Effect of Angina in the Week Before Myocardial Infarction on Long-Term Cardiovascular Morbidity and Mortality After Hospital Discharge

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The occurrence of angina in the week preceding myocardial infarction is associated with a reduction in cardiovascular complications in the acute phase. However, little is known about it relationship with prognosis after hospitalization (eg, cardiovascular death and the development of heart failure or ischemic cardiomyopathy). The study included 290 consecutive patients admitted for a first myocardial infarction: 107 (36.9%) had preceding angina while 183 did not. Those with a history of ischemic cardiomyopathy of more than 1 week or structural cardiopathy were excluded. There was no difference in baseline characteristics between the 2 groups. Moreover, there was no difference in the rates of cardiovascular complications after hospital discharge: cardiovascular death (7% vs 12.6%; *P*=.3), heart failure (7.4% vs 11.6%; *P*=.2), and myocardial ischemia, including myocardial infarction and unstable angina, requiring hospitalization (41.2% vs 31.3%; *P*=.3). The occurrence of angina in the week before a first myocardial infarction did not influence cardiovascular complications after hospital discharge (odds ratio = 0.75 [0.51–1.11]; *P*=.15).

Key words: *Unstable angina. Infarction. Prognosis.*

Influencia de la angina preinfarto en la semana previa en la morbimortalidad cardiovascular tardía tras el alta hospitalaria

La angina preinfarto precoz (semana previa) se asocia a una reducción de las complicaciones cardiovasculares en la fase aguda del infarto, pero es escasa la información sobre su relación con el pronóstico tras la fase hospitalaria (muerte cardiovascular y desarrollo de insuficiencia cardiaca e isquemia miocárdica). Estudiamos a 290 pacientes consecutivos ingresados con un primer infarto, 107 con angina precoz (36,9%) y 183 sin ella. Se excluyó a los pacientes con antecedentes de cardiopatía isquémica de más de 1 semana o cardiopatía estructural de base. No se aprecian diferencias en las características basales de ambos grupos. No hay diferencias en las complicaciones cardiovasculares tras el alta hospitalaria (mortalidad cardiovascular, 7 frente a 12,6%; p = 0,3), insuficiencia cardiaca (7,4 frente a 11,6%; p = 0,2) o isquemia miocárdica (infarto o angina inestable, 41,2 frente a 31,3%; p = 0,3) que motiven ingreso hospitalario. La angina precoz no es un factor asociado a complicaciones cardiovasculares tras el alta hospitalaria (*odds ratio* = 0,75; intervalo de confianza del 95%, 0,51-1,11; p = 0,15).

Palabras clave: *Angina inestable. Infarto de miocardio. Pronóstico.*

INTRODUCTION

The occurrence of angina in the week before the onset of a myocardial infarction is associated with a significant reduction in hospital mortality.[1] Additionally, fewer cardiovascular complications are reported to occur during the acute phase of myocardial infarction and in the medium term.[2] This may be associated with the greater amount of viable myocardium[3] and the greater recovery of ventricular function.[4] This better prognosis in the hospital phase appears to be due to slowing of the process of cell death caused by the previous angina.[5] The underlying pathophysiologic mechanism for this phenomenon could be explained by ischemic preconditioning, by the appearance of collateral circulation or earlier and more efficient reperfusion when fibrinolytic treatment is given or a primary angioplasty is performed.[1,6] Previous chronic angina,

however, is associated with a poor late prognosis (due to greater multivessel disease) and it presents a developed collateral network.[7]

Scientific evidence about the effect of prodromal preinfarction angina and the long-term prognosis after hospital discharge is very scarce. The aim of this study was to analyze the association between these 2 factors.

METHODS

We carried out a retrospective study of 290 patients admitted to our hospital during 1995 and 1996 with a first acute myocardial infarction, according to classical criteria, before the use of troponins. Patients who had had chest pain compatible with angina for more than 1 week were excluded. The intra-hospital complications have been described in a previous report.[2] A total of 107 patients had preinfarction angina of recent onset, whereas the remaining 183 patients did not. We used a first infarction as an inclusion criterion in order to avoid confounding bias in patients with a history of ischemic heart disease (silent ischemia) and we considered angina during the previous week (as collected in the history by a specific questionnaire) given the possible beneficial effect of a second window of protection described in the phenomenon of ischemic preconditioning.[6] Cardiovascular complications after discharge were defined as those that caused heart failure or residual ischemia (reinfarction or unstable angina) that required hospital admission, and cardiovascular death as that occurring during the follow-up for the reasons described, including sudden death. The follow-up data were obtained at a clinic check-up or telephone interview. The mean follow-up was 56.4 (2.57) months (5.6% were lost to follow-up).

Statistical Analysis

The quantitative data are expressed as the mean (standard deviation) and the qualitative data as percentages. We performed a univariate analysis with the Student t test for continuous variables and the $\chi 2$ test for discrete variables. We used Cox multivariate regression analysis to evaluate the factors that contributed to the cardiovascular complications after hospital discharge, including the variables age, sex, localization of the infarction (anterior or non-anterior), depressed ventricular function (defined as an ejection fraction <40% from visual estimation during the hospital phase by an expert echocardiographer), use of thrombolytic therapy, prior angina, hypertension, hypercholesterolemia, diabetes, smoking, and heart failure during the acute phase of the infarction. The differences were considered to be statistically significant if the P<.05. The calculations were done with the statistical package SPSS 11.0.

TABLE 1. **Baseline Characteristics of the Patients According to Whether or Not They Had Recent Onset Preinfarction Angina**

	With Angina (n=107)	Without Angina (n=183)
Age, y	61.9 (11.9)	63 (12.1)
Male, %	75.7	75.4
Cardiovascular risk factors, %		
Hypertension	42.4	46.7
Smoking	57.9	62.8
Diabetes mellitus	23.4	25.2
Hypercholesterolemia	34.6	25.1
Anterior localization of the infarction[a]	38.3	34.4
Thrombolytic therapy	72.9	67.2
Depressed EF during admission[b]	23.4	67.2

EF indicates ejection fraction determined by echocardiography.
[a]Determined by electrocardiography.
[b]Statistically significant difference (P<.009).
The data are expressed as the overall percentage of each group or as the mean (standard deviation).

RESULTS

Clinical Characteristics

Table 1 gives a summary of the clinical characteristics in both groups of patients. Of the 290 patients, 107 (36.9%) had had a previous angina. No significant differences were seen between the 2 groups concerning age, sex, risk factors, the localization of the infarction, or the use of fibrinolytic therapy, though there was a significant difference in the percentage of patients with depressed ventricular function.

Cardiovascular Complications After Hospital Discharge

Table 2 presents the cardiovascular complications after hospital admission and the overall complications. The percentage of cardiovascular complications during the follow-up of the patients with prior angina compared to those without was: cardiovascular death, 7% versus 12.6% (P=.3); readmission due to heart failure, 7.4% versus 11.6% (P=.2); readmission due to infarction or unstable angina, 41.2% versus 31.3% (P=.3). Analysis of the factors associated with total complications after hospital discharge showed that prior angina was not an associated factor (odds ratio [OR]=0.75; 95% confidence interval [CI], 0.51-1.11; P=.15), whereas age (OR=1.02; 95% CI, 1.01-1.04; P=.02), heart failure during the acute hospital phase (OR=3.44; 95% CI, 2.07-5.7; P=.001), use of fibrinolysis (OR=0.64; 95% CI, 0.44-0.94; P=.02), and diabetes mellitus (OR=1.53; 95% CI, 1.03-2.28; P=.03) were all associated factors.

TABLE 2. Total Complications and Complications During Follow-up According to Whether the Patient Had Had Angina During the Week Before or Not

	Total Complications		P	Complications After Discharge		P
	Yes (n=107)	No (n=183)		Yes (n=103)	No (n=162)	
Cardiovascular death	11 (10.3)	44 (24)	.004	7 (7)	23 (12.6)	.3
Heart failure or shock	12 (11.4)	44 (24)	.006	8 (7.4)	21 (11.6)	.2
Residual ischemia	45 (42.1)	69 (37.7)	.5	40 (41.2)	57 (31.3)	.3
Total complications	52 (48.6)	101 (55.2)	.3	45 (42.5)	89 (48.6)	.3

Residual ischemia during the follow-up is hospital admission for unstable angina or reinfarction. Heart failure during the follow-up is hospital admission with the main diagnosis of heart failure.
The data are expressed as the number of patients (percentage of the total number in each group) or mean (standard deviation).

DISCUSSION

The occurrence of angina in the week before the onset of myocardial infarction reduces mortality and the intra-hospital cardiovascular complications of patients with myocardial infarction.[1,2] The main finding of this study is the absence of differences in cardiovascular complications after hospital discharge (death, heart failure, angina, and reinfarction leading to readmission to hospital) in a group of 290 patients with a first myocardial infarction and no history of ischemic heart disease. Nevertheless, other associated factors, such as age, onset of heart failure during hospital admission, the use of fibrinolysis, and diabetes mellitus were associated with long-term prognosis.

Little information is available about the long-term prognosis of recent-onset prior angina. Ishihara et al[8] studied a group of 350 patients with a previous infarction treated with primary angioplasty that achieved reperfusion in 84% (TIMI II-III) and found a long-term protective effect of angina in the 24 h before the infarction (24% of the patients), but not if they had had angina at any time earlier (9% of the patients with previous infarction); the authors considered both hospital events and those occurring after discharge (intra-hospital cardiovascular death, 6% vs 14% according to whether they had had angina during the previous 24 h or not; mortality after discharge, 8% vs 13%; and overall mortality at 5 years, 14% vs 27%; *P*<.001). Bahr et al,[9] in a subgroup of 204 patients belonging to the GUSTO-1 clinical trial (all patients treated with fibrinolysis) and considering previous angina for up to 2 weeks before the onset of myocardial infarction, found that the patients who had had previous angina experienced a lower long-term mortality (5 years) in general (23.2% vs 31%), but mortality after the first month was 16% in patients with angina versus 20% in those without. Our study differs from these earlier studies in the analysis carried out, as it just focused on complications after discharge. Though the improvement in cardiovascular mortality was not statistically significant, it was similar in terms of percentage (around 5% reduction in cardiovascular mortality) to the studies by Ishihara et al[8] and Bahr et al[9] with 5 years of follow-up.

The benefit of prodromal angina is associated with a reduction in hospital complications in these 3 series,[2,8,9] even though they have important clinical differences regarding the use of reperfusion therapies (primary angioplasty, 100%; fibrinolysis, 70%), a history of prior infarction (9%, 20%, and 0%), definition of prior angina (24 h, 2 weeks, and 1 week) and anterior localization of the infarction (100%, 42%, and 36%). Nevertheless, all the studies reported a similar percentage of reduction in cardiovascular death after hospital discharge, though only our study examined this as a separate issue in this period, and no significant differences were found between the groups.

Ischemic preconditioning,[6] a fast and efficient mechanism that delays cell death if early and effective reperfusion is achieved,[10] could explain the hospital benefit of previous angina, though it does not appear to show a benefit after hospital discharge.

Limitations of the Study

The study obviously involves a selection bias as we only included patients who arrived at the hospital alive. We are therefore unable to determine the influence of angina during the week before the onset of infarction prior to the hospital phase and whether this influences the early and late prognosis. The degree of reperfusion attained may also affect the results found,[10] as may the medication given before and after the hospital phase. Determining the exact time of the onset of myocardial infarction in patients with prodromal angina is difficult. We have no knowledge of the coronary anatomy of most patients, due to the poor availability of coronary angiography during the study period.

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