



## Original Article

# Cardiovascular risk factors profile in patients with acute coronary syndrome with particular reference to left ventricular ejection fraction

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## ABSTRACT

**Background:** Acute coronary syndrome (ACS) remains a leading cause of death in the United States. Numerous studies have shown that the degree of LV systolic dysfunction is a major if not the most important determinant of long-term outcome in ACS.

**Objectives:** To identify the most important risk factors and other clinical predictors which might have impact on left ventricular ejection fraction in patients with ACS.

**Results:** The total patients (299) admitted to our center from July, 2015 till December, 2015; with established diagnosis of ACS were classified in to two groups: Group I: 193 patients with impaired LVEF < 40% (64.5%), Group II: 106 patients with LVEF equal or > 40% (35.5%). The patients of group I were significant elderly compared to those of group II (60.9 ± 11.2 vs 56.9 ± 10.6; p = 0.002), had significant history of DM and CKD (66.3% and 31.1% VS 49.1% and 19.8%; p = 0.004 and 0.036 respectively), presented mainly with STEMI- ACS (51.3% VS 28.3% respectively; p < 0.001) with +v cardiac biomarker (troponin) (90.2% VS 66.0%; p < 0.001). Moreover, patients of group I had more significant ischemic MR compared to the patients of group II (24.9% VS 3.8% respectively; p < 0.001) with higher rate of LV thrombus discovered by echocardiography (25.4% VS 1.9%; p < 0.001). Extensive significant CAD disease was observed to be higher among patients of group I (69.4% VS 57.5%; p = 0.039) and those patients treated mainly with PCI revascularization therapy (68.9% VS 52.8%; p = 0.002) compared to patients of group II who mainly treated medically (34.9% VS 17.6 %; p < 0.001). Multiple logistic regression analysis demonstrated that DM (odd ratio (OR): 2.64, 95% confidence interval (CI): 1.45–4.79, P = 0.01), presence of significant ischemic MR (OR: 13.7, 95% CI: 2.84–66.1, p = 0.001) and presence of significantly diseased coronary vessels (odd ratio (OR): 5.06, 95% confidence interval (CI): 1.14–22.6, P = 0.033.) all were independent predictors for significant LV dysfunction (LVEF < 40%) which predict poor outcome in ACS patients.

**Conclusion:** We concluded that DM, presence of significant ischemic MR, and increased number, severity of diseased coronaries all were independent predictors of LV dysfunction (LVEF < 40%) which is known to predict poor outcome. Identification of those risk predictors upon patient evaluation could be helpful to identify high risk-patients, in need of particular care, aggressive therapy and close follow-up to improve their poor outcome.

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## 1. Introduction

Acute coronary syndrome (ACS) remains a leading cause of death in the United States .1 There is racial variation in its epidemiology and outcome.2–4 It describes the range of myocardial ischemic states that includes unstable angina (UA), non-ST

elevated myocardial infarction (NSTEMI), or ST-elevated myocardial infarction (STEMI). The diagnosis and classification of ACS is based on clinical features, electrocardiogram (ECG) findings and biochemical markers of myocardial necrosis.5

Numerous studies have shown that the degree of LV systolic dysfunction is a major if not the most important determinant of long-term outcome in ACS.6 Among patients with ACS, impaired LV systolic function(LVEF <40%) is associated with increased 1-year mortality or hospitalization for HF, regardless of the method or timing of the LVEF assessment.7

The World Health Organization has recognized obesity, diabetes mellitus(DM), hypertension(HTN), chronic kidney disease

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(CKD), hypercholesterolemia, and smoking among the top10 traditional risk factors for premature death and morbidity.<sup>8</sup> The ultimate importance of knowing those risk factors is to determine and identify the individual risk.

In this study, we aim to perform a brief overview of prevalence of relatively important risk factors and other clinical predictors which might have impact on left ventricular ejection fraction in patients with ACS admitted to our center.

## 2. Methods

It is a descriptive, prospective, single center, observational study of all consecutive acute coronary syndrome patients admitted to our center. A total 299 patients presented to our cardiac center from July, 2015 till December, 2015; with established diagnosis of ACS (by clinical symptoms, ECG changes and/or elevated cardiac biomarkers) and sent to our center for further evaluation and providing the suitable line of management. The study of the subjects was divided in to two groups: Those with LVEF <40% (Group I), and those with LVEF equal or >40% (Group II). Ejection fraction was determined by echocardiography, in which the volumes of the heart's chambers are measured during the cardiac cycle. Ejection fraction can then be obtained by dividing the volume ejected by the heart (stroke volume) by the volume of the filled heart (end-diastolic volume).<sup>9</sup>

We analyzed the baseline demographic and clinical characteristics (age, gender, BMI, presence of DM, HTN, dyslipidemia, smoking and CKD), clinical presentation (STEMI, NSTEMI, and UA), and cardiac biomarker (Troponin). Echocardiographic findings (LVEF, presence and severity of MR and LV thrombus evidence) were all recorded. The number of significantly diseased vessel (>50% stenosis in left main or >70% in LAD, LCX and RCA) were identified with coronary angiography were also assessed. We defined patients with severe coronary artery disease as those who had left main disease and/or had two, three significantly stenosed coronaries. However, line of treatment selected to each patient (medical treatment, PCI and CABG) was also assessed.

Our study is designed to be the part of the standard of patient care, to measure and improve quality of ACS management, and has received approval of the ethics committee/institutional review board of the King Abdullah Medical City.

### 2.1. Statistical analysis

The collected data were tabulated and analyzed using SPSS version 16 soft ware (Spss Inc, Chicago, ILL Company) and Microstat W software (India, CNET Download.com). Categorical

data were presented as number and percentages while quantitative data were expressed as mean  $\pm$  standard deviation. Chi square test ( $X^2$ ), "Z" test were used to analyze categorical variables. Quantitative data were tested for normality using Kolmogorov Smirnov test, assuming normality at  $P > 0.05$ , using Student "t" for normally distributed variable. Binary logistic regression analysis was used to detect the significant predictors of significant LV dysfunction

(LVEF < 40). The accepted level of significance in this work was stated at 0.05 ( $P < 0.05$  was considered significant).

$P > 0.05$  is non significant (NS)

$P < 0.05$  is significant (S)

$P \leq 0.001$  is highly significant (HS)

## 3. Results

The total patients (299) admitted to our center from July, 2015 till December, 2015; with established diagnosis of ACS were classified in to two groups: Group I: 193 patients with impaired LVEF <40% (64.5%), Group II: 106 patients with LVEF equal or >40% (35.5%). We categorized our data into three main categories: baseline characteristics, clinical measures and line of treatment selected to each patient.

### 3.1. Baseline characteristics

The patients of group I were older compared to those of group II ( $60.9 \pm 11.2$  vs  $56.9 \pm 10.6$ ;  $p = 0.002$ ). Compared to group II, patients of group I had significant history of DM and CKD (66.3% and 31.1% vs 49.1% and 19.8%;  $p = 0.004$  and  $0.036$  respectively). There were no observed significant differences between group I and group II patients regarding the gender, BMI, rates of HTN, hyperlipidemia and smoking ( $p$  value = 0.78, 0.48, 0.65, 0.15 and 0.071 respectively) (Table 1).

### 3.2. Clinical measures

With regard to the type of ACS presentation, group II patients presented mainly with UA (33% vs 11.4%;  $p < 0.001$ ) while group I patients presented mainly with STEMI (51.3% vs 28.3% respectively;  $p < 0.001$ ). Moreover, patients of group I mostly had +ve cardiac biomarker (troponin) (90.2% vs 66.0%;  $p < 0.001$ ). Also, there was observed increase in the severity of MR among group I patients as incidence of patients who had moderate and severe MR in this group were (24.9% vs 3.8% respectively;  $p < 0.001$ ). Interestingly, the rate of LV thrombus discovered by echocardiography was higher among high risk group patients (group I) (25.4% vs 1.9%;  $p < 0.001$ ) (Table 2).

**Table 1**  
Comparison between the two groups according to demographic data.

Variable	Group I (LVEF < 40%) (N = 193)	Group II (LVEF > 40%) (N = 106)	Test	P- value
AGE (mean $\pm$ SD)	60.9 $\pm$ 11.2	56.9 $\pm$ 10.6	St. "t" = 3.05	0.002 (S)
Gender (no, %)	Male	141 (73.1)	$X^2 = 0.08$	0.78 (NS)
	Female	52 (26.9)		
BMI (no, %)	25–30	83 (62.4)	0.49	0.48 (NS)
	Obese > 30	50 (37.6)		
DM (no, %)	128 (66.3)	52 (49.1)	8.51	0.004 (S)
HTN (no, %)	128 (66.3)	73 (68.9)	0.2	0.65 (NS)
Hyperlipidemia (no, %)	80 (41.5)	53 (50)	2.03	0.15 (NS)
Smoking (no, %)	19 (9.8)	18 (17)	3.2	0.071 (NS)
CKD (no, %)	60 (31.1)	21 (19.8)	4.4	0.036 (S)

BMI: body mass index; CKD: chronic kidney disease, DM; diabetes mellitus; HTN: hypertension.

**Table 2**  
Comparison regarding to Clinical predictors:

VARIABLE	Group I (LVEF< 40%)	Group II (LVEF> 40%)	Z test	P- value
UA presentation (no, %)	22 (11.4)	35 (33.0)	4.55	<0.001 (HS)
NSTEMI presentation (no, %)	72 (37.3)	41 (38.7)	0.23	0.81 (NS)
STEMI presentation (no, %)	99 (51.3)	30 (28.3)	3.84	<0.001 (HS)
+ve troponin (no, %)	174 (90.2)	70 (66.0)	5.15	<0.001 (HS)
Significant MR (no, %)	48 (24.9)	4 (3.8)	4.6	<0.001 (HS)
LVT +ve (no, %)	49 (25.4)	2 (1.9)	5.17	<0.001 (HS)

LVT: left ventricular thrombus; MR: mitral regurge; NSTEMI: Non- ST elevation myocardial infarction; STEMI: ST elevation myocardial infarction; UA; unstable angina.

### 3.3. Coronary angiography findings and treatment strategies

Significant diseased coronaries were observed to be higher among patients of group I (69.4% vs 57.5%;  $p=0.039$ ). With regard to the management strategy selected in each group, group II patients treated medically (34.9% vs 17.6%;  $p<0.001$ ) while group I patients treated mainly with PCI (68.9% vs 52.8%;  $p=0.002$ ). There was no observed significant difference in utilization of CABG by the patients of two groups ( $p=0.76$ ) (Table 3).

Multiple logistic regression analysis demonstrated that DM (odd ratio (OR): 2.64, 95% confidence interval (CI): 1.45–4.79,  $P=0.01$ ), presence of significant ischemic MR (OR: 13.7, 95% CI: 2.84–66.1,  $p=0.001$ ) and presence of significantly diseased coronary vessels (odd ratio (OR): 5.06, 95% confidence interval (CI): 1.14–22.6,  $P=0.033$ ) all were independent predictors for significant LV dysfunction (LVEF < 40%) which predict poor outcome in ACS patients (Table 4).

## 4. Discussion

It is known that patients with CAD at risk for subsequent cardiovascular events, but the risk varies among patients. The long-term prognosis or survival rate is poor in patients with impaired LV function.<sup>7</sup> This study is designed to investigate the pattern of different risk factors, clinical measures and treatment strategies of patients with ACS admitted to our cardiac center, and to compare the prevalence of all these risk factor in the two groups of patients (Group I, those with impaired LVEF < 40% and group II, those with LVEF equal or >40%. In this study, approximately, 299 patients were admitted to our cardiac center and diagnosed as ACS.

### 4.1. Baseline characteristics

Patients of group I with significant systolic dysfunction (LVEF < 40%), were significantly older,

**Table 3**  
Comparison regarding Angiographic findings and management strategies:

Variable	Group I (LVEF< 40%)	Group II (LVEF> 40%)	Z	P- value
Single vessel disease	55 (28.5)	30 (28.3)	0.04	0.96 (NS)
Significant CAD	134 (69.4)	61 (57.5)	2.06	0.039 (S)
Medical treatment	34 (17.6)	37 (34.9)	3.36	<0.001 (HS)
PCI	133 (68.9)	56 (52.8)	2.76	0.002 (S)
CABG	26 (13.5)	13 (12.3)	0.3	0.76 (NS)

CABG: coronary artery bypass grafting; CAD: coronary artery disease; PCI: percutaneous coronary intervention.

**Table 4**  
Binary regression analysis for the predictors of LVEF< 40%.

Variable	B	S.E	OR	95% CI	P-value
Age > 60	0.141	0.308	1.16	0.63–2.1	0.65
DM +ve	0.970	0.305	2.64	1.45–4.79	0.01
CKD	0.201	0.360	1.22	0.6–2.47	0.57
Troponin +ve	2.000	1.204	7.39	0.69–78.3	0.097
STEMI presentation	0.679	1.211	1.97	0.18–21.3	0.57
MR	2.617	0.803	13.7	2.84–66.1	0.001
Significant diseased coronaries	1.623	0.762	5.06	1.14–22.6	0.033

CKD: chronic kidney disease; DM: diabetes mellitus; MR: mitral regurge; STEMI: ST-elevation myocardial infarction.

( $P=0.002$ ). This is expected as with aging process, the heart thickness, stiffness increase and significant functional deficit with stress occur which in turn result in decreasing cardiac reserve and function.<sup>10</sup> Similar to our finding, a study concluded that age is independent predictor of LV systolic dysfunction after ACS which can be easily detectable on initial evaluation of the patient.<sup>11</sup>

Also, prevalence of DM was significantly more in group I compared to group II patients. It is known that diabetic patients presenting with acute coronary syndrome (ACS) have a worse prognosis.<sup>12</sup> Moreover, patients with diabetes were found to have worse left ventricular systolic dysfunction and a higher-risk coronary anatomy.<sup>13</sup> Similarly, Antonio et al. identified DM as a strong predictor of LV dysfunction which could predict poor outcome in patients with ACS.<sup>11</sup> Also, diabetic patients showed comparable depression in LV longitudinal systolic indices when compared with age- and gender-matched healthy controls; the co-existence of diabetes leads to further impairment in LV longitudinal systolic function in an additive manner.<sup>14</sup> Recently, Amin, et al. also concluded that chronic hyperglycemia in diabetic patients may be a risk factor for developing LV systolic dysfunction in patients presenting with ACS and glycated hemoglobin level may predict LV dysfunction in those patients.<sup>15</sup>

Moreover, patients with history of CKD were identified significantly more in group I. This is predicted as it is known that CKD is closely associated with a higher risk of cardiovascular disease (CVD), and the presence of CKD is a potent predictor of a worse prognosis among patients with coronary artery disease.<sup>16–19</sup> Patients with CKD have structural changes in the myocardium as well as diastolic dysfunction and even systolic failure occur frequently.<sup>20</sup> Similarly, Dohi, et al. concluded that CKD was associated with higher long-term all cause and cardiovascular mortality after ACS.<sup>21</sup> In another study CKD was considered as independent predictor of in-hospital HF and NSTEMI-ACS.<sup>22</sup> This result is predicted as CKD alone is an independent risk factor for the development of CAD, associated with increased mortality after ACS and is considered a CAD risk equivalent.<sup>23</sup>

With respect to other risk factors, there were no significant differences observed in the prevalence of gender, BMI, HTN, dyslipidemia and smoking between the two groups of patients.

### 4.2. Clinical measures and treatment strategies

Group I patients presented mainly with STEMI and positive cardiac troponin, which might predict the high risk outcome compared to group II patients who mainly presented with UA-ACS. STEMI patients had higher long-term mortality due to higher mortality of the acute event within six months.<sup>24</sup> Similar to our finding, Antonio, et al conducted a study and concluded that ST-elevation myocardial infarction was significantly more frequent in patients with LV systolic dysfunction and those patients showed higher levels of myocardial markers of necrosis.<sup>11</sup>

Moreover, with respect of the presence of a significant MR, group I patients had significant ischemic MR compared to those

patients of group II and this significant ischemic MR seems to have prognostic implications and provided independent information for prediction of adverse outcome. Development of MR during ACS may be due to ischemic injury of the papillary muscle apparatus and/or dilation of the left ventricle and has been linked to death and development of heart failure in patients with acute MI independently of LVEF and clinical confounders.<sup>25,26</sup> In addition, MR has been linked with adverse outcome in patients with STEMI undergoing a percutaneous coronary intervention.<sup>27</sup> Similarly, Persson, et al. conducted a study and

concluded that information concerning MR grade provides important prognostic information across the spectrum of ACS and should be taken in account in evaluation of long term prognosis.<sup>28</sup>

Interestingly, the percentage of LV thrombus detected by echocardiography was higher among group I patients. This can be explained by most of those patients presented with STEMI, had LVEF < 40% with high prevalence of significant coronary artery disease, all these factors were recently established to be strongly linked to the development of LV thrombus.<sup>29,30</sup>

Moreover, patients of group I showed significant diseased coronaries compared to group II and this is expected as those patients had more prevalent risk factors (elderly, DM and history of CKD) with aggressive ACS presentation (STEMI) and higher levels of myocardial necrosis biomarkers which all associated with poor outcome post ACS. Similar to that Van der Schaaf, et al. who conducted a study and concluded that patients with STEMI and MVD have a higher long-term mortality than those without MVD, which can be explained by a smaller LVEF and a high prevalence of associated risk factors in this group of patients.<sup>31</sup>

Also, group I patients were treated mainly with PCI- revascularization and this is expected as those patients predominantly presented with STEMI-ACS, had higher rate of primary intervention and had significant coronary artery disease with impaired LVEF. It is known that CABG is the standard of care of CAD patients with 3-vessel disease and it is associated with significantly lower rates of death, MI, and repeat revascularization while PCI is an acceptable revascularization strategy for those with low SYNTAX score.<sup>32</sup>

Lastly, in conclusion DM, significant MR and significant CAD all were statistically identified as independent predictors for LV dysfunction (LVEF < 40%) in patients with ACS. The present study clearly demonstrated that the risk factors differed between the patients according to their LVEF which is known to be strongly predictor that could differentiate high- and low- risk CAD patients. However, the reason for the difference and the mechanism by which these risk factors worsen the outcome need to be investigated.

#### 4.3. Study limitation

Our data was collected from observational study, which is a limitation. Moreover, the number of enrolled patients is small due to the nature of single center study and short duration selected. Furthermore, this limited number of patients in our study may limit the degree to which our findings can be generalized. We hope to reduce the effect of this limitation by sharing with other hospitals to conduct similar studies in the future.

#### 5. Conclusion

We concluded that DM, presence of significant ischemic MR, and increased number, severity of diseased coronaries all were independent predictors of LV dysfunction (LVEF < 40%) which is known to predict poor outcome. So, evaluation of those risk predictors in patients with ACS could provide complementary

prognostic information to conventional clinical risk factors. Identification of those risk predictors upon patient evaluation could be helpful to identify high risk-patients, in need of particular care, aggressive therapy and close follow-up to improve their poor outcome. Future researches are required to investigate the prevalence of those predictors in multicenter and to determine the short and long term clinical outcomes of those patients.

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