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Original Article

Impact of percutaneous coronary intervention on patients with impaired baseline renal function

Deepti Yadav, Ankit Kumar Sahu, Roopali Khanna, Pravin K. Goel*

Department of Cardiology, Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPGIMS), Lucknow, 226014, Uttar Pradesh, India

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ABSTRACT

Background: Acute kidney injury (AKI) frequently co-prevails with acute coronary syndromes (ACS), which could improve post percutaneous coronary intervention (PCI). We sought to evaluate the impact of PCI on post-procedural renal function in patients with impaired baseline serum creatinine (Cr).

Methods: Retrospective evaluation of 185 patients undergoing PCI with impaired basal serum Cr (≥ 1.5 mg/dl) was done, including 88 (47.5%) patients with recent ACS (≤2 weeks old) in group I and 97 (52.4%) patients in group II (stable angina or ACS >2 weeks old). Patients were classified into worsening or improving renal function based on a corresponding increase or decrease of ≥0.5 mg/dl (ΔCr) in serum Cr 24–48 h post PCI. ΔCr < 0.5 mg/dl was termed as no change.

Results: A trend towards improving renal function was seen in the study cohort (mean serum Cr: 2.37 ± 1.25 mg/dl vs 2.28 ± 1.59 mg/dl); ($p = 0.09$) with decrease in group I from 2.28 ± 1.09 mg/dl to 2.12 ± 1.44 mg/dl ($p = 0.03$) and in group II from 2.45 ± 1.38 mg/dl to 2.43 ± 1.71 mg/dl ($p = 0.81$). Post PCI, worsening occurred in 20/185 (10.8%) patients in the total study cohort, 5/88 (5.6%) in group I and 15/97 (15.4%) in group II ($p = 0.03$). Improvement in serum Cr was seen in 49/185 (26.4%) in the total study cohort, 30/88 (34.1%) in group I and 19/97 (19.6%) patients in group II ($p = 0.03$).

Conclusion: – Post PCI, only a small proportion of patients with impaired baseline creatinine showed worsening in renal function. Improved renal function was observed in at least one-third of the patients with recent ACS.

1. Introduction

Acute kidney injury (AKI) post percutaneous coronary intervention (PCI) shows early (within days) worsening of renal function, with clinical manifestations ranging from minimal increase in serum creatinine to anuric renal failure requiring renal replacement therapy.[1] Acute kidney injury also frequently co-exists with acute coronary syndrome (ACS) per se, wherein hemodynamic instability is often the precipitating factor which can improve post PCI. Changes in volume status, nephrotoxic drugs, contrast usage, athero-embolism, intra-aortic balloon pump counterpulsation and non-access site related major bleeding are some of the common factors in patients undergoing PCI that may contribute to the development of AKI.[2–4] We therefore sought to evaluate the impact of coronary revascularization on renal function in patients with impaired baseline creatinine levels in consecutive patients undergoing PCI and also to see if there was any difference with respect to ACS status or not.

2. Material and methods

Consecutive patients with impaired baseline serum creatinine levels (≥1.5 mg/dl) undergoing PCI from February 2006 to August 2019 were included in the study. Patients were taken up for PCI, provided adequate urine output (≥0.5 ml/kg/h) was present. Also, consultation from department of nephrology was sought in every case and optimal peri-procedural management including hydration and N-acetyl cysteine was given pre procedure in all. We excluded patients with incomplete data on serum creatinine levels before and/or post PCI. Preprocedural serum creatinine values were measured prior to PCI, with a preference given to the value closest to the time of PCI for the purpose of analysis. The decision to perform PCI was made at the discretion of the operating cardiologist on the basis of patient's clinical profile, lesion characteristics and patient preference. A written informed consent was obtained

* Corresponding author.
E-mail address: golf_pgi@yahoo.co.in (P.K. Goel).

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prior to the procedure in all patients as per institutional protocol. All data related to the procedure, including details on clinical presentation and follow-up was retrieved from a computerized database software wherein all patient details were recorded as a part of department protocol on a day to day basis. Incomplete records were refreshed using telephonic contact with the patients. All patients with baseline renal dysfunction undergoing PCI were either not initiated or if already taking, were discontinued the following drugs [angiotensin converting enzyme inhibitor (ACEI)/angiotensin receptor blocker (ARB)/mineralocorticoid receptor antagonist (MRA)]. Post PCI, only those patients where renal function improved to normal were these drugs reinstated and that too in lower doses at discharge or during outpatient follow-up visits.

2.1. Procedure protocol

All patients were pre-loaded with dual antiplatelets (aspirin and clopidogrel 600 mg or ticagrelor 180 mg or prasugrel 60 mg) depending upon patient's clinical profile and contraindications, if any. Unfractionated heparin was given at the time of procedure and titrated to maintain activated clotting time (ACT) > 280 seconds. During procedure adequate hydration was maintained and only iso-osmolar contrast media (Iodixanol) was used during PCI. Glycoprotein IIb/IIIa inhibiting agent (abciximab only) was given at discretion of the operator in view of complexity of the lesion, stent length, multiple stents and patient's clinical status. Post procedure all patients were prescribed dual antiplatelet drugs for at least one year and advocated aspirin for whole life. Other cardioactive medications were prescribed in accordance with patient's clinical need and guideline-based recommendations from time to time. Complete revascularization was aimed at in all patients except those who presented with acute coronary syndrome (ACS) where depending on clinical situation culprit vessel only strategy was followed in some as per decision of the treating physician. Post-procedural serum creatinine level was obtained at 24–48 h post procedure. If two post PCI values were available, then the higher value was considered for analysis. The N-acetyl cysteine (NAC) dosage used was 1.2 gm twice daily for 24 h prior to the procedure and up to 48 h post procedure. The following hydration protocol was followed in all patients viz. normal saline at the rate of 1–2 ml/kg/hr for at least 6 h pre-PCI and for 12–24 h post-PCI to maintain a minimum urine output of >1 ml/kg/hr as a standard protocol in all the patients. Intermittent IV furosemide bolus injection (0.25–0.5 mg/kg) followed by infusion at the rate of 0.1–0.2 mg/kg/hr was given in selected patients of mild to moderate renal dysfunction with fluid overload to maintain a net negative fluid balance.

2.2. Definitions

Patients were divided into 2 groups based on their clinical presentation. Group I included patients presenting with recent ACS (<2 weeks duration). Group II included all other patients including those presenting with stable angina or old ACS (>2 weeks duration). The study groups so framed were then analyzed to look for worsening, no change or improvement in their renal function post PCI based on the change in serum creatinine value (ΔCr) obtained 24–48 h after PCI. Worsening in renal function was defined as an increase of ≥0.5 mg/dl in ΔCr. Improvement in renal function was defined as decrease of ≥0.5 mg/dl in ΔCr and the rest were labelled as no change in renal function. ACS was referred to any group of clinical symptoms compatible with acute myocardial ischemia irrespective of troponin elevation and covered the spectrum of clinical conditions ranging from unstable angina to NSTE-ACS and STEMI.[5] Clinical outcome parameters including in-hospital mortality and need for renal replacement therapy (RRT) post procedure were also recorded.

2.3. Statistical analysis

Demographic data was described across the two groups as mean ± standard deviation for continuous variables and number (%) for categorical variables. Pearson's Chi-square test was used for comparison of categorical variables and student paired-t test for continuous variables. Profile plots were drawn for pictorial comparison of pre and post procedural creatinine change. *p*-value of ≤0.05 was taken asstatistically significant. Statistical analyses were performed using IBM SPSS® statistical software (SPSS version 20.0, Chicago, IL, USA).

3. Results

Between February 2006 and August 2019, 196 consecutive patients with impaired basal serum creatinine underwent PCI. 11 patients were excluded from analysis as per predefined exclusion criteria. Of the 185 then included in the study the clinical, demographic, and procedural characteristics of patients stratified into group I and group II are shown in Table 1. Group I patients were on an average 6 years younger than group II patient ($p < 0.001$). The risk factor profile and sex distribution were similar between the two groups. For obvious reasons, group I patients had more single

Table 1
Baseline characteristics.

Variables	Total cohort (n = 185)	Group I (n = 88)	Group II (n = 97)	P-value
Mean age, years	62.50±10.06	65.28±10.15	59.98±9.32	<0.001
Sex, n (%)				
Male	156 (84.3)	74 (84.1)	82 (84.5)	0.934
Female	29 (15.7)	14 (15.9)	15 (15.5)	
Co-morbid risk factors				
Diabetes mellitus	111 (60.0%)	48 (54.5%)	63 (64.9%)	0.177
Hypertension	128 (69.2%)	58 (65.9%)	70 (72.2%)	0.426
Smoker	48 (25.9%)	23 (26.1%)	25 (25.8%)	1.000
Known CKD	40 (21.6%)	17 (19.3%)	23 (23.7%)	0.481
Mean LVEF (%)	47.38±8.90	46.80±8.86	47.91±8.94	0.398
No of vessels intervened				
1	116 (62.7%)	65 (73.9%)	51 (52.6%)	0.003
2	58 (31.4%)	17 (19.3%)	41 (42.3%)	0.001
3	11 (5.9%)	6 (6.8%)	5 (5.2%)	0.633
Contrast volume (ml)	190±70.98	181.42±69.18	197.94±72	0.114

Plus-minus values are mean±SD. CKD= chronic kidney disease. LVEF= left ventricular ejection fraction.

vessel and less double vessel intervention as compared to group II. Also, a non-significant trend towards lower contrast volume usage in recent ACS patients was noted (181.42 ± 69.18 ml vs 197.94 ± 72 ml; $p = 0.114$).

Fig. 1 shows the profile plot of serum creatinine values pre and post PCI in the individual patients of the two study groups separately. Post PCI there was a nonsignificant decreasing trend in mean serum creatinine from 2.37 ± 1.25 mg/dl to 2.28 ± 1.59 mg/dl ($p = 0.08$), in the study cohort as a whole, with only the decrement in group I being significant (2.28 ± 1.09 mg/dl to 2.12 ± 1.44 mg/dl; $p = 0.03$) (Fig. 2). Fig. 3 shows the proportion of patients having worsening, no change or improvement in serum creatinine values post PCI in the two study groups. Post PCI worsening of renal function occurred in 20/185 (10.8%) patients in study cohort as a whole, 5/88 (5.6%) in group I and 15/97 (15.4%) in group II ($p = 0.03$). Improvement in serum creatinine was seen in 49/185 (26.4%) patients in study cohort as a whole, 30/88 (34.1%) in group I and 19/97 (19.6%) in group II ($p = 0.02$). There was no change in 116/185 (62.7%) patients of study cohort as a whole, 53/88 (60.2%) patients of group I and 63/97 (64.9%) patients of group II ($p = 0.50$) (Table 2). A total of 10/185 (5.4%) patients needed RRT in same admission and a total of 2/185 (1.1%) had in-hospital mortality. Table 3 shows the distribution of patients needing RRT and death in the three different outcome subgroups vide worsening, no change or improvement in renal function.

In the univariate analysis, age (OR 1.07 [95% CI:1.00–1.14]; $p = 0.04$), diabetic status (OR 4.62 [95% CI:1.20–17.82]; $p = 0.03$), ACS presentation (OR 0.21 [95% CI:0.07–0.68]; $p = 0.009$) and known CKD (OR 10.37 [95% CI:3.13–34.40]; $p < 0.0001$) risk factors were predictive of a significant change in renal status post PCI comparing those who worsened versus those who improved with only ACS group showing a favorable effect. Baseline LVEF (47.8 ± 7.6% vs 46.43 ± 8.9%; $p = 0.548$) and contrast volume (182.50 ± 80.6 ml vs 189.1 ± 75.8 ml; $p = 0.749$) was found to be

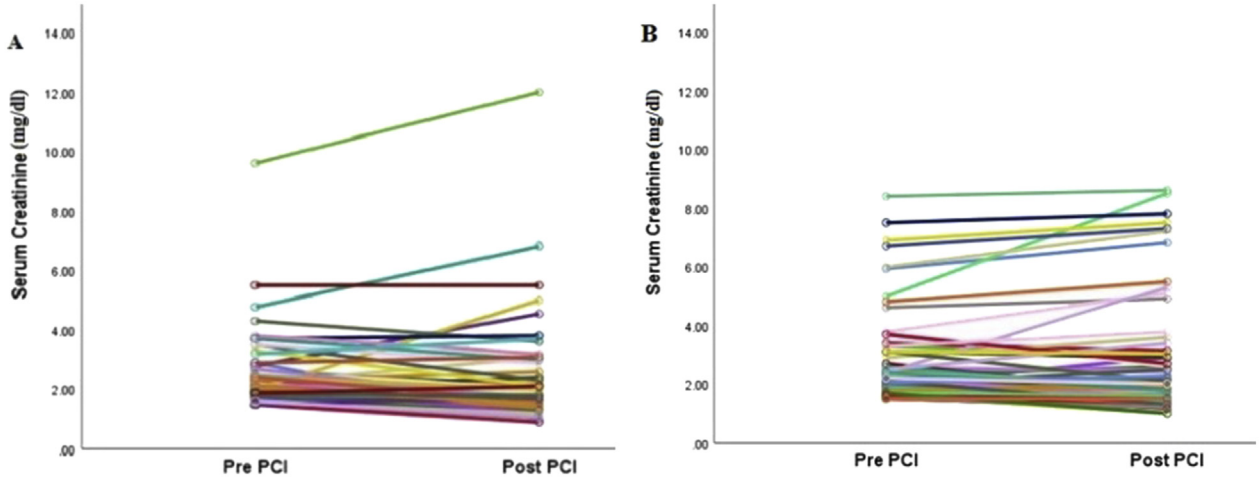

Fig. 1. Profile plot showing individual serum creatinine values pre and post PCI in group I (panel A) and group II (panel B). Abbreviations: PCI=percutaneous coronary.

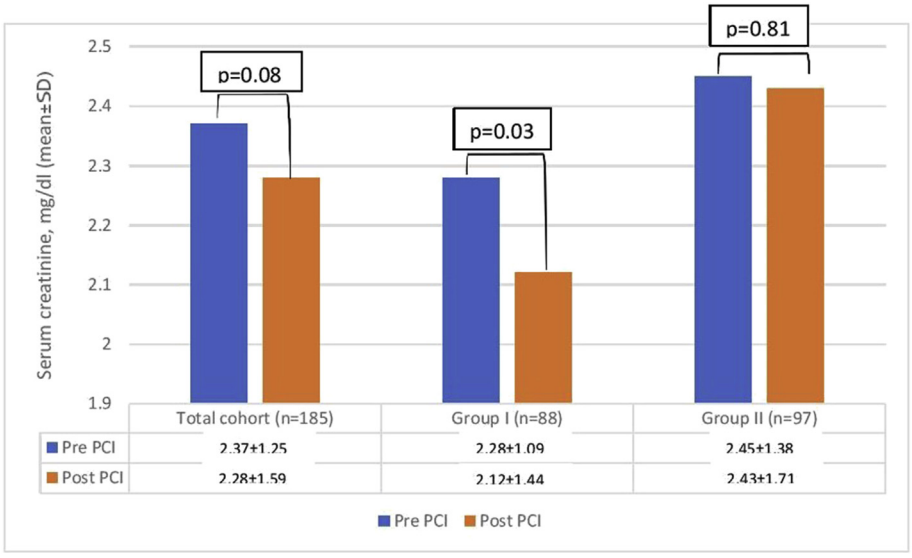

Fig. 2. Post PCI change in the mean serum creatinine value (mg/dl) from baseline in the two study groups. Abbreviations: SD=standard deviation.

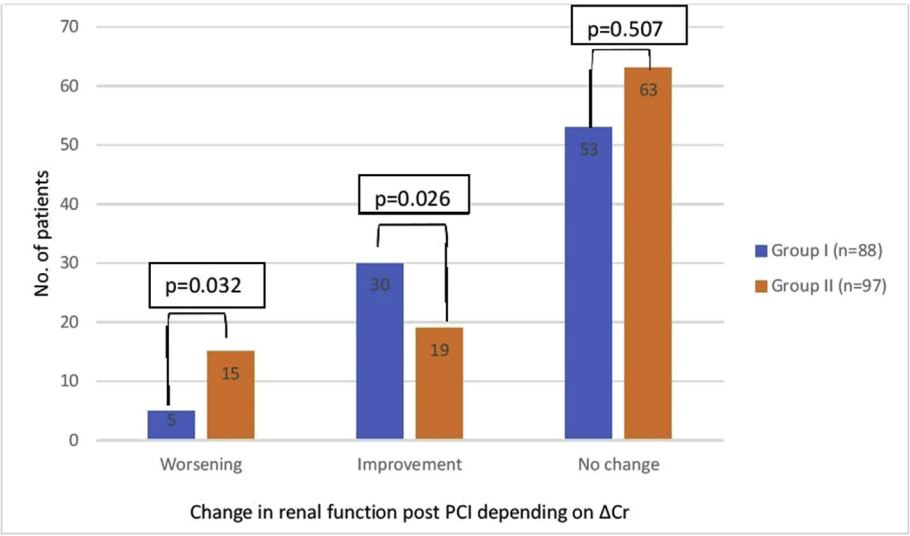

Fig. 3. Worsening, improvement and no change in the renal function status post PCI depending on the change in serum creatinine levels (ΔCr) in the two study groups.

Table 2
Outcomes of the two study groups in accordance with change in serum creatinine levels post PCI.

Study group	Change in serum creatinine (ΔCr) post PCI		
	Worsening	Improvement	No change
Total cohort (n=185)	20 (10.8%)	49 (26.5%)	116 (62.7%)
Group I (n=88)	59 (5.7%)	30 (34.1%)	53 (60.2%)
Group II (n=97)	15 (15.5%)	19 (19.6%)	63 (64.9%)
P-value	0.032	0.026	0.507

PCI=percutaneous coronary intervention.

similar in the patients who had worsening or improvement of renal function post PCI. On multivariate analysis, only recent ACS presentation (<2 weeks) (aOR 0.04 [95% CI:0.005–0.38]; $p = 0.005$) and known CKD status (aOR 41.67 [95% CI:4.93–333.33]; $p = 0.001$) were found to independently correlate with a significant change in renal functional status post PCI, with recent ACS setting favoring improvement in serum creatinine and known CKD status being associated with worsening renal function post PCI (Table 4).

Table 3
Clinical outcomes in patients showing worsening, improvement or no change in serum creatinine post-PCI.

Clinical outcomes	Total cohort (n=185)	Change in serum creatinine (ΔCr) post PCI			P-value
		Worsening (n=20)	Improvement (n=49)	No change (n=116)	
In-hospital mortality, *n (%)*	2 (1.1)	1 (5.0)	1 (2.0)	0 (0)	0.102
Need for RRT, *n (%)*	10 (5.4)	7 (35.0)	0 (0)	3 (2.6)	0.0001
on MHD	6 (3.2)	3 (15.0)	0 (0)	3 (2.6)	0.998
First time in-hospital RRT	4 (2.1)	4 (20.0)	0 (0)	0 (0)	NA

PCI=percutaneous coronary intervention. MHD=maintenance hemodialysis. RRT=renal replacement therapy. NA=not applicable.

Table 4
Univariate analysis of clinical variables with respect to worsening or improvement of renal function post PCI.

Variable	Change in serum creatinine (ΔCr) post PCI		P-value (univariate)
	Worsening (n=20)	Improvement (n=49)	
Age (years)	59.35±8.8	64.41±9.1	0.038
Sex, n(%)			
Male	14 (70.0)	42 (85.7)	0.131
Female	6 (30.0)	7 (14.3)	0.131
Co-morbid risk factors			
Diabetes mellitus	17 (85.0%)	27 (55.1%)	0.019
Hypertension	19 (95.0%)	29 (59.2%)	0.193
Known CKD	14 (70.0%)	9 (18.4%)	<0.001[a]
Clinical presentation			
Recent ACS (<2 weeks)	5 (33.3%)	30 (61.2%)	0.006[a]
Mean LVEF (%)	47.8±7.6	46.43±8.9	0.548
Procedural factors			
No of vessels intervened			
1	13 (65.0%)	30 (61.2%)	0.77
2	7 (35.0%)	15 (30.6%)	0.72
3	0 (0%)	4 (8.2%)	0.18
Contrast volume (ml)	182.50±80.6	189.1±75.8	0.749

Plus-minus values are mean±SD. CKD= chronic kidney disease. LVEF= left ventricular ejection fraction. PCI=percutaneous coronary intervention. ACS=acute coronary syndrome. NA=not applicable.
[a] denotes variables that independently predict worsening of renal function post-PCI on multivariate analysis.

4. Discussion

Our study has primarily three main observations. Firstly, not all patients with impaired baseline serum creatinine levels had further worsening in creatinine values after percutaneous interventions. Secondly, recent ACS (<2 weeks) patients had a significantly lesser incidence of further worsening in renal functions after percutaneous intervention when compared to the other group. And thirdly, a reasonable number of patients of in the study also showed improvement in serum creatinine values post PCI, more so in the predefined ACS group.

We also observed a trend towards decrease in mean serum creatinine value post PCI in the study patients as a whole but the same was significant in the predefined ACS group alone. Serum creatinine post PCI had no significant change in a large majority of patients but improved in about a third of recent ACS patients with lesser number of patients in this group showing worsening. It is possible that in ACS patients the cause for high pre procedure serum creatinine values was more often secondary to pre-renal factors, and with PCI improving the hemodynamics in this patient subset there was a net improvement of serum creatinine values in this group in spite of a contrast load factor also added by the PCI procedure.

AKI being a multifactorial phenomenon is influenced by multiple contributing factors during ACS including key factors like systemic and renal hemodynamic changes secondary to impaired cardiac output ('arterial underfilling') and increased venous congestion ('venous overfilling') that lead to decreased glomerular filtration rate (GFR).[2,6] Moreover, an imbalance of endogenous vasodilating and vasoconstrictive factors appears to be involved in ACS which is characterized by a progressive activation of several neurohormonal systems that exert profound effects on renal perfusion and function. Additionally, a burst of immunological and inflammatory factor activation are among the potential causes of progressive renal injury.[7,8] Indeed, enhanced inflammatory response, increased oxidative stress and sympathetic activation have been shown to synergistically accelerate AKI in patients with ST-segment elevation myocardial infarction (STEMI).[9] Finally, metabolic factors including acidosis and acute hyperglycemia, may be implicated in AKI development.[10]

Tsai et al[11] studied consecutive patients undergoing PCI and found that at least 7% of all patients undergoing a PCI, develop AKI. In our study with baseline serum creatinine values impaired in all included patients, further worsening after PCI was seen in 10.8% of study cohort, which is more than the Tsai et al study.[11] This could be largely because of the baseline renal impairment in all included patients which in itself becomes a risk factor for further deterioration of renal function post PCI. Furthermore, since we did not include patients with normal serum creatinine pre procedure, it would be unreasonable to compare our incidence of worsening renal function with that of Tsai et al.

A recent study, the ISCHEMIA-CKD trial[12] showed that intervention in stable CAD patients with advanced kidney disease did not increase the need for initiation of dialysis with respect to medical management which in a way suggests that all patients with renal dysfunction would not be at higher risk of future renal worsening because of the intervention per se. This corroborates with our finding that almost equal number of patients in non-ACS group had worsening and improvement or no change of renal function post PCI. The argument that in mild CKD patients withholding ACEIs, using minimal contrast load and good hydration can reduce the rise in post PCI serum creatinine, is valid to a large extent. However, our study included patients with not only mild renal impairment but also advanced renal failure sometimes even needing renal replacement therapy.

Moreover, in our study baseline LVEF did not affect the procedural outcome with respect to worsening or improvement of renal function. Post PCI LVEF was not considered for outcome analysis, as often the time taken for LV function improvement is highly variable and depends on a large number of other factors. Rather alternate estimates of myocardial functional recovery could be made with gated equilibrium radionuclide angiocardiography or cardiac magnetic resonance imaging (cMRI). Also, contrast volume was not found to be associated with worsening or improvement of renal function post PCI. This may be explained by the fact that since all patients included in the study had renal dysfunction at baseline hence additional precaution were taken in all including an attempt to limit contrast volume to minimum thereby eliminating variability in contrast use during the procedure. Surprisingly though, diabetes was not found to independently predict the worsening of renal function post PCI.

4.1. Study limitations

This study has few limitations. Firstly, this is a single center, retrospective, non-randomized, observational study having cross-sectional analysis design with a small sample size. Secondly, since this is a long-drawn retrospective study spanning over 13 years therefore some degree of variability in the form of changing definition of ACS, changing practice of invasive management of CAD, protocols in use of contrast, pre-procedural use of N-acetylcysteine and hydration cannot be ruled out completely. Thirdly, patients were not followed up for long term clinical outcomes (cardiovascular or renal). Fourthly, since we did not have body weight records of all patients included in the study, therefore creatinine clearance (eGFR) was not used in the study. Lastly, data regarding completeness of revascularization in the study patients was not available for analysis. Therefore, larger multicenter studies with prospective randomized design are needed to test the hypothesis generated on larger scale.

5. Conclusion

We conclude that not all patients with impaired basal serum creatinine will show worsening in renal function post PCI and a good number of ACS patients with raised baseline serum creatinine value, often show stabilization or improvement in the serum creatinine values rather than worsening after a successful PCI.

5.1. Clinical implication

It may be more useful to intervene in recent ACS patients (<2 weeks duration) in spite of impaired renal function rather than deferring intervention on them for the fear of worsening renal function.

Author contributions

Pravin K Goel: Conceived the basic idea for the study and actively participated in the interpretation and editing of the manuscript. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

Deepti Yadav: Collected the raw data, did preliminary statistical analysis and generated crude results.

Ankit Kumar Sahu: Did advance statistical analysis, refined the results and prepared the draft of this manuscript. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

Roopali Khanna: Provided logistical support including clinical assessment during patient follow-up and assisted in the coronary revascularization procedure of the patients involved in the study.

Financial disclosure

None.

Declaration of competing interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ihj.2020.07.006.

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