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Research Article

Persistent Ischemia in Recovery Predicts Mortality after Myocardial Infarction in Patients Undergoing Dobutamine Stress Echocardiography

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Abstract

Objectives: After myocardial infarction (MI), patients are at high risk for major cardiovascular events (MI or cardiac death). Several study shows that dobutamine stress echocardiography (DSE) helps to stratify cardiovascular risk and to assess prognosis of patients after myocardial infarction but the predictors of mortality are different. The aim of our study is to identify what these predictive factors.

Method: It is a prospective study on 146 patients with an acute coronary syndrome with ST segment elevation (STEMI), thrombolysis or not, admitted to the cardiology department, since the beginning of September 2012 to the end of August 2013 and has undergo a pharmacological stress echocardiography with Dobutamine (DSE), an average of 4 weeks after the acute episode, and followed for a year.

Results: Of 146 patients, the average age was 55 ± 8 years, 41% were diabetic. Thrombolysis was performed in 63% of patients. The left ventricular ejection fraction (LVEF) at stress estimated 48.2 ± 6.8%. 89% of patients have benefited from coronary angiography (130 patients). Cardiovascular mortality at 1 year was 3.1% (n = 5), 19.2% of MI (n = 28). In multivariate analysis, independent predictors of 1-year mortality are the absence of viability (p = 0.0001) and persistent ischemia in recovery (p = 0.01). Only the absence of viability was an independent risk factor for MI at 1 year (p = 0.01). In univariate analysis, in addition to the other factors, the biphasic response (viability at low doses of dobutamine, ischemia at high doses) was a risk factor for death (p = 0.004) and MI (p = 0.01) at 1 year.

Conclusion: Dobutamine stress echocardiography predicts the prognosis of patients one year after myocardial infarction. Persistent ischemia in recovery is a new independent predictor for cardiac death.

Keywords: *myocardial infarction; dobutamine stress echocardiography; viability; persistent ischemia in recovery; prognosis.*

Abbreviations: MI: myocardial infarction; DSE: Dobutamine stress echocardiography; STEMI: ST elevation myocardial infarction; LVEF: left ventricular ejection fraction; WMI: wall motion index; MACE: major cardiovascular events; CABG: Coronary arteries bypass graft.

Introduction

After a myocardial infarction, patients are at high risk for major cardiovascular events (death or reinfarction). The stratification of cardiovascular risk is crucial. The troubles of left ventricular kinetics after acute coronary syndrome may be permanent or reversible depending on time of reperfusion and collateral circulation. The identification of myocardial viability has important prognostic and therapeutic implications due to the improvement of the contractility after revascularization. Revascularization of patients with myocardial viability decreases by 3 the occurrence of a coronary event within three years after a myocardial infarction [1].

Several studies have investigated this and demonstrated that dobutamine stress echocardiography (DSE), allowed to determine the prognosis of these patients after an acute coronary syndrome; but the predictors of mortality are many and different. The aim of our study was to determine the rate of major cardiovascular events (death or reinfarction) at 1 year of a myocardial infarction and to identify short- and medium-term predictors of mortality in our population by dobutamine stress echocardiography.

Materials and Methods

This is a prospective study, involving 146 patients who had an acute coronary syndrome with ST segment elevation (STEMI), thrombolysis or not admitted to the cardiology department, since early September 2012 at the end of August 2013, who underwent dobutamine stress echocardiography (DSE) after discharge from the hospital, and after eliminating obviously against-indications to exploration (left intraventricular thrombus, severe left ventricular dysfunction with LVEF < 35%, uncontrolled arrhythmias, pulmonary hypertension, aortic stenosis).

The EDS is performed on average 4 weeks after the acute episode, as a pharmacological stress protocol to dobutamine based on 3-minutes stages of 5, 10, 20, 30 and 40 µg/kg/mn infusion with additional atropine up to 1 mg at stage 30 µg/kg/mn (accelerated Protocol) if required, to achieve the 85% of age-predicted maximum heart rate (220- age). Heart rate, blood pressure and 12-lead electrocardiogramm (ECG) were recorded at rest, during each stage of DSE and in recovery. Metoprolol is used as antagonist.

Echocardiographic images were recorded on a PHILIPS HD EnVisor device. The left ventricle was divided into 16 segments according to the ASE (American Society of Echocardiography). A score is assigned to each segment as follows:

a. Normal kinetics
b. GHypokinesia
c. Akinesia
d. Dyskinesia
e. Aneurysm with calculation of WMI (Wall motion index) at rest and at peak exercise.

Coronary angiography is performed when stress echocardiography is positive (biphasic response with viability in low doses of dobutamine and ischemia at high doses). The results of the exploration and the therapeutic will be specified (medical treatment, percutaneous revascularization with angioplasty or by surgical CABG).

Patients are followed for a year with a consultation to 3 months, 6 months and 1 year. Each consultation will be mentioned the patient's symptomatology, data from the physical examination and electrocardiogram, echocardiographic data including estimation of LVEF, analysis of segmental wall motion, assessment of left filling pressures and pulmonary pressures, and finally the therapeutic conduct.

Major cardiovascular events MACE (death or reinfarction) are also noted.

For the statistical analysis, all data entry is performed on SPSS version 17 software: calculation of percentages and averages with standard deviations, parametric tests: The Chi 2 test to compare qualitative variables and Student's t test to compare the quantitative variables; and when it comes to a comparison of each patient with his own witness (WMI at rest and at peak exercise), we used the paired tests. Test F Fisher- Snedecor for comparison of several averages, and finally non parametric tests for ordinal variables grouped.

The relationships between variables are determined for a significance level $p \leq 0.05$ for a 95% confidence interval.

Results and Discussion

Of 146 patients, the average age was 55 ± 8 years (min 28 years, max 74 years), 85% men (n = 125), 41% of diabetics, 36% had hypertension and 31% had dyslipidemia. One third of patients were over 3 cardiovascular risk factors. The hospital stay was averaging 8 ± 3 days.

The complications of MI are dominated by heart failure Killip stage 2 and 3 (17.7%). The characteristics of our population are resumed in table1.

Patients Characteristics	N = 146
Age (Years)	55 ± 8
Male gender (%)	85
Hypertension (%)	36
Diabetes mellitus (%)	42
Hyperlipidemia (%)	31
MI location, anterior wall (%)	58
Killip classification 2 and 3 at the arrival (%)	12
Thrombolytic therapy (%)	63
Q wave MI (%)	88
LVEF ≤ 40% (%)	26,8

Table 1: *Patients characteristics.*

LVEF the day of stress was evaluated and estimated at 48.2 ± 6.8%. 10 patients had an LVEF <40% and benefited from research of viability only (low doses of dobutamine).

WMI at rest is estimated to average 1.7 ± 0.4. WMI at the peak of the stress is estimated to 1.9 ± 0.4 with a ΔWMI calculated for each patient ($p < 0.0001$).

At the end of the examination, 28% of patients had typical chest pain requiring cessation test, 9% of benign ventricular arrhythmia (extrasystoles).Test responses are summarized in the table2.

Viability	95%
Sustained viability	8,9%
Biphasic response	84,7%
Persistent ischemia in recovery	2,7%
Ischemia in other territories	33%

Table 2: *Stress echocardiography responses.*

89% of patients (130 patients) underwent coronary angiography: more than three quarters of patients had involvement of the anterior descending artery. There is a predominance of single-vessel disease (42%); 33% of double-vessel disease; the triple vessel lesions accounted for only 14.6% of patients. Nearly 2/3 of patients underwent percutaneous revascularization, and 16.9 % underwent coronary artery bypass graft (CABG). Angiographic and intervention data are specified in table3.

Revascularization	89% (N = 130)
Bare metal stent (BMS)	44,6%
Drug eluting stent (DES)	14,6%
CABG	16,9%

Table 3: *Angiographic and intervention parameters.*

Regarding the MACE at 1 year, cardiovascular mortality rate was 3.1% (N = 5 patients), 19.2% of reinfarction (N = 28).

During follow-up, there is an improvement in LV ejection fraction at 1 year, and significantly (p = 0.0001), as shown in table 4. Third of patients have a normal LVEF ≥ 60 % at 1 year.

Nearly ¾ of patients who had a viability in DSE improved their LVEF at 1 year (sensitivity 97% and specificity 75%) and p = 0.004.

	Stress	1 an	p
LVEF (%)	48,2 ± 6,8	52,8 ± 8,1	0,0001

Table 4: *Comparison between LVEF at stress and at 1 year.*

In multivariate analysis, independent predictors of 1-year mortality are the absence of viability at DSE (p < 0.0001) and persistent ischemia in recovery (p = 0.01). The risk of cardiac death is multiplied by 4.9 when there is an absence of viability and multiplied by 3.8 in cases of persistent ischemia in recovery objectified by the dobutamine stress echocardiography. Obviously, patients who have viability to DSE have better survival

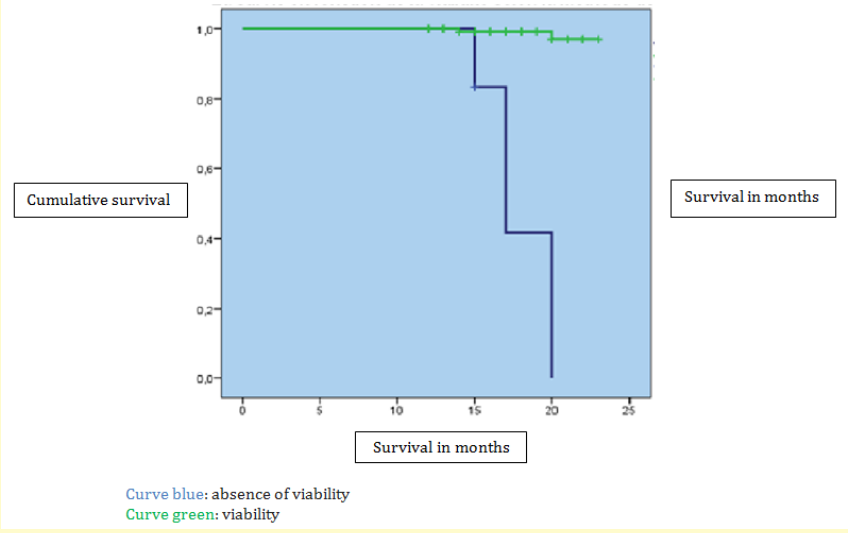

Figure 1: *Survival vs. viability according to the Kaplan-Meier method.*

Only the absence of viability was an independent risk factor for reinfarction at 1 year (p = 0.01).

In univariate analysis, and in addition to the other factors, the biphasic response was a risk factor for death (p = 0.004) and reinfarction (p = 0.01) at 1 year of a myocardial infarction.

The cardiovascular risk stratification after myocardial infarction represents a real challenge for cardiologists, particularly using non-invasive techniques for this lamination such as stress echocardiography [2,3]. Stress echocardiography, dobutamine essentially, has been studied in this indication and the results are promising. Its role in the detection of myocardial ischemia has been well established [4-7]. Many studies have focused on this topic [2,8-16] and have identified, for the most, predictive of mortality in multivariate analysis, but the independent risk factors are different. Carlos et al are the first to have demonstrated that the absence of viability was a risk factor for death after an acute coronary syndrome [8]. In Sicari et al study [2], WMI pic was a predictive factor of mortality. The biphasic response was found in three studies [10,11,13]. This parameter has been objectified in our study only in univariate analysis. Detection and clinical usefulness of a biphasic response was also found during exercise echocardiography early after myocardial infarction [17]. Del Mar de la Torre et al identified that ischemia induced by stress echocardiography and WMI at rest are independent factors of MACE after myocardial infarction. Bangalore et al study showed no independent predictors of cardiac events in multivariate analysis, but demonstrated that patients with normal stress echocardiography after myocardial infarction have benign (< 1% event rate/year) prognosis for up to 18 months after which the event rate increases greatly and patients with abnormal stress echocardiography have a high event rate [14]. Recent studies, mostly interested in comparing the DSE with other stress imaging techniques or DSE combined with new modalities such as speckle tracking, have insisted that dobutamine stress echocardiography has always its own place in the detection of myocardial viability and risk stratification of patients [18-21].

Finally, the results of the present study show that stress echocardiography effectively stratifies risk of patients after myocardial infarction. In addition to the absence of viability, persistent ischemia in recovery predicts cardiovascular mortality at 1 year of myocardial infarction, and it significantly (p = 0.01), since it multiplies by 3.8 the risk of major cardiovascular events at 1 year. Our study has confirmed the prognostic role of stress echocardiography in the prediction of major cardiovascular events after myocardial infarction. Patients, who have no viability in the test, and those with ischemia at high doses of dobutamine, especially if ischemia persisted in recovery, have a greater risk of death.

Conclusion

"Optimal" stratification of cardiovascular risk after myocardial infarction is still uncertain. Dobutamine stress echocardiography can predict the prognosis of patients 1 year after myocardial infarction. Persistent ischemia in recovery is a new independent predictor of cardiovascular mortality that can stratify the cardiovascular risk of our patients to improve their care. This technical approach used to guide cardiologists in their treatment decisions towards a more aggressive approach to invasive revascularization of patients at risk who would benefit from a better prognosis.

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