

The 1997 American Diabetes Association Criteria Versus the 1985 World Health Organization Criteria for the Diagnosis of Abnormal Glucose Tolerance

Poor agreement in the Hoorn Study

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OBJECTIVE — Recently, the American Diabetes Association (ADA) introduced new diagnostic criteria. These new criteria are based on fasting plasma glucose levels, avoiding the burdensome oral glucose tolerance test (OGTT). We compared the 1997 ADA criteria with the 1985 World Health Organization (WHO) criteria with respect to the prevalence of diabetes and the cardiovascular risk profile in the population of the Hoorn Study.

RESEARCH DESIGN AND METHODS — The Hoorn Study is a population-based survey of 2,484 men and women, aged 50–75 years. An OGTT was performed and cardiovascular risk factors were determined in 2,378 subjects without known diabetes. Subjects were categorized according to both sets of diagnostic criteria.

RESULTS — Although the prevalence of diabetes was similar for both sets of criteria, 47 of 120 (39.2%) subjects who were diagnosed with diabetes according to the 1997 ADA criteria were not classified as having diabetes when using the 1985 WHO criteria. Similarly, of 285 subjects diagnosed with impaired fasting glucose by the 1997 ADA criteria, 195 (68.4%) were classified as having normal glucose tolerance by the 1985 WHO criteria. The overall agreement was poor (κ 0.33; 95% CI 0.28–0.38). Subjects who were diagnosed as having diabetes by either set of criteria had an adverse cardiovascular risk profile, which was between the cardiovascular risk profiles of concordant normal and concordant diabetic subjects.

CONCLUSIONS — In this study, both sets of criteria diagnosed a similar number of diabetic subjects, but many of the subjects shifted between glucose intolerance categories. With either set of criteria, a considerable number of subjects at risk of developing diabetes and subjects carrying an increased risk of cardiovascular disease, as reflected by an adverse cardiovascular risk profile, will be missed.

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Abbreviations: ADA, American Diabetes Association; CVD, cardiovascular disease; FPG, fasting plasma glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; NFG, normal fasting glucose; NGT, normal glucose tolerance; NHANES, National Health and Nutrition Examination Survey; OGTT, oral glucose tolerance test; PG, plasma glucose; sBP, systolic blood pressure; TG, triglyceride; WHO, World Health Organization; WHR, waist-to-hip ratio.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

The most widely used diagnostic criteria for glucose intolerance are those of the World Health Organization (WHO) (1). These criteria, published in 1985, are based on fasting plasma glucose (FPG) values and glucose values measured 2 h after a standard 75-g glucose load (2-h plasma glucose [PG]) (Table 1). The cutoff points for these diagnostic criteria are based mainly on the prevalence of microvascular complications, in particular, retinopathy. In 1995, an international expert committee working under the sponsorship of the American Diabetes Association (ADA) was established to review the scientific literature since 1979, and to decide whether changes in the diagnostic criteria for diabetes were required. Recently, this committee introduced new diagnostic criteria, which were subsequently endorsed by the ADA (2). These new diagnostic criteria, published in 1997, are based on FPG only, providing a more simple test for diagnosing diabetes (Table 1). Because of its inconvenience to patients and the perception by many physicians that the oral glucose tolerance test (OGTT) is not necessary, the OGTT is at present rarely used for diagnosing diabetes in clinical practice (3). Furthermore, concerning the prevalence of microvascular complications, several studies have shown that measurement of 2-h PG values did not contribute additional information to the predictive value of FPG (4,5). One major complication of glucose intolerance is macrovascular disease (6–8). By lowering the FPG value, the diagnosis of diabetes in clinical practice is expected to occur at an earlier stage of the disease (9). This will most likely also affect the cardiovascular risk factors in the various glucose intolerance groups. Therefore, we compared the 1997 ADA criteria with the 1985 WHO criteria with respect to the prevalence of diabetes and the cardiovascular risk profile in a population-based study of 2,378 men and women, aged 50–75 years, without previously known diabetes.

Table 1—Diagnostic criteria for glucose intolerance according to WHO and ADA

	FPG (mmol/l)		2-h PG (mmol/l)
1985 WHO criteria (1)			
Diabetes	≥7.8	or	≥11.1
IGT	<7.8	and	7.8–11.1
NGT	<7.8	and	<7.8
1997 ADA criteria (2)			
Diabetes	≥7.0		—
IFG	6.1–7.0		—
NFG	<6.1		—

RESEARCH DESIGN AND METHODS

Study population

The Hoorn Study is a survey of glucose intolerance in a general Dutch population. The study population and research design have been described in detail previously (10). In summary, 3,553 men and women, aged 50–75 years, were randomly selected from the population register of the middle-sized Dutch town of Hoorn. Of the 2,540 subjects (71.5%) who agreed to participate, 56 non-Caucasians were excluded. Therefore, the study cohort consisted of 2,484 men and women. All subjects gave their informed written consent. The study was approved by the ethics committee of the Vrije Universiteit Academic Hospital.

Glucose intolerance

Before the physical examination, a fasting blood sample was taken from all subjects. Subsequently, an oral 75-g glucose load was given. FPG and 2-h postload PG levels were determined with a glucose dehydrogenase method (Merck, Darmstadt, Germany). Subjects were classified according to both the 1985 WHO criteria (1) and the 1997 ADA criteria (2) (Table 1). Subjects who were already using insulin, glucose-lowering agents, or a diet for diabetes were classified as having “known diabetes” ($n = 90$). This group was excluded from all analyses. We also excluded 16 subjects for whom information on the PG values was missing. Consequently, all analyses were done in the remaining study population of 2,378 subjects.

Examinations

Blood pressure was measured twice, using a random-zero sphygmomanometer (Hawksley-Gelman, Lancing, U.K.), on the right arm with subjects sitting in a chair. The average of duplicate measurements was used

for analyses. Subjects were considered hypertensive when systolic blood pressure (sBP) was ≥ 160 mmHg, diastolic blood pressure was ≥ 95 mmHg, or when using antihypertensive medication (11). Weight and height were measured with subjects wearing underwear only, and BMI was calculated as the ratio of weight and height squared. Waist and hip circumferences were measured according to a standardized procedure (12). Waist-to-hip ratio (WHR) was defined as waist circumference divided by hip circumference. Triglycerides (TGs), total cholesterol, and HDL cholesterol were determined from fasting blood samples by enzymatic techniques (Boehringer Mannheim, Mannheim, Germany). The Friedewald formula was used to calculate the level of LDL cholesterol (13). Glycated hemoglobin (HbA_{1c}) was determined by ion-exchange high-performance liquid chromatography, using a modular diabetes monitoring system (Bio-Rad, Veenendaal, The Netherlands; normal range 4.3–6.1%). Fasting specific insulin level was quantified with an insulin-specific double-antibody radioimmunoassay (antibody SP21; Linco, St. Louis, MO). Information on smoking habits was obtained by a translated questionnaire from the London School of Hygiene (14).

Statistical methods

Prevalences of glucose intolerance were calculated for both sets of diagnostic criteria.

To examine the agreement between the two sets of criteria, a cross-table was made. The overall κ , which measures the agreement across all categories of glucose intolerance, was calculated. A value of 1 indicates perfect agreement, while a value of 0 indicates that agreement is no better than chance. Values >0.75 may be taken to represent excellent agreement, values <0.40 may be taken to represent poor agreement, and values between 0.40 and 0.75 may be taken to represent fair to good agreement (15). Cardiovascular risk factors and metabolic characteristics were compared among several concordant and discordant glucose intolerance groups. Differences among these groups were tested with analysis of covariance for continuous variables and with logistic regression for proportions, adjusted for age and sex. All analyses were performed using the Statistical Package for the Social Sciences (SPSS) for Windows 6.1 (16). P values were based on two-sided tests, and the cutoff point for statistical significance was 0.05.

RESULTS

Glucose intolerance

The study population consisted of 1,102 men with a mean age of 61.2 ± 7.3 years and 1,276 women with a mean age of 61.8 ± 7.4 years. All subjects were categorized according to both the 1997 ADA criteria and the 1985 WHO criteria. The overall prevalence of diabetes did not differ between the two sets of criteria: 120 vs. 118 subjects were diagnosed with diabetes using the 1997 ADA and the 1985 WHO criteria, respectively (both 5%) (Table 2). However, of the 118 subjects diagnosed with diabetes according to the 1985 WHO criteria, only 73 (61.9%) were also diagnosed with diabetes according to the 1997 ADA criteria. Of the 45 subjects (38.1%) not diagnosed with diabetes by the latter criteria, 26 were classified as having impaired fasting glucose (IFG) and 19 were classified as having normal

Table 2—Agreement between the 1985 WHO criteria and the 1997 ADA criteria for glucose intolerance in a population without known diabetes: the Hoorn Study

	NGT (WHO)	IGT (WHO)	Diabetes (WHO)	Total
NFG (ADA)	1,791	163	19	1,973
IFG (ADA)	195	64	26	285
Diabetes (ADA)	22	25	73	120
Total	2,008	252	118	2,378

Table 3—Glycemic parameters and various cardiovascular risk factors for the concordant and discordant diabetic subgroups according to the 1985 WHO criteria and the 1997 ADA diagnostic criteria

	No diabetes (WHO)/ No diabetes (ADA)	Diabetes (WHO)/ No diabetes (ADA)	No diabetes (WHO)/ Diabetes (ADA)	Diabetes (WHO)/ Diabetes (ADA)
n	2,213	45	47	73
FPG (mmol/l)	5.4 ± 0.5	6.1 ± 0.6*†	7.2 ± 0.2*‡	9.6 ± 3.3*
2-h PG (mmol/l)	5.6 ± 1.7	12.5 ± 1.4*†	8.1 ± 1.9*‡	16.7 ± 6.4*
Fasting specific insulin (pmol/l)	75.5 (56.1, 103.7)	107.6* (71.7, 166.3)	99.0* (70.6, 130.3)	112.2* (73.2, 158.5)
HbA _{1c} (%)	5.3 ± 0.5	5.7 ± 0.5*	5.8 ± 0.5*	7.3 ± 2.0*
Age (years)	61.3 ± 7.3	65.5 ± 6.3*†	61.8 ± 7.2‡	65.8 ± 7.0*
Sex (% men)	46.1	40.0	55.3	50.7
sBP (mmHg)	134.1 ± 19.7	148.5 ± 19.3*	149.5 ± 24.7*	145.7 ± 19.8*
Hypertension (%)	28.6	64.4*	55.3*	52.1*
BMI (kg/m ²)	26.3 ± 3.4	28.2 ± 4.1*	28.1 ± 3.6*	28.8 ± 4.2*
WHR	0.89 ± 0.09	0.94 ± 0.08*†	0.93 ± 0.08*‡	0.96 ± 0.09*
Cholesterol (mmol/l)	6.66 ± 1.18	6.67 ± 1.25	6.74 ± 1.12	6.67 ± 1.45
HDL cholesterol (mmol/l)	1.34 ± 0.37	1.25 ± 0.33*	1.25 ± 0.30	1.13 ± 0.32*
LDL cholesterol (mmol/l)	4.63 ± 1.11	4.48 ± 1.16	4.67 ± 0.99	4.37 ± 1.34*
TG (mmol/l)	1.30 (0.90, 2.00)	1.80* (1.10, 2.70)	1.60* (1.02, 2.44)	2.20* (1.38, 3.12)
Current smokers (%)	48.4	33.3	32.4	45.5

Data are means ± SD, median (20th, 80th percentile), or %. TGs and fasting specific insulin are tested with log-transformed data. *Significantly different from 2,213 concordant nondiabetic subjects (age- and sex-adjusted, two-sided, $P < 0.05$); †significantly different from 47 subjects diagnosed as having diabetes according to the ADA criteria only (age- and sex-adjusted, two-sided, $P < 0.05$); ‡significantly different from 45 subjects diagnosed as having diabetes according to the WHO criteria only (age- and sex-adjusted, two-sided, $P < 0.05$).

fasting glucose (NFG). Similarly, 47 of 120 (39.2%) subjects who were diagnosed as having diabetes according to the 1997 ADA criteria were not diagnosed as having diabetes by the 1985 WHO criteria. By using the 1997 ADA criteria, 285 subjects (12.0%) were classified as having IFG, compared with 252 subjects (10.6%) classified as having impaired glucose tolerance (IGT) by the 1985 WHO criteria. A total of 163 subjects (64.7%) categorized as having IGT by the latter criteria were classified as having NFG by the 1997 ADA criteria. Overall, the percentage of agreement between the two diagnostic criteria was 81%; 450 subjects (19%) shifted among glucose intolerance groups. The overall κ was 0.33 (95% CI 0.28–0.38), indicating poor agreement (15).

Cardiovascular risk profile

Glycemic parameters and some cardiovascular risk factors were compared among concordant diabetic subjects, both discordant categories, and concordant nondiabetic subjects (Table 3). FPG, 2-h PG, insulin, and HbA_{1c} values were significantly higher for the discordant and concordant diabetic subjects compared with the concordant nondiabetic subjects ($P < 0.05$). The subjects in these diabetic groups were also more often hypertensive and had higher values of BMI and WHR compared with the concordant nondiabetic subjects ($P < 0.05$).

The cardiovascular risk profile of subjects who were diagnosed as having diabetes by only one set of criteria was between the cardiovascular risk profiles of concordant nondiabetic and concordant diabetic subjects. We also compared both discordant categories with each other. Compared with the 47 subjects classified as having diabetes according to the 1997 ADA criteria only, the 45 subjects who were classified as having diabetes by only the 1985 WHO criteria had—as a consequence of the definition—lower FPG, significantly higher 2-h PG (12.5 vs. 8.1 mmol/l; $P < 0.05$), and higher fasting insulin (median 107.6 vs. 99.0; $P = 0.19$). The subjects were also older (65.5 vs. 61.8 years; $P < 0.05$) and had higher WHRs (0.94 vs. 0.93; $P < 0.05$).

Table 4 shows glycemic parameters and some cardiovascular risk factors for the concordant normal subjects, concordant IGT/IFG subjects, and the discordant categories IGT/NFG and normal glucose tolerance (NGT)/IFG (both WHO/ADA criteria). Compared with the concordant normal subjects, FPG, 2-h PG, insulin, and HbA_{1c} were significantly higher for the two discordant categories and concordant IGT/IFG subjects ($P < 0.05$). Also, these groups had a more adverse cardiovascular risk profile compared with the concordant NGT/NFG group. Comparing the two discordant categories, the 163 subjects classified as having

IGT according to the WHO criteria only had—as could be expected from the definition—lower FPG (5.6 vs. 6.3 mmol/l; $P < 0.05$), higher 2-h PG (8.9 vs. 5.8 mmol/l; $P < 0.05$), and lower serum insulin (median 85.4 vs. 92.7 pmol/l; $P < 0.05$) compared with the 195 subjects classified as having IFG according to the ADA criteria only. The subjects were also significantly older, were more often women, and had lower HDL cholesterol and higher TG levels ($P < 0.05$). When the two sets of diagnostic criteria were compared with respect to the identification of newly diagnosed diabetes plus IGT or IFG, more cases were found when using the ADA criteria (405 vs. 370). The cardiovascular risk profiles of these two groups were very similar (data not shown).

CONCLUSIONS

Glucose intolerance

In this study of 2,378 men and women with a mean age of 61.6 years, we analyzed the consequences of using the 1997 ADA criteria and the 1985 WHO criteria with respect to the prevalence of glucose intolerance and some cardiovascular risk factors. Compared with classification according to the 1985 WHO criteria, 18.9% of all subjects shifted to another glucose intolerance group when applying the 1997 ADA criteria, without affecting the overall prevalence of diabetes.

Table 4—Glycemic parameters and various cardiovascular risk factors for the concordant and discordant IGT subgroups according to the 1985 WHO criteria and the 1997 ADA diagnostic criteria

	NGT (WHO)/NFG (ADA)	IGT (WHO)/NFG (ADA)	NGT (WHO)/IFG (ADA)	IGT (WHO)/IFG (ADA)
n	1,791	163	195	64
FPG (mmol/l)	5.3 ± 0.4	5.6 ± 0.4*†	6.3 ± 0.2*‡	6.4 ± 0.3*
2-h PG (mmol/l)	5.1 ± 1.2	8.9 ± 0.9*†	5.8 ± 1.2*‡	9.1 ± 0.9*
Fasting specific insulin (pmol/l)	73.2 (55.3, 98.0)	85.4*† (56.5, 128.3)	92.7*‡ (70.7, 123.3)	96.8* (65.5, 141.7)
HbA _{1c} (%)	5.3 ± 0.5	5.5 ± 0.5*	5.5 ± 0.5*	5.7 ± 0.5*
Age (years)	60.8 ± 7.2	65.1 ± 7.1*†	61.9 ± 6.8*‡	64.4 ± 8.1*
Sex (% men)	45.3	38.7†	58.5*‡	50.0
sBP (mmHg)	132.0 ± 19.2	142.6 ± 19.4*	142.2 ± 16.8*	148.2 ± 24.8*
Hypertension (%)	25.6	42.3*	37.4*	51.6*
BMI (kg/m ²)	26.0 ± 3.3	27.4 ± 3.6*	27.4 ± 3.7*	28.3 ± 3.6*
WHR	0.88 ± 0.08	0.91 ± 0.08*	0.93 ± 0.08*	0.94 ± 0.08*
Cholesterol (mmol/l)	6.64 ± 1.19	6.73 ± 1.20	6.77 ± 1.08*	6.76 ± 1.01
HDL cholesterol (mmol/l)	1.35 ± 0.37	1.27 ± 0.36*†	1.32 ± 0.37†	1.21 ± 0.30*
LDL cholesterol (mmol/l)	4.63 ± 1.12	4.59 ± 1.07	4.72 ± 1.06	4.66 ± 0.93
TG (mmol/l)	1.30 (0.90, 1.90)	1.70*† (1.20, 2.50)	1.50*‡ (1.10, 2.10)	1.70* (1.20, 2.40)
Current smokers (%)	49.9	34.8*	44.6	47.5

Data are means ± SD, median (20th, 80th percentile), or %. TGs and fasting specific insulin are tested with log-transformed data. Concordant and discordant diabetic subjects were excluded in this table ($n = 165$). *Significantly different from 1,791 concordant normal subjects (age- and sex-adjusted, two-sided, $P < 0.05$); †significantly different from 195 subjects diagnosed as having IFG according to the ADA criteria only (age- and sex-adjusted, two-sided, $P < 0.05$); ‡significantly different from 163 subjects diagnosed as having IGT according to the WHO criteria only (age- and sex-adjusted, two-sided, $P < 0.05$).

However, 38.1% of the subjects diagnosed as having diabetes by the WHO criteria were classified as either IFG or as NFG by the ADA criteria. Also, 39.2% of the subjects diagnosed as having diabetes according to the ADA criteria were not diagnosed as having diabetes by the WHO criteria.

The threshold for FPG has been lowered to 7.0 mmol/l by the ADA, because of the assumption that using the FPG criterion alone should result in the diagnosis of a similar number of patients as that diagnosed using the 1985 WHO criteria, which is based on FPG and 2-h PG values together (2,4,5,17–20). However, in our study population, the agreement between the 1997 ADA criteria and the 1985 WHO criteria was poor, as reflected in the overall κ of 0.33 (15). Because the study population was a random selection from the population registry of Hoorn, we can exclude selection bias.

FPG and 2-h PG in this population were assessed only once. In a subpopulation of 1,109 subjects, a second OGTT was performed after 2–6 weeks. As we previously reported, the intra-individual coefficient of variation was 6.5% for FPG and 16.7% for 2-h PG, indicating that the variability of 2-h PG is larger than that of FPG (21). This variability may have caused some random misclassification in glucose intolerance categories. In this subpopulation, with

repeated measurements, when the diagnostic criteria of the ADA and the WHO were applied to the means of the duplicate FPG and 2-h PG values, an overall κ of 0.43 (95% CI 0.37–0.48) was observed, indicating fair to good agreement (15). So duplicate measurements improve agreement.

Harris et al. (9) recently studied the consequences of using the 1997 ADA criteria on the prevalence of diabetes in the National Health and Nutrition Examination Survey (NHANES) III population. They found a prevalence of undiagnosed diabetes of 4.4% by using the 1997 ADA criteria and of 6.4% by using the 1985 WHO criteria, but they did not comment on the fact that, overall, a large proportion of all subjects shifted between categories. In agreement with our findings, in the NHANES III study, 46.9% of subjects classified as having diabetes according to the 1985 WHO criteria were classified as either normal or having IFG by the 1997 ADA criteria, and 22.7% of the subjects classified as having diabetes according to the ADA criteria were not classified as having diabetes by the WHO criteria.

In both the Hoorn Study and the NHANES III study, a substantial number of subjects shifted between IGT/IFG and normal. Nijpels et al. (22), in a prospective study in subjects with IGT over an average period of 3 years, found that 2-h PG rather

than FPG was the most important predictor of conversion to NIDDM (22). This observation has been confirmed in other studies (23). Therefore, measurement of 2-h PG may be very important when investigating the pathogenesis of diabetes and for the identification of subjects at risk for conversion to diabetes. Conversion rates of subjects with IFG have not yet been published.

Cardiovascular risk profile

The changes in glucose intolerance categories also influence the level of cardiovascular risk factors. The main risk factors for macrovascular complications of diabetes are generally the same as those in the non-diabetic population, but they are more prevalent among subjects with abnormal glucose tolerance. This phenomenon has been attributed to the so-called insulin resistance syndrome: a clustering of metabolic disorders, including glucose intolerance, obesity, hypertension, and lipid abnormalities (24–26). It is well accepted that guidelines for the treatment of diabetes should include target values for these established cardiovascular disease (CVD) risk factors (6,27–29). With either set of criteria, a considerable number of subjects who carry an increased risk of CVD, as reflected by an adverse cardiovascular risk profile, will be missed. This again demonstrates that it does not suffice to screen

subjects at risk for CVD on the basis of glucose levels. The results of the present study indicate no differences in cardiovascular risk factors between newly diagnosed diabetic plus IGT or IFG subjects using either criteria. Therefore, for CVD risk stratification, the presence of cardiovascular risk factors like hypertension and obesity may be a reason to determine fasting glucose. Subjects with several risk factors and IFG might benefit from glucose-lowering advice, primarily lifestyle interventions.

In conclusion, the major advantage of the 1997 ADA criteria is that one only needs to measure FPG. The OGTT may no longer be needed for diagnosis, but it remains an important tool in pathogenetic research. In clinical practice, measurement of FPG only may lead to improved detection of subjects with previously undiagnosed diabetes and IFG, as is reflected by the younger age of the subjects diagnosed with diabetes and IFG when using the 1997 ADA criteria. To answer the question whether application of the new criteria will result in earlier detection and lower mortality and morbidity, prospective studies are needed.

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