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CME

Modest Visceral Fat Gain Causes Endothelial Dysfunction in Healthy Humans

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CME Objective for This Article: At the conclusion of this activity, the learner should be able to identify the effects of fat gain on endothelial function.

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Modest Visceral Fat Gain Causes Endothelial Dysfunction in Healthy Humans

Objectives The aim of this study was to determine the impact of fat gain and its distribution on endothelial function in lean healthy humans.

Background Endothelial dysfunction has been identified as an independent predictor of cardiovascular events. Whether fat gain impairs endothelial function is unknown.

Methods A randomized controlled study was conducted to assess the effects of fat gain on endothelial function. Forty-three normal-weight healthy volunteers were recruited (mean age 29 years; 18 women). Subjects were assigned to gain weight (approximately 4 kg) (n = 35) or to maintain weight (n = 8). Endothelial function (brachial artery flow-mediated dilation [FMD]) was measured at baseline, after fat gain (8 weeks), and after weight loss (16 weeks) for fat gainers and at baseline and follow-up (8 weeks) for weight maintainers. Body composition was measured by dual-energy X-ray absorptiometry and abdominal computed tomographic scans.

Results After an average weight gain of 4.1 kg, fat gainers significantly increased their total, visceral, and subcutaneous fat. Blood pressure and overnight polysomnography did not change after fat gain or loss. FMD remained unchanged in weight maintainers. FMD decreased in fat gainers (9.1 ± 3% vs. 7.8 ± 3.2%, p = 0.003) but recovered to baseline when subjects shed the gained weight. There was a significant correlation between the decrease in FMD and the increase in visceral fat gain (rho = −0.42, p = 0.004), but not with subcutaneous fat gain (rho = −0.22, p = 0.15).

Conclusions In normal-weight healthy young subjects, modest fat gain results in impaired endothelial function, even in the absence of changes in blood pressure. Endothelial function recovers after weight loss. Increased visceral rather than subcutaneous fat predicts endothelial dysfunction. (Fat Gain and Cardiovascular Disease Mechanisms; NCT00589498) (J Am Coll Cardiol 2010;56:662–6) © 2010 by the American College of Cardiology Foundation

Endothelial dysfunction is considered a systemic process and an early event in the atherosclerotic process (1). Brachial artery flow-mediated dilation (FMD) reflects coronary endothelial function (2,3) and has been associated with a higher prevalence of coronary artery disease (1) and is an independent predictor of cardiovascular events in patients with and without established atherosclerosis (4,5).

Increased body fat has been linked to a higher risk for cardiovascular disease. Previous studies assessing obesity and endothelial dysfunction have been cross-sectional in nature, and thus no causal interaction can be defined (6,7). Although visceral obesity is predictive of increased cardiovascular risk, there are no data on the interactions between visceral obesity and endothelial function. We tested the hypothesis that endothelial function is impaired after weight gain and recovers after reversal of weight gain. We also tested the hypothesis that impaired endothelial function is linked to visceral or subcutaneous fat accumulation.

Methods

We recruited 43 healthy volunteers with baseline body mass indexes (BMIs) of 18.5 to 24.9 kg/m^2. Subjects were excluded if they were smokers, were pregnant, were taking any medication, or had any acute or chronic illness. This study was approved by the Mayo Clinic institutional review board, and all subjects provided written informed consent.

Fat gainer and weight maintainer protocols. After a weight maintenance period of 3 days, subjects were randomly assigned to be in the fat gainer or weight maintainer group, with a 20% chance of being a weight maintainer. For the fat gainer group, for the first 8 weeks, each subject received 1,000 kcal/day (40% carbohydrate, 40% fat, and 20% protein) in addition to weight maintenance requirements. The goal was to gain 3 to 4 kg of total body fat (a 5% increase in weight). After the fat gain, subjects underwent a diet program to return to their basal weights. Dietary counseling was available to all participants, and their weights were monitored by a dietitian throughout the study. Exercise treadmill testing was conducted to assess changes in levels of physical fitness during the study.

Body composition. We measured height by wall stadiometer, weight by electronic scale, and waist and hip circumferences by nonelastic tape. The volunteers underwent computed tomographic measures of visceral fat area (single-slice computed tomography at the L2 to L3 interspace) and dual-energy X-ray absorptiometry (Lunar Radiation, Madison, Wisconsin) at baseline and after 8 weeks for both groups and after weight loss (16 weeks) for fat gainers. For logistic reasons, computed tomographic and dual-energy X-ray absorptiometry measures were obtained in all 35 subjects before and after weight gain and in 16 subjects after weight loss.

Vascular studies. All subjects were asked to abstain from alcohol and caffeine for 24 h before the study. Subjects underwent complete overnight polysomnography to exclude the development of sleep apnea using the apnea-hypopnea index (events/h) (8) with weight gain. FMD was measured in the morning with the subjects fasting, with high-resolution ultrasound following a standard protocol as previously described (9).