Coronary Risk Assessment in Subjects With Type 2 Diabetes Mellitus. General Population-Based Scores or Specific Scores?

Rubén Hernáez,^a Lucía Choque,^a Margarita Giménez,^a Ángels Costa,^a Juan I. Márquez,^a and Ignacio Conget^{a,b}

^aServicio de Endocrinología y Diabetes, Hospital Clínic i Universitari, Barcelona, ^bÁrea 3, Hígado, sistema digestivo y metabolismo, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain.

Coronary risk in patients with type 2 diabetes mellitus can be calculated using population-based scores or diabetes-specific scores. Our objective was to compare the results with both scores in a group of patients with type 2 diabetes and no history of cardiovascular disease. We analyzed the results for 101 patients aged 40 to 65 years with type 2 diabetes and no prior cardiovascular disease. Two scales were used, one based on the general population (Framingham function adapted from the REGICOR study), and the other based on the population with type 2 diabetes mellitus (UKPDS risk engine). The average 10year likelihood of coronary events was 5.8 (2.5)% and 15.7 (8.4)% for the REGICOR risk score and the UKPDS risk score, respectively (P<.001), with a Pearson correlation coefficient of 0.525 (P<.01). Risk was higher in men (19.2 [8.7]% based on the UKPDS score, and 5.6 [2.8]% based on the REGICOR score, P<.001). The figures for women were 11.3 [5.9]% and 5.9 [2.1]% with the UKPDS and REGICOR scores, respectively (P<.001). Our results suggest that substantially different findings are obtained when general population-based scores or specific scores are used to assess cardiovascular risk in subjects with type 2 diabetes.

Key words: Cardiovascular risk. Coronary artery disease. Coronary heart disease risk functions. Type 2 diabetes mellitus.

Estimación del riesgo coronario en pacientes con diabetes mellitus tipo 2. ¿Escalas de población general o escalas específicas?

El riesgo coronario de los pacientes con diabetes tipo 2 puede calcularse mediante escalas de población general o específicas para diabéticos. Hemos comparado los resultados al aplicar ambas escalas en una muestra de pacientes con diabetes tipo 2 sin enfermedad cardiovascular previa. Se seleccionó a 101 pacientes con diabetes, sin antecedentes cardiovasculares, con edades comprendidas entre los 40 y los 65 años. Se aplicó la escala basada en población general (calibración de la escala de Framingham según el estudio Registre Gironí del Cor [REGICOR]) y otra basada en población diabética (UKPDS [United Kingdom Prospective Diabetes Study] risk engine). La estimación del riesgo a 10 años mediante REGICOR fue de 5,8 \pm 2,5% y por UKPDS fue de 15,7 \pm 8,4% (p < 0,001), con una correlación de Pearson de 0,525 (p < 0,01). Los varones tuvieron un mayor riesgo (19,2 ± 8,7 con UKPDS, y 5,6 ± 2,8 para REGICOR; p < 0,001); en mujeres el resultado fue de 11,3 \pm 5,9 y 5,9 \pm 2,1 para las escalas UKPDS y REGICOR, respectivamente (p < 0,001). Nuestros datos sugieren que al aplicar ambos tipos de escalas se obtienen resultados sustancialmente distintos.

Palabras clave: *Riesgo cardiovascular. Enfermedad coronaria. Ecuaciones de riesgo cardiovascular. Diabetes mellitus tipo 2.*

Correspondence: Dr. I. Conget. Hospital Clínic i Universitari. Servicio de Endocrinología y Diabetes. Villarroel, 170. 08036 Barcelona. España. E-mail: iconget@clinic.ub.es

Received 30 September, 2003, Accepted for publication 5 February, 2004.

INTRODUCTION

In Spain, the prevalence of type 2 diabetes mellitus (DM2) in the population older than 30 years old fluctuates around 6%-10%, and half of the patients have not been diagnosed.^{1,2}

The importance of DM2 in the social and health context is basically due to it being a demonstrated risk factor for cardiovascular disease (CVD). In patients with DM2, CVD is the leading cause of death, is frequently encountered, and has a worse prognosis.^{3,4} Thus, the consensus is that the risk of a patient with DM2, but without previous CVD, presenting a CVD episode is comparable to that of a patient without DM2 and with known CVD.⁵

The most frequently used scale to estimate coronary risk derives from the Framingham cohort. However, DM2 has recently been excluded from this scale due to it being considered equivalent to coronary disease.⁶ Although the reliability of the Framingham scale as applied to different populations has been demonstrated, it would be advisable to obtain functions derived from each population to improve its precision.⁷ Thanks to Marrugat et al,⁸ there is an equation calibrated for the Spanish population for the Framingham scale which includes the presence or absence of DM2, taking as the reference population the one used in the Registre Gironí del Cor (REGICOR) study.⁹

Our aim was to compare the estimation of coronary risk obtained by applying a scale based on the Spanish general population (REGICOR) with another specific to patients with DM2 (UKPDS [United Kingdom Prospective Diabetes Study] risk engine)¹⁰ to a sample of patients with DM2 and no previous coronary disease.

PATIENTS AND METHODS

From November 2002 to April 2003, 101 patients were consecutively selected in our outpatient clinic. Patients with DM2 from 40 to 65 years old without previous cardiovascular disease were included and

578 Rev Esp Cardiol 2004;57(6):577-80

TABLE. Characteristics of the Patients Included in the Study*

Patients, n	101
Age, years	57.9±6.3
Male/female, n	58/43
Duration DM2, years	10.5±7.4
HbA _{1c} , %	7.0±1.4
FH of ischemic heart disease, %	12.9
SAP	135±10
Total cholesterol, mg/dL	207±39
LDL-C, mg/dL	127±31
HDL-C, mg/dL	53±13
Triglycerides	152±97

*FH indicates family history; HDL-C, cholesterol bound to high-density lipoproteins; LDL-C, cholesterol bound to low-density lipoproteins; DM2, type 2 diabetes mellitus; HbA_{1c}, glycosylated hemoglobin; SAP, systolic arterial pressure.

variables covered sex, age, duration of DM2, hemoglobin glycosylate (HbA_{1c}), family history of early ischemic heart disease, smoking, presence of atrial fibrillation, total cholesterol, cholesterol bound to high-density lipoproteins (HDL-C), cholesterol bound to low-density lipoproteins (LDL-C), triglycerides, systolic blood pressure (SAP), and treatment with hypolipemics, platelet aggregation inhibitors and hypotensives. All the patients had an electrocardiogram (ECG) done during the previous year and were placed on a special diet and given oral hypoglycemics and insulin therapy as treatment for DM2.

Coronary risk at 10 years was estimated with the REGICOR equation that includes the variables sex, age, the presence or absence of DM2, total cholesterol, SAP and diastolic blood pressure, smoking and a correction based on the value of HDL-C on the obtained total result. We also used a specific scale for the diabetic population (UKPDS risk engine version 1.0). This scale includes the variables sex, age, ethnic group, duration of DM2 in years, HbA_{1c}, smoking, SAP, presence of atrial fibrillation, total cholesterol, and HDL-C.

Data analysis was done with the Statistical Package for Social Sciences (SPSS) version 10. Quantitative variables were expressed as mean \pm SD. Dummy qualitative variables were presented as percentages. Mean differences were calculated with Student's *t* test and statistical significance was established at *P*<.05. Pearson's test was used to obtain correlation between variables.

RESULTS

Sample characteristics are shown in the Table. Seventy-nine percent of the patients included in the study did not smoke. Forty-nine percent received treatment with hypotensives, 58% received hypolipemics and

ABBREVIATIONS

Study.

DM2: type 2 diabetes mellitus.

ECG: electrocardiogram. CVD: cardiovascular disease.

SAP: systolic arterial pressure.

lipoproteins.

lipoproteins.

REGICOR: Registre Gironí del Cor. HbA_{1c}: glycosylated hemoglobin.

LDL-C: cholesterol bound to low-density

HDL-C: cholesterol bound to high-density

UKPDS: United Kingdom Prospective Diabetes

24% received platelet aggregation inhibitors. Taking the recommendations of the American Diabetes Association as the reference, 17.8% of the sample presented SAP lower than 130 mm Hg; 54.1% had LDL-C lower than 130 mg/dL; 18.4%, LDL-C lower than 100 mg/dL; 84%, HDL-C higher than 40 mg/dL; and 61.4%, triglycerides lower than 150 mg/dL. Regarding glycemic control 53.5% of the sample had HbA_{1c} values below 7.0%.

Average coronary risk at 10 years estimated with UKPDS was $15.7\pm8.4\%$ in our patients, whereas this was $5.8\pm2.5\%$ (*P*<.001) with REGICOR. A significant correlation was found between the estimations, with *r*=0.525 (*P*<.01). Coronary risk at 10 years was 19.2±8.7% versus $5.6\pm2.8\%$ (*P*<.001) in males and 11.3±5.9% versus $5.93\pm2.1\%$ (*P*<.001) in females, with the UKPDS and the REGICOR scales, respectively.

DISCUSSION

Our data suggest that when applying a scale for calculating coronary risk based on the general population to a group of patients with DM2 but no previous CVD, the results obtained differ from those obtained with a scale specific for DM2.

To date, some comparisons have been made (not in Spain) between general scales applied to patients with DM2 with varying results.^{11,12} When applying coronary risk scales to patients with DM2 but without previous CVD we are ignoring the equivalence of coronary risk this metabolic disease is supposed to have. This assumption, mainly based on the study by Haffner et al,5 has been called into question in recent years.¹³⁻¹⁵ The limitations of this study and the publication of new ones with different results has revived the need for evaluating cardiovascular risk in patients with DM2 to establish the most appropriate treatment objectives both individually and for each population. According to our results, when applying the UKPDS scale, the estimation of coronary risk at 10 years (especially in males) is closer to the theoretical figure of 20% at 10 years which is accepted as "equivalent." The figure estimated with the REGICOR scale is substantially lower. These results are not surprising if we take into account that the specific scale used derives from the results obtained in the UKPDS study. More than 5000 patients with DM2 and without previous CVD were included in this study and were followed up for more than a decade. For the first time the duration of DM2 and the HbA_{1c} values were taken into account, both parameters being closely related to cardiovascular risk.¹⁶ If we consider disease duration in the sample studied, we see that it is closer to studies that incorporate DM2 and equivalent coronary risk which would explain the substantial theoretical risk our patients present. This risk estimation is even more relevant if we take into account the substantial proportion of subjects who are found within the values considered "optimal" for glycemic control, lipid profile and blood pressure. Obviously, our cross-sectional study of cardiovascular risk estimation would require prospectively following-up the population studied to verify the results obtained. In our case, we should also take into account the fact that the specific scale for DM2 used comes from an Anglo-Saxon population, with the consequent problems regarding extrapolation of the results.

The basis of any scale for the calculation of coronary risk is to identify, motivate, initiate, and modulate therapeutic measures in individuals at high coronary risk. Regardless of any specific risk, the fact is that patients with DM2 present high morbidity and mortality due to cardiovascular events, and in recent years the reduction in mortality that has been observed in the general population has not been seen in this group.¹⁷ These facts should motivate us to specify more precisely risk in this group of patients and act accordingly.

In conclusion, when calculating cardiovascular risk for patients with DM2 it should be born in mind that the use of scales either for the general population or those specific for this type of patient can yield substantially different results.

REFERENCES

- Bosch X, Alfonso F, Bermejo J. Diabetes y enfermedad cardiovascular. Una mirada hacia la nueva epidemia del siglo XXI. Rev Esp Cardiol 2002;55:525-7.
- Goday A. Epidemiología de la diabetes y sus complicaciones no coronarias. Rev Esp Cardiol 2002;55:657-70.
- Cho E, Rimm EB, Stampfer MJ, Willet WC, Hu FB. The impact of diabetes mellitus and prior myocardial infarction on mortality form all causes and from coronary heart disease in men. J Am Coll Cardiol 2002;40:954-60.
- Grundy SM, Benjamín IJ, Burke GL, Chait A, Eckel RH, Howard BV. Diabetes and cardiovascular disease: a statement for healthcare professionals from the American Heart Association. Circulation 1999;100:1134-46.
- Haffner SM, Lehto S, Ronnema T, Pyorala K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and nondiabetic subjects with and without prior myocardial infarction N Engl J Med 1998;339:229-34.
- Expert Panel on detection, evaluation, and Treatment of High Blood Cholesterol in adults. Executive summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001; 285:2486-97.
- D'Agostino RB, Grundy SM, Sullivan LM, Wilson P. Validation of the Framingham coronary heart disease prediction scores. Results of a multiple ethnic groups investigation. JAMA 2001;286: 180-7.
- Marrugat J, Solanas P, D'Agostino RB, Sullivan L, Ordovas J, Cordón F, et al. Estimación del riesgo coronario en España me-

diante la ecuación de Framingham calibrada. Rev Esp Cardiol 2003;56:253-61.

- Masiá R, Pena A, Marrugat J, Sala J, Vila J, Pavesa M, et al. High prevalence of cardiovascular risk factors in Gerona, Spain, a province with low myocardial infarction incidence. J Epidemiol Community Health 1998;52:707-15.
- Stevens RJ, Kothari V, Adler AI, Stratton IM, Holman RR on behalf of the United Kingdom Prospective Diabetes Study (UKPDS) Group. The UPKDS risk engine: a model for the risk of coronary heart disease in type II diabetes (UKPDS 56). Clin Sci 2001;101:671-9.
- Game FL, Jones AF. Coronary heart disease risk assessment in diabetes mellitus —a comparison of PROCAM and Framingham risk assessment functions. Diabet Med 2001;18: 355-9.
- Yeo WW, Rowland K. Predicting CHD risk in patients with diabetes mellitus. Diab Med 2001;18:341-4.

- Evans JM, Wang J, Morris AD. Comparison of cardiovascular risk between patients with type 2 diabetes and those who had a myocardial infarction: cross sectional and cohort studies. BMJ 2002;324:939-42.
- Gu K, Cowie CC, Harris MI. Diabetes and decline in heart disease mortality in US adults. JAMA 1999;281:1291-7.
- Winocour PH, Fisher M. Prediction of cardiovascular risk in people with diabetes. Diabet Med 2003;20:515-27.
- Turner RC, Millns H, Neil HA, Stratton IM, Manley SE, Matthews DR, et al. Risk factors for coronary artery disease in non-insulin dependent diabetes mellitus: United Kingdom Prospective Diabetes Study (UKPDS: 23). BMJ 1998;316:823-8.
- Gu K, Cowie CC, Harris MI. Mortality in adults with and without diabetes in a National cohort of the U.S. population, 1971-1993. Diabetes Care 1998;21:1138-45