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Unlocking the Impact of Renal Function on Acute Coronary Syndrome: Insights from a Cohort of 318 Cases

Hanaa El Ghiati[1], Hind Ouaouicha[2], Hamza Chraibi[3], Zineb Fassi Fehri[4], Najat Mouine[5], Zouhair Lakhal[6], Aatif Benyass[7]

[1]Cardiology, Military Teaching Hospital of Rabat, Rabat, Morocco
[2,3]Cardiology, Cardiology Department of Avicenne Hospital, Rabat, Morocco
[4]Cardiology Center, V Military Instruction Hospital of Rabat, Mohammed V University, Rabat, Morocco
[5]Cardiology, Mohammed V Military Hospital, Rabat, Morocco
[6]Military hospital of instruction mohammed V, Department of Cardiology, Mohammed V University, Rabat, Rabat, Morocco
[7]Cardiology Center, Mohammed V Military Instruction Hospital of Rabat, Mohammed V University, Rabat, Morocco

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Corresponding Author:
Hanaa El Ghiati

ABSTRACT

Introduction: Chronic kidney disease (CKD) represents a distinct risk factor by itself for the development of coronary artery disease (CAD). Notably, CAD stands as the primary driver of both sickness and death among individuals diagnosed with CKD. Furthermore, individuals with CKD tend to experience worse outcomes when it comes to CAD. In addition to conventional risk factors, numerous factors associated with uremia, including inflammation, oxidative stress, endothelial dysfunction, coronary artery calcification, elevated homocysteine levels, and the use of immunosuppressants, have been linked to an increased risk of accelerated atherosclerosis.

Objective and method: In this study, we aim to assess the differential effect of renal impairment across the spectrum of patients with acute coronary syndrom. We conducted this study in the intensive care unit of cardiology in the Military Teaching Hospital of Rabat.

Results: A total of 318 patients were included in the study. The average age was 63.8 +/- 9.41 years and 77% (244/318) were male. Normal kidney function was reported in 72.8% (220/318) of patients. Of the 318 included patients, 121(38.3%) were presented with STEMI, 154 (48.7%) with NSTEMI, and 41 (13%) with unstable angina. The difference of age was significant with a p-value of <.001 with a mean of age of 61.8 in patients with normal renal function vs 68.1 in impaired renal function patients.

Patients with impaired GFR had more history of previous PCI (21) compared to those with normal GFR (23) with a p value of 0.001. Hb was lower (12.5vs 13.9 p<0.01) and Grace score was higher (45 vs44 p<.001) in patients with impaired GFR vs patients with normal GFR.

Percentage of cardiogenic shock and death was respectively higher in renal impairment (12(60%) vs 8 (40%) with p of 0.004); (10(62.5%) vs 6(37.5%) with p 0.005.

Conclusion: The magnitude of renal impairment is significant in our study in the most deadly complication: cardiogenic shock and death; which confirms that outcomes of coronary artery disease especially in acute coronary syndrome are significantly poorer in patient with kidney disease.

Categories: Cardiology

KEYWORDS: Keywords: non-st segment elevation myocardial infarction (nstemi), st-elevation myocardial infarction (stemi), coronary artery disease, chronic kidney disease (ckd), : acute coronary syndrome, impaired renal function

INTRODUCTION

Chronic kidney disease (CKD) is a well-established independent risk factor for the development of coronary artery disease (CAD), and it plays a pivotal role in the health outcomes of affected individuals. CAD is the leading cause of both morbidity and mortality among CKD patients, underscoring the critical need for comprehensive management strategies in this population. The interplay between CKD and CAD is complex and multifactorial, with various uremic factors and comorbidities contributing to an

elevated risk of accelerated atherosclerosis. Understanding these intricate relationships is crucial for optimizing the care and outcomes of CKD patients with CAD.

Numerous prior investigations have indicated that there may be an association between modest to moderate rises in serum creatinine levels and elevated rates of all-cause mortality and cardiovascular-related deaths.

However, it remains uncertain whether chronic kidney disease autonomously amplifies the risk of various cardiovascular conditions. [1]

In our study, we will strive to determine whether renal impairment independently contributes to the heightened risk of various cardiovascular diseases and how it may influence both mortality rates and the occurrence of other cardiovascular complications.

MATERIALS AND METHODS

Study Population:

In this retrospective study, we enrolled a total of 318 patients who sought medical attention in the emergency room due to acute coronary syndrome.

Duration and Location:

The study was carried out over a two-year period spanning from 2019 to 2021. It took place within the intensive cardiac care unit of the Military Teaching Hospital of Rabat, which served as the primary setting for data collection.

Inclusion Criteria:

Patients were included in the study if they met any of the following conditions: Presenting with ST-segment elevation myocardial infarction (STEMI). Presenting with non-ST-segment elevation myocardial infarction (NSTEMI). Presenting with Unstable Angina.

Exclusion criteria:

Participants were excluded from the study if they met any of the following conditions:

Possessing incomplete or missing data that were relevant to the study's variables. Failing to meet the predetermined inclusion and exclusion criteria.

STATISTICAL ANALYSIS

To assess the normality of data distribution, the Shapiro-Wilk test was employed. The study data were summarized using either the mean and standard deviation or the median and interquartile range, depending on their suitability. Continuous variables were compared using either an unpaired t-test or the Mann- Whitney U test, as appropriate. Conversely, frequency comparisons were performed using the Chi-Squared test. Adjusted and unadjusted models were used to compare the impact of cardiovascular risks and especially the impairment of renal function in the occurence of the total occlusion of artery and thus the STEMI presentation.

RESULTS

A total of 318 patients were included in the study. The population was divided into two groups based on renal function: Normal renal function (N=220), Impaired renal function (N=98). (Table 1)Of the 318 included patients, 121(38.3%) were presented with STEMI, 154 (48.7%) with NSTEMI, and 41 (13%) with unstable angina. (Figure1)

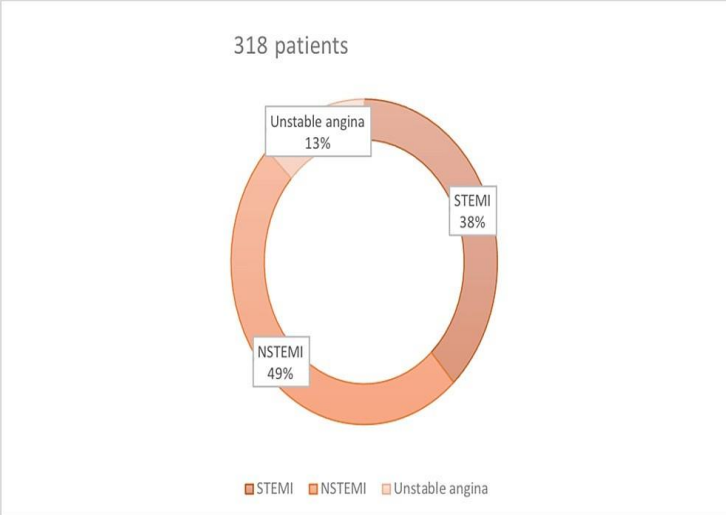

Figure 1: Clinical presentation of our population

Table 1: Sociodemographic characteristics

	Total Population N= 318	Normal renal function N= 220	Impaired renal function N= 98	P value
Age (mean ±SD)	63.8 ± 9.41	61.8 ± 9.14	68.1 ± 8.55	<0.001*
Males, n (%)	244 (77.0)	189 (63)	55 (37)	0.201
Diabetes, n (%)	155 (48.9)	89 (57.4)	66 (42.6)	<0.001*

Hypertension, n (%)	136 (42.9)	76 (55.9)	60 (44.1)	<0.001*
Dyslipidemia, n (%)	109 (34.)	70 (64.8)	38 (35.2)	0.409
Active smoker, n (%)	175 (55.2)	129 (74.1)	45 (25.9)	0.072
Previous MI, n (%)	38 (12.1)	19 (50)	19(50)	0.007*
Previous PCI, n (%)	44 (14.0)	21 (47.7)	23 (52.3)	0.001*
Previous CABG, n (%)	5 (1.6)	3 (60)	2 (40)	0.665
Hb (mean ±SD)	13.5 ± 1.87	13.9 ±1.53	12.5 ± 2.16	<0.01
GRACE > 140, n (%)	89 (29.5)	44 (49.4)	45 (50.6)	<0.001*
Impaired LVSF < 50%, n (%)	113 (37.5)	63 (55.8)	50 (44.2)	<0.001*
Culprit LAD, n (%)	105 (33.2)	76 (72.4)	29 (27.6)	0.054
Acute heart failure, n (%)	57 (18.1)	35 (61.4)	22 (38.6)	<0.01
Cardiogenic shock, n (%)	20 (6.3)	8(40)	12 (60)	0.004*
Severe secondary MR, n (%)	7 (2.2)	4 (57.1)	3(42.9)	0.497
Pericarditis, n (%)	20 (6.3)	13 (65)	7 (35)	0.683
PCI, n (%)	145 (46.0)	105 (72.4)	40 (27.6)	0.212
Inhospital Death, n(%)	16 (5.1)	6 (37.5)	10(62.5)	0.005*

MI: Myocardial Infarction, PCI: Percutaneous Coronary Intervention, CABG: Coronary Artery Bypass Graft,GRACE: Global Registry of Acute Coronary Events, LVSF : Left Ventricular Systolic Function, LAD : Left Artery Descendant artery, MR: Mitral Regurgitation

* $p<0.05$

Among all the risk factors, impaired renal function appears to be incriminated in the occurrence of Myocardial infarction with ST elevation, which is the ultimate evolution of ischemic heart disease and therefore the most serious condition.

We chose to study the factors that may lead to this condition and we evaluated them both in unadjusted models and adjusted models.(Table 2)

We included then the universal cardiovascular risk factors which happened to be significant in our previous comparison study and we added the impaired renal function.

Table 2: Odds ratios (OR) and their corresponding confidence intervals (CI) for various factors in predicting the occurrence of STEMI

	Unadjusted			Adjusted		
Factors	OR	95%	p	OR	95%	p
Impaired renal function	4.02	1.42-11.4	0.005	3.850	0.0426 - 2.6537	0.043
Male	0.758	0.210-2.74	0.672	1.258	-1.3852 - 1.8448	0.780
Age				1.018	-0.0527 - 0.0887	0.618
Smoking	1.24	0.453-3.39	0.676	0.682	-1.7352 - 0.9703	0.579
Diabetes mellitus	0.420	0.142-1.24	0.106	1.398	-0.9421 - 1.6119	0.607
Hypertension	0.744	0.272-2.04	0.564	1.579	-0.7773 - 1.6915	0.468
Hyperlipidemia	1.62	0.508-5.13	0.412	0.710	-1.6042 - 0.9190	0.595
Hemoglobin				0.900	-0.4458 - 0.2358	0.546

In the unadjusted model, individuals with impaired renal function have an odds ratio of 4.02 (95% CI: 1.42- 11.4) compared to those with normal renal function. This indicates that individuals with impaired renal function are approximately four times more likely to experience the Myocardial Infarction with ST elevation. After adjusting for other variables, the odds ratio is 3.850 (95% CI: 0.0426-2.6537), suggesting a significant association between impaired renal function and the outcome (p-value = 0.043).

DISCUSSION

Epidemiological aspects:

Epidemiological studies consistently demonstrate a strong association between cardiovascular (CV) events and chronic kidney disease (CKD). A landmark population-based study conducted by Go et al. [1] involving over 1.1 million adults established that a decline in glomerular filtration rate (GFR) is a primary independent risk factor for CV events, such as peripheral artery disease (PAD), coronary artery disease (CAD), congestive heart failure (CHF), and stroke. This association remains significant even after accounting for other confounding risk factors. Moreover, the progressive

decline in GFR is associated with a gradual increase in mortality. In contemporary medical practice, CKD is recommended to be considered on par with CAD due to its significant impact on cardiovascular health.

Pathophysiological aspects:

The pathophysiology of vascular disease in individuals with chronic kidney disease (CKD) differs significantly from that seen in the general population.In addition to conventional risk factors such as hypertension, diabetes, dyslipidemia, and advancing age, there is a prevalence of novel risk factors in CKD and end-stage renal failure (ESRF) patients. These factors, including endothelial dysfunction (ED), abnormalities associated with CKD-mineral and bone disorder (CKD-MBD) like hyperphosphatemia and hyperparathyroidism, along with vascular calcifications, increased oxidative stress, and inflammation, appear to exert a more substantial influence on vascular disease in CKD and ESRF patients when compared to healthy individuals [2,3].

Despite considering these factors, the reasons why CKD patients are more susceptible to adverse cardiovascular (CV) outcomes remain somewhat elusive. In the general population, many individuals with coronary artery disease (CAD) develop collateral circulation in response to atherosclerotic coronary artery obstructions. Charytan et al. have postulated that CKD patients may have a reduced capacity for collateral blood supply to ischemic myocardial areas. This hypothesis could offer a partial explanation for the notably worse CV outcomes and mortality observed in CKD patients [4].

It's important to highlight the significant role of vascular calcification (VC) in this context. VC is highly prevalent and tends to worsen with declining kidney function in CKD and ESRF patients. The significance of this process has been underscored by the strong correlation between VC and heightened cardiac mortality in this patient population [4].

Clinical aspects:

A study conducted by Moisi et al. [5] found that when it comes to Acute Coronary Syndrome (ACS), the symptoms often deviate from the typical pattern. Individuals with normal kidney function tend to primarily report thoracic pain. In contrast, CKD (Chronic Kidney Disease) subjects show a statistically significant association with dyspnea. Research indicates that CKD patients are more likely to experience silent ischemia or atypical symptoms upon admission. In a trial involving 356 patients, it was observed that painless myocardial infarction occurred more frequently in the CKD group compared to those without CKD, with statistical significance [6]. This phenomenon is believed to be influenced by common conditions among CKD patients, such as diabetic neuropathy and neuropathy induced by the uremic environment [6].

When ACS manifests with dyspnea as the primary symptom, it can be mistaken for angina equivalent. Sosnov et al. reported that CKD subjects were 43% less likely to report specific thoracic pain, even when diabetic neuropathy was not a factor. This observation aligns with our study, which also revealed a notable incidence of shortness of breath in the CKD subgroup [7].

The presence of few symptoms and angina-like manifestations in ACS cases among CKD patients is crucial in developing a comprehensive screening protocol [8]. Numerous studies, including a significant one by Go et al. [1] that encompassed CKD subjects, emphasize the role of cardiovascular risk factors independently of renal function. This research demonstrated that impaired renal function significantly increases the hospitalization rate for ischemic CAD, peripheral artery disease (PAD), or congestive heart failure, irrespective of concurrent cardiovascular risk factors. It underscores the independent predictive role of CKD in major cardiovascular events.

Prognosis aspects:

Patients with Chronic Kidney Disease (CKD) who also have Coronary Artery Disease (CAD) tend to face a more unfavorable outlook compared to those with healthy kidney function. This disparity is marked by higher rates of in-hospital complications and long-term mortality, particularly in individuals undergoing hemodialysis [9,10]. Several factors contribute to this bleak prognosis [11], including hypertension, diabetes, advanced age, hypervolemia, decreased glomerular filtration rate, proteinuria, inflammation, oxidative stress, and other related factors.

The CKD patient group exhibits a greater frequency of complications, such as acute pulmonary edema or cardiogenic shock, in contrast to individuals with normal kidney function. The presence of severe CAD, left ventricular ejection fraction (EF) impairment, ischemia in the papillary muscles of the mitral valve, and secondary severe mitral valve insufficiency, coupled with impaired renal function, underpins the negative prognosis and the common occurrence of complications in these patients.

Conversely, individuals with Acute Coronary Syndrome (ACS) and normal kidney function tend to experience a more favorable disease progression, characterized by lower rates of cardiogenic shock and in-hospital mortality. Our research findings highlight the importance of tailoring the management of ACS patients with CKD in the emergency department to account for their distinctive clinical course and negative prognosis.

Given the increased prevalence of multivessel coronary disease and hemodynamic instability frequently observed in CKD patients, special emphasis should be placed on comprehensive echocardiographic assessments.

Treatment aspects:

The management of Acute Coronary Syndrome (ACS) in individuals with Chronic Kidney Disease (CKD) presents a challenging clinical scenario. Historically, advanced CKD patients and those undergoing dialysis have not been included in randomized trials assessing ACS treatments, both medical and interventional.

Consequently, our knowledge about this subgroup of patients is primarily derived from limited observational studies, and as of now, there is no universally accepted treatment strategy for them.

Coronary Reperfusion Strategies:

When it comes to treating CKD patients in the early stages of ST-segment Elevation Myocardial Infarction (STEMI), several uncertainties exist, particularly regarding the adoption of aggressive reperfusion approaches like fibrinolytic therapy and primary percutaneous coronary intervention (PCI). Although significant trials have clearly demonstrated the life-saving benefits of thrombolytic agents in STEMI, none of these trials conducted specific subgroup analyses focusing on CKD patients. As a result, there is minimal data available on the use of thrombolytics in this population. Notably, a study led by Wright et al. [12] found that only 13% of their study population received intravenous fibrinolytic therapy, and 10% underwent primary PCI. The utilization of reperfusion therapy was notably lower among patients with varying degrees of CKD compared to those without CKD. Furthermore, a study by Beattie et al. [13] indicated a decreasing trend in the use of life-saving treatments like primary angioplasty and thrombolysis with worsening renal function, suggesting a potential treatment bias in favor of patients with less advanced renal dysfunction.

While the reduced use of PCI can be partly justified due to concerns about the elevated risk of contrast- induced nephropathy (CIN) and its associated high mortality, it does not fully explain the lower adoption of thrombolysis. It's crucial to emphasize that CKD should not inherently hinder the success of percutaneous or pharmacological reperfusion therapies, but it may be associated with a higher incidence of major adverse events. A study by Gibson et al. [14] examined the impact of CKD in STEMI patients receiving fibrinolytic therapy. Despite appropriate treatment with thrombolytics and additional therapies for acute myocardial infarction, including early PCI in some cases, there was a consistent reduction in survival as renal function declined, extending up to two years of follow-up. The incidence of intracranial hemorrhage was also higher in CKD patients, suggesting that primary PCI might be a more favorable option. Nevertheless, the outcomes of primary PCI in STEMI patients with CKD have remained poorly understood due to their exclusion from clinical trials.

In the management of Non-ST-segment Elevation Myocardial Infarction (NSTEMI), previous studies and guidelines have favored an invasive strategy over an initial conservative approach, with an early invasive strategy generally preferred over a delayed one. However, the KAMIR study showed that an invasive strategy within 24 hours of admission reduced mortality compared to a conservative approach, except for those with severe CKD. Regarding the timing of the invasive strategy, trends suggested that an early approach was superior to a delayed one in patients with mild CKD, although this advantage diminished as renal function worsened [15].

In a prospective study, CKD patients were randomized to receive either Coronary Artery Bypass Grafting (CABG) or stent placement. This study found no significant differences in terms of mortality, myocardial infarction (MI), or stroke, although repeat revascularization procedures were more common in the stent group [16].

Limits and perspectives:

This is a retrospective study where the majority of population had a normal function which may have biased the comparative statistics.

Our perspective is to conduct a prospective case control study with larger population.

CONCLUSIONS

The findings from our study underscore the profound impact of renal impairment on the most severe and life-threatening complications, specifically cardiogenic shock and mortality. These results serve as a stark reminder that the outcomes of coronary artery disease, particularly in the context of acute coronary syndrome, are markedly worse in patients with coexisting kidney disease.

The substantial association between renal dysfunction and adverse cardiac events, such as cardiogenic shock and death, sheds light on the critical need for specialized care and tailored treatment strategies for individuals at the intersection of coronary artery disease and chronic kidney disease. It emphasizes the urgency of developing comprehensive clinical guidelines that account for the unique challenges and risks faced by this vulnerable patient population.

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