Comparison of Body Size Measurements as Predictors of NIDDM in Pima Indians

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OBJECTIVE — To determine and compare the abilities of various anthropometric measurements to predict the development of non-insulin-dependent diabetes mellitus (NIDDM) in Pima Indian men and women.

RESEARCH DESIGN AND METHODS — A total of 290 male and 443 female Pima Indians were followed for up to 6 years for the development of NIDDM. A proportional hazards analysis was used to assess the ability of anthropometric measurements evaluated at baseline to predict NIDDM. Receiver operating characteristic (ROC) curves were used to compare individual variables in predicting NIDDM.

RESULTS — In separate models controlled for age and sex, body mass index (BMI), waist circumference, thigh circumference, waist-to-thigh ratio (WTR), weight, and percentage body fat (PBF) estimated by bioelectric resistance each predicted NIDDM, which developed in 30 men and 52 women. The highest incidence rate ratios (IRRs; for 1 SD of a variable) were for WTR in men and for PBF in women, although the confidence interval (CI) for PBF was wide. In stepwise analyses, WTR was the most significant predictor in men (IRR for 1 SD = 1.58, 95% CI = 1.20–2.07), and BMI was the most significant predictor in women (IRR for 1 SD = 1.65, 95% CI = 1.29–2.11). However, by ROC analyses, thigh circumference was the only variable significantly worse than WTR in men or BMI in women at predicting NIDDM.

CONCLUSIONS — Measurements such as waist circumference, WTR, weight, and BMI may be as useful as more complicated measurements, such as PBF by bioelectric resistance, for identifying groups of individuals whose body habitus places them at high risk of developing NIDDM.

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BMI, body mass index; CI, confidence interval; IRR, incidence rate ratio; NIDDM, non-insulin-dependent diabetes mellitus; PBF, percentage body fat; ROC, receiver operating characteristic; WTR, waist-to-thigh ratio.

Measures of generalized obesity, such as body mass index (BMI) (kg/m^2), and of central fat distribution, such as waist-to-thigh ratio (WTR), are associated with subsequent development of non-insulin-dependent diabetes mellitus (NIDDM) (1–7). Studies have shown that centralized obesity is associated with diabetes risk factors (8–12) and may be more predictive than overall obesity for the incidence of NIDDM (1–7).

The Pima Indians of the Gila River Indian Community of Arizona are obese and have a high incidence of NIDDM (13,14). In prior studies, BMI (14) and WTR (6) predicted the development of NIDDM in this population. If other body size measurements are better predictors or add significantly to the prediction of NIDDM, they might be used to identify those at risk for developing diabetes.

The aim of our present study is to evaluate the relative predictive ability of percentage body fat (PBF) estimated by bioelectric resistance (15) and to compare the ability of other anthropometric measurements, including waist circumference, thigh circumference, WTR, weight, and BMI, to predict the development of NIDDM in Pima Indians.

RESEARCH DESIGN AND METHODS

An epidemiological study of diabetes has been conducted in the Pima Indian population since 1965 (13). Subjects are invited to biennial examinations consisting of a medical history and a physical examination with measurements of height, weight, waist and thigh circumferences, and bioelectric resistance. A 75-g oral glucose tolerance test is performed with venous sampling at fasting and 2 h for measurement of plasma glucose concentrations, and subjects are classified according to World Health Organization criteria (16).

Starting in February 1988, bioelectric resistance data were collected on an RJL Systems body composition analyzer. PBF was calculated from an equa-

Table 1—*Correlations between body size measurements at the baseline examination*

	BMI	Waist circumference	Thigh circumference	WTR	Weight	PBF
Men						
BMI	1.000	—	—	—	—	—
Waist	0.900	1.000	—	—	—	—
Thigh	0.757	0.634	1.000	—	—	—
WTR	0.414	0.667	−0.143	1.000	—	—
Weight	0.963	0.891	0.774	0.386	1.000	—
PBF	0.866	0.840	0.651	0.468	0.858	1.000
Women						
BMI	1.000	—	—	—	—	—
Waist	0.914	1.000	—	—	—	—
Thigh	0.732	0.649	1.000	—	—	—
WTR	0.500	0.689	−0.096	1.000	—	—
Weight	0.957	0.900	0.768	0.441	1.000	—
PBF	0.813	0.844	0.566	0.590	0.790	1.000

Pearson product-moment correlations are shown. $P < 0.0001$ for each positive correlation; $P < 0.05$ for the negative correlations between WTR and thigh circumference.

tion derived from this population (17) using age, sex, weight, height, and bioelectric resistance measurements (15).

Subjects examined in this study included nonpregnant adult Pima Indians who attended biennial examinations in the Gila River Indian Community in Arizona and were at least 18 years old during the period from February 1988 to May 1994. All subjects had either normal or impaired glucose tolerance at baseline examination, had at least one follow-up visit during the study period, and were followed for a minimum of 1 year from the first examination until the last examination before May 1, 1994, or to the diagnosis of NIDDM, whichever occurred first.

Statistical analysis

Proportional hazards regression analysis was used to determine the ability of anthropometric measurements individually and in combination to predict the development of NIDDM. Age-adjusted (with a quadratic term) stepwise proportional hazards models were used to select those body size measurements in each sex that significantly predicted diabetes. Three-year cumulative incidence rates of NIDDM as functions of individual body size measurements were estimated from the survival function and parameter estimates of the proportional hazards model.

Because the anthropometric measurements were highly correlated, their predictive abilities were compared directly by receiver operating characteristic (ROC) curves. This method examines the ability of a variable to predict diabetes by depicting sensitivity as a function of 1 − specificity. The area under the ROC curve represents the probability of correctly distinguishing one individual, chosen at random from those who developed NIDDM, from another, chosen from those who did not develop NIDDM (18). The area under the curve ranges from 0.5, i.e., an ability to distinguish individuals that is equal to that of chance, to 1.0, or perfect predictive ability. The significance of the difference between the areas under two ROC curves was determined by the CLABROC program (19).

RESULTS — Of 1,428 potentially eligible subjects, 1,095 had an examination at least 3 years before the end of the study and, thus, had ample time for follow-up. The 658 (60.1%) with and the 437 (39.9%) without follow-up were of similar obesity (mean BMI = 33.6, 95% confidence interval [CI] = 33.0–34.2, and

Table 2—*Age-adjusted IRR for individual body size measurements as predictors of NIDDM among Pima Indians from the Gila River Indian Community of Arizona*

				IRR (95% CI)		
Variable	Men	Women	Both	Men	Women	Both
BMI (kg/m^2)	32.1 ± 7.4	34.5 ± 8.1	33.5 ± 7.9	1.40 (1.02–1.93)	1.65 (1.29–2.11)	1.54 (1.27–1.88)
Waist circumference (cm)	103.4 ± 19.8	109.0 ± 18.5	106.8 ± 19.2	1.57 (1.16–2.12)	1.49 (1.14–1.96)	1.53 (1.24–1.88)
Thigh circumference (cm)	62.0 ± 8.9	68.9 ± 8.3	66.2 ± 9.2	1.19 (0.82–1.73)	1.37 (1.05–1.79)	1.33 (1.05–1.68)
WTR	1.7 ± 0.2	1.6 ± 0.2	1.6 ± 0.2	1.58 (1.20–2.07)	1.30 (0.97–1.73)	1.44 (1.17–1.78)
Weight (kg)	94.5 ± 24.2	88.2 ± 22.3	90.7 ± 23.3	1.33 (0.98–1.82)	1.57 (1.23–2.01)	1.44 (1.19–1.74)
PBF (%)	27.2 ± 7.3	38.2 ± 5.4	33.8 ± 8.2	1.43 (0.94–2.19)	1.79 (1.24–2.58)	1.84 (1.29–2.64)

Data are means ± SD. Each variable was tested in a model containing that variable plus age and age^2 (men and women separately) or age, age^2, and sex (both). IRRs are given for an increase of 1 SD of the predictor variables for men, women, and both; 95% CIs were computed from the SE of each estimate.

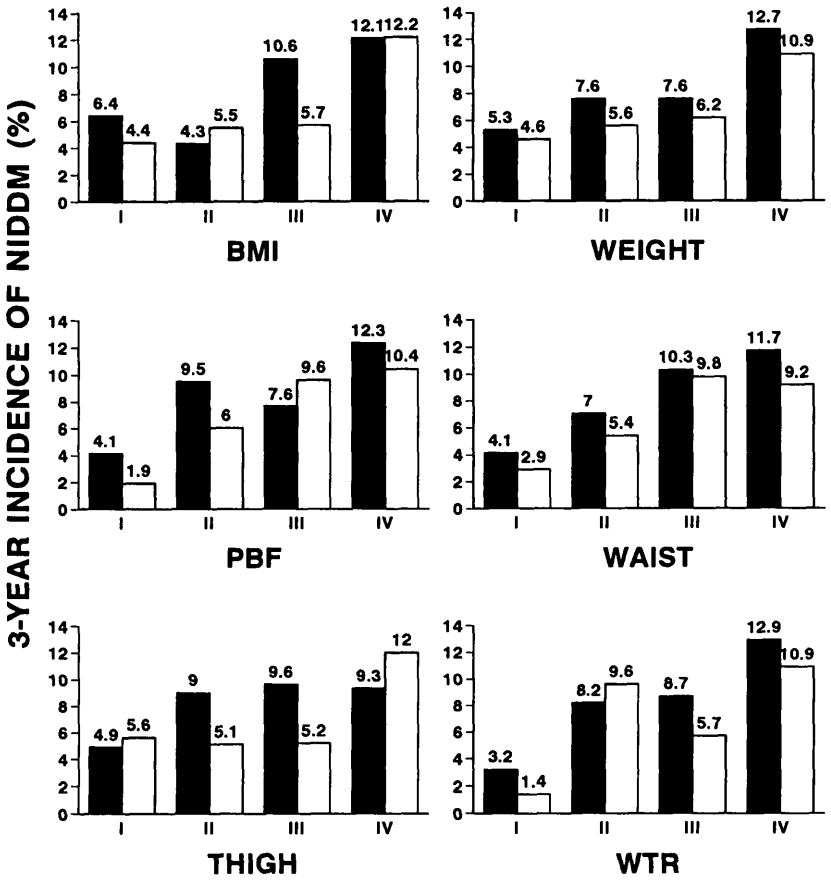

Figure 1—*Three-year cumulative incidence rates of NIDDM as a function of BMI, weight, PBF, waist and thigh circumferences, and WTR quartiles among residents of the Gila River Indian Community in Arizona.* ■, *men;* □, *women. The points dividing the quartiles for BMI were 26.9, 31.4, and 36.1 kg/m^2 (men) and 28.6, 33.5, and 39.3 kg/m^2 (women). The points dividing the quartiles for weight were 78, 92, and 109 kg (men) and 72, 84, and 101 kg (women). The points dividing the quartiles for PBF were 23.8, 28.0, and 31.9% (men) and 34.7, 38.7, and 42.2% (women). The points dividing the quartiles for waist were 91, 102, and 113 cm (men) and 96, 108, and 121 cm (women). The points dividing the quartiles for thigh were 56, 61, and 69 cm (men) and 64, 69, and 75 cm (women). The points dividing the quartiles for WTR were 1.5, 1.7, and 1.8 (men) and 1.4, 1.6, and 1.7 (women).*

mean BMI = 33.2, 95% CI = 32.4–34.0, respectively). An additional 75 subjects (BMI = 33.5, 95% CI = 31.6–35.3) returned within 3 years. Thus, 733 subjects (290 men and 443 women) were followed for a mean of 3.2 years (range 1.1–6.3 years), during which time 82 subjects, 30 men (10.3%) and 52 women (11.7%), developed NIDDM. The body size measurements were highly correlated (Table 1), and correlations were similar in men and women. Each measurement, controlled for age and sex, significantly predicted NIDDM ($P < 0.05$). The 3-year cumulative incidence of NIDDM predicted by BMI, weight, PBF, waist, thigh, and WTR, controlled for age, is shown in Fig. 1.

Table 2 shows the incidence rate ratios (IRR) for these variables analyzed as continuous variables. When the sexes were combined, there was a significant positive relationship between each measurement and the incidence of NIDDM ($P < 0.05$). When the sexes were analyzed separately, BMI, waist, and WTR significantly predicted NIDDM in men, while BMI, waist, thigh, weight, and PBF significantly predicted NIDDM in women (Table 2). For women alone and for the sexes combined, PBF had the highest IRR for a difference of 1 SD of a variable. However, because it also had the widest CI, the estimate is less precise. For men, WTR had the highest IRR and the smallest CI.

In age-adjusted stepwise proportional hazards analyses with all six anthropomorphic variables available to the model, WTR alone was selected as the most statistically significant predictor of NIDDM among men (IRR = 1.58, 95% CI = 1.20–2.07) and BMI alone was the most statistically significant predictor among women (IRR = 1.65, 95% CI = 1.29–2.11). While no other body size measurement significantly added to the prediction of diabetes in these models, this was partially due to the high correlations between variables. ROC analyses indicated that neither WTR in men nor BMI in women was significantly superior to any of the other measures, except for thigh circumference.

CONCLUSIONS— The relationship between obesity and NIDDM was determined prospectively in 733 subjects. Participation in the follow-up examinations was unrelated to obesity. Central body fat distribution is associated with elevated insulin and glucose concentrations, possibly as a result of an increased concentration of free fatty acids released into the portal vein by abdominal adipose tissue (20). Elevated portal-vein free fatty acids inhibit hepatic insulin clearance (21,22) and stimulate hepatic gluconeogenesis (23,24), resulting in hyperinsulinemia and hyperglycemia, which are risk factors for NIDDM (25).

High BMI is a strong risk factor for the development of diabetes in the Pima Indians (14). In our present study, anthropomorphic measurements other than BMI, such as weight, waist circumference, thigh circumference, WTR, and PBF, were equally predictive of diabetes when controlled for the known effects of age and sex (14). Studies conducted in other

populations have also found measurements of fat distribution to be predictive of diabetes and to add significantly to the prediction of general obesity (1–5,7). However, in contrast with these other studies, estimates of fat distribution in our present study were not significantly better than general estimates of obesity. Rather, the various measurements were equally predictive of diabetes, and fat distribution added little to the predictive ability of BMI alone. Perhaps the predictive value of BMI was equivalent to that of measures of abdominal obesity (waist circumference or WTR) because of a greater range in BMI in the Pima Indians than in other populations (14) or because the Pima population has a more uniform somatotype. For whatever reason, since ROC curve analyses indicate that the simple measures of weight, BMI, waist circumference, and WTR are not significantly different from PBF as predictors of NIDDM, these inexpensive measurements may be sufficient for assessing obesity as a risk factor for diabetes in this population. A better understanding of the relationship between NIDDM and obesity may point to the mechanisms involved in the development of diabetes in susceptible individuals. The high incidence and prevalence of NIDDM and obesity in this and other populations make research into these two conditions and their prevention of considerable priority.

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References

1. Ohlson LO, Larsson B, Svärdsudd K, Welin L, Eriksson H, Wilhelmsen L, Björntorp P, Tibblin G: The influence of body fat distribution on the incidence of diabetes mellitus: 13.5 years of follow-up of the participants in the study of men born in 1913. *Diabetes* 34:1055–1058, 1985
2. Lundgren H, Bengtsson C, Blohme G, Lapidus L, Sjöström L: Adiposity and adipose tissue distribution in relation to incidence of diabetes in women: results from a prospective population study in Gothenburg, Sweden. *Int J Obes* 13:413–423, 1989
3. Bergstrom RW, Newell-Morris LL, Leonetti DL, Shuman WP, Wahl PW, Fujimoto WY: Association of elevated fasting C-peptide level and increased intra-abdominal fat distribution with development of NIDDM in Japanese-American men. *Diabetes* 39:104–111, 1990
4. Haffner SM, Stern MP, Mitchell BD, Hazuda HP, Patterson JK: Incidence of type II diabetes in Mexican-Americans predicted by fasting insulin and glucose levels, obesity, and body fat distribution. *Diabetes* 39:283–288, 1990
5. Cassano PA, Rosner B, Vokonas PS, Weiss ST: Obesity and body fat distribution in relation to the incidence of non-insulin-dependent diabetes mellitus. *Am J Epidemiol* 136:1474–1486, 1992.
6. Lillioja S, Mott DM, Spraul M, Ferraro R, Foley JE, Ravussin E, Knowler WC, Bennett PH, Bogardus C: Insulin resistance and insulin secretory dysfunction as precursors of non-insulin-dependent diabetes mellitus. *N Engl J Med* 329:1988–1992, 1993
7. Chan JM, Rimm EB, Colditz GA, Stampfer MJ, Willett WC: Obesity, fat distribution, and weight gain as risk factors for clinical diabetes in men. *Diabetes Care* 17:961–969, 1994
8. Gerber LM, Madhavan S, Alderman MH: Waist-to-hip ratio as an index of risk for hyperglycemia among hypertensive patients. *Am J Prev Med* 3:64–68, 1987
9. Peiris AN, Sothmann MS, Hennes MI, Lee, MB, Wilson CR, Gustafson AB, Kissebah AH: Relative contribution of obesity and body fat distribution to alterations in glucose insulin homeostasis: predictive values of selected indices in premenopausal women. *Am J Clin Nutr* 49:758–764, 1989
10. McKeigue PM, Pierpoint T, Ferrie JE, Marmot MG: Relationship of glucose intolerance and hyperinsulinaemia to body fat pattern in South Asians and Europeans. *Diabetologia* 35:785–791, 1992
11. Haffner SM, Mitchell BD, Stern MP, Hazuda HP, Patterson JK: Public health significance of upper body adiposity for non-insulin-dependent diabetes mellitus in Mexican Americans. *Int J Obes* 16:177–184, 1992
12. Sosenko JM, Kato M, Soto R, Goldberg RB: A comparison of adiposity measures for screening non-insulin-dependent diabetes mellitus. *Int J Obes* 17:441–444, 1993
13. Knowler WC, Bennett PH, Hamman RF, Miller M: Diabetes incidence and prevalence in Pima Indians: a 19-fold greater incidence than in Rochester, Minnesota. *Am J Epidemiol* 108:497–505, 1978
14. Knowler WC, Pettitt DJ, Savage PJ, Bennett PH: Diabetes incidence in Pima Indians: contributions of obesity and parental diabetes. *Am J Epidemiol* 113:144–156, 1981
15. Lukaski HC, Johnson PE, Bolonchuk WW, Lykken GI: Assessment of fat free mass using bioelectrical impedance measurements of the human body. *Am J Clin Nutr* 41:810–817, 1985
16. World Health Organization: *Diabetes Mellitus: Report of a WHO Study Group.* Geneva, World Health Org., 1985 (Tech. Rep. Ser., no. 727)
17. Rising R, Swinburn B, Larson K, Ravussin E: Body composition in Pima Indians: validation of bioelectrical resistance. *Am J Clin Nutr* 53:594–598, 1991
18. Hanley JA, McNeil BJ: The meaning and use of the area under a receiver operating characteristic curve. *Radiology* 143:29–36, 1982
19. Metz CE, Wang P, Kronman HB: A new approach for testing the significance of differences between ROC curves measured from correlated data. In *Proc. VIIIth Conference on Information Processing in Medical Imaging.* Deconinck F, Ed. The Hague, Nijoff, 1984, p. 432–445
20. Björntorp P: Abdominal obesity and the development of noninsulin-dependent diabetes mellitus. *Diabetes Metab Rev* 4:615–622, 1988

21. Faber OK, Christensen K, Kehlet H: Decreased insulin removal contributes to hyperinsulinemia in obesity. *J Clin Endocrinol Metab* 53:618–621, 1981
22. Bonora E, Zavaroni J, Coscelli C, Butturini U: Decreased hepatic insulin extraction in subjects with mild glucose intolerance. *Metabolism* 32:438–446, 1983
23. Ferrannini E, Barrett EJ, Bevilacqua S, DeFronzo RA: Effect of fatty acids on glucose production and utilization in man. *J Clin Invest* 72:1737–1744, 1983
24. Bevilacqua S, Bonadonna R, Buzzigoli G, et al.: Acute elevation of free fatty acid levels leads to hepatic insulin resistance in obese subjects. *Metabolism* 36:502–506, 1987
25. Knowler WC, Pettitt DJ, Saad MF, Bennett PH: Diabetes mellitus in the Pima Indians: incidence, risk factors and pathogenesis. *Diabetes Metab Rev* 6:1–27, 1990