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Research article

Prevalence of contrast-induced nephropathy after primary percutaneous coronary intervention at a tertiary referral hospital

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ABSTRACT

Objective: This study aimed to quantify the incidence of Contrast-induced nephropathy (CIN) in patients undergoing primary percutaneous coronary intervention (PPCI) due to acute ST-elevation myocardial infarction (STEMI).

Methods: From April 2019 to March 2022, a prospective, observational study enrolled 213 consecutive STEMI patients referred to a tertiary hospital for PPCI. Participants were divided into tow groups based on the presence or absence of contrast-induced nephropathy. The chi-square test ($\chi 2$) and Student's t-test evaluated the data, with logistic regression identifying CIN's independent predictors.

Results: Results: In this study, the incidence of contrast-induced nephropathy was observed at 13.1% (N = 28). Several factors were more prevalent among patients exhibiting contrast-induced nephropathy. These factors encompassed: radial access for coronary angiography over the femoral method (P = 0.021), elevated contrast volume (P = 0.003), smoking (P = 0.009), diabetes (P = 0.04), heart failure (P = 0.049), a history of coronary artery bypass graft (P = 0.006), diminished left ventricular ejection fraction indicating systolic dysfunction (P = 0.012), cardiogenic shock (P = 0.046), increased BUN at the time of admission (P = 0.043), decreased initial GFR (P = 0.004), and prior consumption of medications such as aspirin (P = 0.002), diuretics (P = 0.046), beta blockers (P = 0.04), angiotensin-converting enzyme inhibitors (P = 0.033), angiotensin receptor blockers (P = 0.02). Other relevant conditions included anemia (P = 0.012), leukocytosis (P = 0.011), hypercholesterolemia (P = 0.034), and reduced HDL levels (P = 0.004). Through logistic regression, key predictors for the onset of contrast-induced nephropathy were determined, which included heart failure (OR: 5.52; 95% CI: 1.08–28.24), radial access (OR: 12.71; 95% CI: 1.45–110.9), hypercholesterolemia (OR: 1.02; 95% CI: 1.004–1.04), increased BUN upon admission (OR: 1.11; 95% CI: 1.006–1.24), and leukocytosis (OR: 2.03; 95% CI: 1.18–3.49).

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Conclusions: While heart failure, radial access, hypercholesterolemia, elevated BUN at admission, and leukocytosis significantly influenced renal filtration deterioration post-PPCI, it's evident that CIN is multifactorial. Further studies are crucial to elucidate the underlying factors.

1. Introduction

The broad diagnostic and therapeutic applications of intravenous contrast media (ICM) in radiological procedures have increased the risk of renal function impairment [1]. This iatrogenic renal function impairment called contrast-induced nephropathy (CIN), is a predictable consequence that will become a cornerstone for ongoing cardiovascular and nephrology research. CIN is the third leading cause of hospital-acquired renal insufficiency after impaired renal perfusion and nephrotoxic medications, leading to acute renal failure [2]. Researchers have reported that CIN incidence in primary percutaneous coronary interventions (PCI) procedures varies from 4% to 28%, depending on the intravenous contrast media and CIN criteria used. Coronary angiography and PCI have the highest incidence of CIN due to the intermittent intravenous contrast media administration [3].

CIN is a serious complication of primary PCI in acute ST-elevation myocardial infarction (STEMI), playing a major role in short-term and long-term cardiovascular and renal morbidity and mortality [4]. The CIN incidence rate in primary PCI in an emergency setting is higher than elective coronary angiography, possibly due to heart failure and hemodynamic instability [5]. Although CIN occurs through different mechanisms, some known pathways are vascular endothelial dysfunction, inflammation, vasoconstriction, altered distribution of renal blood flow, tubular cell toxicity, free-radical damage, reactive oxygen species (ROS), and oxidative stress, all of which contribute to CIN pathogenesis [6,7].

In previous studies, several factors have been identified as significant and independent predictors of CIN. Widely proposed risk factors for CIN include decreased baseline renal function, age, gender, patient dehydration, diabetes mellitus, hypertension, prior myocardial infarction, heart failure, decreased left ventricular ejection fraction $<40\%$, lower estimated glomerular filtration rate and the contrast medium volume. These are closely associated with CIN in PPCI, reported by several studies, though their influence requires further evaluation [8]. Clinicians should be aware of CIN incidence after PPCI and recognize its risk factors early for preventive measures. Beyond the previously mentioned risk factors, we conducted a more comprehensive study to evaluate more laboratory and cardiac indexes to add some valuable insight to CIN prediction. Therefore, this study aimed to determine independent predictors for CIN development in STEMI patients managed by PPCI, to determine the independent predictors for CIN development in patients with STEMI managed by PPCI.

2. Method

2.1. Study design and population

The present study was conducted as a prospective observational study enrolled 213 consecutive hospitalized adults diagnosed with STEMI who underwent primary emergency PCI between April 2019 and March 2022.

2.2. Exclusion criteria

Patients with these criteria are excluded from the study: cardiopulmonary resuscitation, active infection, collagen vascular disease, inflammatory disease, hematologic disorders, advanced liver disease, severe structural heart disease, long-term hemodialysis, end-stage renal disease (eGFR <15 mL/min/1.73 m^2), pregnancy or lactation, severe anaerobic condition, administration of intravascular CM within 2 weeks from PPCI, nephrotoxic medication use like angiotensin-converting enzyme inhibitors(ACEI), angiotensin receptor blockers(ARB), nonsteroidal anti-inflammatory drugs (NSAIDs) such as Naproxen, metformin, aminoglycosides, sodium bicarbonate, Cisplatin, corticosteroids, Cyclosporine, etc two weeks before PPCI and also lack accurate and sufficient data.

2.3. ST-elevation myocardial infarction diagnosis

STEMI diagnosis was based on having [1] typical chest pain lasting >30 min [2], ST-segment elevation >0.2 mV in contiguous electrocardiogram (ECG) chest leads, or >0.1 mV in at least two contiguous limb leads or new left bundle branch block, and [3] positive cardiac enzymes for myocardial infarction per current guidelines [9].

Patients matching the specified criteria were selected for data collection, with their anonymous data utilized for analysis. Clinical and laboratory attributes were obtained from medical records. Patients were followed for 10 days, and laboratory tests were conducted following the administration of contrast media during coronary angioplasty. Kidney function tests, specially sCr, are monitored to determination of CIN.

2.4. Primary PCI

The cardiologist with experience of 5 years used femoral or radial access for all PPCI procedures with a nonionic, iso-osmolar contrast medium (Iodixanol or Iohexol, Ireland). According to the American Heart Association(AHA) guidelines, all patients

received 300 mg chewable acetylsalicylic acid, P2Y12 receptor antagonist loading dose (180 mg ticagrelor or 300 mg clopidogrel), and intravenous unfractionated heparin before PPCI [10].

2.5. PCI prophylaxis

After PPCI, prophylaxis for the AKI was started for all patients according to the latest guidelines based on patients' GFR estimation and LVEF: protocol of intravenous isotonic saline at a rate of (1.0–1.5 ml/kg/h), started immediately after PPCI up to 24 h and in the condition of reduced left ventricular ejection fraction (LVEF) < 40%, isotonic(0.9%) saline prescribed in a reduced rate of 0.5 mL/kg/h, [11,12].

2.6. Contrast-induced nephropathy determination

After PPCI, patients were classified into CIN and non-CIN groups per CIN definition: absolute Scr increase ≥0.3 mg/dL from baseline within 48 h, relative Scr increase ≥50% from baseline within 3 days, or urine output decrease to 0.5 mL/kg/hr for 6 h after ICM [13,14].

Patients were clinically assessed with a detailed history including diabetes, hypertension, cardiac/vascular disease, prior CABG, lab tests, vascular access, contrast media type/volume, diseased vessels, clinical outcomes like hypotension during/pre-PCI with cardiogenic shock, monitored for 3 days after PPCI by trained staff.

2.7. Echocardiography

Echocardiography was carried out on the first day and again at discharge to determine the ejection fraction of the patients and evaluation the cardiac index's association with CIN.

2.8. Statistical analysis

Statistical data analysis was done using SPSS version 27 (Statistical Package for the Social Science, version 20, IBM, and Armonk, NY). The Kolmogorov–Smirnov test was used to assess the compatibility of our data with normal distribution. Numerical continuous variables were demonstrated as mean ± standard deviation, while nominal variables were expressed as frequency by number and percentage. A comparison of different data of the nominal variables was made by using the Chi-square test ($\chi 2$). Fischer's exact test was used whenever any of the expected cells were less than five. For the comparison of the mean of two different quantitative variables with normally distributed, the Student t-test was used.

In contrast, Mann-Whitney's test was used for not normally distributed ones. The confidence interval level was kept at 95%, and the P value of significance was set at $P < 0.05$. Logistic regression analysis was used to identify independent predictors of CIN.

2.9. Ethical considerations

The study was approved by the Ethics Committee of Qom University of Medical Sciences under the code of IR.MUQ.REC.1400.020. All participants provided written informed consent after being informed about the study's purpose. Ensuring participant anonymity and data confidentiality was paramount, with personal identifiers removed and data securely stored. Participants had the right to withdraw at any point without repercussions. Equal treatment was guaranteed for all participants regardless of their background. Throughout the research, ethical standards were continuously monitored to ensure their consistent application.

Table 1
Demographic factors comparison between two CIN and Non-CIN groups of patients.

Variable	subgroups	Acute Kidney Injury (No)	Non-Acute Kidney injury(No)	P. Value
Sex	male	22 (10.3%)	139 (65.3%)	0.816
	female	6 (2.8%)	46 (21.6%)	
Site of Angiography	Radial artery	19 (8.9%)	161 (75.6%)	0.021
	Femoral artery	9 (4.2%)	24 (11.3%)	
Numbers of narrowed coronary arteries	single vessel	8 (3.8%)	56 (26.3%)	0.895
	two vessels	13 (6.1%)	90 (42.3%)	
	three vessels	7 (3.3%)	39 (18.3%)	
Contrast Type	Iodixanol	8 (3.8%)	90 (42.3%)	0.06
	Iohexol	20 (9.4%)	95 (44.6%)	
Variable		**(Meas±S.D.)**	**(Meas±S.D.)**	
Age		64 ± 9	63 ± 8	0.625
BMI		26 ± 4	26 ± 3	0.752
Contrast.Volume		160 ± 35	139 ± 35	0.003
Admission days		7 ± 1	3 ± 1	

3. Results

In the study, over 300 patients who underwent PPCI were assessed. Of these, 213 patients who fulfilled the eligibility criteria were included. The average age of the patients was 63.4 years, with a standard deviation of 8.28, ranging from 39 to 80 years. Out of the total participants, 161 (75.6%) were male, while the remainder were female. No significant difference was observed between males and females in terms of CIN presence when compared to the non-CIN groups (P = 0.81), as detailed in Table 1.

Among the patients studied, 24.9% (n = 53) were smokers, 44.6% (n = 95) had diabetes mellitus, and 71.8% (n = 153) had hypertension, as highlighted in Table 2. The baseline serum creatinine (sCr) levels prior to contrast introduction showed no significant disparity between the CIN and Non-CIN groups (P = 0.79), estimated to be 1.17 ± 0.19 for the CIN group and 1.16 ± 0.21 for the Non-CIN group. After undergoing PPCI, the patients were segmented into two groups: the CIN group, which accounted for 28 (13.1%) cases, including 22 males and 6 females, and the non-CIN group, with 185 (86.9%) patients. Fig. 1 provides a detailed account of the daily variations in sCr levels post-primary coronary angioplasty in the CIN cases.

Among the patients who underwent PPCI, 28 were classified into the CIN group. Upon thorough evaluation, we identified several potential risk factors for CIN, including hypertension, diabetes mellitus, smoking, and anemia, all of which were significantly associated with CIN occurrence.

Also, some other certain risk factors were notably associated with CIN in our study. These include the use of radial access in angiography over the femoral approach (P = 0.021), the volume of contrast (P = 0.003), smoking habits (P = 0.009), diabetes mellitus (P = 0.04), and heart failure (P = 0.049). Patients with a history of CABG (P = 0.006), a reduced LVEF attributable to LV systolic dysfunction (P = 0.012), cardiogenic shock (P = 0.046), elevated BUN at admission (P = 0.043), and a high baseline GFR (P = 0.004) also demonstrated significant association with CIN. Moreover, consumption of specific drugs like ASA (P = 0.002), diuretics (P = 0.046), beta-blockers (P = 0.04), ACE inhibitors (P = 0.033), and ARB inhibitors (P = 0.02) which are mentioned in Table 3, as well as conditions such as anemia (P = 0.012), leukocytosis (P = 0.011), Hypercholesterolemia (P = 0.034), and low HDL levels (P = 0.004), were strongly correlated with CIN.

Variables such as gender (P = 0.81), age (P = 0.62), BMI(P = 0.75), site of culprit lesion in angiography (P = 0.89), hypertension (P = 0.65), Previous MI (P = 0.31), Previous PCI(P = 0.39), cardiac valves disease (P = 1), history of CVA(P = 0.09), peripheral vascular disease (P = 0.57), history of COPD and lung disease (P = 0.13), arrhythmia in electrocardiography (P = 0.09), statin consumption (P = 0.15), Blood sugar at admission (P = 0.051) didn't have a significant relationship with CIN in this research. The patients' clinical, imaging and laboratory data are summarized in Tables 4 and 5.

Through logistic regression analyses aimed at identifying predictors of CIN, the factors most closely linked to CIN development were Heart Failure (OR: 5.52; 95% CI: 1.08 to 28.24), Radial Access (OR: 12.71; 95% CI: 1.45 to 110.9), Hypercholesterolemia (OR: 1.02; 95% CI: 1.004 to 1.04), BUN at the time of admission (OR: 1.11; 95% CI: 1.006 to 1.24), and Leukocytosis (OR: 2.03; 95% CI: 1.18 to 3.49) as detailed in Table 6.

Patients who developed CIN were treated through hydration and adjustments to nephrotoxic drugs. Once their GFR improved and sCr levels returned to admission levels (indicating renal recovery), they were discharged. Thankfully, none of the patients required renal replacement therapy or hemodialysis.

Table 2
Risk factors comparison between two CIN and Non-CIN groups of patients.

Risk Factor	Presence	Contrast induced nephropathy	Non-Contract induced nephropathy	P-Value
Smoking	Yes	13 (6.1%)	40 (18.8%)	**0.009**
	No	15 (7.0%)	145 (68.1%)	
Diabetes	Yes	18 (8.5%)	77 (36.2%)	**0.04**
	No	10 (4.7%)	108 (50.7%)	
Hypertension	Yes	19 (8.9%)	134 (62.9%)	0.65
	No	9 (4.2%)	51 (23.9%)	
previous MI	Yes	6 (2.8%)	14 (6.6%)	0.31
	No	22 (10.3%)	171 (80.3%)	
Heart Failure	Yes	15 (7.0%)	134 (62.9%)	0.049
	No	13 (6.1%)	51 (23.9%)	
previous PCI	Yes	3 (1.4%)	10 (4.7%)	0.38
	No	25 (11.7%)	175 (82.2%)	
Cardiac valves disease	Yes	2 (0.9%)	12 (5.6%)	1
	No	26 (12.2%)	173 (81.2%)	
previous CABG	Yes	4 (1.9%)	3 (1.4%)	**0.006**
	No	24 (11.3%)	182 (85.4%)	
previous CVA	Yes	3 (1.4%)	6 (2.8%)	0.09
	No	25 (11.7%)	179 (84.0%)	
COPD	Yes	2 (0.9%)	3 (1.4%)	0.09
	No	26 (12.2%)	182(85.4%)	
Peripheral vascular disease (PVD)	Yes	1 (0.5%)	5 (2.3%)	0.57
	No	27 (12.7%)	180 (84.5%)	

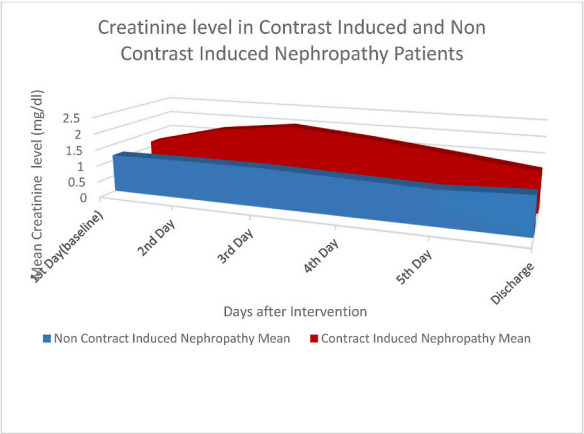

Fig. 1. Timeline of Serum Creatinine (mg/dL) in the hospitalization days.

Table 3
Medications comparison between two CIN and Non-CIN groups of patients.

Medications	Intake	Contract induced nephropathy	Non-Contract induced nephropathy	P-Value
acetylsalicylic acid	Yes	17 (8.0%)	54 (25.4%)	**0.002**
	No	11 (5.2%)	131 (61.5%)	
Clopidogrel	Yes	15 (7%)	14 (6.6%)	0.19
	No	13 (6.1%)	171 (80.3%)	
Diuretic	Yes	2 (0.9%)	1 (0.5%)	**0.046**
	No	26 (12.2%)	184 (86.4%)	
Beta-Blockers	Yes	8 (3.8%)	23 (10.8%)	**0.04**
	No	20 (9.4%)	162 (76.1%)	
calcium channel blockers	Yes	4 (1.9%)	52 (24.4%)	0.167
	No	24 (11.3%)	133 (62.4%)	
angiotensin converting enzyme inhibitor	Yes	15 (7%)	59 (27.7%)	**0.033**
	No	13 (6.1%)	126 (59.2%)	
angiotensin II receptor blockers	Yes	10 (4.7%)	30 (14.1%)	**0.02**
	No	18 8.5%)	155 (72.8%)	
Statin	Yes	8 (3.8%)	25 (11.7%)	0.051
	No	20 (9.4%)	160 (75.1%)	

Table 4
Laboratory Tests comparison between two CIN and Non-CIN groups of patients.

Laboratory Test	Contrast-induced nephropathy (Mean ± S.D.)	Non-Contract induced nephropathy (Mean ± S.D.)	P-value
Blood sugar at admission	172 ± 36	162 ± 42	0.15
BUN at admission	25 ± 10	21 ± 7	**0.043**
Serum Cr baseline	1.17 ± 0.19	1.16 ± 0.2	0.79
Serum Cr on discharge	1.2 ± 0.18	1.21 ± 0.2	**0.09**
White blood cells	8.5 ± 1.6	7.8 ± 1.4	**0.011**
RBC	4.6 ± 0.4	4.6 ± 0.4	0.681
Hemoglobin (g/L)	12.2 ± 2.2	13.4 ± 2.2	**0.012**
Platelet count	254.8 ± 42.6	247.6 ± 47.5	0.443
Total cholesterol	187 ± 42	169 ± 32	**0.034**
HDL-cholesterol	35 ± 7	39 ± 7	**0.004**
Triglycerides	153 ± 27	150 ± 22	0.938
LDL-cholesterol	98 ± 23	91 ± 18	0.143

4. Discussion

From the data of 213 patients, 28 were categorized into the CIN group. Upon detailed examination of previously proposed CIN predictors, we discovered that some held a significant association with CIN incidence in our analysis. However, some predictors did not demonstrate a noteworthy correlation, which will be discussed subsequently.

Table 5
Outcomes comparison between two CIN and Non-CIN groups of patients.

Outcomes	Subgroup	Contract induced nephropathy	Non-Contract induced nephropathy	P-Value
LVEF dysfunction	Normal	20 (9.4%)	168 (78.9%)	**0.012**
	mild	5 (2.3%)	10 (4.7%)	
	moderate	3 (1.4%)	7 (3.3%)	
	Severe (LVEF< 30%)	0 (0.0%)	0 (0.0%)	
arrhythmia	No arrhythmia	22 (10.3%)	167 (78.4%)	
	VT	4 (1.9%)	7 (3.3%)	0.092
	VF	0 (0.0%)	3 (1.4%)	
	AF.	2 (0.9%)	8 (3.8%)	
	others	0 (0.0%)	0 (0.0%)	
Cardiogenic shock	Yes	2 (0.9%)	1 (0.5%)	**0.046**
	No	26 (12.2%)	184 (86.4%)	
Death	Yes	2 (0.9%)	0 (0.0%)	**0.017**

Table 6
Independent predictors of post PPCI CIN in stepwise logistic regression.

CIN Predictors	P Value	Odds ratio	95% CI.	
			Lower	Upper
age	.776	1.014	.919	1.120
sex	.130	4.428	.644	30.455
BMI	.082	.836	.682	1.023
Diabetes Mellitus	.364	.476	.096	2.360
smoking	.163	.268	.042	1.704
Heart Failure	**.040**	**5.527**	**1.082**	**28.244**
Contrast Volume	.121	1.017	.996	1.039
Radial Vs. femoral access for angiography	**.021**	**12.712**	**1.456**	**110.996**
Cardiogenic Shock	.706	.099	.000	15983.612
CABG(Previous)	.394	.193	.004	8.503
ASA (Pre-procedure Consumption)	.582	.586	.087	3.928
ACEi (Pre-procedure Consumption)	**.016**	**.098**	**.015**	**.645**
ARBi (Pre-procedure Consumption)	**.004**	**.050**	**.006**	**.382**
Beta Blocker (Pre-procedure Consumption)	.859	.805	.073	8.861
Diuretics (Pre procedure Consumption)	**.040**	**.001**	**.000**	**.741**
Clopidogrel (Pre procedure Consumption)	.004	.054	.008	.384
Low HDL	**.002**	**.052**	**.008**	**.350**
Hypertriglyceridemia	.185	1.021	.990	1.054
Hypercholesterolemia	**.021**	**1.026**	**1.004**	**1.048**
BUN. at Admission	**.039**	**1.118**	**1.006**	**1.243**
Cr baseline	.423	7.459	.055	1016.396
Hyperglycemia at admission	.077	1.017	.998	1.036
Anemia	.373	.413	.059	2.890
Leukocytosis	**.010**	**2.038**	**1.189**	**3.493**
CKD	.115	.120	.009	1.675

5. Contrast-induced nephropathy prevalence

CIN is a frequent but often reversible complication of coronary angiography, which can aggravate a patient's situation and, in some cases, lead to mortality and morbidity in a hospital setting. The incidence of CIN varies in different studies depending on the CIN definition, type and volume of their contrast media. As a main finding of our research, CIN prevalence is 13.1%. In Johanne Silvain et al.'s (2018, France) study, contrast-induced AKI occurred in 18.3% [15]. Amar Narula et al., 2014 the incidence of contrast-induced AKI in a cohort study was 16.1% [16]. Also, the incidence rate of CIN in the Manari, Antonio study (2014, Italy) was 18.1% [17]. Abdellatif El-Ahmadi's study(2019 Denmark) CIN occurred in 765 (19.1%) [18]. The CIN rate in the present study was similar to previous studies.

6. CIN pre-procedural possible risk factors

1 Age, Sex, Body mass index, Smoking:

6.1. Sex

CIN was reported in 10.3 % (N = 22) males and 2.8% (N = 6) females, with no difference between genders (P = 0.81) and BMI (P =

0.75) in this study. Omer Toprak (2006,USA) a study reported female sex was an independent predictor of CIN (p = 0.0001), maybe due to Ovarian hormones' effect on the renin-angiotensin system and renal blood flow [19].

6.2. Age

Due to the presence of reno-vascular diseases and atherosclerotic lesions in renal arteries, older patients are more prone to CIN. Still, our study didn't show any difference in the age of CIN cases (P = 0.62). Abdellatif El-Ahmadi et al.(2019, Denmark) research reported that the age of more than 60 is an independent risk factor for AKI(20). In Manari, Antonio et al. study in 2014, age was significantly associated with an increased risk of CI-AKI [17]. In John P.Vavalle et al. study in 2016, the strongest predictor of AKI was the age of more than 60 years [20].In the Dileep Kumar et al. (2020, Pakistan) study, no association between CIN and gender or age was reported [21]. This finding is consistent with our research.

6.3. Smoking

Smoking affects CIN (P = 0.009) in this research significantly. Smoking by producing reactive oxygen species can damage renal tubules and make them sensitive to the contrast media in PPCI [22]. In a study conducted by Dileep Kumar et al. (2020, Pakistan), no association between CIN and smoking was reported [21].

2 Site of coronary angiography access, contrast volume, contrast media type, and the number of coronary artery diseases:

Radial artery access for angiography more than the femoral approach led to CIN (P = 0.021) in our study; maybe it's due to numerous radial cases, which is more than the femoral ones, but in contrast to the results of our research Giuseppe Andò et al. (2016, Italy) suggested that *trans*-radial intervention is associated with a lower incidence of CIN after PCI than femoral access [23].

In the iso-osmolar Contrast type (Iodixanole vs. Iohexole), we didn't find the difference in CIN occurrences (P = 0.06). Although CIN has been reported with low osmolar and iso-osmolar contrast media administration, Iodixanol (iso-osmolar) is considered a safe contrast media in the high-risk patient for CIN since its lower osmolarity and nonionic properties has the least damage to the kidney tubules [24].

The mean volume of contrast administered was significantly associated with the incidence of nephrotoxicity (P = 0.003). The contrast volume used in PPCI was higher among patients developing CIN (90 ± 31.2 ml) than patients who did not (71 ± 25.2 ml) in this analysis.

Previous studies have also demonstrated a dose-dependent risk of CIN similar to the results of our study; for example, Abdurrezzak Börekçi et al., in 2014 declared that contrast medium amounts were found to be an independent predictor for CIN(23). Yong Liu et al. (2015, China) stated that there is a significant association between a higher volume contrast media to Cr clearance ratio(CM/CrCl) and CIN risk (P < 0.001) [25].

Ahmadreza Assareh et al. (2016 Iran) reported a significant association between CIN and mean volume of contrast administration (P = 0.001) [26]. Charanjit S. Rihal et al. study demonstrated a significant association with the volume of contrast medium administered with baseline Cr < 2.0 reported [27]. In a study conducted by Sandeep Kumar et al. (2017, India), the total volume of contrast administered to the CIN group (175 ± 59.3) was not significant as compared to that of the non-CIN (159.1 ± 56) group (P = 0.334) [28]. Johanne Silvain et al. (2018, France) proved that contrast-media volume was not correlated to increased sCr level [15].

Variables such as the site of culprit lesion in angiography (P = 0.89) and the number of coronary artery diseases (SVD,2VD,3VD) (P = 0.89) hadn't a significant relationship with CIN in this study.

According to Toprak et al. study, it was found that multivessel coronary involvement increases the risk of CIN since other vessels in the body, such as the renal artery, can be involved at the same time, and as renal blood supply decreases, the kidneys become more susceptible to CIN [29].

3 History of Cardiac disease:

Heart failure (P = 0.049), history of CABG(P = 0.006), reduced LVEF (LV systolic dysfunction) (P = 0.012), and cardiogenic shock (P = 0.046) had a significant association with CIN in our study. Previous MI (P = 0.31), previous PCI (P = 0.39), and cardiac valvular disease (P = 1.00) didn't show a significant role in CIN. Manari, Antonio's study in 2014 from Italy showed that cardiogenic shock and ejection fractions 35% or less were significantly associated with an increased risk of CI-AKI [17]. Charanjit S. Rihal et al. study in 2002 revealed that acute renal failure had a significant association with previous acute myocardial infarction and shock patients [27].

Gaetano La Manna et al. (2010, Italy) experiment showed that the risk of CIN increased in patients with comorbidities like diabetes mellitus, a previous myocardial infarction, and ventricular dysfunction [30].

Johannes Schmucker et al. (2018 Germany) revealed an 18% incidence of CIN in STEMI patients, and higher AKI stages were associated with lower mean systolic blood pressure at admission and left-heart-failure/cardiogenic shock as well as larger infarctions (peak creatine kinase >3000 U/L were independently associated with a greater risk for CIN [31].

7. Arrhythmia

In our study, no significant associations between CIN and arrhythmia in electrocardiography were obtained (P = 0.09) however, in

the Narut Prasitlumkum 2018 [32] and Tufan Çinar 2018 [33] study, baseline AF in ECG increased risk of CIN after cardiac catheterization.

4 Past Medical History

7.1. Hypertension

Hypertension in our analysis didn't show any relationship with CIN (P = 0.65), but in Sandeep Kumar et al. study in 2017 India, hypertension was the only observed risk factor, and CIN was observed to be more common in patients with hypertension than in those without hypertension (P = 0.0158) [28].

7.2. Diabetes mellitus

The role of diabetes in increasing comorbidities and organ damage is clear to physicians. In our analysis, diabetes had a prominent role (P = 0.04) in CIN prevalence, which met the previous results of articles on this issue. In Abdurrezzak Börekçi et al. analysis in 2014, diabetes was reported as an independent predictor for CIN(23). YU-HAN QIN (2017, China) showed that hyperglycemia on admission and elevated HbA1c were associated with CIN, and hyperglycemia was an independent predictor of CIN [34]. Ahmadreza Assareh et al. (2016, Iran) reported a significant association between CIN and diabetes (P = 0.001) [26]. In the study of Charanjit S. Rihal et al., on 7586 patients, 254 (3.3%) experienced CIN, and the risk of CIN was higher among diabetic patients [27]. In the study of Dileep Kumar et al. (2020, Pakistan), CIN was found to be statistically significantly associated with diabetes mellitus [21].

7.3. Chronic kidney disease

The results of this study showed that known chronic kidney disease (CKD) patients with high BUN at admission time (P = 0.04), lower GFR(P = 0.004), and a history of renal impairment had a significant relationship with CIN occurrence. It seems that in these patients, because of reduced adaptive capacity for intravenous contrast media, the prevalence of CIN is higher than in normal kidneys. Still, it doesn't always mean CIN in cases with pre-existing renal insufficiency would happen.

Charanjit S. Rihal et al. study demonstrated the CIN association with baseline serum Cr reported [27]. John P.Vavalle et al. study stated that the rate of CIN had a substantial relationship with patients' baseline eGFR ($P < 0.0001$) [20]. In Manari, Antonio et al. study (2014, Italy) high basal sCr and CKD was significantly associated with an increased risk of CI-AKI [17].

In the study of YosukeNegishi (2019, Japan), CIN was observed in 31 patients (9.7%) with advanced renal dysfunction, so CIN was not high in Japanese patients with advanced renal dysfunction [35].

8. Cerebrovascular accident, cerebrovascular accident and chronic obstructive pulmonary disease

History of CVA (P = 0.09), Peripheral vascular disease (P = 0.57), and history of COPD and lung disease (P = 0.13) had no

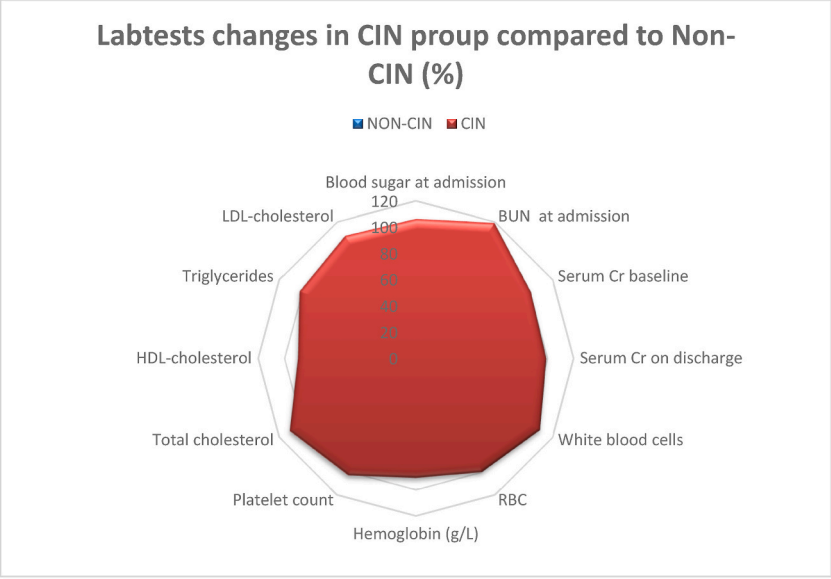

Fig. 2. Labtests changes in CIN proup compared to Non-CIN (%).

significant association with CIN in our research. Rihal et al. and Bartholomew et al. studies reported peripheral vascular disease as a CIN risk factor in coronary angiographies(P = 0.0001) [29] while it did not work in our study.

5 Drug History

History of previous drug consumptions such as ASA(P = 0.002), Diuretic(P = 0.046), Beta blocker (P = 0.04), ACEi (P = 0.033), ARBi (P = 0.02) had a significant role in CIN occurrence. Statin consumption (P = 0.15) didn't he any role, while in some studies, Statins had a protective role against CIN. Of course, Gaetano La Manna's research (2010, Italy) did not confirm furosemide therapy is associated with a moderately increased risk of nephropathy [30].

6 Laboratory Data

BUN at admission time (P = 0.043), baseline GFR (P = 0.004), Anemia (P = 0.012), leukocytosis (P = 0.011), Hypercholesterolemia (P = 0.034) and low HDL (P = 0.004) found to have a significant association with CIN. As the BUN level increases in blood samples, the rate of CIN will level up, so can be indicated to the role of hydration in emergency status as a preventive measure of CIN. Alongside our study, Gaetano La Manna et al. (2010, Italy) also observed that the risk of CIN increases in an anemic state [30].

Blood sugar at admission (P = 0.051) didn't have a significant relationship with CIN in this research. YU-HAN QIN 2017 China proposed that pre-operative blood cholesterol, hyperglycemia on admission, and elevated HbA1c account for considerable risk for CIN, and hyperglycemia is an independent predictor of CIN [34]. Fig. 2 demonstrates the comparision of laboratory tests findings among two groups.

It is not easy to predict which patients are prone to developing CIN after PPCI, so in this survey, we evaluate different possible predictors that may help point those at higher risk for CIN. High-risk patients should be identified and targeted for preventive strategies like hydration, close sCr and renal function monitoring during hospitalization and prompt intervention. We should consider this issue that not only patients with previously damaged kidney filtration power are prone to CIN, but a variety of factors, besides CKD, like heart failure, radial access, leukocytosis, Hypercholesterolemia and high BUN at admission, proposed to be the predictors of CIN which should be considered in emergencies especially PPCI for early implementation of preventive strategy like hydration to reduce the acute decline in renal function rate in PPCI.

9. Strategies to prevent contrast-induced nephropathy in patients undergoing cardiac interventions

Contrast-induced nephropathy (CIN) poses a significant concern for patients undergoing percutaneous coronary intervention (PCI). Its prevention is crucial due to its association with prolonged hospital stays, increased costs, and adverse prognoses. Such complications arise not only in PCI but also in other cardiac interventions [36]. To mitigate CIN risks, strategies like patient preparation, use of iso-osmolar or low-osmolar contrast agents, and minimizing contrast media volume have been recommended. Proper risk assessment is foundational. An initial step of risk assessment is crucial.

In a study by Bartholomew et al., a Radiocontrast-induced nephropathy (RCIN) score was established using various criteria. The incidence of RCIN post-PCI increased with each additional point. The occurrence of RCIN was particularly prominent in patients with higher scores [37]. The Contrast Media Safety Committee, emphasizing the choice of contrast medium and preventive measures, noted a lower CIN risk with intravenous as opposed to intra-arterial iodinated mediums [38]. A retrospective study from 2017 to 2020 involving 378 ACS patients indicated a 12.7% AKI development rate attributed to various prognostic factors [39].

It's advised to use the least amount of contrast necessary for procedures. For instance, Bartholomew BA highlighted the volume of contrast media as a primary risk factor [37]. Also, In a study by H Costa et al., they tried to calculate a safe contrast volume that can be used without injury to the patients. They concluded that, Notably, a VolC/CrCl ratio of less than 3.7 was effective in preventing AKI within 24 h but not after; however, a ratio below 2.0 was efficient in mitigating both early and late AKI [39]. Conclusively, for ACS PCI patients, AKI onset, especially after 24 h, significantly elevates mortality rates. The findings suggest a preferable VolC/CrCl ratio of under 2.0, which offers a reliable measure of VolC, assisting in averting both early and late AKI in specific ACS [39]. In another study by Mun J-H et al., they identified the CV/eGFR ratio as more predictive of AKI than the absolute amount of contrast used, suggesting its utility using the safe amount of contrast for cardiovascular procedures. A CV/eGFR ratio of 3.84 emerged as the most suitable cutoff, offering both high sensitivity and specificity [40].

Hydration is one of the most important considerable points which should be taken seriously to prevent CIN. Pre- and post-procedure hydration, typically with isotonic saline, is a key preventive strategy [41]. In a study of 450 ST-elevation–myocardial infarction (STEMI) patients undergoing primary percutaneous coronary intervention (PCI), the efficacy of intravascular volume expansion in preventing contrast-induced acute kidney injury (CI-AKI) was examined. Patients were divided into three groups: early hydration (pre- and post-procedure with sodium bicarbonate), late hydration (post-procedure with isotonic saline), and a control (no hydration). CI-AKI occurred in 20.6% of patients. The early hydration group had the lowest incidence at 12%, compared to 22.7% in the late hydration group and 27.3% in the control group. The results suggest that pre- and post-procedure hydration using sodium bicarbonate is more effective than post-procedure hydration with isotonic saline alone in preventing CI-AKI in STEMI patients [42].

The hydration agent that is used is also important. In a study by Gregory J et al. on Contrast-induced nephropathy, they evaluated the randomized trial to compare the preventive hydration effects of sodium bicarbonate to sodium chloride before and after administering radiographic contrast. The results showed that only 1.7% of those hydrated with sodium bicarbonate developed contrast-induced nephropathy, as opposed to 13.6% in the sodium chloride group. Thus, hydration with sodium bicarbonate was found

to be more effective than sodium chloride in preventing contrast-induced renal failure [43].

The specific causes behind contrast-induced nephropathy (CIN) remain uncertain, but the osmotic properties of contrast media (CM) are in the interested areas of investigation. CM's osmotic effects on the kidneys can cause temporary reductions in blood flow and filtration. A notable side effect is an osmotically driven increase in urine production which can lead to dehydration. While clinical studies comparing CIN occurrences between different CM classes based on osmolality suggested minimal benefits from lower osmolality, recent animal tests indicate that a mild osmotic urine production, triggered by iso-osmolar agents, might counteract the harmful kidney effects of high viscosity-caused CM buildup within the tubules [44]. So, using iso-osmolar or low-osmolar contrast agents instead of high-osmolar contrast agents can reduce the risk of CIN.

In the near future, we expect the appearance of more helmless contrast agents, which will substitute the conventional agents. For example, in a pilot study focused on acute ischemic syndromes treatment requiring iodinated X-ray contrast agents, Rowe ES et al. used Sulfobutylether beta cyclodextrin combined with iohexol (SBECD-iohexol) for its renal safety and cardioprotective properties. Current clinical trials are assessing its safety in cardiovascular procedures, particularly since preclinical studies indicated that it minimized contrast-induced kidney injury in rodents [45]. Of course, further studies need to use these diagnostic agents extensively.

10. Conclusion

The current study underscores the significance of understanding CIN predictors in emergent coronary angioplasty, given the observed increase in hospital-day admissions, associated comorbidities, and AKI-related mortality. Our findings highlight that heart failure, radial access, leukocytosis, hypercholesterolemia, and elevated BUN at admission are primary risk factors for the CIN phenomenon. However, it's evident that other factors, beyond those mentioned, play a role. Physicians should be acutely aware of these concerns, and additional large-scale studies are crucial to identify new risk factors.

Data availibility

Data is sourced from the Healthcare Information System (HIS) of Shahid Beheshti Hospital in Qom, Iran. While it is not stored in a centralized repository, it is accessible in an anonymized format upon request for anyone interested.

Complementary

Abbreviations in the tables of study; BMI(Body mass index), DM (Diabetes mellitus), HTN(Hypertension), MI(Myocardial infarction), PCI(Percutaneous coronary intervention), CABG(Coronary artery bypass graft), CVA (Cerebrovascular accident), CKD(Chronic kidney disease), PVD (peripheral vascular disease), COPD(Chronic obstructive pulmonary disease), LVEF(Left ventricle ejection fraction), BUN (Blood urea nitrogen), GFR(Glomerular infiltration rate), HDL(High-density lipid), LDL(Low-density lipid), SVD(single vessel disease).

CRediT authorship contribution statement

Zahra Masoomi: Data curation, Software, Validation. **Ali Mohammad Nasirian:** Writing – review & editing. **Mansoor Namazi:** Data curation, Writing – original draft. **Mohammad Shahidi:** Writing – review & editing. **Moein Zangiabadian:** Writing – review & editing. **Abdoreza Dayani:** Validation. **Mohammad Shahidi:** Writing – review & editing. **Hossain Saghafi:** Visualization. **Amir Ghaffari Jolfayi:** Conceptualization, Formal analysis, Methodology, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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