Novel Predictors of Left Ventricular Systolic Function Recovery in Patients with ST Elevation Myocardial Infarction who Underwent Reperfusion Therapy

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Introduction

Measurement of left ventricular systolic function has been widely accepted as a primary method of risk stratifying patients after ST-elevation myocardial infarction (STEMI). Left ventricular systolic function is predictive of early and late complications and mortality in these patients [1-4]. To further emphasize this important measurement, recently published guidelines by the American College of Cardiology/American Heart Association (ACC/AHA) have included the evaluation of left ventricular systolic function as a performance measure for all patients admitted with acute myocardial infarction [5].

However, measurement of left ventricular systolic function shortly after the ischemic event can be misleading, as a majority of patients with left ventricular systolic dysfunction show improvement in their left ventricular ejection fraction (LVEF) over time. A study performed in 2001 showed that 90 days after a myocardial infarction treated with reperfusion therapy 22% of patients had complete recovery of left ventricular systolic function and an additional 36% had partial recovery. The majority of functional improvement occurred in the first 14 days [6,7] The only significant predictor of left ventricular systolic function recovery was a lower CK-MB peak level.

A more recent study found that, the larger the extent of left ventricular systolic dysfunction in the acute phase, the greater the potential for improvement. These investigators also showed that a smaller infarct and an improvement in left ventricular systolic function had beneficial effects on long term survival [8]. Functional recovery of stunned and hibernating myocardium has been proposed as the main factor responsible for this improvement in left ventricular systolic function after myocardial infarction [6-9].

Recently published data demonstrated that enzymatic infarct size (as estimated by peak CK-MB levels), time from onset symptoms to reperfusion, extent and severity of baseline LV wall motion abnormalities and female gender were independent predictors of left ventricular systolic function recovery [10].

The presence of elevated cardiospecific biomarkers (troponin T and troponin I) demonstrate excellent correlation with infarct size and LVEF. A recent study showed that single time, peak and area under the curve troponin I and troponin T levels correlated strongly with a larger infarct size and a lower LVEF thirty days after myocardial infarction [11]. However, there is no data regarding the utility of cardiospecific markers to predict the recovery of left ventricular systolic function after STEMI. We aimed to determine if peak troponin levels can accurately

Abstract

Assessment of the left ventricular ejection fraction (LVEF) is important in patients admitted with myocardial infarction as a decreased LVEF is an indicator of poor prognosis. However, early measurement of LVEF can be misleading as patients can show delayed recovery of LVEF. Limited evidence exists regarding the use of predictors of LVEF recovery in patients with ST-elevation myocardial infarction (STEMI). Our aim was to determine if a lower level of cardiac biomarkers and electrocardiographic resolution of the ST elevation (ST–segment resolution of >50%) predicted LVEF recovery in patients with STEMI. We included patients admitted with STEMI to Einstein Medical Center from 2006 to 2008, with an LVEF of <50% during that admission, and a follow-up echocardiogram between 1 to 6 months after the event. A retrospective chart review was performed and 59 patients who underwent reperfusion therapy were included. Patients were identified as having recovery of myocardial function if the LVEF improved ≥ 10% (absolute value) on the subsequent echocardiogram. Both groups (improvement vs. non-improvement) had similar baseline characteristics. Mean age was 62. Forty percent were female, 71% were hypertensive and 46% were diabetic. Predictors of LVEF improvement were absence of dyslipidemia (p=0.01), resolution of the ST-segment elevation (p=0.04) and lower troponin levels (highest quartile vs. other 3 quartiles p=0.04). Furthermore, one year mortality was higher in the group that had no LVEF improvement compared to the group with LVEF improvement (26% vs. 0). In conclusion, in patients with STEMI, ST-segment resolution and a lower peak troponin level accurately predicted LVEF recovery 1 to 6 months after the event. If the LVEF improved ≥ 10%, the one year mortality was negligible.

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predict left ventricular systolic function recovery in patients with STEMI. We also sought to determine whether clinical parameters, electrocardiographic changes and angiographic data might also predict left ventricular systolic function recovery.

Methods

Consecutive patients with STEMI, as defined by current guidelines, [12,13] admitted to Einstein Medical Center between January of 2006 and December of 2008 were included in this study. All patients underwent primary percutaneous coronary intervention (PCI). Patients who died during the admission (24 patients), who had an ejection fraction (EF) >50% during hospitalization (115 patients), who did not have assessment of LVEF during the admission and who did not have a follow up echocardiogram between one and six months after the STEMI (65 patients) were excluded. Data on demographics, cardiac risk factors, and medications received on admission, during the hospitalization and at discharge, troponin and CK-MB levels were obtained. Electrocardiograms (ECG) [14] were reviewed prior to and immediately after revascularization. The ST-segment elevation was measured manually at the J-point to the nearest 0.5 mm in all leads. The sum of ST-segment elevation in all leads was determined for the individual ECG, and ST-segment resolution was assessed by the reduction in ST-segment elevation between the baseline ECG and the subsequent ECG as the percentage of baseline ST-segment elevation. ST-segment resolution after revascularization was defined as a resolution of the ST-segment elevation of at least 50% after revascularization. We determined the time from symptom onset to revascularization. We did not use the door-to-balloon times as it is predictable and consistent at our institution as we are a 24/7 PCI center. Angiographic data including the epicardial TIMI (Thrombolysis in Myocardial Infarction) flow after revascularization, the number and type of vessels diseased according to the Coronary Artery Surgery Study (CASS) system were obtained. One year mortality was obtained through the Social Security Death Index.

Echocardiogram reports were reviewed and the LVEF was recorded. All measurements of LVEF were performed by board certified echocardiologists. All patients underwent an echocardiogram after revascularization. Patients were considered to have left ventricular dysfunction if their EF during the admission was <50%. Patients were divided in two groups. The first group included patients that showed recovery of their left ventricular function. They were included if their LVEF improved ≥ 10% (absolute) in the subsequent echocardiogram. The second group included patients that did not show recovery of their left ventricular function. These were included if their LVEF did not improve ≥ 10% in the subsequent echocardiogram. Prior studies have considered complete recovery of LVEF as an improvement to normal values or partial recovery as any improvement in LVEF [6]. More recently, LVEF improvement was considered when the LVEF improved more than 3% (absolute percentage) [9].

Statistical Analysis

Categorical data were expressed as percentages and continuous data were expressed as means ± standard deviation. Differences between the two groups were analyzed using Fisher’s exact test for categorical variables and two-sample t-test with equal variances for continuous variables. A stepwise multivariable logistic regression model was used to analyze variables that were statistically associated with LVEF improvement on univariate analysis. We considered significant predictors for further inclusion in a multivariate model if the two-tail p-value was <0.10. We looked for predictors using parsimonious modeling construction (forward, backward and mixed analyses). All analyses were performed using JMP statistical software (Cary, NC, USA).

Results

We identified 263 patients who had STEMI during the study period. Of those, 59 (11%) had left ventricular dysfunction identified during the admission and had a subsequent echocardiogram performed between one and six months after the event. Forty two of the 59 patients (71%) had no improvement of their LVEF during the study period. Baseline characteristics are shown in Table 1.

There were no statistically significant differences between STEMI patients with and without LVEF recovery with respect to age, hypertension, diabetes, smoking history, prior myocardial infarction and chronic kidney disease. At presentation, more patients who did not improve their LVEF had a history of dyslipidemia (38 vs. 12% p=0.04).

Medications during the admission and at discharge were similar between both groups (Table 2).

After analyzing electrocardiographic data (Table 1), there were no statistically significant differences between the two groups in regards to localization or magnitude of the ST segment elevation, the presence of ST segment resolution after revascularization or the presence of reciprocal changes in other electrocardiographic leads.

We also recorded angiographic data (Table 1). We did not find statistically significant differences in regards to the number of stents placed or the time from symptom onset to revascularization. The incidence of cardiogenic shock and the presence of multi-vessel disease were similar between groups. We found that circumflex artery involvement was more commonly associated with patients who did not have LVEF recovery (24% vs. 0 p=0.02).

Regarding cardiac biomarkers, patients whose LVEF recovered had a lower peak troponin I, but the results were not statistically significant (181 vs. 115 ng/dl p=0.197). Furthermore, peak CK-MB levels were not significantly different between the two groups. We did not find a difference between both groups in the time from symptom onset to the peak troponin I level.

We performed a stepwise logistic regression analysis, and we determined that after analyzing troponin levels in different quartiles, patients with the highest troponin I quartile (>239 ng/dl) had a significant association with the absence of left ventricular function recovery (p=0.048). Other factors studied included a history of dyslipidemia (p=0.01) and resolution of the ST segment elevation (p=0.055). The results are reported in Table 3. The different quartiles of troponin I levels are depicted in Figure 1.

Among patients whose left ventricular function recovered, all were alive at one year. In contrast, there were 11 deaths (26%) among the group with no left ventricular function recovery (p=0.019).

We attempted to determine which factors were associated with higher one year mortality. When compared to patients who were alive at one year, (Table 4) those who died were more likely to be female (72% vs. 33% p=0.016), have a history of diabetes mellitus (72% vs. 39% p=0.047), and history of a prior myocardial infarction (63 vs. 31% p=0.005). In regards to cardiac biomarkers, patients who were deceased at one year had a higher peak troponin I level, but the results were not statistically significant (225 vs. 148 ng/dl p=0.191).

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Variable | LVEF recovery (n=17) | No LVEF recovery (n=42) | P-value
--- | --- | --- | ---
Age (mean ± SD) | 60.2 ± 3.4 | 63.1 ± 1.9 | 0.45
Sex, n (%) | | | |
Male | 10 (59) | 25 (59) | 0.96
Female | 7 (41) | 17 (41) | |
African American race, n (%) | 13 (76) | 34 (81) | 0.12
Past Medical History, n (%) | 13 (76) | 29 (69) | 0.56
Diabetes Mellitus | 6 (35) | 21 (50) | 0.30
Dyslipidemia | 2 (11) | 16 (38) | 0.04
Myocardial infarction | 2 (11) | 15 (36) | 0.06
Smoking | 8 (47) | 27 (64) | 0.22
Congestive heart failure | 1 (5.9) | 5 (11) | 0.46
Obesity | 2 (12) | 6 (14) | 0.79
Chronic kidney disease | 1 (5) | 7 (16) | 0.27
Laboratory Values
Troponin I (peak in ng/dl ± SD) | 115 ± 33 | 181 ± 28 | 0.19
CPK-MB (peak in ng/dl ± SD) | 2808 ± 63 | 2899 ± 334 | 0.89
Electrocardiographic changes
Anterior infarction, n (%) | 12 (71) | 29 (69) | 0.90
Inferior infarction, n (%) | 5 (29) | 13 (31) | 0.90
ST segment resolution after PCI, n (%) | 14 (82) | 27 (64) | 0.17
Reciprocal changes, n (%) | 13 (76) | 27 (64) | 0.36
slR ST segment elevation, n (%) | 0 | 1 (2.7) | 0.52
Development of Q waves, n (%) | 8 (47) | 15 (36) | 0.41
Highest ST segment elevation (in mm ± SD) | 4.24 ± 0.3 | 4.36 ± 0.28 | 0.80
ST segment elevation sum (in mm ± SD) | 12.4 ± 1.5 | 10.3 ± 0.71 | 0.17
Angiographic data
Number of stents placed (mean ± SD) | 1.24 ± 0.2 | 1.31 ± 0.13 | 0.75
Left anterior descending artery stented, n (%) | 14 (82) | 28 (67) | 0.22
Right coronary artery stented, n (%) | 4 (23) | 6 (14) | 0.39
Circumflex artery stented, n (%) | 2 (11) | 10 (21) | 0.02
Mean time to revascularization (in hrs ± SD) | 9.06 ± 2.4 | 8.17 ± 1.3 | 0.72
Mean time to peak Troponin I (in hrs ± SD) | 21 ± 2.4 | 18 ± 1.53 | 0.19
Baseline-ejection fraction (% ± SD) | 35 ± 2.06 | 30 ± 1.55 | 0.04
Change in ejection fraction, n (%) | +18.2% ± 8.5 | -3.5% ± 7.5 | 0.0001
Incidence of cardiogenic shock, n (%) | 2 (12) | 8 (14) | 0.79
Multivessel disease, n (%) | 6 (35) | 17 (40) | 0.71
Mortality at one year (%) | 0 | 26% | 0.01

Table 1: Baseline characteristics of the two STEMI groups.

Medication, n (%) | LVEF recovery (n=17) | No LVEF recovery (n=42) | P-value
--- | --- | --- | ---
Aspirin | 16 (94) | 42 (100) | 0.28
Clopidogrel | 16 (94) | 41 (98) | 0.50
Statin | 17 (100) | 40 (95) | 0.36
Beta Blocker | 15 (88) | 39 (93) | 0.56
ACE inhibitor | 15 (88) | 30 (81) | 0.16
Glycoprotein IIb/IIa inhibitor (during admission) | 37 (88) | 13 (76) | 0.26

Table 2: Medical treatment of the 2 STEMI groups.

Discussion
A significant number of patients develop left ventricular dysfunction after acute myocardial infarction. Prior studies have shown that significant left ventricular dysfunction improves in more than 50% of cases [6]. Assessment of left ventricular function has become one of the core performance measures for patients admitted with acute myocardial infarction [5]. The goal of our study was to determine factors that were associated with a lack of left ventricular function recovery following STEMI.

We found that 71% of the patients who were admitted with STEMI and had depressed left ventricular systolic function on the index echocardiogram did not have an improvement in their left ventricular function 1 to 6 months after the event. These results contrast with prior publications that noticed a significant improvement in the majority of patients [6,7]. Possible explanations for this difference may include different populations, as our study group had a high percentage of African American patients, high prevalence of diabetes, hypertension and history of myocardial infarction. We analyzed baseline clinical characteristics, and found that patients that had no left ventricular function recovery were more likely to have a history of dyslipidemia when compared to those whose ventricular function improved (38 vs. 12% p=0.04). This finding warrants further investigation in future studies.

We also found that peak troponin I levels were higher in the group that had no left ventricular function recovery, but the results did not reach statistical significance, likely due to the low number of patients in each study group. The presence of elevated troponin I levels has been well described in prior literature as an excellent predictor of poor outcomes [15,16].

However, after performing a logistic regression analysis, we did find that troponin I levels in the highest quartile was associated with a lack of left ventricular function recovery when compared to the other 3 quartiles. The absence of ST-segment elevation resolution after PCI was also associated with a lack of left ventricular function recovery. Numerous studies from the fibrinolytic era have found that
the absence of ST-segment elevation resolution after reperfusion has been associated with poor outcomes, including larger infarct size and increased mortality [17, 18].

Lastly, we assessed the one year mortality for both groups. We found a striking difference, with no deaths in the group of patients with left ventricular function recovery and 11 deaths (26% of the patients) in the group with no recovery. This finding is consistent with prior studies, including Studies of Left Ventricular Dysfunction (SOLVD) [19], in which patients with left ventricular dysfunction had a greater mortality in the long term, despite the absence of congestive heart failure symptoms [1].

Limitations of our study include its retrospective nature. Also, only 11% of patients who presented with STEMI had left ventricular dysfunction identified during the admission and had a subsequent echocardiogram performed between one and six months after the event, thus limiting our sample size. The baseline LVEF was 35% in the group that recovered their LVEF versus 30% in the group that did not recover their LVEF. This difference was statistically significant. While this could represent a type I statistical error given the sample size, we cannot rule out a physiological basis for better recovery in those with an initial better LVEF; though clinically, these LVEF’s are both in the moderately to severe left ventricular dysfunction range. Our limitations will be addressed in a future prospective trial.

In conclusion, we found that higher troponin levels and the lack of ST-segment elevation resolution were each associated poor recovery of left ventricular function after a myocardial infarction. Such patients have significant one year mortality and may warrant aggressive therapy.

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