CONTRAST INDUCED NEPHROPATHY IN PATIENTS UNDERGOING ELECTIVE PCI IN A TERTIARY CARE CENTRE IN COASTAL KERALA

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ABSTRACT

BACKGROUND

Contrast induced nephropathy after PCI is associated with significant morbidity and mortality after PCI. Patients undergoing PCI who had risk factors for renal compromise are at higher risk.

The aim of this study was to evaluate the incidence, predictors and in-hospital outcome of contrast-induced nephropathy (CIN) after elective percutaneous coronary intervention (PCI) for stable ischaemic heart disease patients.

MATERIALS AND METHODS

In 630 consecutive patients undergoing ad hoc PCI, we measured serum creatinine concentration (Cr) at baseline and daily for the following three days; contrast-induced nephropathy was defined as a rise in Cr of 0.5 mg/dL.

RESULTS

Overall, CIN occurred in 40 (6.51%) patients. Patients who develop CIN had baseline Cr. of 1.27 ± 0.23 with mean increase in S. cr value of 0.9 ± 0.47 mg/dL. In multivariate analysis diabetes ($p < 0.0001$), baseline Cr. clearance < 60 mL/min ($p < 0.0001$), contrast agent volume > 300 mL ($p < 0.0001$) and complex PCIs were independent correlates of CIN. No correlation was found between development of CIN and age, HTN and smoking. CIN patients had longer hospital stay and more complicated clinical course.

CONCLUSION

Contrast induced nephropathy frequently complicates clinical course of patients undergoing PCI, even in patients with normal renal function. Thus, preventive strategies are needed, particularly in high-risk patients.

KEYWORDS

PCI, CIN, AKI, Elective PCI.

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BACKGROUND

Contrast induced nephropathy (CIN) is the third leading cause of acute renal failure in admitted patients, accounting for 10% of all cases.¹ Percutaneous intervention using iodinated contrast media has seen a tremendous surge in recent time as a first line and most efficacious treatment for coronary disease spectrum from acute myocardial infarction to stable ischaemic heart disease. With all its benefit of easy accessibility and immediate benefit, it comes with an iatrogenic risk attributed to use of contrast medium leading to Contrast Induced Nephropathy (CIN). Although, the risk of CIN is low (0.6 – 2.3%) in the general population, it may be very high (up to 50%) in selected subsets, especially in patients with major risk factors such as advanced chronic kidney disease and diabetes mellitus and in those undergoing emergency percutaneous coronary interventions (PCI).

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This entity is a type of renal AKI and treatment is also on the same line, but strikingly it is a potentially preventable disease with proper prevention and timely intervention. Despite all efforts, many a times however, especially in high risk subset patients CIN leads to complicated clinical course and morbidity. With increasing technological advancements in the field of interventional cardiology, number of PCI using iodinated contrast media being performed per year in more complex and high risk patients are increasing and so the number of CIN. Many scholars have researched and evaluated the risk scores, risk predictors to assess the predictability of CIN, its prevention and cures. Studies have shown that CIN is associated with increased morbidity and mortality, extended length of hospital stay and increased costs.^{2,3}

MATERIALS AND METHODS

Study Type

Single centre prospective observational study.

Study Population and Protocol

Between January 1, 2014 and December 2014, all patients with CAD scheduled to undergo CAG with elective PCI enrolled into the present study. Patients were excluded if: (1) Acute myocardial infarction (AMI) at admission; (2) Severe LV systolic dysfunction, i.e. EF $< 30\%$; (3) Known case of ESRD on medical management; (4) Patients on chronic peritoneal or haemodialytic treatment; (5) Contrast allergy; (6)

Administration of contrast agent in last 7 days; (7) History of AKI in last 7 days; (8) No written formal consent from patients.

Study Protocol

All patients were treated by 0.9% saline given intravenously at a rate of 1 mL/kg/h starting from 12 h before scheduled time for coronary angiogram and 0.5 mL/kg/hr for 6 hours after PCI. The use of drugs including beta-adrenergic blockade, angiotensin-converting enzyme inhibitors and diuretics was according to cardiologist's discretion. Baseline S. cr values were taken before the procedure and post PCI serum creatinine values were recorded daily for next 3 days daily.

PCI

PCI was performed as per approved guidelines and institutional protocols. Only low osmolar contrast media was used all through the study. Selection of transfemoral or transradial approach, contrast dose, PCI technique and supportive pharmacologic therapies were left to operator's choice.

Defining CIN

Rise in S. cr can be expressed either in absolute terms (0.5 to 1.0 mg/dL) or as a proportional rise in S. cr of 25% or 50% above the baseline value. Generally, most commonly used criteria for CIN is a rise in S. cr of 0.5 mg/dL or a 25% increase from the baseline value assessed at 48 h after the procedure. The European Society of Urogenital Radiology defines contrast-induced AKI as renal dysfunction (an increase in S. cr by > 0.5 mg/dL or > 25% within 3 days after intravascular administration of contrast medium) without an alternative aetiology.⁴ The Acute Kidney Injury Network definition⁵ is a rise in S. cr > 0.3 mg/dL with oliguria.

Statistical Analysis

Continuous data are expressed as the mean value $\pm$ SD. Categorical data are expressed as absolute values and percentages. Comparison of continuous variables was performed by means of Student 't' test. Chi-square test was used for comparison of categorical variables as appropriate. A p value < 0.05 was considered statistically significant.

RESULTS

Among 630 patients under study, 520 (82.54%) were males and 110 (17.46%) were females with mean age of 56.48 ± 9.15 years; 184 (29.20%) were diabetic and 203 (32.22%) were hypertensive. Chronic tobacco use was found in 193 (30.63%) patients. Indications for PCI were old AW MI with EA > II (129, 20.47%) old IWMI with EA > II (69, 10.95%), NSTEMI (149, 23.65%), UA (134, 21.27%) and SIHD refractory to medical management with EA FC II/III (149, 23.65%). History of coronary angiogram or PCI were present in 94 (14.92%) patients, 51 of which were those who underwent CAG before and scheduled for planned PCI later, rest 41 had primary PCI in the past. Pre-existing renal dysfunction (defined as eGFR < 60 mL/min/1.73 m²) was present in 210 (33.33%) with mean GFR of 52.22 ± 6.35 mL/min/1.73 m², patients with normal renal function had mean eGFR of 79.05 ± 21.8 . Baseline S. cr value was 1.24 ± 4.28 mg/dL. Baseline LV EF being $56 \pm 4.28\%$. Baseline characteristics are presented in Table 1.

Post PCI CIN was noted in total of 41 patients (6.51%). Patient who develop CIN had baseline Cr values of 1.27 ± 0.23

with mean increase in S. cr value of 0.9 ± 0.47 mg/dL against baseline cr of 1.24 mg/dL increase of 0.34 mg/dL in patients who did not develop CIN. Patients who developed CIN had mean eGFR of 61.2 ± 38.0 in comparison to 82.43 ± 40.67 in patients who did not develop CIN. Patient who developed CIN had longer hospital stay (5.59 ± 1.26 vs 2.59 ± 0.84). Patients with eGFR < 60 had higher rates of CIN (26, 12.38% vs 14, 3.34%, $p < .0001$). Diabetics also had higher numbers of CIN (28, 15.28% vs 12, 26.90%, $p < .0001$). Mean contrast volume used was 204.29 ± 74.29 mL and it showed direct correlation with development of CIN when CV is higher than 300 mL (17, 16.67% vs 23, 4.35%, $p < 0.0001$). Patients undergoing multivessel or complex PCI were at higher risk of CIN (31, 7.91% vs 9, 3.18%, $p = 0.003$). Parameters which did not show positive correlation with development of CIN were HTN (14, 6.9% vs 26, 6.09%, $p = 0.08$), smoking (16, 7.77% vs 24, 5.72% $p = 0.33$), male gender (34, 6.54% vs 06, 5.45%, $p = 0.7$) and age > 65 (11, 8.33% vs 29, 5.82%, $p = 0.29$).

Clinical Outcome

Usually, as depicted CIN has a mild indolent clinical course and self-resolution of renal impairment in 5 - 7 days. In our study also, patients who develop CIN had to be monitored serially with RFT and urine output for several days with only 2 patients had to undergo dialysis for CIN. None of the patients died as after consequence of CIN. Patients with CIN had longer hospital stay.

Baseline Characteristics of Patients (N= 630)		
Age (Years)	N	%
<40	24	3.81
40-50	130	20.63
50-60	228	36.2
60-70	205	32.54
>70	43	6.83
Sex		
M	520	82.54
F	110	17.46
Diabetic	184	29.2
Hypertension	203	32.22
Smokers	193	30.63
Baseline EF (%)		
<40	87	13.81%
40-55	136	21.59%
>55	407	64.60%
Indications of PCI		
H/O AWMI	129	20.47
H/O IWMI	69	10.95
NSTEMI	149	23.65
UA	134	21.27
SIHD	149	23.65
H/O Previous Intervention		
CAG	51	8.10%
PCI	42	6.82%
Baseline S. cr	1.24 ± 4.79 mg/dL	
Baseline eGFR	81.88 ± 37.59	
eGFR in mL/min/1.73 m2, AWMI- Anterior Wall Myocardial Infarction, IWMI- Inferior Wall Myocardial Infarction, NSTEMI- Non-ST Elevation Myocardial Infarction, UA- Unstable Angina, SIHD- Stable Ischaemic Heart Disease		
Table 1. Baseline Characteristics of Patients		

Results	CIN	No CIN	P
Total	40	590	
DM	28	156	<0.0001
NO DM	12	434	
eGFR > 60	14	406	<0.001
eGFR < 60	26	184	
Contrast > 300 mL	17	85	<0.001
Contrast < 300 mL	23	505	
EF= 30 - 40%	12	75	<0.001
EF > 40%	28	515	
SVD	9	274	0.003
MVD	31	316	
HTN	14	189	0.08
No HTN	26	434	
> 65	11	121	0.29
< 65	29	469	
Smoking	15	178	0.33
No smoking	25	412	
Baseline eGFR	52.22	79.05	
Mean S. cr	1.27±2.3	1.25±4.87	
Increase in cr	0.9±.47	0.11±0.47	
Mean Cv	255.85±111.87	200.7±69.82	
Hospital Stay (days)	5.59 ± 1.26	2.59 ± 0.84	

Table 2. Difference in Results of Patients who developed CIN vs Who Did Not

eGFR in mL/min/1.73 m², CV- Contrast Volume, EF- Ejection Fraction, DM- Diabetes Mellitus, HTN- Hypertension, SVD- Single Vessel Disease, MVD- Multivessel Disease.

Chart - Difference in Baseline and Increase in S. cr

DISCUSSION

This study evaluate the incidence of CIN in stable CAD patients with relatively normal baseline renal parameters and it also validates the risk predictors already established for causation of CIN in relatively normal subjects undergoing elective PCI. This study shows that CIN is a common complication of PCI in normal subjects and complicates clinical course and increase hospital stay.

Evidences suggest that PCI is the most effective treatment for CAD spectrum for acute MI to stable ischaemic heart disease. Our study encompasses study population who had PCI scheduled electively for UA, old MI, NSTEMI and stable angina refractory to OMT. In all mentioned indications patient did not have acute decompensation or acute LVF, most of the patients had preserved LVEF with minority patients having significant LV systolic dysfunction. Similarly, majority of the

patients had baseline S. cr value < 1.5 mg/dL with calculated eGFR > 60 mL/min/m². Unlike previous studies^{6,7} which showed rare CIN in stable patient undergoing elective PCI (1.2% - 1.7%), our study showed relatively higher incidence of CIN, probably owing to higher number of multivessel (two vessel and three vessel) and complex PCI's and prolonged procedures requiring higher dose of contrast volume due to technological advancement in the field.

Our study proved that diabetes mellitus is strong and independent risk predictor for CIN even in patients with normal renal parameters. In a large study in patients with normal baseline serum creatinine levels, diabetes was an independent predictor of CIN (odds ratio [OR], 1.90; 95% confidence interval [CI], 1.38 - 2.61).⁸ Dangas and Associates⁹ also showed that diabetes is an independent risk factor for CIN (OR, 1.55; 95% CI, 1.26 - 1.91) in patients with normal renal function (mean baseline eGFR < 88.0 mL/min per 1.73 m² in patients with CIN, 81.1 mL/min per 1.73 m² in patients without CIN). In another analysis, Rihal et al showed that diabetes increased the risk of post-PCI renal failure in patients with normal or mildly impaired renal function or mild impairment (serum creatinine > 1.2 mg/dL [$> 106.1 \mu\text{mol/L}$] or 1.2 - 1.9 mg/dL [$106.1 - 168.0 \mu\text{mol/L}$]).¹⁰

Our study also supports that pre-existing renal compromise is an independent predictor for CIN. Almost all studies mentioned pre-existing renal impairment as the first and foremost risk for contrast induced nephropathy.¹¹⁻¹⁴ In a registry from Michigan Cardiovascular consortium, it was shown that of 16,592 PCIs the incidence of CIN increased with worsening baseline renal function¹⁵ which was also confirmed in a series of 1,826 patients.¹⁶ Another registry study showed that the incidence of renal failure after PCI increased from 2.5% in patients with mild renal impairment (serum creatinine 1.2 - 1.9 mg/dL) to 30.6% in those with more severe impairment (serum creatinine > 3.0 mg/dL). Using a model developed by Davidson CJ et al, to predict the risk of CIN it was found that the risk was relatively constant at baseline serum creatinine levels of > 1.1 mg/dL ($> 97.2 \mu\text{mol/L}$) and increased at levels of > 1.2 mg/dL ($> 106.1 \mu\text{mol/L}$).¹⁷

Contrast volume also serves as an independent predictor for CIN and it has been shown by previous studies.^{18,19} Consensus panel regarding type and volume of contrast volume states that low osmolality CM (including CM that is iso-osmolar to plasma) are recommended for all patients. There is insufficient evidence at to recommend one specific CM over another for its potential to cause less nephrotoxicity in patients with renal insufficiency. The volume of CM administered, particularly to high-risk patients should be the minimum amount needed for diagnosis and intervention. Strategies to minimise CM volume such as use of CM with high iodine content, use of saline flushes or power injectors may provide additional benefit.

Increasing age is a risk factor for CIN in many studies, possibly reflecting the decline in renal function with advancing age. However, in some studies, age remains an independent predictor in multivariate analyses.²⁰ Old age is associated with increased vascular stiffness and a decline in endothelial function resulting in reduced vasodilator responses as well as decreased capacity for vascular repair with pluripotent stem cells.²¹ These factors may increase the risk of CIN in the elderly patient and reduce the potential for prompt recovery. Our study failed to show that positive correlation between age and

development of CIN is probably because of small sample size of elderly patients not enough to reach a definite conclusion.

Limitation of Study

1. Small sample size with less power to reach a definite conclusion.
2. Relatively stable patient with near normal renal parameters were included, excluding a whole set of patient population on higher risk of development of CIN.
3. Patients were not followed up and hence clinical implication of CIN could not be determined.

CONCLUSION

CIN is common in patients undergoing elective PCI with near normal renal parameters and haemodynamically stable state. Pre-existing renal impairment, diabetes mellitus, contrast volume being strong and independent predictors of development of CIN.

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