.36, p<0.001)
Smoking	No	308 (93.3)	22 (6.7)	-	-
	Yes	165 (97.1)	5 (2.9)	0.42 (0.14-1.06, p=0.089)	0.52 (0.09-2.64, p=0.450)
Dyslipidemia	No	339 (93.4)	24 (6.6)	-	-
	Yes	134 (97.8)	3 (2.2)	0.32 (0.07-0.92, p=0.064)	4.43 (0.27-79.27, p=0.299)
BMI	Mean (SD)	29.1 (3.7)	28.1 (3.8)	0.93 (0.85-1.03, p=0.152)	1.08 (NA-1.59, p=0.699)
HB	Mean (SD)	12.7 (0.8)	12.0 (1.3)	0.41 (0.25-0.66, p<0.001)	0.26 (0.12-0.53, p<0.001)
TLC	Mean (SD)	5.4 (1.1)	5.5 (1.0)	1.05 (0.74-1.40, p=0.777)	1.48 (0.97-2.27, p=0.061)
PLT	Mean (SD)	278.5 (58.9)	301.3 (68.5)	1.01 (1.00-1.01, p=0.055)	1.01 (1.00-1.02, p=0.028)
TAG	Mean (SD)	154.2 (28.5)	147.1 (29.9)	0.99 (0.98-1.00, p=0.214)	1.00 (0.98-1.03, p=0.699)
Cholesterol	Mean (SD)	196.8 (38.8)	174.1 (32.8)	0.98 (0.97-0.99, p=0.004)	0.95 (0.92-0.98, p<0.001)
LDL	Mean (SD)	119.1 (22.2)	109.1 (28.9)	0.99 (0.98-1.00, p=0.118)	1.05 (1.02-1.08, p=0.002)
HDL	Mean (SD)	55.0 (6.6)	51.2 (6.8)	1.11 (1.04-1.22, p=0.008)	1.21 (1.03-1.46, p=0.030)
HBA1C	Mean (SD)	6.4 (1.5)	6.3 (1.6)	0.96 (0.73-1.24, p=0.777)	0.70 (0.26-1.98, p=0.495)

AKI: acute kidney injury; OR: odds ratio; BMI: body mass index; HB: hemoglobin; TLC: total leukocytic count; PLT: platelet count; TAG: triacyl glyceride; LDL: low-density lipoprotein; HDL: high-density lipoprotein; and HbA1C: glycosylated hemoglobin.

In table (4), the increased amount of used contrast significantly increased the risk of AKI [adjusted OR = 1.01 (1.00-1.03, p=0.049)].

Table (4): Univariate and multivariate logistic regression analysis of echocardiographic parameters and the AKI

		NO (n = 473)	YES (n = 27)	OR (univariable)	OR (multivariable)
LVEF	Mean (SD)	52.9 (6.6)	51.4 (7.0)	0.97 (0.91-1.03, p=0.282)	1.02 (0.94-1.11, p=0.575)
LVEDD	Mean (SD)	5.6 (0.5)	6.0 (0.5)	4.10 (1.93-8.99, p<0.001)	3.93 (1.37-11.61, p=0.011)
LVESD	Mean (SD)	3.2 (0.6)	3.5 (0.5)	1.95 (1.01-3.75, p=0.044)	1.12 (0.42-2.91, p=0.812)
IVS	Mean (SD)	1.0 (0.2)	1.2 (0.2)	15.33 (2.68-91.96, p=0.002)	1.04 (0.01-166.56, p=0.986)
LVPW	Mean (SD)	1.0 (0.2)	1.2 (0.2)	14.15 (2.79-74.95, p=0.001)	8.79 (0.07-958.84, p=0.366)

AKI: acute kidney injury; LVEF: left ventricular ejection fraction; LVEDD: left ventricular end-diastolic dimensions; LVESD: left ventricular end-systolic diameter; IVS: interventricular septum; and LVPW: Left ventricle posterior wall. Data are presented as median and interquartile range.

DISCUSSION

In this cohort study, we aimed to investigate the risk factors associated with CIN after PCI angiography and the differences in these factors among diabetic and non-diabetic patients. PCI procedures are rising annually due to advancements in technology and equipment, and the use of CM is becoming more widespread. After intravascular CM injection, CIN is a common complication and is the second most frequent cause of AKI in hospitalized patients, highlighting the clinical relevance of this study [8]. We found that hypertension, increased LDL, platelet count, and decreased HDL are significant risk factors for AKI, while a higher level of hemoglobin is protective. Patients who developed AKI had greater LVEDD, LVESD, IVS, and LVPW, indicating deterioration in cardiac functions. These findings align with previous literature demonstrating the association between age, hyperlipidemia, hypertension, contrast volume, decreased hemoglobin level, and post-PCI CIN [9-13].

Our study reported that hypertension significantly increases the risk of AKI (P<0.001). This finding aligns with the results of **Mehran *et al.*** [9] who found a significant association between hypertension and the development of CIN after PCI (P<0.0001). **Kumar *et al.*** [11] reported that hypertension emerged as the sole identified risk factor, with CIN being more prevalent among patients with hypertension compared to those without hypertension (P = 0.0158). This agreement strengthens the evidence of the negative effect of hypertension. The damage to small vessels in the kidney in patients with hypertension, which are responsible for filtering waste products, may explain the increased risk of CIN in this population [14]. Another association should be acknowledged from our study is the link between hypertension and cardiac function. CIN may be a result of decreased cardiac function in our cohort instead of hypertension itself. Our study concurs with **Mehran *et al.*** [9] that age and hyperlipidemia are independent risk factors for CIN (P<0.0001 and P=0.0004 respectively). Vasculopathy-mediated hyperlipidemia may significantly contribute to the increased incidence of CIN. It can damage blood vessels throughout the body, including the small vessels supplying the kidney, impairing blood flow and reducing the kidneys' ability to filter waste products [15]. The increased occurrence of CIN in older individuals supports current evidence of age-related renal function decline.

Contrast volume is also correlated with CIN in our study, which is consistent with the findings of **Cigarroa *et al.*** [12] and **Mehran *et al.*** [9]. Contrast volume has been linked to an increased risk of AKI, although the exact mechanism is not clearly defined. A prognostic study conducted on three million people found an association between contrast volume and AKI, but it was limited by baseline differences between groups [16].

Our results suggested that a higher baseline hemoglobin level is protective, which aligns with the findings of **Ying *et al.*** [13].

This protection may stem from the contrast agent's tendency to generate free radicals in the kidney, leading to tissue and tubular damage through oxidative stress (OS) [17]. Elevated hemoglobin levels may bolster defences against OS. Furthermore, contrast agents can increase blood viscosity and promote vasoconstriction, potentially reducing blood flow to the kidneys and inducing hypoxia [18]. Adequate hemoglobin levels could facilitate better oxygen supply to the kidneys, thereby preserving renal function and reducing the risk of CIN.

Patients who developed AKI had greater LVEDD, LVESD, IVS, and LVPW highlighting the association between pre-operative impaired cardiac functions and the increased risk of AKI following PCI. **Masoomi *et al.*** [19] reported heart failure is an independent risk factor for developing CIN after PCI (P=0.04).

This report by **Masoomi *et al.*** [19] supports our hypothesis. These findings may be attributed to weak renal perfusion in patients with impaired cardiac functions, consequently reducing blood flow to the kidneys. This compromised perfusion decreases the kidneys' ability to filter waste products effectively, making them more susceptible to ischemia and injury from contrast, thereby increasing the risk of CIN.

In our study, diabetes was not a risk factor for CIN after PCI. Our results align with that was reported in the study by **Kumar *et al.*** [11]. However, our results are contradicting that was reported by **Masoomi *et al.*** [19]. In our study, there was no differences in hA1c between those who developed CIN and those who didn't (P = 0.5).

This observation shows the overall good glycemic control in our study, which was not achieved in **Masoomi *et al.*** [19]. **Zhang *et al.*** [20] showed that the risk of CIN in diabetic patients is significant only with HA1c level higher than 9.5. Moreover, **Parfrey *et al.*** [21] showed that diabetic patients with preserved kidney function had a CIN rate comparable to that of individuals without diabetes. The two studies suggest that diabetes with good control may not be a risk for developing CIN, as we reported. Another possible cause for not observing diabetes as a risk factor in our study was the limited occurrence of CIN in our study (0.5%).

STRENGTHS AND LIMITATIONS

Our study delves into a crucial clinical concern, examining various potential risk factors for AKI and underscoring the significance of addressing pre-existing health conditions and optimizing patients' profiles before PCI. Evaluating cardiac function and ensuring good blood pressure control prior to PCI could serve as valuable strategies in minimizing AKI risk. This study aimed to explore the risks in Egyptian patients who were not adequately studied in the literature. Furthermore, our study emphasized the importance of conducting a thorough risk-benefit assessment when planning for PCI procedures, including efforts to minimize contrast volume to enhance patient safety and reduce the likelihood of post-procedural complications such as CIN. However, given its retrospective nature, our study's evidence may be somewhat limited in its power. Additionally, the relatively small sample size and being a single-center study may affect the generalizability of the results. Future research endeavors with larger sample sizes and a prospective approach could enhance our understanding of the relationship between pre-existing conditions, PCI, and AKI. Moreover, exploring strategies to mitigate the contrast's impact on kidney function would be invaluable in improving patient outcomes.

CONCLUSION

This study concluded that hypertension, dyslipidemia, contrast volume, and impaired cardiac parameters are risk factors for AKI after PCI, and higher hemoglobin level was protective. Diabetes was not a risk in the current report.

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