Weight Loss Reduces Abdominal Fat and Improves Insulin Action in Middle-Aged and Older Men With Impaired Glucose Tolerance

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Aging is associated with an increased accumulation of abdominal fat, glucose intolerance, and insulin resistance. We tested the hypothesis that diet-induced weight loss would reduce the abdominal distribution of fat and improve glucose tolerance and insulin action in a group of obese middle-aged and older men with normal or impaired glucose tolerance (IGT). Oral glucose tolerance tests (OGTTs) were performed at baseline and after 9 months of diet-induced weight loss in 35 men (mean age, 60 ± 8 years). Fifteen men of comparable age and degree of obesity who did not participate in the weight loss intervention served as controls. Subjects lost 9.0 ± 2.0 kg (mean ± SD) body weight ($P < .001$), resulting in a 19% reduction in percent body fat (30.0 ± 4.0% to 24.0% ± 4.0%, $P < .001$), an 8% reduction in waist circumference (104.0 ± 7.0 to 96.0 ± 7.0 cm, $P < .001$), and a 2% reduction in waist to hip ratio [WHR] (0.97 ± 0.06 to 0.95 ± 0.06, $P < .01$). Weight loss improved glucose tolerance: nine men with IGT at baseline reverted to normal glucose tolerance following the intervention. Glucose area during the OGTT was significantly reduced after weight loss (−22.0%, $P < .001$), while it increased in control subjects (+32%, $P < .004$). In multiple regression analysis, the improvement in glucose area following weight loss in these 35 men was attributed to the reduction in waist circumference ($P < .01$) and baseline glucose area ($P < .05$). Insulin response to glucose and tissue sensitivity to endogenous insulin were measured in a subset of eight men using the hyperglycemic clamp technique. Weight loss resulted in significant reductions in acute ($P < .05$) and second-phase ($P < .01$) insulin responses and a significant increase in the rate of glucose utilization ([M] $P < .05$), indicative of increased tissue sensitivity to insulin. Our results support the hypothesis that weight loss significantly improves glucose tolerance and insulin action in obese middle-aged and older men with normal glucose tolerance or IGT, in part by reducing the distribution of fat in upper-body sites.

AGING IS ASSOCIATED with an increased prevalence of impaired glucose tolerance (IGT).[1] Approximately 40% of the population over the age of 60 years have IGT. The pathophysiology of IGT in the elderly is multifactorial, involving insulin resistance, hyperinsulinemia, impaired β-cell function, and increased hepatic glucose production.[2,3] Although "primary" postreceptor defects have been identified in older individuals with IGT,[4] the deterioration in glucose tolerance and insulin sensitivity often associated with aging may be related to an increase in total and abdominal adiposity,[5] as well as to decreased levels of physical activity and reduced muscle mass.[6]

A large number of subjects with IGT, particularly those with central obesity, progress to non–insulin-dependent diabetes mellitus and suffer significant morbidity and mortality from atherosclerotic complications, specifically coronary artery disease.[7-11] The heightened risk for non–insulin-dependent diabetes mellitus and coronary artery disease in older subjects with IGT suggests that clinical strategies are needed to normalize glucose tolerance. In this study, we hypothesized that reductions in total and regional adiposity would improve or normalize glucose tolerance, reduce the magnitude of glucose-stimulated insulin response, and improve insulin action in obese middle-aged and older men with either normal glucose tolerance or IGT. The oral glucose tolerance test (OGTT) and the hyperglycemic clamp technique were used to examine the effects of total and regional weight loss on glucose tolerance and insulin action.

SUBJECTS AND METHODS

Subjects

The Fitness After Forty-Five program is a prospective study of the effects of exercise and weight loss on metabolic and cardiovascular function in healthy, nonsmoking men over the age of 45 years.[12] Subjects were screened by telephone to determine whether they met entry criteria for the study. Telephone screening was used to ascertain medical histories. Subjects with a history of diabetes mellitus, coronary artery disease, hypertension (blood pressure > 160/90 mm Hg), hyperlipidemia, or comorbid diseases were excluded. Individuals who were eligible for further testing underwent physical examination. Screening blood chemistries excluded men with hyperlipidemia, defined as a plasma triglyceride or low-density lipoprotein level greater than the 90th percentile for age and gender according to the Lipid Research Clinics criteria,[13] and diabetes mellitus, defined as a fasting plasma glucose greater than 140 mg/dL (7.8 mmol/L or greater than 200 mg/dL (11.1 mmol/L) at 120 minutes during an OGTT.[14]

Seventy-three men were randomized to a sequential intervention of 3 months of an isocaloric step I American Heart Association (AHA)[15] diet followed by 9 months of a hypocaloric weight-reducing step I AHA diet, and 26 to a control group that received 3 months of an isocaloric step I AHA diet followed by 9 months of weight maintenance. Forty-eight men randomized to the weight

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loss group completed the intervention; the other 25 men dropped out because of lack of interest. Of 48 men who completed the intervention, four had incomplete data and nine lost less than 5 kg body weight. Noncompliance with the caloric restriction was considered the major reason for lack of weight loss in these nine men. Thus, we report data on 35 men who lost at least 5 kg during the intervention and completed retesting. Of 26 men in the control group, one had incomplete data and 10 dropped out due to loss of interest and would not return for reevaluation. We report control data on the remaining 15 men. All subjects provided informed consent according to guidelines approved by the University of Maryland and the Francis Scott Key Center Human Studies Institutional Review Boards.

Dietary and Weight Loss Program

After receipt of a detailed 7-day food record, all subjects were first instructed for 3 months by registered dietitians on the principles of an isocaloric AHA step I diet. Subjects were instructed not to lose weight or change their level of physical activity during this period of diet instruction. Body weights were checked weekly to ensure weight maintenance (±1.0 kg), and 7-day food records were reviewed biweekly to monitor adherence to the AHA step I diet. After 3 months on the AHA step I weight-maintaining diet, subjects were provided an isocaloric metabolic diet of comparable composition to their own AHA step I diet from the General Clinical Research Center metabolic kitchen for 5 days before and during baseline metabolic testing. Subjects in the weight loss group then began a 9-month AHA step I hypocaloric diet, while the men in the control group continued to consume an isocaloric (weight-maintaining) AHA step I diet for an additional 9 months. The control group attended weekly 1-hour dietary counseling meetings to ensure compliance with the AHA step I diet, while the weight loss group attended weekly 1-hour weight loss behavioral-modification sessions to reinforce successful weight loss and better eating habits. The behavioral techniques focused on elimination of needless associations between food and daily life situations, development of patterns of self-control to limit overeating and reduce caloric intake, understanding the influences of mood and emotions on eating behavior, and learning guidelines for the maintenance of weight loss after completion of the program. Body weight and compliance with the AHA step I diet were monitored weekly by a registered dietitian. Energy intake for subjects undergoing the 9-month weight loss program were adjusted to ensure a gradual weight loss of approximately 0.25 to 0.5 kg/wk. Target weight loss for the 9-month intervention was 10% of initial body weight. After completing the 9-month weight loss intervention, subjects were weight-stabilized on an AHA step I diet for 1 month before repeat metabolic testing. All subjects were provided an isocaloric metabolic diet of similar composition to their own AHA step I diet from the General Clinical Research Center kitchen for 5 days before and during repeat metabolic testing.

Dietary Intake

Subjects in the weight loss and control groups were instructed to record all foods and beverages consumed for 7 consecutive days at baseline, after completion of the 3-month isocaloric AHA step I diet, and after completion of the 9-month interventions. Food-exchange lists were evaluated at least biweekly and often weekly to monitor and ensure compliance with the 3- and 9-month interventions. Subjects received detailed verbal and written instructions and were provided food scales before completion of a 7-day food record. Dietary records were then reviewed with the subjects to ensure completeness, preparation methods, and food description.

Metabolic Testing

Blood samples for determination of fasting glucose and insulin levels were drawn into chilled EDTA (1 mg/mL blood) tubes after a 12- to 14-hour overnight fast on day 4 of the metabolic diet. Reported fasting values are the mean of two determinations drawn at −15 and 0 minutes. Blood samples were then drawn 30, 60, 90, and 120 minutes after ingestion of glucose 40 g/m^2 body surface area (body surface area = weight$^{0.425}$ · height$^{0.725}$ · 71.84) to normalize dose to body size. This dose was chosen to permit comparison of these results to results of OGTTs performed over a 35-year period by collaborating investigators from the Baltimore Longitudinal Study of Aging. The average oral glucose dose administered during the OGTT was 79 g, and there was no significant correlation between this dose and the glucose area ($r = -.08$) or the 2-hour glucose level ($r = -.04$). IGT was defined as a fasting blood glucose concentration less than 7.8 mmol/L and a 2-hour glucose concentration between 7.8 and 11.1 mmol/L.[14] Plasma glucose level was measured by the glucose oxidase method (Beckman Glucose Analyzer; Fullerton, CA). Plasma immunoreactive insulin levels were measured by radioimmunoassay.[16] Glucose and insulin areas above the basal level were calculated from 0 to 120 minutes using the trapezoidal rule.

Body Composition

Hydrostatic weighing was performed, and percent body fat was calculated using the Siri equation.[17] Fat-free mass (FFM) was calculated as kilograms of body weight minus kilograms of fat mass. Waist circumference was determined at the point of minimal abdominal circumference. The waist to hip ratio (WHR) was determined as the ratio of waist circumference to the circumference at the maximal gluteal protuberance and was the index of regional fat distribution.

Maximal Aerobic Capacity

To ensure that metabolic changes were not influenced by changes in physical activity, maximal aerobic capacity ($\dot{V}O_2$max) was determined before and after weight loss using a modified Balke protocol as previously described.[12] All $\dot{V}O_2$max tests fulfilled at least two of the following three criteria: (1) heart rate at maximal exercise was greater than 95% of the age-adjusted maximal heart rate (220 − age), (2) respiratory exchange ratio was greater than 1.10, and (3) a plateau in oxygen uptake was achieved on the basis of a change in $\dot{V}O_2$ of less than 0.2 L/min during the final two oxygen collections. Tests not meeting these criteria were repeated. $\dot{V}O_2$max is expressed in liters per minute.

Hyperglycemic Clamp Protocol

Hyperglycemic clamps were performed in eight men as previously described.[18] Three arterialized venous blood samples were obtained 10 minutes apart in heparinized syringes before the start of the clamp for measurement of baseline plasma glucose and insulin levels. An infusion of 20% dextrose solution was begun in a primed-continuous manner to increase each subject's fasting plasma glucose concentration by 7.9 mmol/L, and was then adjusted using a variable-speed infusion pump (Harvard Apparatus, Boston, MA) to sustain hyperglycemia for 120 minutes. Heparinized blood samples were drawn at 2, 4, 6, 8, and 10 minutes and then at 5-minute intervals during the remaining 110 minutes for measurement of plasma glucose and insulin levels. Plasma glucose levels were determined immediately using the glucose oxidase method (Beckman Instruments). Plasma for determination of insulin was stored at −70°C until measured by radioimmunoassay[16] at a later date so that samples obtained before and after weight loss could be

measured in the same assay. Glucose utilization (M) rates are glucose infusion rates corrected for filling of the whole-body glucose space and urinary disposal.

The mean M rate during hyperglycemic clamp studies was calculated as the mean of the five M rates (millimoles per kilogram FFM per minute) measured over 20-minute intervals from 20 to 120 minutes. Mean first- and second-phase insulin responses to glucose infusion were calculated as the mean insulin concentrations from 0 to 10 and 20 to 120 minutes, respectively. Areas under the curves for early- and late-phase insulin responses were calculated above the basal level using a trapezoidal model. The coefficient of variation for plasma glucose concentration was 5.1% during the pre–weight loss clamp and 5.6% during the post–weight loss clamp.

Index of Insulin Sensitivity

Because the relationship of M to plasma insulin concentration (I) was linear during the last 100 minutes of the hyperglycemic clamp, tissue sensitivity was calculated by linear regression analysis. Plots of M versus I during the last five 20-minute intervals of the clamp were constructed for each subject. The means of eight individual intercepts and slopes were used to determine the overall regression equation between M and I for the group before and after weight loss.

Statistical Methods

Data were checked for normality. Insulin values were not normally distributed and required nonparametric analysis (Wilcoxon signed-rank test and Spearman correlations). Paired *t* tests were performed to compare variables before and after weight loss. Pearson product-moment values were calculated to determine correlations between anthropometric, physical, and metabolic variables. Stepwise multiple linear regression analysis was performed with change in glucose area due to weight loss as the dependent variable and change in waist circumference, change in percent body fat, and baseline glucose area as independent variables. A similar model was constructed in which the change in fat mass replaced the change in percent body fat. Results of these two models were similar and therefore, for ease of presentation, we only report results of the model that includes percent body fat. The Wilcoxon signed-rank test was used to compare the change in slopes of M versus I before and after weight loss. A P value not greater than .05 was considered significant. Data are expressed as the mean ± SD.

RESULTS

Subject Characteristics

The 35 obese sedentary men in the weight loss group had an upper-body distribution of fat, as indexed by a high waist circumference and WHR (Table 1). Fifty-seven percent (20 of 35) of the men had IGT. The 15 men in the control group had similar baseline characteristics, and 40% (six of 15) had IGT.

The weight loss group lost a mean of 9.0 ± 2.0 kg (range, 5.2 to 20.7; $P < .001$), or 10% of their initial body weight ($P < .001$), during the intervention period, resulting in a 19% reduction in percent body fat ($P < .001$), an 8% reduction in waist circumference ($P < .001$), a 2% reduction in WHR ($P < .01$), and a 3% reduction in FFM ($P < .01$). By design, the level of cardiovascular fitness ($\dot{V}O_2max$) did not change following weight loss. Body weight, body composition, and level of cardiovascular fitness of the control group did not change significantly during the intervention period.

Table 1. Physical Characteristics of Weight Loss and Control Subjects

	Weight Loss (n = 35)		Control (n = 15)	
Characteristic	Baseline	Post–Weight Loss	Baseline	Follow-up
Age (yr)	60.0 ± 8.0	—	62.0 ± 7.0	—
Weight (kg)	91.0 ± 10.0	82.0 ± 8.0†	89.0 ± 13.0	90.0 ± 13.0
BMI (kg/m²)	30.0 ± 2.0	27.0 ± 2.0†	30.0 ± 3.0	30.0 ± 3.0
% fat	30.0 ± 4.0	24.0 ± 4.0†	29.0 ± 5.0	29.0 ± 6.0
Waist circumference (cm)	105.0 ± 6.0	97.0 ± 7.0†	103.0 ± 8.0	103.0 ± 9.0
WHR	0.97 ± 0.06	0.95 ± 0.06*	0.97 ± 0.04	0.98 ± 0.04
$\dot{V}O_2max$ (L/min)	2.6 ± 0.5	2.5 ± 0.5	2.6 ± 0.6	2.5 ± 0.5
FFM (kg)	63.9 ± 6.3	62.1 ± 6.0*	62.5 ± 7.7	62.9 ± 7.0

NOTE. Data are the mean ± SD.
*$P < .01$, †$P < .001$: significance of difference from baseline.

Effects of Weight Loss on Glucose Tolerance and Insulin Sensitivity

Weight loss improved glucose tolerance, as indicated by a decrease in the prevalence of IGT from 57% (20 of 35) to 40% (14 of 35). Nine men converted from impaired to normal and three from normal to impaired, 11 remained impaired, and 12 remained normal following the weight loss intervention. In contrast, the prevalence of IGT in the control group increased from 40% (six of 15) to 67% (10 of 15) following the intervention period. Six subjects converted from normal to impaired and two from impaired to normal, while four remained impaired and three remained normal.

The improvement in glucose tolerance after weight loss was reflected by a reduction in plasma glucose levels during the OGTT (Fig 1). Fasting plasma glucose levels did not significantly change in either the weight loss or control group (5.4 to 5.3 and 5.5 to 5.6 mmol · min/L, respectively), but the glucose area decreased by 25% (378 to 306 mmol · min/L, $P < .001$) in the weight loss group and increased by 32% (288 to 396 mmol · min/L, $P < .004$) in control subjects. Changes in glucose area were significantly different between the two groups ($P < .001$). Similar changes in plasma insulin values during the OGTT were seen after weight loss (Fig 1). Fasting insulin levels decreased by 20% (90 to 72 pmol/L, $P < .001$) with weight loss, and insulin area decreased by 28% (56,700 to 40,500 pmol · min/L, $P < .005$). There were no significant changes in fasting insulin level or insulin area in the control group (72 to 78 pmol/L and 43,920 to 49,140 pmol · min/L, respectively). Thus, the changes in insulin area differed significantly between groups ($P < .01$).

The eight weight loss subjects who underwent hyperglycemic clamps had baseline characteristics similar to those of the group as a whole and lost a similar amount of body weight (Table 2). Weight loss was accompanied by a significant reduction in body mass index (BMI), percent

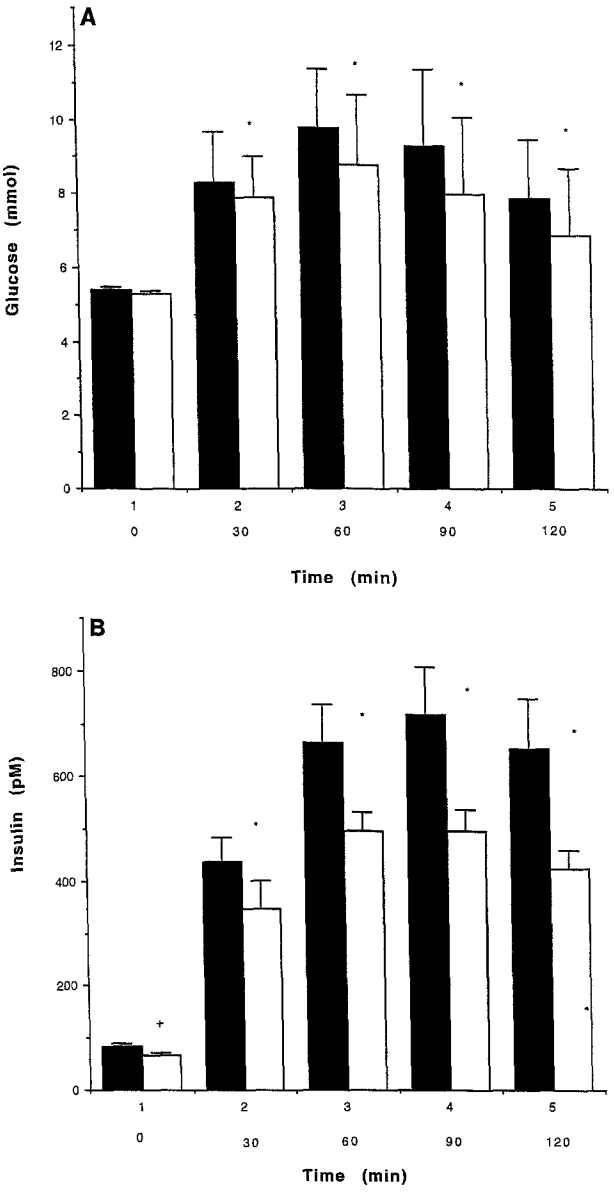

Fig 1. Plasma (A) glucose and (B) insulin concentrations during the OGTT (■) before and (□) after weight loss. +$P < .05$, *$P < .01$.

body fat, and waist circumference, but no significant changes in WHR or $\dot{V}O_2$max. Four of eight men had IGT at baseline, and three of these men converted to normal following weight loss. The four men with normal glucose tolerance at baseline remained normal following the weight loss intervention. Glucose and insulin levels and areas during the OGTT decreased significantly following weight loss in eight men who underwent hyperglycemic clamps (data not shown).

Fasting plasma glucose levels at the time of the clamps were similar before (5.3 mmol/L) and after (5.1 mmol/L, $P = .06$) weight loss, as were mean glucose levels during the clamps before (13.3 mmol/L) and after (13.0 mmol/L) weight loss ($P = .12$). Weight loss resulted in a significant decrease in acute-phase insulin response (0- to 10-minute area, $P < .05$), as well as second-phase insulin response (20- to 120-minute area, $P < .01$), during the hyperglycemic clamp (Fig 2). Weight loss was also associated with an overall increase (21%, $P < .05$) in the M rate over the 120-minute clamp (Fig 2). Together, these results indicate that less insulin was required to metabolize a greater amount of glucose following weight loss. The slope of the relationship of M to I during the last 100 minutes of the clamp was calculated as an index of tissue sensitivity to endogenously secreted insulin during the clamp (Fig 3). The relationship of M to I was shifted to the left with weight loss, and the mean slope increased significantly ($P < .01$). This increase in glucose metabolism at each level of insulin after weight loss is consistent with greater tissue sensitivity to endogenously secreted insulin.

Table 2. Physical Characteristics of Eight Men Who Underwent Glucose Clamp Studies

Characteristic	Baseline	Post–Weight Loss
Age (yr)	59.0 ± 10.6	—
Weight (kg)	90.0 ± 10.6	79.0 ± 7.9†
BMI (kg/m²)	30.0 ± 2.6	27.0 ± 2.6†
% fat	31.0 ± 2.6	25.0 ± 2.6†
Waist circumference (cm)	104.0 ± 15.9	96.0 ± 10.6*
WHR	0.98 ± 0.05	0.96 ± 0.05
$\dot{V}O_2$max (L/min)	2.5 ± 1.6	2.4 ± 1.3

NOTE. Data are the mean ± SD.
*$P < .01$, †$P < .001$: significance of difference from baseline.

Relationship of Changes in Glucose Area to Body Composition

There were significant correlations between the weight loss–induced change in glucose area during the OGTT and

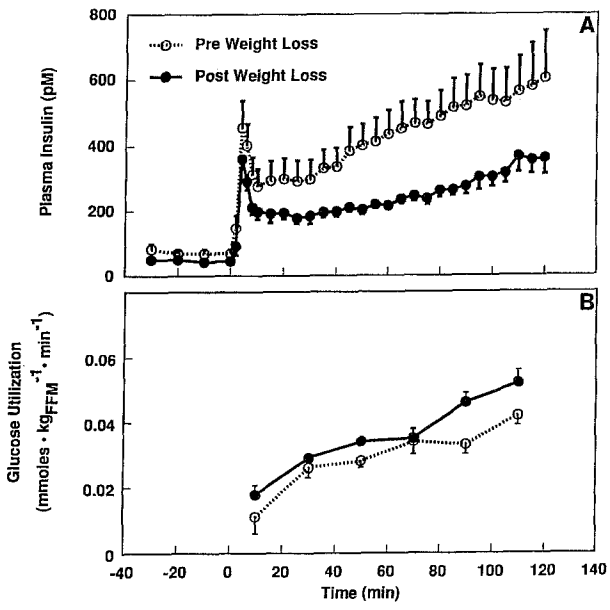

Fig 2. Plasma (A) insulin concentrations, acute-phase (0 to 10 minutes) and second-phase (20 to 120 minutes), and (B) glucose utilization (M) rate during the hyperglycemic clamp before and after weight loss.

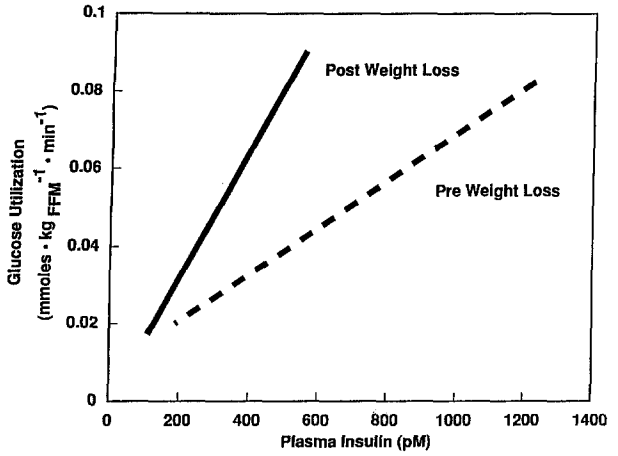

Fig 3. Relationships between glucose utilization (M) rates and plasma insulin concentrations during the hyperglycemic clamp are represented by regression lines. The mean slope of the line before weight loss differed significantly from the mean slope after weight loss ($P < .01$). Pre–weight loss regression equation: M = 0.0088 + 0.00006 · insulin; post–weight loss regression equation: M = −0.0005 + 0.00016 · insulin.

the change in waist circumference ($r = .49$, $P = .005$), the change in fat mass ($r = .40$, $P = .02$), the baseline glucose area ($r = -.37$, $P = .02$), and the change in percent body fat ($r = .36$, $P = .03$). There were no significant correlations between change in glucose area and baseline percent body fat, baseline waist circumference, baseline WHR, or change in WHR. There were also no correlations between baseline insulin area or change in insulin area during the OGTT after weight loss with changes in the measures of body composition. To identify independent determinants of the change in glucose area following weight loss, a stepwise multiple regression analysis was performed with change in glucose area as the dependent variable and initial glucose area, change in waist circumference, and change in percent body fat as the independent variables. This model explained 27% of the variance in change in glucose area (Table 3). The change in waist circumference explained 16% ($P < .01$) of the variance, and the baseline glucose area explained an additional 11% ($P < .05$) of the variance. The change in percent body fat (or the change in fat mass) did not add significantly to the model.

DISCUSSION

These results show that weight loss induced by energy restriction improves glucose tolerance and insulin action in overweight middle-aged and older men with either normal glucose tolerance or IGT. Moreover, in multiple regression analysis, improvement in glucose metabolism was related to reduction in central body fat, as estimated by a reduction in waist circumference. In addition, these improvements were greatest in men with the most severe glucose intolerance at baseline. These results suggest that middle-aged and older subjects with IGT and an upper-body fat distribution will benefit significantly from weight loss. It is also likely that some older individuals with the insulin resistance syndrome and its associated metabolic abnormalities might derive substantial benefit from weight loss interventions.[19]

Table 3. Independent Determinants of the Weight-Loss–Induced Improvement in Glucose Area

Independent Variable	Partial R^2	β	P
Change in waist circumference	16%	2.5	.02
Initial glucose area	11%	−0.3	.03
Change in percent body fat	—	0.6	.70

There is evidence from cross-sectional studies that both total and abdominal obesity are associated with IGT, insulin resistance, and development of hyperinsulinemia.[20-22] However, few studies have examined the effects of weight loss on glucose tolerance and insulin sensitivity in obese older subjects. In a previous study, we showed that diet-induced weight loss improved glucose tolerance and reduced insulin levels during an OGTT more effectively than exercise training in 10 obese, older, nondiabetic men.[5] Results of the present study confirm the beneficial effects of weight loss on glucose and insulin metabolism as measured during an OGTT in a larger sample of obese middle-aged and older men. Moreover, the hyperglycemic clamp provides direct assessment of the effects of weight loss on glucose disposal and insulin action and indirect assessment of peripheral tissue sensitivity to endogenously secreted insulin. Weight loss was associated with an increase in the glucose disposal rate and a reduction in the glucose-stimulated insulin response, consistent with a significant improvement in insulin sensitivity.

Weight loss of 20 kg following gastric bypass surgery in eight morbidly obese women also improved peripheral tissue sensitivity to endogenous insulin.[23] In that study, obese individuals had a significant reduction in insulin secretion, as well as an increase in insulin clearance by the liver. In another study of middle-aged overweight subjects with non–insulin-dependent diabetes mellitus and glucose intolerance, weight loss through caloric restriction improved fasting glucose levels and meal tolerance.[24] Improvements in glucose metabolism were attributed to an increase in hepatic insulin sensitivity and a reduction in basal endogenous glucose production. However, in contrast to the results of our study, peripheral insulin sensitivity as measured by the hyperinsulinemic-euglycemic clamp technique did not change following weight loss of 10 kg. There are several possible explanations for the disparate results between our study and that reported by Bogardus et al.[24] First, there were no subjects with diabetes in our study. The presence of diabetes suggests more severe defects in insulin action and secretion; therefore, a weight loss of 10 kg might not have been sufficient to normalize the defects in skeletal muscle insulin receptor kinase activity and other postreceptor mechanisms mediating insulin action.[25] Second, the men in our study had a significant reduction in upper-body distribution of fat, as indexed by a reduction in waist circumference, whereas subjects in the study reported by Bogardus et al did not appear to have a change in the regional distribution of body fat. Finally, greater reductions

in FFM following weight loss in their subjects as compared with our subjects may have blunted increases in insulin sensitivity. Thus, the ability of diet-induced weight loss to improve insulin sensitivity may be affected not only by the degree of total weight loss, but also by the change in regional fat distribution, the rate and composition of the weight loss, and the degree of glucose intolerance at baseline.

Weight loss in our subjects was associated with a significant reduction in WHR, waist circumference, and percent body fat. Similar to other reports, there was a significant correlation between the change in glucose area during an OGTT and the change in waist circumference, independent of the change in percent body fat.[21,26] There were no associations between change in glucose and insulin levels and change in WHR. In our subjects, concomitant and relatively equal reductions in waist and hip circumferences with weight loss resulted in a narrow range for the change in WHR. This truncated range may account for the lack of association between change in glucose area and change in WHR. Additionally, the change in WHR that accompanies weight loss may not accurately reflect the reduction in intraabdominal fat, particularly in the elderly. In our laboratory, we found no correlation between change in intraabdominal fat, measured by computed tomographic scan, and change in WHR ($r = .06$) in 14 weight-reduced postmenopausal women (B. Nicklas and A. Goldberg, unpublished data, April 1994). Cross-sectional data indicate that waist circumference is a more accurate index of abdominal visceral fat content and correlates better with glucose and insulin levels than WHR.[27] In a study of young and older men and women, waist circumference was an independent predictor of glucose disposal rate during a euglycemic clamp, explaining greater than 40% of the variance in insulin sensitivity.[28] In male subjects, WHR was not associated with insulin sensitivity after waist circumference was taken into account statistically. In a longitudinal study of the effects of exercise and weight loss on body composition in older men, a 2% reduction in WHR accompanied a 20% reduction in intraabdominal fat measured by computed tomographic scan.[29] Collectively, these findings suggest that it would be advantageous to use computed tomographic scans to quantify the change in intraabdominal fat that follows diet-induced weight loss in older patients. Studies are now in progress to examine the effects of exercise and weight loss on intraabdominal fat content in older men and women.

In addition to age-associated changes in body composition and physical activity that contribute to the increased prevalence of insulin resistance and glucose intolerance in the elderly, age-related changes in sex hormone levels appear to play a role in this metabolic dysfunction. In men, testosterone levels decline with advancing age.[30] Although we did not measure testosterone levels in our subjects, other investigators report that low testosterone levels are associated with increased levels of visceral fat in men.[31,32] Moreover, recent data indicate that moderate doses of exogenous testosterone decrease visceral fat mass and improve glucose tolerance in middle-aged men.[33] However, to our knowledge, it is unknown whether loss of visceral fat and accompanying improvements in metabolic function are associated with a change in testosterone levels.

In conclusion, older individuals with IGT have an increased risk of development of non–insulin-dependent diabetes mellitus[7] and coronary artery disease.[8] Forty-five percent of the men in this study with IGT at baseline had a normalized glucose tolerance following weight reduction. Aerobic exercise also increases insulin sensitivity in older men.[34] The combined effects of exercise and weight loss may be synergistic in improving glucose and insulin metabolism by reducing fat mass and increasing muscle mass and $\dot{V}O_2max$.[35] It is possible that even more of the obese sedentary men with IGT would have a normalized glucose tolerance if they also engaged in regular aerobic exercise. It will be important to continue to evaluate these subjects longitudinally; if the weight loss can be maintained, the improved glucose and insulin metabolism may translate into decreased risk for diabetes and associated comorbidities.

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