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Experimental Weight Gain Increases Ambulatory Blood Pressure in Healthy Subjects: Implications of Visceral Fat Accumulation

Naima Covassin, PhD; Fatima H. Sert-Kuniyoshi, PhD; Prachi Singh, PhD; Abel Romero-Corral, MD; Diane E. Davison, RN; Francisco Lopez-Jimenez, MD; Michael D. Jensen, MD; and Virend K. Somers, MD, PhD

Abstract

Objective: To examine whether experimentally induced weight gain raises ambulatory blood pressure (BP) in healthy subjects and identify any relationship between changes in BP and changes in regional fat distribution.

Patients and Methods: Twenty-six normal weight subjects were randomized to 8 weeks of weight gain through overfeeding (n=16; age, 30.4±6.6 years) or to weight maintenance (controls; n=10; age, 27.1±7.7 years) between July 2004 and August 2010. Measures of body composition via dual energy X-ray absorptiometry and computed tomography, circulating biomarkers, and 24-hour ambulatory BP were obtained at baseline and after the 8-week experimental phase.

Results: Overfeeding resulted in 3.7 kg (95% CI, 2.9-4.5) increase in body weight in weight gainers, with increments in total (46.2 cm^2; 95% CI, 27.6-64.9), visceral (13.8 cm^2; 95% CI, 5.8-21.9), and subcutaneous fat (32.4 cm^2; 95% CI, 13.5-51.3). No changes occurred in the maintenance group. Increases in 24-hour systolic BP (4 mm Hg; 95% CI, 1.6-6.3), mean BP (1.7 mm Hg; 95% CI, 0.3-3.3), and pulse pressure (2.8 mm Hg; 95% CI, 1.1-4.4) were evident after weight gain in the experimental group, whereas BP remained unchanged in controls. Changes in mean BP correlated only with changes in visceral fat (ρ=0.45; P=.02), but not with changes in other body composition measures.

Conclusion: Modest weight gain causes elevation in 24-hour BP in healthy subjects. The association between increased BP and abdominal visceral fat accumulation suggests that visceral deposition of adipose tissue may contribute specifically to the enhanced risk of hypertension associated with weight gain.

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From the Department of Cardiovascular Medicine (N.C., F.H.S.-K., P.S., A.R.-C., D.E.D., F.L.-J., V.K.S.) and the Division of Endocrinology, Department of Medicine (M.D.J.), Mayo Clinic, Rochester, MN.

Excess body weight is widely recognized as a leading contributor to morbidity and mortality,[1,2] being associated with enhanced vulnerability to various cardiovascular and noncardiovascular diseases including hypertension. Current estimates on the prevalence of hypertension show that 36% to 47% of the obese population suffers from high blood pressure (BP), compared with 20% of normal weight individuals,[3,4] and prospective studies have consistently identified increased body weight as a determinant of BP elevation and new-onset hypertension.[5-7]

Nevertheless, there is substantial variability in the disease risk conferred by excess weight when individuals are stratified solely on the basis of their body mass index (BMI; calculated as the weight in kilograms divided by the height in meters squared). In spite of its conventional use as a surrogate for total body adiposity, BMI does not discriminate between lean mass and fat mass, nor does it take into account fat partitioning among various depots. In this regard, growing evidence indicates that the anatomic location of fat accumulation is a key feature in determining risk status,[8-10] suggesting that interindividual differences in disease propensity may be partially ascribed to the heterogeneity in regional adiposity distribution existing at any given BMI. Specifically, abdominal visceral obesity has recently emerged as the obesity-phenotype conveying the most unfavorable health profile.

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In comparison to total and subcutaneous adiposity, visceral fat is more closely related to cardiometabolic risk factors, such as fasting glucose, lipids, and endothelial function,[11-13] as well as to the presence of overt diseases such as coronary atherosclerosis and stroke.[14] In addition, visceral adiposity has been showed to perform better than other anthropometric measures as a predictor of cardiovascular and all-cause deaths.[15,16]

The critical role of visceral fat in obesity-related hypertension is increasingly apparent. Several population-based studies, including the Framingham and the Jackson cohorts, have linked visceral fat deposition to heightened BP values and greater prevalence of hypertension,[11,12,17,18] with these associations being independent of total body weight and subcutaneous adiposity. More recently, observational longitudinal data on the impact of visceral fat accumulation on incident hypertension have also been reported.[17,19-21]

Nevertheless, unlike the relative abundancy of observational evidence connecting visceral fat deposition to high BP, there is a paucity of interventional, mechanistic studies addressing the effects of experimental fat gain, and specifically of increases in visceral fat, on BP in human subjects.

Building upon these considerations, we conducted a randomized controlled study to examine whether experimental weight gain raises 24-hour ambulatory BP in healthy individuals (primary outcome) and to define the relative contribution of changes in regional fat distribution (secondary outcome). We hypothesized that overfeeding-induced weight gain would increase ambulatory BP and that fat deposition in the visceral compartment would be preferentially associated with larger BP increments.

PATIENTS AND METHODS

Study Population

Twenty-six nonobese, healthy individuals (16 males; mean ± SD age, 29.1±7.1 years; BMI, 23.6±3.1 kg/m^2) were recruited as part of a larger project on the effects of weight gain on cardiometabolic health.[22-24] Eligible subjects had to be sedentary, nonsmokers, free of overt medical or psychiatric diseases, and not taking any medications aside from the birth control pill for women. Absence of undiagnosed medical conditions was confirmed by physical examination, collection of medical history, and polysomnography to rule out sleep disordered breathing. A negative pregnancy test result was required for women.

The protocol was approved by the Mayo Clinic Institutional Review Board and informed consent was obtained from all participants. These studies were conducted between July 1, 2004, and August 31, 2010.

Study Design

Subjects underwent an initial 3-day period of weight maintenance, during which they adhered to a dietary regimen consisting of 40% carbohydrate, 40% fat, and 20% protein. The individual calorie intake required for weight stability was determined by research dieticians after consultation with each participant.

Following baseline evaluation, enrolled subjects were randomized to an 8-week experimental protocol of either moderate weight gain (5% increase in body weight) or weight maintenance. Subjects assigned to the weight gain group (n=16) were instructed to increase their habitual food intake by increasing their portion sizes or by consuming 400 to 1200 extra kcal/d via dietary supplements. Available supplements were chocolate bars (king-size Snickers bar, 510 kcal; Mars Inc), ice-cream shakes (402 kcal), and nutritional energy drinks (Boost Plus, 360 kcal/8 oz; Nestle Nutrition). Participants randomized to weight maintenance (n=10) were instructed to continue with their normal diet for the 8-week experimental phase. Weight measures were obtained 5 times/wk or more during the study and caloric intakes were adjusted to achieve the targeted increase in body weight in gainers. Adherence to usual diet was reinforced in maintainers if they exhibited ±2% changes in body weight. All subjects were advised to maintain their usual lifestyle routines throughout the study period with the exception of avoiding caffeine and alcohol consumption for 24-hour before and on the day scheduled for measurements. Body composition, BP, and blood specimen measures were taken at study entry and after completion of the 8-week experimental protocol.