

## ORIGINAL ARTICLE

# Association of Creatinine Clearance with Left Ventricular Ejection Fraction in Patients with Acute Coronary Syndrome

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**ABSTRACT**

**Background:** Renal dysfunction is an independent predictor of adverse cardiovascular outcomes among patients with acute coronary syndrome. However, the relationship between creatinine clearance and left ventricular systolic function remains incompletely characterized. This study aimed to evaluate the association between creatinine clearance and left ventricular ejection fraction, and to assess clinical outcomes in ACS patients with varying degrees of renal function. **Methods & Materials:** The prospective observational study was conducted at the Department of Cardiology at Mymensingh Medical College Hospital between October 2022 and September 2023, including 100 consecutive patients with first-episode ACS within 24 hours of symptom onset. The patients were divided into two groups according to their calculated creatinine clearance: Group I (CrCl  $\geq$  70 ml/min, n = 31) and Group II (CrCl < 70 ml/min, n = 69). The study included a comprehensive clinical assessment, echocardiographic evaluation, and in-hospital monitoring. Data were analyzed using SPSS version 26 with appropriate statistical analysis. **Results:** The mean age of patients was 51.7 $\pm$ 8.5 years, with 88% males. Patients with reduced creatinine clearance were significantly older (53.4 $\pm$ 8.4 vs 47.8 $\pm$ 7.2 years, p=0.002) and had a higher prevalence of diabetes mellitus (56.5% vs 22.6%, p=0.002). Mean LVEF was significantly lower in the abnormal clearance group (49.4 $\pm$ 6.7% vs 56.5 $\pm$ 6.0%, p=0.001). In-hospital morbidity was substantially higher in patients with CrCl <70 ml/min (84.0% vs 29.0%, p=0.001), including increased rates of heart failure (28.9% vs 9.6%, p=0.030), ventricular tachycardia (28.9% vs 6.4%, p=0.010), post-MI angina (34.7% vs 6.4%, p=0.002), and cardiogenic shock (21.7% vs 3.2%, p=0.020). **Conclusion:** Among ACS patients, reduced creatinine clearance is an independent correlate of lower LVEF and significantly higher in-hospital morbidity. Early recognition of renal dysfunction and aggressive risk stratification are strategies that may improve outcomes in this high-risk population.

**Keywords:** Acute coronary syndrome, Creatinine clearance, Renal dysfunction, Left Ventricular Ejection Fraction.

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**INTRODUCTION**

Acute coronary syndrome represents a spectrum of ischemic cardiac states, including ST-elevation myocardial infarction, non-ST-elevation myocardial infarction, and unstable angina, and continues to be one of the leading causes of cardiovascular morbidity and mortality worldwide<sup>[1]</sup>. Despite advances in both reperfusion strategies and pharmacological treatments, outcomes among patients with ACS continue to be highly variable, depending on a diverse array of clinical and biochemical factors. Renal impairment has emerged as an important, albeit largely unrecognized, contributor to these outcomes. Given the growing interest in the interaction between heart and kidney, the cardiorenal syndrome has become a focus of cardiovascular investigation and clinical practice<sup>[2]</sup>. CKD has been described in a substantial minority of patients with ACS, though the reported prevalence varies widely, between 30% and 60%, according to population characteristics and thresholds for diagnosis<sup>[3]</sup>. CKD in the setting of ACS often coexists with more extensive coronary disease, reduced utilization of evidence-based therapies, and significantly higher rates of adverse events both during

hospitalization and over longer-term follow-up<sup>[4]</sup>. Notably, even mild to moderate renal dysfunction has been associated with a gradient of increased mortality and complication rates as estimated glomerular filtration rate decreases<sup>[5]</sup>. Calculated creatinine clearance, by means of the Cockcroft-Gault equation, is commonly used clinically to estimate renal function. Large registries, such as the Global Registry of Acute Coronary Events (GRACE), have consistently shown that it independently predicts in-hospital mortality and major bleeding in ACS patients<sup>[6]</sup>. The mechanisms for the association between impaired renal function and poor cardiovascular outcome are multifaceted, including accelerated atherosclerosis, persistent inflammation, oxidative injury, endothelial dysfunction, disturbances in mineral metabolism, and activation of neurohormonal pathways such as the renin-angiotensin-aldosterone system<sup>[7]</sup>. LVEF, which is the most applied measure of systolic function in post-ACS management, remains a cornerstone for risk stratification. A reduced LVEF is inextricably linked with increased mortality, susceptibility to heart failure, and risk of sudden cardiac death<sup>[8]</sup>. The influence of renal impairment on LVEF is

bidirectional; renal impairment might enhance the degree of myocardial injury via both thrombotic and inflammatory pathways<sup>[9]</sup>, while impaired cardiac output may aggravate renal hypoperfusion and neurohormonal activation, which further accelerates deterioration in both organs. Although renal function and LVEF are individual determinants of prognosis, their direct relationship remains poorly defined in ACS patients, especially in resource-constrained settings. Establishing this relationship can enable the earlier identification of high-risk patients, guide revascularization and medical therapy, and inform monitoring strategies<sup>[10]</sup>. In light of this, this study aimed to assess the correlation between creatinine clearance and LVEF among patients with ACS and the impact of renal dysfunction on complication rates during hospitalization.

**METHODS & MATERIALS**

This prospective study was conducted in the Department of Cardiology at Mymensingh Medical College Hospital between October 2022 and September 2023. A total of 100 patients of both sexes were enrolled through purposive sampling. The reduced sample size was due to the limited study period. Eligible participants included adults aged 65 years or younger who presented with their first episode of acute coronary syndrome within 24 hours of symptom onset. Patients with

previous ACS, valvular heart disease, cardiomyopathy, prior heart failure, or a history of PTCA with stenting or CABG were excluded. Renal function was assessed using calculated creatinine clearance, and patients were stratified into two groups: Group I with CrCl  $\geq 70$  ml/min and Group II with CrCl  $< 70$  ml/min. After obtaining informed written consent, each patient underwent detailed history taking, physical examination, and 12-lead ECG assessment. Blood samples were collected for cardiac biomarkers, serum creatinine, glucose, lipid profile, and echocardiography or other investigations as indicated. All findings were documented in a standardized, IRB-approved data collection form. Patients were monitored throughout hospitalization for the development of complications such as heart failure, cardiogenic shock, mechanical complications, arrhythmias, post-MI angina, reinfarction, or death. Data were entered and analyzed using SPSS version 26. Continuous variables were expressed as mean  $\pm$  standard deviation and compared using an independent samples t-test. Categorical variables were presented as frequencies and percentages, and compared using the chi-square test or Fisher's exact test as appropriate. Analysis of variance (ANOVA) was employed for comparing multiple group means. A p-value  $< 0.05$  was considered statistically significant for all analyses.

**RESULTS**

**Table – I: Distribution of baseline demographic and risk factors of the study population (n=100)**

Variables	Male (n= 88) (88%)		Female (n=12) (12%)		Total (N=100)		p-value
	n	%	n	%	n	%	
Age (in years)	-	-	-	-	-	-	-
30-39	7	8%	1	8.3%	8	8%	-
40-49	24	27.3%	1	8.3%	25	25%	-
50-59	37	42%	6	50%	43	43%	-
60-65	20	22.7%	4	33.3%	24	24%	-
Mean $\pm$ SD (Range)	51.3 $\pm$ 8.5 (30-65)		54.4 $\pm$ 8.1 (30-65)		51.7 $\pm$ 8.5 (30-65)		0.230
Risk Factors	-	-	-	-	-	-	-
Smoking	70	79.5	1	8.3	71	71%	-
Hypertension	48	54.5	11	91.7	59	59%	-
Diabetes mellitus	38	43.2	8	66.7	46	46%	-
Dyslipidaemia	42	47.7	4	33.3	46	46%	-
Family H/O IHD	39	44.3	4	33.3	43	43%	-
Mean $\pm$ SD (Range)	2.7 $\pm$ 0.9 (1-5)		2.3 $\pm$ 1.1 (1-5)		2.6 $\pm$ 0.9 (1-5)		0.250

Table I represents baseline demographics and risk factors of the study population. The study consisted of 100 patients (mean age 51.7 $\pm$ 8.5 years, range 30-65 years) with a predominance of males (88%). Age distribution was 50-59

years (43%), 40-49 years (25%), and 60-65 years (24%). Traditional cardiovascular risk factors were very common, including smoking in 71% of the patients, hypertension in 59%, diabetes mellitus, and dyslipidemia in 46% each.

**Table – II: Haemodynamic parameters of the Study population (n=100)**

Parameters	Male (n=88)	Female (n=12)	p-value
	Mean $\pm$ SD	Mean $\pm$ SD	
Pulse/minute	79.5 $\pm$ 13.9 (40-120)	71.9 $\pm$ 13.9 (52-105)	0.080
Systolic blood pressure (mmHg)	120.7 $\pm$ 28.9 (60-220)	132.9 $\pm$ 30.9 (100-220)	0.170
Diastolic blood pressure (mmHg)	77.7 $\pm$ 18.9 (40-120)	80.0 $\pm$ 14.1 (70-120)	0.680

Table II shows the haemodynamic parameters of the study population with a mean pulse rate of 79.5 $\pm$ 13.9 bpm for males versus 71.9 $\pm$ 13.9 bpm for females, systolic blood pressure of

120.7 $\pm$ 28.9 mmHg for males versus 132.9 $\pm$ 30.9 mmHg for females, and diastolic blood pressure of 77.7 $\pm$ 18.9 mmHg for males versus 80.0 $\pm$ 14.1 mmHg for females.

**Table – III: Age, sex, and heart failure distribution of study population with normal and abnormal renal function (n=100)**

Variables	Creatinine Clearance				Total		p-value
	Normal clearance (≥70) (n=31)		Abnormal clearance (<70) (n=69)		n	%	
	n	%	n	%			
Age (in years)	-	-	-	-	-	-	-
30 - 39	3	9.7%	5	7.9%	8	8%	-
40 - 49	13	41.9%	12	17.4%	25	25%	-
50 - 59	14	45.2%	29	42%	43	43%	-
60 - 65	1	3.2%	23	33.3%	24	24%	-
Total	31	100%	69	100%	100	100%	-
Mean ± SD (Range)	47.8±7.2 (30-60)		53.4±8.4 (35-65)		51.7±8.5 (30-65)		0.002
Sex	-	-	-	-	-	-	-
Male	28%	90.3%	60	87%	88	88%	0.630
Female	3%	9.7%	9	13%	12	12%	
Heart failure	-	-	-	-	-	-	-
Class I	28%	90.3%	49	71%	77	77%	0.030
Class II	2%	6.5%	11	15.9%	13	13%	
Class III	1%	3.2%	3	4.3%	4	4%	

Table III depicts the age distribution of patients with normal and abnormal renal function. Patients with abnormal renal function were older than those with normal clearance (53.4±8.4 vs 47.8±7.2 years), with only 3.2% of normal-clearance patients in the 60-65 years compared to 33.3% of those with abnormal clearance. Of importance, heart failure

classification differed significantly between the groups (p=0.030), with 90.3% of normal-clearance patients in class I compared to only 71.0% of reduced-clearance patients, while class II was present in 6.5% versus 15.9% and class III in 3.2% versus 4.3%, respectively.

**Table – IV: Risk factors of patients with normal and abnormal creatinine clearance (n=100)**

Risk factors	Creatinine Clearance				Total (N=100)		p-value
	Normal clearance (≥70) (n=31)		Abnormal clearance (<70) (n=69)		Number	%	
	Number	%	Number	%			
Smoking	22	71%	49	71%	71	71%	0.990
Hypertension	16	51.6%	43	62.3%	59	59%	0.310
Family history of IHD	15	48.4%	28	40.6%	43	43%	0.460
Diabetes mellitus	7	22.6%	39	56.5%	46	46%	0.002
Dyslipidaemia	17	54.8%	29	42%	46	46%	0.230
Mean ± SD (Range)	2.45±0.76 (1-4)		2.72±1.01 (1-5)		2.64±0.98 (1-5)		0.190

Table IV shows the risk factors of patients with normal and abnormal creatinine clearance. The stratification of the cardiovascular risk factors by renal function revealed notable similarities in smoking (71.0% vs 71.0%), hypertension

(62.3% vs 51.6%), family history of ischemic heart disease (40.6% vs 48.4%, p=0.460), and dyslipidemia (42.0% vs 54.8%, p=0.230) between the abnormal and normal creatinine clearance groups.

**Table – V: Pattern of acute coronary syndrome in patients with normal and abnormal renal function (n=100)**

Pattern of ACS	Creatinine Clearance				Total (N=100)		p-value
	Normal clearance (≥70) (n=31)		Abnormal clearance (<70) (n=69)		n	%	
	n	%	n	%			
Anterior	19	61.3%	27	39.1%	46	46%	0.200
Inferior	9	29%	34	49.3%	43	43%	
NSTEMI	1	3.2%	4	5.8%	5	5%	
UA	2	6.5%	4	5.8%	6	6%	

Table V shows the pattern of acute coronary syndrome in patients with normal and abnormal renal function. The distribution of ACS subtypes was as follows: anterior myocardial infarction, 46% overall (61.3% in normal

clearance vs 39.1% in reduced clearance); inferior myocardial infarction, 43% overall (29.0% vs 49.3%); NSTEMI, 5% overall (3.2% vs 5.8%); and unstable angina, 6% overall (6.5% vs 5.8%).

**Table - VI: Mean percent of ejection fraction of patients with normal and abnormal creatinine clearance (n=100)**

Ejection fraction (percent)	Creatinine Clearance				Total (N=100)		p-value
	Normal clearance (≥70) (n=31)		Abnormal clearance (<70) (n=69)				
	Number	%	Number	%	Number	%	
30 - 39	0	0%	3	4.3%	3	3%	-
40 - 49	4	12.9%	33	47.8%	37	37%	-
50 - 59	16	51.6%	29	42%	45	45%	-
60 - 69	11	35.5%	4	5.8%	15	15%	-
Mean ± SD (Range)	56.5±6.0 (43-66)		49.4±6.7 (30-66)		51.6±7.3 (30-66)		0.001

Table VI denotes the Mean percent of ejection fraction of patients with normal and abnormal creatinine clearance. The mean LVEF was substantially lower in patients with reduced creatinine clearance, 49.4±6.7% vs. 56.5±6.0%. Distribution of ejection fraction categories showed that no patients with

normal clearance had severely depressed function, 30-39% range, while 4.3% of those with abnormal clearance fell into this category. At the other extreme, 35.5% of normal-clearance patients achieved LVEF ≥60%, whereas only 5.8% of reduced-clearance patients did.

**Table - VII: Pattern of cardiac complications of patients with normal and abnormal creatinine clearance (In-hospital morbidity (n=100))**

Complications	Creatinine Clearance				Total (N=100)		p-value
	Normal clearance (≥70) (n=31)		Abnormal clearance (<70) (n=69)				
	n	%	n	%	n	%	
Heart failure (Killip II- IV)	3	9.6%	20	28.9%	23	23%	0.030
Atrial fibrillation	3	9.6%	14	20.2%	17	17%	0.190
Ventricular tachycardia	2	6.4%	20	28.9%	22	22%	0.010
Ventricular fibrillation	0	0%	4	5.7%	4	4%	0.170
Post MI angina	2	6.4%	24	34.7%	26	26%	0.002
Heart Block	0	0%	7	10.1%	7	7%	0.060
Mechanical complication	0	0%	2	2.9%	2	2%	0.330
Cardiogenic shock	1	3.2%	15	21.7%	16	16%	0.020

Table VII demonstrates the Pattern of cardiac complications of patients with normal and abnormal creatinine clearance (In-hospital morbidity. Heart failure (Killip II-IV) occurred in 28.9% versus 9.6%, ventricular tachycardia in 28.9% versus

6.4%, post-MI angina in 34.7% versus 6.4%, and cardiogenic shock in 21.7% versus 3.2%, atrial fibrillation (20.2% vs 9.6%), ventricular fibrillation (5.7% vs 0%), heart block (10.1% vs 0%), and mechanical complications (2.9% vs 0%).

**Table - VIII: In-hospital morbidity and Mortality of patients with normal and abnormal creatinine clearance (n=100)**

	Creatinine Clearance				p-value
	Normal clearance (≥70) (n=31)		Abnormal clearance (<70) (n=69)		
	n	%	n	%	
Morbidity	-	-	-	-	-
Yes	9	29%	58	84%	0.001 <sup>s</sup>
No	22	71%	11	16%	
Mortality	-	-	-	-	-
Yes	0	0%	4	5.8%	0.17 <sup>ns</sup>
No	31	100%	65	94.2%	

Table VIII shows the in-hospital morbidity and Mortality of patients with normal and abnormal creatinine clearance. Overall, in-hospital morbidity affected 84% of those with abnormal clearance compared with 29% in those with normal clearance (p=0.001). In-hospital mortality occurred in 0% patients with normal clearance versus 5.8% in the abnormal clearance group.

**DISCUSSION**

The study demonstrates a clear and clinically meaningful relationship between impaired creatinine clearance and reduced left ventricular ejection fraction in patients with acute coronary syndrome, with a substantially higher burden of in-hospital morbidity. An absolute 7.1% reduction in mean LVEF among patients with impaired renal function strengthens previous findings by Køber et al., that renal dysfunction significantly exacerbates cardiac systolic impairment and increases the risk of adverse outcomes<sup>[11]</sup>. The high

percentage of patients in this cohort with creatinine clearance below 70 ml/min is consistent with Keough-Ryan et al. major registry findings, indicating that renal impairment is common among ACS populations worldwide<sup>[12]</sup>. Data from large registries like the GRACE registry demonstrate that declining creatinine clearance independently predicts hospital mortality and major bleeding across the spectrum of ACS<sup>[13]</sup>. Correspondingly, the findings of Reddan et al. indicate that even small reductions in renal function confer incremental risk of mortality, emphasizing the prognostic implications of mild renal impairment<sup>[14]</sup>. Chronic renal disease accelerates atherosclerosis through sustained inflammation, oxidative injury, endothelial dysfunction, and accumulation of atherogenic uremic toxins<sup>[15]</sup>. These processes increase coronary disease severity and predispose to larger infarcts during ischemia. Furthermore, renal impairment is also involved in the development of coronary microvascular disease, which in turn has been related to worse infarct size

and post-ischemic ventricular remodeling<sup>[16]</sup>. Uremic toxins such as indoxyl sulfate and p-cresyl sulfate further destabilize plaques and enhance thrombogenicity, promoting more extensive myocardial injury<sup>[17]</sup>. The notably higher prevalence of diabetes within the reduced clearance group underlines the importance of metabolic factors within the cardiorenal axis. Indeed, emerging evidence has pointed out that insulin resistance, as quantified by the triglyceride-glucose index, partly serves as a mediator between renal impairment and adverse cardiovascular outcomes in ACS<sup>[18]</sup>. Thus, the triad of diabetes, renal dysfunction, and ACS forms a high-risk clinical phenotype that requires more frequent monitoring and intensified therapeutic strategies. The high morbidity in the reduced clearance group (84% vs 29%) indicates the significant clinical consequence of renal impairment during the acute phase. Complications like heart failure, ventricular tachycardia, post-MI angina, and cardiogenic shock were recorded with far greater frequency, which is in tune with the findings of Nabais et al., who demonstrated that renal dysfunction carries heightened risk independently of the traditional ACS risk scores<sup>[19]</sup>. The increased arrhythmia burden is consistent with the report by Yalta et al., including electrolyte disturbances, autonomic imbalance, and changes in myocardial structure related to uremia<sup>[20]</sup>. Temporal analyses demonstrate that though therapies have evolved, the gains in outcome have been much less marked for those with impaired renal function, partly because of underutilization of therapies related to bleeding risk, concern about contrast exposure, and altered pharmacokinetics<sup>[21]</sup>. These findings emphasize the need for individual adjustments of therapy, rather than withholding beneficial treatments. Clinical implications include the routine inclusion of creatinine clearance in risk stratification to facilitate early identification of vulnerable patients. The shock index-creatinine score is an emerging tool that will likely further refine prognostic assessment in ACS<sup>[22]</sup>. Management should be focused on renal-protective strategies, judicious fluid balance, avoidance of nephrotoxic exposures, and guideline-directed medical therapy, with appropriate dose adjustment. Evidence to support SGLT2 inhibitors and renin-angiotensin-aldosterone system blockers suggests that there could be a benefit even in those patients with advanced renal dysfunction.

**Limitations of the Study:** The limitations of this study are its small sample size and single-center design, which may restrict the generalization of findings to broader populations with different demographic and clinical characteristics. The absence of long-term follow-up data precludes assessment of chronic outcomes, ejection fraction recovery patterns, and sustained impact of renal dysfunction on cardiovascular morbidity and mortality beyond the acute hospitalization period.

## CONCLUSION

This study among patients with acute coronary syndrome shows that reduced creatinine clearance is independently associated with a significantly lower left ventricular ejection fraction and substantially increased in-hospital morbidity. The findings underline the paramount importance of early assessment of renal function in ACS risk stratification and point out a particular need for intensive monitoring and targeted interventions in patients with concomitant cardiac and renal dysfunction. The integration of creatinine clearance into routine clinical evaluation may improve predictive accuracy and enable appropriate therapeutic decision-making in this vulnerable population.

**Recommendations:** Future studies need to be prospective and multicenter, with larger cohorts and longer follow-up, to confirm these findings and establish optimal management strategies for ACS patients with renal dysfunction.

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