Predictors of Left Ventricular Dysfunction in Patients with First Acute Anterior Myocardial Infarction Undergoing Primary Angioplasty

Ashraf Hamdan MD, Ran Kornowski MD, Alejandro Solodky MD, Shmuel Fuchs MD, Alexander Battler MD and Abid R. Assali MD

Cardiac Catheterization Laboratories, Department of Cardiology, Rabin Medical Center (Beilinson Campus), Petah Tiqva, Israel
Affiliated to Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

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Abstract

Background: The degree of left ventricular dysfunction determines the prognostic outcome of patients with acute myocardial infarction.

Objectives: To define the clinical, angiographic and procedural variables related to LV dysfunction in patients with anterior wall AMI referred for primary percutaneous coronary intervention.

Methods: The sample included 168 patients treated by primary PCI for first anterior wall AMI. Clinical, demographic and medical data were collected prospectively into a computerized registry, and clinical outcome (death, reinfarction, major cardiovascular event) were evaluated during hospitalization and 30 days after discharge. Patients were divided into three groups by degree of LV dysfunction (mild, moderate, severe) and compared for clinical, angiographic and procedural variables.

Results: LV dysfunction was associated with pre-PCI renal failure (serum creatinine > 1.4 mg/dl), peripheral vascular disease, high peak creatine kinase level, longer door to balloon time, low TIMI flow grade before and after PCI, and use of an intraaortic balloon pump. On multivariate analysis adjusted for baseline differences, peak creatine kinase level (r = 0.3, P = 0.0001) and door to needle time (r = 0.2, P = 0.008) were the most significant independent predictors of moderate or severe LV dysfunction after anterior AMI.

Conclusion: Abnormal LV function after first anterior AMI can be predicted by door to balloon time and the size of the infarction as assessed by creatine kinase levels. Major efforts should be made to decrease the time to myocardial reperfusion.

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Left ventricular dysfunction after acute myocardial infarction is the most important factor affecting morbidity and mortality [1], and every effort should be made to minimize it. The primary objective of reperfusion therapy is to restore epicardial flow and to reperfuse the myocardial tissue in order to maintain myocyte integrity and function. Guidelines for reperfusion strategies for ST-elevation AMI favor primary percutaneous coronary intervention to achieve rapid restoration of coronary artery patency after AMI and increase threatened myocardium salvage, thereby preserving ventricular function and patient survival [2].

LV = left ventricular
AMI = acute myocardial infarction
PCI = percutaneous coronary intervention

Excellent epicardial blood flow, as assessed by the TIMI (Thrombolysis In Myocardial Infarction) flow grade, is associated with reduced mortality and improved LV functional recovery [3]. However, in some cases lack of microvascular reperfusion and, consequently, significant LV dysfunction persist despite the rapid and sustained restoration of blood flow through a previously occluded epicardial coronary artery. Thus, early identification of patients at increased risk of developing LV dysfunction after AMI could aid physicians in targeting more aggressive therapy. Studies have shown that older age, diabetes mellitus, total occlusion of the culprit artery, and delayed ST-segment resolution may predict LV dysfunction and heart failure in patients treated with thrombolysis for AMI [4-6]. However, predictors of LV dysfunction in patients treated with primary PCI for first ST-segment elevation anterior wall AMI have not been clearly determined. We sought to evaluate the effect of clinical, angiographic and treatment variables at first presentation on LV function and clinical outcomes in patients with first acute anterior myocardial infarction treated by primary PCI.

Patients and Methods

Beginning in January 2001, all patients with ST elevation AMI who underwent emergency PCI at the Rabin Medical Center were prospectively observed and the data were entered into a uniform registry format. At our medical center we adopted a therapeutic strategy of "around the clock" emergency PCI for AMI patients, and a senior interventional cardiologist performs all PCI procedures. The registry includes detailed demographic, clinical, angiographic and procedural data. All patients signed an informed consent prior to the catheterization procedure. Immediate and in-hospital events were recorded, and each patient was surveyed by telephone with a standardized questionnaire at 30 days follow-up. Routine follow-up angiography was not performed unless clinically indicated.

The sample for the present study included all patients with first anterior wall AMI treated by primary PCI angioplasty in our catheterization laboratory from January 2000 through August 2003. The diagnostic criteria were ST-segment elevation ≥ 1 mm in at least two contiguous leads out of V1-4 with confirmation by troponin elevation. Patients were included if they had chest

pain for less than 6 hours until hospital arrival. Patients with cardiogenic shock were excluded.

Primary angioplasty technique

All patients received aspirin (325 mg) and heparin (5000 IU) before the procedure. The decision to administer glycoprotein IIb/IIIa blockade was made by the interventional cardiologist. In these patients, a bolus of 0.25 mg/kg eptifibatide was given during angioplasty, followed by 12 hours infusion at 0.125 µg/kg/min. An intra-aortic balloon pump was inserted in patients with TIMI flow < 3, or systolic blood pressure < 100 mmHg at the end of the procedure, or coexisting congestive heart failure symptoms. Following the procedure, patients received aspirin at a dose of at least 100 mg once daily and clopidogrel at a loading dose of 300 mg followed by 75 mg daily for at least one month.

Angiographic analysis

Angiographic films were reviewed at our angiographic core laboratory using the MDView™ Quantitative Angiographic System (Medcon™ Telemedicine Technology, Israel). An experienced cardiologist who was blinded to the clinical outcome performed the analysis. TIMI flow grades were assessed as previously described [7] before and immediately after angioplasty. Successful angioplasty was defined as TIMI grade 3 flow in the treated vessel with < 30% residual stenosis.

Echocardiography

Standard 2D echocardiogram (Sonos 5500 ultrasound device, Phillips) was obtained in all patients within 24 hours of presentation. To evaluate ejection fraction an experienced cardiologist who was blinded to the clinical outcome performed the analysis. LVEF was calculated by Simpson's rule [8]. On the basis of the findings, the patients were divided into three groups of LV dysfunction: normal-mild (EF > 40%), moderate (EF = 30–40%), and severe (EF < 30%).

Statistical analysis

Results are given as means ± standard deviations. Pearson's correlation coefficient (r) and its significance (P) were calculated between the variables. Clinical characteristics, and angiographic and treatment variables [Tables 1 and 2] were compared across groups by means of one-way ANOVA for continuous variables. To predict LV dysfunction, a series of multivariate stepwise logistic regression models were fitted to the data. Statistical analysis was performed using STATISTICA software, and P values ≤ 0.05 were considered statistically significant.

Results

Baseline characteristics

Altogether, 168 patients were enrolled in the study: 58 (34.5%) with mild, 87 (51.8%) with moderate, and 23 (13.7%) with severe LV dysfunction. Their background and clinical characteristics are shown in Table 1. There were no significant differences among the three groups with regard to risk factors. Patients with severe LV dysfunction were more likely to have peripheral vascular disease (P = 0.01) and pre-PCI renal failure (serum creatinine > 1.4 mg/dl) (P = 0.01) than those with mild or moderate LV dysfunction. Patients with moderate or severe LV dysfunction had a longer door to needle time as compared to patients with mild LV dysfunction (P = 0.04). There were no differences between the groups according to the adjunctive medications given prior to PCI.

Table 1. Clinical characteristics stratified by LV dysfunction

	Degree of LV dysfunction			
Characteristics	Mild (n=58)	Moderate (n=87)	Severe (n=23)	*P*
Age (yrs)	58.6 ± 12.8	59.8 ± 13.8	64.1 ±14.7	0. 2
Male gender (%)	76	77	70	0.7
Diabetes mellitus (%)	31	30	43	0.5
Hyperlipidemia (%)	44	44	30	0.5
Hypertension (%)	42	41	52	0.6
Current smoker (%)	33	30	30	0.8
Peripheral vascular disease (%)	4	2.5	23	0.01
Renal failure (%)	6	5	27	0.01
Prior stroke (%)	3.9	5	9	0.7
Systolic BP (mmHg)	136 ± 26	136 ± 22	126 ± 20	0. 7
Diastolic BP (mmHg)	77 ± 13	80 ± 10	74 ± 10	0.07
Prior CABG (%)	2	0	0	0.3
Symptoms to door time (hrs)	2.1 ± 1.4	2.3 ± 1.3	2.4 ± 1.5	0.5
Median (25–75%)	1.6 (1–3)	2 (1.5–1.3)	2 (1–4)	
Door to balloon time (hrs)	1.2 ± 1.4	3.2 ± 5.2	2.9 ± 4.0	0.04
Median (25–75%)	1 (0.5–1.5)	1.5 (1–3.5)	1 (1–3.5)	
Peak CK (U/L)	1721 ± 1590	3253 ± 2338	3820 ± 3469	0.0001

CABG = coronary artery bypass graft

Table 2. Angiographic characteristics stratified by LV dysfunction

	Degree of LV dysfunction			
Angiographic features	Mild LV	Moderate	Severe	*P*
TIMI flow before PCI (0-1) (%)	63	79	73	0.08
TIMI flow after PCI (3) (%)	99	96	64	0.0001
Intra-aortic baloon pump (%)	3	7	26	0.003
Glycoprotein IIb/IIIa Inhibitors (%)	81	85	82	0.9
Multivessel disease (%)	43	50	68	0.3
Pre-PCI diameter stenosis (%)	95 ± 10	93 ± 15	98 ± 3	0.2
Post-PCI diameter stenosis (%)	4 ± 7	5 ± 15	6 ± 21	0.7
Lesion length (mm)	13 ± 6	14 ± 5	16 ± 6	0.2
Reference vessel diameter (mm)	3.1 ± 0.4	3.9 ± 0.6	3.0 ± 0.5	0.9
Pre-PCI minimal lumen diameter (mm)	0.17 ± 0.43	0.1 ± 0.22	0.0 ± 0.05	0.11
Post-PCI minimal lumen diameter (mm)	2.9 ± 0.6	3 ± 0.8	2.7 ± 1	0.4
No/slow-reflow (%)	6	8	20	0.2
Fluoroscopy time (min)	12 ± 10	15 ± 8	14 ± 7	0.3
Contrast media quantity (ml)	146 ± 0	179 ± 51	182 ± 61	0.008

Angiography [Table 2]

Patients with severe LV dysfunction were more likely to have TIMI grade 0-1 flow before PCI: 73% (severe) vs. 79% (moderate), 63% (mild); P = 0.08. They also achieved TIMI grade 3 flow significantly less often after PCI (64% vs. 99%, 96%; P = 0.0001). Patients with severe LV dysfunction were more likely to be treated

EF = ejection fraction

Table 3. Univariate predictors of LV function in patients with first AMI

Predictors	Correlation coefficient	*P*
Renal failure	0.22	0.009
Peripheral vascular disease	0.2	0.02
Peak CK	0.3	0.0001
TIMI flow 0-1 before PCI	0.2	0.03
TIMI flow 3 after PCI	-0.34	0.0003
Door to Balloon time	0.22	0.008

TIMI = thrombolysis in myocardial infarction

with IABP (26% vs. 3%, 7%, $P = 0.003$) compared to patients with mild or moderate LV dysfunction. But there was no difference in the use of glycoprotein IIb/IIIa blockade or in other angiographic characteristics [Table 2].

Clinical outcomes

As compared to patients with mild or moderate LV dysfunction, patients with severe LV dysfunction had a higher risk of in-hospital (26% vs. 0%, 3.4%, $P = 0.0001$) and 30 day mortality (35% vs. 0%, 5.8%, $P = 0.0001$), as well 30 day major adverse cardiovascular events (death, re-AMI and target vessel revascularization: 43% vs. 6.9%, 12.6%; $P = 0.002$).

Univariate predictors of LV function were renal failure, peripheral vascular disease, door to balloon time, peak CK, TIMI flow before and after PCI, and the need for IABP [Table 3]. Multivariate analysis adjusted for baseline characteristics, medical treatment and angiographic findings identified peak CK ($r = 0.3$, $P = 0.0001$) as well as door to balloon time ($r = 0.2$, $P = 0.008$) as the most significant predictors of LV dysfunction after first anterior AMI.

Discussion

The principal finding of this study is that late reperfusion time, peak CK level, renal failure, peripheral vascular disease, use of IABP, and low TIMI flow grade before and after angioplasty are associated with depressed LV function in patients with anterior AMI. Of these, the most powerful predictors of LV function were door to balloon time and peak CK.

The time delay to myocardial reperfusion is important for survival and recovery of LV function in patients undergoing thrombolytic therapy for AMI [9]. However, the importance of time to treatment with primary PCI is controversial. Stone and colleagues [10] showed that time to treatment may be less important for survival after primary percutaneous transluminal coronary angioplasty than after thrombolysis. However, Brodie et al. [11] found that up to 2 hours reperfusion time with primary PCI is a major factor in survival and recovery of LV function. After 2 hours however, recovery of LV function was modest and survival was relatively independent of the time to reperfusion, suggesting that factors other than myocardial salvage may be involved. Miura and team [12] showed that patients who presented less than 4 hours before primary PCI exhibited better LV function than those who presented later. In the present study, LV function decreased with an increase in door to needle time, however patients with moderate and severe LV dysfunction had similar door to balloon time, which may be related to other factors affecting LV function after AMI; these may be TIMI frame count, myocardial blush and ST resolution.

Peak CK following primary angioplasty was one of the most powerful predictors of LV function in our study. A significant linear relation between peak CK and LVEF in AMI patients treated with either thrombolysis [13] or primary PCI was also found by others [14].

Baseline renal failure has been reported to be a powerful predictor in patients with AMI undergoing primary PCI. Sadeghi et al. [15] found that patients with renal failure undergoing primary PCI were more likely to have a reduced LVEF; however, this was not the primary endpoint of their study. Kashani and associates [16] reported that creatinine clearance < 60 ml/min was one of the four most powerful correlates of heart failure in patients treated with thrombolysis following ST-elevation AMI. Our study clearly demonstrated that renal failure is a predictor of LV dysfunction in ST-elevation AMI treated by primary angioplasty. Possible mechanisms by which renal failure acutely exacerbates LV function include cardiomyopathy changes induced by nephropathy, severe restenosis, infarct artery reocclusion and more diffuse atherosclerosis [15,16].

Studies have shown that patients who have a history of PVD have a higher rate and more extensive degree of coronary artery disease than those without such a history [3]. PVD correlates with poor outcome and is associated with adverse outcome in patients with acute coronary syndrome, due to the bigger burden of atherosclerosis [17] and chronic CAD. Our study demonstrated that patients with severe LV dysfunction were more likely to have PVD than patients with mild or moderate LV dysfunction. The same finding was observed by Cotter et al. [17]. The latter authors also found that patients with acute coronary syndrome and extracardiac vascular disease, including PVD, cerebrovascular accident, and transient ischemic attack, have a high likelihood of decreased EF.

TIMI 3 flow in the infarct-related artery before and after angioplasty predicted residual LV function. This finding confirms the importance of achieving early TIMI 3 flow, as previously reported by others [19,20]. The use of IABP improves LV function in acute myocardial infarction complicated by cardiogenic shock [21] and persistent ST elevation after primary PCI [22]. In our study, however, IABP was a predictor of reduced LV function, perhaps because we used IABP in patients with initially depressed LV function and/or symptoms of congestive heart failure.

Patients at high risk for LV dysfunction and subsequent death following anterior wall ST-elevation AMI can be identified by clinical and angiographic variables that are readily available at the time of initial assessment. We demonstrated that high peak

IABP = intra-aortic balloon pump
CK = creatine kinase

PVD = peripheral vascular disease
CAD = coronary artery disease

CK and long interval from symptom onset to hospital arrival time are the most important predictors of LV function. Therefore, patients with these features may represent a subgroup at risk of excessive mortality. Our study emphasizes that maximal attempts should be made to decrease the time from onset of chest pain to coronary reperfusion. Additional studies are needed to determine the role of adjunctive pharmacotherapy (e.g., delaying myocardial necrosis and preventing reperfusion injury) and other approaches (e.g., systemic cooling and hyperbaric oxygen treatment) in augmenting the chances of preserving the LV function and improving prognosis following AMI.

Limitations

This is an observational, non-controlled study, and is affected by all the limitations of these kinds of studies. On the other hand, because of the prospective real-time database implementation, we have minimal missing data and all our patients were consecutive, which limits possible patient selection bias.

LV function was assessed at the first 24 hours after AMI, but depressed LV function in the first days/weeks after AMI may be affected by stunning rather than permanent myocardial damage. However, LV function assessed in our study correlated with in-hospital and 30 day outcome, emphasizing the importance of LV function assessment in the first hours after AMI.

Another limitation is the assessment of TIMI flow, which was one of the predictors of LV dysfunction in our study. Methods for assessment of myocardial perfusion are ST resolution, myocardial blush and TIMI frame count. Other authors confirm the importance of achieving TIMI flow [19,20].

Conclusion

The principal finding of this study is that abnormal left ventricular function after first AMI can be predicted by longer door to balloon time and larger infarction size as assessed by peak CK levels.

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Correspondence: Dr. A.R. Assali, Dept. of Cardiology, Rabin Medical Center (Beilinson Campus), Petah Tiqva 49100, Israel.
Phone: (972-3) 937-6441
Fax: (972-3) 923-1016
email: aassali@clalit.org.il