Original Article

Impact of Baseline Admission Serum Creatinine Level in ST Segment Elevated Myocardial Infarction (STEMI) Patient Undergoing Primary PCI: An Important Predictor of in-hospital and 12-month Survival Outcome

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Abstract:

Key Words :
CIN, Creatinine, Primary PCI, Ischaemic heart disease

Background: *Several studies has shown that impaired renal function might be an important predictor of adverse cardiovascular events in patient with ST elevated myocardial Infarction (STEMI) undergoing primary percutaneous intervention (pPCI). Exact data on clinical impact of baseline or admission serum creatinine level of STEMI patient undergoing pPCI in our patient population not well established. Therefore, we have carried out this non-randomized study to see the effects of S. creatinine level on major adverse cardiovascular outcomes among STEMI patient undergoing pPCI.*

Methods: *Patients were enrolled in this observational non-randomized prospective cohort between November 2017-July 2019, who were presented into our emergency department with acute onset of severe chest pain or angina with ECG evidenced of acute ST elevated myocardial infarction. Total 137 patient (F 12; Male 125) were enrolled in this study.*

Results: *Out of 137 patients, female :12 (8.75%) vs Male: 125 (91.2%). Among, these patient females were more obese (BMI: Female 27.0 ± 2.2 vs   male 25.4 ± 4.9) and developed CAD in advance age (Female 59.1 ± 14.5   vs Male 53.4 ± 10.5). Among the 137 patients, 89 (65%) were dyslipidemia, 72 (52.6%) were hypertensive, Diabetic 66(48%), Smoker 70 (51%) and FH positive for CAD were 31 (22.6%). According to the involvement of myocardium infarction, STEMI diagnosis of Anterior MI were 48.9% (n=67) and Inferior MI 51.1% (n=70). An elevated serum creatinine level was defined as creatinine >1.2mg/dl. Based on baseline serum creatinine level, patients were divided into group-A and Group-B. In Group-A. Total 68 patients have S. Creatinine level <1.2 and in Group-B, 69 patients have S. Creatinine level >1.2. Anterior MI were higher in group -B patient than Group-A; Ant MI as 35 (50.4%) vs 31(45.6%), Inf MIL: 34 (49.35) vs 34 (50%), Shock 11 (15.9%) vs 6 (8.8%0, CHB 4 (5.8%) vs 4 (5.9%), Death 12 (17.4%) vs 2 (2.9%) and LVF 5(7.2%) vs 1(1.5%) with 7 days in-hospital stay after primary PCI. Territory wise involvement of vessel in Group-B patient has more involvement of LAD 35 (50.7%) and Group-A has RCA 26(38.2%).*

Conclusion: *In this present study, we found, that in acute STEMI patients, baseline higher serum creatinine level is associated with more AMI related complications and death than in lower serum creatinine level. Thus, we may conclude that baseline admission serum creatinine level may be an important predictor for both in-hospital and 12-month survival outcomes in STEMI patients undergoing pPCI.*

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Introduction:

It is well known that the contrast-induced nephropathy (CIN) is a possible complication of coronary diagnostics and interventional procedures. Its development has been associated with increased in-hospital and long-term morbidity and mortality, prolonged hospitalization, long-term renal impairment.[1-2] Chronic kidney disease (CKD) is a strong predictor for fatal and nonfatal cardiovascular events.[3] Even mildly decreased

kidney function with an estimated glomerular filtration rate (eGFR) of 60-90mL/min/1.73m2 independently predicts long-term mortality among STEMI patients undergoing primary PCI (pPCI).[4]

Primary PCI, defined as intervention in the culprit vessel within 12 hours after the onset of chest pain without previous thrombolytic or clot dissolving therapy, is the best available strategy for treatment of STEMI.[5] Increasing evidence suggested that pPCI obtains rapid restoration of coronary artery patency and increases threatened myocardial salvages, thus preserving ventricular function and improving STEMI survival outcomes.[6] STEMI Patients treated with pPCI may represents the population at higher risk of contrast induced nephropathy (CIN) than those of elective PCI. CIN is associated with marked increase in hospital morbidity and mortality, which may partially thwart the survival benefit of pPCI in patients who develop this serious renal complication.[7-8]

 CIN is defined as a relative increase in serum creatinine of > 25% or an absolute rise > 44micromol/L, this is low(<3%) in patient without renal dysfunction, but it is <50% in known renal dysfunction patients.[9-10] In case of pPCI, the risk of CIN is 10-20%.[11] In this setting of STEMI, hypotension, shock, a large volume of contrast during coronary intervention and the impossibility of starting renal prophylactic therapy might be the key factors. The impact of this factors on renal function and clinical relevance of CIN in the scenario of pPCI in STEMI patient remain unknown. Wright et al,[12] demonstrated that renal insufficiency and AMI represents a high-risk combination.

As pPCI is common practice to treat STEMI patient in our center 24/7 hrs., round the year. We don't have exact data how these group of patient papulation, may develop CIN after primary PCI if any. Therefore, we have carried out this observation non-randomized prospective study to see the effects of baseline or preprocedural admission as well as post procedural serum Creatine level on the mortality and morbidity in STEMI patient undergoing primary PCI.

Methods:
We conducted this prospective observational study, a single center based tertiary care hospital open

for 24/7 primary PCI services for STEMI patient between November 2017-July 2019. Patient were excluded if emergency cardiac surgery for STEMI related mechanical complications or Patient on long peritoneal or hemodialysis or died during PCI.

Protocol:

The diagnosis of STEMI was established by a typical history of chest pan, diagnostic ECG changes and serial ECG; elevation of cardiac biomarkers.[13] Blood samples drawn pre-PCI. Primary PCI performed in patients with ongoing symptoms <12 hrs. in duration, Complications like cardiogenic shock or need for IABP, need for emergent CABG, mechanical ventilation or heart failure episodes treated conservatively, clinically, significant arrhythmia requiring pacemaker or major bleeding requiring blood transfusion.

PCI Procedures:
 24 hr. on call interventional team performed PCI according to standard clinical practice by using standard 6F guide catheter, guide wires, balloon catheters mostly via the femoral routes or radial routes. Patient received 5000-unit bolus of heparin, followed by an additional 2000 units during the procedure. Coronary stent was performed with standard technique, contrast dose left to individual operator discretion. All patient received non-ionic low -osmoler contrast (Iopamerol). After the pPCI, patients were hydrated with IV normal saline (0.9%) for 12 hrs. and or N-Acetylcysteine. In patient with impaired or low LVEF, IV saline dose reduced to 0.5ml/kg. Patient were loaded with either Ticagrelor or clopidogrel along with Aspirin and loading and maintenance doses of gpIIb/IIIa receptor blocker abciximab.

Laboratory parameters
Serum creatinine was determined upon hospital presentation to ER with the c/o chest pain and ECG evidenced STEMI and post PCI in intensive care unit stay. Other routine biochemical tests were measured by standard analyzer at our center.

Statistical analysis
All data were summarized and displayed as mean +/- standard deviation and in percentage.

Results:
Table I. Shows the profile of studied patients in this prospective observational study. Figure 1.,

showed total 137 patients were enrolled in the study, female:12 (8.75%) vs Male: 125 (91.2%). Among, these patient females were more obese (BMI: Female 27.0 ± 2.2 vs   male 25.4 ± 4.9) and developed CAD in advance age (Female 59.1 ± 14.5 vs Male 53.4 ± 10.5). Among the 137 patients, 89 (65%) were dyslipidemia, 72 (52.6%) were hypertensive, Diabetic 66(48%), Smoker 70 (51%) and FH positive for CAD were 31 (22.6%) as shown in Figure 2.
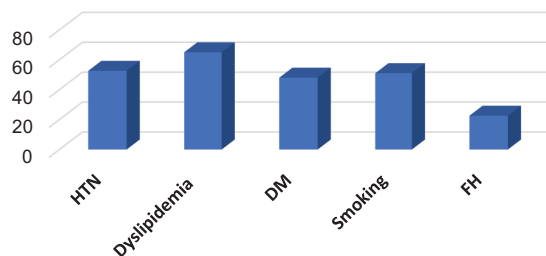
Table-I
Demographic Profile of the patients

	S. creatinine <1.2	S. Creatinine >1.2
Number	68(F9/M59)	69(F3/M66)
Age (yrs)	51.0±11.0	56.0±10.0
BMI(kg/m^2)	27.0±2.9	25.0±5.8
SBP(mmHg)	123.0±23.0	120.0±21.0
DBP(mmHg)	76.0±12.0	74.0±9.6
No. of CAD Risk Factor	3.1±1.0	3.1±1.0

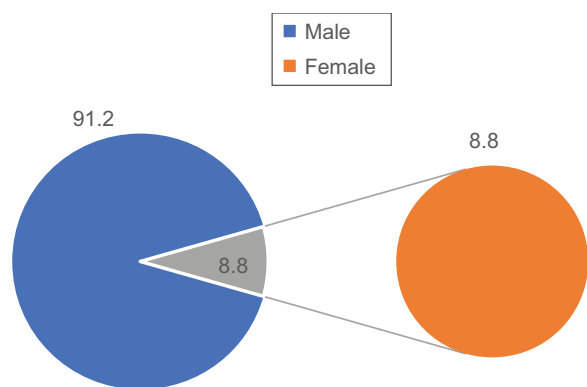# Data were presented as Mean ± SD

Fig.-1: *Percentage Distribution of Male and Female*

Table-II
Chest pain, Door to Balloon time and S. Trop – I levels

	S. creatinine <1.2	S. Creatinine >1.2
Duration of Chest Pain (min)	124.4±56.9	113.2±57.9
Door-to- balloon time (min)	51.6±14.9	50.6±20.2
S. Troponin-I level	2.7±5.6	3.5±5.4
LVEF (%)	43±6.1	43±5.7

Data were presented as Mean ± SD

Fig.-2: *Percentage distribution of CAD Risk factors*
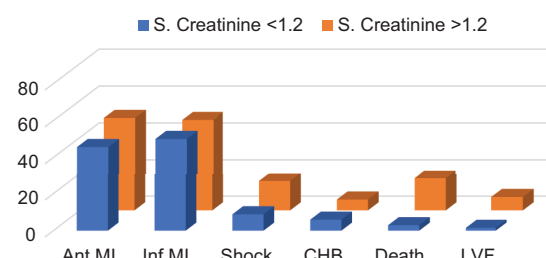

Fig.-3: *Percentage distribution of Clinical Scenario between the two group*

According to the involvement of myocardium infarction, STEMI diagnosis of Anterior MI were 48.9% (n=67) and Inferior MI 51.1% (n=70). Table. II has shown the Chest pain, Door to Balloon time and S. Trop – I levels. An elevated serum creatinine level was defined as creatinine >1.2mg/ dl. Based on baseline serum creatinine level, patient was divided into group-A and Group-B. In Group-A, total 68 patients have S. Creatinine level <1.2mg/dl and in Group-B, 69 patients have S. Creatinine level >1.2 mg/dl.

Table-III
Average size of Stent

	S. creatinine <1.2	S. Creatinine >1.2
Stent diam(mm)	3.1±0.4	3.0±0.4
Length (mm)	27.4±8.4	26.3±8.6

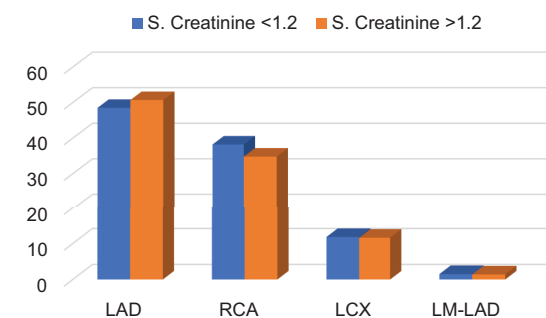# Data were presented as Mean ± SD

Fig.-4: *Territory wise Percentage distribution of vessel in the studied population.*

As shown in Figure 3, the Percentage distribution of Clinical scenario between the two group. Anterior MI, Shock, LVF and death were higher in group -B patient than Group-A; Ant MI as 35 (50.4%) vs 31(45.6%), Inf MI: 34 (49.35) vs 34 (50%), Shock 11 (15.9%) vs 6 (8.8%), CHB 4 (5.8%) vs 4 (5.9%), Death 12 (17.4%) vs 2 (2.9%) and LVF 5(7.2%) vs 1(1.5%) within 7 days in-hospital stay after primary PCI. As shown in Figure 4, territory wise involvement of vessel in Group-B patient has more involvement of LAD 35 (50.7%) and Group A has RCA 26(38.2%). Total 153 stents were deployed in 137 vessels. Table III. shows the average length and diameter of the stents used. Figure 5 showed the Percentage Distribution of various stents. Figure 6 has shown the percentage distribution of total Vessel and stents. Table IV. Shows the Baseline admission S. Creatinine level and amount of contrast used. We did not find any gross increase of S. creatinine level after primary PCI. Table V. Shows the Biochemical parameters of the studied population.

Table-IV
Baseline admission S. Creatinine level and amount of contrast used

	S. creatinine <1.2	S. Creatinine >1.2
S. Creatinine	1.02±0.11	1.5±0.4
Contrast (ml)	86.2±15.3	85.4±15.4

Data were presented as Mean ± SD

Table V
Biochemical parameters of the studied population

	S. creatinine <1.2	S. Creatinine >1.2
Blood Sugar	8.8±3.8	11.7±12.9
HbA1C	7.7±2.1	7.5±1.7
TC mg/dl	182.0±62.0	171.0±61.0
TG mg/dl	187.0±135.0	157.0±183.0
HDL mg/dl	34.0±9.3	35.0±9.1
LDL mg/dl	113.0±50.0	112.0±61.8
Athero index	5.3±2.3	5.3±1.9

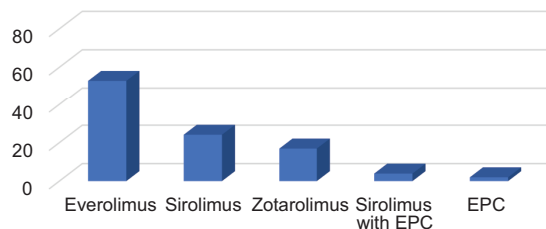# Data were presented as Mean ± SD

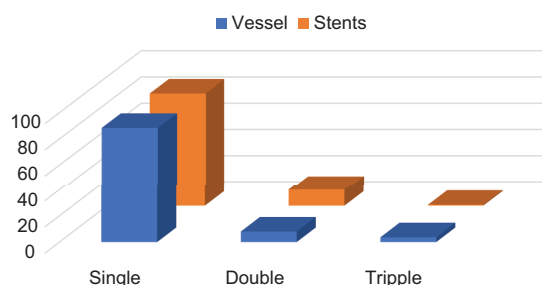**Fig.-5:** *Percentage Distribution of various stents*

Fig.-6: *Percentage distribution of total Vessel and stents*

Discussion:
Impaired renal function has been established as a significant and independent predictor of adverse cardiovascular events among patient with STEMI treated by primary PCI.[14] There have been limited studies that investigated the role of admission Serum Creatinine on major adverse clinical events in patients with STEMI. Recent studies have demonstrated a positive correlation between decreased eGFR and increased risk of atherosclerosis and reduced left ventricular ejection fraction. These studies found that patients with eGFR <60mL/min/1.73 m^2 had a 7-8-fold higher mortality as compared to patients with an eGFR:>60mL/min/1.73m^2.[15-16]

Very recently, Poornima et al,[17] has shown that in the setting of STEMI, elevated serum creatine and eGFR <60mL/min/1.73m^2 was associated with an increased risk of developing major adverse events including cardiogenic shock, bleeding and heart failure.

Data of STEMI patient's Serum creatinine level and subsequent complications is not well understood in our patient perspectives. Therefore, we have carried out this observation prospective study. Based on baseline serum creatinine level, patient was divided into group-A and Group-B. In Group-A. Total 68 patients have S. Creatinine level <1.2 mg/dl and in Group-B, 69 patients have S.

Creatinine level >1.2 mg/dl. Group B patients are older and having higher FBS, S. Creatinine level and high baseline S. Troponin-I. Duration of chest pain were more in Group A patient than Group B, possibly the group B patient developed post STEMI complication earlier than Group A and were brought to ER. Door to Balloon time was almost same in both groups as our Cath lab is having 24 hours primary PCI team available on site. Average stent size was almost same in both groups. Total 153 stents were deployed in 137 vessels of 137 STEMI patients. Average smaller diameter stents in both group of patients indicating the small size coronary artery in this part of world.

Male are more frequent to developed STEMI and Dyslipidemia may be one of the important CAD risk factors followed by DM, HTN, FH and Smoking. LAD is the most affected vessel in both group and were more in Group B. STEMI and its associated complications including, Shock, CHB, LVF and Death were more observed in patient with higher baseline S. Creatinine group B patients.

Contrast induced nephropathy (CIN) is a well-known and important side effects of contrast media during performing CAG or PCI. Usually CIN develops within 2 to3 days with a peak in serum creatinine level 3-5 days after contrast exposure and normalizes within 7 to 10 days after contrast exposure. However, impaired renal function may persist after primary PCI in half of the STEMI patient with CIN.[18] The effect of contrast media on renal function is complex. Initially, a reduction of GFR occurs because of changes of intrarenal and systemic regulatory mechanisms.[19]

Endothelial dysfunction, erythrocyte aggregation with increased viscosity and a decrease erythrocyte velocity are followed by a decrease oxygen tension together with a directly toxic effect on the tubular apparatus contributing to the reduction in renal function.[20] Previous studies showed that patient with renal insufficiency were at increased risk for both cardiovascular disease and adverse cardiovascular outcomes.[21-22]

Patient particularly on dialysis with AMI are thought to have high mortality from cardiac causes and poor long-term survival. Renal insufficiency, measured as corrected creatinine clearance, blood urea nitrogen and serum creatinine clearance,

blood urea nitrogen or serum creatinine level has found to be independent predictor of survival in patients with acute coronary syndrome.[23]

In general, patients with normal renal function and no risk factors, a transient increase in serum creatinine in general is spontaneously normalized.[24] But, in known reduced renal function or renal risk factors where a permanent reduction in renal function with poorer prognosis may be consequences.[25] To avoid all these, reduce contrast dose as much as possible, optimal hydration before and after pPCI by intravenous normal saline.[26] Patients treated for STEMI with pPCI are more often exposed to contrast without preexisting knowledge of renal function, and the patients are in different conditions of hydration

Yamaguchi et al,[27] showed that serum creatinine level on admission in patients with AMI predicts long term mortality. Conditions that heighten the risk of CIN such as chronic kidney disease, diabetes, congestive heart failure, hemodynamic instability and anemia are typically not modifiable at the time of emergency catheterization, but other strategies have emerged to minimize the nephrotoxicity of contrast media.[28] Among these, the proven effective preventive measures against CIN in PCI patients includes hydration with normal saline and minimize contrast volume (CV).[29] The benefits of N acetylcysteine or isotonic sodium bicarbonate remains controversial.[30] Thayssen et al.[31],has demonstrated that NAC or NaHCO3 did not reduce the rate of acute CIN significantly. But, combined treatment with these two may reduce the risk of renal dysfunction after 30 days.

In the current study, patients of both group A and Group B, S creatinine level were not changed much in subsequent sample after PCI, as we minimize the total uses of contrast volume in both group of patients. Serum creatinine level in group-A were; Pre-PCI (1.02±0.12): Post-PCI (1.06±0.18) and in Group-B Pre-PCI (1.5±0.4); Post-PCI (1.56±0.9). In both group Pre and Post-PCI, S. Creatinine level was not changed much, possibly due to average uses of contrast <80ml in this selected group of patients. Patients were doing well at 12 months after PCI and regularly followed up into our OPD and none of them developed CIN. Pre-treatment with Statin before admission for primary PCI, might have impact to reduce CIN as stated

elsewhere.[32] In addition, we found that the admission blood glucose level was higher in group-B patients (S. Creatinine >1.2), indicating that DM is an important predictor of renal impairment in these group of patient and carries risk for MI associated complications.

Patients with STEMI who are not undergoing primary PCI, may also have acute worsening of renal function with the same prognostic implication as for CIN [24], which suggest that acute kidney injury may results from hemodynamic compromise rather than from CIN per se. In addition, pPCI in STEMI patients may require a larger amount of contrast. Thus, an optimal procedural result should be carefully weighed against risk for CIN. The association of contrast volume, as an absolute and a weight- and creatinine-adjusted value; CIN incidence; and clinical outcome in the setting of pPCI remain unknown in our patient population.

Conflict of Interest - None.

Conclusion:
It has been well documented that STEMI patient who underwent primary PCI to treat the infarcted artery with the reestablishment of coronary flow, thus to provide better myocardial salvage, are in high risk of development of Contrast induced nephropathy and increases the morbidity and mortality in this subset of patient population. Many of the patient are not known about their creatinine status prior lifesaving primary PCI and later, who might develop CIN. [7] Therefore, effective CIN prevention strategy may further improve the clinical outcome of STEMI patients who receive primary PCI. Also, we should keep in mind that the development of early acute kidney injury may associate worse outcome, even renal function comes to baseline level, patients with early AKI tended to be high risk of mortality.[33] Potential preventive strategies include protecting kidney from contrast-or ischemic -induced injury and limiting the amount of contrast administered. Some of the studies with antioxidant agents N-acetylcysteine have promising result [8] to reduce CIN after pPCI when uses with sodium bicarbonate. [34] Some of the author demonstrated that simple hydration or IV normal saline before and after the procedure, can better prevent CIN in pPCI of STEMI patient.

In this present study, we found, that baseline higher serum creatinine level of acute STEMI patients at presentation to our ER, is associated with more AMI related complications and death than in lower serum creatinine level. Zhao et al, [35] has shown that the Elevated admission serum creatinine was an independent predictor of poor myocardial perfusion and a higher rate of 1-year mortality in STEMI patients undergoing primary PCI. Our present study was very much consistent with Zhao et al, results. Thus, we may conclude that baseline serum creatinine level may be an important predictor for both in-hospital and 12-month survival outcomes in STEMI patients undergoing pPCI. In addition,

Post-PCI serum creatinine level may not change much or remain same as of pre-PCI level because of reduced and controlled uses of contrast and hydration with normal saline along with N-Acetylcysteine. Therefore, we may recommend limiting the amount of contrast uses as low as possible, especially in primary PCI of STEMI patients.

Future perspectives:
Acute ST elevated myocardial infarction (STEMI) is a leading cause of death in our patient population, that needs immediate intervention to reestablish blood flow through the occluded vessel and preserve better myocardial salvages. Now, a day's very few centers doing pPCI. At our center, we are doing pPCI round the clock in 365 days. We found that patient with higher baseline hospital admission creatinine has more complications after pPCI. Hence, recommend involving more center to form a common guideline in assessing the patients and comorbidities, uses of contrast amounts which can lead to potential hazardous CIN and thus increase pPCI related mortality and morbidity in STEMI patient.

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