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REVIEW ARTICLE

Impact of Renal Dysfunction on In-Hospital Outcomes in Patients with Acute Coronary Syndrome

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Abstract:

Background:The outcome is poor in patients with acute myocardial infarction (MI) who have renal dysfunction in long-term follow-up. Less is known about the outcome of acute MI in the short term.

Objectives: We aimed to evaluate the outcome of patients with acute coronary syndrome (ACS) across varying degrees of renal dysfunction.

Materials and methods: Seventy patients presenting with ACS, including ST-segment elevation MI (STEMI), non-ST-segment elevation MI (NSTEMI), and unstable angina (UA), were enrolled in this prospective observational study. Sociodemographic and clinical characteristics and in-hospital outcomes were compared for patients according to glomerular filtration rate (GFR).

Results: Patients with moderate to severe renal dysfunction were elderly females and associated with more comorbidities and adverse outcomes if compared with patients who had normal to mild renal dysfunction. When the enrolled patients were divided into two groups, STEMI and NSTEMI/UA, a significant difference was observed between these two groups. There was no significant association between STEMI with the occurrence of adverse outcomes and the presence of moderate to severe renal dysfunction. On the other hand, there is a significant association with the occurrence of adverse outcomes among patients in the NSTEMI/UA group.

Conclusion: Moderate to severe renal impairment is a predictor of in-hospital morbidity and mortality in ACS.

Keywords: Acute coronary syndrome; Renal dysfunction; Mortality; Morbidity

Introduction

In the literature, studies have shown that any stage of renal dysfunction (mild to severe) is an independent risk factor for short- and long-term mortality among patients with myocardial infarction (MI), suggesting that cardiovascular disease may develop early in the course of renal dysfunction. [1, 2, 3]

A comprehensive review of the literature showed that even mild to moderate renal dysfunction or early stages of chronic kidney disease significantly worsen outcomes following both coronary artery bypass grafting and percutaneous coronary intervention. Also, it highlights higher in hospital mortality, increased postoperative complications, and poorer long term survival in CKD patients undergoing coronary intervention. [4,5] A recent meta-analysis and systematic review study reported that chronic kidney disease is a strong and independent predictor of mortality in patients with acute MI. The increased risk for adverse outcome applies to both early and late outcomes and persists across different stages of kidney dysfunction, highlighting the need for early risk stratification and tailored management in MI patients with renal dysfunction. [2]

These findings have led some investigators to propose for the inclusion of renal function as a significant prognostic factor at the time of acute coronary syndrome (ACS). Several prior studies found renal impairment to be a substantial predictor of cardiovascular morbidity and mortality, while others investigated a broader variety of ACS comorbidities. Although some researchers have examined all clinical manifestations of ACS, research has traditionally concentrated on ST-elevation myocardial infarction (STEMI) rather than non-ST-elevation myocardial infarction (NSTEMI) or unstable angina (UA). In contrast, the current analysis includes all types of ACS and its associated comorbidities. [6, 7, 8]

The main aims of the present study were to evaluate characteristics of patients with varying degrees of renal dysfunction

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among patients hospitalized with all types of ACS, as well as to compare outcomes of all types of acute coronary syndrome across varying degrees of renal function.

Patients and Methods

Seventy patients with ACS admitted to the coronary care unit (CCU) in Al-Sadr Teaching Hospital in Annajaf from March 2008 to March 2009 were enrolled in the present study. Exclusion criteria were as follows: (1) delayed hospitalization (>48 hr); (2) patient who had chronic kidney disease or was on dialysis; (3) cardiogenic shock at time of presentation (prolonged decline in systolic blood pressure <80 mm Hg with poor tissue perfusion where it requires positive inotropic drugs to maintain); (4) death within 24 hours; and (5) patient who is discharged early from hospital (<3 days).

Diagnosis of MI depends on the classic World Health Organization (WHO) criteria that require at least two of the following three elements to be present: a history of ischemic-type chest discomfort, evolutionary changes on serially obtained ECG tracings, and a rise and fall in serum cardiac markers. [9] UA was defined according to the Braunwald classification. Class I includes new onset of severe angina or accelerated angina without rest pain, while Class III refers to the occurrence of one or more anginal episodes at rest within the preceding 48 hours. [10] Baseline data were obtained about patients' sociodemographic characteristics, including age, sex, and marital status, as well as comorbidities, including previous history of diabetes mellitus, hypertension, ischemic heart disease, smoking, and family history of premature ischemic heart disease (male < 55 years, female < 65 years). The height of the patients was measured by using a metallic tape measure and approximated to the nearest 0.5 cm, and the weight of the patient was taken to calculate the body mass index (BMI) = weight in kg / (height in meters). 2. Serial ECGs were conducted for each patient using the MAC 500 ECG device. Two blood samples were collected to measure creatine kinase-MB (CK-MB) isoenzyme levels—one at 12 to 24 hours and another at 72 hours—to detect the characteristic rapid rise and fall in CK-MB. Serum creatinine was also measured by using commercial kits (BIOLABO REAGENT: CK-MB Iso enzyme immune inhibition method and Biomaghreb: creatinine kinetic test). CK-MB levels were used to differentiate between NSTEMI and UA in patients presenting with ST-segment depression; however, these groups were combined in the analysis due to a small sample size.

The patients who met WHO diagnostic criteria for MI and those classified as Class I and III of the Braunwald classification for UA were included in the study. All enrolled patients were monitored clinically and electrocardiographically throughout their hospital stay, which ranged from 5 to 10 days. Clinical adverse outcomes were recorded during hospital stay.

Determination of renal function

Patients were categorized according to the estimated GFR at baseline with the use of the abbreviated Modification of Diet in Renal Disease study group equation (MDRD) [11]:

Estimated GFR = 186 × (serum creatinine level in mg/dl) - 1.154 × (age in years) - 0.203

For women and Blacks, the product of this equation was multiplied by a correction factor of 0.742 and 1.21, respectively, where GFR is in ml/min/1.73 m^2. Calculations were done by eGFR calculator software, and the patients were grouped as follows: GFR ≥ 60 ml/min/1.73 m^2 was considered as normal to mild renal impairment, and GFR < 60 ml/min/1.73 m^2 as moderate to severe renal impairment.

Statistical analysis

The chi-square test was used for categorical variables; a p-value <0.05 was considered to indicate statistical significance. Measurements were done by interactive chi-square software.

Results

Of the seventy patients with ACS, 33 patients had normal to mild renal impairment (mean GFR of 80 ± 16), and 37 patients had moderate to severe renal impairment (mean GFR of 44 ± 11). The study included 44 males (27 with normal to mild renal impairment and 17 with moderate to severe renal impairment) and 26 females (six with normal to mild renal impairment and 20 with moderate to severe renal impairment).

The mean age of patients with normal to mild renal impairment was 57 ± 9, and for patients with moderate to severe renal impairment, it was 63 ± 7. The mean serum creatinine was 1 ± 0.1 in normal to mild renal impairment and 1.5 ± 0.3 in moderate to severe renal impairment. The baseline characteristics of patients with ACS according to the degree of renal impairment are presented in Table 1.

The adverse outcomes included atrial fibrillation (2 patients), ventricular fibrillation (15 patients), ventricular tachycardia (2 patients), complete heart block (1 patient), bifascicular block (1 patient), ventricular and atrial premature complexes (2 patients), heart failure (2 patients), pulmonary edema (1 patient), mitral regurgitation (1 patient), hypotension (1 patient), extension of ischemia (1 patient), pericarditis (1 patient), and death (15 patients). There was a significant association between in-hospital mortality and morbidity and moderate to severe degrees of renal impairment, as in Table 2. Another finding was the significant association between the number of risk factors and the moderate to severe degree of renal impairment (Table 3).

Regarding types of ACS, 33 patients out of seventy had STEMI, 16 patients had normal to mild renal impairment (mean GFR of 86 ± 17), and 17 patients had moderate to severe renal impairment (mean GFR of 44 ± 12); 21 males (14 with normal to mild renal impairment and 7 with moderate to severe renal impairment) and 12 females (2 with normal to mild renal impairment and 10 with moderate to severe renal impairment); the mean age of patients was 60 ± 9 in normal to mild renal impairment and 63 ± 8 with moderate to severe renal impairment; and the mean serum creatinine was 0.95 ± 0.1 in normal to mild renal impairment and 15 ± 0.4 in moderate to severe renal impairment (Table 4).

There was no significant association between sex and the degree of renal impairment. However, older patients and those who had hypertension had more severe renal impairment. Additionally, there was no significant association observed between the occurrence of adverse outcomes and the degree of renal impairment, as shown in Table 5.

Among thirty-seven patients with NSTEMI/UA, 17 patients had normal to mild renal impairment (mean GFR was 74 ± 14), and 20 patients had moderate to severe renal impairment (median GFR was 43 ± 9). The group included 23 males (13 with normal to mild renal impairment and 10 with moderate to severe renal impairment) and 14 females (4 with normal to mild renal impairment and 10 with moderate to severe renal impairment). The mean age of patients was 55 ± 8 in normal to mild renal

impairment and 63 ± 6 with moderate to severe renal impairment. The mean serum creatinine was 1 ± 0.1 in normal to mild renal impairment and 15 ± 0.2 in moderate to severe renal impairment. There was no relation between sex or hypertension and degree of renal impairment (Table 6). There was significant association between adverse outcomes and degree of renal impairment, as outlined in Table 7.

Discussion

In this study, it was found that as age increased, renal function declined significantly, and this was in agreement with other studies. [12, 13, 14] A recent systematic review reported that age is independently linked with progressive GFR decline, and this decline is more pronounced in individuals following MI. Notably, patients over 40 lose approximately 1 mL/min/1.73 m² per year, with an accelerated decline post-MI. [12] Findings from a U.S. tertiary center reveal that about 25% of patients presenting with acute chest pain and measured troponin had CKD, and renal dysfunction significantly diminished the diagnostic performance of troponin for MI. [14]

Rivera FB et al. and Rocamora-Horrach M et al. studies found a significant association between female sex and moderate to severe renal dysfunction, and this was consistent with the results of this study due to women presenting at the hospital with ACS being almost older than men; that may explain the predominance of women among patients with impaired renal function. [15, 16] Pitsavos C et al. found cigarette smoking was less frequent among patients with moderate to severe renal dysfunction and low body mass index, but this is in disagreement with the findings of this study, where cigarette smoking is more frequent but not significant, and there was no difference in body mass index in patients with varying degrees of renal dysfunction. [17] This study is in agreement with other studies, such as Pitsavos C et al. and Anavekar NS et al., regarding the association of moderate to severe renal dysfunction with hypertension. [17, 18]

It was found that with increasing ischemic risk factors, renal function declines because of the shared impact of these factors on both cardiovascular and renal systems in addition to the impact of renal dysfunction on the cardiovascular system. Many coronary risk factors, particularly diabetes mellitus and hypertension, are established predictors for the progression of renal disease. [18]

In the present study, a cutoff value for an estimated GFR of less than 60 ml/min/173 m² was a predictor of adverse cardiovascular outcome, consistent with the findings of other studies. [19, 20, 21]

Furthermore, fatal and non-fatal complications are significantly higher in patients with moderate to severe renal dysfunction than those with normal to mild dysfunction, and this is in agreement with the Pitsavos C et al. and Anavekar NS et al. studies. [17, 18]

When the data were stratified into subgroups, including NSTEMI/UA, neither sex nor hypertension showed significant association with moderate to severe renal dysfunction. This contrasts with findings from other studies. [22, 23] This discrepancy may be attributed to the relatively small sample size in the present study. In the STEMI group, the occurrence of fatal and non-fatal complications in relation to moderate to severe degrees of renal impairment is not significant in contrast to other studies that reported a significant association between adverse clinical outcomes and moderate to severe renal impairment, particularly in patients with STEMI. These differences in the findings may be partially explained by the phenomenon of therapeutic nihilism that has been observed in certain settings. [24, 25] In these settings, patients with moderate to severe renal dysfunction were less likely to receive risk-modifying cardiovascular medications and to undergo coronary revascularization due to complications, such as bleeding and stroke, encountered in those patients. [25, 26]

Several linked factors likely contribute to the adverse prognosis of patients with both impaired renal function and ACS. These include the high prevalence of comorbidities such as diabetes, dyslipidemia, and hypertension in patients with chronic and end-stage kidney disease. [27] Furthermore, the underuse of cardio protective therapies, including angioplasty, thrombolytic agents, and revascularization, may play a role. Therapy toxicity and abnormal vascular integrity, characteristic of chronic kidney disease, have a role as well. While the exact interplay of these factors in increasing adverse outcomes remains unclear, they are actively being investigated. [28, 29]

The present study has several limitations. The total number of patients is relatively small, particularly when stratified into subgroups, and this may limit the statistical power to detect significant associations, particularly in subgroup analyses. Also, this is a single-center study, and hence the findings may not be generalizable to other populations. Future studies with larger, multicenter cohorts and long-term follow-up are required to confirm these observations and explore the underlying potential mechanisms.

In conclusion, moderate to severe renal function impairment is a predictor of in-hospital morbidity and mortality for patients hospitalized with ACS.

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Conflict of Interest: The authors declare that they have no conflict of interest.

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Table 1: Baseline characteristics of patients with Acute coronary syndrome(ACS) according to the degree of renal impairment

Patient criteria		No. of patients with normal/mild renal impairment (33)	No. of patients with moderate/severe renal impairment (37)	P value
Total No.(70)				
Age(yr)	<60 (29)	21(72%)	8(28%)	<0.001
	≥60(41)	12(29%)	29(71%)	
Sex	Male(44)	27(61%)	17(39%)	<0.002
	Female(26)	6(23%)	20(77%)	
History of ischemic heart disease(21)		8(38%)	13(62%)	0.4
History of hypertension(40)		13(32%)	27(68%)	<0.007
History of DM(37)		16(43%)	21(57%)	0.6
Current smoking(34)		13(38%)	21(62%)	0.1
BMI kg/m²	<25	8(40%)	12(60%)	0.5
	≤25	25(50%)	25(50%)	

Table :2 The outcome (complications and mortality) in patients with ACS according to the degree of renal impairment

Outcome	No. of patients with normal/ mild renal impairment (33)	No. of patients with moderate/severe renal impairment (37)	P value
Total(70)			
Occurrence of complications (28)	8(28%)	20(72%)	< 0.01
Mortality (15)	3(20%)	12(80%)	< 0.01

Table 3: Relationship between number of risk factors &degree of renal impairment in acute coronary syndrome

NO. OF RISK FACTORS Total (70)	No. of patients with normal/ mild renal impairment (33)	No. of patients with moderate/severe renal impairment (37)
≤ 3	21(75%)	7(25%)
>3	12(28%)	30(72%)

P value< 0.0005

Table 4: Baseline characteristics of patients with STEMI according to degree of renal impairment

Patient criteria		No. of patients with normal/ mild renal impairment (16)	No. of patients with moderate/ severe renal impairment (17)	P value
Total No.(33)				
Age(yr)	<60(14)	10(71%)	4(29%)	<0.01
	≥60(19)	6(31%)	13(69%)	
Sex	Male(21)	14(67%)	7(33%)	<0.01
	Female(12)	2(17%)	10(83%)	
History of ischemic heart disease(5)		1(20%)	4(80%)	0.1
History of hypertension(19)		6(31%)	13(69%)	<0.01
History of DM(17)		8(47%)	9(53%)	0.5
Current smoking(19)		7(37%)	12(63%)	0.1

BMI K/m²	<25(8)	3(37%)	5(67%)	0.3
	≤25(25)	13(52%)	12(48%)	

Table 5: Outcomes (complications and mortality) in patients with STEMI according to degree of renal impairment

Outcome Total(33)	No. of patients with normal/mild renal impairment (16)	No. of patients with moderate/severe renal impairment (17)
Occurrence of complications (15)	5(33%)	10(67%)
MORTALITY (7)	2(28%)	5(72%)

P value=0.1

Table 6: Baseline characteristics of patients with NSTEMI/UA according to degree of renal impairment

Patient criteria Total No.(37)		No. of patients with normal/mild renal impairment (17)	No. of patients with moderate/ severe renal impairment (20)	P value
Age (yr)	<60(15)	11(73%)	4(27%)	<0.01
	≥60(22)	6(27%)	16(73%)	
SEX	Male(23)	13(56%)	10(44%)	0.09
	Female(14)	4(28%)	10(72%)	
History of ischemic heart disease(16)		7(44%)	9(56%)	0.8
History of hypertension(21)		7(33%)	14(67%)	0.07
History of DM(20)		8(40%)	12(60%)	0.4
Current smoking(15)		6(40%)	9(60%)	0.5
BMI Kg/m²	<25(12)	5(42%)	7(58%)	0.7
	≤25(25)	12(48%)	13(52%)	

Table 7: Outcomes (complications & mortality) in patients with NSTEMI /UA according to the degree of renal impairment

Outcome Total No.(37)	No. of patients with normal/ mild renal impairment (17)	No. of patients with moderate/ severe renal impairment (20)
Occurrence of complications (13)	3(23%)	10(77%)
MORTALITY (8)	1(12%)	7(88%)

P value<0.03