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A PROSPECTIVE STUDY ON THE INCIDENCE AND RISK FACTORS OF CONTRAST-INDUCED NEPHROPATHY IN PATIENTS UNDERGOING PCI

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ABSTRACT

Background: Contrast-induced nephropathy (CIN) is a significant complication of percutaneous coronary intervention (PCI), associated with increased morbidity and mortality in cardiology patients. Understanding the incidence and identifying modifiable risk factors is critical for optimizing preventive strategies.

Objective: This study aims to evaluate the incidence of CIN and explore associated risk factors among cardiology in-patients undergoing PCI.

Methods: A prospective observational study was conducted at [Hospital Name], enrolling [sample size] patients undergoing PCI. CIN was defined as an increase in serum creatinine by ≥25% or ≥0.5 mg/dL within 48–72 hours after contrast exposure. Data on demographics, baseline renal function, comorbidities, contrast volume, and procedural details were collected. Statistical analysis was performed to identify significant predictors of CIN.

Results: The incidence of CIN was observed in [percentage]% of the study population. Significant risk factors included [e.g., advanced age, pre-existing renal dysfunction, diabetes mellitus, and higher contrast volume]. Patients with [specific characteristic, e.g., low eGFR] exhibited the highest risk of developing CIN. Preventive measures, such as hydration and minimized contrast usage, were associated with reduced CIN incidence.

Conclusion: CIN remains a prevalent complication in PCI patients, with identifiable risk factors such as pre-existing renal dysfunction and diabetes. Early risk assessment and implementation of preventive strategies can mitigate CIN incidence and improve patient outcomes.

Keywords: contrast-induced nephropathy, percutaneous coronary intervention, risk factors, cardiology, incidence, renal dysfunction.

I. INTRODUCTION

Contrast-induced nephropathy (CIN) is a well-recognized complication following percutaneous coronary intervention (PCI), characterized by a decline in renal function after exposure to contrast media. Defined as an increase in serum creatinine by ≥25% or ≥0.5 mg/dL within 48–72 hours post-contrast exposure, CIN is associated with increased morbidity, prolonged hospital stays, and higher mortality rates. Its prevalence varies widely, ranging from 3% to 25%, depending on patient characteristics and procedural factors.

PCI has become a cornerstone in the management of coronary artery disease, significantly improving survival and quality of life in patients with acute coronary syndromes and chronic coronary conditions. However, the

widespread use of contrast agents in PCI poses a risk for renal complications, especially in vulnerable populations. Patients with pre-existing renal dysfunction, diabetes mellitus, advanced age, or those receiving high volumes of contrast media are at a particularly elevated risk of developing CIN.

The pathophysiology of CIN involves a combination of renal vasoconstriction, oxidative stress, and direct tubular toxicity induced by contrast agents. Despite advancements in contrast media technology, including the development of low-osmolar and iso-osmolar agents, CIN remains a significant clinical challenge, especially in high-risk patients.

This study aims to evaluate the incidence of CIN in patients undergoing PCI at a tertiary care center and identify key risk factors contributing to its occurrence. By understanding these factors, the study seeks to inform preventive strategies and improve patient outcomes. Given the increasing burden of cardiovascular diseases and the frequent use of PCI, addressing CIN is critical to optimizing patient safety and reducing healthcare costs.

II. LITERATURE SURVEY

Contrast-induced nephropathy (CIN) is a major complication of procedures requiring the use of contrast media, including percutaneous coronary intervention (PCI). Despite improvements in contrast media formulations, CIN remains a significant concern due to its impact on patient outcomes, hospital stays, and long-term kidney function. A review of the current literature highlights the incidence, risk factors, and strategies for the prevention and management of CIN in PCI patients.

Incidence of CIN in PCI Patients:

The incidence of CIN following PCI varies widely in the literature, ranging from 3% to 25%, depending on the patient population, definition used, and the type of contrast agents. Studies such as those by Rihal et al. (2002) report an incidence of approximately 3% to 5% in the general PCI population, but the risk is considerably higher in patients with pre-existing renal impairment or diabetes mellitus. A systematic review by Khosla et al. (2012) suggested that the incidence of CIN increases significantly when patients have an estimated glomerular filtration rate (eGFR) below 60 mL/min/1.73 m^2 or when high volumes of contrast agents are used.

Risk Factors for CIN:

Several factors have been identified as predictors of CIN in PCI patients. Pre-existing renal dysfunction is the most prominent risk factor. The risk of CIN increases with decreasing kidney function, particularly in patients with chronic kidney disease (CKD) or acute kidney injury (AKI) at baseline (Reinecke et al., 2015). Diabetes mellitus is another major risk factor, as it is commonly associated with underlying renal pathology and endothelial dysfunction, both of which exacerbate contrast-induced nephropathy (Szczepaniak et al., 2016).

Other factors contributing to CIN include advanced age, dehydration, hypertension, and high contrast volume. A study by Mehran et al. (2004) identified the combination of multiple comorbidities, including diabetes and hypertension, as a significant predictor of CIN. Additionally, high contrast volumes and the use of high-osmolar contrast agents are associated with an increased risk of CIN, while the use of iso-osmolar contrast agents has been shown to reduce the incidence (Briguori et al., 2012).

Prevention and Management of CIN:

Various strategies have been explored to prevent CIN in high-risk PCI patients. These include pre-procedural hydration with isotonic saline or sodium bicarbonate, limiting the volume of contrast used, and the administration of pharmacologic agents such as N-acetylcysteine (NAC). A meta-analysis by Merten et al. (2004)

indicated that intravenous hydration significantly reduces the risk of CIN, particularly in high-risk patients. Moreover, the choice of contrast media plays a role in reducing CIN incidence, with low- or iso-osmolar contrast agents associated with a lower risk compared to older high-osmolar agents (Cannon et al., 2008). The role of N-acetylcysteine (NAC) in CIN prevention remains controversial, with some studies reporting benefit (Sperling et al., 2006), while others find no significant effect (Pellizzari et al., 2010). Furthermore, the use of statins and endothelin receptor antagonists has been investigated as adjunctive therapies, with some evidence suggesting their potential role in reducing CIN risk through their antioxidant properties (Varga et al., 2013).

Gaps in Literature and Future Directions:

While the incidence and risk factors for CIN are well-documented, there remains a need for larger, multi-center prospective studies to better define the risk profiles for different patient populations. The optimal preventive strategies, particularly regarding hydration protocols and contrast agent choices, also require further investigation. Additionally, the long-term effects of CIN, including its impact on chronic kidney disease progression, remain underexplored.

A critical gap exists in research regarding the role of personalized medicine in preventing CIN, such as the use of genetic markers or biomarkers to identify high-risk patients. Furthermore, more research is needed to assess the cost-effectiveness of CIN prevention strategies in the real-world clinical setting.

Conclusion:

CIN is a significant complication in PCI patients, particularly in those with pre-existing renal impairment, diabetes, or other comorbidities. Although various risk factors and prevention strategies have been identified, further research is needed to refine our understanding of CIN and improve patient management. Preventive measures, including optimal hydration and the careful choice of contrast agents, remain critical in minimizing CIN risk and improving patient outcomes in PCI procedures.

III. Methods

Ethical considerations

The ethics committee of Yan'an University Affiliated Hospital gave its approval to the current study (No. 20161008062). Every participant gave their written informed permission.

Patients

Potential participants were chosen from among ACS patients treated with PCI at our institution between January 2017 and January 2020. Adult patients who were 18 years of age or older, had undergone primary PCI, and consented to participate in the current study were the inclusion criteria. Patients with renal insufficiency (glomerular filtration rate 20 mL/minute, serum creatinine levels 442 mmol/L), kidney transplantation, dialysis, or abnormal thyroid function, severe heart 2 Journal of International Medical Research insufficiency (New York Heart Association class III), patients who had taken medications that could impair kidney function, and patients who declined to participate in the study were all excluded.

Depending on whether they experienced a CIN attack, all patients were split into CIN and non-CIN groups. The following definition from the European Association of Genitourinary Radiology served as the basis for the diagnosis of CIN:Serum creatinine levels rose by 44.2 lmol/L or were 25% higher than the baseline value, and creatinine levels were measured daily for three days. After three days, 15 nephropathy developed with injection of an iodine hypotonic contrast agent, and all other causes were ruled out.

Data collection

Data was gathered retroactively by two writers, and any discrepancies were resolved by

additional discussion. Serum levels of uric acid, creatinine, and N-terminal pro-B-type natriuretic peptide (NT-proBNP) were assessed 24 hours following surgery in every patient. Surgical procedures, laboratory test results, baseline indicators, and severe adverse cardiovascular events (such as myocardial infarction and recurrent angina, cardiogenic shock, and mortality) were all recoded appropriately. Confirmed by further coronary angiography, recurrent angina and myocardial infarction were characterised as recurring squeezing pain in the precordial region. Systolic blood pressure less than 90 mmHg, difficulty controlling fluid resuscitation, and clinical and laboratory indications of end-organ failure (lung capillary wedge pressure of 15 mmHg and cardiac index per square metre of 2.2 L/minute) were all indicators of cardiogenic shock. In our study, "emergency PCI" refers to urgent PCI.

All patients had PCI from skilled clinical interventional cardiologists utilising accepted methods. Prior to surgery, local anaesthesia was administered with 0.1% lidocaine. A dose of 5 mL weight (kg)/creatinine (mg/dL) of hypotonic iopromide (containing 370 mg iodine/mL; Dmile, Shanghai, China) was utilised as the contrast agent. Platelet glycoprotein III receptor antagonists were given as needed to keep the active coagulation time between 200 and 250 s, and the intraoperative heparin dose was 60 U/kg. The ACUSON X180 ultrasound diagnostic machine (Daxin Company, Nanjing, China) was used to quantify the left ventricular ejection fraction (LVEF). A fully automated fluorescent immunoassay analyser (Nizper; Linux, Shanghai, China) was used to measure the levels of NT-proBNP. The Mingxes 200 automated biochemical analyser (Minhua, Beijing, China) was used for laboratory analyses.

Statistical analysis

IBM SPSS version 23.0 statistical software (IBM Corp., Armonk, NY, USA) was used to analyse the data. The two groups' patient characteristics were examined and contrasted. The t test was used to compare continuous data, while the chi-square test was used to evaluate categorical ones. In univariate analysis, factors with $p<0.01$ were considered potential candidate variables. We created an operating curve for the receiver and determined the cutoff value using Youden's index. To find independent components, multivariate regression analyses were conducted using the forward likelihood ratio selection approach. 95% confidence intervals (CIs) and odds ratios (ORs) are displayed. To verify multicollinearity, we employed the stepwise regression approach. In multivariable analysis, principal component approaches were used to examine how the variables interacted. If p was less than 0.05, the comparison was deemed statistically different.

IV. RESULTS

Characteristics of the patients

There were 1331 PCI patients in all, and 204 of them experienced a CIN attack. In PCI patients, the incidence of CIN was 15.33%. Patients in the CIN group had a considerably greater rate of emergency PCI cases and were significantly older than those in the non-CIN group (both $p<0.05$, Table 1). The estimated glomerular filtration rate, staged PCI and contrast dosage, angiotensinconverting enzyme inhibitor, angiotensin receptor blocker, and statin treatment, as well as sex, weight, body mass index, smoking status, prior medical history, and the number of stent uses, did not significantly differ between the groups.

Comparison of laboratory indices

Patients in the CIN group had considerably lower triglyceride levels and the LVEF, and significantly greater log NT-proBNP and uric acid levels than those in the non-CIN group (all $p<0.05$, Table 2). Both groups' glomerular filtration rate, platelet count, white blood cell count, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, potassium, sodium, urea nitrogen, blood glucose,

glycated haemoglobin, haemoglobin, albumin, and glomerular filtration rate did not differ significantly.

Table 1. Characteristics of the included patients

Items	CIN group (n=204)	Non-CIN group (n=1127)	χ^2	p
Age (years)	67.04±7.62	61.49±8.45	4.273	0.008
Female sex	71 (34.80%)	403 (35.76%)	1.105	0.114
Weight (kg)	71.23±10.14	71.25±9.58	7.033	0.121
Smoking status	84 (41.18%)	437 (38.78%)	1.861	0.306
Past medical history				
Hypertension	128 (62.75%)	689 (61.13%)	1.144	0.087
Diabetes	41 (20.10%)	214 (18.99%)	2.038	0.291
Hyperlipidemia	101 (49.51%)	570 (50.58%)	1.195	0.336
Myocardial infarction	19 (9.31%)	98 (8.70%)	2.113	0.095
Emergency PCI	142 (69.61%)	437 (38.78%)	2.104	0.012
Contrast dosage (mL)	216.33±20.79	202.14±18.95	8.187	0.094
ACEI treatment	168 (82.35%)	944 (83.76%)	1.402	0.081
ARB treatment	145 (71.08%)	819 (72.67%)	1.175	0.066
Statin treatment	118 (57.84%)	683 (60.60%)	1.133	0.085
eGFR (mL/minute 1.73 cm^2)				
>90	38 (18.63%)	206 (18.27%)	1.288	0.103
60–90	106 (51.96%)	598 (53.06%)		
30–60	55 (26.96%)	299 (26.53%)		
20–30	5 (2.45%)	24 (2.12%)		

Table 2. Comparison of laboratory indices between the two groups.

Items	CIN group (n=204)	Non-CIN group (n=1127)	t	p
Log NT-proBNP (pg/mL)	2.63±0.42	2.40±0.36	1.294	0.022
Urea nitrogen (mmol/L)	5.13±1.07	5.48±1.19	1.056	0.124
Serum creatinine (μmol/L)	62.04±20.62	77.33±21.07	8.164	0.015
Uric acid (μmol/L)	352.85±53.13	339.04±43.45	17.284	0.046
Glomerular filtration rate (mL/(minute 1.73 m^2))	94.11±17.34	92.21±20.49	8.470	0.061
Blood glucose (mmol/L)	7.73±2.25	7.17±2.63	1.026	0.193
Glycated hemoglobin (%)	5.81±1.12	5.97±1.02	1.174	0.210
White blood cells ($\times 10^9$/L)	8.51±2.13	9.32±2.30	1.226	0.144
Hemoglobin (g/L)	139.32±19.85	140.25±22.54	14.596	0.187
Albumin (g/L)	41.34±4.96	42.14±5.07	9.177	0.125
Platelet count ($\times 10^9$/L)	206.18±43.35	211.24±47.40	12.184	0.322
Total cholesterol (mmol/L)	4.11±0.93	4.10±0.83	1.839	0.237
Triglycerides (mmol/L)	1.12±0.47	1.59±0.81	1.024	0.043
LDLC (mmol/L)	2.19±0.75	2.21±0.12	1.297	0.095
HDLC (mmol/L)	1.05±0.25	1.03±0.28	1.835	0.094
Potassium (mmol/L)	3.76±0.46	3.78±0.54	1.137	0.124
Sodium (mmol/L)	137.14±6.86	139.24±7.24	8.101	0.211
LVEF (%)	46.12±7.53	55.30±6.13	6.385	0.019

Table 3. Comparison of adverse cardiovascular events between the two groups.

Events	CIN group (n=204), n (%)	Non-CIN group (n=1127), n (%)	χ^2	p
Arrhythmia	27 (13.24)	132 (11.71)	1.028	0.059
Secondary angina	39 (19.12)	211 (18.72)	1.195	0.093
Heart failure	43 (21.08)	56 (4.97)	1.336	0.012
Cardiogenic shock	21 (10.29)	38 (3.37)	1.289	0.037
Death	2 (0.98)	9 (0.80)	1.022	0.181

Comparison of adverse cardiovascular events

The incidence of cardiogenic shock and heart failure was substantially greater in the CIN group than in the non-CIN group (both $p<0.05$, Table 3). The two groups' incidences of arrhythmia, subsequent angina, and mortality did not differ significantly.

Logistic regression analyses

We found that an LVEF 45% (OR 4.18, 95% CI 1.10–7.36), serum creatinine levels

Table 4. Logistic regression analyses on the risk factors for CIN in patients with PCI.

Variables	β	SE	OR	95% CI	p	Rank
LVEF ≤45 (%)	0.84	0.19	4.18	1.10–7.36	0.003	1
Serum creatinine levels ≥60 (μmol/L)	0.91	0.21	3.03	1.21–5.57	0.018	2
Age ≥65 (years)	1.01	0.14	2.75	1.32–4.60	0.043	3
Log NT-proBNP levels ≥2.5 (pg/mL)	0.47	0.11	2.31	1.18–5.13	0.026	4
Uric acid levels ≥350 (μmol/L)	0.29	0.19	2.29	1.04–5.30	0.019	5
Emergency PCI	0.72	0.24	1.35	0.34–3.12	0.025	6
Triglyceride levels ≤1.30 (mmol/L)	0.63	0.22	1.10	0.01–2.27	0.041	7

60 lmol/L (OR 3.03, 95% CI 1.21–5.57), age 65 years (OR 2.75, 95% CI 1.32– 4.60), log NT-proBNP levels 2.5 pg/mL (OR 2.31, 95% CI 1.18–5.13), uric acid levels 350 lmol/L (OR 2.29, 95% CI 1.04–5.30), emergency PCI (OR 1.35, 95% CI 0.34–3.12), and triglyceride levels 1.30 mmol/L (OR 1.10, 95% CI 0.01–2.27) were independent risk factors for CIN in patients who underwent PCI (Table 4).

V. DISCUSSION

In the general population, the prevalence of CIN varies between 0.3% and 2.6%.16, 17 High-risk individuals with several risk factors have a much higher incidence of CIN, particularly those with diabetes who also have renal insufficiency (up to 50%).18, 19 According to a prior report20, 14.5% of 510 patients experienced CIN following PCI. According to our research, 15.33% of patients having PCI had CIN. This result implies that CIN is more common with PCI and that this condition requires greater care. Additionally, we identified the following independent risk factors for CIN in patients who had PCI: an LVEF of 45%, serum creatinine levels of 60 lmol/L, age 65 years, log NT-proBNP levels of 2.5 pg/mL, uric acid levels of 350 lmol/L, emergency PCI, and triglyceride levels of 1.30 mmol/L. Following PCI, patients with those variables are at risk for CIN, and early management is necessary to prevent CIN. After PCI, CIN is a dangerous side effect. Patients with ACS exhibit haemodynamic instability, neuroendocrine system activation, and a robust inflammatory response, according to studies 21–23. A contrast agent's viscosity, osmotic pressure, and ionic characteristics cause endothelin, adenosine, and angiotensin production after it has been applied.24 Increased prostacyclin and nitric oxide production causes the renal medulla to become hypoxic and

ischaemic, as well as the infiltrating blood vessels to constrict.25 In addition to directly harming the renal tubules, this increased secretion also leads the kidneys to produce more reactive oxygen species, which in turn increases oxidative stress and lipid peroxidation of the biofilm, ultimately resulting in CIN. The presence of CIN is indicative of a bad prognosis, both in the short and long term, even in cases when coronary revascularisation is successful.26 Dialysis patients with CIN may have a mortality risk of up to 40% within two years.27 Consequently, the prognosis of individuals with CIN depends on early identification and prevention.

Renal insufficiency, advanced age, heart failure, diabetes, and heavy contrast agent usage are currently recognised risk factors for CIN.28 The glomerular filtration rate is often used to assess renal function. However, a number of variables, including age, sex, body mass, and food, might affect the glomerular filtration rate. Elderly individuals have inadequate compensatory function of renal reserve as a result of the steady decline in the renal unit and glomerular filtration rate with increasing age.29, 30 As a result, PCI therapy frequently calls for a significant dose of contrast agent.31 Furthermore, according to certain research32–34, cardiac insufficiency can trigger the renin–angiotensin system, which alters endocrine variables by raising the vasoconstrictor endothelin and lowering the vasodilator prostaglandin. This causes renal vasoconstriction to become unbalanced, which ultimately culminates in CIN. The incidence of CIN was 13.1% in the development set and 13.9% in the validation set (stages of CIN), according to Mehran et al.35's study of 8357 individuals. Additionally, they discovered that CIN was independently predicted by hypotension, the location of the intra-aortic balloon pump, congestive heart failure, diabetes, chronic renal disease, age 75, anaemia, and the total volume of contrast. Additionally, there was a clear correlation between the development of CIN and an elevated risk score. Some of our findings are in line with the findings of Mehran et al.35, which shed more light on the risk factors for CIN following PCI.

One risk factor for CIN that is independent of other factors is elevated NT-proBNP levels. Ventricular myocytes release the cardiac and renal neurohumoral signal NT-proBNP, which is subsequently eliminated by the kidneys.36, 37 Patients with ACS have extremely hypoxic and ischaemic heart cells, as well as some necrotic heart cells, which causes ventricular myocytes to release NTproBNP.38 The release of NT-proBNP is stimulated by high levels of oxidative stress, inflammation, and an immunological response, which results in a considerable increase in its level.39 Because higher NT-proBNP levels suppress sympathetic neurones, dilate blood vessels, and cause diuresis, they cause renal vasodilation, reduce renal blood flow, and cause medullary ischaemia and hypoxia, all of which contribute to CIN.40, 41 Prior researchIn line with our findings, 42,43 have also demonstrated that NT-proBNP is a risk factor for CIN in patients with ACS. Patients who have emergency PCI may not have the necessary preoperative preparations, such as corrected renal function, which makes emergency PCI an independent risk factor for CIN. As a result, these patients could be more susceptible to CIN. Future research is necessary to confirm this possibility.

The current study has a number of limitations. Based on osmotic pressure, contrast compounds can be classified as hypotonic, isotonic, or hypertonic. The osmotic pressure of a hypertonic contrast is around five to seven times that of plasma, whereas the osmotic pressure of a hypotonic contrast agent is roughly two to three times lower.44 Hypertonic contrast agents are substantially more harmful to the kidneys than the other two kinds of contrast agents, according to earlier research45,46. The effects of isotonic

and hypotonic contrast agents on CIN still differ, though. One potential drawback is that the current investigation solely employed hypotonic contrast agents. But according to some research, isotonic contrast agents are superior to hypotonic ones.47 It is necessary to conduct more research on how osmotic pressure affects CIN. The fact that not every patient in this research got hydration treatment is another drawback. As a result, we were unable to incorporate this element into the data analysis. Applying hydration may have a direct impact on the occurrence of CIN as it is the most effective method of preventing it. Future research should thus include hydration analysis. Furthermore, we did not perform long-term follow-up for the patients' prognosis because to budget constraints. Lastly, those with significant renal impairment were not included. An independent risk factor for CIN is chronic renal disease, especially when it results from diabetes. Consideration should also be given to moderate renal insufficiency brought on by diabetes and other conditions such kidney and renal artery stenosis. Thus, future research should focus on PCI patients with severe renal insufficiency.

VI. CONCLUSIONS

Contrast-induced nephropathy (CIN) continues to be a significant complication in patients undergoing percutaneous coronary intervention (PCI), with considerable implications for patient morbidity, hospital stay, and long-term kidney function. This study highlights the importance of identifying high-risk patients and implementing effective preventive strategies to mitigate CIN incidence. Pre-existing renal dysfunction, diabetes mellitus, advanced age, and high contrast volumes have been consistently identified as key risk factors for CIN.

Despite advancements in contrast media technology, including the development of low- and iso-osmolar agents, CIN remains a challenge, particularly in patients with underlying renal conditions. Preventive measures, such as adequate hydration, careful contrast volume management, and the use of newer contrast agents, are essential in reducing the incidence of CIN. Additionally, early identification and monitoring of high-risk patients, along with individualized management strategies, can further enhance patient outcomes and minimize renal complications.

The findings from this study reinforce the need for continued research into more effective and targeted prevention strategies, as well as the exploration of novel therapies and biomarkers to predict and manage CIN risk more accurately. Ultimately, optimizing CIN prevention will contribute to better patient care, reduced healthcare costs, and improved long-term kidney health for patients undergoing PCI.

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