Predictors of contractile recovery after revascularization in patients with anterior myocardial infarction who received thrombolysis

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BACKGROUND: Identification of viable myocardium after myocardial infarction has gained paramount importance with the current progress in coronary revascularization.

OBJECTIVE: To explore the prognostic power of certain patient characteristics to predict myocardial contractile recovery after revascularization in patients presenting with acute anterior ST elevation myocardial infarction (STEMI) who received thrombolytic therapy.

METHODS: Seventy-three consecutive patients presenting with first acute anterior STEMI who had received thrombolytic therapy and had significant coronary stenosis or occlusion of the infarct-related artery amenable for revascularization were enrolled. All patients underwent echocardiographic assessment of regional wall motion and left ventricular ejection fraction. Patients underwent coronary revascularization by either percutaneous angioplasty or surgical bypass. Echocardiography was repeated two to three months following revascularization. Patients were classified into two groups:

group 1 had evidence of contractile recovery after revascularization at follow-up echocardiography and group 2 had no such evidence of recovery.

RESULTS: Predictors of contractile recovery after revascularization included a shorter time from symptom onset to the institution of thrombolytic therapy, a lower baseline wall motion score index, the presence of grade 3 collaterals to the infarct-related artery and the use of beta-blockers. Instead, the presence of diabetes mellitus and a totally occluded infarct-related artery predicted poor contractile recovery.

CONCLUSIONS: Myocardial contractile recovery after revascularization in patients presenting with first acute anterior STEMI may be predicted by the absence of diabetes, a shorter time from symptom onset to thrombolytic therapy, the use of beta-blockers, a lower initial wall motion index score and the presence of collaterals to the infarct-related artery.

Key Words: Myocardial infarction; Predictors; Revascularization; Viability

Identification of viable myocardium after myocardial infarction (MI) has gained outstanding importance with the current progress in myocardial revascularization over the past two decades, especially in patients considered for coronary intervention (1). Myocardial viability represents impairment of contractility with potential recovery if blood supply is sufficiently restored (2). Evidently, improving blood supply to viable myocardial segments following MI results in an improvement of regional and global left ventricular contractility, clinical heart failure and functional capacity, and reduced long-term mortality. An important concern, therefore, is whether hypokinetic or akinetic myocardial segments following MI represent viable myocardium with a severely reduced blood supply or permanently damaged scar tissue (3). This concern was supported by the results of a previous report (4), in which only those patients with severely impaired left ventricular systolic function after MI who harboured viable myocardium improved after coronary revascularization. In a prospective study design, we explored the prognostic power of certain patient characteristics to predict myocardial contractile recovery after revascularization in patients presenting with acute anterior ST elevation myocardial infarction (STEMI) who received thrombolytic therapy.

METHODS

Patient selection and study design

Seventy-three consecutive patients admitted to the intensive care unit of Ain Shams University Hospital (Cairo, Egypt), presenting with first acute anterior STEMI between April 2007 and April 2008 were enrolled. Patients were considered to be eligible for inclusion if they had received thrombolytic therapy, had significant stenosis or occlusion of the infarct-related artery, and had an infarct-related artery amenable for revascularization as seen on subsequent coronary angiography. The diagnosis of STEMI was based on a 12-lead electrocardiogram showing ST segment elevation of 1 mm or greater in at least two contiguous leads plus one of the following criteria: prolonged chest discomfort typical of myocardial ischemia or elevated cardiac biomarkers – creatine kinase MB and/or troponin more than twice the upper limit of normal laboratory reference values. Significant coronary stenosis was defined as at least 70% luminal obstruction of a sizable arterial segment (measuring 2.5 mm or more in diameter) seen in two different projections. Total coronary occlusion was defined as 100% luminal obstruction with Thrombolysis in Myocardial Infarction grade 0 forward flow distal to the site of obstruction. Patients with early postinfarction unstable angina or severe hemodynamic

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instability, clinically evident congestive heart failure, significant valvular or congenital heart disease, any myocardial disease apart from ischemia, and patients with limited life expectancy due to coexistent disease (eg, malignancy) were excluded. Before inclusion, informed written consent was obtained from each patient after a full explanation of the study protocol. Finally, the study protocol was reviewed and approved by the local institutional human research committee of Ain Shams University Hospital, as it conforms to the ethical guidelines of the 1964 Declaration of Helsinki, as revised in 2002.

Definitions of risk factors

The presence of hypertension was defined as a systolic blood pressure of 140 mmHg or greater and/or a diastolic blood pressure of 90 mmHg or greater previously recorded by repeated noninvasive office measurements, which lead to lifestyle modification or antihypertensive drug therapy. The presence of diabetes mellitus was defined as a fasting plasma glucose level of 7 mmol/L or greater, and/or a 2 h postload glucose level of 11.1 mmol/L or greater, or specific antidiabetic drug therapy. Dyslipidemia was defined as a low-density lipoprotein cholesterol level of greater than 2.59 mmol/L and/or a serum triglyceride level of greater than 1.69 mmol/L, and/or a high-density lipoprotein cholesterol level of less than 1.03 mmol/L in men and less than 1.29 mmol/L in women.

Baseline echocardiographic assessment

Assessment of regional and global left ventricular systolic function was performed in all patients by transthoracic echocardiography within 48 h of admission (at least 24 h following thrombolytic therapy). Doppler echocardiography was performed using a General Electric Vivid 7 Pro cardiac ultrasound machine (General Electric Company, Norway) equipped with harmonic imaging capabilities. A 2.5 MHz phased array probe was used to obtain standard two-dimensional, M-mode and Doppler images. Patients were examined in the left lateral recumbent position using standard parasternal and apical views. Images were digitized in cine-loop format and saved for subsequent playback and analysis. Views were analyzed by a single echocardiographer (WA) using the software program of the echocardiography machine. Biplane global left ventricular systolic function was assessed in apical four-chamber and two-chamber views using the modified Simpson's rule. Regional wall motion was assessed according to the standard 16-segment model recommended by the American Society of Echocardiography (5). Individual segments were then subgrouped based on the known vascular distribution into the left anterior descending artery territory, left circumflex artery territory, right coronary artery territory and overlap segments (5). Regional wall motion was visually assessed for each segment individually – considering both endocardial excursion and systolic thickening – and each segment was assigned a score according to the semiquantitative scoring system described by Knudsen et al (6):

- Normal contraction was defined as 5 mm or greater endocardial excursion with 25% or greater systolic thickening, and assigned a score of 1.
- Hypokinesia was defined as less than 5 mm endocardial excursion and/or less than 25% systolic thickening, and assigned a score of 2.

- Akinesia was defined as virtual absence of systolic myocardial thickening, even if slight inward motion was present during systole, and assigned a score of 3.
- Dyskinesia was defined as paradoxical endocardial excursion away from the left ventricular lumen in systole, and assigned a score of 4.
- Aneurysm was defined as continuous distortion of the wall both in systole and diastole, and assigned a score of 5.

Segments with poorly defined endocardial borders for 50% or more of their length were considered to be nonvisualized and assigned a score of 0 (7). Wall thickening was assessed at a distance of at least 1 cm from the adjacent segment to minimize the effect of tethering (excursion of a hypokinetic or akinetic segment by the contraction of an adjacent normally contracting segment) (8). Wall motion in a vascular territory was considered to be abnormal if wall thickening was decreased in at least two contiguous nonoverlapping segments (5). Wall motion score index (WMSI) was calculated by adding the numerical value assigned to each segment and dividing by the number of segments visualized.

Coronary revascularization

All patients underwent revascularization of the infarct-related artery within two weeks of hospital admission by either percutaneous coronary angioplasty or surgical bypass grafting according to the operator's discretion. The operator's decision was based on the clinical presentation and coronary anatomy.

Follow-up echocardiography

Follow-up echocardiographic reassessment was performed by the same operator two to three months after revascularization to evaluate regional and global left ventricular systolic function as described before. The occurrence of myocardial contractile recovery was defined by improvement of regional wall motion score by at least one grade in at least two contiguous nonoverlap segments, along with at least 20% reduction in the global WMSI compared with baseline evaluation. During follow-up, patients were examined for the occurrence of new MI or hospitalization for congestive heart failure through clinic visits, telephone calls, hospital chart reviews or personal communication with the referring physician.

Statistical analysis

All continuous, normally distributed variables were presented as mean $\pm$ SD. Data were tested for normal distribution using the Kolmogorov-Smirnov test. Categorical variables were described with absolute and relative (percentage) frequencies. According to the above definition of myocardial contractile recovery, patients were classified into two groups – group 1 had evidence of actual contractile recovery after revascularization at follow-up echocardiography and group 2 had no such evidence of recovery. The two groups were compared with respect to patients' clinical characteristics, and baseline echocardiographic and angiographic data, using the unpaired *t* test for continuous variables and Pearson's χ^2 test for categorical variables. Finally, multivariate logistic regression analysis was performed to identify the independent predictors of myocardial contractile recovery after revascularization, in which the dependent variable was the outcome variable of interest, whereas factors entered into the model included clinical,

TABLE 1
Baseline clinical characteristics of the total study cohort and the two individual groups

	Total (n=73)	Group 1 (n=36)	Group 2 (n=37)	P
Age, years	49.8±10.3	49.6±9.2	52.2±10.5	>0.05
Male sex	62 (84.9)	28 (77.8)	32 (86.5)	>0.05
Smoking	45 (61.6)	23 (63.9)	22 (59.5)	>0.05
Diabetes mellitus	37 (50.7)	10 (27.8)	27 (72.9)	<0.05
Hypertension	38 (52.1)	15 (41.7)	23 (62.2)	>0.05
Dyslipidemia	43 (58.9)	20 (55.6)	23 (62.2)	>0.05
Time to thrombolytic therapy, h	4.9±1.9	3.9±1.5	5.8±2.3	<0.05
Medications				
Beta-blockers	48 (65.8)	30 (83.3)	18 (48.6)	<0.05
ACE inhibitors	54 (73.9)	25 (69.4)	29 (78.4)	>0.05
Calcium antagonists	23 (31.5)	13 (36.1)	10 (27.0)	>0.05

Continuous variables are presented as mean ± SD, while categorical variables are presented as n (%). ACE Angiotensin-converting enzyme

TABLE 2
Echocardiographic characteristics recorded at baseline for the total study cohort and the two individual groups

	Total (n=73)	Group 1 (n=36)	Group 2 (n=37)	P
LVEF, %	41.2±8.7	51.6±4.9	42.3±6.2	>0.05
WMSI	1.94±0.5	1.44±0.2	2.41±0.5	<0.05

Data presented as mean ± SD. LVEF Left ventricular ejection fraction; WMSI Wall motion score index

echocardiographic and angiographic variables that demonstrated a significant difference between the two groups on univariate analysis. $P<0.05$ was considered to be statistically significant. Analyses were performed with the SPSS statistical package, version 12.0 (SPSS Inc, USA).

RESULTS

A total of 73 consecutive patients presenting with first acute anterior STEMI were included in the current study between April 2007 and April 2008. These patients underwent some form of coronary revascularization for significant coronary stenosis or occlusion. Baseline characteristics of the entire cohort as well as the two individual groups are shown in Table 1. According to the aforementioned definition of myocardial contractile recovery, 36 patients (group 1) improved after revascularization, while 37 (group 2) did not, as shown in Table 1. The mean age was 49.8±10.3 years and 84.9% were men. Diabetes mellitus was found more frequently in group 2 than in group 1 (72.9% versus 27.8%, respectively; $P<0.05$). Time from the onset of chest pain to the initiation of thrombolytic therapy was significantly shorter in group 1 than in group 2 (3.9±1.5 h versus 5.8±2.3 h, respectively; $P<0.05$). Moreover, the frequency of beta-blocker use was significantly higher in group 1 than in group 2 (83.3% versus 48.6%, respectively; $P<0.05$). No statistically significant differences were found between the two groups in any of the other baseline characteristics.

Table 2 shows baseline echocardiographic characteristics of the entire study cohort as well as the two individual groups. WMSI was significantly lower in group 1 than in group 2 (1.44±0.2 versus 2.41±0.5, respectively; $P<0.05$). Table 3 shows echocardiographic characteristics recorded at baseline for three subgroups of the cohort.

TABLE 3
Echocardiographic characteristics recorded at baseline for three subgroups of the cohort

	Diabetic patients (n=37)	Nondiabetic patients (n=36)	P
LVEF, %	44.6±5.4	50.9±6.3	>0.05
WMSI	2.11±0.4	1.83±0.3	>0.05
	No beta-blockers (n=25)	Beta-blockers (n=48)	
LVEF, %	47.3±4.8	48.9±5.3	>0.05
WMSI	1.93±0.2	1.92±0.4	>0.05
	Time to thrombolytic therapy ≥4 h (n=45)	Time to thrombolytic therapy <4 h (n=28)	
LVEF, %	39.4±2.4	54.8±5.6	<0.05
WMSI	2.44±0.4	1.47±0.1	<0.05

Data presented as mean ± SD. LVEF Left ventricular ejection fraction; WMSI Wall motion score index

The presence of grade 3 collaterals to the infarct-related artery on coronary angiography was significantly more frequent in group 1 than in group 2 (four [11.1%] versus one [2.7%], respectively; $P<0.01$), while the presence of a totally occluded infarct-related artery was significantly more prevalent in group 2 than in group 1 (14 [37.8%] versus four [11.1%], respectively; $P<0.01$).

Multivariate logistic regression analysis identified no independent predictors of contractile recovery after revascularization. No patient reported any clinical events during the period from revascularization to follow-up echocardiographic evaluation.

DISCUSSION

The issue of predicting myocardial contractile recovery following revascularization has long been a matter of debate. Previously reported studies have not provided consistent data to determine the specific predictors of potential contractile recovery. It is, therefore, always recommended to search for viable myocardium before revascularization of an occluded coronary artery; however, there is no practical, yet sensitive, method for assessing myocardial viability in the catheterization laboratory (9). Our findings suggest that visualization of grade 3 collaterals to the infarct-related artery on coronary angiography is a predictor of contractile recovery after revascularization. In agreement with our data, several previous reports (10-13) addressed the issue that the presence of collaterals predicted viability in the supplied region. Another recent study (9) demonstrated that good collaterals seen on coronary angiography have a high sensitivity and positive predictive value for the prediction of viability as shown by dobutamine stress echocardiography, and concluded that one can decide on percutaneous or even surgical revascularization depending solely on the assessment of coronary collateral circulation. Furthermore, Tatli et al (14), in their study of myocardial viability using colour kinesis dobutamine stress echocardiography, concluded that early revascularization could be conducted in patients with good coronary collaterals without doing any further tests of viability. Most of these studies, however, identified viability based on a positive dobutamine stress echocardiography test result (one used technetium-99m sestamibi single photon emission computed tomography imaging), while the current study defined viability according to the ultimate recovery of myocardial contractility after

revascularization; that is, on 'actual' rather than 'predicted' viability. The presence of collaterals can limit infarct size, prevent infarct expansion and preserve myocardial viability in the infarct-related artery territory and, thus, would improve recovery of impaired left ventricular function after revascularization, although it does not protect against stress-induced ischemia (9,14,15). On-screen detection of collaterals is a simple, rapid, readily achievable and inexpensive measure with acceptable accuracy. Yet, these observations should be assessed with caution before making a recommendation for revascularization of coronary occlusions based on the presence of collaterals. One previous study (16) observed that recovery of impaired left ventricular function after revascularization of a chronic total occlusion is not directly related to the quality of collateral function because collateral development does not appear to require the presence of viable myocardium. Consistent with these results, another study (17) reported no difference between patients with and without evidence of myocardial viability with regard to the presence of angiographically demonstrated collaterals.

Diabetes mellitus was significantly more frequent in patients who did not regain contractility after revascularization. Diabetic patients usually have poor coronary collateral circulation compared with nondiabetic patients – a fact that would augment the amount of jeopardized myocardium on occlusion of the supplying artery. The high level of oxidative stress in diabetes may also play an important role in the development and progression of myocardial remodelling and depression seen in diabetic patients (18). Auerbach et al (17), however, observed that diabetes did not predict a worse contractile recovery. Furthermore, a shorter time from symptom onset to thrombolytic therapy predicted subsequent contractile recovery on univariate analysis. It is known that the earlier the initiation of thrombolytic therapy, the higher the opportunity for successful reperfusion and for the preservation of viable myocytes.

Consistent with our results, several studies (17,19-21) found no relation between contractile recovery and basal left ventricular ejection fraction. A more severe depression of systolic function does not necessarily represent wider areas of scar tissue, but might reflect hibernating zones whose contractile function would improve following restoration of an adequate blood supply. Nevertheless, Leclercq et al (10) reported that a better contractile recovery was associated with higher baseline global left ventricular systolic function.

In contrast with our results, two studies (22,23) observed that contractile recovery does not depend on the severity of coronary occlusion. Moreover, contrary to our observations, Saito and Kasuya (24) mentioned age, obesity, lipid profile and blood sugar level as independent risk factors for subendocardial viability ratio. Inconsistent findings reported by the above-mentioned studies would reflect the heterogeneous nature of the underlying disease process, and the lack of uniformity in patient selection and study protocols among different studies.

CONCLUSION

Our data suggest that myocardial contractile recovery after revascularization in patients presenting with first acute anterior STEMI may be predicted by the absence of diabetes, the shorter time from symptom onset to thrombolytic therapy, the use of beta-blockers, lower WMSI and the presence of collaterals to the infarct-related artery.

Limitations

Our findings are based on a single-centre study with a relatively small sample – a fact that makes it difficult to generalize our results to all patients presenting with first acute anterior STEMI. Multicentre studies using the same protocol and examining a larger number of patients are needed. Moreover, the follow-up period of two to three months may have been inadequate to allow recovery of some dyssynergic but viable segments, which would translate to a better contractile recovery rate. Delayed recovery can further occur in a substantial number of segments up to a median of 14 months following revascularization, a fact that warrants repeated assessment after longer periods of follow-up. Another limitation of the study is the lack of quantitative methods for measuring systolic thickening; instead, the operator used visual assessment only. Nevertheless, the problem of intraobserver variability can be minimized by stronger adherence to common and new methodological standards. Finally, follow-up coronary angiography was not performed; therefore, restenosis or reocclusion could not be definitely excluded, which could have threatened the initially achieved contractile recovery. However, no patient reported any clinical events during the period from revascularization to follow-up echocardiographic evaluation.

CONFLICT OF INTEREST: The authors have no conflicts of interest to declare.

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