Do Measures of Body Fat Distribution Provide Information on the Risk of Type 2 Diabetes in Addition to Measures of General Obesity?

Comparison of anthropometric predictors of type 2 diabetes in Pima Indians

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OBJECTIVE — To investigate which anthropometric measurements of obesity best predict type 2 diabetes in a population of Pima Indians and whether additional information on diabetes risk could be obtained by combining measures of general obesity with measures of body fat distribution.

RESEARCH DESIGN AND METHODS — We conducted a prospective study of 624 men and 990 nonpregnant women >18 years of age without diabetes. Subjects were followed a mean of 5.25 years for the development of type 2 diabetes (using 1997 American Diabetes Association criteria).

RESULTS — A total of 322 new cases of type 2 diabetes (107 men and 215 women) were diagnosed during follow-up. Baseline obesity measurements were highly correlated and predicted diabetes in proportional hazards models adjusted for age. BMI had the highest hazard ratio in men and women, with age-adjusted hazard ratios per SD of 1.73 (95% CI 1.44–2.07) and 1.67 (1.45–1.91), respectively. According to receiver-operating characteristic analysis, BMI and waist-to-height ratio were the best predictors of diabetes in men, while in women BMI, waist-to-height ratio, waist circumference, and waist-to-thigh ratio were the best predictors. The predictive abilities of models containing BMI were not significantly improved by including other measures of general obesity or measures of the body fat distribution.

CONCLUSIONS — Throughout its range, BMI was an excellent predictor of type 2 diabetes risk in Pima Indians and was not significantly improved by combining it with other measures of general adiposity or body fat distribution.

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General measures of obesity (weight, BMI, and percent body fat) and measures of central fat distribution (waist circumference, waist-to-hip ratio, waist-to-thigh ratio, and waist-to-height ratio) predict the risk of type 2 diabetes in prospective studies regardless of age or ethnicity (1–8).

The strong association between the quantity of intra-abdominal fat and metabolic disorders, however, has led some to suggest that anthropometric measurements that describe central fat distribution (such as waist circumference) may be better than general measures of obesity as predictors of diabetes. For example, in the San Antonio Heart Study (5), the waist circumference was the best predictor of diabetes risk in a population of Mexican Americans among the variables BMI, waist-to-hip ratio, hip circumference, and the sum of skinfold thicknesses. In other prospective studies (3,4,7) the risk of diabetes increased with increasing quantities of central fat within a BMI category, suggesting that both measures are important in predicting the risk of diabetes. Two studies have demonstrated that the effect of these measures of body fat distribution depends on the value of BMI (5,6). The San Antonio study showed a stronger effect of body fat distribution on diabetes risk in subjects with a BMI <27 kg/m^2 (odds ratio per 1-SD difference = 6.0; 95% CI 1.8–20.1) compared with those with a BMI >27 kg/m^2 (1.7, 1.1–2.7) (5). However, Ohlson (6) demonstrated the opposite effect, with the strongest effect of increasing waist-to-hip ratio tertiles on the risk of type 2 diabetes in the subjects within the highest BMI tertile.

The aim of the present study was to examine whether general measures of obesity or measures of body fat distribution were more important in determining the risk of type 2 diabetes in Pima Indians. A previous analysis in this population suggested that the best predictors of diabetes were BMI, waist circumference, and waist-to-thigh ratio in men and waist circumference, thigh circumference, weight, and percent body fat in women (1). When

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Abbreviations: ADA, American Diabetes Association; HRR, hazard rate ratio; OGTT, oral glucose tolerance test; ROC, receiver-operating characteristic.

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

these anthropometric measurements were compared using receiver-operating characteristic (ROC) analysis, none was superior to the others (1). The present study extends these analyses to a longer follow-up time and includes almost four times as many incident cases of diabetes. This provides additional statistical power not only to compare anthropometric variables, but also to assess whether combining measures of body fat distribution with a measure of general obesity improves the ability to predict diabetes. We were also able to explore whether BMI modified the effect of body fat distribution on diabetes incidence.

RESEARCH DESIGN AND METHODS

— The population studied was part of an ongoing epidemiological study of diabetes conducted in Pima Indians since 1965 (9). People from the community are invited to participate in biennial examinations consisting of a focused medical history, physical examination, and laboratory tests.

Trained investigators obtained the anthropometric data. Measurements were taken without the subjects wearing shoes or heavy outdoor clothing. Height was measured to the nearest centimeter using a stadiometer with the subject standing erect on the floor with the back against a vertical mounted ruler. Weight was obtained from an electronic digital scale. The hip circumference was measured at the maximum circumference around the hips, and the thigh circumference was measured under the gluteal fold with the patient standing. Waist circumference was obtained at the level of the umbilicus with the subject supine. The Bioelectric resistance (RJL systems, Detroit, MI) was used to calculate percent body fat from an equation for fat-free mass derived from the Pima population (see APPENDIX). A 75-g oral glucose tolerance test (OGTT) was performed after an overnight fast in all subjects. Plasma glucose was measured using the glucose oxidase method with a glucose analyzer.

Subjects were defined as having diabetes if they met the American Diabetes Association (ADA) criteria (fasting plasma glucose ≥7.0 mmol/l or 2-h blood glucose after a 75-g OGTT ≥11.1 mmol/l) or if there was documented evidence of diabetes in the medical records. The date of diagnosis of diabetes was the date on which the subject had a diagnostic fasting or 2-h blood glucose or the earliest date on which the diagnosis of diabetes had been made if the participant was diagnosed between biennial examinations.

All nonpregnant Pima Indians ≥18 years of age with the anthropometric measurements of interest (weight, height, waist circumference, thigh circumference, hip circumference, and bioelectrical impedance) and who were free of diabetes at their baseline examination were eligible for this analysis, providing they had at least one follow-up visit before 1 April 2002. Subjects were followed from their first examination with complete data (August 1990, when all the relevant variables were being measured) until the development of diabetes or to the time of their last diabetes-free examination before 1 April 2002.

Statistical analysis

The relationship between anthropometric variables was tested using Spearman's correlation coefficient. Sex-specific proportional hazards models were used to determine the ability of each anthropometric measurement to predict type 2 diabetes. Age and age-squared terms were included in each model, as diabetes incidence did not increase linearly with age. For each anthropometric variable the hazard rate ratios (HRRs) are presented per sex-specific SD difference. Anthropometric variables that were not normally distributed were log transformed before standardization. ROC analysis was used to compare the ability of the age-adjusted variables to predict type 2 diabetes. The ROC curve tests the ability of a variable to predict an outcome by plotting sensitivity against 1-specificity. Sensitivity and specificity were computed assuming that each variable was positively related to the incidence of diabetes. The area under the curve represents the probability of being able to identify an individual who will develop the outcome of interest, in this case diabetes. For variables that positively predict the outcome, areas under the ROC curve vary from >0.5 to 1.0 (with 1.0 representing perfect prediction). An area of 0.5 indicates no predictive value, and one <0.5 indicates that the variable is negatively predictive (i.e., a lower value is related to greater probability of the outcome developing).

As the anthropometric measurements were highly correlated, the HRRs obtained from including more than one variable in a proportional hazards model were difficult to interpret because of colinearity (10). ROC analysis was used to determine whether a model containing a combination of anthropometric variables would be better able to discriminate between subjects who were likely to develop diabetes and those who would not develop the disease. The area under the ROC curve from the prediction of age-adjusted models containing age and BMI in each sex were compared with the area under the ROC curve from the prediction of more complex models containing age, BMI, one anthropometric measure of body fat distribution, and the interaction term between that measurement and BMI. The equivalence of the ROC curve areas was compared using the method of DeLong (11), which accounts for the correlation among variables. To explore modification of the strength of measures of body fat distribution to predict diabetes risk at differing BMI levels, sex-specific BMI quartiles were generated and ROC analysis comparing the anthropometric measurements was repeated after restricting the population to men and women with a BMI in the first or fourth quartiles.

RESULTS

— Altogether 1,614 subjects (624 men and 990 women) were evaluated, and 322 (107 men and 215 women) new cases of diabetes were diagnosed during the follow-up period, averaging 5.25 years per person.

At baseline, men were significantly taller, heavier, and had higher waist-to-thigh and waist-to-hip ratios than women. The women, however, had a higher BMI, waist circumference, and percent fat than men (Table 1). The baseline anthropometric obesity measurements were highly correlated with each other in men and women (Table 2).

Subjects who developed diabetes were older and more obese at baseline examination than those who did not develop the disease. In prospective analysis, each of the anthropometric variables was a good predictor of type 2 diabetes (Table 1). BMI had the highest HRR in both sexes (HRR per SD 1.73, 95% CI 1.44–2.07 in men and 1.67, 1.45–1.91 in women). Of the measures of body fat distribution, the waist-to-height ratio was the best predictor of diabetes in men and women (1.57, 1.34–1.85 and 1.61, 1.41–1.84, respectively). BMI continued to have the highest HRR in men and women, even

Table 1—*Means ± SD and age-adjusted* hazard ratios (95% CIs) for type 2 diabetes per SD difference for each anthropometric marker of obesity presented by sex*

	Men		Women	
n	624		990	
BMI (kg/m^2)†	32.7 ± 7.1	1.73 (1.44–2.07)	34.9 ± 8.0	1.67 (1.45–1.91)
Weight (kg)†	97.3 ± 23.7	1.66 (1.37–2.01)	89.6 ± 21.5	1.60 (1.39–1.83)
Waist-to-height ratio	0.61 ± 0.09	1.57 (1.34–1.85)	0.68 ± 0.12	1.61 (1.41–1.84)
Waist (cm)	105 ± 16.8	1.56 (1.32–1.85)	109 ± 18.6	1.58 (1.39–1.80)
Percent fat	33.3 ± 6.7	1.62 (1.32–1.99)	47.0 ± 7.8	1.58 (1.34–1.83)
Hip (cm)†	110 ± 13.3	1.51 (1.28–1.78)	120 ± 16.5	1.59 (1.38–1.82)
Thigh (cm)†	62.9 ± 7.4	1.47 (1.21–1.79)	67.1 ± 7.4	1.33 (1.15–1.53)
Waist-to-hip ratio	0.95 ± 0.06	1.56 (1.27–1.90)	0.90 ± 0.06	1.24 (1.07–1.45)
Waist-to-thigh ratio†	1.70 ± 0.17	1.51 (1.25–1.82)	1.60 ± 0.22	1.47 (1.27–1.69)

Data are means ± SD or HRR (95% CI). *Age included as a continuous and squared term in determining the hazard ratios. †Variables log transformed prior to standardization and use in determining hazard ratio.

with adjustment for glucose tolerance at the baseline examination.

The anthropometric variables were then compared using ROC analysis. In men there was no statistically significant difference between BMI and the waist-to-height ratio in the ability to distinguish between subjects who developed type 2 diabetes and those who did not. In women there was no statistically significant difference between BMI and the waist circumference, waist-to-height ratio, and the waist-to-thigh ratio in predicting type 2 diabetes (Table 3 and Fig. 1).

When the analysis was restricted to subjects with a BMI in the first quartile (18.5–28.0 kg/m^2 in men and 18.2–29.3 kg/m^2 in women), results similar to those of the full population were obtained. Measures of body fat distribution were not superior to measures of general obesity in their ability to determine who might develop diabetes (Table 4). In both men and women no measures of obesity proved to be superior at predicting diabetes when the analysis was restricted to subjects with a BMI in the fourth quartile (36.2–64.0 kg/m^2 in men and 39.0–66.6 kg/m^2 in women). In men none of the anthropometric measures of obesity remained significant predictors of diabetes risk once analysis was restricted, only to subjects in the highest BMI quartile (Table 4).

In men and women, age-adjusted models for predicting diabetes containing BMI were not improved by adding other measures of general adiposity or body fat distribution with or without their interaction term (data not shown).

CONCLUSIONS — In a previous analysis of 733 Pima Indians (30 incident cases of type 2 diabetes in men and 52 in women) using stepwise proportional hazard analysis, BMI was the best predictor of diabetes in women (HRR per SD 1.68, 95% CI 1.29–2.11), while waist-to-thigh ratio was the best predictor in men (1.58, 1.20–2.07). Weight, BMI, percent fat, waist circumference, and waist-to-thigh ratio were equally good predictors of diabetes in men and women when they were compared using ROC analysis (1).

The present study extends these observations to a larger number of individuals with almost four times as many incident cases of type 2 diabetes, which increased the power of the analysis. There was also a longer mean follow-up time (5.25 compared with 3.2 years), allowing the incidence of type 2 diabetes to be assessed over a longer time period. In the present analysis, while all the anthropometric measures of obesity evaluated were good predictors of diabetes in age-adjusted proportional hazard models, BMI and waist-to-height ratio were the best measures of general obesity and distribution of obesity in men and women. Using ROC analysis they were equivalent in their ability to differentiate between

Table 2—*Spearman's correlation coefficients between various anthropometric markers of obesity*

	Weight	BMI	Percent fat	Waist	Hip	Thigh	Waist-to-height	Waist-to-hip	Waist-to-thigh
Weight	1.000	*0.953*	*0.854*	*0.862*	*0.945*	*0.766*	*0.796*	*0.297*	*0.464*
BMI	0.943		*0.871*	*0.888*	*0.951*	*0.734*	*0.879*	*0.343*	*0.518*
Percent fat	0.859	0.874		*0.857*	*0.885*	*0.678*	*0.837*	*0.373*	*0.530*
Waist	0.934	0.948	0.902		*0.904*	*0.606*	*0.980*	*0.659*	*0.756*
Hip	0.945	0.929	0.855	0.913		*0.735*	*0.871*	*0.302*	*0.536*
Thigh	0.808	0.786	0.735	0.728	0.815		*0.557*	*0.096*	*−0.014**
Waist-to-height	0.849	0.944	0.880	0.968	0.860	0.676		*0.674*	*0.772*
Waist-to-hip	0.587	0.635	0.648	0.763	0.469	0.355	0.774		*0.771*
Waist-to-thigh	0.483	0.523	0.559	0.650	0.449	0.021*	0.664	0.739	*1.000*

Correlation coefficients for men are presented in the lower left side of the table, while those for women are in the upper right corner in italics. All correlations have a *P* value <0.01 unless otherwise stated; **P* value >0.05 for Spearman's coefficient.

Table 3—*ROC areas for each of the age-adjusted anthropometric variables by sex*

	ROC area	
	Men	Women
BMI	**0.700**	**0.695**
Waist-to-height ratio	**0.689**	**0.695**
Waist	0.679	**0.689**
Hip	0.676	0.682
Weight	0.674	0.684
Percent fat	0.657	0.677
Thigh	0.644	0.646
Waist-to-thigh ratio	0.638	**0.668**
Waist-to-hip ratio	0.633	0.644

The anthropometric variables equivalent to BMI in predicting type 2 diabetes for men and women are presented in bold. Equivalence of ROC curve areas for anthropometric measurements with that of BMI was established by comparing the area under the ROC curves using the method suggested by DeLong (11) for correlated data. Variables were considered equivalent to the BMI if in the comparison of the ROC curve areas *P* value for χ^2 statistic was >0.05.

subjects who would and would not develop type 2 diabetes.

In Mexican Americans (5), U.S. Nurses (4), older women from Iowa (3), and Swedish men (6) and women (7), there is a significant increase in the risk of type 2 diabetes with increasing waist circumference or waist-to-hip ratio measurements within BMI categories, suggesting that both measures of general obesity and body fat distribution are important in assessing diabetes risk. As the measures of general obesity and body fat distribution were highly correlated (1,5,6), an increasing risk of diabetes with increasing waist circumference, waist-to-thigh ratio, or waist-to-hip ratio within a BMI category may also have resulted from increasing BMI within each category (and not just an increase in the measure of body fat distribution).

To identify whether these measures of body fat distribution were important determinants of risk, we compared age-adjusted models containing one variable with more complex models containing multiple anthropometric variables using ROC analysis. In men and women we found little improvement in our ability to discriminate between subjects who would and would not develop type 2 diabetes by combining BMI with other measures of general obesity or body fat distribution and their interaction terms. This suggested that once the BMI was known, little additional information on type 2 diabetes risk is obtained from other measurements.

It has been suggested that the inability to demonstrate the importance of body fat distribution on diabetes risk in the Pima Indians may be a result of effect modification between BMI and measures of body fat distribution, with measures of body fat distribution being more important in the less obese subjects (5). However, this was not found in several other studies examining this issue. The study of Swedish men demonstrated an opposite relationship between the waist-to-hip ratio and BMI, with the waist-to-hip ratio having the most dramatic effect on diabetes risk in the subjects with the highest BMI (6). In the Nurses Health Study (4) and the study of Iowa women (3) there was no modification of the effect of body fat distribution on diabetes risk by BMI category. When our analysis of the Pima population was restricted to subjects with a BMI in the lowest sex-specific quartiles, there was no advantage of measures of body fat distribution over the general measures of obesity in men or women. For men in the highest BMI quartile, all measurements lost their ability to predict type 2 diabetes. This would suggest that the effect of body fat distribution and other measures of general obesity become less important at high BMI levels but are not better than the BMI at lower BMI levels.

The importance of measures of body fat distribution in predicting diabetes may vary with age and ethnicity. Previous studies evaluating the effect of body fat on diabetes risk have predominantly explored the relationship in middle-aged and elderly Caucasian populations. The Pima Indians in this study had a lower mean age at baseline than participants in most of these other studies.

In a study of Native Canadians from several tribes, BMI was the strongest determinant of diabetes (12). The population was similar in age to ours. BMI was one of the most significant determinants of diabetes in stepwise regression analysis in this population, and waist-to-hip ratio and the subscapular-to-triceps ratio (measures of central adiposity) did not provide information on diabetes risk that was independent of BMI (12). In a Jamaican cohort (predominantly black), BMI, waist circumference, waist-to-hip ratio, and waist-to-thigh ratio were excellent predictors of diabetes, and none was superior when age- and sex-adjusted models containing each variable were compared. The additional effect of measures of body fat distribution on diabetes risk once a measure of general obesity had been obtained was not reported (2).

Advantages of our study include the use of a large population-based sample with a large number of subjects developing diabetes. A large number of anthropometric measurements, including bioelectric impedance, was obtained by trained investigators. Diabetes was determined by a combination of an OGTT and review of patient medical records and did not depend on self-reporting of the disease.

The study population consisted of Native Americans, with predominantly Pima or Tohono O'Odham heritage, and the extent to which the results are generalizable to other populations is uncertain. Within this population the anthropometric measures of body fat distribution and general adiposity were highly correlated; this may have resulted in too little heterogeneity in body fat distribution within BMI groups to demonstrate the importance of body fat distribution on diabetes risk.

Of the anthropometric variables examined, BMI and waist-to-height ratio (one a measure of general obesity and the other body fat distribution) were excellent predictors of type 2 diabetes risk in Pima Indians. Little additional information on diabetes risk in men or women was gained from including other measures of general obesity or body fat distribution once BMI was known.

APPENDIX

Derivation of predictive equations for percent body fat in Pima Indians

Predictive equations for fat-free mass were developed from the bioelectrical impedance measurement using the fat-free mass estimate obtained from dual-energy X-ray absorbiometry (DEXA) as the gold standard measurement.

Resistance and reactance measurements have been obtained with the Body Composition Analyzer System (Model BIA-103; RJL systems, Detroit, MI) since 1988. Disposable electrodes were placed on the right hand and right foot according to the manufacturer's directions. DEXA measurements (DPX-IQ; Lunar, Madison, WI) were performed on the same day. Subjects wore hospital gowns for DEXA

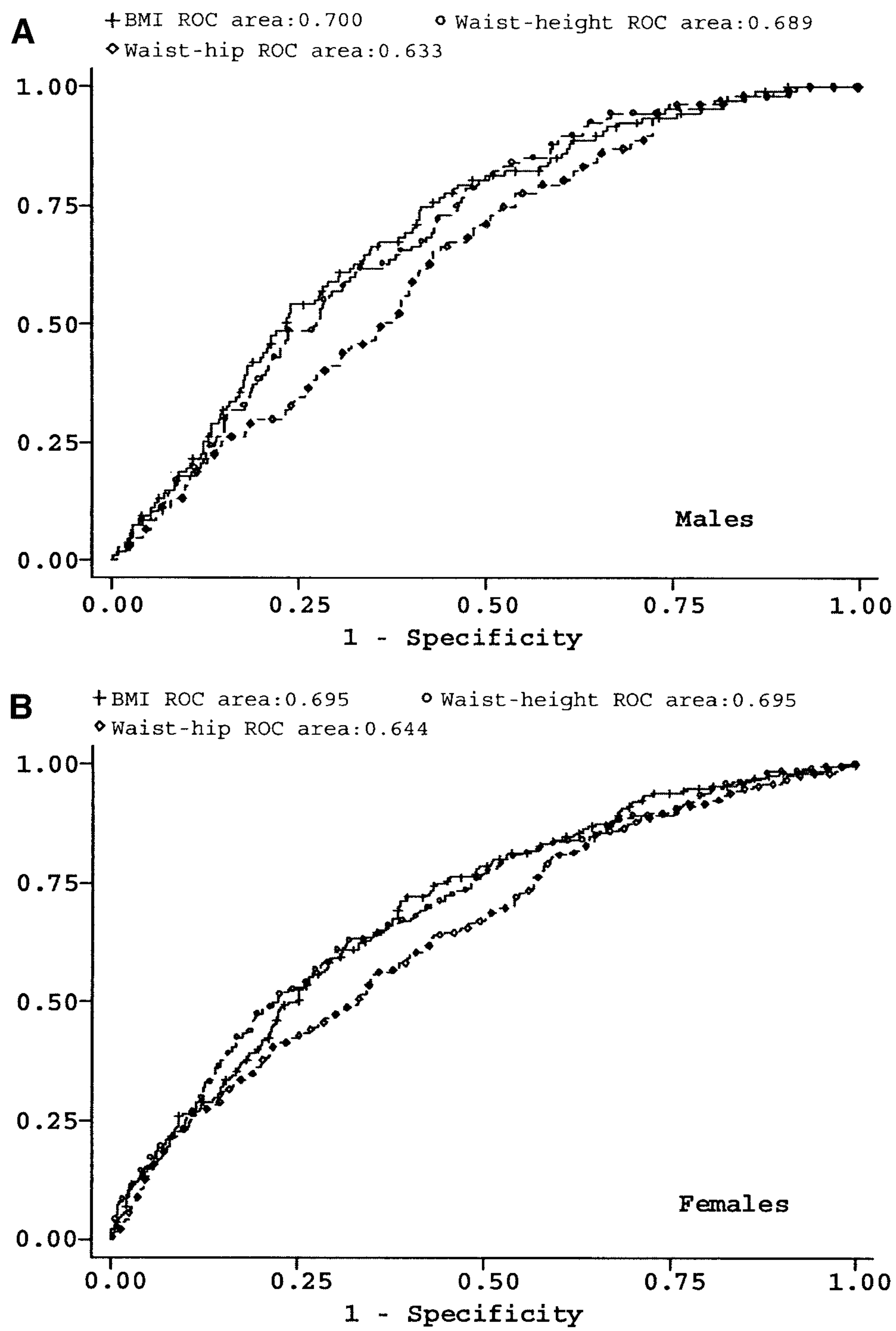

Figure 1—*ROC curves for BMI, waist-to-height ratio, and waist-to-hip ratio for prediction of type 2 diabetes in Pima men* (A) *and women* (B)*.*

scans after removing jewelry and other metal objects. If the subject was able to fit into the scanning area, the operator performed a whole body scan. In larger subjects who did not fit into the scanning area, a saggital half-body scan was performed (13). The percent body fat was obtained from the DEXA scan, and the fat-free mass was calculated using body weight.

Altogether, 308 (132 men and 176 women) nonpregnant subjects without diabetes (by 1997 ADA criteria), 18–43 years of age, with a bioelectrical impedance measurement, DEXA-derived percent body fat, and normal renal function at the time of their examination were used to derive the predictive equations.

The predictive equations were obtained from regression analysis, with the DEXA-derived fat-free mass as the dependent variable. Models were derived using combinations of height, resistance, reactance, age, weight, and sex. The coeffi-

Table 4—*ROC areas for each of the age-adjusted anthropometric variables by sex*

	BMI first quartile*		BMI fourth quartile*	
	Men	Women	Men†	Women
n	156 (9)	249 (26)	156 (49)	247 (87)
BMI	**0.655**	**0.661**	**0.519**	**0.590**
Waist-to-height ratio	**0.636**	**0.624**	**0.490**	**0.610**
Waist	**0.664**	0.609	**0.482**	**0.606**
Hip	**0.605**	**0.655**	**0.500**	**0.574**
Weight	**0.652**	0.631	**0.496**	**0.583**
Percent fat	**0.657**	**0.660**	**0.461**	**0.571**
Thigh	0.496	0.610	**0.492**	**0.559**
Waist-to-thigh ratio	**0.742**	**0.589**	**0.488**	**0.590**
Waist-to-hip ratio	**0.672**	0.569	**0.467**	**0.594**

Anthropometric variables equivalent to the BMI in predicting type 2 diabetes for men and women in the highest and lowest BMI quartiles are presented in bold. New cases of diabetes presented in parenthesis beside sample size. *For men first BMI quartile 18.5–28.0 kg/m^2, fourth BMI quartile 36.2–64.0 kg/m^2; for women first BMI quartile 18.2–29.3 kg/m^2, fourth BMI quartile 39.0–66.56 kg/m^2. †ROC curve areas were not significantly different from 0.5 and had a predictive ability equal to chance. Equivalence of ROC curve areas for anthropometric measurements with that of BMI was established by comparing the area under the ROC curves using the method suggested by DeLong for correlated data.

cient of determination (R^2) was used to measure the explanatory power and goodness of fit, and the root mean square error (RMSE) was used to determine the precision of each model. Interaction terms for sex were included to examine the need for sex-specific models. Analysis of residuals was used to determine whether the final models met the assumptions of linear regression.

The final model selected included age, sex, weight, and the resistive index (height^2/resistance). As there was significant interaction between the resistive index and sex, gender-specific models were derived. Plots of the residuals of these models did not demonstrate any heteroskedacity. The final models used in our analysis are presented below.

Men

Fat-free mass = 12.5 − 0.03 (age) + 0.22 (weight) + 0.50 (height^2/resistance)

$R^2 = 0.87$; RMSE = 2.97 kg

Women

Fat-free mass = 7.60 − 0.03 (age) + 0.23 (weight) + 0.44 (height^2/resistance)

$R^2 = 0.92$; RMSE = 2.25 kg

where age is measured in years, weight in kilograms, height in centimeters, and resistance in ohms.

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