Impaired Fasting Glucose or Impaired Glucose Tolerance

What best predicts future diabetes in Mauritius?

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OBJECTIVE — To determine if impaired fasting glucose (IFG; fasting plasma glucose level 6.1–6.9 mmol/l) can predict future type 2 diabetes as accurately as does impaired glucose tolerance (IGT; 2-h plasma glucose level 7.8–11.0 mmol/l).

RESEARCH DESIGN AND METHODS — A longitudinal population-based study was performed with surveys in 1987 and 1992 on the island of Mauritius, assessing diabetes status by the oral glucose tolerance test. A total of 3,717 subjects took part in both surveys. Of these subjects, 3,229 were not diabetic in 1987 and formed the basis of this study.

RESULTS — At baseline, there were 607 subjects with IGT and 266 subjects with IFG. There were 297 subjects who developed diabetes by 1992. For predicting progression to type 2 diabetes, the sensitivity, specificity, and positive predictive values were 26, 94, and 29% for IFG and 50, 84, and 24% for IGT, respectively. Only 26% of subjects that progressed to type 2 diabetes were predicted by their IFG values, but a further 35% could be identified by also considering IGT. The sensitivities were 24% for IFG and 37% for IGT in men and 26% for IFG and 66% for IGT in women, respectively.

CONCLUSIONS — These data demonstrate the higher sensitivity of IGT over IFG for predicting progression to type 2 diabetes. Screening by the criteria for IFG alone would identify fewer people who subsequently progress to type 2 diabetes than would the oral glucose tolerance test.

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The American Diabetes Association (ADA) has recently proposed a revision of the criteria for diagnosing diabetes (1). The main change was a lowering of the fasting plasma glucose (FPG) threshold to 7.0 mmol/l. Furthermore, impaired fasting glucose (IFG) (FPG value of 6.1–7.0 mmol/l) was created as a new category of abnormal glucose metabolism. These changes recognize that an FPG value of 7.8 mmol/l usually reflects a greater degree of hyperglycemia than does a 2-h plasma glucose (PG) value of 11.1 mmol/l (2,3). Also, these changes are supported by data indicating that the risks of both retinopathy and coronary heart disease start to rise at FPG values of ~6.0 mmol/l (4–6).

The report further suggests that with the lowering of FPG thresholds, the oral glucose tolerance test (OGTT) could become unnecessary in the face of "a simpler and equally accurate test—fasting plasma glucose" (1). However, while the lowering of FPG thresholds is based on available epidemiological data, the suggestion that FPG can adequately substitute for the OGTT is not. However, it depends on an assumption that the relationship between FPG and 2-h PG is such that one can substitute for the other. Thus, uncertainty centers mainly on the possible abandonment of the OGTT rather than the validity of the new thresholds.

Impaired glucose tolerance (IGT), which can only be diagnosed with an OGTT, is highly predictive of subsequent type 2 diabetes (7). As such, it has a potentially important role in public health and as a target for experimental strategies for prevention of type 2 diabetes. If the OGTT is to be abandoned and IFG is to replace IGT, then it is important to determine how well IFG compares with IGT in predicting type 2 diabetes.

In a 1987 population-based survey from the island of Mauritius, we determined glucose tolerance status by OGTT. Diabetes, almost universally type 2 diabetes, was found in 11.9% of adults aged 25–74 years (8). A follow-up survey in 1992, again measuring both FPG and 2-h PG with the OGTT, allowed us to compare the ability of IFG and IGT to predict the development of type 2 diabetes.

RESEARCH DESIGN AND METHODS

— Mauritius is an Indian Ocean island nation ~800 km east of Madagascar. The population consists of 70% Asian Indians, 2.1% Chinese, and 27.9% "general population" who are predominantly people of African ancestry (Creoles) with varying amounts of European, Malagasy, and Indian admixture. Since World War II, Mauritius has experienced industrialization, a rise in living standards, and an increase in the prevalence of noncommunicable diseases. The 1987 survey included 86.2% of all enumerated adults (both diabetic and nondiabetic), aged 25–74 years, living in 10 randomly selected population centers, plus a purposely selected area of Chinatown in the

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Abbreviations: ADA, American Diabetes Association; FPG, fasting plasma glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test; PG, plasma glucose; PPV, positive predictive value.

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

Table 1—*Classification of subjects at baseline according to fasting and 2-h PG*

	FPG (mmol/l)		
2-h PG (mmol/l)	<6.1	6.1–6.9	≥7.0
<7.8	2,474*	148*	10
7.8–11.0	489*	118*	32
≥11.1	45†	61†	151

Data are *n*. Subjects on treatment for diabetes were excluded. *Included in primary and secondary analysis; †included in secondary analysis only.

Table 2—*Prediction of progression to diabetes, according to glucose tolerance category and sex*

	All (*n* = 3,229)			Male (*n* = 1,492)			Female (*n* = 1,737)		
	IFG	IGT	IFG or IGT*	IFG	IGT	IFG or IGT*	IFG	IGT	IFG or IGT*
n	266	607	755	147	222	314	119	385	441
Sensitivity (%)	26	50	61	24	37	50	26	66	74
Specificity (%)	94	84	80	92	84	83	95	81	79
PPV (%)	29	24	24	27	27	26	29	23	22

*Includes all subjects with either IFG or IGT. Because IFG and IGT overlap, the number in the "IFG or IGT" column is less than the sum of the numbers in the IFG and IGT columns.

capital, Port Louis. Full details have been published previously (8). For the 1992 survey, all adults from the 1987 survey were invited. The survey methodology was the same on both occasions. All eligible adults were asked to attend a survey site between 0800 and 1000 after an overnight fast. After registration, all subjects had fasting blood samples taken, and all subjects except those on treatment for diabetes had an OGTT (75 g dextrose monohydrate in 250 ml water). Fasting and 2-h PG values were determined immediately on site with a YSI glucose analyzer (Yellow Springs, OH). For this analysis, classifications of diabetes and IGT and IFG values were based on the recent ADA recommendations (1). In the primary analysis, diabetes was diagnosed on the basis of a 2-h PG value of ≥11.1 or an FPG value of ≥7.0 mmol/l or current treatment with insulin or oral hypoglycemic drugs. IGT was defined as an FPG value of <7.0 mmol/l, together with 2-h PG values of ≥7.8 and <11.1 mmol/l. IFG was defined as FPG values of ≥6.1 and <7.0 mmol/l, with a 2-h PG value of <11.1 mmol/l. Subjects who had both IFG and IGT were included in the data for each category of glucose metabolism. Subjects who progressed to diabetes were designated as any subject classified as having diabetes in 1992 and not having diabetes in 1987. Both the fasting and the 2-h values at both surveys were used to determine progression. In the secondary analysis, only fasting values were used to classify diabetes and IFG in the two surveys.

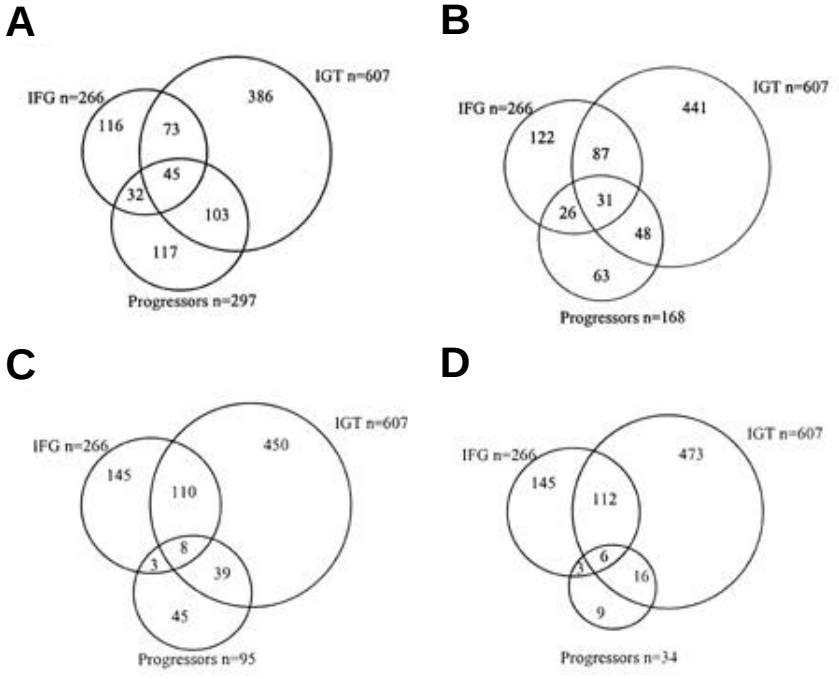

Figure 1—*Progression to diabetes over 5 years according to baseline glucose tolerance status and diabetes diagnostic criteria. A: All subjects who progressed to diabetes, as defined by FPG or 2-h PG values or hypoglycemic treatment in 1992. B: Progression to type 2 diabetes by virtue of FPG ≥7.0 mmol/l, irrespective of 2-h PG, in 1992. C: Progression to type 2 diabetes by virtue of only 2-h PG ≥11.1 mmol/l, in 1992. D: Progression to type 2 diabetes by virtue of taking hypoglycemic treatment in 1992. Data shown are numbers. Circles represent subjects with IFG or IGT at baseline, in 1987, and those who had progressed to diabetes at follow-up, in 1992. Areas of circles and regions of overlap are not necessarily to scale.*

RESULTS — There were 3,717 subjects who took part in both surveys, 189 of whom were already on treatment for diabetes in 1987. Table 1 shows how the subjects were classified by FPG and 2-h PG values at baseline. The 3,229 subjects who were not diabetic in 1987 (FPG <7.0 mmol/l, 2-h PG <11.1 mmol/l, and not on treatment for diabetes) formed the basis for the primary analysis in this study. In 1987, there were 631 subjects with IGT according to the World Health Organization (1985) criteria (FPG <7.8 mmol/l and 2-h PG 7.8–11.0 mmol/l), 24 of whom had an FPG value of ≥7.0 mmol/l. The primary analysis includes only the 607 subjects with IGT who had an FPG value of <7.0 mmol/l, and the 266 subjects with IFG who had nondiabetic 2-h PG levels. The IFG and IGT groups each contain the 118 subjects who had both.

Primary analysis

Figure 1*A* illustrates the numbers of subjects in the primary analysis with IFG and IGT at baseline who progressed to diabetes by 1992. IFG predicted 26% (77 of 297) of subjects that progressed to diabetes. A further 35% (103 of 297) could be identified by also considering IGT. Table 2 shows the sensitivity, specificity, and positive predictive value (PPV) of IFG, IGT, and the combination of IFG and IGT (i.e., all subjects who had either IFG or IGT). The sensitivity for the prediction of diabetes was markedly higher for IGT, and this was par-

ticularly striking in women (IGT, 66%; IFG, 26%); however, IFG was the more specific test in both sexes. The combination of IFG or IGT as a screening test was the most sensitive, with only small declines in specificity and PPV, compared with IGT alone. There were similar trends in the different ethnic groups (each of which had similar sex distributions). Among Chinese subjects, IFG had the same sensitivity as IGT (35%), but this was still considerably lower than the sensitivity of IFG and IGT combined (35 vs. 59%).

Figure 1*B–D* shows the prediction of progression to type 2 diabetes according to the criteria for diagnosing diabetes in the follow-up survey. IGT had a higher sensitivity for the prediction of type 2 diabetes than did IFG, whether diabetes status at follow-up was determined by FPG (47 vs. 34%), 2-h PG values alone (49 vs. 12%), or current hypoglycemic treatment (65 vs. 26%).

Secondary analysis

In the secondary analysis, using only FPG values in both surveys to determine progression (defined as those who had an FPG value of <7.0 mmol/l at baseline, and developed an FPG value of ≥7.0 mmol/l, or started hypoglycemic treatment at follow-up) and including the 106 subjects whose baseline 2-h PG was in the diabetic range (but FPG value was <7.0 mmol/l [Table 1]), the number of subjects who progressed to diabetes was 256 (138 men). The percentages of these subjects who progressed to diabetes and had IFG, IGT, and either IFG or IGT at baseline (i.e., sensitivity) were 38, 30, and 57% in men and 43, 51, and 75% in women, respectively. From the 61 subjects whose baseline FPG value was classified as IFG but whose 2-h PG value was >11.0 mmol/l, 38 (62%) developed diabetes based on fasting criteria at follow-up. Similarly, 16 of 45 (36%) of those with a normal FPG value (<6.1 mmol/l) and a diabetic 2-h PG value at baseline progressed to diabetes at follow-up. When subjects with diabetes on 2-h value alone at baseline are excluded, but diabetes at follow-up is still diagnosed based on the fasting value only, then the sensitivity of IFG falls to 31% in men and 34% in women, while that of IGT rises to 37% in men and 67% in women.

CONCLUSIONS — There is concern that because the new category of IFG might not represent the same subjects as the IGT category, IFG would not be predictive of type 2 diabetes to the same degree as IGT. Though the ADA committee did not explicitly state that IFG was defined so as to make it identical to IGT, it is important to compare the two categories. This prospective population-based study shows that in predicting diabetes, there is a considerable increase in sensitivity using the OGTT compared to relying on IFG. This is similar to earlier findings in French middle-aged men, where IGT identified more of the subjects progressing to diabetes than did IFG (9). The present study shows that whatever criteria are used to diagnose type 2 diabetes at follow-up, IGT at baseline is a better predictor of type 2 diabetes than is IFG (Fig. 1). Only when diabetes was diagnosed based on FPG values, and when subjects with normal baseline FPG values but with a 2-h PG value ≥11.1 mmol/l were included in the analysis (and then only in men), did IFG have a higher sensitivity than IGT. However, even in this setting, performing the OGTT still identified an additional 19% of subjects who progressed to diabetes that were not found by IFG alone. Furthermore, this approach fails to identify 106 (21%) of those with diabetes (based on FPG and 2-h PG values) at baseline.

For IGT, we found a lower specificity, which relates mainly to the higher prevalence of IGT compared with IFG, with only a minor contribution from the slightly lower risk of progression from IGT than from IFG (PPV). Nevertheless, specificity of IGT was >80% in all analyses.

Our data show a striking difference between men and women. In women performing only a fasting test, IFG identified only 26% of subjects who progressed, but when the OGTT was performed, 74% were identified. In men, the figures were 26 and 50%, respectively, showing the additional benefit of the OGTT over a fasting test to be somewhat smaller, but still considerable.

The presence of a large number of subjects (n = 106) with an FPG value of <7.0 mmol/l, but a 2-h PG value in the diabetic range, and the observation that most of the IGT subjects have FPG values that are well within the normal range (FPG ≤5.5 mmol/l in 54%), demonstrate the limitations of FPG alone in classifying hyperglycemia. Furthermore, the higher sensitivity of IGT for predicting type 2 diabetes shows, at least in this population, that over 5 years, IGT is a more common antecedent of diabetes than is IFG.

If the purpose of diagnosing intermediate categories of glucose metabolism is to initiate treatment (lifestyle modification or drug therapy) that will reduce the risk of progression to diabetes (10), then it is important that IFG identifies either the same subjects as does IGT, or at least a group with a similar risk for progression. As can be seen from our data, the individual's risk of progression (as indicated by the PPV) is slightly higher for IFG than IGT. However, from the population perspective, the considerably lower sensitivity of IFG indicates that far fewer cases of diabetes could be prevented by targeting preventive measures on subjects with IFG than could be by targeting IGT subjects.

One of the advantages of relying on FPG rather than 2-h PG values is the superior reproducibility of the former (11). Indeed, the lower reproducibility of the 2-h PG might theoretically partially explain the higher sensitivity for progression from IGT that we have found. If, as a result of the variability of the 2-h value, rather than genuine progression, significant numbers of IGT subjects had at follow-up 2-h values over 11.0 mmol/l, the proportion of subjects progressing to diabetes (i.e., sensitivity) identified by IGT would appear to be higher than that for the more reproducible IFG. However, studies performing two OGTTs within a short time have shown that the low reproducibility of 2-h PG mainly results in IGT subjects being reclassified as normal, with only 7–12% of them being reclassified as having diabetes (11–13). Additionally, in the present study, IGT was still a better predictor of type 2 diabetes when it was diagnosed by FPG alone (Fig. 1*B*).

This study has focused on a comparison of IFG and IGT as recently defined by the ADA (1). Other issues relating to the definition of these two states, such as the change in IGT that has resulted from lowering the fasting criterion from <7.8 to <7.0 mmol/l and the choice of 6.1 mmol/l as the lower limit of IFG, are also important and remain to be explored.

For clinical practice, IFG can be more easily diagnosed than IGT. Therefore, IFG now offers the possibility of identifying people at risk of future diabetes, without having to do an OGTT. Also, as long as its limitations are borne in mind, it may provide a more accessible risk assessment in clinical practice than IGT.

In summary, these data show that IGT has a much higher sensitivity for predicting progression to diabetes than does IFG. This occurs at the cost of only a small reduction

in specificity and PPV. Thus, while the new category of IFG may broaden and improve our description of states of intermediate glucose metabolism, it should be seen as complementary to, rather than a replacement for, IGT. If data from other populations confirm these findings, then screening programs aimed at identifying people at risk for diabetes would lose a considerable amount of information by relying on fasting values alone rather than the OGTT.

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