Contrast-induced nephropathy in patients undergoing primary angioplasty for acute myocardial infarction: incidence, a simple risk score, and prognosis

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Abstract

Introduction: Patients undergoing primary angioplasty for ST-segment elevation myocardial infarction (STEMI) may be at increased risk of contrast-induced nephropathy (CIN) because of inadequate prophylaxis. We investigated the incidence, predictive factors, and outcomes of CIN after primary percutaneous coronary intervention (PCI).

Material and methods: 2521 consecutive STEMI patients (mean age 56.5 ±11.8, years, 2091 male, baseline creatinine 0.97 ±0.3 mg/dl) undergoing primary PCI were retrospectively enrolled in the present study.

Results: Contrast-induced nephropathy was defined as an increase in serum creatinine level ≥ 0.5 mg/dl or ≥ 25% from baseline within 72 h of radiocontrast administration. 630 patients (25%) developed CIN. Patients with baseline creatinine > 1.5 mg/dl developed CIN more often than those with creatinine ≤ 1.5 mg/dl (45.9 vs. 24%, $p < 0.001$). The following factors were predictors of CIN: diabetes mellitus (odds ratio [OR] 1.34, 95% confidence interval [CI] 1.03-1.75; $p = 0.03$), time to reperfusion ≥ 6 h (OR 1.46, 95% CI 1.07-2.00, $p = 0.02$), use of intra-aortic balloon pump (OR 2.46, 95% CI 1.30-4.67, $p = 0.006$), radiocontrast medium volume > 250 ml (OR 1.34, 95% CI 1.01-1.78, $p = 0.04$), age ≥ 75 years (OR 2.07, 95% CI 1.36-3.12, $p = 0.001$), anterior infarction (OR 1.26, 95% CI 0.99-1.60, $p = 0.05$). Higher in-hospital mortality rate was observed in patients developing CIN (9.5 and 1.2%, $p < 0.001$). Cox regression analysis showed that CIN was a predictor of long-term cardiovascular mortality (hazard ratio [HR] 1.90, 95% CI 1.16-3.12, $p = 0.01$) and major cardiovascular events (HR 1.34, 95% CI 1.04-1.72, $p = 0.025$).

Conclusions: Contrast-induced nephropathy in patients with STEMI undergoing primary PCI is associated with a markedly increased risk of major cardiovascular events as well as in-hospital and long-term mortality.

Key words: primary angioplasty, acute myocardial infarction, contrast-induced nephropathy.

Introduction

Radiographic contrast media are used on a daily basis by invasive cardiologists. Contrast-induced nephropathy (CIN) is a possible complication of coronary diagnostic and interventional procedures. A commonly used

definition of CIN is an absolute increase in serum creatinine (SCr) ≥ 0.5 mg/dl or a relative increase ≥ 25% from baseline within 72 h of intravenous contrast administration [1-5]. Contrast-induced nephropathy is the third leading cause of hospital-acquired renal failure and is associated with significant morbidity and mortality [1]. Several risk factors for CIN have been identified. Chronic renal failure, diabetes mellitus (DM), age, volume of contrast medium, and heart failure are considered important risk factors [6-9].

Primary percutaneous coronary intervention (PCI) achieves rapid restoration of coronary artery patency and preserves ventricular function in patients presenting with an ST-elevation myocardial infarction (STEMI). On the other hand, patients treated via primary PCI may be at increased risk of CIN because of haemodynamic alterations such as hypotension or shock, the use of large volumes of contrast medium, and inadequate prophylaxis for CIN [10, 11].

However, there are few studies assessing kidney function in the setting of primary PCI, and examining the clinical association of CIN with outcomes. The aim of the present study was to evaluate the incidence, clinical predictors, and outcome of CIN after primary PCI for STEMI in a large population.

Material and methods

Patient population

We retrospectively evaluated 2825 consecutive patients with STEMI who were admitted to the emergency department of our hospital and underwent urgent cardiac catheterization procedures between October 2003 and March 2008. Patients were enrolled in the study if they fulfilled the following criteria: (1) presenting within 12 h (18 h for cardiogenic shock) from the onset of symptoms (typical chest pain lasting for > 30 min); (2) ST-segment elevation ≥ 2 mm in at least two contiguous electrocardiogram (ECG) leads or new onset of complete left bundle-branch block; (3) treatment with primary PCI (angioplasty and/or stent deployment). 304 patients were excluded because of chronic dialysis (n = 8), no indication for PCI (n = 96), treated with coronary bypass surgery (i.e. not suitable for PCI) (n = 85), death in the first 24 h (n = 63), missing or unavailable kidney function (n = 52). Therefore, the final study population consisted of 2521 patients. The study protocol was approved by the hospital's Ethics Committee.

Data sources

Demographic information and the clinical history of risk factors such as age, gender, DM, hypertension, hypercholesterolaemia, smoking, family history for coronary artery disease, MI history, PCI or bypass history were determined from medical records. Angina-to-reperfusion time, and door-to-balloon time were calculated.

Blood values (including SCr) were determined at hospital admission (prior catheterization procedures) and on a daily basis during the hospital stay. A 12-lead ECG was recorded in each patient just after hospital admission.

Admission glomerular filtration rate (GFR) was estimated by the simplified MDRD (Modification of Diet in Renal Disease) equation [12, 13].

Transthoracic echocardiography was performed by using System V (Vingmed, GE) with a 2.5 MHz phased-array transducer. Recordings were taken on patients positioned in the left lateral decubitus position. The left ventricular ejection fraction (EF) was measured using modified Simpson's rule [14].

Coronary angiography, primary angioplasty and stenting

All patients received chewable aspirin (300 mg, unless contraindicated), and clopidogrel (300 mg loading dose) before coronary angiography. Angiographic data of the patients were obtained from the cardiac catheterization laboratory records. Emergency coronary angiography was performed by the percutaneous femoral approach.

In all cases, non-ionic low-osmolality contrast media were used. These were iopromide 74.7% (Ultravist, Schering AG, Germany), iopamidol 23% (Iopamiro, Bracco S.p.A. and Patheon Italia S.p.A., Italy), iobitridol 1.6% (Xenetix, Guerbet, France), and iohexol 0.7% (Omnipaque, Amersham Health, Ireland).

First the non-infarcted artery and then the infarct-related artery (IRA) was injected. IRA was graded according to the Thrombolysis In Myocardial Infarction (TIMI) classification (TIMI 0, 1, 2, 3) [15]. Heparin (10,000 U) was administered after coronary anatomy was defined. Coronary artery stenosis > 50% was considered clinically significant. Occlusion of the IRA was crossed by using a 0.014-inch guide wire. Primary coronary interventions including balloon angioplasty and/or stent implantation were performed only for IRA according to lesion anatomy. For each procedure, interventional success at the acute phase was defined as an obstruction and stenosis of the IRA having been reduced to < 50% stenosis with TIMI 2 or 3 flow after primary PCI. After angioplasty, all patients were admitted to the coronary care unit, where 500 U/h of intravenous heparin or 1 mg/kg/day of subcutaneous low molecular weight heparin was given; 100 mg aspirin and 75 mg clopidogrel were continued in all patients. The use of tirofiban, type of contrast medium, contrast dose, hydration schedule (type of fluid therapy and dose), and the need for renal

replacement therapy were left to the discretion of the operator.

Definitions

Contrast-induced nephropathy was defined as an increase in serum creatinine level ≥ 0.5 mg/dl or ≥ 25% from baseline (admission) within 72 h of radiocontrast administration [5]. Anaemia was defined as a baseline haemoglobin concentration < 13 mg/dl in men and < 12 mg/dl in women. Cardiogenic shock was defined as marked and persistent (> 30 min) hypotension with systolic pressure less than 80 mmHg with signs of hypoperfusion due to left ventricular dysfunction, right ventricular infarction, and mechanical complications. Patients were also evaluated according to Killip clinical examination classification [16]. Advanced heart failure was defined as New York Heart Association (NYHA) classification ≥ 3. Multivessel disease was defined by a stenosis of > 50% in three major epicardial coronary arteries. Hypertension (HT) was defined as a history of HT and/or use of antihypertensive drugs [17], and DM was defined as a history of DM and/or use of anti-diabetic drugs before the hospital admission [18]. Admission hyperglycaemia was defined as admission plasma glucose ≥ 200 mg/dl regardless of diabetic status. Hypercholesterolaemia was defined as total cholesterol ≥ 200 mg/dl. Positive family history for coronary artery disease (CAD) was defined as documented evidence of CAD in a parent or sibling before 60 years of age. Acute stent thrombosis is defined as an abrupt onset of cardiac symptoms (i.e., an acute coronary syndrome) along with an elevation in levels of biomarkers or electrocardiographic evidence of myocardial injury after stent deployment in the first 24 h which is accompanied by angiographic evidence of a flow-limiting thrombus near a previously placed stent.

Cardiovascular mortality was defined as unexplained sudden death or death due to acute MI, heart failure or arrhythmia. Reinfarction was described as elevation of serum CK-MB enzyme levels by twice the upper limit of normal and ST-segment re-elevations.

Follow-up

Follow-up data were obtained from hospital records or by interviewing (directly or by telephone) patients, their families, or their personal physicians. Major adverse cardiac events (MACE) were defined as cardiovascular mortality, reinfarction, and repeat target-vessel revascularization (TVR) (percutaneous or surgical). Only cardiovascular mortality was recorded. Serious ventricular arrhythmias (ventricular tachycardia and/or fibrillation), stroke, cardiopulmonary resuscitation, advanced heart failure, atrioventricular block, transient pace intervention, intra-aortic balloon pump, atrial fibrillation, major bleeding requiring ≥ 2U of blood, dialysis, acute stent thrombosis, and MACE were also recorded during the in-hospital period.

Statistical analysis

Quantitative variables were expressed as mean value ± SD, and qualitative variables were expressed as percentages (%). Comparison of parametric values between two groups was performed by means of two-tailed Student's *t* test. Categorical variables were compared by the likelihood-ratio χ^2 test or Fisher's exact test. Variables were selected by use of backward stepwise logistic regression analysis, entering all those with a significant or borderline ($p < 0.1$) association with CIN. Backward stepwise multivariate Cox regression analysis which included variables with $p < 0.1$ was performed to identify independent predictors of cardiovascular mortality and MACE. Gender, age ≥ 75, time-to-reperfusion > 6 h, DM, hypertension, hypercholesterolaemia, smoking habit, MI history, multivessel disease, unsuccessful procedure, anterior MI, cardiogenic shock, CIN, admission glucose and anaemia were entered into the model. The cumulative survival curves for cardiovascular mortality and MACE were constructed using the Kaplan-Meier method with differences assessed with the log-rank test. A p value < 0.05 was considered statistically significant. All statistical studies were carried out with the program SPSS (version 15.0, SPSS, Chicago, Illinois, USA).

Results

Patient characteristics

The baseline characteristics in the two groups are summarized in Table I. Among the 2521 study patients (mean age 56.5 ±11.8 years, 2091 male), baseline SCr was 0.97 ±0.3 mg/dl. 630 patients (25%) developed CIN. Patients developing CIN were slightly to be female, significantly older, and more commonly had hypertension, DM, anterior MI, cardiogenic shock, more advanced Killip class, and longer reperfusion time (Table I).

Laboratory findings

Table II lists the laboratory data of the patients. CIN was more frequent in patients with admission GFR < 60 ml/min/1.73 m^2 (15.2 vs. 10.6%, $p = 0.002$) and baseline creatinine level > 1.5 mg/dl (6.2 vs. 2.4%, $p < 0.001$). Patients with baseline creatinine > 1.5 mg/dl developed CIN more often than those with creatinine ≤ 1.5 mg/dl (45.9 vs. 24%, $p < 0.001$). Higher enzymatic peak (correlated with anterior MI), and higher admission glucose were observed in patients with CIN (Table II).

Angiographic and procedural characteristics

Angiographic and procedural characteristics are depicted in Table III. Mean left ventricular ejection

fraction (LVEF) was less in patients with CIN. Left anterior descending (LAD) coronary artery as a culprit lesion and proximal location of the lesion were more common in patients developing CIN. In patients with CIN, pre-procedural and post-procedural epicardial flow and procedural success were worse than in patients without CIN. Smaller and longer stents were used in patients with CIN. In addition, they received a higher volume of contrast medium during PCI than patients without CIN (Table III).

Table I. Baseline characteristics of study patients

	CIN (n = 630)	No CIN (n = 1891)	p Value
Age [years]	58.8 (12.7)	55.7 (11.4)	< 0.001
Age ≥ 75 years	80 (12.7)	121 (6.4)	< 0.001
Male	507 (80.5)	1584 (83.8)	0.06
Anterior MI	348 (55.2)	882 (46.6)	< 0.001
Hypertension	271 (43)	721 (38.1)	0.02
Hypercholesterolaemia	209 (33.2)	661 (35)	0.44
DM	185 (29.4)	435 (23)	0.001
Current smoker	354 (56.2)	1105 (58.4)	0.7
Family history for CAD	110 (17.5)	299 (15.8)	0.21
Bypass	13 (2.1)	59 (3.1)	0.17
PCI	61 (9.7)	141 (7.5)	0.08
MI history	67 (10.6)	199 (10.5)	0.93
Admission cardiogenic shock	30 (4.8)	31 (1.6)	< 0.001
Killip > 1	73 (11.6)	81 (4.3)	< 0.001
Reperfusion time [hour]	3.8 (2.7)	3.1 (2.2)	< 0.001
Door-to-balloon time [min]	33 (21)	29 (25)	0.47
Admission systolic pressure [mmHg]	124.7 (31.5)	126.3 (32.4)	0.34

Mean values (SD) and % (n) are reported for continuous and categorical variables, respectively, CIN – contrast-induced nephropathy, MI – myocardial infarction, CAD – coronary artery disease, DM – diabetes mellitus, PCI – percutaneous coronary intervention

In-hospital outcomes

Table IV presents the in-hospital adverse outcomes after primary PCI. In-hospital mortality rate was higher in patients with CIN than without CIN (9.5 vs. 1.2%, $p < 0.001$). MACE were more frequent (14.9 vs. 4.7%, $p < 0.001$) and the length of hospital stay longer (8 vs. 7.1 days, $p < 0.001$) in patients with CIN than without CIN. Dialysis was required in 0.6%. There was a more complicated in-hospital outcome in patients with CIN, with a higher incidence of stroke, advanced heart failure, atrial fibrillation, acute stent thrombosis, more episodes of serious ventricular arrhythmia and a higher percentage of cardiopulmonary resuscitation, intra-aortic balloon pump, dialysis, transient pacemaker, and blood transfusion (Table IV).

Predictive factors for CIN and risk scoring

We performed a multivariate analysis to determine the factors that were associated with CIN. The following were considered independent variables: DM (OR 1.34, 95% CI 1.03-1.75, $p = 0.03$), time to reperfusion ≥ 6 h (OR 1.46, 95% CI 1.07-2.00, $p = 0.02$), use of intra-aortic balloon (OR 2.46, 95% CI 1.30-4.67, $p = 0.006$), radiocontrast medium volume > 250 ml (OR 1.34, 95% CI 1.01-1.78, $p = 0.04$), age ≥ 75 years (OR 2.07, 95% CI 1.36-3.12, $p = 0.001$), and anterior infarction (OR 1.26,

Table II. Laboratory findings of patients

	CIN (n = 630)	No CIN (n = 1891)	p Value
Creatinine concentration at admission [mg/dl]	0.95 (0.4)	0.98 (0.2)	0.23
Admission GFR (MDRD) < 60 ml/min/1.73 m^2	96 (15.2)	200 (10.6)	0.002
Creatinine concentration at admission > 1.5 mg/dl	39 (6.2)	46 (2.4)	< 0.001
Peak CK-MB [U/l]	247.7 (206.5)	209.9 (170)	< 0.001
Total cholesterol [mg/dl]	186.9 (42.4)	189.4 (42.5)	0.28
LDL cholesterol [mg/dl]	117.4 (34.7)	117.9 (35.6)	0.8
HDL cholesterol [mg/dl]	41.4 (10.1)	40.7 (8.8)	0.17
Triglycerides [mg/dl]	147.9 (107)	152.1 (108.3)	0.47
Admission blood glucose concentration [mg/dl]	168.2 (88.3)	151.5 (67.9)	< 0.001
Anaemia at admission	159 (25.2)	455 (24.1)	0.57
Admission hyperglycaemia	134 (21.3)	280 (14.8)	< 0.001

Mean values (SD) and % (n) are reported for continuous and categorical variables, respectively, GFR – glomerular filtration rate, MDRD – modification of diet in renal disease, CIN – contrast-induced nephropathy

95% CI 0.99-1.60, $p = 0.05$). We used a risk scoring system taking into account the value of the odds ratio. A value of 2 points for each was assigned to intra-aortic balloon usage and older age (≥ 75 years), and 1 point to the other variables. For each patient, the score was calculated as the sum of these values. The incidence of CIN and in-hospital mortality significantly increased with score (Figures 1 and 2). Of note, contrast and stent type showed no sign of association with CIN in univariate analysis.

Long-term prognosis

The median follow-up time was 21 months. Follow-up data after discharge were not obtained for 42 patients without CIN (2.2%) and 4 (0.6%) patients with CIN. Table V presents the long-term adverse outcomes. The Kaplan-Meier survival plot for cardiovascular death is presented in Figure 3. Cardiovascular mortality, MACE, reinfarction, and advanced heart failure were significantly higher in patients developing CIN. Patients with CIN had a statistical tendency of significantly higher incidence of TVR. Long-term cardiovascular mortality was 30.4% in patients with CIN risk score

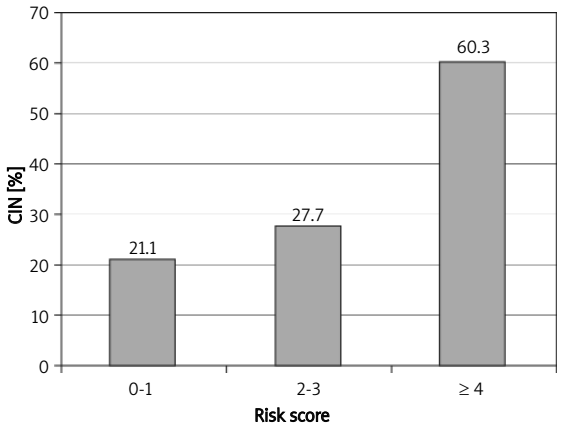

Figure 1. Incidence of contrast-induced nephropathy (CIN) according to the risk score ($p < 0.001$)

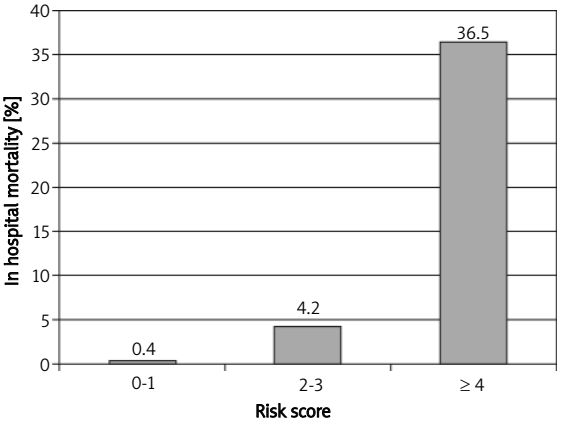

Figure 2. Incidence of in-hospital mortality according to the risk score ($p < 0.001$)

Table III. Angiographic and procedural characteristics of patients

	CIN ($n = 630$)	No CIN ($n = 1891$)	p Value
Culprit lesion:			
LMCA	0 (0)	2 (0.1)	0.76
LAD	347 (55.1)	890 (47.1)	0.02
CX	73 (11.6)	259 (13.7)	0.36
RCA	207 (32.9)	722 (38.2)	0.21
Bypass graft	3 (0.5)	14 (0.7)	0.43
Intermediate artery	0 (0)	4 (0.2)	0.25
No. of diseased vessels:			
1	264 (41.9)	804 (42.5)	0.78
2	209 (33.2)	607 (32.1)	0.65
3	157 (24.9)	480 (25.4)	0.54
Pre TIMI grade:			
0/1	575 (91.3)	1632 (86.3)	0.003
2	35 (5.5)	172 (9)	0.41
3	20 (3.2)	87 (4.6)	0.75
Post TIMI grade:			
0/1	89 (14.1)	131 (6.9)	< 0.001
2	32 (5.1)	95 (5)	0.93
3	509 (80.8)	1665 (88)	0.38
Stent	509 (80.8)	1563 (82.6)	0.35
Stent length [mm]	20.2 (7.3)	19 (6.5)	0.001
Stent diameter [mm]	3.07 (0.32)	3.13 (0.35)	0.001
Stent type:			
BMS	500 (98.2)	1512 (96.7)	0.21
PES	4 (0.8)	23 (1.5)	0.18
SES	5 (1)	28 (1.8)	0.16
Proximal location of the lesion	361 (57.3)	973 (51.5)	0.01
LVEF (%)	45.4 (12.4)	48.1 (10.7)	< 0.001
Tirofiban	309 (49)	912 (48.2)	0.87
Volume of contrast medium [ml]	250.3 (103.6)	232.6 (90.5)	< 0.001
Volume of contrast medium > 250 ml	147 (23.3)	322 (17)	< 0.001
Success of the procedure	540 (85.7)	1756 (92.9)	< 0.001

Mean values (SD) and % (n) are reported for continuous and categorical variables, respectively, CIN – contrast-induced nephropathy, LMCA – left main coronary artery, LAD – left anterior descending coronary artery, CX – circumflex coronary artery, RCA – right coronary artery, TIMI – thrombolysis in myocardial infarction, BMS – bare metal stent, PES – paclitaxel-eluting stent, SES – sirolimus-eluting stent, LVEF – left ventricular ejection fraction

Table IV. In-hospital cardiac events and complications

	CIN (n = 630)	No CIN (n = 1891)	p Value
In-hospital mortality	60 (9.5)	23 (1.2)	< 0.001
Reinfarction	24 (3.8)	29 (1.5)	0.001
Target-vessel revascularization	42 (6.6)	70 (3.7)	0.002
MACE	94 (14.9)	89 (4.7)	< 0.001
Stroke	11 (1.7)	7 (0.4)	< 0.001
Serious ventricular arrhythmia	57 (9)	54 (2.9)	< 0.001
Cardiopulmonary resuscitation	67 (10.6)	34 (1.8)	< 0.001
Advanced heart failure	142 (22.5)	193 (10.2)	< 0.001
Intra-aortic balloon pump	63 (10)	40 (2.1)	< 0.001
Renal failure requiring dialysis	15 (2.4)	1 (0.05)	< 0.001
New atrial fibrillation	20 (3.2)	17 (0.9)	< 0.001
Complete atrioventricular block requiring transient pacemaker	36 (5.7)	55 (2.9)	0.001
Major bleeding requiring blood transfusion	41 (6.5)	58 (3)	< 0.001
Acute stent thrombosis	13 (2.1)	10 (0.5)	< 0.001
Time of hospital stay [days]	8 (5.9)	7.1 (6.1)	0.003

Mean values (SD) and % (n) are reported for continuous and categorical variables, respectively, CIN – contrast-induced nephropathy, MACE – major adverse cardiac events (cardiovascular death, reinfarction, target-vessel revascularization)

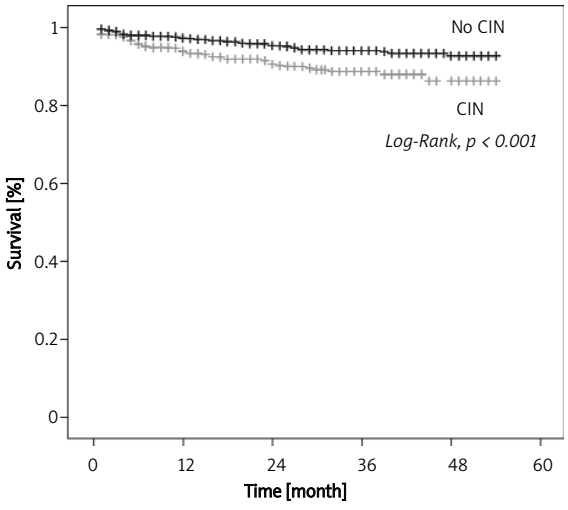

Figure 3. Kaplan-Meier curve for long-term survival according to the development of contrast-induced nephropathy (CIN)

Table V. Long-term cardiac events

	CIN (n = 566)	No CIN (n = 1826)	p Value
Cardiovascular mortality	47 (8.3)	79 (4.3)	< 0.001
Reinfarction	56 (9.9)	136 (7.4)	0.02
Target-vessel revascularization	102 (18)	281 (15.4)	0.05
MACE	151 (26.7)	372 (20.4)	< 0.001
Advanced heart failure	65 (11.5)	116 (6.4)	< 0.001

*% (n) are reported for categorical variables, CIN – contrast-induced nephropathy, MACE – major adverse cardiac events (cardiovascular death, reinfarction, target-vessel revascularization), *n = 566 for CIN (there is no follow-up for 4 patients and 60 patients died in hospital), *n = 1826 for no CIN (there is no follow-up for 42 patients and 23 patients died in hospital)*

≥ 4, 8.1% for 2-3, and 2.9% for 0-1 (p < 0.001, p < 0.001, respectively). Independent predictors of cardiovascular mortality and MACE were determined by Cox proportional hazards analysis. CIN was independently associated with a 90% increase in the risk of long-term cardiovascular mortality (HR 1.90, 95% CI 1.16-3.12, p = 0.01) and 33% increase in the risk of long-term MACE (HR 1.34, 95% CI 1.04-1.72, p = 0.025).

Discussion

The major findings of the present single centre study, the largest to date examining the impact of CIN in patients undergoing primary PCI for STEMI, are that CIN is observed frequently after primary PCI, even in patients with normal renal function, and it is associated with a striking increase in in-hospital and long-term morbidity and mortality with longer hospital stay. Contrast-induced nephropathy was one of the strongest independent predictors of diminished long-term survival. Adverse clinical events occurred more frequently in patients with CIN score ≥ 4.

The reported incidence of CIN varies widely across the literature, depending on the patient population and the baseline risk factors. The most commonly used definition in clinical trials is an increase in serum creatinine of 0.5 mg/dl, or a 25% increase from the baseline value, assessed at 48-72 h after the procedure [5]. Its reported incidence ranges from 8 to 15% in the general population [19]. For example, in a study by McCullough *et al.* [6] that analyzed data on 1,826 patients undergoing PCI, CIN occurred in 14.5% of the cases. Dialysis as a result of CIN in that study was required in 0.3%. In the present study, incidence of CIN was higher and dialysis was required in 0.6%. The difference may be due to the exclusion of patients with known renal failure or those in cardiogenic shock, the definition of CIN, and the lack of routine daily creatinine measurements.

The mechanisms by which CIN worsens early and late outcomes in patients undergoing primary PCI are multifactorial. We found that patients with CIN were more often elderly and female, presented later, had larger infarct size, and were more likely to have a reduced left ventricular EF. Pre-existing renal disease with an elevated level of creatinine is a crucial risk factor in the development of CIN; rates in patients with underlying renal disorder are extremely high, ranging from 14.8 to 55% [20]. As shown in a study by Hall [21] if baseline plasma creatinine level is ≤ 1.2 mg/dl, the incidence of CIN was only 2%. However, in patients with values of creatinine in the range of 1.4-1.9 mg/dl, the incidence of CIN increased to 10.4%, and in patients with baseline creatinine level ≥ 2.0 mg/dl, 62% developed CIN after angiography. Generally, estimated GFR < 60 ml/min/1.73 m^2 is considered a cut-off value for increased risk of CIN [20]. In our population, the incidence of CIN was increased to 45.9% in patients with values of baseline creatinine > 1.5 mg/dl.

In addition to baseline renal failure, many risk factors for developing CIN after PCI have been identified. Most importantly, these appear to be related to demographic factors such as advanced age, DM, periprocedural factors such as haemodynamic instability or heart failure, and evidence of volume depletion [23]. Additional factors include the use of intra-aortic balloon pumps and nephrotoxic medications. A key and potentially modifiable factor is the use of high volumes of contrast medium. For example, Cigarroa *et al*. [24] have suggested a formula for maximum allowable contrast dose (5 × body weight/SCr).

Over the last several years, several risk-prediction models have been developed to predict a patient's risk of developing CIN after PCI. In 208 patients, Marenzi *et al*. [25] showed that age ≥ 75 years, use of an intra-aortic balloon pump, anterior MI, time to reperfusion ≥ 6 h, and contrast medium volume ≥ 300 ml were predictors of CIN after primary PCI. Bouzas-Mosquera *et al*. [26] identified predictors of CIN in 315 patients after primary PCI. In this model, volume of contrast medium was not associated with CIN. A model by Mehran *et al*. [27] developed in 8357 patients undergoing PCI uses eight variables to calculate a risk score for predicting CIN. But in that model, patients treated with primary PCI and patients in shock were excluded. So our model defined the actual information within the setting of urgent cardiac catheterization in a large population.

Contrast-induced nephropathy is one of the most common sources of acute renal failure among hospitalized patients. It is associated with prolonged in-hospital stay and increased morbidity, mortality, and costs. In our population, patients with CIN had worse in-hospital outcome; mortality in this group was 9.5%, but was 1.2% in patients without CIN. Similarly, Marenzi *et al*. [25] reported that in-hospital mortality rates were higher in patients that developed CIN (31%) compared with those without CIN (0.6%) after primary PCI. In the study by Bouzas-Mosquera *et al*. [26] in-hospital mortality was 13.9% in patients with CIN versus 0.7% in patients with preserved renal function.

In patients undergoing primary PCI for MI, short- and long-term mortality rates were also significantly higher in those who developed CIN: 16.2% at 30 days and 23.3% at 1 year for those with CIN, compared with 1.2 and 3.2%, respectively, for those without CIN ($p < 0.001$) [28]. Contrast-induced nephropathy was shown to be an independent predictor of 1-year mortality in consecutive patients after PCI (OR 2.7, $p < 0.001$) [29]. In our population, cardiovascular mortality and the MACE rate during long-term follow-up were higher in the group that developed CIN. And also, CIN was a strong and independent predictor of mortality and MACE.

Study limitations

This study has the well-known limitations of the retrospective design. We showed the independent adverse effects of contrast medium but we cannot determine the role of atheroembolism, haemodynamic alterations, cardiogenic shock and longer ischaemia time. These factors could play a role in kidney hypoperfusion and injury. There was no standard hydration procedure for prevention but we used normal saline solution, not bicarbonate or N-acetylcysteine peri- or post-procedure. And also we do not have enough information about the percentage of use of ACE-I, ARB, and diuretics. Patients receiving statins at the time of the procedure show a significantly reduced incidence of CIN. This evidence strongly supports routine use of statins as adjuvant pharmacological therapy before PCI [30]. In the MIRACL study, high dose atorvastatin (80 mg) was used [31]. Our patients were given different doses of atorvastatin on admission but data about doses are not enough for evaluation.

Clinical implications

This study shows that patients who develop CIN have worse clinical outcomes, higher complication rates, longer hospital stays, and higher mortality, both in hospital and post-discharge, than patients who do not develop CIN. In the setting of urgent catheterization, where the benefit of very early imaging outweighs the risk of waiting for the results of blood tests, it may be necessary to proceed without SCr assessment or GFR estimation. So useful and actual risk scoring may guide the determination of high-risk patients. Then it is

meaningful to make all attempts at the time of intervention to prevent CIN in high-risk patients, including adequate hydration [32], minimization of contrast use [6], use of low-osmolar contrast [33], and possibly administration of N-acetylcysteine [34, 35].

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