

In-Hospital Mortality of Acute Myocardial Infarction in Patients with and Without Renal Dysfunction

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Objective: To compare in-hospital mortality of acute myocardial Infarction in patients having normal renal functions with renal dysfunction patients. **Setting:** Emergency ward, Coronary care units and cardiology wards of the Punjab Institute of Cardiology Lahore. **Study design:** It was a comparative study. **Sample size:** 1000 consecutive patients presenting with acute myocardial infarction admitted to the Punjab Institute of cardiology Lahore were studied from 1st March 2004 to 15th August 2004. **Results:** After fulfilling the inclusion criteria 1000 patients were studied. The mean age of the study population was 60.8±9.38 years. Total number of males in the study population was 642(64.2%) while female patients were 358(35.8%). Patients with any degree of renal dysfunction, except those with end-stage renal disease were more likely to present with anterior MI than were patients without renal dysfunction. Patients with end-stage renal disease and more severe renal dysfunction were more likely to develop heart failure during hospitalization, to experience atrial fibrillation, and to have mechanical complications. Streptokinase therapy was used less frequently in patients with any degree of renal dysfunction than in patients without renal dysfunction, despite a similar incidence of MI. In-hospital mortality was 51(12%) in Group I patients, 46(16.6%) in Group II patients, 36(22%) in Group III patients, 35(27.7%) in Group IV patients and 5(35.7%) in Group V patients with a p value of <0.0001. Severe renal insufficiency had the maximum in-hospital mortality with OR of 5.4 and 95% confidence interval of 2.9-10.3 followed by end stage renal disease OR 5.1 (CI 2.2-12.1), moderate renal insufficiency OR 4.1 (CI 2.3-7.2) and mild renal insufficiency OR 1.9(CI 1.1-3.1) with a p value of <0.0001. Similarly congestive heart failure during hospital stay was observed in 20(4.7%) patients in Group I, 17(6.1%) patients in Group II, 15(9.4%) patients in Group III, 16(12.6%) patients in Group IV and 4(28.6%) patients in Group V. Similar trends were observed in mechanical complications and post myocardial arrhythmias in the study population. **Conclusion:** Patients with renal dysfunction who have acute MI are a high-risk population and suffer from increased mortality once they are admitted to the hospital. This is because of presence of more risk factors in this sub set of patients. **Key words:** Acute myocardial infarction, renal failure, in-hospital mortality, mechanical complications.

Acute myocardial infarction continues to be a major public health problem in the developed world, despite revolutionary achievements in diagnosis and management over the last three decades¹⁻². In the United States nearly 1.5 million patients annually suffer from acute myocardial infarction³. Although the death rate from acute myocardial infarction has declined by about 30 percent over the last decade, its development is still a fatal event in approximately one third of patients³.

Patients with end-stage renal disease have increased cardiovascular death and morbidity⁴⁻¹³. In the United States, approximately 44% of all deaths can be attributed to cardiovascular disease⁷ and more than one in five cardiac deaths can be attributed to acute myocardial infarction⁵.

Patients with end-stage renal disease who require maintenance dialysis have markedly increased mortality after myocardial infarction compared with other patients¹⁴. In a recent study in-hospital mortality rates were 30% in these patients as compared to 2% in patients with normal renal function⁴.

After acute myocardial infarction end-stage renal disease patients are less likely than normal patients to receive aggressive therapy, such as thrombolytic therapy, Aspirin, Beta blockers and Angiotensin Converting Enzyme Inhibitors¹⁶.

In Pakistan mortality of a cute myocardial infarction has been studied previously¹⁷⁻¹⁹ but little data is available about prognosis of patients with acute myocardial infarction having end-stage renal disease. Patients with renal insufficiency have a greater risk for cardiovascular disease events, but the association between mild and moderate renal insufficiency and survival after myocardial infarction has not been evaluated in-depth previously. This study was designed to compare the in-hospital mortality of acute myocardial infarction in patients with and without renal insufficiency.

Materials and methods:

After fulfilling the inclusion criteria 1000 consecutive patients presenting with acute myocardial infarction admitted to the Punjab Institute of Cardiology Lahore from 1st March 2004 to 15th August 2004 were studied.

Patients presenting with a cute myocardial infarction were included in the study on the basis of presence of any two of the following criteria.

- 1) Chest pain consistent with acute myocardial infarction.
- 2) Electrocardiographic changes i.e. ST-Segment elevation >0.2 mv in at least two contiguous chest leads or >0.1 mv in at least two contiguous limb leads.
- 3) New or presumably New Left Bundle Branch Block on electrocardiogram.

4) Raised levels of cardiac enzyme CK-MB, (more than double the reference value).

Patients having Non ST elevation myocardial infarction were excluded from the study.

A full history was taken particularly age, sex, occupation, address, history of smoking, diabetes mellitus, hypertension, ischemic heart disease and family history of ischemic heart disease were inquired. Location of acute MI was classified as anterior, inferior, or other. Time of initial presentation was defined as the time of arrival at the hospital. Primary reperfusion therapy was defined as use of intravenous streptokinase therapy. The use of adjunctive therapy during hospitalization was recorded. Killip classification was defined at admission.²⁰ Renal function was estimated according to a calculated creatinine clearance derived from creatinine concentration at admission by using the Cockcroft-Gault formula²¹.

$$\text{Creatinine Clearance} = \frac{140 - \text{age (in years)} \times \text{body weight (in Kilograms)} \times 72 (\text{in men})}{\text{Serum Creatinine}}$$

$$\text{Creatinine Clearance} = \frac{140 - \text{age (years)} \times \text{body weight (in Kilograms)} \times 0.85 (\text{in women})}{\text{Serum Creatinine}}$$

Patients were then divided into five groups according to creatinine clearance.

- Group 1 Patients with normal renal function
- Group 2 Patients with mild renal insufficiency.
- Group 3 Patients with moderate renal insufficiency.
- Group 4 Patients with severe renal insufficiency.
- Group 5 Patients with end-stage renal disease.

Major complications of acute MI were identified by documentation of death, mechanical complications, ischemic complications, or electrical complications. Death was classified as in-hospital (death before discharge during a patient's admission to the hospital. Mechanical complications included cardiac tamponade, acute ventricular septal defect, papillary muscle rupture, or free-wall rupture. Ischemic complications included recurrent MI, cardiogenic shock, or congestive heart failure, and electrical complications included cardiac arrest, electromechanical dissociation, or ventricular arrhythmia. Laboratory tests like CK-MB levels, S Creatinine level, Urea level, Serum Sodium and Potassium levels and Random blood sugar level were documented for all patients. Baseline weight of all patients was done. All patients were treated according to the treatment protocol of the Cardiology Unit. Patients were followed up daily and pulse, blood pressure, ECG changes and complications if any were monitored till death or discharge of the patient.

Operational definitions:

1. Renal dysfunction:

- 1) Patients having Serum Creatinine \leq 1 mg/dl were considered as normal.
- 2) Patients having Serum Creatinine \geq 1 mg/dl were further classified into mild, moderate and severe renal

dysfunction by calculating Creatinine clearance derived from Creatinine concentration, body weight, age and gender of the patient by using the Cockcroft-Gault formula²¹.

2. **Mild renal insufficiency:** Creatinine clearance >0.84 ml/sec (>50 ml/min) but ≤ 1.25 ml/sec (≤ 75 ml/min).

3. **Moderate renal insufficiency:** Creatinine clearance ≥ 0.59 ml/sec (>35 ml/min) but ≤ 0.84 ml/sec (≤ 50 ml/min).

4. **Severe renal insufficiency:** Creatinine clearance <0.59 ml/sec (<35 ml/min)

5. **End-stage renal disease:** Patients on maintenance hemodialysis.

6. Killip Classification:

Class I: No evidence of Heart Failure

Class II: Presence of third Heart Sound and Crackles on both bases of Lungs

Class III: Presence of third Heart Sound and chest full of Crackles on both sides

Killip IV: Presence of third Heart Sound and Cardiogenic Shock

Statistical analysis: All the data were analyzed by SPSS (Statistical Package for Social Sciences) Version 10.0 for Windows. In-hospital mortality for different groups was compared using Chi-square test and p values were calculated. P value less than 0.05 was taken as significant. All tests applied were two tailed. In order to assess the impact of various confounding factors (ESRD, Severe Renal Insufficiency, Moderate Renal Insufficiency, Mild Renal Insufficiency, Mechanical Complications i.e. Killip Class >1 and CHF, Diabetes mellitus and Female sex) on in-hospital mortality multiple logistic regression was applied and Odds Ratios were calculated.

Results:

Baseline Characteristics After fulfilling the inclusion criteria 1000 patients were studied at Punjab Institute of Cardiology, Lahore. Group I was the largest group which consisted of 424 (42.4%) patients; these were the patients who had normal renal functions. Group II consisted of 277 (27.7%) patients, Group III 159 (15.9%) patients, Group IV 126 (12.6%) patients and Group V consisted of 14 (0.14%) patients. (Fig 1)

The mean age of the study population was 60.8 ± 9.38 years. Mean age of Group I patients was 50.65 ± 4.31 years, Group II patients was 61.45 ± 3.75 years, Group III patients was 65.3 ± 5.43 years, Group IV patients was 63.8 ± 4.7 years and mean age of Group V patients was 68.21 ± 3.54 years. It was noted that patients in end stage disease group (Group V) were older at the time of presentation than patients in other groups.

Total number of males in the study population was 642 (64.2%) while female patients were 358 (35.8%). Group I consisted of 339 (80%) male patients and 85 (20%) females, Group II 168 (60.64%) males and 109 (39.35%) females, Group III 75 (47.16%) males and 84 (53.8%) females, Group IV 52 (41.6%) males and 74 (61.9%) females,

females and group V consisted of 8(57%) males and 6(42.8%) female patients. Patients with any degree of renal dysfunction were older, were more likely to be women, and had more cardiovascular comorbid conditions than those without renal dysfunction (Table 1). In group I 102(24.5%) patients were diabetic and there was an increasing trend towards diabetes with advanced renal disease as in Group V 6(42.8%) patients were diabetic. Similarly 142(35%) patients were hypertensives in Group I, 134(48.4%) patients in Group II, 93(58.4%) in Group III, 84(66.6%) in Group IV and 9(64.28%) patients in Group V.

No difference was observed in the prevalence of MI related to ST-segment elevation. Patients with any degree of renal dysfunction, except those with end-stage renal disease were more likely to present with anterior MI than were patients without renal dysfunction. Patients with any degree of renal dysfunction were more likely to present with symptoms of heart failure (Killip class > I); incidence of such symptoms was highest in patients with end-stage renal disease. Patients with end-stage renal disease and more severe renal dysfunction were more likely to develop heart failure during hospitalization, to experience atrial fibrillation, and to have mechanical complications.

Treatment strategies: Streptokinase therapy was used less frequently in patients with any degree of renal dysfunction than in patients without renal dysfunction, despite a similar incidence of MI with ST-segment elevation (Table 2). Patients with any degree of renal dysfunction were more likely to have contraindications to reperfusion therapy than those without renal dysfunction. The use of aspirin, β-blockers, and intravenous heparin during the first 24 hours of hospitalization was less

frequent in patients with end-stage renal disease and moderate to severe renal dysfunction.

Outcome data: In-hospital mortality rates increased with worsened renal function. (Table 3)

In-hospital mortality was 51(12%) in Group I patients, 46(16.6%) in Group II patients, 36(22%) in Group III patients, 35(27.7%) in Group IV patients and 5(35.7%) in Group V patients with a p value of <0.0001. Similarly congestive heart failure during hospital stay was observed in 20(4.7%) patients in Group I, 17(6.1%) patients in Group II, 15(9.4%) patients in Group III, 16(12.6%) patients in Group IV and 4(28.6%) patients in Group V. Similar trends were observed in mechanical complications and post myocardial arrhythmias in the study population.

Predictors of survival: As far as in-hospital mortality is concerned, predictors of death were endstage renal disease, severe renal dysfunction, and moderate renal dysfunction, along with mechanical complications, congestive heart failure on admission (Killip class > I), congestive heart failure during hospitalization, diabetes, and advanced age (Table 4). Female sex was associated with reduced risk for in-hospital death with Odds Ratio of 0.7(0.5-1.5)

In order to assess the impact of various confounding factors on in-hospital mortality multiple logistic regression was applied and Odds Ratios were calculated. Severe Renal insufficiency had the maximum OR of 5.4 with in-hospital mortality and 95% Confidence Interval of (2.9-10.3) followed by End stage renal disease 5.1(2.2-12.1), moderate renal insufficiency 4.1(2.3-7.2) and mild renal insufficiency 1.9(1.1-3.1) all these were having a p value of <0.0001. Mechanical complications, killip class, congestive heart failure and diabetes were also significantly associated with in-hospital mortality. (Table 4).

Table 1: . Baseline characteristics.

Characteristics	Group I (n=424)	Group II (n=277)	Group III (n=159)	Group IV (n=126)	Group V (n=14)	p value
Age mean years	50.65±4.31	61.45±3.76	65.3±5.43	63.8±4.7	68.21±3.54	
Male	339(80%)	168(60.64%)	75(47.16%)	52(41.3%)	8(57%)	<0.0001
Female	85(20%)	109(39.35%)	84(52.8%)	74(61.9%)	6(42.8%)	<0.0001
Diabetes	102(24.05%)	79(28.5%)	48(30%)	41(32.5)	6(42.8%)	<0.0001
Smoking	252(59.4%)	136(49%)	85(53.45%)	52(41.26%)	8(57%)	<0.0001
Hypertension	142(33%)	134(48.4%)	93(58.4%)	84(66.6%)	9(64.28%)	<0.0001
Dyslipidemia	178(41%)	118(42.6%)	67(42%)	58(46%)	6(42.8%)	<0.0001
F/H of IHD	71(16.7%)	60(21.6%)	45(28.3%)	38(30.15%)	5(35.7%)	<0.0001

Table 2. Presentation characteristics.

Characteristics	Group I (n=424)	Group II (n=277)	Group III (n=159)	Group IV (n=126)	Group V (n=14)	p value
Site of MI						
Anterior wall	214(50.5%)	141(51%)	84(52.8%)	69(54.7%)	8(57%)	0.043
Inferior wall	178(41%)	118(42.6%)	60(37.73%)	41(32.5%)	4(28.6%)	0.205
Others	37(8.7%)	17(6.1%)	15(9.43%)	16(12.6%)	2(14.3%)	0.051
Killip Class >I	54(12.73%)	60(21.6%)	48(30%)	52(41.26%)	9(64%)	<0.0001
Streptokinase	246(58%)	140(50%)	78(49%)	52(41.26%)	4(28.6%)	<0.0001

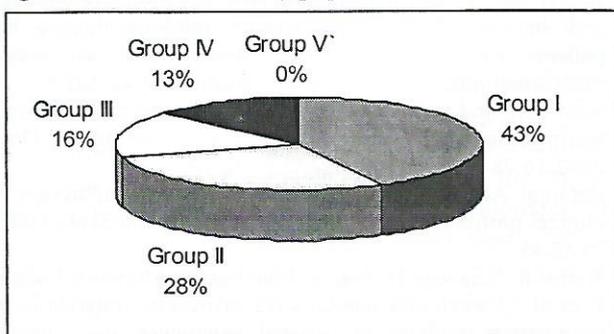
Table 3. In-hospital outcome.

Variables	Group I (n=424)	Group II (n=277)	Group III (n=159)	Group IV (n=126)	Group V (n=14)	p value
CHF during hospital stay	20(4.7%)	17(6.1%)	15(9.4%)	16(12.6%)	4(28.6%)	<0.001
Mechanical complications	9(2.12%)	7(2.6%)	5(3.14%)	7(5.53%)	1(7.14%)	<0.066
Arrhythmias	5(1.17%)	12(4.3%)	7(5%)	5(4%)	1(7.14%)	<0.001
In-hospital mortality	51(12%)	46(16.6%)	36(22%)	35(27.7%)	5(35.7%)	<0.0001

Table 4. Predictors of outcome.

Multiple Logistic Regression Results	In-hospital mortality	
	OR (95% CI)	p value
ESRD	5.1(2.2-12.1)	<0.001
Severe Renal Insufficiency	5.4(2.9-10.3)	<0.001
Moderate Renal Insufficiency	4.1(2.3-7.2)	<0.001
Mild Renal Insufficiency	1.9(1.1-3.1)	0.017
Mechanical Complication	2.9(1.5-5.3)	<0.001
Killip Class >1	2.7(2.0-3.7)	<0.001
CHF	1.7(1.1-2.8)	0.021
Diabetes mellitus	1.4(1.0-1.9)	0.062
Female vs male	0.7(0.5-1.5)	0.012

Fig 1. Distribution of study population in groups



Discussion:

Acute myocardial infarction is a major cause of death in the modern world. Patients with renal dysfunction have an increased risk of cardiovascular death and morbidity following an acute myocardial infarction. Patients with end stage renal disease on maintenance dialysis have markedly increased mortality after acute myocardial infarction compared with other patients. After acute myocardial infarction, end stage renal disease patients are less likely than normal patients to receive aggressive therapy such as thrombolytic therapy, aspirin, beta blockers and angiotensin converting enzyme inhibitor therapy.

The observations of the current study are consistent with previously published reports demonstrating increased mortality from acute MI in patients with end-stage renal disease^{5,6} and renal failure^{11,13}. The work done by Beattie et al¹³ demonstrates that the increased gradient of risk is present even in mild renal dysfunction and that patients with renal dysfunction develop more acute MI-related complications, including arrhythmias, congestive heart failure and mechanical complications. Previous work has demonstrated the influence of advanced age, sex, congestive heart failure, and diabetes as important

predictors of survival in patients with end-stage renal disease and acute MI.^{5,6} We confirm those observations in Asian population and demonstrate the association of other comorbid conditions with survival. Our data also indicates that established, aggressive modern reperfusion^{5,6,13} and adjunctive medical therapies are not used frequently in patients with renal dysfunction. The patients who received such treatments appeared to fare better. Taken together, previous work^{5,6,11-13} and current study observations underscore the poor prognosis of patients with end-stage renal disease and any degree of chronic renal insufficiency who have acute MI⁵⁻¹³.

Impact of treatment strategies: Current study also considers the impact of treatment. As in previous work^{8,13}, our data demonstrates that acute reperfusion therapy is used less frequently in patients with end-stage renal disease who develop acute MI. Others have noted statistically significantly less use of β -blockers, aspirin, and ACE inhibitors in patients with end-stage renal disease despite increased prevalence of hypertension, congestive heart failure, and coronary artery disease in this group.¹³ Current study extends these observations to patients with mild and moderate renal failure, suggesting gradients of increased risk and less aggressive care that parallel the degree of renal dysfunction.

Reperfusion therapy: Previous studies have examined the use of reperfusion therapy in patients with end-stage renal disease and renal failure who have acute MI.^{5,6,13} In current study it was observed that reperfusion therapy, when administered, was associated with improved survival. One potential mechanism for this association may have been improved left ventricular function, which has translated over the long term into improved survival in previous studies of patients without renal failure.²²⁻²³ In our study, many patients with renal failure had relative contraindications to intravenous streptokinase therapy, a

common occurrence in clinical practice. Preferential use of primary percutaneous coronary intervention for reperfusion in patients with acute MI and renal failure may reduce the risk of hemorrhagic complications but may also lead to contrast-induced worsening of renal function and volume overload. The current data suggests an association between reduced use of acute reperfusion therapy in these patients and poor long-term survival and highlights the need for different approaches to management.

Conclusion:

Patients with renal dysfunction who have acute MI are a high-risk population and suffer from increased mortality as compared to patients with normal renal function. This is because of presence of more risk factors in this sub set of patients. Furthermore they are treated less aggressively consequent to presence of contraindications to aggressive therapies.

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