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Effect of Obesity and Overweight on Left Ventricular Diastolic Function

A Community-Based Study in an Elderly Cohort

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Objectives The purpose of this study was to assess the independent effect of increased body size on left ventricular (LV) diastolic function.

Background Obese and overweight persons are at increased risk of heart failure. Left ventricular diastolic dysfunction is an asymptomatic condition associated with future heart failure. It is unclear whether obesity and overweight are independently associated with LV diastolic dysfunction.

Methods The LV diastolic function was evaluated in 950 participants from the CABL (Cardiovascular Abnormalities and Brain Lesions) study by traditional and tissue Doppler imaging. Peak early transmitral diastolic flow velocity (E), late transmitral diastolic flow velocity (A), and early diastolic mitral annulus velocity (E′) were measured, and E/A and E/E′ were calculated. The study sample was divided into 3 groups: normal weight (body mass index [BMI] $<$25.0 kg/m^2), overweight (BMI 25.0 to 29.9 kg/m^2), and obese (BMI $\geq$30 kg/m^2).

Results In multivariate analyses, BMI was independently associated with higher E, A, and E/E′, an indicator of LV filling pressure (all $p \leq 0.01$). Overweight and obese had lower E′ (both $p < 0.01$) and higher E/E′ (both $p < 0.01$) than normal weight participants. The E/A was lower in obese subjects than in normal weight subjects ($p < 0.01$). The risk of diastolic dysfunction was significantly higher in overweight subjects (adjusted odds ratio: 1.52, 95% confidence interval: 1.04 to 2.22) and obese subjects (adjusted odds ratio: 1.60, 95% confidence interval: 1.06 to 2.41) compared to normal weight subjects.

Conclusions Increased BMI was associated with worse LV diastolic function independent of LV mass and associated risk factors. The increased risk of LV diastolic dysfunction in both overweight and obese persons may partially account for the increased risk of heart failure associated with both conditions. (J Am Coll Cardiol 2011;57:1368–74) © 2011 by the American College of Cardiology Foundation

The prevalence of obesity is steadily increasing worldwide, and constitutes a major health issue because of its association with morbidity, mortality, and cardiovascular diseases (1–3). Obesity is an independent predictor of incident heart failure in the general population, and evidence exists that overweight also carries an increased risk of heart failure, which is intermediate between that of obese and lean persons (4,5). An increase in body size, besides being associated with cardiovascular risk factors such as hypertension, diabetes mellitus, and hyperlipidemia, directly affects cardiac structure and function. The excess in body fat determines an increase in both pre-load and afterload due to a hyperdynamic circulation, chronic volume overload, and increase in peripheral resistance (6,7). In addition, it has been demonstrated that increased adiposity enhances the effect of blood pressure on left ventricular (LV) mass growth (8). As a result, LV dilation and increased LV mass are frequent findings in persons with increased body weight, with both eccentric and concentric LV geometric patterns described in these conditions (9–11).

Left ventricular diastolic dysfunction is a condition that reflects an impairment of the filling properties of the left ventricle that has been demonstrated to be a predictor of future development of heart failure in population settings (12–15). Left ventricular diastolic dysfunction might, therefore, represent one of the pathophysiological links between

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an increased body weight and the future occurrence of heart failure. Cardiovascular risk factors and cardiac structural changes associated with obesity/overweight are also major determinants of LV diastolic function (16,17). Whether an increased body weight is associated with an impairment of LV diastolic mechanics, independent of associated risk factors, has not been fully established. Accordingly, the aims of our study were: 1) to analyze the association between body size and LV diastolic function, assessed by transthoracic echocardiography, in a community-based cohort of subjects over age 50 years; 2) to evaluate the impact of associated risk factors on this relationship; and 3) to investigate the effect of different degrees of increased body size on the risk of LV diastolic dysfunction.

Methods

Study population. The study cohort was derived from the NOMAS (Northern Manhattan Study), a population-based prospective study evaluating the incidence, risk factors, and clinical outcome of stroke in the population of northern Manhattan. Study design and methodological details have been described previously (18). From September 2005, the NOMAS subjects >50 years of age who voluntarily agreed to undergo a brain magnetic resonance imaging study and a more extensive echocardiographic evaluation including diastolic function assessment were included in the CABL (Cardiac Abnormalities and Brain Lesion) study. This subset of subjects constitutes the study population of the present report. Informed consent was obtained from all study participants. The study was approved by the institutional review board of Columbia University Medical Center.

Risk factors assessment. Hypertension was defined as systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg at the time of the visit (mean of 2 readings), or the patient's self-reported history of hypertension or use of antihypertensive medications. Diabetes mellitus was defined as fasting blood glucose ≥126 mg/dl or the patient's self-reported history of diabetes or use of diabetes medications. Hypercholesterolemia was defined as total serum cholesterol >240 mg/dl, and the patient's self-report of hypercholesterolemia or use of lipid-lowering treatment. Body mass index (BMI) was calculated as weight (kg) divided by height-squared (m^2). According to a standard definition, overweight was defined as BMI between 25.0 and 29.9 kg/m^2, and obesity as BMI ≥30 kg/m^2 (19).

Echocardiographic assessment. Transthoracic echocardiography was performed using a commercially available system (iE 33, Philips, Andover, Massachusetts) by a trained registered sonographer following a standardized protocol. The LV linear dimensions were measured from a parasternal long-axis view according to the recommendations of the American Society of Echocardiography (20). The LV mass was calculated with a validated formula (21) and indexed both for body surface area (BSA) and height$^{2.7}$ (22). The LV relative wall thickness was calculated as follows: (2 × posterior wall thickness) divided by end-diastolic diameter (23). The LV ejection fraction was calculated by biplane modified Simpson's rule.

Abbreviations and Acronyms

BMI = body mass index

BSA = body surface area

CI = confidence interval

LV = left ventricular

OR = odds ratio

TDI = tissue Doppler imaging

Left ventricular diastolic function assessment has been described previously in detail (17). Briefly, from an apical 4-chamber view, transmitral flow was sampled by pulsed-wave Doppler at the level of mitral valve leaflet tips. Peak velocities of the early phase (E) and late phase (A) of the mitral inflow were measured, and their ratio (E/A) was calculated. Left ventricular myocardial velocities were evaluated by tissue Doppler imaging (TDI). Pulsed TDI sample volume was placed at the level of the lateral and septal mitral valve annulus, and the peak early diastolic velocities (E′) were measured and then averaged (24). The ratio between E and E′ (E/E′) was calculated as an index of LV filling pressures (25). Diastolic dysfunction was defined as 1) E/A ≤0.7 (impaired relaxation, grade I); or 2) E/A >0.7 and ≤1.5 and E′ <7 cm/s (pseudonormalized pattern, grade II); or 3) E/A >1.5 and E′ <7 cm/s (restrictive pattern, grade III) (17,24).

Statistical analysis. Data are presented as mean ± SD for continuous variables and as proportions for categorical variables. Differences between groups were assessed by 1-way analysis of variance and post-hoc multiple comparisons were performed using the Bonferroni correction. The Fisher's exact test was used to test differences between proportions. Multiple linear regressions were used to assess the independent association of BMI with diastolic function parameters. The predictors and the outcome variables were standardized with corresponding standard deviations and both nonstandardized (B) and standardized (β) coefficient estimates and relative standard errors were reported. Covariates (age, sex, LV mass/height$^{2.7}$, heart rate, hypertension, and diabetes) were entered in the models in a stepwise fashion, with entry and removal criteria set at a $p < 0.1$. Analysis of covariance was conducted to assess differences in diastolic function parameters between groups after adjusting for covariates. Estimated marginal means adjusted for covariates and 95% confidence intervals (CIs) were derived. Multivariate logistic models were used to assess the risk of diastolic dysfunction associated with body size measures, and odds ratios (ORs) and relative 95% CI were derived.

For all statistical analyses, a 2-tailed $p < 0.05$ was considered significant. Statistical analyses were performed using SPSS software version 17.0 (SPSS, Inc., Chicago, Illinois).