Short Reports

Receiver Operating Characteristic Analysis on Fasting Plasma Glucose, HbA_{1c}, and Fructosamine on Diabetes Screening

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Objective: To determine the efficacy of HbA_{1c} and fructosamine as alternatives to fasting plasma glucose (FPG) for diabetes screening. Research Design and Methods: Receiver operating characteristic (ROC) analysis was conducted on the above tests. Comparison among tests was based on the area under ROC curve of a test. World Health Organization criteria for classifying glucose tolerance status of the subjects was used. The study consisted of subjects (*n* = 583) who visited the clinic from September to October 1989 and all diabetic cases (*n* = 36) from November 1989 to March 1990, after excluding those <40 yr of age or with hypoglycemic therapies (469 were normal, 88 with impaired glucose tolerance [IGT], and 62 with diabetes). Results: Area under ROC curve of HbA_{1c} was not different from that of FPG. Area under curve of fructosamine was significantly smaller than that of FPG. For all tests, overall efficacy of a test to detect IGT and diabetes was considerably diminished compared with detection of diabetes alone. Conclusions: The discriminating ability of HbA_{1c} is almost the same as that of FPG, therefore HbA_{1c} is a good alternative to FPG. Fructosamine is not suitable for diabetes screening. *Diabetes Care* 14:1075–77, 1991

Plasma glucose measurement for diabetes screening has practical disadvantages: it is easily influenced by recent physical activity, food intake, and metabolic stress. HbA_{1c} and fructosamine, markers of glycemic control, have gained increasing attention as potential alternatives because their values are relatively stable regardless of the above conditions (1,2).

The purpose of this study was to assess the efficacy of HbA_{1c} and fructosamine as alternatives to fasting plasma glucose (FPG) for diabetes screening by receiver operating characteristic (ROC) analysis. The use of ROC analysis, based on the curve plotting the relationship between the true positive rate (TPR) and the false positive rate (FPR) over a range of cutoff points of a test, is increasing for comparison of the discriminating ability of various clinical tests (3–5). Comparison is based on the measurement of the area under the curve (AUC) of ROC. AUC represents the probability that a randomly chosen person with a disorder has a higher test score than a randomly chosen person without the disorder. Tests with greater AUCs are considered superior when ROC curves of tests do not overlap (3–5).

RESEARCH DESIGN AND METHODS

We examined individuals who visited the health checkup clinic of Tezukayama Hospital in Osaka City, Japan. The subjects, mostly white-collar workers, received checkups as an industrial health service sponsored by their employers. Consequently, most were asymptomatic. The study population consisted of two groups. Group 1 consisted of all subjects who visited the clinic from September to October 1989, and group 2 consisted of diabetic patients chosen from the examinees from November 1989 to March 1990. Those <40 yr old and diabetic subjects receiving hypoglycemic therapies such as oral medication or insulin were excluded. From group 1, 166 were excluded because of age, and 4 because of diabetic therapy. Group 1 was composed of 583 subjects (370 men, 213 women), and group 2 was composed of 36 subjects (33 men, 3 women). The mean ± SD age of the sample was 51.1 ± 7.33 yr (range 40–88 yr).

After an overnight fast, blood was drawn from the antecubital vein for FPG, HbA_{1c}, and fructosamine. Then, a 75-g oral glucose tolerance test (OGTT) was performed with glucose determinations at 60 and 120 min. FPG was measured by glucose oxidase (Auto Analyzer 7250, Hitachi, Tokyo), HbA_{1c} by high-performance liquid chromatography (HPLC; Toyo-Soda, Tokyo; with reagent HLC 723 GHb, Nihon-Kemifa, Tokyo) with a normal range of 3.5–6.5%, and fructosamine by Nitroblue-Tetrazolium (AU700, Olympus, Tokyo; fructosamine test, Roche, Tokyo) with a normal range of 2.1–2.8 mM. All measurement was performed by Shionogi (Osaka, Japan). For the examinees from November 1989 to March 1990, results of the OGTT were reported on STAT basis, and then HbA_{1c} and fructosamine were measured in the diabetic subjects (group 2) only. The subjects were classified as nondiabetic, impaired glucose tolerant (IGT), or diabetic according to World Health Organization criteria (6), which define diabetes as FPG ≥8 mM and/or plasma glucose (PG) at 120 min ≥11 mM, IGT as FPG <8 mM and PG at 120 min within 8–11 mM, and nondiabetic as FPG <8 mM and PG at 120 min <8 mM.

Sensitivity and specificity for each test were calculated over a range of cutoff points (FPG, every 0.56 mM from 4.48 to 10.08 mM; HbA_{1c}, every 0.2% from 4.6–7.0%; fructosamine, every 0.1 mM from 1.6–3.4 mM). The accuracy of the tests was compared by ROC curves. The AUC and standard error for each test was measured by the method of Hanley and McNeil (4,5), and the significant difference among AUCs was examined accordingly. For all statistical analyses, $P < 0.05$ was considered significant.

RESULTS

In group 1, 469 were classified as nondiabetic, 88 as IGT, and 26 as diabetic. There were no significant differences by *t* test between diabetic cases of group 1 and group 2 in age, body mass index, biochemical values such as FPG, PG at 60 and 120 min of OGTT, HbA_{1c}, fructosamine, serum cholesterol, and triglyceride. χ^2 tests were not significant for sex composition and lifestyle factors such as smoking and drinking habits between groups. Accordingly, diabetic cases of both groups were combined for the analysis.

Mean ± SD FPG was 5.06 ± 0.46 mM in nondiabetic subjects, 5.40 ± 0.54 mM in IGT subjects, and 7.42 ± 2.09 mM in diabetic subjects. Mean HbA_{1c} was 5.67 ± 0.41% in nondiabetic subjects, 5.85 ± 0.46% in IGT subjects, and 7.50 ± 1.49% in diabetic subjects. Mean fructosamine was 2.24 ± 0.26 mM in nondiabetic subjects, 2.33 ± 0.23 mM in IGT subjects, and 2.80 ± 0.47 mM in diabetic subjects. PG at 120 min of OGTT was 5.89 ± 1.10 mM in nondiabetic subjects,

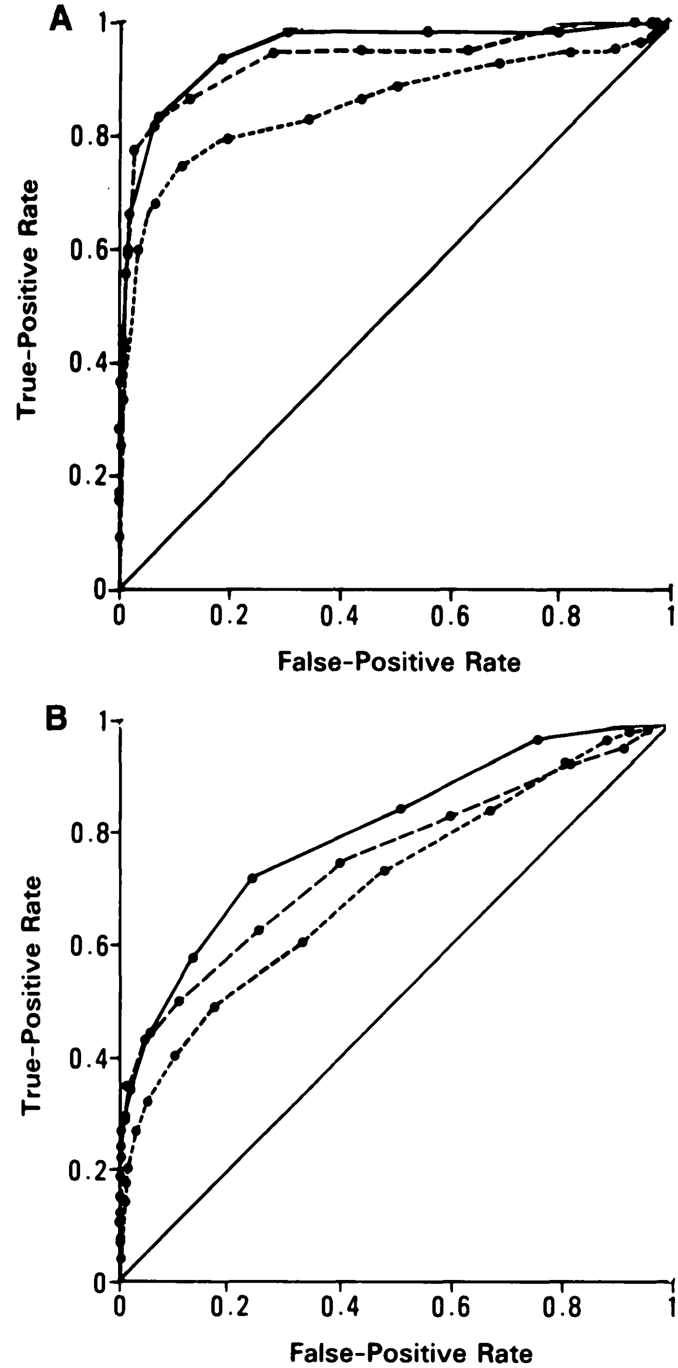

FIG. 1. Empirical receiver operating characteristics curves for fasting plasma glucose, HbA_{1c}, and fructosamine. *A*: diabetic as disease present, impaired glucose tolerance (IGT), and nondiabetic as disease absent. *B*: diabetic and IGT as disease present, nondiabetic as absent.

8.84 ± 0.83 mM in IGT subjects, and 15.06 ± 3.67 mM in diabetic subjects. One-way analysis of variance was significant for each test ($P < 0.05$).

Figure 1*A* shows ROC curves when considering diabetic as disease present and IGT and nondiabetic as disease absent. AUC of FPG (0.944 ± 0.020) was not different from that of HbA_{1c} (0.935 ± 0.022), but that of fructosamine (0.856 ± 0.031) was significantly smaller than those of the other two ($P < 0.05$). Figure 1*B* shows ROC curves when regarding both IGT and diabetic as disease present and nondiabetic as disease absent. AUC of FPG (0.785 ± 0.016) was larger than that of HbA_{1c} (0.753 ± 0.026), although it was not statistically significant. AUC of fructosamine (0.706 ± 0.026) was significantly smaller than that of FPG ($P < 0.05$) but not of HbA_{1c}.

CONCLUSIONS

Our study sample included all subjects who visited a community hospital–based health checkup clinic during a given period. There was no influence of hypoglycemic therapy on the results because diabetic subjects treated with insulin or oral hypoglycemic agents were excluded from the analysis. Prevalence of diabetes and distributions of FPG, HbA_{1c}, and fructosamine at each glucose tolerance status in this study were consistent with other studies in Japan (7–9). Accordingly, the sample of this study is considered representative of the Japanese population.

The ROC analysis indicated that the discriminating ability of fructosamine was far inferior to both FPG and HbA_{1c}, thus the use of fructosamine as a screening test for diabetes is of no value. The diagnostic accuracy of HbA_{1c} for detecting diabetes, judged by the size of AUC, was almost the same as that of FPG, suggesting that HbA_{1c} is an alternative to FPG.

Another implication from this study is that the efficacy of all tests in detecting diabetes and IGT was considerably diminished compared with detection of diabetes alone. AUC of each test became smaller for diabetes and IGT than for diabetes alone, due to the considerable overlap between the test values of IGT and those of nondiabetic subjects. The efficacy in detecting IGT cases by these screening methods is inherently limited.

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Received for publication 18 September 1990 and accepted in revised form 13 March 1991.

ACKNOWLEDGMENTS

This study was supported in part by a Grant-in-Aid from the Ministry of Education, Japan (No. 02770281) and by the Japanese Association of Social Insurance (Zenkoku Shakai-hoken Rengou).

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Altering Triglyceride Concentrations Changes Insulin-Glucose Relationships in Hypertriglyceridemic Patients

Double-Blind Study With Gemfibrozil With Implications for Atherosclerosis

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Objective: To determine whether reducing triglyceride concentrations in humans reduces serum insulin levels and consider the implications of this for the insulin resistance of hypertriglyceridemia. Research Design and Methods: Insulin and glucose levels were determined during an oral glucose tolerance test (OGTT) in 14