Clin. Cardiol. 15, 260–264 (1992)

Predictors of Spontaneous Predischarge Ischemia Following Acute Myocardial Infarction

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Summary: To determine if the occurrence and the consequences of spontaneous predischarge postinfarction ischemia could be predicted early after hospital admission, a consecutive series of patients with acute myocardial infarction was studied and followed for 3 years. No patient was treated by thrombolysis. Spontaneous predischarge ischemia was defined as angina that occurred at rest before hospital discharge, at least 3 days after the acute event, and that was accompanied by electrocardiographic changes, but not by an increase in cardiac enzymes. Patients who died within the first 3 days were excluded from analysis. Among the 943 patients who survived at least 3 days, 165 (17.5%) had spontaneous ischemia before discharge. They had a higher 1-year post-hospital mortality (16 vs. 10%), but did not have significantly higher total 3-year mortality rates. Four independent, early available variables predictive of the occurrence of spontaneous ischemia were selected from a stepwise logistic discriminant analysis: history of angina before infarction, non-Q-wave infarct, absence of smoking, and higher age. Among the 165 patients with spontaneous ischemia, 3 independent variables predictive of 3-year mortality were selected stepwise: left ventricular function score, history of previous infarction, and absence of smoking.

Key words: ischemia, myocardial infarction, prognosis, smoking

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Received: August 1, 1990
Accepted with revision: January 18, 1992

Introduction

Previous studies have suggested that early postinfarction ischemia may identify patients with high mortality who should be suited for prompt cardiac catheterization with aggressive medical and surgical therapy.[1,2] However, these studies analyzed the outcome of small selected populations, most patients being referred specifically because of postinfarction complications. To better select the indications for diagnostic and therapeutic interventions in this setting, efforts should be made to determine the incidence and prognostic implications of postinfarction ischemia in a large, unselected group of patients.

The purpose of this study was not only to determine the incidence of spontaneous predischarge ischemia following acute myocardial infarction, but also to identify simple clinical variables which could predict the occurrence and the deleterious consequences of spontaneous ischemia.

Patients and Methods

The study population consisted of 1013 consecutive patients admitted to coronary care unit with acute myocardial infarction and followed for 3 years after infarction or until earlier death. Acute myocardial infarction was diagnosed by an increase in creatine kinase to at least twice the normal level in the clinical setting of prolonged acute chest pain and serial electrocardiographic changes. No patient was treated by thrombolysis. After hospital discharge, the patients were managed by their primary physicians and therapy was not controlled. Mortality within 3 years was the endpoint of this study and this information was obtained in all patients. Recurrent nonfatal infarction was not included as a specific endpoint because the information could not be reviewed for uniform categorization.

Spontaneous predischarge ischemia following infarction was defined as typical chest pain or discomfort that occurred at rest before hospital discharge at least 72 h after the acute event and was accompanied by electrocardiographic changes, but not by an increase in cardiac enzymes. The

information was prospectively obtained in all 1013 patients. Because of the definition, the 42 patients who died within the first 72 h were excluded from analysis. Also excluded were 28 patients in whom confrontation of clinical, electrocardiographic, and biochemical data did not aim to assert definitely the presence or absence of spontaneous ischemia. The remaining 943 patients form the study population.

A series of parameters were coded, stored and studied in a prospective manner. They included age, sex, history of diabetes mellitus and smoking habits, medications taken before infarction, delay of admission to the coronary care unit, electrocardiographic site, type of infarct (Q-wave or non-Q-wave) and peak creatine kinase level (serum levels were measured at 4-h intervals up to 72 h and daily thereafter). The following in-hospital complications were also included: in-hospital recurrent infarct; development of pericardial friction rub; left ventricular function score coded from 0 to 4 (0 = no rales, 1 = basilar rales, 2 = rales up to scapular level, 3 = acute pulmonary edema, 4 = cardiogenic shock); bradycardia (<50 min^{-1}), atrial flutter or fibrillation; frequent premature ventricular complexes (>30 $hour^{-1}$); ventricular tachycardia; ventricular fibrillation; second- or third-degree atrioventricular block; and right or left bundle branch block. Although concomitant electrocardiographic changes were required to define spontaneous ischemia, the location and extent of these abnormalities were not stored. Predischarge exercise testing was performed in only a minority of patients.

The mean value and standard deviations were computed for all quantitative variables, and proportions were computed for binary or discrete clinical findings. Means and proportions for patients with and without spontaneous predischarge ischemia were compared using the Student's *t*-test or the chi-square test, respectively. Results were considered significant at the 5% critical level. To identify significant clinical predictors of ischemia following infarction, variables were examined with a stepwise logistic discriminant analysis.[3] To specify the clinical predictors associated with an unfavorable outcome, univariate and multivariate analyses were also used to compare survivors and nonsurvivors at three years in patients with spontaneous ischemia.

Results

Among the 943 patients who survived at least 3 days after acute myocardial infarction, 165 (17.5%) had spontaneous ischemia before hospital discharge. The clinical characteristics of patients with and without postinfarction ischemia are listed in Table I. The following variables were significantly more frequent among patients with than those without spontaneous ischemia: a history of angina pectoris before infarction, particularly chronic angina and/or unstable angina, non-Q-wave infarct, in-hospital recurrent infarction, and 1-year post-hospital mortality. Patients with ischemia were more frequently nonsmokers and had a lower peak serum creatine kinase level. The total 3-year mortality rates were not significantly different in the 2 patient groups.

Four independent variables predictive of the occurrence of spontaneous ischemia were selected stepwise from the multivariate analysis. All were available early after admission: history of angina before infarction, non-Q-wave infarct, absence of smoking habits, and higher age (Table II).

Within the group of 165 patients with spontaneous ischemia, the 52 patients who died during a 3-year period were compared with the 113 patients who were alive after 3 years (Table III). Nonsurvivors were more frequently nonsmokers. They were older; more often had a history of previous infarction; presented more frequently with an anterior Q-wave infarction; and more often had left ventricular failure, pericardial friction rub, and ventricular fibrillation during hospital stay.

Among patients with spontaneous ischemia, 3 independent variables predictive of 3-year mortality were selected stepwise from the logistic discriminant analysis: left ventricular function score (chi-square = 27.8, p<0,0001), history of previous infarction (chi-square = 7.3, p = 0,007) and absence of smoking habits (chi-square = 8.4, p = 0,004). Considering the left ventricular function score as high when >1, 52% of the nonsurvivors presented with 2 or 3 independent variables. On the other hand, 88% of the 3-year survivors had none or one of these three characteristics (Fig. 1).

Discussion

The results of this study indicate that the occurrence of spontaneous predischarge ischemia in patients not treated

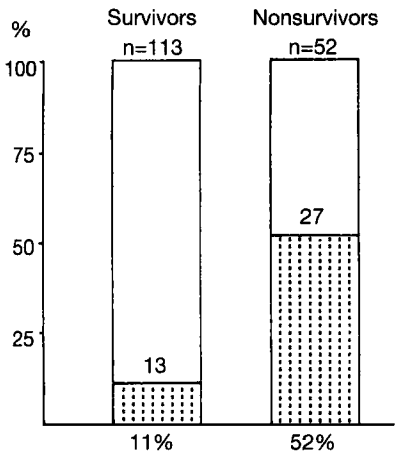

FIG. 1 Prediction of mortality among patients presenting with spontaneous predischarge postinfarction ischemia, using 3 simple clinical variables: left ventricular function score > 1, history of previous infarction, and absence of smoking. The presence of 2 or 3 variables is indicated by the dotted lines in the groups of survivors and nonsurvivors.

TABLE I Comparison between patients with or without spontaneous predischarge ischemia

	Group 1 (ischemia)	Group 2 (without ischemia)	p
Patients (n)	165	778	
Time interval between onset of pain and admission (h)	8 ± 22	9 ± 16	NS
Mean age (years)	58 ± 10	59 ± 10	NS
Sex (% women)	23	17	NS
History of infarction (%)	33	26	NS
History of angina (%)	81	65	<0.0001
History of chronic angina (%)	64	41	<0.001
History of unstable angina (%)	40	23	<0.001
Smoking (%)	76	86	<0.001
Site of infarction			
Non-Q-wave (%)	23	12	<0.001
Anterior (%)	35	39	NS
Inferior (%)	40	46	NS
Unknown (%)	2	3	NS
Peak creatine kinase (IU/l)	1205 ± 960	1463 ± 1113	<0.005
LV function score >1 (%)	35	43	NS
In-hospital recurrent infarction (%)	7	2	<0.005
Pericardial friction rub (%)	24	27	NS
Bradycardia (%)	15	16	NS
Atrial fibrillation (%)	10	15	NS
Frequent PVCs (%)	47	46	NS
Ventricular tachycardia (%)	6	6	NS
Ventricular fibrillation (%)	8	9	NS
Atrioventricular block (%)	10	12	NS
Bundle-branch block (%)	8	10	NS
In-hospital mortality (%)	7	8	NS
Post-hospital mortality			
1st year (%)	16	10	<0.05
2nd and 3rd years (%)	8	7	NS
Total mortality (%)	31	26	NS

Abbreviations: LV = left ventricular; NS = not significant; PVCs = premature ventricular complexes.

with a thrombolytic agent is predictable from clinical variables that are available early after admission. Distinction between patients with this complication who have a favorable prognosis and those who have a deleterious outcome may be possible with very simple clinical data before undergoing further exploration.

TABLE II Prediction of spontaneous predischarge ischemia by stepwise logistic discriminant analysis

	Chi-square	p
1. History of angina before infarction	16.50	0.0001
2. Non-Q-wave infarction	7.18	0.007
3. Absence of smoking	6.12	0.01
4. Age	5.58	0.02
Creatine kinase	3.03	0.08

The reported occurrence of in-hospital postinfarction angina pectoris varies from 6 to 60%,[2,4-7] reflecting the broad clinical definition for angina. In contrast, the incidence of spontaneous ischemia, defined as typical chest pain with concomitant ischemia electrocardiographic changes, is highly stable in the literature: 17.5% in the study by Schuster *et al.*,[2] 18% in the study by Bosch *et al.*,[8] and 17.5% in this study.

The 1-year post-hospital mortality rate was higher in patients with than those without predischarge ischemia. The proportions (16 vs. 10%) were similar to those found by Bosch *et al.*[8] (17 vs. 8%) who followed their patients for 14 ± 8 months. On the other hand, mortality rates were similar in our groups during the second and third years (8

TABLE III Comparison between nonsurvivors and suvivors at 3 years in the 165 patients with spontaneous predischarge ischemia

	Nonsurvivors	Survivors	p
Patients (n)	52	113	
Time interval between onset of pain and admission (h)	5 ± 12	7 ± 25	NS
Mean age (years)	62 ± 10	56 ± 10	<0.002
Sex (% women)	27	22	NS
History of infarction (%)	56	22	<0.0001
History of angina (%)	87	79	NS
History of unstable angina (%)	60	31	<0.001
Smoking (%)	62	81	<0.05
Site of infarction			
Non-Q-wave (%)	13	27	NS
Anterior (%)	50	28	<0.01
Inferior (%)	29	44	NS
Unknown (%)	8	1	NS
Peak creatine kinase (IU/l)	1270 ± 1052	1170 ± 915	NS
LV function score >1 (%)	61	23	<0.0001
In-hospital recurrent infarction (%)	10	6	NS
Pericardial friction rub (%)	38	19	<0.01
Bradycardia (%)	13	16	NS
Atrial fibrillation (%)	19	6	<0.01
Frequent PVCs (%)	50	45	NS
Ventricular tachycardia (%)	10	4	NS
Ventricular fibrillation (%)	17	4	<0.01
Atrioventricular block (%)	10	10	NS
Bundle-branch block (%)	13	6	NS

Abbreviations as in Table I.

vs. 7%). In the studies which determined the prognostic significance of early postinfarction angina, this symptom was associated with an increased risk of mortality only when it occurred frequently.[5,7,9]

The occurrence of spontaneous ischemia, at least 3 days after the acute event and before hospital discharge, may be predicted by simple clinical parameters, already available during the first day of hospital stay: a history of antecedent angina, non-Q-wave infarction, absence of smoking, and higher age. A history of angina before infarction is associated with the presence of well-developed collateral vessels,[10,11] multivessel coronary artery disease,[11,12] and significant residual stenosis of the infarct-related artery.[13] This explains why a clinical history of antecedent angina identifies a subgroup of patients at an increased risk for recurrent cardiac events[14] and late mortality.[15]

Patients with non-Q-wave infarction have been characterized as being at higher risk for recurrent cardiac events,[16] thought to be due to a higher frequency of a patent infarct-related artery[17] with myocardium at jeopardy in the territory perfused by this artery.

Smoking is a risk factor for the development of acute myocardial infarction.[18] Because of an increased thrombogenicity,[19] smoking precipitates myocardial infarction at an earlier age,[20] and also at a lesser degree of coronary artery disease.[21] Thus nonsmokers are more likely to have more extensive coronary artery disease at the time of their infarct and a more guarded prognosis.[22] In this study, absence of smoking was the only clinical variable which predicted both occurrence and deleterious consequences of spontaneous ischemia.

Among our patients who suffered from spontaneous predischarge ischemia, the higher incidence of pericardial rub in nonsurvivors suggests a higher incidence of transmural infarct in this subgroup, as pericardial rub is the only noninvasive way of identifying anatomically transmural infarction.[23] This characteristic and the more frequent history of previous infarction in nonsurvivors suggest that nonsurvivors were more likely to have ischemia at a distance than ischemia in the infarct zone.[1] In the former, the combination of irreversible complete infarction and reversible ischemia may lead to in-hospital transient pulmonary congestion which is an early warning signal of a poor prognosis.[14]

This study has several limitations. First, it could not be ascertained in some patients whether recurrent nonfatal myocardial infarction did or did not occur during the 3-year follow-up; therefore, this endpoint could not be studied. Second, thrombolytic therapy, which was not performed in this study population, has changed the incidence and clinical significance of recurrent predischarge ischemia. Early spontaneous ischemic events occur more fre-

quently (18 to 32%),[24,25] predominently in the infarct zone. They are also associated with a decreased survival.[25] Contrary to our results found in patients not submitted to thrombolysis, recurrent in-hospital ischemia in the thrombolytic era is not predictable,[24] and mortality risk with recurrent ischemia is not stratified with readily available clinical variables.[25] Our findings are clearly not applicable to the patients with acute myocardial infarction who are treated with thrombolytic therapy. It must, however, be remembered that still a minority of patients admitted to hospitals with acute myocardial infarction receives this treatment [only 140,000 of 700,000 (20%) in 1989].[26]

In summary, spontaneous predischarge ischemia may be predicated early and easily after acute myocardial infarction not submitted to thrombolysis. The predictive variables are associated with patent infarct-related artery (non-Q-wave infarction) or more severe and extensive atherosclerosis (previous angina, absence of smoking, and higher age).

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