Age, BMI, and Race Are Less Important Than Random Plasma Glucose in Identifying Risk of Glucose Intolerance

The Screening for Impaired Glucose Tolerance Study (SIGT 5)

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OBJECTIVE — Age, BMI, and race/ethnicity are used in National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and American Diabetes Association (ADA) guidelines to prompt screening for pre-diabetes and diabetes, but cutoffs have not been evaluated rigorously.

RESEARCH DESIGN AND METHODS — Random plasma glucose (RPG) was measured and 75-g oral glucose tolerance tests were performed in 1,139 individuals without known diabetes. Screening performance was assessed by logistic regression and area under the receiver operating characteristic curve (AROC).

RESULTS — NIDDK/ADA indicators age >45 years and BMI >25 kg/m^2 provided significant detection of both diabetes and dysglycemia (both AROCs 0.63), but screening was better with continuous-variable models of age, BMI, and race and better still with models of age, BMI, race, sex, and family history (AROC 0.78 and 0.72). However, screening was even better with RPG alone (AROCs 0.81 and 0.72). RPG >125 mg/dl could be used to prompt further evaluation with an OGTT.

CONCLUSIONS — Use of age, BMI, and race/ethnicity in guidelines for screening to detect diabetes and pre-diabetes may be less important than evaluation of RPG. RPG should be investigated further as a convenient, inexpensive screen with good predictive utility.

Diabetes Care 31:884–886, 2008

Because development of type 2 diabetes is preceded by pre-diabetes, a state in which progression to diabetes can be prevented or delayed (1), the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the American Diabetes Association (ADA) recommend screening for pre-diabetes if individuals have risk factors of age >45 years and BMI >25 kg/m^2 and consideration for age <45 years if BMI is >25 kg/m^2 and another risk factor is present (2). However, screening is infrequent; in one survey, only 70% of patients had any glucose measurement over 3 years and 95% of the measurements taken were random plasma glucose (RPG) (3). Since there has been little critical examination of the conventional risk factors (age >45 years, etc.), we compared them with continuous-variable models and with RPG, an alternative screen that is convenient, inexpensive, and commonly performed.

RESEARCH DESIGN AND METHODS

— The Screening for Impaired Glucose Tolerance (SIGT) study from 1 January 2005 through 31 May 2007 involved 1,155 subjects aged 18–84 years who had no prior knowledge of diabetes, were not pregnant, nursing, or taking glucocorticoids, and were well enough to have worked the previous week. RPG was measured at the first visit, without a prior fast. The second visit (2–3 weeks later) included an oral glucose tolerance test (OGTT) begun before 11:00 A.M. following an overnight fast. Glucose was measured in the Grady Health System clinical laboratory. Glucose tolerance was defined by World Health Organization criteria; we focused on identifying diabetes and dysglycemia (diabetes, IGT, or impaired fasting glucose 110–125 mg/dl) because such levels confer increased mortality (4).

Discriminative effectiveness in 1,139 subjects with complete data was evaluated by receiver operating characteristic analysis, defining OGTT as the gold standard that identified all cases. Prediction of diabetes and dysglycemia was modeled by logistic regression as a continuous-variable function of risk factors with and without RPG; models were assessed by the *c* statistic, equivalent to area under ROC curves (AROCs). Calibration slope (agreement between predicted and observed probabilities) was calculated as [(model χ^2) − (model d.f. − 1)]/(model χ^2); slope close to 1 indicates good calibration while slope <1 indicates overfitting (5). Maximum prediction error was calculated as absolute difference between observed and calibrated probabilities.

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Received for publication on 30 November 2007 and accepted in revised form 15 February 2008.

Published ahead of print at http://care.diabetesjournals.org on 29 February 2008. DOI: 10.2337/dc07-2282.

Abbreviations: ADA, American Diabetes Association; AROC, area under the receiver operating characteristic curve; IGT, impaired glucose tolerance; NIDDK, National Institute of Diabetes and Digestive and Kidney Diseases; OGTT, oral glucose tolerance test; RPG, random plasma glucose.

Table 1—*Multivariate analysis of contributions of race, age, BMI, sex, family history, and RPG to risk of different categories of glucose intolerance*

	Diabetes		Diabetes or IGT		Diabetes or IGT or IFG 110 mg	
	Odds ratio	*P*	Odds ratio	*P*	Odds ratio	*P*
Model A						
Age (5 years)	1.39	<0.001	1.31	<0.001	1.33	<0.001
BMI (5 kg/m^2)	1.49	<0.001	1.39	<0.001	1.43	<0.001
Race (black)	1.46	0.198	1.40	0.032	1.22	0.193
Model B						
Age (5 years)	1.37	<0.001	1.27	<0.001	1.30	<0.001
BMI (5 kg/m^2)	1.42	0.001	1.32	<0.001	1.37	<0.001
Race (black)	2.05	0.028	1.68	0.002	1.47	0.018
Sex (female)	0.52	0.043	0.71	0.043	0.64	0.005
Family history	1.69	0.1	1.34	0.072	1.31	0.082
RPG (10 mg/dl)	1.53	<0.001	1.37	<0.001	1.40	<0.001

Data are odds ratios and probabilities, $n = 1139$ for each analysis. (ADA/NIDDK have recommended that screening be performed on individuals who have age >45 years and are overweight [BMI >25 kg/m^2] and be considered on the basis of age >45 years or age <45 years if BMI is >25 kg/m^2 and at least one other risk factor is present [family history of diabetes, gestational diabetes, or having had a baby weighing >9 lb, non-Caucasian, dyslipidemia, or hypertension] [2]). IFG, impaired fasting glucose 110–125 mg/dl.

Models were validated using bootstrap methods (5); 100 bootstrap replicates were drawn (with replacement) to calculate bias-corrected indexes of model fit and discrimination. Statistical analyses were conducted using S-Plus and STATA.

RESULTS — The subjects had average age 49 years, BMI 30.4 kg/m^2, and RPG 99 mg/dl and were 54% black and 63% female; 5.1% had diabetes, and 25.0% had dysglycemia. Compared with those with normal glucose tolerance, those with dysglycemia were older (53.5 vs. 46.0 years), were heavier (BMI 32.8 vs. 29.3 kg/m^2), and had higher RPG (111 vs. 94 mg/dl), all $P < 0.001$. We first evaluated the cutoffs of age >45 years, BMI >25 kg/m^2, and black race. Cutoffs of age >45 years + BMI >25 kg/m^2 carried a significant risk of both diabetes (odds ratio 3.44 [95% CI 1.80–6.56]) and dysglycemia (3.16 [2.35–4.25]), but these risks were not increased with the model age >45 years + BMI >25 kg/m^2 + black race (2.37 [1.39–4.04] and 2.10 [1.58–2.78]) because whites with diabetes or dysglycemia would be missed. Age >45 years + BMI >25 kg/m^2 provided a *c* statistic of 0.63 (0.58–0.69) for diabetes and 0.63 (0.60–0.66) for dysglycemia, and inclusion of black race lowered performance to 0.60 and 0.58, values that are statistically significant but weak for screening.

As continuous variables, age and BMI contributed independently to risk of diabetes, diabetes or IGT, and dysglycemia (Table 1, model A, all $P < 0.001$), while the trend for black race was nonsignificant except for diabetes or IGT. However, subjects of black race were significantly more likely to have a family history of diabetes (56 vs. 40%) or to be female (69 vs. 57%), both $P < 0.001$. In models containing age, BMI, race, sex, and family history along with RPG (Table 1, model B), the contributions of age, BMI, and race were all significant, but RPG also contributed independently, and the impact of 10 mg/dl higher RPG was greater than that of 5 additional years of age or 5 kg/m^2 more of BMI.

The usefulness of different screening strategies was evaluated by ROC analysis. AROCs for RPG alone as a screen for diabetes (0.81) and dysglycemia (0.72) were highly significant ($P < 0.001$) and significantly higher than both the age >45 years + BMI >25 kg/m^2 cutoffs (both 0.63) and the age + BMI + black race cutoffs (0.63 and 0.58), $P < 0.001$. Compared with screening with the continuous-variable model containing age + BMI + race + sex + family history, screening with RPG was slightly better for diabetes (0.81 vs. 0.78) and comparable for dysglycemia (both 0.72), all P = NS. AROCs for detection of diabetes and dysglycemia by RPG were comparable in subpopulations grouped by age, BMI, family history, etc., and at different times after meals; detection of diabetes was also unaffected by time of day, but detection of dysglycemia was less effective late in the day (not shown).

As an "index of concern," an RPG cutoff level of 125 mg/dl is likely to be cost-effective because of high specificity (6). It provided 93% specificity, 41% sensitivity, and a positive predictive value of 23% for identification of diabetes and 94% specificity, 23% sensitivity, and a positive predictive value of 51% for dysglycemia; such a level could be used to prompt further evaluation.

CONCLUSIONS — Glucose intolerance is more likely in individuals who are older, heavier, and have minority race/ethnicity, and such factors are often included in models to identify prevalent diabetes. AROCs ranged from 0.58–0.80 with risk factor models in previous studies (7–11), comparable with or lower than RPG alone in the present study. However, we find that combination of risk factors and RPG improves AROC significantly (not shown).

The strengths of our study include large sample size, sex and race balance, range of age and BMI, and a true screening paradigm—measuring RPG at a visit separate from the OGTT. Limitations include subject self-selection, although RPG AROCs were comparable in those with and those without a family history of diabetes (not shown). Further studies will be required to confirm our findings in unselected populations and in other racial/ethnic groups.

Age, BMI, and race/ethnicity can be used to identify risk of diabetes and dysglycemia, but the screening performance of recommended cutoffs is weak and lower than that of continuous-variable models. However, such models might be cumbersome to use, and their

performance is no better than RPG alone. Widespread screening via use of RPG levels could aid detection of unrecognized glucose intolerance, as needed to permit early initiation of preventive management.

Acknowledgments— This work was supported in part by grants DK07298, DK062668, RR017643, DK066204, and RR00039 from NIDDK and the National Center for Research Resources.

Parts of this study were presented in abstract form at the 67th annual meeting of the American Diabetes Association, Chicago, Illinois, 22–26 June 2007.

We thank Circe Tsui, Jack Kaufman, Rincy Varughese, Eileen Osinski, Elizabeth Barrera, and Aisha Bobcombe for their assistance.

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