Influence of Mild to Moderate Obesity on Left Ventricular Stress Filling Pattern in Hypertension

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In resting condition, obese subjects are described as having impaired diastolic filling. To examine the effect of mild to moderate obesity on left ventricular diastolic performance during stress in hypertension, we determined the filling responses to dynamic submaximal exercise in 19 obese hypertensive patients (body mass index, 26 to 30 kg/m²) with a normal left ventricular structure, 19 age- and sex-matched, non-obese hypertensive patients, and 19 age- and sex-matched, non-obese normotensive controls (mean age, 55 ± 3 yr). Doppler echocardiographic studies were performed at baseline and 1 min after exercise on a supine ergometer bicycle. At rest, systolic function and filling indices, peak velocities of early (E) and late (A) filling, and their ratio (E/A), were similar in the two hypertensive groups, while normotensive controls had higher peak velocities of E and E/A. At a maximum workload of 75 W, blood pressure and heart rate increased similarly in the two hypertensive groups. Peak velocities of E and A increased significantly after exercise. The percentage change in the peak velocity of E was greater in obese hypertensive patients than in non-obese hypertensive patients and normotensive controls (23 ± 4 vs. 12 ± 3 and 14 ± 3%, p < 0.05). Percentage changes in A and E/A were similar in the three groups. Our study suggests that mild to moderate obesity does not further worsen left ventricular diastolic filling at rest and mitigates diastolic filling abnormalities after exercise in hypertensive patients. (Hypertens Res 1998; 21: 245-250)

Key Words: obesity, hypertension, pulsed Doppler echocardiography, diastolic function

Although the association between obesity and hypertension is well established (I-3), studies of the influence of obesity on cardiovascular morbidity in patients with hypertension have yielded inconsistent results (4-7). Barrett-Connor and Khaw (4) have demonstrated that in hypertensive patients obesity attenuates the risks of cardiovascular morbidity and mortality because of relatively low peripheral resistance. In addition, Cambien et al. (5) reported in two studies a negative interaction between blood pressure and body mass index with respect to cardiovascular mortality. In contrast, Chiang et al. (6) found that obese hypertensive patients have a shorter life span because of the increased risk of coronary artery disease. The Framingham Study showed that hypertension and obesity have an additive impact on cardiovascular morbidity especially among very obese patients (7). These discrepancies have stimulated comparative studies in an effort to define basic pathophysiologic mechanisms leading to the increased risk of cardiovascular disease in obese patients with hypertension.

Most previous studies have focused on left ventricular systolic function. Obese hypertensive patients have a higher cardiac output and a lower total peripheral resistance with an augmented venous return than lean patients at any given level of arterial hypertension (8, 9). Emerging evidence suggests that left ventricular diastolic dysfunction is one of the earliest expressions of cardiac malfunction (10-12) and may lead to congestive heart failure (13). Because the increase in left ventricular filling pressure correlates most closely with the degree of exercise limitation, independently of the severity of systolic dysfunction (14, 15), the left ventricular filling profile during stress may determine the likelihood of congestive heart failure before any alteration of systolic function. Diastolic filling abnormalities occur early in the course of hypertension (10, 11, 16), and morbid obesity impairs left ventricular diastolic filling (17). However, it is unclear whether mildly to moderately obese hypertensive patients, which constitute the majority of the hypertensive population, differ from their non-obese counterparts with regard to diastolic performance during exercise. We therefore assessed the left ventricular filling profile during dynamic exercise in mild to moderate obese patients with hypertension.

Methods

Study Population
The study participants were hypertensive patients enrolled from the annual screening program at our

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hypertension outpatient clinic. Subjects were stratified according to body mass index (BMI) into 2 groups. BMI was calculated as body weight (kg) divided by the square of height (m). The obese hypertension group consisted of 19 hypertensive patients with a BMI of >26 but <30 kg/m², including 16 men and 3 women (mean age 55 ± 3 yr). The non-obese hypertension group was composed of 19 age- and sex-matched, non-obese hypertensive patients whose BMI was <26 kg/m². Mean BMI was 27.1 ± 1.2 in the obese hypertensive group and 22.7 ± 2.0 in the non-obese hypertensive group. The following criteria were used to define patient eligibility for the study: (1) blood pressure in the range of 140-180/90-110 mmHg on at least 2 of 3 consecutive visits at 2-wk intervals; (2) no previous antihypertensive treatment; (3) no evidence of any coexisting cardiovascular disease as assessed by clinical examination, electrocardiography, chest radiography, and echocardiography; and (4) no electrocardiographic or echocardiographic evidence of left ventricular hypertrophy. We excluded very obese individuals from this study because of an association with left ventricular hypertrophy, difficulty in Doppler echocardiographic recording, or both. A group of 19 age- and sex-matched, non-obese normotensive volunteers was used to generate control Doppler echocardiographic data. They had no evidence of heart disease as evaluated by history, physical examination, and echocardiography. Their mean BMI was 22.8 ± 2.6 kg/m². Baseline characteristics of the study groups are summarized in Table 1. After 3 consecutive baseline visits, all participants underwent two-dimensional directed M-mode and pulsed Doppler echocardiographic studies at rest and 1 min after exercise on a supine ergometer bicycle. Echocardiographic studies were performed at the same time in the morning. The protocol was approved by our institution's ethical committee, and informed consent was obtained from all participants.

Echocardiographic Examination
Two-dimensional directed M-mode echocardiograms of the left ventricle were obtained from the parasternal window. The instrument used was an Aloka SSD-870 echocardiograph (Tokyo, Japan) with a 3.5-MHz transducer. The interventricular septum, LV internal dimension, posterior wall thickness, and left atrial dimension were measured according to the recommendations of the American Society of Echocardiography (18). Ejection fraction was assessed by the Teichholz method (19). Left ventricular mass was assessed using the Pen formula (18): LV mass = 1.04 × [(LV internal dimension + interventricular septum thickness + posterior wall thickness)³ - LV internal dimension] - 13.6. A LV mass index greater than 125 g/m² was defined as echocardiographic left ventricular hypertrophy.

Pulsed Doppler Echocardiography
Using a 2.5 MHz transducer, we recorded mitral inflow velocity at rest and after stopping exercise, when the heart rate had slowed sufficiently to allow discrimination between diastolic early flow and late flow velocities, as described previously (16). Postexercise echograms were generally completed 1 min after termination of exercise. Tracings of 3 to 5 consecutive cardiac cycles having the highest velocity in early filling were analyzed by 3 experienced echocardiographers blinded to the study design. The following variables were examined: peak velocity of early filling (E); peak velocity of late filling (A); and their ratio (E/A). Left ventricular exercise filling response was defined as the percentage change in E, A, and E/A from rest to 1 min during the recovery period. The interobserver and intraobserver coefficients of variation for Doppler indices at our laboratory have been reported previously (20).

Exercise Testing
Moderate exercise was performed on a supine ergometer driven at a constant speed of 50 cycles/min for 9 min. The workload was started at 25 W and increased in a stepwise fashion by 25 W every 3 min until a maximum workload of 75 W was attained. During the test, blood pressure, heart rate, and the electrocardiogram were continuously monitored with an automatic device (Nippon Colin STBP-6807, Tokyo, Japan) and recorded once every minute.

Statistical Analysis
Analyses were done using BMDP statistical software (BMDP Statistical Software, Berkeley, California). Data are expressed as means ± SEM. When appropriate, Student’s t-test and analysis of variance were used to assess statistical significance. The level of significance was set at a probability of less than
Results

Left Ventricular Echocardiographic Indices

Echocardiographic features of the patients in the two hypertensive groups and the normotensive controls are listed in Table 2. LV internal dimension, wall thickness, ejection fraction, LV mass index, and left atrial dimension were similar in the two hypertensive groups. Normotensive controls had slightly but not significantly lower values for wall thickness and LV mass index. No wall motion abnormality was seen in any subject.

Hemodynamic Effect of Exercise

The hemodynamic data in the two hypertensive groups are summarized in Table 3. Blood pressure and heart rate were similar in the two groups at rest, maximum exercise, and 1 min after the cessation of exercise. During exercise, 70% to 75% of the submaximal heart rate predicted by age for untrained subjects (116 to 124 beats/min) was reached in all subjects within 6 to 9 min. No ST-T depression occurred, and no patient was forced to discontinue the exercise because of cardiac symptoms or the development of lethal arrhythmias. Doppler echocardiography was performed at a similar heart rate in the two groups at rest and during recovery as shown in Table 2. In the normotensive control group, blood pressure rose from 116 ± 3/70 ± 2 to 180 ± 9/95 ± 4 mmHg at peak exercise, and the Doppler echocardiogram was recorded at a mean heart rate of 66 ± 2 at rest and 80 ± 3 during after exercise.

Effect of Exercise on Filling Profile

At rest, the peak velocities of E (42 ± 3 cm/s for obese patients vs. 44 ± 2 cm/s for non-obese patients, ns), A (55 ± 3 vs. 53 ± 2, ns), and their ratio (0.76 ± 0.10 vs. 0.83 ± 0.06, ns) did not differ significantly between the two hypertensive groups (Fig. 1). Normotensive controls had a higher peak velocity of E and E/A ratio than the hypertensive groups. As shown in Fig. 2, different filling responses were observed after exercise. The percentage change in the peak velocity of E was greater in obese hypertensive patients (23 ± 4%) than in non-obese hypertensive patients (12 ± 3%) and normotensive controls (14 ± 3%). The percentage change in the peak velocity of A (19 ± 4, 13 ± 2, and 13 ± 2%, respectively) and the percentage change in E/A (4 ± 5, 0 ± 3, and -10 ± 5%, respectively) were similar for the three groups.

Discussion

An important finding of this study is that despite similarities in blood pressure, cardiac structure, systolic function, and LV filling profile at rest, obese and non-obese hypertensive patients showed a disparate filling response to dynamic exercise. To allow a direct comparison of obese with non-obese hypertensive patients, care was taken to enroll only patients with similar clinical characteristics except for body mass. Heart rate, an independent determinant of LV filling, was similar in the two groups when the filling signals were recorded. Systolic and diastolic blood pressures were also similar in the two groups at rest, maximum exercise, and 1 min after the cessation of exercise. In addition, the lack
Obesity impairs left ventricular diastolic filling (17, 21-23) and has long been considered a cause of cardiac morbidity (24). Nevertheless, in our well-defined hypertensive population, obesity did not negatively affect LV filling pattern. This contrasts with the results of a previous study by Grossman et al. (25), who found a greater degree of impairment of left ventricular filling in obese hypertensive patients. Unlike our study, conducted in mildly to moderately obese patients, they studied severely obese patients who had evidence of cardiac disease, such as an increased left ventricular mass and left ventricular enlargement. Their results might have been affected by these confounding factors. In fact, it has been suggested that impaired left ventricular filling is closely associated with morbid obesity and left ventricular remodeling (17, 22). The exclusion of obese patients with cardiac structural changes from our study does not permit extension of our observations to this subgroup of patients.

The exercise-induced increase in peak velocity of E was higher in obese hypertensive patients than in their non-obese counterparts, whereas the exercise-induced increase in the peak velocity of A was similar in the two groups. Earlier studies did not examine the effect of exercise on LV filling profile in obese hypertensive patients. Since Doppler velocities represent instantaneous pressure gradients, the disparate filling response to exercise in our study indicates that the early diastolic transmitral pressure in obese hypertensive patients differs from that in their non-obese counterparts. Various factors, such as left ventricular contractility, loading conditions, a suction effect, and delayed relaxation of the left ventricle may influence the exercise-induced response of Doppler filling patterns (26-28) and may account for the observed results. Although the present study could not determine all factors potentially affecting the response to exercise, the greater enhancement of early filling in obese hypertensive patients may be mediated by exercise-induced catecholamine release. Exercise increases secretion of catecholamines in obese borderline hypertensive patients (29). Moreover, Udelson et al. (26) reported that isoproterenol stimulation reduced LV minimal diastolic pressure and induced negative left ventricular pressure. This increase in negative left ventricular pressure may facilitate the rapid phase of diastolic filling of the left ventricle and mask impaired relaxation due to hypertension. However, we did not measure plasma catecholamines in the present study. Alternatively, higher postexercise E values may reflect more subtle phenomena such as...
changes in hemodynamic factors or loading conditions, independent of intrinsic properties of the heart. Obesity increases the venous return and the preload of the left ventricle (8). An increase in ventricular preload enhances peak velocity of E and, to a lesser degree, that of A (28). Indeed, a similar response of filling patterns was obtained immediately after exercise in the obese hypertensive patients in this study. We also observed that the exercise-induced increase in peak velocity of E in the obese hypertensive patients was greater than that in the normotensive non-obese controls, whereas the percentage changes in peak velocities of A and of E/A were similar. The capacity to increase peak velocity of A during exercise decreases in patients with left ventricular diastolic dysfunction (30). The response of late filling velocity in our obese hypertensive patients was similar to that in normotensive controls, thus strengthening the hypothesis that the postexercise increase in E is independent of the intrinsic diastolic properties of the heart. The lack of concomitant monitoring of intracardiac pressure and cardiac output represents a limitation of our study. Further studies are needed to clarify the mechanism(s) of this disparate filling response to exercise.

Exercise-induced systolic dysfunction in patients with hypertension is caused by impaired left ventricular filling (31). In studies of the filling response to exercise in patients with hypertrophic cardiomyopathy, Iwase et al. (32) found a marked increase in peak late filling velocity, and only a mild increase in early filling velocity. This increase in peak late velocity was considered a compensatory mechanism for poor ventricular distensibility. In our study, the magnitude of change in late filling velocity was similar in the two hypertensive groups and the normotensive control group, whereas the change in early filling velocity from rest to immediately after exercise was greater in the obese hypertensive group. This suggests that hypertensive patients with mild to moderate obesity who have an apparently normal left ventricular structure have a greater reserve for exercise in the active phase of diastole despite impaired relaxation at rest. The left ventricular diastolic compliance observed in these obese hypertensive patients permits good left ventricular systolic performance (33).

In conclusion, mild to moderate obesity associated with a normal left ventricular structure did not further worsen left ventricular diastolic filling at rest in hypertensive patients and, moreover, mitigated diastolic filling abnormalities after exercise. These results suggest that obesity, at least when mild or moderate, does not additively increase the risk of ventricular dysfunction in patients with hypertension.

References


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