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

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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.

Keywords: ST-elevation myocardial infarction; Left ventricular ejection function; Troponin; ST-segment resolution; Dyslipidemia

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

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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 mean ± 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).

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 (%)			
Hypertension	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)	0.48
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 mg/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
avR 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
Circunflex artery stented, n (%)	0	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 ± 2.42	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)	6 (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

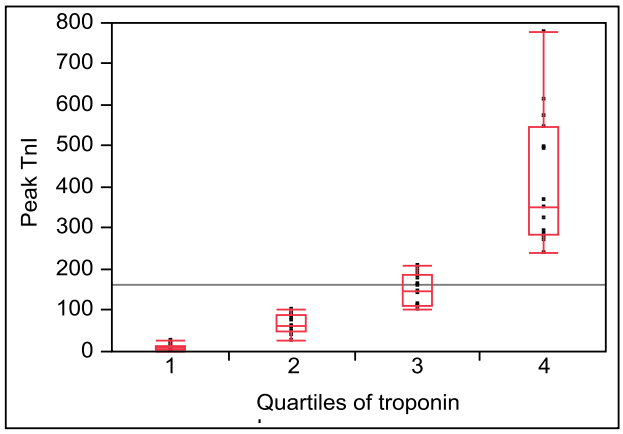
Variable	B-Estimate	Chi²	P-value
Dyslipidemia	1.1028	5.57	0.01
Resolution of ST segment elevation	0.79	3.01	0.055
First 3 quartiles TnI*	0.81	3.35	0.048

Table 3: Multivariable regression analysis for left ventricular function recovery.

Variable (%)	Dead at 1 year n=11	Alive at 1 year n=48	P-value
Female sex	73%	33%	0.016
Diabetes Mellitus	73%	39%	0.047
Hyperlipidemia	45%	27%	0.233
Myocardial infarction	63%	21%	0.005
Chronic kidney disease	27%	10%	0.141
No LVEF improvement	100%	64%	0.019

*Highest quartile is Troponin I ≥ 239 ng/dl *vs*. the rest.

Table 4: Patient characteristics according to one year mortality.



Quartiles of Troponin I

Level	Minimum	10%	25%	Median	75%	90%	Maximum
1	1	1.06	4.525	9.28	13.625	23.15	25
2	25.4	33.44	47.4	62	87	97.2	102
3	104	107.6	112	146	188	207	210
4	239	257	285	350	548	679.2	777

Figure 1: Quartiles of Troponin I.

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.

References

1. Heger JJ, Weyman AE, Wann LS, Rogers EW, Dillon JC, et al. (1980) Cross-sectional echocardiographic analysis of the extent of left ventricular asynergy in acute myocardial infarction. Circulation 61: 1113-1118.
2. Gibson RS, Bishop HL, Stamm RB, Crampton RS, Beller GA, et al. (1982) Value of early two dimensional echocardiography in patients with acute myocardial infarction. Am J Cardiol 49: 1110-1119.
3. Nishimura RA, Tajik AJ, Shub C, Miller FA Jr, Ilstrup DM, et al. (1984) Role of two-dimensional echocardiography in the prediction of in-hospital complications after acute myocardial infarction. J Am Coll Cardiol 4: 1080-1087.
4. Horowitz RS, Morganroth J (1982) Immediate detection of early high-risk patients with acute myocardial infarction using two-dimensional echocardiographic evaluation of left ventricular regional wall motion abnormalities. Am Heart J 103: 814-822.
5. Krumholz HM, Anderson JL, Bachelder BL, Fesmire FM, Fihn SD, et al. (2008) ACC/AHA 2008 performance measures for adults with ST-elevation and non-ST-elevation myocardial infarction. J Am Coll Cardiol 52: 2046-2099.
6. Solomon SD, Glynn RJ, Greaves S, Ajani U, Rouleau JL, et al. (2001) Recovery of ventricular function after myocardial infarction in the reperfusion era: the healing and early afterload reducing therapy study. Ann Intern Med 134: 451-458.
7. Sheehan FH, Doerr R, Schmidt WG, Bolson EL, Uebis R, et al. (1988) Early recovery of left ventricular function after thrombolytic therapy for acute myocardial infarction: an important determinant of survival. J Am Coll Cardiol 12: 289-300.
8. Bolli R (1992) Myocardial 'stunning' in man. Circulation 86: 1671-1691.
9. Ndrepepa G, Mehilli J, Martinoff S, Schwaiger M, Schömig A, et al. (2007) Evolution of left ventricular ejection fraction and its relationship to infarct size after acute myocardial infarction. J Am Coll Cardiol 50: 149-156.
10. Parodi G, Memisha G, Carrabba N, Signorini U, Migliorini A, et al. (2007) Prevalence, predictors, time course, and long-term clinical implications of left ventricular functional recovery after mechanical reperfusion for acute myocardial infarction. Am J Cardiol 100: 1718-1722.
11. Chia S, Senatore F, Raffel OC, Lee H, Wackers FJ, et al. (2008) Utility of cardiac biomarkers in predicting infarct size, left ventricular function, and clinical outcome after primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. JACC Cardiovasc Interv 1: 415-423.
12. Thygesen K, Alpert JS, White HD; Joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction (2007) Universal definition of myocardial infarction. J Am Coll Cardiol 50: 2173-2195.
13. Antman EM, Anbe DT, Armstrong PW, Bates ER, Green LA, et al. (2004) ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction; A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of patients with acute myocardial infarction). J Am Coll Cardiol 44: E1-E211.
14. McDonagh TA, Morrison CE, Lawrence A, Ford I, Tunstall-Pedoe H, et al. (1997) Symptomatic and asymptomatic left-ventricular systolic dysfunction in an urban population. Lancet 350: 829-833.
15. Giannitsis E, Müller-Bardorff M, Lehrke S, Wiegand U, Tölg R, et al. (2001) Admission troponin T level predicts clinical outcomes, TIMI flow, and myocardial tissue perfusion after primary percutaneous intervention for acute ST-segment elevation myocardial infarction. Circulation 104: 630-635.
16. Ohman EM, Armstrong PW, White HD, Granger CB, Wilcox RG, et al. (1999) Risk stratification with a point-of-care cardiac troponin T test in acute myocardial infarction. GUSTOIII Investigators. Global Use of Strategies To Open Occluded Coronary Arteries. Am J Cardiol 84: 1281-1286.

17. de Lemos JA, Braunwald E (2001) ST segment resolution as a tool for assessing the efficacy of reperfusion therapy. J Am Coll Cardiol 38: 1283-1294.

18. Schröder R, Wegscheider K, Schröder K, Dissmann R, Meyer-Sabellek W (1995) Extent of early ST segment elevation resolution: a strong predictor of outcome in patients with acute myocardial infarction and a sensitive measure to compare thrombolytic regimens. A substudy of the International Joint Efficacy Comparison of Thrombolytics (INJECT) trial. J Am Coll Cardiol 26: 1657-1664.

19. [No authors listed] (1992) Effect of enalapril on mortality and the development of heart failure in asymptomatic patients with reduced left ventricular ejection fractions. The SOLVD Investigattors. N Engl J Med 327: 685-691.