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Cover Page Footnote

Please add the second affiliations of the authors at the footer as followings: 1-Sheeren Khaled is affiliated with Benha University- Benha- Egypt. 2-Ghada Shalaby is affiliated with Zagazig University- Zagazig- Egypt.

Severe Left Ventricular Dysfunction Earlier after Acute Myocardial Infarction Treated with Primary Percutaneous Coronary Intervention: Predictors and In-Hospital Outcome— A Middle Eastern Tertiary Center Experience

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Abstract

Improving or maintaining heart function following percutaneous coronary intervention (PPCI) is not identified in all patients. Our aim in the current study is to investigate the prevalence, factors associated with early left ventricular (LV) dysfunction following successful revascularization of myocardial infarction patients.

Methods: A single-center retrospective study included 2863 myocardial infarction patients who were admitted to our center and treated with successful PPCI.

Results: Out of 2863 consecutive patients who underwent PPCI from May 2018 to August 2021, 1021 (36%) developed server LV dysfunction. They showed a higher history rate of ischemic heart disease and previous revascularization before AMI (P = 0.05 and 0.001 respectively). Also, they presented more with anterior myocardial infarction (P < 0.001) and heavy thrombus burden (P = 0.002 and 0.004 for indication of peri-procedural glycoprotein IIb/IIIa inhibitors use and thrombus aspiration) compared to the other group of patients. Moreover, they also had a more critical anatomy of coronary artery disease (P < 0.001 for both left main and multi-vessel coronary artery disease). The independently associated predictors for early severe LV dysfunction post-AMI treated with PPCI were anterior localization of AMI, the greater value of troponin, renal impairment, and severe coronary artery disease (P = <0.001, 0.036, 0.002, and <0.07 respectively). Despite optimal treatment for those patients, they showed poor outcomes including in-hospital morbidity and mortality (P < 0.001)

Conclusion: Sizable proportion of patients following successful PPCI develop severe LV systolic dysfunction and associated with poor clinical outcomes. Larger myocardial infarction, renal impairment, and severe coronary artery disease are independent predictors of severe LV systolic dysfunction post-PPCI.

Keywords: Myocardial infarction, Left ventricular dysfunction, Primary percutaneous coronary intervention

1. Background

L eft ventricular (LV) systolic dysfunction after acute myocardial infarction (AMI) is the most crucial factor affecting morbidity and mortality. The reperfusion strategy aims to restore epicardial flow and reperfuse the myocardium. However, not all the patients present improvement, and a group of patients may experience depression in cardiac function [1].

Mortality rates because of AMI have decreased significantly over the past years [2]. Moreover, early reperfusion therapy including mechanical means and adjunctive antithrombotic treatment has been proven to lower mortality [3,4]. Notably, the mechanical reperfusion strategy with PPCI in



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patients with AMI can limit the infarct size and preserve left ventricular systolic function [5,6]. However, a proportion of patients may show decreased cardiac function even after undergoing successful PPCI and are prone to further congestive heart failure [7,8].

Prevalence and predictors that may associate left ventricular dysfunction post AMI despite treatment with PPCI have been investigated in some studies [9,10]. However, limited data and information concerning this are available in the Middle Eastern countries and results are still few.

The current study aims to provide insights into the prevalence and associated predictors of severe LV systolic dysfunction post-AMI treated with PPCI & its influence on in-hospital outcomes by analyzing the experience of a tertiary care center within a unique location in the holy city of Makkah, having a large sample of patients with a variable background.

2. Patients and method

2.1. Patients and study design

This retrospective study was held at the only cardiothoracic center in the Holy Makkah region, which provided tertiary-level cardiac services. We reviewed the records of 2863 AMI patients who were treated with PPCI during the period from May 2018 to August 2021. Successful PPCI was defined as post-intervention residual stenosis <30% with thrombolysis in myocardial infarction flow grade III. This study is designed to be part of the standard of patient care and has received approval from the ethics committee/institutional review board of our institution.

2.1.1. Inclusion criteria

AMI patients who were treated with successful PPCI and had completed recorded data.

2.1.2. Exclusion criteria

Patients known to have LV dysfunction before AMI, those who presented with AMI and had a cardiogenic shock, cardiac arrest, or connected to mechanical ventilation, those who received thrombolytic therapy or were referred for rescue percutaneous coronary angioplasty, those with unsuccessful angioplasty, and those who did not have post-procedure completed data.

Abbreviations

AMI	Acute myocardial infarction
BMI	Body Mass Index
CVA	Cerebrovascular accidents
DBT	Door to balloon time
DM	Diabetes Mellitus
EDV	End-diastolic volume
EF	Ejection fraction
ESV	End systolic volume
HTN	Hypertension
IHD	Ischemic heart disease
LAD	Left anterior descending artery
LCX	Left circumflex artery
LM	Left main
LV	Left Ventricle
LVEF	Left ventricular ejection fraction
LVT	Left ventricular thrombus
PPCI	Primary percutaneous coronary intervention
RCA	Right coronary artery
STEMI	ST-Elevation Myocardial Infraction
SV	Stroke volume

2.2. Data collection

Data were collected from cath lab records and their case notes including electronic records, echocardiographic and coronary angiographic reports include all of the following:

2.2.1. Clinical data

All demographics, baseline patient characteristics, and cardiovascular risk factors. Electrocardiographic data included the territory of AMI: anterior vs non-anterior. Laboratory data included troponin levels, serum creatinine, and glycosylated hemoglobin. Angiographic data included the presence of left main (LM) disease and the number of significantly diseased coronary arteries; defined as stenosis >50% for the left main and >70% for the left anterior descending (LAD) arteries, left circumflex artery (LCX), and right coronary artery (RCA). Data regarding treatment including anti-thrombotic treatment were also collected.

2.2.2. Echocardiography*

All patients underwent a baseline transthoracic Doppler echocardiography within 24 hours of hospitalization for acute myocardial infarction and PPCI. It was performed with a Vivid 7 ultrasound system assessing the slandered parameters. Left ventricular ejection fractions (LVEF) are the fraction of chamber volume ejected in systole (stroke

^{*} Severe left ventricular dysfunction is defined as LVEF<30% as per the American Society of Echocardiography and the European Association of Cardiovascular Imaging [11].

volume) concerning the volume of the blood in the ventricle at the end of diastole (end-diastolic volume). Stroke volume (SV) is calculated as the difference between end-diastolic volume (EDV) and end-systolic volume (ESV). LVEF is calculated from LVEF: [SV/EDV] x 100.

2.2.3. In-hospital outcomes

Data include post-myocardial infarction complications; pulmonary edema, cardiogenic shock, history of mechanical ventilation, cardiac arrest, left ventricular thrombus (LVT), length of hospital stay, and in-hospital death.

2.3. Statistical analysis

Statistical analysis was performed by use of the SPSS software package (SPSS Inc.; Chicago, Ill), version 21.0. Continuous data were expressed as mean \pm standard deviation and compared using the Student t-test. Categorical data were given as a percentage and compared with a chi-square test. A Chi-square test was also used to compare the existence of ventricular dysfunction pre-and post-operatively. Regression analysis was also performed. For all analyses a *p*-value <0.05 was considered significant and not significant if it is > 0.05).

3. Results

3.1. Key results

A total of 2865 consecutive patients who met the criteria were included in the analysis. Severe LV dysfunction was detected in 36% of the patients. There was a sizable proportion of patients who developed significant LV dysfunction despite treatment with successful PPCI. There are ethnic/racialrelated differences in the development of left ventricular dysfunction post-PPCI treated AMI. The previous history of ischemic heart disease and revascularization predispose for further significant LV dysfunction post-AMI. Those patients showed poor in-hospital outcomes including mortality. Large myocardial infarction, renal impairment, and severe coronary artery disease have the greatest effect on LV dysfunction post AMI despite optimal treatment with PPCI.

3.1.1. Patients and baseline characteristics

The baseline characteristics of the whole cohort are shown in Table 1. We classified our patients into two groups: Group I; AMI patients treated with PPCI and had severe LV dysfunction: 1021 patients

Table 1. Characteristic data for the whole patient group.

Variable	Number %
Age (years) Mean ± SD	56.1 ± 12.2
Male	2385 (83%)
Pilgrims	919 (32%)
South Asian	861 (30%)
Arabic speakers	1760 (61%)
BMI (kg/m2) Mean \pm SD	27.8 ± 5.9
DM	1565 (55%)
HTN	1527 (53%)
Smoking	951 (33%)
Dyslipidemia	408 (14%)
Obesity (BMI >30 kg/m2)	782 (27%)
Old CVA	85 (3%)
History of IHD	583 (20%)
Previous revasculrization	183 (6%)
Serum creatinine (mg/dL) Mean \pm SD	1.2 ± 5.1
Troponin (ng/mL) Mean \pm SD	66 ± 235
Clinical presentation Anterior STEMI	1588 (55%)
Multi-vessel coronary artery disease	433 (15%)

BMI: Body Mass Index; CVA: Cerebrovascular accidents; DM: Diabetes Mellitus; HTN: Hypertension; IHD: Ischemic heart disease; STEMI: ST- Elevation Myocardial Infraction.

(36%) and Group II: 1842 patients (64%) without severe LV dysfunction. We compared the two groups of patients in all parameters. Pilgrims, the South Asian population, and Non- Arabic speaking patients were more prevalent among the severe LV dysfunction group. Neither age nor gender showed an impact on LV dysfunction among our variable population. Also, the prevalence of most cardiovascular risk factors showed no significant statistical difference among both groups except for smoking as it was less prevalent among patients with severe LV dysfunction (P = 0.03). History of ischemic heart disease and revascularization were strongly significant among patients with severe LV dysfunction group compared to the other group of patients (P = 0.05 and 0.001 respectively) Table 2.

3.1.2. Clinical data and LV dysfunction

Patients in group I presented more with anterior myocardial infarction and greater myocardial injury reflected with higher values of troponin compared to the other group of patients (P < 0.001) Table 2. They also showed severe coronary artery disease in their coronary angiogram (P < 0.001 for both LM disease and multi-vessel coronary artery disease prevalence). Moreover, they showed greater thrombus burden and were in higher need of aggressive antithrombotic treatment (P = 0.004 and 0.002 for glycoprotein IIb/IIIa inhibitors utilization and thrombus aspiration during coronary angiogram respectively) Table 3.

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Table 2. Comparing	' clinical characteristic o	t patients with and without severe L	<i>V</i> dysfunction post PPCI treated AMI.

Variable	Group I with severe LV dysfunction $N = 1021 (36\%)$	Group II without severe LV dysfunction $N = 1842$ (64%)	P value
Age (years) $M \pm SD$	56.77 ± 11.7	55.64 ± 11.8	NS
Male	857 (84%)	1528 (83%)	NS
Pilgrims	367 (36%)	552 (30%)	0.002
South Asian	327 (32%)	534 (29%)	0.08
Non- Arabic speakers	439 (43%)	664 (36%)	0.003
DM	571 (56%)	994 (54%)	NS
HTN	551 (54%)	976 (53%)	NS
Smoking	306 (30%)	645 (35%)	0.03
Dyslipidemia	132 (13%)	276 (15%)	NS
Obesity	285 (28%)	497 (27%)	NS
Old CVA	30 (3%)	55 (3%)	NS
History of IHD	234 (23%)	349 (19%)	0.05
Previous revascularization	91 (9%)	92 (5%)	0.001
Anterior STEMI	796 (78%)	792 (43%)	< 0.001
Troponin (ng/mL) Mean \pm SD	140.8 ± 343.7	67.2 ± 189.1	< 0.001
Serum creatinine (mg/dL) Mean \pm SD	1.3 ± 4.1	1.2 ± 0.09	NS

AMI: Acute myocardial infarction; CVA: Cerebrovascular accidents DM: Diabetes Mellitus; HTN: Hypertension; IHD: Ischemic heart disease; LV: Left Ventricle; PPCI: Primary percutaneous coronary intervention; STEMI; ST-Elevation myocardial infarction.

Table 3. Comparing coronary angiographic findings and peri procedural antithrombotic treatment of patients with and without severe LV dysfunction post PPCI treated AMI.

Variable	Group I with severe LV dysfunction $N = 1021$ (36%)	Group II without severe LV dysfunction $N = 1842$ (64%)	P value
DBT <90 minutes for PPCI	306 (30%)	589 (32%)	NS
LM disease	51 (5%)	36 (2%)	< 0.001
Multi-vessel disease	194 (19%)	239 (13%)	< 0.001
Glycoprotein IIb/IIIa inhibitors	285 (28%)	424 (23%)	0.004
Thrombus aspiration	153 (15%)	203 (11%)	0.002

DBT: Door to balloon time; LM: Left main; LV: Left ventricle.

3.1.3. Predictors of LV dysfunction and prognosis

Variables significantly associated with post PPCI-LV dysfunction were anterior localization of myocardial infarction with higher values of peak troponins, peri-procedural renal impairment, and severe coronary artery disease at the time of AMI (P < 0.001, 0.03, 0.002, and 0.07 respectively) Table 4. The in-hospital outcomes were different as the severe LV dysfunction group of patients showed a longer in-hospital length of stay (P = 0.002), higher incidence of post-myocardial infarction complications, and in-hospital mortality (P < 0.001) Table 5.

4. Discussion

Our study provides beneficial insights into the prevalence of severe LV dysfunction post-PPCI treated myocardial infarction, risk predictors, and prognosis. We observed the following: First, there is more than a third of the population developed significant LV dysfunction post PPCI which has a major concern in the in-hospital stay. The second history of ischemic heart disease and/or previous revascularization was strongly predicting further LV dysfunction post-myocardial infarction. Third, the independent variables associated with severe LV dysfunction included anterior myocardial infarction, renal impairment, and severe coronary artery disease. Fourth, the severe LV dysfunction postmyocardial infarction status is associated with poor in-hospital outcomes including mortality despite the optimal treatment with PPCI and aggressive antithrombotic treatment.

A significant finding in our study is the incidence (36%) of severe LV dysfunction early in post-acute

Table 4. Cox Regression analysis for severe LV dysfunction post PPCI treated AMI.

Variable	В	S.E	EXP (B)	P value
Anterior STEMI	-1.501	0.139	0.223	< 0.001
Troponin	0.001	0.000	1.001	0.036
Serum creatinine	0.527	0.173	1.693	0.002
LM disease	0.822	0.471	2.274	0.08
Multi-vessel disease	0.394	0.222	1.483	0.07

AMI; Acute myocardial infarction; LM: Left main; LV: Left ventricle; PPCI: Primary percutaneous coronary intervention; STEMI: ST- Elevation myocardial infarction.

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Variable	Group I with severe LV dysfunction $N = 1021 (36\%)$	Group II without severe LV dysfunction $N = 1842$ (64%)	P value
Pulmonary edema	71 (7%)	37 (2%)	< 0.001
Cardiogenic shock	70 (7%)	36 (2%)	< 0.001
History of mechanical ventilation	84 (8%)	35 (2%)	< 0.001
Cardiac arrest	82 (8%)	50 (3%)	< 0.001
LVT	174 (17%)	74 (4%)	< 0.001
Length of hospital stay	6.6 ± 7.6	5.1 ± 8.1	0.002
In hospital death	51 (5%)	18 (1%)	< 0.001

Table 5. Comparing in-hospital outcome parameters of patients with and without severe LV dysfunction post PPCI treated AMI.

AMI: Acute myocardial infarction; LV: Left ventricle; LVT: Left ventricular thrombus; PPCI: Primary percutaneous coronary intervention.

infarct despite successful reperfusion with PPCI. Our finding is consistent with other studies from the contemporary era of coronary stenting, reporting a prevalence ranging from (27%-60%) [12–15]. The relatively elevated prevalence of severe LV dysfunction (36%) in our study can be explained by the site and size of myocardial infarction in our population. The majority of the LV dysfunction group (78%) had anterior AMI vs 43% in group II without severe LV dysfunction (P < 0.001). Anterior STEMI is known to be associated with the highest prevalence of LV dysfunction and this is identified in previous studies [9,16].

Interestingly, the unique location of our tertiary cardiac center in the holy city of Makkah near Haram and holy sites, as it received all AMI indicated for interventions including different pilgrim patients from variable background places. The present study showed pilgrims, the South Asian population and Non- Arabic speaking patients were more prevalent among the severe LV dysfunction group. This finding is also concordant with another study aimed to address the AMI pilgrim's related disparities [17]. Also, there was no statistically significant impact of age, gender, diabetes mellitus, or other cardiovascular risk factors on the development of LV dysfunction post-AMI treated with PPCI, and this was in concordance with other studies [9,18]. On the other hand, another study stated that age might predict higher rates of depressed LV function in patients with STEMI [19]. Regarding gender, another study concluded that female patients demonstrated lower systolic LV function, despite receiving similar treatment as male patients [20]. Of note, the presence of diabetes mellitus; decreased myocardial energy supply, endothelial dysfunction, and oxidative stress all harm LV function post-AMI and this is reported by another study [21]. This discrepancy could be explained by the difference in the sample volume, variable means of age, and different revascularization modalities. Moreover,

many factors are related to our diverse populations including genetic variation and the degree of atherosclerosis. However, a prior history of ischemic heart disease was found as a crucial predictor of decreased LV function post-AMI [10] and this is concordant with our findings.

Our study support previous data (9&10) that anterior myocardial infarction has the highest risk for early LV dysfunction post-AMI treated with PPCI. Anterior myocardial infarctions lead to more noticeable LV dysfunction and hence further negative impact on LV remodeling compared with myocardial infarction in other areas [22]. The present study demonstrated that troponin level was also significantly associated with LV dysfunction and this was agreed by other studies [10,23]. Another independent predictor for LV dysfunction and poor prognosis was elevated serum creatinine, which is consistent with previous reports [24,25] as renal impairment plays a pivotal role in post-AMI cardiac remodeling and cardiovascular outcomes. Moreover, patients with multi-vessel diseases including LM were at high risk for further LV dysfunction once got acute myocardial infarction. This is consistent with other studies, which reported that multi-vessel AMI had a higher prevalence of left main disease and poor in-hospital outcomes and mortality [26-28]. Finally, patients with severe LV dysfunction post-AMI treated with PPCI have poor in-hospital outcomes and mortality and this is proven by many other studies [29,30].

5. Conclusion

We demonstrated a sizable proportion of AMI develops severe LV dysfunction despite treatment with successful PPCI. Variables significantly associated with early LV dysfunction were larger myocardial infarction, renal impairment, and severe coronary artery disease. Although those patients were treated maximally with both mechanical revascularization and proper antithrombotic, they showed poor prognosis including mortality. Identification of those risk predictors upon patient evaluation could be helpful to identify high-risk- a group of patients, in need of particular care, aggressive therapy, and close follow-up to improve their poor outcomes. This may serve as a warning, allow the proper identification of those high-risk patients, and hence further development of a high prediction score for LV dysfunction& more effective therapeutic strategies. The key to this management consists of early identification, proper recognition of LV dysfunction, and rapid proper treatment. Moreover, this study also refers to the need for proper utilization of services available in the tertiary centers including further advanced heart failure treatment Sacubitril-Valsartan or/and an implantable cardioverter-defibrillator.

5.1. Study limitations

The number of patients included is limited due to the nature of the single center. Symptoms to balloon time could not be accurately assessed, as the majority of the patients were referral cases from other hospitals directly transferred to the cath lab (missing this data in their records). The limitation of follow-up data is due to being a tertiary center as most of the cases were followed in our center for a few months post-PPCI and then complete their follow-up in the primary and secondary hospitals. In addition to this, more than a third of our population were pilgrims and had no follow-up in the region. We hope to reduce the effect of this limitation by sharing with other hospitals in the region to conduct similar studies in the future including proper follow-up data.

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The authors declare no funding.

Conflict of interest

None.

Author contributions

Conception and design of Study: SK, GS. Literature review: SK. Acquisition of data: SK. Analysis and interpretation of data: SK, GS. Research investigation and analysis: SK, GS. Data collection: SK, GS. Drafting of manuscript: SK, GS. Revising and editing the manuscript critically for important intellectual contents: SK. Data preparation and presentation: SK. Supervision of the research: SK. Research coordination and management: SK.

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