BRIEF REPORT

Influence of Diabetes Mellitus on the Management and Prognosis of Non-ST-Elevation Acute Coronary Syndrome

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The presence of diabetes mellitus worsens prognosis in acute coronary syndromes. The aim of our study was to analyze retrospectively the influence of diabetes mellitus on the management and prognosis of patients with non-ST-segment elevation acute coronary syndrome. We compared the baseline clinical characteristics of 273 patients (93 diabetic and 180 non-diabetic) admitted consecutively to our department with the diagnosis of non-ST-segment elevation acute coronary syndrome. In both groups, we assessed the medical treatment given during hospitalization and the use of coronary angiography, percutaneous coronary intervention, and coronary artery bypass grafting. Finally, we determined the incidence of heart failure during hospitalization and mortality at 28 days and 6 months in both groups. Multifactorial analysis revealed that diabetes was an independent risk factor for mortality during the study period. Data from our registry indicate that these findings were not associated with more extensive use of interventions in diabetic patients.

Key words: *Unstable angina. Diabetes mellitus. Prognosis.*

Influencia de la diabetes mellitus en el tratamiento y el pronóstico del síndrome coronario agudo sin elevación del segmento ST

La diabetes mellitus condiciona un peor pronóstico del síndrome coronario agudo. Presentamos un estudio retrospectivo cuyo objetivo fue analizar la influencia de la presencia de diabetes en el pronóstico y el tratamiento de pacientes con síndrome coronario agudo sin elevación del segmento ST. Se compararon las características clínicas de 273 pacientes (93 pacientes diabéticos frente a 180 no diabéticos) ingresados en nuestro centro con el diagnóstico de síndrome coronario agudo sin elevación del segmento ST. Durante la hospitalización analizamos en ambos grupos el tratamiento médico y la realización de coronariografía, intervencionismo y cirugía coronaria. Finalmente, analizamos la incidencia acumulada de insuficiencia cardiaca intrahospitalaria y la mortalidad a los 28 días y 6 meses en ambos grupos. El análisis multifactorial demostró que la diabetes fue un predictor independiente de mortalidad durante el período de seguimiento. Estos hallazgos no se acompañaron en nuestro registro de un tratamiento más intervencionista en el grupo de pacientes diabéticos.

Palabras clave: *Angina inestable. Diabetes mellitus. Pronóstico.*

INTRODUCTION

In recent years, the definition of acute coronary syndrome (ACS), formulated parallel to the development of diagnostic and therapeutic advances of considerable clinical impact, has included the various forms of acute ischemic heart disease. In particular, in the last decade non-ST-elevation acute coronary syndrome (NSTEACS) and its prognostic stratification has raised interest among the various scientific societies[1-3] in the past decade. Even with the current therapeutic possibilities, however, NSTEACS still presents high morbidity and mortality.[4] Diabetes mellitus (DM), one of the most prevalent diseases, is intrinsically linked to the development of arteriosclerosis and cardiovascular disease.[5] There is abundant evidence to sustain that the prognosis of ACS among diabetic patients is poorer than among nondiabetics.[6,7] The current epidemiology of DM in

TABLE 1. Baseline Clinical Characteristics and Angiography and Revascularization Therapy (Percutaneous or Surgical) During Hospitalization Among the Diabetic and Nondiabetic Groups*

	Group With DM (n=93)	Group Without DM (n=180)	P
Age, mean±SD, y	67±12	65±10	.24
Men	56 (60%)	121 (67%)	.35
HT	46 (50%)	56 (31%)	.001
Dyslipidemia	45 (48%)	65 (36%)	.001
Smoker	44 (47%)	59 (33%)	.002
History of infarction	21 (23%)	27 (15%)	.01
Coronary angiography	28 (30%)	58 (32%)	.34
PTCA	26 (28%)	56 (31%)	.34
Coronary bypass surgery	6 (6%)	7 (4%)	.30

*DM indicates diabetes mellitus; HT, hypertension; PTCA, percutaneous transluminal coronary angioplasty; SD, standard deviation.

TABLE 2. Development of Heart Failure During Admission and Cumulative Incidence of Cardiovascular Mortality at 28 Days and at 6 Months in Both Groups*

	Group With DM (n=93)	Group Without DM (n=180)	P
Heart failure during admission	16 (17%)	13 (7%)	.001
28-day mortality	3 (3.2%)	3 (1.4%)	.001
6-month mortality	8 (8.3%)	8 (4.4%)	.01

*DM indicates diabetes mellitus.

Spain readily explains the growing interest of the cardiologic community in the association between DM and cardiovascular disease.[8,9] The purpose of our study was to analyze the influence of DM on the prognosis and the clinical and therapeutic approach toward patients with NSTEACS.

METHODS

Study Population and Design

A historical cohort study was conducted with 273 patients (204 men and 69 women) admitted to our hospital from January 2001 to December 2002 with a diagnosis of NSTEACS according to published criteria.[1-3] Among the total study population, 93 patients (34.1%) had DM versus 180 who were not diabetics. The patients were classified as diabetics if they had been diagnosed with DM, were receiving hypoglycemic therapy, or presented repeatedly high baseline blood sugar levels (>126 mg/dL in at least 2 fasting measurements) during admission. Among the

group of diabetics, 43.4% were on insulin therapy, 37.1% were receiving oral antidiabetic therapy, and 19.5% were managed by diet.

Data Analyzed

The following variables were collected in both groups: age, sex, history of cardiovascular risk factors (hypertension, dyslipidemia, and smoking), history of ischemic heart disease, drug therapy received, coronary angiography, and revascularization therapy (percutaneous or surgical) during the hospitalization. Lastly, we analyzed the onset of major cardiovascular events, defined as heart failure during admission and cardiovascular mortality at 28 days and at 6 months. This information was obtained by a review of the medical histories, personal interviews, and a phone survey of the patients.

Statistical Analysis

SPSS (Statistical Package for Social Sciences, version 10.0 for Windows) was used for the data analysis. The quantitative variables are expressed as mean±SD and the qualitative variables as percentages. The χ^2 test was used to compare the qualitative variables. Quantitative variables were compared using the Student's t test. Cox proportional-hazards regression models were used to estimate the hazard ratio of clinical variables significantly different in the single-factor analysis[10] (hypertension, dyslipidemia, smoker, history of myocardial infarction, and use of angiotensin-converting enzyme inhibitors [ACE inhibitors]).

RESULTS

The baseline characteristics of the patient population are shown in Table 1. There were no differences in age or sex between the 2 groups. In contrast, diabetic patients presented a higher prevalence of hypertension, dyslipidemia, previous myocardial infarction, and, paradoxically, smoking. Coronary angiography, percutaneous transluminal coronary angioplasty, and coronary bypass surgery was similar in the 2 groups, as is shown in Table 1.

Both groups had similar characteristics with regards to beta-blocker, acetylsalicylic acid, clopidogrel, heparin, and statin therapy during the hospitalization and follow-up phases. However, ACE inhibitors were more commonly used among diabetics (60% vs 37%; $P<.05$).

With regard to the onset of major cardiovascular events, a higher incidence of heart failure during admission and a higher cumulative incidence of cardiovascular mortality at 28 days and at 6 months was found among the patients with DM (Table 2). The multivariate analysis showed that DM was an independent predictor of mortality *(hazard*

ratio [HR]=2.2; 95% confidence interval [95% CI], 1.4-3.6; *P*<.05).

DISCUSSION

The results of our study show that diabetic patients with NSTEACS have a significantly poorer prognosis than nondiabetics. Interestingly, however, the diagnosis-therapeutic approach used among diabetic patients was not more invasive than among the nondiabetics.

In our study, diabetic patients had a higher prevalence of other cardiovascular risk factors and previous coronary artery disease than nondiabetics, a finding consistent with recent studies, except for smoking, which was generally lower in the diabetic population.[6,7] In any case, DM *per se* is independently associated with a higher risk and poorer prognosis after ACS.[5-7,9] In this regard, scientific associations such as the American Heart Association have gone on to consider it an "equivalent" of cardiovascular disease rather than merely a risk factor.[11] Therefore, diabetic patients who have not experienced an ACS have the same risk of presenting it as nondiabetics who have had it previously.[12]

In our study, at least the pharmacologic treatment used for NSTEACS was similar in both groups, except for ACE inhibitors, which were used most frequently among diabetic patients. Other authors have obtained similar findings.[6,7] Despite the published recommendations,[1-3,13] we observed that clopidogrel is not routinely utilized in NSTEACS and our diabetic population (at greater risk) also fails to benefit differentially from greater use of this agent.

Consistent with other authors,[6,7] we found that there were no significant differences between the study groups in the use of invasive strategies (interventional procedures and coronary bypass surgery).

In our study, heart failure during admission was more frequent among the diabetics. Diabetes mellitus and heart failure have been related to extensive coronary artery disease, autonomic dysfunction, and a high prevalence of hypertension.[11] Likewise, the higher mortality observed among our diabetic patients could be due to a higher prevalence of hypertension and previous coronary artery disease.[6-8] However, multivariate analysis maintained DM as an independent predictor of mortality.

Consequently, we feel that DM should prompt a different risk stratification after NSTEACS than that of a nondiabetic patient. Considering NSTEACS a high-risk event is a determining factor in deciding on an invasive therapeutic approach, clearly superior in general terms to a conservative approach (with results that can be extrapolated to the diabetic population, although noticeably lower).[7,14,15] According to the European Society of Cardiology guidelines, the mere presence of DM is a high risk in NSTEACS, regardless of the presence of other high-risk criteria (clinical, electrocardiographic, or biochemical).[2] In contrast, of the U.S. guidelines[1] and thase of the Sociedad Española de Cardiología (Spanish Society of Cardiology)[3] propose that DM per se determines an intermediate risk.

Limitations of the Study

This is a single-center, retrospective study with all the limitations inherent to this kind of design. In addition, the new therapeutic recommendations for ACS were published around the time of the study period and may explain the sub-optimal use of some of the therapeutic strategies, now clearly defined for ACS.

CONCLUSIONS

Our study demonstrates that DM confers a special risk status among patients with NSTEACS and we believe that it is possible to optimize treatment for this large subgroup of patients. The decisive findings of epidemiological studies and projections on DM and its cardiovascular impact might indicate the need to adopt more interventional strategies for the treatment of ACS among the diabetic population, thus contributing in part to improve their prognosis following NSTEACS.

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