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Retrospective Study

Impact of Chronic Kidney Disease on Major Adverse Cardiac Events in Patients with Acute Myocardial Infarction: A Retrospective Cohort Study

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Abstract

Background: Acute Myocardial Infarction (AMI) results in a reduction in patients' life expectancy. Different risk factors affect the risk of Major Adverse Cardiac Events (MACE). Although the role of kidney dysfunction in patients with Chronic Kidney Disease (CKD) in cardiac events has been identified, many patients with AMI are unaware of their underlying kidney disease. This study aimed to compare the incidence of adverse cardiovascular events and identify predictors of major adverse cardiovascular events in the medium term among patients with and without renal dysfunction following AMI.

Methods: This retrospective cohort study was conducted on 1039 patients who were hospitalized for Acute Myocardial Infarction (AMI) between 2018 and 2019. The patient cohort comprised 314 women (mean age: 69.8 ± 13.2 years) and 725 men (mean age: 60.5 ± 13.8 years). Patient data were obtained from the registry of patients with acute myocardial infarction and the participants were followed up for a minimum of one year following hospital discharge to assess the incidence of MACE.

Results: The study found that patients with a Glomerular Filtration Rate (GFR) level below 60 had a significantly higher mortality rate than those with a GFR level of 60 or above (15.7% *vs.* 3.5%, $p < 0.0001$). The multivariate analysis showed that Diabetes Mellitus (DM), GFR, and Non-ST Elevation Myocardial Infarction (NSTEMI) are significant risk factors for cardiovascular events. ($p = 0.016$, $p = 0.015$, $p = 0.006$ respectively), while variables such as sex, age, and Hypertension (HTN) were not significant risk factors. There was a negative correlation between GFR and death ($0.241 - = r$, $p < 0.0001$)

Conclusion: This study highlights the importance of detecting kidney disease during an AMI and managing risk factors for cardiovascular disease to improve health outcomes and reduce the risk of mortality.

More Information

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Introduction

Acute Myocardial Infarction (AMI) is a significant public health concern, representing a leading cause of morbidity and mortality worldwide. Renal impairment commonly coexists in patients with cardiovascular disease, thereby increasing the risk of major adverse cardiovascular events [1-4]. The severity of renal dysfunction serves as a vital prognostic factor for subsequent cardiovascular events [5]. Early identification of renal dysfunction is of paramount importance for optimal management, as its presence can have a negative impact on diagnostic and therapeutic interventions during both the acute and long-term phases of AMI [6,7]. Notably, patients with Chronic Kidney Disease (CKD) who experience ST-elevation myocardial infarction (STEMI) face a particularly high risk of adverse outcomes, including death, hospitalization, and cardiovascular events [8-10].

The primary objective of this study is to conduct a comprehensive comparative analysis of adverse cardiovascular events in patients with and without renal dysfunction following acute myocardial infarction. Additionally, the secondary

objective is to identify the predictors of such occurrences in the medium term. By examining the relationship between renal dysfunction and cardiovascular outcomes in AMI patients, this research aims to enhance our understanding of the impact of renal impairment on the prognosis of individuals with AMI. The findings from this study hold the potential to contribute to the development of improved strategies for risk stratification, early detection and management of renal dysfunction in AMI patients. Ultimately, this could lead to better patient outcomes and potentially alleviate the burden of cardiovascular events in this population.

Methods

This retrospective cohort study included a total of 1039 patients who were admitted to Afshar Hospital between 2018 and 2019 and diagnosed with Acute Myocardial Infarction (AMI). The sample size for the study was determined based on an assumed Major Adverse Cardiovascular Events (MACE) rate of approximately 4%. With a desired level of significance (α) of 0.05 and a power (1-β) of 0.80, the sample size of 1039 patients was estimated to be sufficient to detect significant differences in MACE rates.

The study followed ethical guidelines and principles set by the institutional review board at Azad Medical School of Yazd. Ethical approval was obtained from the review board before starting the research, based on the code of ethics (1400.315. IR.IAU.KHUISF.REC) provided by the ethics committee. Informed consent was obtained from all participants, and their privacy and confidentiality were safeguarded throughout the research process.

Patient data was extracted from a registry database that included myocardial infarction patients in Yazd province. The study included patients between 25 and 70 years old who had a confirmed diagnosis of myocardial infarction according to the fourth universal definition of MI. Patients with a history of heart failure before the myocardial infarction or those who did not provide consent were excluded from the study.

The collected patient data encompassed various demographic variables such as age, gender, weight, blood pressure, diabetes, smoking status, alcohol consumption, and high blood pressure. Additionally, information on laboratory test results, symptoms at the time of referral, type and severity of myocardial infarction, and details of the treatment received were recorded. The Glomerular Filtration Rate (GFR) was calculated for each patient using the Modification of Diet in Renal Disease (MDRD) formulas. The study aimed to evaluate the impact of renal dysfunction on adverse cardiovascular events following acute myocardial infarction by comparing patients with a GFR greater than 60cc/min to those with a GFR equal to or less than 60cc/min. This cutoff point allowed for a clear differentiation between patients with relatively normal kidney function and those with impaired kidney function.

Patients were followed up for at least one year, during which occurrences of death, hospitalization, and repeat revascularization were evaluated as Major Adverse Cardiovascular Events (MACE) in the study.

The collected data were analyzed using SPSS-18 software. Quantitative data were analyzed using t-tests and ANOVA tests, while qualitative variables were analyzed using the chi-square test. Post-hoc analysis using the Tukey test was conducted when necessary. A p - value less than 0.05 was considered statistically significant, indicating meaningful differences between the groups being compared.

Results

This study included a total of 314 women, with a mean age of 69.8 ± 13.2 years, and 725 men, with a mean age of 60.5 ± 13.8 years. The characteristics of the patients are presented in Table 1. The loss rate for follow-up and assessment of Major Adverse Cardiovascular Events (MACE) was 7.7%, which accounted for 80 patients. During the one-year follow-up period, 8.7% of the patients died (Table 2). The study found a significant relationship between low Glomerular Filtration Rate (GFR) levels and higher mortality rates. Patients with a GFR below 60 had a mortality rate of 15.7%, compared to 3.5% for those with a GFR of 60 or above (Table 3). Age, sex,

Table 1: Baseline Characteristics of Study Population.

Character	Mean ± SD
	N(%)
Age (yr)	
-Male	13.8 ± 60.5
-Female	13.2 ± 69.8
Sex	
-Male	725(69.8)
-Female	314(30.2)
BMI > = 30 kg/ m2	190(18.3)
Risk factor	
-DM	352(33.9)
-HTN	494(47.5)
-HLP	384(37)
-Smoking	252(24.3)
-Opium addiction	158(15.2)
MI type	
-STEMI	652(62.8)
-NSTEMI	365(35.1)
-LBBB	9(0.9)
-undetermined	13(1.2)
Treatment option	
-Medical	550(52.9)
-PCI	489(47.1)

Table 2: Association between Glomerular Filtration Rate and Adverse Cardiovascular Outcomes.

Event	N	%	Total
Death	84	8.7	959
Rehospitalisation	263	27.4	959
Repeat Revascularization	161	16.8	959
MACE	508	52.9	959

MACE: Major Adverse Cardiovascular Events.

GFR, and Diabetes Mellitus (DM) were identified as significant risk factors for MACE, while smoking, opium addiction, and Hypertension (HTN) did not show a significant association (Table 4). Patients with lower GFR levels were found to have a higher likelihood of experiencing MACE compared to those with higher GFR levels. Multivariate regression analysis revealed that DM, GFR, and Non-ST Elevation Myocardial Infarction (NSTEMI) were significant risk factors for cardiovascular events ($p = 0.016$, $p = 0.015$, $p = 0.006$, respectively). However, variables such as sex, age, and HTN were not significant risk factors (Table 5). There was a negative correlation between GFR and death ($r = -0.241$, $p < 0.0001$) (Figure 1).

Discussion

Chronic Kidney Disease (CKD) is a significant global health issue affecting millions of individuals worldwide [11,12]. It is a progressive condition characterized by a gradual decline in kidney function, leading to the accumulation of toxins and waste products in the body [13]. CKD is associated with an increased risk of mortality, cardiovascular disease, and other health complications [14,15]. Glomerular Filtration Rate (GFR) is a measure of kidney function that estimates the amount of blood filtered by the kidneys over time [16].

Table 3: Association between GFR Level and Patient Survival.

GFR level	Alive	Deceased (%)	*p*
≥ 60	528(96.5)	19(3.5)	< 0.0001
< 60	347(84.3)	65(15.7)	

Note: GFR: Glomerular Filtration Rate.

Table 4: Association of Risk Factors with Major Adverse Cardiovascular Events (MACE).

Parameter	With MACE (N)		Without MACE (N)		*p*
	≥ 60	< 60	≥ 60	< 60	
Age ≥ 60 yr	**59**	**136**	**146**	**187**	**0.004**
Male	135	86	325	130	0.034
Female	23	101	41	132	
Smoking	58	21	121	32	0.863
Opium addiction	40	16	77	25	0.353
DM	48	89	92	106	0.039
HLP	45	69	119	131	0.518
HTN	61	112	131	166	0.136
GFR	158	187	366	262	0.001

MACE: Major Adverse Cardiovascular Events. DM: Diabetes Mellitus. HLP: Hyperlipidemia. HTN: Hypertension. GFR: Glomerular Filtration Rate

Table 5: Multivariate Regression Analysis of Risk Factors for Cardiovascular Events.

Variable	Regression coefficient	Odd ratio	Min	Max	*p* - value
HTN	0.112	1.12	0.803	1.557	0.508
DM	0.379	1.46	1.072	1.989	0.016
HLP	-0.469	0.63	0.449	0.871	0.005
MI type STEMI *vs.* NSTEMI	-0.412	0.66	0.495	0.887	0.006
Sex	0.259	1.3	0.919	1.825	0.139
Age	0.4	1.4	0.992	1.015	0.536
GFR	0.419	1.52	1.085	2.133	0.015

HTN: Hypertension; DM: Diabetes Mellitus; HLP: Hyperlipidemia; STEMI: ST-Elevation Myocardial Infarction; NSTEMI: Non-ST Elevation Myocardial Infarction; RC: Risk Category; GFR: Glomerular Filtration Rate.

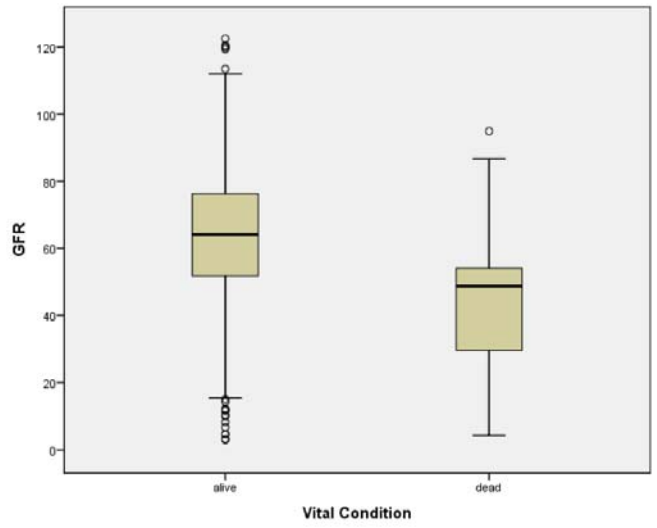

Figure 1: Relationship between Glomerular Filtration Rate and Mortality.

This study used the Glomerular Filtration Rate (GFR) instead of serum creatinine for assessing kidney function. GFR is a more precise measure because it reflects the kidneys' ability to filter blood and remove waste products [17]. Serum creatinine, although commonly used, can be influenced by various factors and may not provide an accurate indicator of kidney function alone. GFR, considers additional factors such as age, sex, race, and serum creatinine levels, resulting in a more accurate estimation of kidney function, especially in individuals with Chronic Kidney Disease (CKD) or those at risk of developing it [18]. GFR is preferred in research studies due to its standardized assessment of kidney function across different populations [19]. It allows for the classification of patients into different CKD stages and the evaluation of their clinical outcomes, including mortality, cardiovascular events, and treatment response [20]. A GFR level below 60 indicates CKD and a GFR level below 15 indicates kidney failure [21]. Our study revealed a significant association between lower GFR levels and higher mortality rates. Specifically, patients with a GFR below 60 had a mortality rate of 15.7%, compared to only 3.5% in patients with a GFR of 60 or above. These findings are consistent with previous research demonstrating a link between lower GFR and increased mortality in Acute Myocardial Infarction (AMI) patients [22-27]. For instance, a study by Ismail, et al. reported a one-year mortality rate of 13.2% in patients with a GFR below 60% compared to 2.4% in those with a GFR above 60% [28].

In addition to mortality, our study investigated the risk factors associated with Major Adverse Cardiovascular Events (MACE). Age and Diabetes Mellitus (DM) were identified as significant risk factors for MACE. DM is a leading cause of CKD and is known to elevate the risk of cardiovascular disease. Interestingly, our study found an inverse relationship between hyperlipidemia and cardiovascular diseases. Further investigation is needed to explore whether statin treatment in patients with this history may provide protective effects

against cardiac events. A meta-analysis indicated that statin administration resulted in a 41% reduction in cardiovascular disease risk in stages 1 - 3 CKD compared to placebo. Statins were also found to significantly reduce the risk of total mortality, coronary heart disease events, and stroke in the same patient population [29].

Studies have extensively examined AMI patients with CKD or End-Stage Renal Disease (ESRD). Renal injury in AMI patients is associated with an increased risk of mortality and CKD progression. Bleeding is the primary cause of mortality in dialysis patients with ESRD, and STEMI patients on dialysis exhibit higher in-hospital mortality rates. AMI patients with ESRD require personalized management and appropriate coronary revascularization. Impaired renal function in STEMI patients is linked to a higher mortality risk, and primary Percutaneous Coronary Intervention (PCI) yields better outcomes than fibrinolysis. These studies emphasize the importance of recognizing and managing renal injury and comorbidities in AMI patients with CKD or ESRD to improve outcomes [24,30-34]. Our study also employed multivariate regression analysis to identify risk factors associated with cardiovascular disease. The analysis revealed that DM and Non-ST Elevation Myocardial Infarction (NSTEMI) are significant risk factors for cardiovascular events. However, variables such as sex, age, and Hypertension (HTN) did not show a significant association. These findings align with previous studies that have identified DM and the type of MI as significant risk factors for cardiovascular events [24,35]. Furthermore, the study found that Percutaneous Coronary Intervention (PCI) was more frequently performed in patients with ST-Elevation Myocardial Infarction (STEMI) compared to those with NSTEMI. This difference in PCI utilization may contribute to the variation in Major Adverse Cardiovascular Event (MACE) incidence between the two groups. Studies suggest that an early invasive strategy may improve outcomes in non-ST-elevation Acute Coronary Syndrome (ACS) patients with CKD [36-38].

The findings of our study underscore the importance of managing risk factors to mitigate the risk of cardiovascular disease and enhance health outcomes. This may involve lifestyle modifications such as adopting a healthy diet, engaging in regular physical activity, and smoking cessation, as well as medication management and regular monitoring of kidney function [39,40].

Limitations

The study was a retrospective analysis of patients with Chronic Kidney Disease (CKD) who had experienced an Acute Myocardial Infarction (AMI). While the study provided important insights into the management and outcomes of this patient population, several limitations had to be considered when interpreting the results.

First, the retrospective nature of the study limited the ability to establish causality or control for potential confounders. This meant that while the study could identify associations between different variables, it could not determine whether one variable directly caused another. Additionally, the study was conducted at a single center, which may have limited the generalizability of the findings to other settings. Another limitation of the study was its relatively short follow-up period of one year. This may have underestimated the incidence of long-term outcomes, such as mortality and cardiovascular events, which are important outcomes for patients with CKD and AMI. Furthermore, the study excluded patients with a history of heart failure before myocardial infarction, which may have limited the generalizability of the findings to this patient population. This was an important limitation, as heart failure is a common complication of CKD and is associated with increased morbidity and mortality. Moreover, the study did not include information on certain variables that may have impacted the outcomes, such as medication use and comorbidities. This was a significant limitation, as the management of CKD and AMI typically involves multiple medications and the presence of comorbidities can impact treatment decisions and outcomes. Finally, the study did not provide information on the specific interventions used to manage patients with CKD and AMI. This was an important limitation, as the choice of interventions can impact outcomes such as mortality and cardiovascular events.

Conclusion

The findings of this study demonstrate a significant association between GFR levels below 60 and increased mortality rates. Patients with lower GFR levels are more likely to experience MACE compared to those with higher GFR levels. Furthermore, GFR emerges as a crucial predictor of mortality and should be incorporated into the assessment of cardiovascular disease risk.

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Author contributions

Abbas Andishmand contributed to the conception and design, drafted the manuscript, gave final approval, and agreed to be accountable for all aspects of the work ensuring integrity and accuracy.

Mahdiah Sadat Namayandah contributed to analysis and interpretation, drafted the manuscript, critically revised the manuscript, gave final approval, and agreed to be accountable for all aspects of the work ensuring integrity and accuracy.

Ehsan Zolfeqari contributed to the acquisition, drafted the manuscript, and prepared and revised the manuscript.

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