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Cardiovascular disease risk and glucose metabolism: agreement and discrepancies between the WHO-85 and ADA-97 classifications

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Aim. To identify the differences between coronary heart disease risk in patients with altered basal glucemia (ABG), oral glucose intolerance (OGI) and type II diabetes mellitus according to the WHO-85 and ADA-97 diagnostic classifications, in an adult population at high risk for diabetes mellitus.
Design. Descriptive, cross-sectional, multicenter study.
Setting. Seven primary health care centers in Spain.
Patient. 970 persons considered the population at risk for type II diabetes mellitus.
Measures. Participants were classified according to the criteria of the WHO-85 (normal, OGI, diabetes) and the ADA-97 system (normal, ABG, diabetes). The following variables were recorded: age, sex, smoking habit, body mass index, systolic blood pressure, diastolic blood pressure, basal glucemia, glucemia 2 h after an oral glucose tolerance test, HbA_{1c}, microalbmuniuria, total cholesterol, HDL, LDL and triglycerides. Coronary heart disease risk was calculated with the 1998 table developed by Wilson et al. on the basis of the Framingham study.
Results. A total of 970 participants were studied. Mean age was 58.6 #+ 12.4 years; 453 were men (46.7%) and 517 were women (53.3%). Our analysis showed that cardiovascular disease risk factors were less frequent in normal subjects, and that their prevalence was higher in persons with diabetes (according to both WHO and ADA classifications). There were no significant differences in coronary heart disease risk or different risk factors between analogous groups in the two classification systems (normal, OGI/ABG or diabetes). Coronary heart disease risk in persons with different types of alterations in glucose metabolism was 11.3% in normal subjects, 14% in persons with OGI and 27.3% in persons with diabetes according to the WHO-85 system, and 11.4% in normal subjects, 15.7% in persons with ABG and 29.5% in persons with diabetes according to the ADA-97 system.
Conclusions. The greater the alteration in carbohydrate metabolism, the greater the coexistence of risk factors and the estimated risk of coronary heart disease. There were no significant differences in the presence of cardiovascular risk factors, or in the relationship between carbohydrate metabolism and coronary heart disease risk, between analogous stages identified with one classification system or the other.

Key words: Primary care. Diabetes. Cardiovascular disease. Risk.

RIESGO CARDIOVASCULAR Y METABOLISMO DE LA GLUCOSA: ACUERDOS Y DISCREPANCIAS ENTRE LAS CLASIFICACIONES OMS-85 Y ADA-97

Objetivo. Conocer las diferencias entre el riesgo coronario de los sujetos con glucemia basal alterada (GBA), intolerancia oral a la glucosa (ITG) y diabetes mellitus tipo 2 según las clasificaciones diagnósticas de la OMS-85 y ADA-97 en una población adulta con un riesgo alto de presentar diabetes mellitus.
Diseño. Estudio descriptivo, transversal, multicéntrico.
Emplazamiento. Atención primaria, 7 centros de salud.
Pacientes. Un total de 970 sujetos considerados población de riesgo para diabetes mellitus tipo 2.
Mediciones. Se clasificaron los sujetos según los criterios OMS-85 (normales, ITG, diabetes) y según la ADA-97 (normales, GBA y diabetes). Se recogieron las siguientes variables: edad, sexo, consumo de tabaco, índice de masa corporal, tensión arterial sistólica, tensión arterial diastólica, glucemia basal, glucemia a las 2 horas de la PTOG, HbA_{1c}, microalbuminuria, colesterol total, cHDL, cLDL, triglicéridos y se estimó el cálculo del riesgo coronario mediante la tabla de Wilson et al de 1998, basada en el estudio Framingham.
Resultados. Se evaluó a 970 sujetos con una edad media de 58,6 ± 12,4 años, 453 varones (46,7%) y 517 mujeres (53,3%). En el análisis de la presencia de factores de riesgo cardiovascular se observa que éstos son menos frecuentes en los sujetos normales y que su prevalencia es más elevada en los diabéticos (OMS y ADA). No existen diferencias significativas entre el riesgo coronario y los diversos factores de riesgo cuando se analizan grupos homónimos OMS–ADA (normales, ITG-GBA o diabéticos). Según la clasificación de la OMS-85, el riesgo coronario en los distintos tipos de alteraciones del metabolismo de la glucosa fue un 11,3% en sujetos normales, un 14% en ITG y un 27,3% en diabéticos, y según la ADA-97 un 11,4% en sujetos normales, un 15,7% en GBA y un 29,5% en diabéticos.
Conclusiones. A mayor grado de patología hidrocarbonada, mayor coexistencia de factores de riesgo y mayor estimación del riesgo coronario. No hay diferencias importantes entre los estadios de las clasificaciones OMS y ADA ni en la presencia de factores de riesgo cardiovascular ni en relación al riesgo coronario.

Palabras clave: Atención primaria. Diabetes. Riesgo cardiovascular.

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Introduction

The clinical diagnosis of diabetes mellitus is based on the determination of cut-off points for glucemia, a continuous laboratory value. In 1980 and 1985 the World Health Organization (WHO) recommended that the diagnosis be established when repeated measures of fasting glucose yielded values of 140 mg/dL or higher, or when glucemia measured after a 2-h oral glucose tolerance test (OGTT) was 200 mg/dL or higher. Values above these numbers indicated in increased risk for microvascular complications.[1] In a specific group of subjects, glucemia after a 2-h OGTT is between 140 and 200 mg/dL and their risk of cardiovascular disease (apart from microangiopathy) is high; these persons have been classified as having impaired glucose tolerance (IGT).[2]

Subsequently, other authors[3-6] showed that the risk of cardiovascular disease was greater in persons with glucemia levels of around 110 mg/dL or higher. In 1997, after reviewing the epidemiological studies that centered on fasting glucose, the American Diabetes Association (ADA) developed new diagnostic criteria, setting the cut-off point at 126 mg/dL for diabetes, and producing a new classification: normal (fasting glucose lower than 110 mg/dL), impaired fasting glucose (IFG, fasting glucose between 110 and 125 mg/dL), and diabetes (fasting glucose 126 mg/dL or higher.[7] Further studies[8-12] have found differences between the WHO and ADA categories, which do not define the same groups of subjects. The DECODE study,[13] for example, showed that agreement between the IFG and IGT categories was low (28%), and recommended that testing to detect OGT not be abandoned in view of its usefulness in predicting evolution to diabetes, and because glucemia after a 2-h OGTT is a better predictor of morbidity and mortality due to cardiovascular disease than is fasting glucose. Some studies[14] considered only IGT to be a risk factor for cardiovascular disease; nonetheless, others[15] have reported that mortality from cardiovascular diseases was higher among patients with IFG.

Most subjects with impaired carbohydrate metabolism (whether IGT, IFG or type 2 diabetes mellitus) also have other clinical and laboratory features (e.g., obesity, hypertension, dyslipedimia, fibrinolytic alterations) that are consistent with the so-called metabolic syndrome (Reaven´s «syndrome X»,)[16] and which lead to an exponential increase in the risk of cardiovascular disease. In persons with diabetes, cardiovascular disease is the most frequent cause of death (accounting for approximately 60%-80% of all deaths in this population).[17-20]

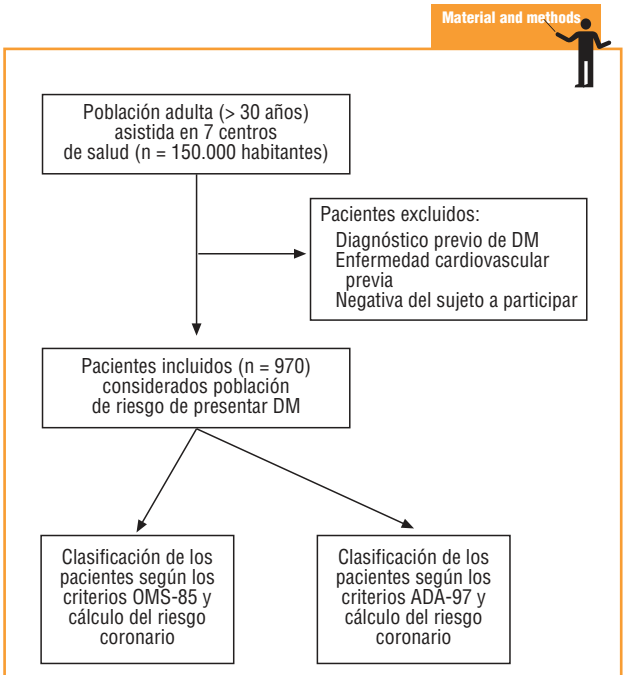
The importance of correctly classifying subjects with a moderate degree of alteration in carbohydrate metabolism (IGT or IFG) lies mainly in determining which persons are at greatest risk of developing diabetes and cardiovascular disease. The main aim of this study was therefore to identify the differences in risk of cardiovascular disease between persons with IFG, IGT and type 2 diabetes mellitus as identified by the WHO-85 and ADA-97 classification systems. Our subjects were an adult population at high risk for diabetes mellitus.

Other aims of this study were to evaluate differences between different risk factors for cardiovascular disease in these patients.

Material and methods

In this descriptive, cross-sectional multicenter study the population was drawn from primary care patients followed at seven urban, semi-urban and rural health centers (total reference population approximately 150 000) in the cities of Barcelona (Raval Sud Basic Health Area), Reus (Reus 1 and Reus 2 Basic Health Areas) and Tarragona (Tarragona-Valss, Sagessa Group) in Spain. All cases were chosen from the population of patients being followed by primary health teams at these centers, and were recruited consecutively from among those who fulfilled the inclusion criteria. In all, we studied 970 persons considered the population at risk for type 2 diabetes mellitus. Sample size was calculated for a 95% confidence interval (95% CI) and an error rate of 3.1%. *Inclusion criteria* were based on risk factors for impaired glucose metabolism (obesity, body mass coefficient >30, antecedents of type 2 diabetes in first degree relatives, antecedents of gestational diabetes, previous disorder in glucose metabolism, and repeated use of glucemia-raising drugs such as diuretics, beta blockers, corticosteroids or estrogens).

The *exclusion criteria* were a prior diagnosis of diabetes mellitus, antecedents or clinical signs of any cardiovascular disease, and refusal to participate in the study.



General scheme of the study

Descriptive, cross-sectional, multicenter study. The differences in risk of coronary heart disease were calculated for subjects belonging to a population at high risk for diabetes mellitus, who were classified according to the WHO-85 and ADA-97 diagnostic criteria.

We studied three sets of variables: *sociodemographic* (age, sex, risk factors for type 2 diabetes mellitus), *clinical* (smoking, body mass coefficient, systolic and diastolic blood pressure) and *laboratory* (fasting glucose, glucemia after a 2-h OGTT, HbA_{1c}, microalbuminuria, total cholesterol, high density lipoprotein cholesterol [HDL-C], low density lipoprotein cholesterol [LDL-C], triglycerides).

Each patient was classified according to the diagnostic criteria of the WHO-85 system, based on fasting glucose and OGTT results, as *normal* (fasting glucose or glucemia after a 2-h OGTT<140 mg/dL), *impaired glucose tolerance* (glucemia after a 2-h OGTT between 140 and 199 mg/dL) or *diabetic* (fasting glucose 140 mg/dL or higher, or glucemia 2 h after OGTT 200 mg/dl or higher). The same patients were each classified again on the basis of the ADA-97 criteria, based on fasting glucose alone, as *normal* (lower than 110 mg/dL), *impaired fasting glucose* (between 110 and 125 mg/dL), or *diabetic* (126 mg/dL or higher).

Global risk of coronary heart disease was calculated for each subject with data from the table of Wilson et al. (1998), which are based on the Framingham study. This table records the following variables: sex, age, diastolic and systolic blood pressure, cigarette smoking, diabetes, total cholesterol and HDL-C.[21] In the present study diabetes was defined according to WHO criteria, and the risk of coronary heart disease was calculated according to the WHO system. Then each patient was classified again with the ADA system, and coronary heart disease risk was again calculated with the latter system. Scores were assigned only for those patients with a diagnosis of diabetes. The final score was the sum of the scores obtained from the table for each variable. These scores were transferred to a new table to predict the percentage likelihood of a new adverse cardiovascular event in the next 10 years. The 10-year risk of coronary heart disease was considered high when the likelihood was >20%, and very high when it was >30%.[22-24]

Descriptive statistics were based on calculation of the mean and standard deviation for quantitative variables, and calculation of the proportions and 95% CI for qualitative variables. Normal distribution was verified with the Kolmogorov-Smirnoff method. Analytical statistics were based on Student´s *t* test and analysis of variance (ANOVA) for quantitative variables, and on the chi-squared test for qualitative variables. The differences were considered significant when $P<.05$. Agreement between the two measurements of the same phenomenon was measured as the kappa coefficient, and was considered very good at >0.75, acceptable at 0.40-0.75, and poor at <0.40.[25]

Results

The study sample consisted of 970 persons (453 men [46.7%], 517 women [53.3%]) with a mean age of

TABLE 1 **General characteristics of the study and presence of cardiovascular risk factors**

	Normal WHO-85, GB y G2h < 140 mg/dl	Normal ADA-97, GB < 110 mg/dl	IGT WHO-85, G2h 140-199 mg/dl	IFG ADA-97, GB 110-125 mg/dl	DM WHO-85, GB ≥ 140 o G2h ≥ 200 mg/dl	DM ADA-97, GB ≥ 126 mg/dl
N = 970	376 (38.8%)	413 (43.3%)	200 (20.6%)	178 (17.31%)	394 (40.61%)	379 (39.07%)
Age (years)	54.3 ± 13.0	55.4 ± 13.0	59.9 ± 12.3	59.5 ± 12.9	61.9 ± 10.4	61.8 ± 10.3
Sex (men)	31.1%	37.3%	18.1%	14.2%	50.8%	48.4%
Smoking habit	31.6%	30.5%	14.3%	14.1%	54.1%	55.4%
BMI	30.9 ± 5.45	31.4 ± 5.44	31.2 ± 5.26	30.5 ± 5.06	29.9 ± 5.12	29.7 ± 5.21
SBP (mmHg)	136.1 ± 19.4	135.9 ± 19.8	139.9 ± 21.3	141.7 ± 19.4	142.4 ± 22.7	142.6 ± 23.0
DBP (mmHg)	83.0 ± 12.2	82.9 ± 11.4	83.7 ± 9.6	84.4 ± 11.2	83.2 ± 11.7	83.2 ± 11.7
BG (mg/dl)	97.3 ± 17.2	92.0 ± 11.1*	108.7 ± 16.1	118.1 ± 4.09*	175.9 ± 70.1	181.3 ± 67.5
Glucemia after 2-h OGTT (mg/dL)	103.1 ± 22.8	127.4 ± 57.4*	167.8 ± 17.8	179.9 ± 64.0*	250.2 ± 70.0	208.7 ± 72.1*
HbA_{1c} (%)	4.86 ± 0.62	4.84 ± 0.56	5.2 ± 0.63	5.25 ± 0.53	6.77 ± 1.98	6.91 ± 1.98
TC (mg/dl)	220.0 ± 40.5	218 ± 40.5	228.6 ±43.2	226.2 ± 38.2	229.5 ± 46.7	233.2 ± 48.5
HDL-C (mg/dl)	54.4 ± 15.4	54.0 ± 14.7	51.5 ± 14.0	50.9 ± 14.0	44.2 ± 12.7	44.1 ± 13.6
LDL-C (mg/dl)	137.3 ± 37.8	137.4 ± 37.9	148.6 ± 40.9	146.0 ± 40.2	152.0 ± 45.9	155.9 ± 46.0
TC/HDL-C	4.33 ± 1.42	4.32 ± 1.34	4.75 ± 1.55	4.80 ± 1.59	5.63 ± 1.90	5.76 ± 1.95
TG (mg/dl)	134.3 ± 101.3	134.3 ± 93.4	142.5 ± 85.6	145.5 ± 105.5	171.8 ± 101.6	172.1 ± 100.5
MA (mg/d)	19.2 ± 29.8	28.4 ± 51.7*	40.0 ± 58.1	28.5 ± 80.4	63.5 ± 172.7	68.6 ± 181.5

Normal indicates normal glucose tolerance; IGT. impaired glucose tolerance; IFG. impaired fasting glucose; DM. diabetes mellitus
BMI. body mass coefficient; SBP. systolic blood pressure; DBP. diastolic blood pressure; BG. fasting glucose; OGTT. oral glucose tolerance test; HbA1C. glucosylated hemoglobin; TC. total cholesterol; HDL-C: high density lipoprotein cholesterol; LDL-C. low density lipoprotein cholesterol: TC/HDL-C. total cholesterol/HDL-C ratio; TG. triglycerides; MA. microalbuminuria.
WHO-85 criteria: normal=basal glucose or glucemia after a 2-h OGTT<140 mg/dL; IGT=glucemia after a 2-h OGTT 140-199 mg/dL; type 2 DM=fasting glucose ≥140 mg/dL or glucemia after a 2-h OGTT ≥200 mg/dL. ADA-97 criteria: normal=fasting glucose <110 mg/dL; IFG=fasting glucose 110-125 mg/dL; type 2 DM=fasting glucose ≥126 mg/dL.
*Statistically significant difference (P<.05).

58.6±12.4 years and a mean body mass coefficient of 30.6±5.34 kg/m^2. Table 1 summarizes the findings for the sociodemographic, clinical and laboratory variables. When we compared different risk factors for cardiovascular disease in subjects with equivalent diagnoses according to the WHO and ADA systems (normal, IGT or IFG, type 2 diabetes mellitus), we found few statistically significant differences. In comparison with the WHO classification, persons considered normal in the ADA system had lower fasting glucose values, higher glucemia values after a 2-h OGTT, and higher 24-h microalbuminuria values. Subjects with IFG had higher fasting glucose and glucemia after a 2-h OGTT than did those diagnosed as having IGT. Subjects considered to have diabetes in the ADA system had lower glucose values after a 2-h OGTT than those found to have diabetes with the WHO system (Table 1).

When we compared the two systems for agreement in diagnosis (Table 2), we found that agreement was acceptable for type 2 diabetes mellitus (kappa coefficient 0.69) and normal status (kappa coefficient 0.54). However, agreement was poor for the OGT and IFG categories (kappa coefficient 0.19), and the two diagnoses matched for only 20.7% of the subjects.

The risk of coronary heart disease, as calculated from the table of Wilson et al. based on the Framingham study (1998), is shown in Table 3 for each category of diagnosis. The values obtained for each risk factor were used to calculate the mean score for each group, expressed as the percentage risk of having an adverse cardiovascular event in the next 10 years. We found that the WHO criteria led to risks of 11.3% in normal subjects, 14.0% in subjects with IGT and 27.3% in subjects with type 2 diabetes mellitus, whereas the ADA criteria yielded values of 11.4% (normal), 15.7% (IFG) and 29.5% (type 2 diabetes mellitus). Thus the diagnosis of IFG and type 2 diabetes mellitus (ADA system) implied a greater risk of coronary heart disease than did the analogous diagnoses with the WHO system (although the difference was statistically significant only for the diagnosis of diabetes). Regardless of which system was used, the risk of coronary heart disease was greater in subjects with IGT or IFG, or diabetes, than in those with normal carbohydrate metabolism (P<.05). When we analyzed different degrees of coronary heart disease risk, we found that the risk was high (>20%) in 27% of the subjects with IGT, 29.2% of those with IFG, 72.1% of those with type 2 diabetes mellitus according to the WHO system, and 76.2% of those with type 2 diabetes mellitus according to the ADA system, whereas this level of risk was found in only 18.1% (WHO system) and 18.8% (ADA system) of the normal subjects (Table 4).

TABLE 2 **Agreement between WHO-85 and ADA-97 diagnostic criteria**

		WHO-85		
		Normal, n = 376 (38.76%)	IGT, n = 200 (20.61%)	DM2, n = 394 (40.61%)
ADA-97	Normal, n = 413 (42.57%)	286 (0.54)	101	26
	IFG, n = 178 (18.35%)	59	65 (0.19)	54
	DM2, n = 379 (39.07%)	31	34	314 (0.69)

Normal indicates normal glucose tolerance; IGT, impaired glucose tolerance; IFG, impaired fasting glucose; DM2, type 2 diabetes mellitus.
Figures in parentheses are kappa statistics for agreement in diagnosis between the two systems. Global weighted kappa coefficient was 0.61.
Agreement is considered very good when kappa >0.75 and acceptable when kappa >0.4-0.75.

TABLE 3 **Quantification of global risk of coronary heart disease, according to the data in the table of Wilson et al. based on the Framingham Heart Study (1998)**

	Normales		IGT/IFG		DM2	
	WHO-85	ADA-97	WHO-85	ADA-97	WHO-85	ADA-97
Mean score	6.47 ± 5.21	6.49 ± 4.94	8.39 ±4.35	8.88 ± 4.40	12.7 ± 4.29	12.8 ± 4.33
Risk of coronary heart disease (%)	11.3 ± 10.7	11.4 ± 9.32	14.0 ± 11.1	15.7 ± 11.6	27.3 ± 13.8	29.5 ± 14.0*

Normal indicates normal glucose tolerance; IGT, impaired glucose tolerance; IFG, impaired fasting glucose; DM2, type 2 diabetes mellitus.
All values are the mean±standard deviation.
WHO-85 criteria: normal=basal glucose or glucemia after a 2-h OGTT <140 mg/dL; IGT=glucemia after a 2-h OGTT 140-199 mg/dL; type 2 DM=fasting glucose ≥140 mg/dL or glucemia after a 2-h OGTT ≥200 mg/dL. ADA-97 criteria: normal=fasting glucose <110 mg/dL; IFG=fasting glucose 110-125 mg/dL; type 2 DM=fasting glucose ≥126 mg/dL.
*Statistically significant difference (P<.05).

TABLE 4 **Degrees of risk of coronary heart disease**

	Normales		IGT/IFG		DM2	
	WHO-85	ADA-97	WHO-85	ADA-97	WHO-85	ADA-97
Risk < 20%	308 (81.9%)	341 (81.2%)	146 (73%)	119 (70.8%)	110 (27.9%)	90 (23.7%)
Risk 20-30%	44 (11.7%)	57 (13.6%)	32 (16%)	26 (15.5%)	152 (38.6%)	90 (23.7%)*
Risk > 30%	24 (6.4%)	22 (5.2%)	22 (11%)	23 (13.7%)	132 (33.5%)	199 (52.5%)*

Figures in parentheses are percentages of the total for each column.
WHO-85 criteria: normal=basal glucose or glucemia after a 2-h OGTT <140 mg/dL; IGT=glucemia after a 2-h OGTT 140-199 mg/dL; type 2 DM=fasting glucose ≥140 mg/dL or glucemia after a 2-h OGTT ≥200 mg/dL. ADA-97 criteria: normal=fasting glucose <110 mg/dL; IFG=fasting glucose 110-125 mg/dL; type 2 DM=fasting glucose ≥126 mg/dL.
*Statistically significant difference (P<.05).

Discussion

Diabetes is associated with a 2-fold to 4-fold greater risk of coronary heart disease than that observed in the population of persons without diabetes; the greater risk, obviously, implies greater mortality.[17-20,26] The risk of atheromatous lesions is also increased in the group of subjects with a moderate degree of alteration in glucose metabolism, e.g., IGT or IFG,[14,15] and even in persons with whose glucemia values are at the upper limit of normality.[27] Therefore, changes in the diagnostic criteria for diabetes can lead to changes in how the risk of cardiovascular disease is assessed. The aim of our study was to compare the influence of the new ADA-97 criteria with that of the older WHO-87 criteria on the assessment of coronary heart disease risk, and to identify the differences between the groups of patients identified as having IGT or IFG.

With regard to our methods, the fact that ours was a multicenter study based on the population seen at primary care centers helped to minimize some of the biases the appear most often in studies of a single, highly selected population, generally in hospital settings (i.e., populations which are less than ideally representative of the general population). To obtain an acceptable number of subjects with impaired carbohydrate metabolism, we worked with a population of subjects who had risk factors for type 2 diabetes mellitus. This may have resulted in selection bias, as our study population might also have had more risk factors for cardiovascular disease in association with diabetes even though their glucose values at the time of the study were normal. This would imply that the differences we observed between the group with a metabolic disorder and the group of normal subjects were smaller than those that would be found in the general population. The strict application of the WHO-87 criteria involves the use of OGTT for most subjects, in contrast with usual clinical practice, in which fasting glucose is the predominant measure (ADA criteria).

To calculate the risk of cardiovascular disease we used the Framingham table, because it is well known in our setting.[28]

With regard to the agreement in diagnosis obtained with the WHO and ADA classifications, the ADA system is relatively useful for diagnosing normal status (k=0.54) and type 2 diabetes (k=0.69). However, agreement for the diagnosis of IGT or IFG was poor (k=0.19), as various authors have shown previously[8-15]. This may be explainable because of differences in physiopathological mechanisms and the stage of glucemia in the two entities. What appears clear is that IGT and IFG do not identify the same subjects or define the same disorder, although both lie in the range between normality and type 2 diabetes mellitus.

Discussion Key points

What is known about the subject

- Diabetes is associated with a 2-fold to 4-fold greater risk of coronary heart disease than in the population without diabetes; this also involves a higher mortality rate in the former.
- Moderate degrees of alteration in carbohydrate metabolism (impaired glucose tolerance, impaired fasting glucose) also involve an increased risk of coronary heart disease.

What this study contributes

- The greater the alteration in glucose metabolism, the greater the presence of cardiovascular risk factors and the greater the risk of coronary heart disease.
- The use of the new ADA-97 criteria does not involve large changes in how the risk of coronary heart disease is quantified.

Subjects classified as normal with both systems had lower fasting glucose levels and fewer risk factors for cardiovascular disease than subjects with IGT or IFG; in turn, there were fewer risk factors in these intermediate groups than in subjects with diabetes. This finding is significant in that it translates as a parallel relationship between the intensity of the carbohydrate disorder and the risk of coronary heart disease the subjects are exposed to.

In the present study we found no significant differences between subjects who were classified as normal with one system or the other. The only finding of note was the lower fasting glucose value in subjects considered normal according to the ADA criterion; this was expected in light of how this diagnosis is defined. There were no differences in any of the other risk factors for cardiovascular disease.

In subjects classified as having IGT or IFG, we found differences only in fasting glucose and glucemia after a 2-h OGTT. In subjects with IFG (ADA-97) the diagnosis is arrived at later (fasting glucose); this probably explains the greater number of risk factors in these persons. Mean 10-year risk of coronary heart disease for subjects with IGT (WHO) was 14.0% for subjects with IGT (WHO) and 15.7% for those with IFG (ADA); this difference was not statistically significant. Although these intermediate stages between normality and diabetes also showed an intermediate degree of risk for cardiovascular disease, the analysis of individuals who satisfied the criteria for both IGT and IFG (about one in every five) is of particular interest. In an earlier study the lipid profile of this subgroup was shown to be much more atherogenic (higher concentration of total and LDL cholesterol) than in subjects with either IGT or IFG.[29] This finding supports the recommendation that the primary prevention of diabetes and its concomitant risk of cardiovascular disease should be aimed specifically at individuals with one or both disorders.

In persons diagnosed according to one criterion or the other as having type 2 diabetes, we found no significant differences in the presence of cardiovascular risk factors, although the global risk of coronary heart disease was 27.3% in patients diagnosed with the WHO criterion, versus 29.5% with the ADA criterion ($P<.05$).

When we compared those subjects most likely to develop atheromatous lesions (with a 10-year risk of coronary heart disease >20%), we noted that this risk was present in 27% of those with IGT and 29.2% of those with IFG. This situation was much more frequent in patients with type 2 diabetes mellitus.

In conclusion, use of the new ADA criteria do not, in global terms, involve significant changes with respect to determining the risk of cardiovascular disease in patients with any of the three grades of glucose metabolism disorder. The Framingham Heart Study used a population residing near Boston, and the use of these data probably overestimated the risk of coronary heart disease in the current Spanish population, as the mortality rate for cardiovascular disease in the USA (close to 500 per 100 000) is higher than that for Spain (lower than 300 per 100 000).[30] Although there are other recognized methods for calculating the risk of coronary heart disease,[31-33] we believe prospective studies in our setting are fundamental, especially for population groups at greatest risk of atherogenesis. We are currently following our sample to determine the actual appearance of cardiovascular events over the next 10 years, in order to determine the validity of predictions based on standard tables.

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COMMENTARY

What is the risk of coronary heart disease in our own patients with diabetes?

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The quantitative calculation of risk of coronary heart disease (CHD) has become increasingly important since the middle of the previous decade for the development of recommendations for the treatment of hypertension and hypercholesterolemia, and such calculations have been included in most of the most influential clinical practice guidelines. In addition to their practical usefulness, risk assessments are also used widely in clinical research, as seen in many articles published in ATENCIÓN PRIMARIA. By way of example, I shall cite only two recently published articles that examine the subject of CHD risk in patients with diabetes.[1,2]

The risk of CHD in diabetes mellitus, and the treatment of dyslipidemia with lipid-lowering drugs, are subjects of current debate, and have given rise to two conflicting stances. The Third Report of the Adult Treatment Panel III[3] considers diabetes a CHD risk equivalent. In other words, a patient with diabetes is at high risk for CHD (10-year risk ≥20%) because of impaired glucose metabolism. Consequently, interventions aimed at diabetes should fulfil the same treatment criteria as in patients with CHD. Moreover, because these patients are by definition at high risk, the recommended risk factor tables are not needed to calculate risk.

The recommendation of the Adult Treatment Panel III to consider diabetes mellitus as a CHD risk equivalent is not shared by other organisms. The European Societies on Coronary Prevention[4] consider diabetes only as a risk fac-

Risk of coronary heart disease in patients with diabetes

- Controversy over the risk of coronary heart disease in patients with diabetes has arisen from two somewhat conflicting assumptions:
  - Diabetes as a coronary heart disease risk equivalent.
  - Diabetes as a risk factor which, together with other risk factors, determines the risk of coronary heart disease.
- Before one of the two assumptions can be accepted, we must:
  - Determine the actual risk in our own patients with diabetes
  - Estimate the possible consequences of accepting one position over the other.

tor; the sum of the scores for this and the rest of the risk factors yields the total coronary risk. Thus interventions aimed at dyslipidemia in persons with diabetes follow the same treatment recommendations as for other risk factors, and the 10-year risk is considered high at ≥20%.

There are arguments in favor of and against cataloging diabetes as a CHD risk equivalent. Some prospective studies offer data that compare the risk in patients with diabetes and in patients who have suffered myocardial infaction.[5] On the other hand, studies of interventions with lipid-lowering drugs in patients with diabetes but without CHD are few, and insufficient to determine whether the benefits of treatment are also equivalent to those in patients with ischemic heart disease.

Against this background of debate over the risk in patients with diabetes, Otzet et al. publish, in this issue of ATENCIÓN PRIMARIA, a study designed to determine the risk of cardiovascular disease associated with alterations in glucose metabolism as classified by the WHO-85 and the ASA-97 systems. According to these authors, there are no differences in risk of CHD or in the prevalence of risk factors between patients diagnosed as having impaired glucose tolerance according to the WHO-85 system and those found to have impaired fasting glucose with the ADA-97 system. However, agreement between the two diagnostic groups was poor. The risk of CHD increases with the degree of impairment of glucose metabolism, and is greatest when diabetes mellitus is diagnosed with either of the two systems. Otzet et al. found that between 72% and 76% -- depending on which system is used-- had a 10-year risk of CHD of ≥20%. On the basis of these figures, most persons with diabetes should be considered at high risk (>20% at 10 years) for CHD, as more than 70% of such individuals were found to be at high risk with calculations based on risk factor tables. However, in another article published in ATENCIÓN PRIMARIA in May 2001,[2] only 31.7% of the persons with diabetes had a risk ≥20%. Although the two studies did not use the same selection criteria and were based on different risk tables with data from different sources, the discrepancy in the percentages of patients with diabetes who were at high risk for CHD was so large as to raise the question: what is the risk in our own patients with diabetes? If most persons with diabetes are not at high risk, and if, in accordance with the higher estimate, they are assumed definition to have CHD risk equivalents, the resources and costs of intervention to achieve a stricter control of cholesterol values will be greater than if—in accordance with the lower figure—almost all persons with diabetes are found to have a risk ≥20% based on calculations with risk tables. Thus the answer to the question posed above is not yet obvious, and further studies will be needed to reach an answer.

In connection with the risk of CHD in patients with diabetes, other questions arise which need to be answered before the criteria developed by influential international organisms can be imported without further consideration. How many persons with diabetes require lipid-lowering treatment? What doses are appropriate if these patients are assumed to have CHD risk equivalents, compared to those for whom treatment is calculated on the basis of risk tables? What would the cost be? In anticipation of the results of clinical assays that are investigating lipid-lowering treatment for the primary prevention of CHD in patients with diabetes, one final question that needs to be asked is: Do the potential benefits make lipid-lowering treatment worthwhile?

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