Changing the Definition of Impaired Fasting Glucose

Impact on the classification of individuals and risk definition

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OBJECTIVE — This study evaluates the impact of lowering the diagnostic threshold for impaired fasting glucose (IFG) from 6.1 to 5.6 mmol/l as proposed by the American Diabetes Association (ADA) on the prevalence of the condition, classification of individuals, and risk definition.

RESEARCH DESIGN AND METHODS — A total of 1,285 employees of the Italian Telephone Company aged 35–59 years without known diabetes underwent an oral glucose tolerance test (OGTT). BMI, serum cholesterol, triglycerides, and blood pressure were measured. Medication use was recorded.

RESULTS — With the new ADA criterion, the proportion of people diagnosed with IFG increased from 3.2 to 9.7%. The newly proposed IFG category identified 41% of all subjects with impaired glucose tolerance (IGT) compared with 16.2% identified with the use of the World Health Organization criterion for IFG; the improvement in accuracy has been achieved at the cost of classifying more previously “normal” subjects as having IFG (from 2.3 to 7.3%). Both IFG and IGT were associated with an unfavorable risk profile for diabetes and cardiovascular disease, with a higher estimated risk for IGT than IFG.

CONCLUSIONS — Even with the revised diagnostic criterion, IFG and IGT identify distinct groups that have a different background risk. The cost/benefit of preventive measures tested in people with IGT may not apply to the new IFG category.

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The American Diabetes Association (ADA) Expert Committee on the Diagnosis and Classification of Diabetes Mellitus has recommended lowering the diagnostic threshold of impaired fasting glucose (IFG) from 6.1 to 5.6 mmol/l (1). The advantages of this change as reported by the committee (1) have been questioned (2,3). Impaired glucose tolerance (IGT) and IFG, as defined by the World Health Organization (WHO) (4), differ in various aspects: IGT is more prevalent than IFG, and postchallenge hyperglycemia is more closely associated with a risk of developing diabetes and cardiovascular disease (CVD) (5–7) than fasting hyperglycemia. Lowering the diagnostic glucose threshold for IFG to 5.6 mmol/l would supposedly result in a similar prevalence of IFG and IGT and increase the concordance between the two groups with respect to risk definition (1). Application of the lower diagnostic threshold would increase the prevalence of IFG, and this has indeed been demonstrated in various, mostly nonwhite populations (3,8). To what extent this would also enhance alignment between IFG and IGT in the classification of individuals and, more importantly, in the definition of risk for diabetes and CVD is less clear and is relevant for the implementation of preventive strategies.

The present analysis was undertaken to evaluate to what extent lowering the IFG diagnostic threshold would increase the concordance between the IFG and IGT categories with regard to classification of individuals, cardiovascular risk, and risk of progression to diabetes in an Italian population of white adults.

RESEARCH DESIGN AND METHODS — Our analysis was conducted with data obtained in a survey of employees of the Italian Telephone Company who resided in the province of Naples (6). All employees aged 35–59 years (n = 1,372) were eligible for this company-sponsored screening program for cardiovascular risk factors, and 95% of the target population was examined. Subjects were examined at their workplace by trained observers according to a standard protocol. The company allowed free time for the examination. Medical records were strictly confidential. In all, 44 subjects reported diabetes or hypoglycemic medication use and were not included in our analysis. A total of 1,245 male and female subjects without self-reported diabetes underwent a 75-g oral glucose tolerance test (OGTT); glucose was measured at fasting and 2-h postload on venous whole blood. The WHO (4) conversion tables were used to correct for differences in glucose measurements between plasma and venous whole blood. Fasting serum cholesterol and triglycerides were also measured by standard methods. Supine blood pressure was measured after a 5-min rest ac-
RESULTS — Complete datasets were available for 1,177 individuals without previously known diabetes. According to the WHO 1999 criterion, 38 people (3.2% of participants) had IFG; among these, 13 (34%) had abnormal postload glucose (11 IGT and 2 diabetes). With the ADA 2003 criterion, 114 people (9.7% of participants) had IFG; among these, 13 (34%) had abnormal postload glucose (28 IGT and 6 diabetes). The newly proposed IFG category identified 41% of all IGT subjects compared with 16.2% identified by the WHO criterion. Furthermore, 43.7% of those with diabetes by OGTT were previously classified “normal,” but now only 18.7% are so classified (Table 1). The improvement in accuracy was achieved at the cost of classifying more previous “normal” subjects as having IGT (from 2.3 to 7.3%). Thus, a lower diagnostic threshold for IFG captured more individuals with postload glucose abnormalities. However, nearly 50% of all cases of IGT still remained undetected. Moreover, of the 76 additional subjects diagnosed with IFG with the new criterion, only 21 had a positive OGTT in this population (Table 1).

As shown in Table 2, IFG and IGT were associated with an unfavorable risk factor profile for future diabetes and CVD. Indeed, subjects with IFG or IGT were older and had a higher BMI, blood pressure, and plasma lipid levels than subjects with neither condition. Subjects diagnosed with IGT (but not those diagnosed with IFG) had a significantly higher prevalence of risk factors, considered both singly and combined, as compared with normoglycemic people.

CONCLUSIONS — By lowering the diagnostic threshold for IFG from 6.1 to 5.6 mmol/l, the proportion of cases of IFG in our sample of relatively young whites increased by nearly 300%. Increases of 200–500% have been reported in population studies of whites and nonwhites (3,8). Despite this large increase in prevalence, IFG and IGT identify largely distinct groups in this study sample. A lower IFG diagnostic threshold identifies more people with abnormal postload glucose abnormalities (IGT and diabetes). However, even with the new criterion, nearly 50% of all cases of IGT still remain undetected.

IFG and IGT are not diseases per se and are totally asymptomatic. Nonetheless, we cannot exclude that by surveying a group of active workers who may be healthier than the general population, we may have underestimated the impact of lowering the IFG diagnostic threshold on the prevalence of these conditions and their associated background risk. Furthermore, we only examined people aged 35–59 years. The truncated age distribution and the relatively small sample size precluded analysis by age, sex, and BMI. Hence, it remains to be established if and how these factors interact with the new definition of IFG in the classification of people. Notwithstanding these limitations, the prevalence figures for IFG obtained in our study coincide with those reported in population-based studies (3,8) and the relation of obesity and age with glucose regulation status was confirmed, thereby providing internal and external support to the results.

Both IFG and IGT were associated with an unfavorable risk profile for diabetes and CVD. More than 80% of both groups had BMI, blood pressure, or
plasma lipid levels above optimal values. Moreover, the percentage of people with three or more risk factors (obesity, hypertension, dyslipidemia, or older age), and hence with a high risk of developing diabetes or CVD according to validated risk scores and population-based studies on the effectiveness of screening procedures (9–12), was significantly higher in the IGT group than in normoglycemic individuals. This was not always the case in subjects with IFG. These results suggest that people with IGT have a higher estimated risk and are in line with data on the incidence of diabetes and CVD in people with IFG reported in two recent prospective studies conducted using the ADA 2003 diagnostic criterion: one in Singapore on a population of Asian ethnicity (62% Chinese, 21% Malay, 15% Asian Indians) and the other in a relatively small group of middle-aged residents of Baltimore, Maryland (13,14).

The metabolic abnormalities of the postprandial phase are more relevant risk markers than previously thought (15,16), and the benefits of preventive strategies tested in people with IGT may be partly due to the correction of postprandial hyperglycemia (17). Even though OGGT is nonphysiological and postchallenge glucose is not the same as glucose after a mixed meal, it can be a better proxy than IFG for the hyperglycemic spikes occurring in the postprandial phase in nondiabetic people (18). Performing OGGT in people with fasting glucose of 5.7–6.9 mmol/L, as recommended by the Canadian Diabetes Association, would help with risk stratification and targeting of intervention in people with IFG, particularly when other risk factors for diabetes or IGT are present (9,19).

In conclusion, a better understanding of the prognostic significance of IFG is relevant for the implementation of preventive strategies and the evaluation of the cost/benefit balance of labeling three times more people with IFG. Based on the evidence available, it is not obvious that the benefits of preventive measures tested in people with IGT will apply, at least quantitatively, in people with IFG defined by the ADA 2003 criterion.

References