Assessment of the New Criteria for Diabetes Mellitus According to 10-year Relative Survival Rates

A. Sasaki

Center for Adult Diseases, Osaka, Japan

Summary. The validity of the new diagnostic criteria for diabetes mellitus for Japanese subjects was assessed by the long-term prognosis of 501 patients, found in an epidemiological survey of 6,681 people in a Japanese town. Ten-year relative survival rates were examined in relation to the 50 g oral glucose tolerance test (serum glucose determined by a ferricyanide method). Subjects were classified using the new criteria. The prognosis of normal subjects (fasting glucose <140 mg/dl (7.8 mmol/l) and 2-hour glucose level <140 mg/dl) and of subjects with fasting glucose <140 mg/dl and 2-h 140–200 mg/dl (7.8–11.1 mmol/l) did not differ from that of the general population. Diabetics (fasting ≥ 140 mg/dl and 2-h ≥ 200 mg/dl) showed a significantly reduced survival rate, corresponding to an excess mortality. Subjects with a fasting level <140 mg/dl and 2-h ≥ 200 mg/dl had a relative survival rate similar to that of normal subjects. As a group, fasting levels ≥ 140 mg/dl indicated a reduced survival rate, regardless of the 2-h level, while those with a 2-h level ≥ 200 mg/dl alone failed to show a significantly reduced survival rate. Thus, the fasting glucose values appeared to be more closely related to death rate than the 2-hour glucose values.

Key words: Diagnostic criteria for diabetes mellitus, glucose tolerance test, fasting serum glucose, impaired glucose tolerance, follow-up study, relative survival rate, prognosis of diabetic patients, epidemiological survey of diabetes mellitus

jects fairly low in order not to overlook genuine diabetes [1–4]. This approach classifies, however, some people with a lesser degree of glucose intolerance as diabetic. Such diagnosis may have an unfavourable psychological impact on some patients. It is desirable, therefore, to set the discriminating point at a more practical and accurate level. Keen et al. [6] recently proposed new diagnostic criteria for diabetes, similar to those proposed by the NIH study group [7], the British Diabetic Association, the Australian Diabetic Society, and by the Expert Committee on Diabetes of the World Health Organization [8]. The new criteria employ, on the basis of epidemiological experience [9–13], glucose levels higher than those formerly proposed for the diagnosis of diabetes. In the present study, the validity of the new criteria was assessed in relation to survival rates of subjects in a 10-year follow-up study on diabetes.

Material and Methods

1. Subjects

The subjects were described in detail previously [14]. Briefly, they came from a diabetic study of the population of a town in Osaka Prefecture from 1964–1965 [15]. A total of 6,681 people (71.2% of the population over 6 years old) responded to the study. Of these subjects, 501 had an oral glucose tolerance test because of postprandial glycosuria and they constituted the subjects of the present study.

2. Methods

OGTT: Blood samples were collected from an antecubital vein before and 1, 2, and 3 h after an oral 50 g glucose load. Serum glucose was determined by an autoanalyser ferricyanide method. The results of the OGTT were classified into five categories as follows: fasting glucose level (F) <140 mg/dl (7.8 mmol/l) and 2-hour glucose level (2-h) <140 mg/dl (normal group); F <140 mg/

Several criteria for diagnosis of diabetes are currently in use [1–5]. Most of these criteria set the discriminating point between normal and abnormal sub-

Fig. 1. Relation between the fasting glucose values and the 2-hour glucose values in 50 g OGTT of 501 subjects studied. Normal: subjects with fasting glucose level (F) < 140 mg/dl and 2-hour glucose level (2-h) < 140 mg/dl. IGT 1: subjects with F < 140 mg/dl and 2-h between 140–200 mg/dl. IGT 2: subjects with F < 140 mg/dl and 2-h ≥ 200 mg/dl. IGT 3: subjects with F ≥ 140 mg/dl and 2-h < 200 mg/dl. Diabetic: subjects with F ≥ 140 mg/dl and 2-h ≥ 200 mg/dl

dl and 2-h between 140–200 mg/dl (7.8–11.1 mmol/l) (IGT 1 group); F < 140 mg/dl and 2-h ≥ 200 mg/dl (IGT 2 group); F ≥ 140 mg/dl and 2-h < 200 mg/dl (IGT 3 group); F ≥ 140 mg/dl and 2-h ≥ 200 mg/dl (diabetic group). IGT 1 is the category originally defined by Keen et al. [6] as “IGT”. IGT 2 and IGT 3 were added by the author (Fig. 1), both of which are classified as “diabetes” according to the NIH and the WHO criteria [7, 8].

Survival Rate: Each subject was followed for 10 years. Those who dropped out of the study due to moving from the town or death were recorded. Those who left the town were identified from community records and those who died were verified by death certificates. The 10-year observed survival rate was computed by the standard life table method [16], based on the information available on each subject concerning date of the initial examination, final date of follow-up, and vital state at that time (alive, dead or moved). The 10-year expected survival rate was estimated from the use of life tables for Japan during the study period, by summing the individual survival probabilities and dividing by the number of subjects involved. The 10-year relative survival rate (RSR) was obtained by dividing the observed survival rate by the expected survival rate. The RSR was expressed as a percentage. Thus, RSR is an age-dependent variable and can be compared between groups of different age-distributions [17]. The significance of the decrease in RSR was estimated by Student's t-test using the standard error of RSR (SER) estimated as follows [17]:

$$SER = \sqrt{\frac{p(1-p)}{n}} / \bar{p}$$

where p is the observed survival rate, $\bar{p}$ is the expected survival rate and n is number of subjects observed.

Results

Figure 1 shows the relation between fasting and 2-h glucose values of the OGTT in the subjects, together with their classification based on the new criteria. This Figure was prepared according to Köbberling et al. [18]. Of 501 subjects, 383 were classified as normal, 42 as IGT 1, 27 as IGT 2, 9 as IGT 3 and 40 as diabetic.

Table 1 presents the 10-year RSR in relation to the classification of subjects made on the basis of their OGTT categories. RSR in the normal group failed to differ significantly from 100%, and RSRs in groups IGT 1 and IGT 2 were slightly higher than 100%, suggesting no excess mortality in these three

groups for the 10-year period compared to the general population in Japan. RSR in group IGT 3 tended to be lower but, with small numbers, the decrease was not statistically significant. RSR in diabetic subjects was decreased significantly, corresponding to an excess mortality in this group. Furthermore, RSR in subjects with $F \geq 140$ mg/dl was significantly less than 100%, whereas RSR in subjects with $2\text{-h} \geq 200$ mg/dl failed to differ significantly from 100%, though it tended to be reduced. In addition, the mean age for each group, which are given in Table 1 along with their SEM, indicated no relation to the RSR. The mean age was much younger in the normal group than in IGT 1 and IGT 2 groups, but there was no difference in RSR between the groups.

Table 2 shows the causes of death in each OGTT category group. A total of 108 deaths was observed during the 10-year follow-up period. Cardiovascular diseases were the leading causes of death in all groups. The proportion of cardiovascular deaths was highest in the diabetic group (75.0%), and next lowest in the normal group (52.3%). The percentages were 63.6%, 66.7% and 50.0% for the IGT 1, IGT 2 and IGT 3 groups respectively, much higher than for the normal group excepting the IGT 3 group, suggesting an increased risk of cardiovascular complications in these groups.

Discussion

Previously, we have reported that the prognoses of diabetic patients were largely dependent on the degree of glucose intolerance at the start of follow-up [14]. In the present study, we have shown a clear relationship between prognosis and the new classification of patients based on the criteria proposed by Keen et al. [6]. The relative survival rate was markedly reduced in diabetic patients compared to normal subjects. Furthermore, a significant decrease in relative survival rate was found in patients with a fasting serum glucose ≥ 140 mg/dl, regardless of glucose intolerance as shown by 2-hour values in OGTT. On the other hand, no marked reduction in the relative survival rate occurred in patients classified on the basis of 2-hour values alone, since the relative survival rates of subjects with impaired glucose tolerance ($2\text{-h} \geq 140$ mg/dl) failed to differ significantly from that of normal subjects, provided that their fasting level was <140 mg/dl, as in IGT 1 and IGT 2.

Taken together, these observations suggest the prognosis of subjects to be related more closely to fasting values than 2-hour values. Our findings support the notion that a fasting level ≥ 140 mg/dl is a

Table 1. Ten-year relative survival rates in relation to OGTT categories at the start of the follow-up

OGTT category	n	Mean age ($\pm$ SEM) (years)	RSR (%)	SER (%)
Normal	383	46.5 $\pm$ 1.0	99.2	2.3
IGT 1	42	60.2 $\pm$ 2.4	109.9	10.3
IGT 2	27	60.3 $\pm$ 2.7	106.8	11.1
IGT 3	9	56.7 $\pm$ 8.3	50.3	23.7
Diabetic	40	61.0 $\pm$ 1.8	69.5 ^a	11.0
$F \geq 140$ mg/dl	49	59.9 $\pm$ 2.1	66.2 ^a	10.1
$2\text{-h} \geq 200$ mg/dl	67	60.7 $\pm$ 1.5	84.3	8.3

^a Denotes a statistically significant difference from 100% ($p < 0.05$)

RSR: 10-year relative survival rate

SER: standard error of the relative survival rate

Normal: subjects with fasting glucose level (F) <140 mg/dl and 2-hour glucose level (2-h) <140 mg/dl

IGT 1: subjects with $F <140$ mg/dl and 2-h between 140–200 mg/dl

IGT 2: subjects with $F <140$ mg/dl and $2\text{-h} \geq 200$ mg/dl

IGT 3: subjects with $F \geq 140$ mg/dl and $2\text{-h} <200$ mg/dl

Diabetic: subjects with $F \geq 140$ mg/dl and $2\text{-h} \geq 200$ mg/dl

Table 2. Number of deaths by specified causes for each OGTT category group

OGTT category	Causes of death			
	All causes (%)	Cardio-vascular (%)	Neoplasms (%)	Others (%)
Normal	65 (100.0)	34 (52.3)	12 (18.5)	19 (29.2)
IGT 1	11 (100.0)	7 (63.6)	3 (27.3)	1 (9.1)
IGT 2	6 (100.0)	4 (66.7)	—	2 (33.3)
IGT 3	6 (100.0)	3 (50.0)	1 (16.7)	2 (33.3)
Diabetic	20 (100.0)	15 (75.0)	1 (5.0)	4 (20.0)

Causes of death were classified according to the eighth revision of the International Classification of Disease

For definition of OGTT categories, see Table 1

more precise criterion than $2\text{-h} \geq 200$ mg/dl for diagnosis of diabetes [18]. It appears reasonable, therefore, that patients with a fasting level of >140 mg/dl are accepted as diabetic as in the reports of the NIH study group and of the WHO Expert Committee. In these reports, patients with $2\text{-h} \geq 200$ mg/dl are also classified as diabetic, regardless of the fasting values, but we find their prognosis to be more favourable in terms of relative survival rate. However, there is evidence of increased risk of cardiovascular complications in these subjects, as discussed by Keen et al. [6].

A glucose load of 50 g was used in the present study, but 75 g is recommended in the new criteria [6, 7, 8]. Too few data are available to determine how

this difference in glucose load affects the 2-hour values in OGTT, though there are many reports on the differences between 50 g and 100 g loads [19]. It is to be noted that the body weight of our subjects averaged 55.7 ± 0.7 kg (SEM) for males and 51.6 ± 0.6 kg for females, which is much less than the average for men and women in Western countries. Consequently, it seems not unreasonable to apply the glucose values recommended in the new criteria to our subjects in this study.

References

1. Wilkerson HLC, Cohen AS, Kenadjian BG (1955) Screening for diabetes. *J Chronic Dis* 2: 464–476
2. Wilkerson HLC, Hyman H, Kaufman M, McCuistion AC, Francis JO'S (1960) Diagnostic evaluation of oral glucose tolerance tests in nondiabetic subjects after various levels of carbohydrate intake. *N Engl J Med* 252: 1047–1053
3. Fajans SS, Conn JW (1954) An approach to the prediction of diabetes mellitus by modification of the glucose tolerance test with cortisone. *Diabetes* 3: 296–304
4. WHO (1965) Diabetes mellitus. Report of a WHO Expert Committee. WHO Tech Rep Ser 310: 11–13
5. Keen H, Rose G, Pyke DA, Boyns D, Chlouverakis C, Mistry S (1965) Blood sugar and arterial disease. *Lancet* II: 505–508
6. Keen H, Jarrett RJ, Alberti KGMM (1979) Diabetes mellitus: a new look at diagnostic criteria. *Diabetologia* 16: 283–285
7. National Diabetes Data Group (1979) Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. *Diabetes* 28: 1039–1057
8. WHO (1980) Diabetes mellitus. Second Report of a WHO Expert Committee. WHO Tech Rep Ser 646: 10–12
9. Jarrett RJ, Keen H, Fuller JH, McCartney M (1979) Worsening to diabetes in men with impaired glucose tolerance ("borderline diabetes"). *Diabetologia* 16: 25–30
10. Diabetes Survey Working Party (1976) Ten-year follow-up report on Birmingham Diabetes Survey of 1961. *Br Med J* II: 35–37
11. O'Sullivan JB, Mahan CM (1968) Prospective study of 352 young patients with chemical diabetes. *N Engl J Med* 278: 1038–1041
12. Jarrett RJ, Keen H (1976) Hyperglycaemia and diabetes mellitus. *Lancet* II: 1009–1012
13. Bennett RH, Rushforth NB, Miller M, LeCompte P (1976) Epidemiologic studies in diabetes in the Pima Indians. *Recent Prog Horm Res* 32: 333–376
14. Sasaki A, Suzuki T, Horiuchi N (1980) Survival rate and causes of death of diabetics in Japan. A 10-year follow-up study. *J Chronic Dis* 33: 341–346
15. Sasaki A, Suzuki T, Fujimoto I, Horiuchi N, Inui H (1971) A population-based epidemiological study on diabetes mellitus in a rural town. Characteristic features of diabetes in Japan. In: Tsuji S, Wada M (eds) *Diabetes mellitus in Asia, 1970*. Int Congr Ser No 221. Excerpta Medica, Amsterdam, p 42–50
16. Cutler SJ, Ederer F (1958) Maximum utilization of the life table method in analyzing survival. *J Chronic Dis* 8: 690–712
17. Ederer F, Axtell L, Cutler SJ (1961) The relative survival rate – a statistical methodology. *Natl Cancer Inst Monogr* 6: 101–121
18. Köbberling J, Creutzfeldt W (1979) Diabetes mellitus: a new look at diagnostic criteria (Letter to Editor). *Diabetologia* 17: 263–264
19. West KM (1978) *Epidemiology of diabetes and its vascular complications*. Elsevier, New York, p 75–80

Received: May 20, 1980,
and in revised form: October 15, 1980

Akira Sasaki, M.D.
Center for Adult Diseases
3 Nakamichi 1-chome
Higashinari-ku
Osaka 537
Japan