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Association of Subclinical Right Ventricular Dysfunction With Obesity

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OBJECTIVES The purpose of this research was to identify the determinants of right ventricular (RV) dysfunction in overweight and obese subjects.

BACKGROUND Right ventricular dysfunction in obese subjects is usually ascribed to comorbid diseases, especially obstructive sleep apnea. We used tissue Doppler imaging to identify the determinants of RV dysfunction in overweight and obese subjects.

METHODS Standard and tissue Doppler echocardiography was performed in 112 overweight (body mass index [BMI] 25 to 29.9 kg/m^2) or obese (BMI >30 kg/m^2) subjects and 36 referents (BMI <25 kg/m^2), including 22 with obstructive sleep apnea but no obesity. Tissue Doppler was used to measure RV systolic (s_m) and diastolic (e_m) velocities and strain indexes.

RESULTS Obese subjects with BMI >35 kg/m^2 had reduced RV function compared with referent subjects, evidenced by reduced s_m (6.5 ± 2.4 cm/s vs. 10.2 ± 1.5 cm/s, $p < 0.001$), peak strain (−21 ± 4% vs. −28 ± 4%, $p < 0.001$), peak strain rate (−1.4 ± 0.4 s^{-1} vs. −2.0 ± 0.5 s^{-1}, $p < 0.001$), and e_m (−6.8 ± 2.4 cm/s vs. −10.3 ± 2.5 cm/s, $p < 0.001$), irrespective of the presence of sleep apnea. Similar but lesser degrees of reduced systolic function ($p < 0.05$) were present in overweight (BMI 25 to 29.9 kg/m^2) and mildly obese (BMI 30 to 35 kg/m^2) groups. Differences in RV e_m, s_m, and strain indexes were demonstrated between the severely versus overweight and mildly obese groups ($p < 0.05$). Body mass index remained independently related to RV changes after adjusting for age, log insulin, and mean arterial pressures. In obese patients, these changes were associated with reduced exercise capacity but not the duration of obesity and presence of sleep apnea or its severity.

CONCLUSIONS Increasing BMI is associated with increasing severity of RV dysfunction in overweight and obese subjects without overt heart disease, independent of sleep apnea. (J Am Coll Cardiol 2006;47:611–6) © 2006 by the American College of Cardiology Foundation

The effect of excess weight on left ventricular (LV) morphology and function has been documented (1), but much less is known about the effects of obesity on right ventricular (RV) characteristics. Right ventricular changes have been attributed to obstructive sleep apnea (OSA) (2), which is highly prevalent in obese subjects, but the contribution of obesity to RV dysfunction is unclear.

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The assessment of RV function using M-mode or two-dimensional echocardiographic indexes is difficult due to its complex geometry. Radionuclide ventriculography, magnetic resonance imaging, and three-dimensional echocardiography can be used accurately to measure volumes and ejection fraction (3), but these indexes are load-dependent. Tissue Doppler imaging (TDI) allows measurement of systolic and diastolic myocardial velocities, has a more favorable signal-noise relationship, and permits the derivation of strain, which is a site-specific parameter. Long-axis velocities of the RV (free wall and tricuspid annulus) and strain indexes have been shown to be accurate and reproducible measures of RV systolic function (4–6), and correlate well with the sonomicrometry (6). We used conventional echocardiographic, TDI, and strain indexes to determine whether RV dysfunction was associated with severity of OSA or body mass index (BMI) and identify the correlates of RV functional changes in a cohort of obese and non-obese subjects.

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METHODS

Patient selection. We studied 148 subjects of both genders and divided into four groups based on degree of obesity: severely obese (BMI >35 kg/m^2, n = 32); mildly obese (BMI 30 to 34.9 kg/m^2, n = 44); overweight (BMI 25 to 29.9 kg/m^2, n = 36); and normal weight referent subjects (BMI <25 kg/m^2, n = 36). To examine the differential effects of sleep apnea and excess weight, we compared 22 consecutive subjects from our sleep laboratory who were non-obese (BMI <30 kg/m^2) but had at least moderate OSA with 22 obese subjects (BMI >30 kg/m^2) who all had confirmed sleep apnea on sleep studies, and a control group of 22 BMI-matched patients. To examine the effect of obesity alone, we compared 19 obese subjects without sleep apnea with the controls (Fig. 1). Obese subjects were recruited from general practice and specialist clinics based at a university hospital. Most of these patients had been involved in a previous study where we demonstrated LV

Abbreviations and Acronyms

AHI = apnea-hypopnea index
BMI = body mass index
LV = left ventricle/ventricular
OSA = obstructive sleep apnea
RV = right ventricle/ventricular
RV e_m = right ventricular early diastolic velocity
RV s_m = right ventricular systolic velocity
$SatO_2$ = oxygen saturation
SR = strain rate
TDI = tissue Doppler imaging
TR = tricuspid regurgitation
VO_2max = peak ventilatory capacity

changes related to obesity (1). The referent group included healthy volunteers in the community.

Organic heart disease was excluded on the basis of a clinical assessment as well as resting and stress electrocardiogram and transthoracic echocardiography. We excluded subjects with ischemic heart disease, hypertension, and diabetes mellitus on the basis of previous history. Informed written consent for participation was obtained, and the hospital ethics committee approved the protocol.

Clinical assessment. Demographic details of age, gender, clinical status, and blood pressures were obtained from standard measurements and questionnaires. A detailed history and physical examination was conducted to exclude obesity-related and cardiovascular comorbidities. Arterial pressure was measured after subjects were rested for >5 min. Anthropometric and fat mass (tetrapolar bioelectrical impedance analyzer) measurements were obtained.

Biochemistry. Biochemical analysis of blood samples includes renal function, electrolytes, fasting insulin (Tosoh AIA-600 immunoassay, Tokyo, Japan), and lipid profile (enzymatic colorimetric assays).

Polysomnography. Sleep studies included measurements of sleep staging, ventilation, and oximetry for oxygen saturation ($SatO_2$) (Compumedics, Melbourne, Australia). Apneas were defined as a cessation of airflow for ≥10 s. Hypopnea was defined as a discrete reduction in any parameter of respiration of ≥10 s duration resulting in ≥3% arterial oxygen desaturation or electroencephalographic arousal. The apnea-hypopnea index (AHI) is the total number of apneas or hypopneas per sleep hour, with an AHI of <5 within normal limits, and numbers of 5 to 15, 15 to 30, and >30 representing mild, moderate, and severe OSA, respectively. The average minimal and median $SatO_2$% readings were recorded.

Metabolic exercise testing. Treadmill exercise testing was performed using an exercise protocol individualized to the patient's exercise capacity. Peak ventilatory capacity (VO_2max) was obtained by breath-by-breath analyses of expired gas (V29C Sensormedics, Yorba Linda, California).

Echocardiography. Images were acquired using a standard ultrasound machine (Vivid 7, GE Vingmed, Horten, Norway) with a 2.5-MHz phased-array probe.

CONVENTIONAL ECHOCARDIOGRAPHY. Images were obtained in the parasternal long- and short-axis and apical four-chamber views. Left ventricular and RV diameter and wall thickness were measured from the M-mode tracings in the parasternal long axis (7); LV mass was determined by Devereux's formula, and indexed to height to the power of 2.7 (8).

Right ventricular end-diastolic and end-systolic volumes and the RV ejection fraction were computed from four-chamber views, using the area-length monoplane method ($V_{RV} = 3/8\pi[area^2/length]$). In patients where an adequate tricuspid regurgitation (TR) spectral Doppler profile was obtainable, pulmonary artery pressure was estimated from the sum of the modified Bernoulli equation ([TR jet velocity]$^2 \times 4$) and the estimated mean right atrial pressure.

TDI. Tissue Doppler imaging provides a number of sensitive parameters of systolic and diastolic function and also correlates with structural change, such as myocardial fibrosis (9). In each apical view, three cardiac cycles were recorded using color tissue Doppler at a high frame rate (120 MHz), giving a temporal resolution of 8 ms. The imaging angle was adjusted to ensure a parallel alignment of the beam with the myocardial segment of interest. Myocardial systolic velocity (s_m) and early diastolic velocity (e_m) were obtained at the

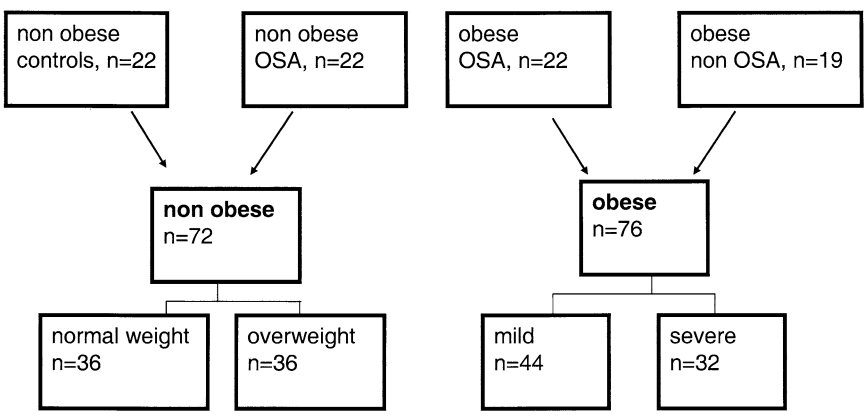

Figure 1. Grouping of subjects' selection. OSA = obstructive sleep apnea.