PROGNOSTIC SIGNIFICANCE OF SILENT MYOCARDIAL ISCHEMIA IN ACUTE MYOCARDIAL INFARCTION

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SUMMARY : Silent myocardial ischemia is proved to be a marker of unfavorable outcomes in coronary artery disease patients. However it has a predictive value in patients early after acute myocardial infarction and its relationship with left ventricular systolic and diastolic dysfunction remains uncertain. The aim of the study is to evaluate the functional changes and specific course of myocardial infarction with symptomatic and silent myocardial ischemia.

119 patients with first Q wave myocardial infarction were included into the study. All of them underwent routine coronary angiography, 24-hour electrocardiographic monitoring, Doppler ECHO of transmitral and transaortal flows with assessment of diastolic and systolic left ventricular function on the 2nd day of disease.

Prospective follow-up was made during 1 year. Factorial and discriminate analysis were undertaken to estimate the most predictable criteria for complicated course of myocardial infarction.

Groups of patients with signs of mixed (symptomatic and silent) and only silent ischemia episodes have more severe coronary artery lesions, pronounced left ventricular systolic and diastolic dysfunction in comparison with group of patients without signs of ischemia. Complicated course of myocardial infarction developed in 52.7%, 45.7% and 12% of patients, respectively ($p<0.05$).

The most predictable criteria for unfavorable prognosis in early post myocardial infarction patients were presence of silent myocardial ischemia, its overall duration more than 60 minutes/per 24 hour, mean number of injured coronary arteries, E value, Ei/ai, aortal flow mean acceleration and EF.

Key Words : Myocardial infarction, silent ischemia, diastolic function, prognosis.

INTRODUCTION

The widely known factors determining survival in MI patients are impaired left ventricular contractility, the extent of coronary lesions, the development of life-threatening arrhythmias, and recurrent anginal attacks, (1-4). Holter ECG monitoring proved useful in the detection of transient episodes of silent myocardial ischemia (SMI) in patients with ischemic heart disease (5-7) which is of special importance in evaluating patients in the early post-infarct period of the disease. Silent myocardial ischemia was observed during exercise testing and prolonged ECG monitoring in post-infarct patients. Several investigators (7-8) are of the opinion that SMI detected soon after myocardial infarction, is an indicator of poor outcome.

It should be noted that impaired diastolic and systolic LV functions are regarded as early manifestations of myocardial ischemia (10,11). At present it seems possible to obtain sufficiently accurate information on these functions with the aid of Doppler EchoCG.

The aim of the present investigation was to study functional changes and specific course of myocardial infarction with manifestations of symptomatic and asymptomatic myocardial ischemia.

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MATERIALS AND METHODS

We studied 119 males aged 30 to 60 years with a first acute Q-wave myocardial infarction. Acute myocardial infarction was diagnosed using conventional WHO (1970) criteria.

According to the results of clinic functional examinations the patients were divided into 3 groups:

Group I consisted of 55 patients who had episodes of symptomatic and silent myocardial ischemia. Group II consisted of 39 patients who only had episodes of silent myocardial ischemia. Group III consisted of 25 patients who had no episodes myocardial ischemia.

Conventional 24-hour ECG monitoring was carried out on days 2-5 of the disease, with evaluation of the frequency of symptomatic or silent ischemia episodes.

The size of MI was determined on the 2nd day of disease by 12-lead ECG's according to the QRS Scoring system (12).

All the patients underwent multi-positional coronary angiography using the Siemens apparatus 'Angioscope D' and the method of Judkings (1967).

Two-dimensional EchoCGs and Doppler EchoCGs were performed on the Toshiba apparatus SSH60A using the 2.5 MHz phased array transducer. Those studies were performed on the second day of disease. Left ventricular end-systolic and end-diastolic volumes were determined using the rule 'area-length'. Pulsed Doppler-EchoCGs were performed in the supine or left lateral recumbent position with recording of Doppler frequency changes in parallel with ECG lead II and phonocardiography on the videotape recorder 'Panasonic'.

Diastolic LV function was assessed by the transmitral flow curve from the position of the apical 4-chamber image of the heart, the sample volume positioned was set at the level of mitral valve cusps.

We assessed the following parameters : myocardial isovolumic relaxation time (IRT, m/sec); peak transmitral flow velocity during early filling (E, cm/sec) and atrial systole (a, cm/sec); their ratio (E/a), the ratio of integral mitral flow velocity early filling to that during atrial systole (ei/ai), and atrial contribution to diastolic filling (%).

Systolic LV function was assessed by the aortal flow curve determined from the suprasternal position, with the sample volume set at the level of the ascending aorta and maximal flow amplitude obtained. The following parameters were assessed : peak aortic flow velocity (PV cm/sec), mean acceleration (MA, m/sec 2).

In order to calculate the values of systolic and diastolic LV function, 3 to 5 cycles of transmitral and aortic flow curves were chosen. The values of systolic and diastolic LV function were analyzed in the absence of ischemia ECG evidence at the time of the study.

Table 1: Clinical characteristics of patients with myocardial infarction.

Parameters	Groups of Patients			
Mean age, years (M±SD)	I(n=55) 48.8±1.7	II (n=39) 49.5±1.9	III (n=25) 48.1±2.3	p NS
Location and size of MI				
Ant. MI, %	54.5	47.2	48	NS
size (balls) (M±SD)	6.3±0.6	5.1±0.6	5.2±0.6	NS
Inf. MI, %	45.5	52.8	52	NS
size (balls) (M±SD)	3.6±0.5	2.8±0.7	3.5±0.7	NS
Anamnesis of				
Angina pectoris, %	47	50	44	NS
Arterial Hypertension, %	42	30	28	NS
Smoking, %	83	75	82	NS
Obesity, %	40	28	30	NS

NS, differences between compared groups are nonsignificant.

Follow-up studies of the patients were maintained for one year. During this period we assessed the incidence of post-infarction unstable angina, recurrent MI, the appearance of signs of heart failure (Killip and Kimball, 1968) and mortality.

In order to determine the predictive value of 45 clinical, electrocardiographic and echocardiographic evidence suggesting an unfavorable outcome in MI patients factorial and discriminant analysis were performed.

RESULTS

All the patients studied were matched for age, sex, risk factors, location and extent of MI (Table 1). Analysis of data on 24-hour ECG monitoring also showed that in 33 MI patients the duration of ischemia exceeded 60 minutes. Thus, the mean frequency of ischemic episodes in this subgroup was 9.0±1.3 and their duration was 109.6±6.8 minutes, while in the other 58 patients the mean frequency of silent myocardial ischemia was 3.0±1.1 and its mean duration was 20.5±2.9 minutes ($p<0.001$).

The state of the coronary bed in MI patients

Comparative analysis of angiographic data in patients with mixed, silent or absent ischemic episodes revealed significant differences in the mean number of diseased coronary arteries (CA), which amounted to 2.5±0.1 in group 1, 2.1±0.1 in group 2 while in group 3 it was 1.6±0.02 (p 1-3 <0.001, p 2-3<0.05).

As it can be observed from Table 2 the highest frequency single-vessel disease was noted in group 3 patients (p>0.001). The frequency of two-vessel disease did not differ significantly between the groups studied, while 3-vessel disease was more frequent in patients with mixed or silent ischemic episodes (p<0.05). The incidence of an infarct-related artery (IRA) occlusion was somewhat higher in patients without ischemic episodes, but the differences were non-significant.

The functional state of the left ventricle in patients with acute MI

Comparison of diastolic function parameters revealed the significant differences between the groups of patients with signs of mixed or silent ischemia and without evidence of ischemia (Table 3). IRT was greater in patients with ischemic episodes than in those without them (p<0.05). Impaired relaxation resulted in decreased myocardial compliance and reduced peak velocity during early filling, as well as in a compensatory increase in atrial filling. Significantly greater changes of E and a velocities were observed in group 1,2 patients as compared to those of group 3 (p<0.05). Decreases in E/a and Ei/ai ratio were also more pronounced in patients with mixed or silent ischemic episodes (p<0.05). The increase in the atrial contribution to diastole in response to decreased early filling was greater in group 1 and group 2 patients as compared to those of group 3 (p<0.001).

The disturbances of diastolic function were accompanied by profound changes in systolic LV function in group 1 and group 2 patients. Aortal flow MA and EF were lower in groups 1 and 2 as compared to group 3 (h1,3-3<0.001) (Table 3).

Predictive value of silent ischemia in acute MI patients

During the follow-up period 6 of group 1 patients (10.9%) and 4 of group 2 patients (10.2%) developed clinically and roentgenologically pronounced signs of heart failure (Killip II) as compared to group 3 where only one subject (4%) had signs of circulatory failure. Acute left ventricular failure developed in 2 group 1 patients and in one group 2 patient.

Follow-up studies revealed that a complicated course of MI developed in 28 group 1 patients (52.7%), in 17 group 2 patients (45.7%), and in 3 group 3 patients (12%) (p1,2-3<0.05). Recurrent MI developed in 5 group 1 patients - after 5 to 11 months, in 4 group 2 patients-within 4 to 12 months, and in 2 group patients - after a year. Within 2 years one patient, in 2 group 2 patients revealed signs of unstable post infarction angina were manifest in 10 group 1 patients and in 5 group 2 patients. Nonfatal ventricular fibrillation developed at the hospital stage in one group 1 and one group 2 patients, one patient in each group died.

Table 2: Coronary angiographic data in patients with myocardial infarction.

Parameters	Groups of Patients			
	I (n=55)	II (n=39)	III (n=25)	P_{1-3}
Left main CA disease, %	8.6	-	6.7	NS
CA Disiease				
1 vessel, %	8.6	18.2*	53.3	<0.001
2 vessel, %	34.3	54.5	33.3	NS
3 vessel, %	31.4	27.2*	13.3	<0.001
IRA occlusion, %	31.3	27.2	33.3	NS

* p<0.05 between II and III. groups.

In assessing the predictive value of prolonged SMI episodes in acute MI patients it was found that during the follow-up period 23 (72.7%) patients with prolonged ischemic episodes had unfavorable outcomes, while in group 2 (SMI of <60 minute duration) only 19 (34.4%) had a complicated disease.

Factorial analysis showed that presence SMI episodes, overall duration ischemic episodes<60 minutes within 24 hours, E volues, Ei/ai, EF and aortal flow MA, mean number of injured CA determined on the 2nd day of disease have the greatest predictive value. The next stage of the statistical study using discriminant analysis showed that the set of the aforementioned factors allows early detection of patients with a possible complicated course of the disease.

DISCUSSION

There are several ways of predicting the course of acute myocardial infarction with manifestations of silent ischemia, that are based on the assessment of predictive value of silent ischemia in post-infarct patients : exercise testing, 24 hour ECG monitoring (5,8,9). However the cited

Table 3: Left ventricular systolic and diastolic function parameters.

Parameters	Groups of Patients			
	I (n=55)	II (n=39)	III (n=25)	P_{1-3}
IRT, msec	92.3±2.1	89.3±3.2	65.1±2.9	<0.05
E, cm/sec	40.1±1.9	42.0±2.2	48.8±2.4	<0.01
a, cm/sec	54.1±1.3	55.2±1.5	50.9±1.1	<0.05
E/a	0.74±0.03	0.76±0.04	0.96±0.03	<0.05
Ei/ai	0.95±0.05	1.0±0.08	1.4±0.06	<0.05
Atrial contribution, %	53.0±1.8	51.3±1.4	43.6±1.6	<0.001
PV, cm/sec	51.2±1.4	54.3±1.2	64.1±1.7	<0.05
MA, m/sec^2	5.8±2.1	6.0±0.3	77.7±0.3	<0.001
EF, %	48.2±0.9	50.0±1.3	56.1±2.3	<0.05

p<0.05 between II and III. groups.

authors evaluated prognosis at the end of the month after onset of disease, although a considerable portion of unfavorable complications develops on the days following the original attack. Therefore it is clear that prognostic evaluation is made with an undue delay and does not include complications observed within 2-3 weeks of the disease. The drawback of the known methods is also their relatively low accuracy which is evidently related to the detection of cases of silent ischemia without taking into account the complicating factor, i.e., impairment of left ventricular function.

Diastolic filling abnormalities are observed in MI patients. It may be due to inherent relaxation rate, early diastolic filling pressure and left ventricular chamber stiffness (13-15). There are two patterns of diastolic filling changes : first impaired relaxation leads to reducing of early peak filling and augmentation of late one and second - pseudo normalization of diastolic curve due to high left ventricular filling pressure (16-17).

Several clinical and experimental studies have uncovered diastolic abnormalities due to acute ischemia (18-20). Clinically it revealed by prolongation of IRT, reduction in early filling rate (10,19). Moreover, these kinds of diastolic alterations disappeared after percutaneous transluminal angioplasty and treatment by Ca channel antagonists in patients with acute MI and unstable angina (21,22).

The present study revealed changes of diastolic function in all the patients with MI, i.e. prolonged IRT, reduced of early filling rate and augmentation of the late filling rate but the characteristics and degree of them were different in different groups. In patients with mixed and SMI episodes diastolic alterations were more pronounced. We explain it by the contribution of ischemia to disturbances of diastolic pattern in MI patients.

A lot of clinical and experimental studies documented that derivates of aortic flow velocity well correlated with myocardial contractile state and EF (23-25). Our data are in agreement with such studies. MA of aortic flow and EF were also significantly lower in patients with ischemia.

Our follow up studies revealed that patients with either mixed or silent ischemia have worse prognosis in comparison with patients who have no signs of ischemia.

Frequency of complications in our groups of patients with signs of mixed (painful and silent) ischemia was 52.7%, only silent ischemia episodes -45.7% and without them 12%. Present study is in agreement with P. Ouang et. al. (8), that in patients with MI and signs of SMI in 52% developed in-hospital complications, in contrast of patients without evidence of ischemia only 22% have such outcomes.

It is evident, that the worse clinical course and prognosis of patients with MI and signs of ischemia are based on Severe CA lesions. Comparison of the nature coronary lesions in the first two groups studied suggests that the frequency of multi vessel disease is higher in patients with symptomatic and myocardial ischemia, which in fact is probably responsible for the presence of ischemic episodes and for the somewhat greater severity of left ventricular dysfunction.

Factorial and discriminant analysis showed that most predictable criteria for complicating course of disease in MI patients are the presence of SI, its duration more than 60 minutes per day, reduced peak flow velocity during early filling, Ei/ai ratio, EF, mean acceleration of aortic flow, mean number of injured coronary arteries.

Silent myocardial ischemia complicates the short and long term prognosis in patients with myocardial infection. Complex evaluation of the clinic functional status of patients with acute myocardial infarction, taken into account the overall duration of ischemic episodes, left ventricular EF, aortic flow MA, early LV filling and relaxation abnormalities, degree of coronary artery lesions, allows early detection of patients with a complicated course of the disease.

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