

Effects of Weight Loss Among Metabolically Healthy Obese Men and Women

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OBJECTIVE — Weight loss among metabolically healthy obese (MHO) individuals may be unnecessary or result in elevated cardio-metabolic risk. We studied the effects of exercise- or diet-induced weight loss on cardio-metabolic risk among MHO and metabolically abnormal obese (MAO) adults.

RESEARCH DESIGN AND METHODS — Participants were 63 MHO and 43 MAO adults who took part in 3 to 6 months of exercise- or diet-induced weight loss intervention. Changes in anthropometry, adipose tissue distribution, and cardio-metabolic risk factors were assessed.

RESULTS — Body weight, waist circumference, and total abdominal and visceral adipose tissue were reduced in all subjects ($P < 0.05$). Improvements in insulin sensitivity were observed in MHO and MAO men and women ($P < 0.05$), but were greater in the MAO individuals ($P < 0.05$). Fasting insulin was the only other cardio-metabolic improvement among MHO individuals ($P < 0.05$).

CONCLUSIONS — Lifestyle-induced weight loss among MHO subjects is associated with a reduction in total and abdominal obesity and improvement in selected cardio-metabolic risk factors.

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Weight loss among metabolically healthy obese (MHO) individuals characterized by low cardio-metabolic risk and low prospective risk of type 2 diabetes and cardiovascular disease may be unnecessary and paradoxically may actually increase health risk (1,2). That weight reduction may be contraindicated for MHO individuals is at odds with the standing recommendation from leading health authorities that weight loss be the primary treatment strategy for all obese patients, regardless of cardio-metabolic status (3). We sought to investigate the effects of exercise- and diet-induced weight reduction on cardio-metabolic risk factors among MHO and metabolically abnormal obese (MAO) adults.

RESEARCH DESIGN AND METHODS

Subjects included Caucasian men and premenopausal and postmenopausal women without overt disease who were recruited from the general public and had participated in previously published lifestyle-based weight loss studies (4–6). For the current investigation, we employed data from men ($n = 20$) and women ($n = 29$) randomized to either the diet-induced or the exercise-induced weight loss intervention (4,5). Additionally, 136 older abdominally obese men and women (aged 60–80 years) participated in a study on the effects of resistance and/or aerobic exercise on risk factors for disease and disability (6). For the current investigation, data from those men ($n = 26$) and women

($n = 34$) randomized to the aerobic exercise or the resistance and aerobic exercise combined group were included. All participants gave informed consent in accordance with the ethical guidelines set by Queen's University.

Definition of MHO versus MAO

We defined MHO men and women as abdominally obese (waist circumference >88 cm in women and 102 cm in men) with one or none of the following risk factors: fasting plasma glucose ≥ 5.6 mmol/l, triglycerides ≥ 1.7 mmol/l, HDL cholesterol <1.0 mmol/l in men and <1.3 mmol/l in women, and blood pressure $\geq 130/85$ mmHg (7). All participants meeting two or more of the above risk factors were classified as MAO. Although we defined the MHO and MAO groups according to a clustering of cardio-metabolic risk factors, our primary observations regarding improvement in insulin sensitivity remained when subjects were categorized solely by tertiles of insulin sensitivity at baseline (these data can be found in supplementary Fig. 1, available in an online appendix at <http://care.diabetesjournals.org/cgi/content/full/dc10-0547/DC1>).

Interventions

Of the 46 men in the current study, 20 were randomly assigned to a diet ($n = 11$) or exercise ($n = 9$) program designed to induce a daily 700-kcal energy deficit for 12 weeks (4). The remaining men were randomized to either 6 months of aerobic exercise ($n = 13$) performed 5 times per week for 30 min or to resistance and aerobic exercise combined ($n = 13$) performed 3 times per week (30 min of aerobic exercise plus ~ 20 min of resistance exercise per session) (6).

Of the 63 women in the current study, 29 premenopausal women were randomized to a diet ($n = 13$) or exercise ($n = 16$) program designed to induce a daily 500-kcal energy deficit for 14 weeks (5). The remaining postmenopausal women were randomized to either 6 months of aerobic exercise ($n = 16$) performed 5 times per week for 30 min or to resistance and aerobic exercise combined

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(n = 18) performed 3 times per week (30 min of aerobic exercise plus ~20 min of resistance exercise per session) (6).

Anthropometric, metabolic, and magnetic resonance imaging measurements

All anthropometric and whole-body magnetic resonance imaging data were obtained using standard procedures (4–6). Blood samples used to determine fasting glucose, insulin, lipid, and lipoprotein values were obtained in the morning after a 12- to 14-h fast. The hyperinsulinemic euglycemic clamp procedure used to determine insulin sensitivity was identical in all studies (4–6).

Statistical analyses

Baseline differences for all variables between groups were assessed using a 2-by-2 (sex-by-metabolic stratification) ANCOVA with age as a covariate. Post hoc analysis was performed using independent-samples *t* tests with a Bonferroni correction for multiple comparisons. Changes in variables (prepost) in response to intervention were assessed using repeated-measures ANCOVA with sex and metabolic stratification as the between-subjects factors with inclusion of age and treatment modality as covariates. Subsequent comparisons were performed with a Bonferroni correction for multiple comparisons. Statistical procedures were performed using SPSS 17.0 software (Chicago, IL).

RESULTS — Subject characteristics and the effects of intervention among MAO and MHO are in Table 1. With the exception of skeletal muscle, all anthropometric and adipose tissue measures reduced significantly in response to intervention among MAO and MHO men and women (*P* < 0.05). Insulin sensitivity increased in both MAO and MHO groups independent of sex (*P* < 0.05); the change was greater in the MAO groups (*P* < 0.05). Improvements in selected cardio-metabolic risk factors also occurred in both MAO and MHO men and women, but were more common in the MAO groups.

CONCLUSIONS — It has been reported that a modest weight reduction achieved via caloric restriction resulted in a 13% deterioration in insulin sensitivity among a group of postmenopausal MHO women (2). Our results counter these observations as insulin sensitivity improved

Table 1—Anthropometric, body composition, and cardio-metabolic outcomes at baseline and in response to intervention in MAO and MHO men and women

	Men				Women			
	MAO	MAO (Δ)	MHO	MHO (Δ)	MAO	MAO (Δ)	MHO	MHO (Δ)
n	20	20	26	26	23	23	40	40
Age (years)	53.1 ± 14.8		61.4 ± 11.8*		46.5 ± 10.7		61.1 ± 12.0*	
Anthropometric								
Body weight (kg)	98.1 ± 9.4	-6.0 ± 2.8†	95.6 ± 12.3	-4.0 ± 2.8†	87.1 ± 8.3*	-4.9 ± 2.4††	81.1 ± 11.4*	-3.0 ± 2.3††
BMI (kg/m ²)	31.4 ± 2.7	-1.9 ± 0.9†	31.0 ± 3.1	-1.3 ± 1.0†	32.7 ± 2.9	-1.8 ± 1.0††	30.4 ± 3.6	-1.1 ± 0.8††
Waist circumference (cm)	109.2 ± 6.0	-6.2 ± 2.8†	111.7 ± 8.3	-5.6 ± 3.2†	101.7 ± 7.8*	-4.6 ± 3.2††	99.3 ± 8.4*	-4.1 ± 3.3††
MRI								
Total AT (kg)	32.6 ± 6.0	-5.1 ± 2.2†	33.6 ± 8.2	-4.1 ± 2.0†	40.0 ± 6.1*	-4.7 ± 2.9††	37.4 ± 7.9*	-3.2 ± 2.3††
Total SM (kg)	33.5 ± 4.5	-0.8 ± 1.3	30.9 ± 3.7	-0.2 ± 1.3	22.7 ± 2.7*	-1.0 ± 1.2	20.1 ± 3.1*	0.1 ± 1.0
Visceral AT (cm ³)	208.7 ± 64.8	-40.1 ± 26.3†	222.8 ± 63.7	-40.5 ± 34.4†	146.0 ± 58.2*	-18.2 ± 24.6††	142.7 ± 44.1*	-19.0 ± 21.7††
Abdominal SAT (cm ³)	301.7 ± 103.1	-40.5 ± 35.4†	294.6 ± 130.2	-28.8 ± 33.8†	403.9 ± 86.0*	-39.5 ± 49.0††	369.2 ± 106.8*	-21.3 ± 40.1††
Cardio-metabolic								
Fasting glucose (mmol/l)	5.3 ± 0.5	-0.6 ± 0.7†	4.9 ± 0.5*	-0.1 ± 0.4	5.5 ± 0.7	-0.3 ± 0.8	4.8 ± 0.4*	0.0 ± 0.4
Fasting insulin (UI)	9.8 ± 5.2	-1.9 ± 4.2	9.8 ± 5.2	-2.0 ± 3.2‡	10.6 ± 6.4	-3.8 ± 4.0†	7.0 ± 4.5*	-0.6 ± 3.9
Cholesterol (mmol/l)	4.3 ± 1.0	-0.0 ± 0.6	4.3 ± 0.8	-0.2 ± 0.4	5.1 ± 0.6*	-0.4 ± 0.5*	5.2 ± 0.9*	-0.1 ± 0.5
HDL cholesterol (mmol/l)	0.8 ± 0.3	0.1 ± 0.1†	1.1 ± 0.2*	0.1 ± 0.1	1.1 ± 0.2*	-0.0 ± 0.1	1.5 ± 0.4*§	0.0 ± 0.2
LDL cholesterol (mmol/l)	2.5 ± 0.8	0.1 ± 0.5	2.6 ± 0.7	-0.2 ± 0.4	3.1 ± 0.7*	-0.2 ± 0.5	3.1 ± 0.8*	-0.1 ± 0.4
Triglycerides (mmol/l)	2.3 ± 0.9	-0.5 ± 0.7†	1.4 ± 0.5*	-0.2 ± 0.4	2.1 ± 0.7	-0.3 ± 0.5†	1.3 ± 0.5*	-0.0 ± 0.3
Insulin sensitivity (mg/kg · SM/min)	10.8 ± 3.4	5.7 ± 4.0†	14.9 ± 7.4*	3.3 ± 4.6†	15.7 ± 7.1*	4.8 ± 4.9†	22.7 ± 7.0*§	4.2 ± 5.4†
(mg/kg · SM/min/ΔμUI/ml)¶	0.21 ± 0.09	0.15 ± 0.12†	0.26 ± 0.17*	0.07 ± 0.11	0.37 ± 0.20§	0.17 ± 0.16†	0.43 ± 0.20*§	0.09 ± 0.12†
Systolic BP (mmHg)	128.4 ± 16.0	-2.1 ± 11.9	122.0 ± 17.7	-3.0 ± 11.0	122.9 ± 17.8	-1.9 ± 18.0	122.4 ± 13.4	0.1 ± 11.3
Diastolic BP (mmHg)	82.2 ± 10.8	-2.9 ± 10.4	76.2 ± 9.3	-2.1 ± 6.4	73.6 ± 7.9	0.3 ± 9.9	72.3 ± 7.0	-1.5 ± 7.1

Data presented as the group means ± SD. (Δ), data presented as the group means ± SD for change scores (prepost). *Significantly different from at-risk group of same sex (*P* < 0.05). †Significant change in variable from pre- to post-intervention (*P* < 0.05). ‡Change in variable different in men vs. women (*P* < 0.05 for interaction by sex). §Significantly different from men (*P* < 0.05). ||Change in variable different in MHO vs. MAO (*P* < 0.05 for interaction risk category). ¶Analyses controlled for age and treatment modality (diet vs. exercise). ††Corrected for differences in measured insulin levels obtained at baseline and during the final 30 min of euglycemia. AT, adipose tissue; BP, blood pressure; MRI, magnetic resonance imaging; SAT, subcutaneous adipose tissue; SM, skeletal muscle.

in MHO men and women by 22 and 18.5%, respectively, regardless of weight-loss modality (these data can be found in supplementary Fig. 2, available in the online appendix). This experimental finding is consistent with recent observational studies wherein MHO and MAO individuals were at similarly elevated risk of cardiovascular disease and all-cause mortality in comparison to metabolically healthy and lean individuals (8,9). Additionally, in comparison to metabolically healthy lean adults, MHO individuals showed signs of subclinical vascular disease marked by a significantly greater intima-media thickness of the common carotid artery and endothelial dysfunction (10).

While limited health care resources dictate the need to prioritize high-risk obese individuals for aggressive treatment, the notion that individuals with uncomplicated obesity would not benefit from lifestyle-induced weight loss seems an inappropriate public health message. This message may be particularly misguided at a time when the prevalence of obesity and its attendant diseases continues to increase despite a greater public awareness of the benefits of weight loss (11). Indeed, our findings reinforce the recommendation that weight or waist circumference reduction in response to lifestyle-based treatment strategies should be considered an appropriate treatment option for all obese men and women regardless of current metabolic status.

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