Simple skinfold-thickness measurements complement conventional anthropometric assessments in predicting glucose tolerance[1–3]

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ABSTRACT

Background: Skinfold-thickness measurements are considered to have limited clinical utility.

Objective: To assess whether skinfold-thickness measurements may be a useful adjunct to conventional anthropometric assessments in predicting glucose and insulin regulation, we studied responses to replicate 75-g oral-glucose-tolerance tests (OGTTs) and performed simple anthropometry in a cross section of subjects.

Design: Thirty-five subjects completed the study: 11 lean [mean (±SEM) age: 33 ± 3.2 y; body mass index (BMI; in kg/m^2): 24.1 ± 0.8; and percentage body fat (%BF): 11.5 ± 1.5%], 12 normal-weight (age: 33 ± 2.9 y; BMI: 23.9 ± 0.7; and %BF: 24.3.5 ± 1.3%), and 12 obese (age: 41 ± 4.5 y; BMI: 34.5 ± 1.7; and %BF: 34.2 ± 1.5%) individuals. The lean and normal-weight groups were selected to have similar BMIs but different %BFs. We measured the participants' heights, weights, %BFs, waist circumferences, hip circumferences, and truncal and peripheral skinfold thicknesses. Subjects received nine 75-g OGTTs and blood samples were collected at 0, 15, 30, 45, 60, 90, and 120 min. Mean plasma glucose and insulin values were used to calculate the insulin sensitivity index.

Results: The obese group had higher plasma glucose concentrations and areas under the curve (AUCs) than did the normal-weight or lean group and higher plasma insulin concentrations and AUCs than did the lean group ($P < 0.05$). Stepwise multiple regression, with adjustment for demographic and anthropometric measurements, identified the following predictors: waist circumference, peripheral skinfold thickness, and BMI for fasting plasma glucose (partial R^2 = 0.20, 0.13, and 0.13, $P < 0.05$); waist circumference and truncal skinfold thickness for plasma glucose AUC (partial R^2 = 0.20 and 0.13, $P < 0.05$); age, waist-to-hip ratio, and peripheral skinfold thickness for fasting plasma insulin (partial R^2 = 0.26, 0.22, and 0.15, $P < 0.05$); truncal skinfold thickness for plasma insulin AUC (partial R^2 = 0.41, $P < 0.001$); and peripheral skinfold thickness for both 2-h plasma glucose (partial R^2 = 0.59, P < 0.001) and the insulin sensitivity index (partial R^2 = 0.49, $P < 0.001$).

Conclusion: Skinfold-thickness measurements may complement other established measurements for predicting abnormal glucose and insulin regulation. *Am J Clin Nutr* 2001;73:567–73.

KEY WORDS Glycemia, insulinemia, oral-glucose-tolerance test, anthropometry, body composition, skinfold thickness

INTRODUCTION

Over the past 4 decades, the prevalences of diabetes and of intermediate classifications of hyperglycemia have increased considerably in both Canada and the United States (1, 2). One of the most powerful contributing factors to this increased prevalence is obesity (1, 2). Most persons who have diabetes are overweight (3) and obesity itself is considered to be the cause of some degree of insulin resistance (4, 5). In this regard, obesity has emerged as an integral feature of the multiple metabolic syndrome that underlies diabetes (6).

Involvement of obesity seems to be site specific. An abdominal fat distribution as measured by waist circumference was shown repeatedly to be a better predictor of various indexes of glucose-insulin homeostasis (7–9) and self-reported diabetes (10) than is body mass index (BMI) alone. These findings were corroborated by use of more accurate and expensive imaging techniques for measuring abdominal fat (8, 9, 11, 12). The waist-to-hip ratio (WHR) is another well-established predictor, but is considered less desirable than waist circumference because it is correlated more weakly with glucose tolerance (8, 9) and is influenced by sex and degree of obesity (13).

Although not considered to have comparable clinical utility (14), additional simple anthropometric assessments such as skinfold-thickness measurements may have predictive value. Vague (15) first proposed almost 50 y ago a possible link between diabetes and central adiposity as determined by caliper measurements. Since then evidence has indicated that truncal skinfold thickness may be a stronger predictor of insulin sensitivity than is abdominal visceral fat as measured by magnetic resonance imaging (12). Cross-sectional (16) and large longitudinal (17–19) studies also

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showed that skinfold-thickness measurements, sums, and their ratios are strong predictors of morbidity. Whether these measurements predict similar or different aspects of glucose and insulin regulation than do conventional anthropometric measurements or whether these may be a useful adjunct is unclear. We therefore studied the relation between 75-g oral-glucose-tolerance-test (OGTT) outcome and various anthropometric variables, including truncal and peripheral skinfold thicknesses, BMI, total body fat, waist circumference, and WHR in a cross-section of lean [low percentage body fat (%BF), normal BMI], normal-weight (normal %BF and BMI), and obese (high %BF and BMI) subjects.

SUBJECTS AND METHODS

Participants

This study represents a further analysis of data from a previous study approved by the Research Ethics Committee at St Michael's Hospital in which the effect of dilution on the reproducibility of a 75-g OGTT was investigated (20). Forty subjects without previously diagnosed dysglycemia were recruited to participate in this study from among the faculty and students of the University of Toronto and though hospital and newspaper advertisements. Of those recruited, 35 completed the study. They were stratified first by BMI and then by %BF into 3 groups: lean (BMI > 19 and ≤27, %BF < 15% for men and <20% for women; $n = 11$), normal-weight (BMI > 19 and ≤27, %BF > 15% for men and >20% for women; $n = 12$), and obese (BMI > 27, %BF > 15% for men and >20% for women; $n = 12$) individuals. The lean and normal-weight groups were selected to have similar BMIs but different %BFs. All subjects gave written, informed consent before starting the study.

Anthropometry

Participants submitted to various anthropometric measurements made by using standard techniques. Each participant's fasting body weight was measured by using a calibrated digital scale while the subject wore light clothing and no shoes. Body circumferences were assessed according to the recommendations of the Airlie Consensus Conference (21): waist circumference was measured at the narrowest part of the torso between the lower rib and the iliac crest and hip circumference at the level of greatest gluteal protuberance. We assessed %BF by use of 2 methods. Total body fat was assessed by the infrared-interactance method with FUTREX-5000 (Futrex Inc, Gaithersburg, MD). This procedure is considered reliable (22) and a reasonably valid alternative to underwater weighing (23). Regional body fat was assessed by the mean of 3 repeated skinfold-thickness measurements made by using Lange skinfold calipers (Cambridge Scientific Industries, Inc, Cambridge, MD) at the 5 most frequently measured sites: triceps, thigh, subscapula, ilium, and abdomen (24). The triceps and thigh measurements were summed to provide an assessment of peripheral skinfold thickness and the subscapular, iliac, and abdominal measurements were summed to provide an assessment of truncal skinfold thickness.

Oral-glucose-tolerance test

A total of nine 75-g Glucodex OGTT meals (Technilab Inc, Chambly, Canada) were administered to participants. These consisted of 3 test meals that differed only in their dilution (300, 600, or 900 mL) repeated 3 times each. The protocol used to administer these meals followed the American Diabetes Association guidelines (25). Participants attended St Michael's hospital on 9 separate mornings after fasting for 10–12 h overnight. They were instructed to maintain the same dietary patterns the evening before each test, to not undertake vigorous exercise the evening or morning before each test, and to consume ≥150 g carbohydrate each day over the 3 d before the test. To ensure that these instructions were followed, we asked participants to complete a questionnaire detailing presession information about their diet and lifestyle patterns and provided them with examples of what constituted 150 g carbohydrate. On commencement of the test, subjects had a catheter inserted into a forearm vein; the catheter was secured by tape and kept patent by saline. A 7-mL blood sample was then collected into a tube containing fluoride oxalate. A randomly selected 75-g OGTT meal was then given with instructions to drink it over a period of exactly 5 min. Additional blood samples were drawn by using the same technique at 15, 30, 45, 60, 90, and 120 min after the start of the meal.

Laboratory analyses

Samples were separated by centrifuge (1240 × g, 15 min, and 4 °C) and the plasma was frozen immediately at –20 °C until analyzed. Banting and Best Diabetes Centre Core Laboratory, Toronto, measured the glucose concentration of each sample by the glucose oxidase method (26) and the insulin concentration by double-antibody radioimmunoassay (27).

Statistical analysis

Plasma glucose and insulin curves were plotted and total areas under the curve (AUCs) were calculated geometrically. The whole-body insulin sensitivity index (ISI) was also calculated by using fasting plasma glucose (FPG), fasting plasma insulin (FPI), and OGTT outcome according to the formula of Matsuda and DeFronzo (28):

$$\mathrm{ISI} = 10\,000/\sqrt{[(\mathrm{FPG} \times \mathrm{FPI}) \times (\mathrm{MPG} \times \mathrm{MPI})]} \qquad (1)$$

where MPG and MPI are mean plasma glucose and insulin, respectively; plasma glucose is expressed in mg/dL (0.0551 mmol/L); and plasma insulin is expressed in μU/mL (6 pmol/L). Results for the 9 repeated tests were averaged for each subject. The replicate mean values were then used for statistical analysis with NUMBER CRUNCHER STATISTICAL SYSTEM (NCSS) 2000 software (NCSS statistical software, Kaysville, UT).

One-way analysis of variance (ANOVA) adjusted for multiple pairwise comparisons by the Tukey-Kramer test was used to assess differences between the 3 groups in the following demographic and anthropometric characteristics: sex, age, weight, BMI, %BF, waist circumference, WHR, and truncal and peripheral skinfold thicknesses. This same statistic was used to assess differences between the 3 groups in the intrasubject CV of weight over the 9 tests; weight changes between each session were assessed by repeated-measures ANOVA. A two-way, repeated-measures ANOVA was used to assess the interactive and independent effects of group (lean, normal weight, and obese) and time (0, 15, 30, 45, 60, 90, and 120 min) on plasma glucose and insulin concentrations. Because the interaction term was significant ($P < 0.001$), individual one-way ANOVAs adjusted for multiple pairwise comparisons by the Tukey-Kramer test were performed to assess differences in replicate mean plasma glucose and insulin concentrations. This same statistic was also used to assess differences in replicate mean

TABLE 1
Demographic and anthropometric characteristics of the subjects[1]

	Lean (n = 9 M, 2 F)	Normal weight (n = 5 M, 7 F)	Obese (n = 4 M, 8 F)
Age (y)	33 ± 3.2	33 ± 2.9	41 ± 4.5
Weight (kg)	75.8 ± 4.1[a]	67.0 ± 3.1[a]	96.3 ± 3.1[b]
BMI (kg/m^2)	24.1 ± 0.8[a]	23.9 ± 0.7[a]	34.5 ± 1.7[b]
%BF (%)	11.5 ± 1.5[a]	24.3 ± 1.3[b]	34.2 ± 1.5[c]
WC (cm)	79.8 ± 2.7[a]	78.7 ± 3.0[a]	106.2 ± 4.4[b]
HC (cm)	97.5 ± 2.3[a]	98.4 ± 2.2[a]	118.4 ± 1.9[b]
WHR	0.82 ± 0.02[a]	0.80 ± 0.02[a]	0.89 ± 0.03[b]
Skinfold thickness (mm)			
Truncal	34.8 ± 4.0[a]	59.4 ± 6.0[b]	108.9 ± 1.6[c]
Peripheral	21.7 ± 2.7[a]	47.6 ± 3.0[b]	72.9 ± 3.1[c]

[1] $\bar{x}$ ± SEM. Means within a row with different superscript letters are significantly different, $P < 0.05$ (one-way ANOVA adjusted for multiple pairwise comparisons with the Tukey-Kramer test). Truncal and peripheral skinfold-thickness measurements are for $n = 10$ in the lean group and were calculated as the mean of 3 repeated caliper measurements at 5 sites: triceps, thigh, subscapula, ilium, and abdomen. The triceps and thigh measurements were summed to provide an assessment of peripheral skinfold thickness and the subscapular, iliac, and abdominal measurements were summed to provide an assessment of truncal skinfold thickness. Percentage body fat (%BF) was calculated by the infrared-interactance method. WC, waist circumference; HC, hip circumference; WHR, waist-to-hip ratio.

plasma glucose and insulin AUCs between the 3 groups. Pearson and Spearman rank correlation coefficients for normally and not normally distributed data, respectively, were used to assess the association between anthropometric variables and 6 selected indexes of glucose and insulin homeostasis: fasting plasma glucose, 2-h plasma glucose, plasma glucose AUC, fasting plasma insulin, plasma insulin AUC, and the ISI. Stepwise multiple regressions were then performed to assess predictors of the 6 indexes, with use of logarithmic transformation for response variables that were not normally distributed. All results are expressed as means ± SEMs and were considered statistically significant if $P < 0.05$.

RESULTS

All 35 subjects were able to follow the study protocol without difficulty. Each subject consumed ≥150 g carbohydrate for 3 d before each session, followed similar activity and dietary patterns the evening and morning before each session, and consumed the test meals in the allotted 5 min. The subjects also kept their body weights constant over the course of the 9 testing sessions; the intrasubject CV for weight did not differ significantly between the lean, normal-weight, and obese groups (0.93 ± 0.1%, 0.94 ± 0.1%, and 1.1 ± 0.09%, respectively). In 3 instances, however, tests were repeated because of violation of the study protocol. Also, skinfold-thickness measurements could not be obtained from one of the lean subjects.

Demography and anthropometry

The demographic and anthropometric data of the 3 groups studied are shown in **Table 1**. The obese group differed significantly from the lean and normal-weight groups in weight, BMI, waist circumference, hip circumference, and WHR measurements. All 3 groups differed significantly from one another in %BF and truncal and peripheral skinfold thicknesses ($P < 0.001$).

Glucose and insulin responses

The mean plasma glucose responses after 9 repetitions of a 75-g OGTT in the lean, normal-weight, and obese groups are shown in **Figure 1**. Plasma glucose concentrations were significantly higher in the obese group than in the normal-weight group at every time point except 0 (fasting), 15, and 30 min and significantly higher than in the lean group at every time point except 30 min. This was reflected in significant differences in the plasma glucose AUCs between the 3 groups ($P = 0.0012$). The obese group had significantly higher AUCs than did either the normal-weight or lean groups (1028.7 ± 34.8 compared with 825.0 ± 15.4 and 786.6 ± 13.6 mmol·min/L). There were no significant differences in plasma glucose concentrations or AUCs between the normal-weight and lean groups. However, there appeared to be a nonsignificant tendency toward lower 2-h plasma glucose in the lean group.

The mean plasma insulin responses after 9 repetitions of a 75-g OGTT in the lean, normal-weight, and obese groups are also shown in Figure 1. Plasma insulin concentrations were significantly higher in the obese group than in lean group at every time point and significantly higher than in the normal-weight group at 0 min (fasting plasma insulin). Again, this was reflected in significant differences in the plasma insulin AUCs between the 3 groups ($P = 0.0031$). Pairwise comparisons, however, showed that only the obese group had significantly higher insulin AUCs than did the lean group (40 232.9 ± 4157.2 compared with 15 636.14 ± 2346.9 pmol·min/L). No other significant differences were detected between the obese and normal-weight groups or the lean and normal-weight groups, although there was a tendency toward a graded difference in insulin secretion across the 3 groups over the last 90 min of the OGTT.

Correlates: glucose and insulin indexes

Shown in **Table 2** are the simple correlations between the anthropometric measurements and the selected indexes of glucose and insulin homeostasis in the entire data set ($n = 35$ or $n = 34$ for truncal and peripheral skinfold-thickness measurements). The strongest correlates of each index, obtained from this table, are shown in **Figure 2**. Fasting plasma glucose was most strongly positively associated with peripheral skinfold thickness, followed by %BF, truncal skinfold thickness, and waist circumference. Two-hour plasma glucose was most strongly correlated with both %BF and peripheral skinfold thickness, followed by truncal skinfold thickness, waist circumference, hip circumference, WHR, and BMI. Plasma glucose AUC was most strongly correlated with waist circumference, followed by WHR, truncal and peripheral skinfold thicknesses, BMI and hip circumference, and %BF. Fasting plasma insulin was most strongly correlated with %BF, followed by peripheral and truncal skinfold thicknesses, BMI, and hip circumference. Plasma insulin AUC was most strongly correlated with truncal skinfold thickness, followed by %BF, peripheral skinfold thickness, waist circumference, WHR, BMI, hip circumference. Last, the ISI was most strongly negatively correlated with peripheral skinfold thickness, followed by %BF, truncal skinfold thickness, waist circumference, BMI, hip circumference, and WHR.

Multivariate predictors: glucose and insulin indexes

Shown in **Table 3** are the correlates that maintained their significance in multivariate analysis after all independent variables (age, sex, weight, BMI, %BF, truncal skinfold thickness,

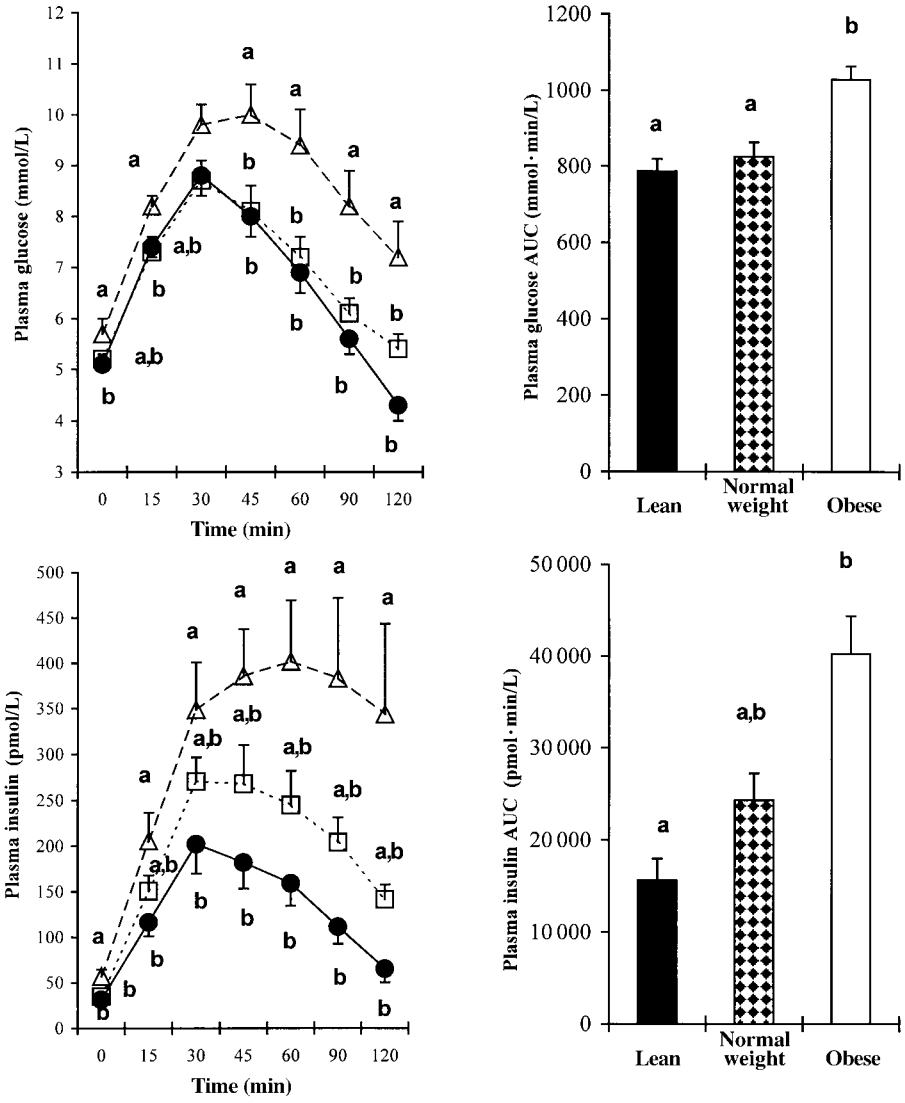

FIGURE 1. Mean (±SEM) plasma glucose and insulin responses after replicate 75-g oral-glucose-tolerance tests in lean (●), normal-weight (□), and obese (△) subjects. A repeated-measures two-way ANOVA was used to assess the interactive and independent effects of group (lean, normal weight, and obese) and time (0, 15, 30, 45, 60, 90, and 120 min) on glucose and insulin concentrations. Because the interaction term was significant ($P < 0.001$), individual one-way ANOVAs adjusted for multiple pairwise comparisons by the Tukey-Kramer test were performed to assess differences in replicate mean plasma glucose and insulin concentrations. Means with different superscript letters are significantly different, $P < 0.05$.

peripheral skinfold thickness, waist circumference, hip circumference, and WHR) were entered into stepwise multiple regression models versus the same indexes of glucose and insulin homeostasis. Waist circumference, peripheral skinfold thickness, and BMI emerged as predictors of fasting plasma glucose ($P < 0.05$). Peripheral skinfold thickness emerged as the sole predictor of both 2-h plasma glucose and the ISI ($P < 0.001$). Waist circumference and truncal skinfold thickness emerged as predictors of the plasma glucose AUC ($P < 0.05$). Age, WHR, and peripheral skinfold thickness were identified as predictors of fasting plasma insulin ($P < 0.05$). Finally, truncal skinfold thickness remained the strongest correlate and sole predictor of the plasma insulin AUC ($P < 0.001$).

Because of the strong relations shown in the literature among some of the independent variables (12, 13, 17, 29), the influence of multicolinearity was considered in the regression models. Correlation coefficients among the independent variables representing general (%BF and BMI) and regional (waist circumference, WHR, and truncal and peripheral skinfold thicknesses) adiposity were all significant ($r = 0.34$ to 0.91, $P < 0.05$), except for the correlation between %BF and WHR ($P = 0.23$). When the demographic variables were considered, age was found to be significantly correlated with peripheral skinfold thickness, waist circumference, and WHR ($r = 0.37$, 0.38, and 0.40 respectively, $P < 0.05$) and sex with peripheral skinfold thickness and WHR ($r = 0.44$ and 0.44, $P < 0.05$). These correlations did not, however, exert a significant influence on the multiple regression models selected by the stepwise regression. No variance inflation factors exceeded 6.2 in any of the models (range: 1.3–6.2), in which >10 is considered a problem. Nor were there any tolerance values <0.16 (range: 0.16–0.76), in which <0.1 is considered a problem.

TABLE 2
Simple correlations between anthropometric measurements and indexes of glucose and insulin homeostasis after replicate 75-g oral-glucose-tolerance tests[1]

	FPG	2-h PG	PG AUC	FPI	PI AUC	ISI
BMI	0.21	0.34[2]	0.55[3]	0.38[2]	0.39[2]	−0.47[4]
%BF	0.53[3]	0.72[3]	0.51[4]	0.65[3]	0.60[3]	−0.69[3]
WC	0.36[2]	0.40[2]	0.67[3]	0.30	0.42[2]	−0.48[4]
HC	0.29	0.39[2]	0.55[3]	0.34[2]	0.35[2]	−0.44[4]
WHR	0.33	0.36[2]	0.66[3]	0.17	0.41[2]	−0.34[2]
Skinfold thickness						
Truncal	0.52[4]	0.67[3]	0.61[3]	0.52[4]	0.62[3]	−0.67[3]
Peripheral	0.54[4]	0.72[3]	0.57[3]	0.59[3]	0.60[3]	−0.70[3]

[1] $n = 35$, except for truncal and peripheral skinfold thickness, for which $n = 34$. Spearman correlation coefficients (for data not normally distributed) are provided for all columns except the insulin sensitivity index (ISI), for which Pearson correlation coefficients are provided. FPG, fasting plasma glucose; 2-h PG, 2-h plasma glucose; PG AUC, plasma glucose area under the curve; FPI, fasting plasma insulin; PI AUC, plasma insulin area under the curve; %BF, percentage body fat; WC, waist circumference; HC, hip circumference; WHR, waist-to-hip ratio.
[2] $P < 0.05$.
[3] $P < 0.001$.
[4] $P < 0.01$.

DISCUSSION

In the present study, general obesity was an important determinant of glucose and insulin regulation. A categorical analysis of the data, in which subjects were stratified on the basis of BMI and %BF as obese, normal weight, and lean, showed significant differences between the 3 groups in glucose and insulin concentrations and AUCs after replicate 75-g OGTTs. A continuous analysis of the data, in which BMI and %BF were correlated with the 6 indexes of glucose and insulin homeostasis, also showed the strong influence of overall adiposity. Both BMI and %BF were significantly correlated with all 6 indexes, except that BMI was not correlated with fasting plasma glucose.

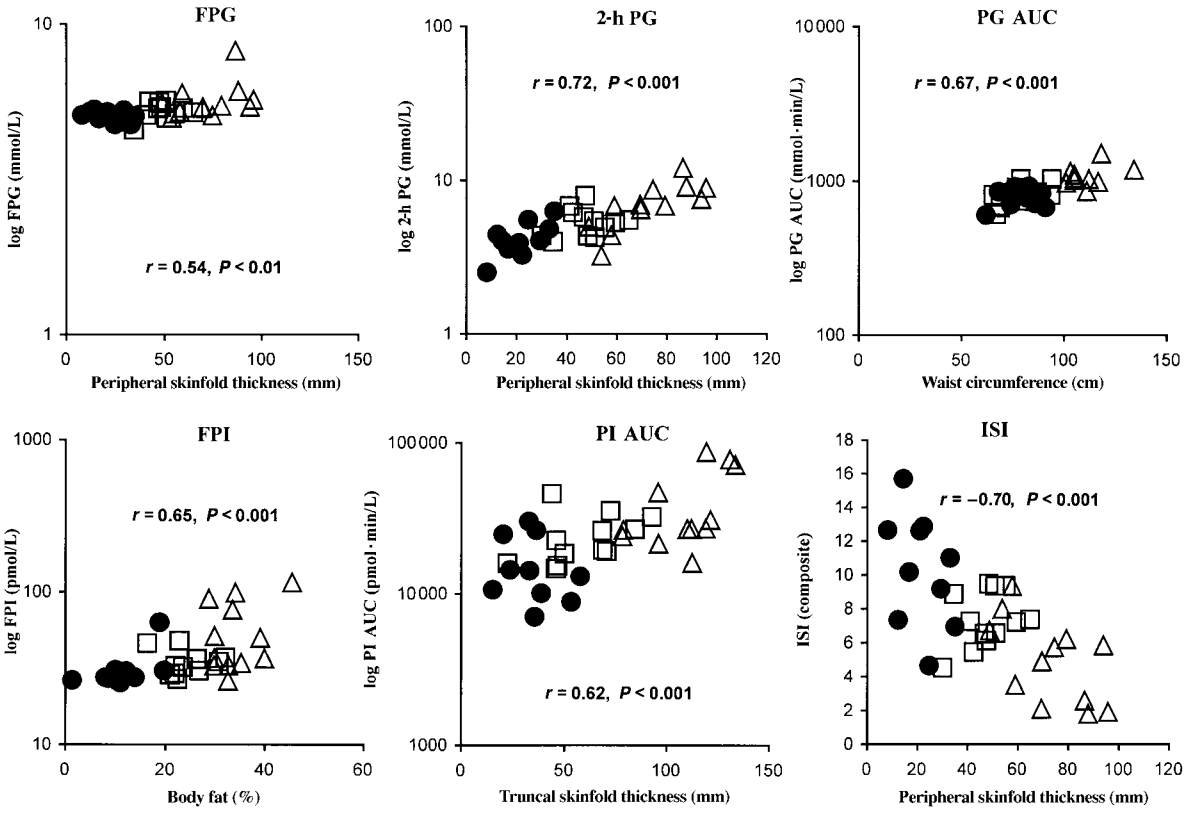

FIGURE 2. Scatter plots of the strongest simple correlates of fasting plasma glucose (FPG), 2-h plasma glucose (2-h PG), plasma glucose area under the curve (PG AUC), fasting plasma insulin (FPI), plasma insulin area under the curve (PI AUC), and the insulin sensitivity index (ISI) after replicate 75-g oral-glucose-tolerance tests in lean (●), normal-weight (□), and obese (△) subjects. FPG, 2-h PG, PG AUC, FPI, and PI AUC were logarithmically transformed to normalize their distributions. The ISI was calculated by using the formula given in the text. Correlations shown are Spearman correlation coefficients, except for the ISI, for which the Pearson correlation coefficient is provided. $n = 35$, except for truncal skinfold-thickness measurements, for which $n = 34$.

TABLE 3
Stepwise multiple regression analyses for predictors of indexes of glucose and insulin homeostasis after replicate 75-g oral-glucose-tolerance tests[1]

Stepwise regression models	β	*P*	Partial R^2	Total R^2
FPG				
BMI	−0.0050	0.046	0.13	
WC	0.0024	0.0096	0.20	
Peripheral skinfold thickness	0.00073	0.041	0.13	0.42
2-h PG				
Peripheral skinfold thickness	0.0048	<0.001	0.59	
PG AUC				
WC	0.0036	0.010	0.20	
HC	−0.0025	0.15	0.069	
Truncal skinfold thickness	0.00096	0.043	0.13	0.59
FPI				
Sex	−0.12	0.083	0.10	
Age	−0.0066	0.0030	0.27	
WHR	1.18	0.0083	0.22	
Peripheral skinfold thickness	0.0030	0.033	0.15	0.56
PI AUC				
Truncal skinfold thickness	0.0046	<0.001	0.41	
ISI				
Peripheral skinfold thickness	−0.96	<0.001	0.49	

[1] $n = 35$, except for truncal and peripheral skinfold thickness, for which $n = 34$. FPG, fasting plasma glucose; WC, waist circumference; 2-h PG, 2-h plasma glucose; PG AUC, plasma glucose area under the curve; HC, hip circumference; FPI, fasting plasma insulin; WHR, waist-to-hip ratio; PI AUC, plasma insulin area under the curve; ISI, insulin sensitivity index. FPG, 2-h PG, PG AUC, FPI, and PI AUC were logarithmically transformed to normalize their distribution for regression analyses.

Specific sites of adiposity appeared to be preferentially driving these observations. After multivariate adjustment, %BF lost significance in relation to all 6 indexes of glucose and insulin regulation measured. This was despite %BF having been the strongest positive correlate of 2-h plasma glucose and fasting plasma insulin in univariate analysis. Instead, waist circumference, peripheral and truncal skinfold thicknesses, WHR, BMI, and age emerged as the most important predictors. Each of these variables explained the variation in different aspects of glucose and insulin regulation: waist circumference, BMI, and peripheral skinfold thickness in fasting plasma glucose; peripheral skinfold thickness in both 2-h plasma glucose and ISI; waist circumference and truncal skinfold thickness in plasma glucose AUC; WHR, peripheral skinfold thickness, and age in fasting plasma insulin; and truncal skinfold thickness in plasma insulin AUC. Because more than one-half of the indexes were explained at least partly by waist circumference, WHR, or truncal skinfold thickness, measures of central adiposity figured prominently.

Comparable observations regarding the importance of central adiposity were made by others. Both Lemieux et al (8) and Ross et al (9) found that women with the greatest abdominal visceral adipose tissue irrespective of overall adiposity showed the greatest deterioration in indexes of glucose and insulin homeostasis measured after a 75-g OGTT. Similarly, Abate et al (12) noticed that after they accounted for specific sites of adiposity, total body fat did not retain significance as a predictor of insulin sensitivity assessed by the hyperinsulinemic euglycemic clamp technique. Instead, subcutaneous abdominal fat emerged as the strongest predictor (12). These findings agree with the notion that total body fat is less important at predicting glucose and insulin regulation than are specific sites of adiposity, especially those that indicate central adiposity.

There is controversy, however, over which central fat compartment plays the greatest role in insulin resistance: visceral or subcutaneous. Visceral fat, the smaller of the 2 fat compartments, was reported to be the stronger determinant of insulin resistance (8, 9, 30), but evidence suggests a possible role for both. Subcutaneous truncal fat assessed by computed tomography was observed previously to be the strongest predictor of the insulin AUC, explaining 34.4% ($P < 0.001$) of the adjusted variation (8). This is similar to the 41% ($P < 0.001$) explained in the present study by subcutaneous truncal skinfold-thickness measurements. Subcutaneous abdominal fat was also thrice noticed to be a stronger predictor of insulin sensitivity than was visceral abdominal fat (11, 16, 17). The suggestion is that the subcutaneous fraction of abdominal fat should also be considered a strong determinant of glucose and insulin regulation.

Peripheral adiposity should not be discounted as another mechanistic factor. Although a decrease in thigh adipose tissue after a 16-wk weight loss was not shown to be significantly correlated with corresponding improvements in insulin sensitivity in a recent analysis by Goodpaster et al (30), we noticed that peripheral skinfold thickness, which included a thigh measurement, was a predictor of 4 of the 6 indexes of glucose and insulin regulation: fasting plasma glucose, 2-h plasma glucose, fasting plasma insulin, and the ISI. Peripheral skinfold thickness explained 13%, 59%, 15%, and 49% ($P < 0.05$), respectively, of the adjusted variation in these indexes and was the sole predictor of 2-h plasma glucose and the ISI. Goodpaster et al (11) also made similar observations in an earlier analysis. They showed that subcutaneous thigh fat, measured as skinfold thickness, and thigh muscle attenuation, an indicator of muscular fat deposition in the peripheral tissue, were significant independent predictors of insulin sensitivity. Both were found to explain more residual variance in insulin sensitivity than did visceral abdominal fat after multivariate adjustment (11). Again, however, the compartment of fat with the greatest influence is a point of debate. The same group showed that the intramuscular and subfacial compartments of thigh fat as measured by computed tomography each had a significant negative correlation with insulin sensitivity (31). On the other hand, the larger subcutaneous fat compartment did not. This latter finding disagrees with both Goodpaster et al's previous observations using skinfold-thickness measurements (11) and our own. Taken together, these data suggest that peripheral fat depots might be mediating glucose and insulin homeostasis, but the relative contributions of intramuscular and subcutaneous peripheral fat are unclear.

Acknowledging that truncal and peripheral subcutaneous fat compartments might be involved in insulin resistance, the question becomes whether skinfold measures of these sites are useful when combined with other established measures of regional adiposity. The addition of peripheral skinfold thickness to waist circumference increased the variance explained in fasting plasma glucose from 23% to 33%, and adding truncal skinfold thickness to waist circumference increased the variance explained in the glucose AUC identically. Furthermore, the variance explained in fasting plasma insulin was increased from 22% to 37% when peripheral skinfold thickness was added to WHR. Greater precision in predicting glucose and insulin regulation might therefore be gained by adding skinfold-thickness measurements to conventional measures of regional adiposity.

In conclusion, concurrent use of several simple anthropometric assessments including skinfold-thickness measurements may provide a more complete picture of risk of abnormal glucose and insulin regulation. Instead of using conventional measurements of BMI and body circumferences alone, practitioners may wish to use several simple measurements that also include skinfold thickness.

How useful skinfold-thickness measurements may be as an adjunct cannot be inferred without further study. These preliminary findings need to be replicated in a larger number of subjects. Allowing separate analyses for men and women would also be useful. Although there is a sex dimorphism in adipose tissue distribution, ie, men have more visceral fat than do women at any given level of general adiposity, that may affect differences in postprandial insulin secretion between persons with high and low amounts of visceral adipose tissue (29), sex was not shown to significantly influence results in previous analyses (30). In the present analyses, there was no significant interaction between group and sex at any time point or for AUC, but the study was underpowered to make this determination fairly. Because our data are applicable to glucose-tolerant subjects, other research avenues of interest might investigate whether our findings hold true in a broader cross section that includes persons at high risk of developing diabetes, such as first-degree relatives of persons with diabetes and those with established impaired fasting glucose or impaired glucose tolerance.

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