DIABETES MELLITUS AND CONCURRENT RENAL INSUFFICIENCY AS PROGNOSTIC INDICATORS FOR ACUTE MYOCARDIAL INFARCTION.

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Abstract

Background:

Prognostic factors for acute myocardial infarction include diabetes mellitus and renal im- pairment (AMI). Few studies, meanwhile, have examined the impact of renal insufficiency in the setting of diabetes and AMI. Here, we looked into the clinical outcomes for individuals with AMI who also had renal impairment and diabetes mellitus.

Method:

400 AMI patients (62±12 years;71% men) were included in this study from March 2022 to February 2023 and divided into 4 groups as follows: Group I (n = 100) did not have either diabetes or renal insufficiency (glomerular filtration rate [GFR] 50 ml/min/1.72m2), Group II (n = 100) did not have either condition, Group III (n = 100) did not have either condition but did have renal insufficiency, and Group IV (n = 100) did. Major adverse cardiac events (MACE), which included a composite of all causes of mortality, myocardial infarction, target lesion revascularization, and coronary artery bypass graft after one year of clinical follow-up, were the main objectives.

Results:

180 (18.1%) patients experienced the primary objectives. In terms of composite MACE, there were differences between the 4 groups that were statistically significant (Group I: 12.4%; Group II: 15.6%; Group III: 30.4%; Group IV: 36.6%; p <0.002). The 12-month mortality increased stepwise from Group III to IV as compared with Group I in a Cox proportional hazards model after multiple covariates were taken into account (hazard ratio [HR], 1.95; 95% confidence interval [CI], 1.33-2.85; p = 0.002; and HR, 2.41; 95% CI, 1.61-3.61; p <0.002, respectively). However, Kaplan-Meier analysis found no significant difference between Group III and IV in the chance of mortality at 1 year (p = 0.287).

Conclusion:

Composite MACE is linked to renal insufficiency, particularly in conjunction with diabetes, and implies a bad prognosis in individuals with AMI. Patients with diabetes and/or renal insufficiency are classified, which is useful data for early risk stratification of AMI patients.

Keywords: renal insufficiency, diabetes mellitus, severe adverse cardiac events, acute myocardial infarction, Submitted: 2023-06-13 Accepted: 2023-06-20

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1. Introduction:

Patients with cardiovascular illness may be at risk for poor long- term prognosis due to cer-

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tain circumstances. Acute myocardial infarction (AMI) cardiovascular complications can be significantly increased by any level of underlying renal impairment [1, 2]. End-stage renal disease (ESRD) has a 1-year mortality rate after AMI of about 60% [3], and renal dysfunction has been reported to be independently predictive of death after admission for acute coronary syndrome [4,5]. These findings show that patients with renal dysfunction have a higher risk of subsequent cardiovascular events than subjects with normal renal function [6,7]. Despite the impending concerns, it is yet unknown howrenal failure contributes to cardiovascular disease.

Worldwide, the incidence of diabetes mellitus has quickly risen. Surprisingly, diabetes mellitus is a recognized risk factor for cardiovascular occurrences such myocardial infarction and cardiovascular death (similar to coronary artery disease) [8,9]. According to the Global Registry of Acute Coronary Events (GRACE), a sizable prospective international registry, individ- uals with diabetes with the acute coronary syndrome have an in-hospital death rate that is about twice as high as patients without diabetes. Furthermore, diabetes has been proposed as a significant independent risk factor for acute coronary syndrome in a recent study [11].

Thus, patients with AMI may have a poor prognosis if they have both diabetes mellitus and renal impairment, either alone or together. There is a paucity of knowledge on the role of renal insufficiency and its relationship with diabetes mellitus in the context of AMI, despite various studies investigating mortality in the presence or absence of diabetes and renal insufficiency following AMI [12,13].

The current study aimed to examine the clinical outcome in individuals with AMI who also had renal impairment and diabetes mellitus.

2. Methods:

2.1. *Patient population and study structure:*

The participants in the study were patients at Patna Medical College & Hospital, Patna from March 2022 to February 2023. Retrospective cohort analysis of 400 patients with the discharge diagnosis of AMI based on clinical symptoms, cardiac enzyme levels, and 10-lead ECG (mean age± SD, 62± 12 years; 71% men) [14]. Patients who were available to determine estimated GFR were included in this investigation. Patients with a primary malignancy were not included. The patients were all followed up for at least 12 months. Each participating institution's ethical committee gave its approval to the study protocol, and all patients received information regarding their participation in the registry.

All patients were divided into 4 groups for ease of analy- sis and presentation based on the presence of diabetes melli- tus and renal insufficiency (glomerular filtration rate [GFR] 50 ml/min/1.72 m2). Group I (n = 100) had neither diabetes melli- tus nor renal insufficiency (GFR 50 ml/min/1.72 m2);Group II (n = 100) had neither renal insufficiency nor diabetes mellitus; Group III (n = 100) did not have either condition; or Group IV (n

= 100) had both conditions.

2.2. *Evaluation of renal function:*

According to the Modification of Diet in Renal Disease (MDRD),

[15] model, renal insufficiency was defined as an estimated GFR of less than 50 ml/min/1.72 m2, taking into account age, ethnic- ity, sex, and serum creatinine: GFR, expressed in ml/min per M2, is equal to 1 86 (serum creatinine [ml/ min] -1 153 (age 0.202 (0.741 [for women]). Using Olympus 5431 equipment, the alkaline picrate technique was used to assess serum creatinine levels. Prior to angiography, the level of creatinine was deter- mined, and renal function was evaluated using an estimated GFR.

2.3. *The objective of the study:*

The main objectives were major adverse cardiac events (MACE) throughout the 12-month clinical follow-up, comprising a com- posite of all cause-of-death, myocardial infarction, target lesion revascularization, and coronary artery bypass graft. Any revas- cularization of the target lesion

resulting from restenosis or reoc- clusion inside the stent or along its 4-mm perimeter was referred to as target lesion revascularization.

2.4. Statistical evaluation:

Categorical variables are reported as the number of cases and percentages, whereas continuous variables are shown as means SD. Analysis of variance (ANOVA) or Student's t-test was used for comparative analysis within the groups or overall. Pearson chi-square test or Fisher's exact test was used for categorical vari- ables. The Kruskal-Wallis test was used to compare continuous variables with skewed distributions presented as median values. Logistic regression was used to determine the independent de- terminants of MACE at a 1-year clinical follow-up. Multivariate Cox regression analysis was modified by previous medical in- sight and autonomously of p-value: age, sex, body mass index, systolic blood pressure on admission, heart rate, Killip class > I, history of hypertension, dyslipidemia, coronary artery disease, smoking, multivessel disease, LVEF <55%, medication of statin, low-density lipoprotein cholesterol, and N-terminal pro-brain natriuretic peptide (NT-pro BNP) of > 2000 pg/ml. The Kaplan- Meier method was used to predict the likelihood of death, and the log-rank test was used to compare curves. All statistical tests were two-tailed, and a significance level of p <0.04 was used. The Statistical Package for Social Sciences, version 22.0, was used to conduct the analyses.

3. Results:

Patients in Group I toward Group IV were older and more often female, had greater rates of prior bouts of hypertension and coronary artery disease, were above Killip class I, and had rising levels of NT-pro BNP and high-sensitivity C-reactive protein. On the other hand, there was a shift from Group I to Group IV in the prevalence of smoking history, family history of coronary artery disease, low-density lipoprotein cholesterol levels, and LVEF. Heart rate, systolic and diastolic blood pressure, prior dys- lipidemia, and

STEMI or NSTEMI varied significantly amongst the groups. Body weight or body mass index, however, did not differ. There were no changes in oral hypoglycemic medicines between the 2 groups, although Group IV received significantly more insulin treatments than Group II. Significantly, Group IV had lower estimated GFR and higher creatinine levels.

3.1. Procedural and angiographic features:

Table 1 provides a summary of the coronary angiographic and procedural features. Patients in Groups I through IV had an increasing number of coronary arteries affected. Moreover, there were an increased number of complex lesions (B2 and C) as determined by the American College of Cardiology/American Heart Association (ACC/AHA). Also, patients in Group IV had reduced post-procedure thrombolysis in myocardial infarction (TIMI) flow compared to Group I patients.

3.2. Hospital mortality and clinical results across time:

After a 2-month and 12-month period of clinical follow-up, Group IV had a significantly greater incidence of composite MACE, myocardial infarction, and mortality. The 12-month com- posite MACE increased progressively in participants in Groups I through IV. The groups did not differ significantly in terms of target lesion revascularization at 1 month or coronary artery by- pass graft at 12 months. Diabetes significantly increased the risk of 12-month composite MACE in individuals in Groups I and II without renal insufficiency (12.4% versus 15.6%, respectively; p =0.002). The same was seen in Groups III and IV individuals who had renal insufficiency (30.5% versus 36.5%, respectively; p = 0.002).

Regarding 12-month mortality in the renal insufficiency groups, there were no appreciable differences between diabetic and non-diabetic patients (25.2% in Group III versus 27.4% in Group IV; p = 0.211). Hence, the rise in 12-month composite MACE in diabetic individuals with renal insufficiency may be in- fluence by both myocardial infarction and target lesion revascu- lar-

ization. Under no renal insufficiency settings, Kaplan-Meier curve analysis showed that individuals with diabetes had signifi- cantly higher death rates than those without diabetes (p = 0.005). Both diabetic and nondiabetic patients with renal insufficiency did not exhibit the same symptoms (p = 0.287).

Table 1 Baseline characteristics of the Patients.

Parameter	Group I	Group II	Group III	Group IV	Overall	Lineart
Age	60±12	61±10	70±20	71±8	<0.002	
Age Groups						
>60	46%	40%	15%	12%		
60-73	37%	44%	41%	55%	<0.002	<0.002
>73	14%	13%	41%	30%		
Male (%)	76%	60%	56%	50%	<0.002	<0.002
Body weight (kg)	64±11	65±11	60±11	61±10	0.094	-
BMI	23±2	24±3	22±2	23±2	0.482	-
HR(beats/minute)	75±21	81±21	80±30	82±25	<0.002	-
Systolic blood pressure(mm Hg)	131±26	131±27	120±34	126±33	<0.002	-
Diastolic blood pressure(mm Hg)	81±18	78±15	73±20	75±34	<0.002	-
Current smoker (%)	64%	57%	43%	36%	<0.002	<0.002
Treatment of Diabetes Mellitus						
No Treatment (%)	99%	13.1%	99%	6%		
Insulin Treatment (%)	1%	5.7%	0%	14%		
Oral hypoglycemic (%)	0%	78%	1%	77%		
Previous hypertension (%)	37%	56%	61%	73%	<0.002	<0.002
Previous dyslipidemia (%)	8%	11%	7%	12%	<0.002	<0.002
Family history of CAD (%)	7%	6%	3%	3%	<0.002	<0.002
Previous CAD (%)	12%	17%	20%	25%	<0.002	<0.002
Killip class >2 (%)	21%	24%	42%	51%	<0.002	<0.002
LDL-C (mg/dl)	121±41	113±37	111±42	111±51	<0.002	-
Hs-CRP	0.16. 3.52	0.22.4.14	0.16.3.52	0.31.6.58	<0.002	-
LVEF (%)	52±11	50±11	48±13	45±13	<0.002	-
STEMI (%)	63%	57%	62%	49%	<0.002	-
Non-STEMI (%)	36%	41%	36%	51%	<0.002	-

3.3. *Cox regression analysis for follow-up mortality:*

To determine the risk factor(s) responsible for the connection between renal insufficiency and diabetes and 12-month mor- tality, multivariable Cox regression analysis was used. After accounting for numerous factors, there were no discernible dif- ferences between Group II (diabetesand no renal insufficiency) and Group I (no diabetes and no renal insufficiency) in terms of 12- month mortality (hazard ratio [HR], 1.21; 95% confidence interval [CI], 0.81-2.01; p = 0.208). However, compared to Group I, the 12-month mortality rose progressively from Group III to Group IV (HR, 1.95; 95% CI, 1.33-2.85; p = 0.002; and HR, 2.41; 95% CI, 1.61-3.61; p <0.002, respectively).

3.4. *Cox regression analysis for follow-up mortality:*

Unbiased indicators of serious adverse cardiac events:

Multivariate logistic regression analysis was used to find the independent predictors of MACE. Killip class > 2, diabetes mel- litus, prior coronary artery disease, a reduction in LVEF of less than 45%, an estimated GFR of less than 50 ml/min/1.72 m2, and a rise in NT-pro BNP levels of more than 2000 pg/ml were all predictors of 12- month MACE. On the other hand, beta-blocker and statin prescriptions while in the hospital were poor indica- tors of 12-month MACE.

4. Discussion:

This study aimed to determine how the presence or absence of renal impairment and diabetes affected the clinical outcomes of individuals with AMI. Several clinical investigations have examined the relationship between renal dysfunction and mor- tality in AMI patients [1, 2, 6, 16] or the impact of diabetes on mortality after acute coronary syndrome [11, 17, 20]. In actuality, diabetes and renal failure are linked to poor clinical outcomes following AMI. The risk of cardiovascular disease in people with

diabetes and renal impairment, particularly after AMI, is not well understood, nevertheless. It is also unknown if people with or without renal failure have different relationships between diabetes and cardiovascular outcomes.

Clinical outcomes and renal insufficiency and diabetes in AMI patients are correlated. These results support other studies' findings [1,2,6,16] that mortality following AMI is predicted by declining renal function. When compared to groups without renal insufficiency, Group III and IV in our study experienced higher composite MACE incidence and mortality following a 12-month follow-up. Renal insufficiency and a rise in cardio- vascular incidents may be related in a number of ways. First of all, renal insufficiency is associated with anemia, elevated ho- mocysteine levels, increased low-density lipoprotein oxidation, and decreased nitric oxide production, which may negatively affect myocardial infarction recovery and hasten atherosclerosis [21–23]. Furthermore, advanced renal failure and left ventricular hypertrophy together pose a significant risk for cardiovascular disease-related mortality.

Because estimated GFR was linked to both intima-media thickness and brachial-ankle pulse wave velocities in a previ- ous study, renal insufficiency may be another helpful surrogate marker for cardiovascular disease in diabetic patients in

the clinical context [24]. Also, compared to diabetic patients with albuminuria and non-reduced estimated GFR, those with non- albuminuric renal impairment had a higher frequency of cardiovascular disease [25–27]. As a result, renal impairment is a strong indicator of morbidity and mortality from cardiovascular disease in diabetes individuals. According to this, in our study, renal insufficiency groups had more severe angiographic results than non-renal insufficiency groups, such as left main coronary artery disease and ACC/AHA lesion ratings.

Clinical results for diabetic patients with AMI are worse than non-diabetic patients [19]. Our results confirmed that inde- pendent of renal insufficiency, individuals with diabetes have greater composite MACE after 1 year of follow-up than patients without diabetes. The increased incidence of negative outcomes in diabetes patients has been attributed to a number of differ- ent factors. These processes include increased endothelial dys- function [29], anomalies of thrombosis and fibrinolysis [30], an aberrant metabolic response to ischemia with inefficient energy usage and accumulation of harmful oxygen-free radicals [28].

Compared to non-diabetic patients, diabetic patients with AMI have worse clinical outcomes [19]. In addition, our results confirmed the fact that patients with diabetes, regardless of renal insufficiency, have a higher composite MACE at 1 year of follow- up than patients without diabetes.

The rise in bad outcomes among diabetes patients has been attributed to a number of reasons. These processes include an aberrant metabolic response to ischemia, which results in in- efficient energy consumption and an accumulation of harmful oxygen-free radicals [28], increased endothelial dysfunction [29], and irregularities of thrombosis and fibrinolysis [30]. In addi- tion, it has recently been shown by Yan et al. [31] that there is a significant correlation between plasma osteopontin levels and the presence and severity of coronary artery disease in diabetic patients. This finding suggests that osteopontin may be crucial in the inflammatory processes leading to accelerated atheroscle- rosis. As evidenced by our study,

patients with diabetes are known to have a higher burden of atherosclerosis and more diffuse and multivessel coronary artery disease.

Combining all of our findings, we propose that the presence of renal insufficiency and diabetes in patients with AMI is a predictive indicator of cardiovascular risk, including composite MACE and all-cause mortality, in addition to representing the severity of the condition or clinical outcome.

4.1. *Clinical significance of the categorization for AMI patients with diabetes and renal impairment:*

The current investigation showed that dividing patients into 4 groups based on the presence or absence of renal insufficiency and diabetes was an effective way to differentiate between pre- dictions of the 1-year clinical outcome following AMI. We dis- covered a stepwise increase in the HR for 12-month mortality from Group I to Group IV, despite multivariate Cox regression analysis showing no significant differences between Group I and Group II. The fact that patients in higher groups were older had higher prevalences of hypertension and prior coronary artery disease and had lower LVEF compared with Group I, all of which may cause atherosclerosis and contribute to an increased cardiovascular mortality, provided additional support for these observations.

In this regard, we also discovered that the levels of a num- ber of molecular markers, such as hs-CRP and NT-pro BNP, increased from Group I through IV. Such markers are influenced by inflammation [32,33], which may have raised the risk of car- diovascular mortality in our patients with AMI. These markers are also influenced by the degree of heart failure. As a result, this study demonstrates that classifying individuals based on the existence of diabetes and renal insufficiency gives useful data for identifying early-risk patients with AMI. A recent single-centre prospective research [13] of AMI patients, separated into groups with and without diabetes, CKD, and diabetes and without CKD, found no significant differences in death or MACE rates between diabetes patients with and without CKD and patients without diabetes.

Diabetes coexisting with CKD, however, was revealed to be one of the strongest independent risk factors for cardiovascular complications and total mortality, in keeping with our findings. On the other hand, our study did find some variations in the clinical outcomes. According to whether or not they had re- nal insufficiency, the non-diabetic patients were split into two groups. Group III non-diabetic patients with renal insufficiency had higher mortality and 12-month composite MACE than dia- betic patients without renal insufficiency (Group II). As opposed to diabetic individuals without renal insufficiency, people with- out diabetes and renal insufficiency (Group I) experienced less severe unfavorable clinical outcomes after AMI (Group II).

After high-risk AMI, Anavekar et al. [12] demonstrated that patients with or without diabetes exhibit a similar relationship between renal insufficiency and cardiovascular risk, including all- cause mortality, death, a composite of heart failure, recurrent AMI, resuscitated sudden cardiac death, and stroke. Similar to a prior study [12], our investigation showed that diabetic and nondiabetic patients with renal insufficiency following AMI ex- perienced the same mortality at a 12-month follow-up. This sug- gests that, regardless of diabetes, persons with renal impairment may be more prone to severe and widespread coronary artery disease. Moreover, these individuals frequently exhibit left ven- tricular hypertrophy and hypertension, indicating a higher risk of cardiovascular disease [34,35].

Patients with diabetes typically exhibit greater proportions of events than non-diabetic patients in response to declining renal function, even though both patients with and without diabetes experience increasing cardiovascular event rates with poor renal function [12].

As a result, a combination of renal insufficiency and diabetes may enhance the risk of cardiovascular events following AMI. Therefore, we empha- sise the significance of categorising patients into 4 broad categories based on the presence or absence of renal insufficiency and diabetes to predict mortality and cardiovascu- lar sequelae in patients with an AMI.

5. Conclusion:

Renal insufficiency, particularly when combined with diabetes, is linked to the development of composite MACE and a poor prognosis in patients with AMI. The classification of individuals depending on the presence or absence of renal insufficiency and diabetes gives important data for the early-risk stratification of AMI patients.

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7. Conflict of interest:

There are no conflicts of interest to declare by any of the authors of this study.

8. Publisher details.

9. References:

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