Noninvasive study of left ventricular performance in obese patients: influence of duration of obesity

TADAHISA NAKAJIMA, M.D., SHIGENORI FUJIOKA, M.D., KATSUTO TOKUNAGA, M.D., KAZUHIKO HIROBE, M.D., YUJI MATSUZAWA, M.D., AND SEIICHIRO TARUI, M.D.

ABSTRACT We studied the performance of the left ventricle in 35 obese patients by means of noninvasive methods, including echocardiography, carotid arterial pulse tracing, and phonocardiography. Patients were divided into two groups according to the duration of obesity: group 1 included patients who had been obese for less than 15 years, and group 2 comprised patients who had been obese for more than 15 years. There were no differences in the degree of obesity and cellularity of adipose tissue between the two groups. Left ventricular dimension and wall thickness, stroke volume, and cardiac output were significantly greater in both groups of obese patients than in nonobese control subjects. Group 2 had a significantly increased end-diastolic dimension index (DDI, calculated as end-diastolic dimension/cube root of body surface area), stroke index (SI), and radius/wall thickness ratio (R/Th) of the left ventricle compared with group 1. Multiple regression analysis showed that DDI, SI, and R/Th correlated significantly with the duration of obesity. We conclude that alterations of cardiac performance in obese patients with left ventricular enlargement and wall thickening is attributed not only to the excess of body weight but also to the duration of obesity.


Obesity causes cardiovascular disturbance,1 and the incidence of cardiovascular disease is higher even in mildly obese patients than in lean subjects.2 Therefore, it is important to evaluate cardiac function and morphology in obese patients even if they have no cardiac symptoms. Although previous studies that used an invasive method showed the presence of a hypervolemic and hyperdynamic state3-9 and myocardial hypertrophy10 in morbidly obese patients, few data have been reported4 regarding the influence of duration of obesity on cardiac performance.

Since obesity is generally a long-standing disease, a noninvasive method is desirable and useful for repeated assessment of cardiac performance. Echocardiographic estimation of function and morphology of the left ventricle is well established11-13 and widely used as a noninvasive procedure.7, 9, 14-18 In this report we studied patients with relatively mild obesity by means of noninvasive methods to clarify the influence of body weight excess and duration of obesity on cardiac performance.

Methods

Thirty-five obese patients who ranged in age from 16 to 60 years old (34.5 ± 12.5 mean ± SD) and weighed 57 to 118 kg (85.1 ± 16.8) were investigated. Their percent of ideal body weight and extent of obesity calculated according to a “weight-for-height chart” published by the Ministry of Health and Welfare, Japan, ranged from 122% to 195% (147 ± 19%) and from 13 to 58 kg (27.2 ± 12.3), respectively. Patients were divided into two groups according to the duration of obesity: group 1 included patients who had been obese for less than 15 years and group 2 comprised patients who had been obese for more than 15 years. There was no difference in percent of ideal body weight, age, and male/female ratio between the two groups. We excluded patients who had a history of hypertension (diastolic pressure >90 mm Hg or systolic pressure >140 mm Hg) and/or normal blood pressure on treatment, significant electrocardiographic changes at rest or after the double Master’s test, cardiothoracic ratio exceeding 0.5, pulmonary diseases on chest x-ray films, evidence of ischemic or valvular heart disease, or signs of heart failure. An oral glucose tolerance test (75 g), thyroid function tests, and adrenal function tests were performed to exclude a diagnosis of diabetes mellitus, hyperthyroidism and hypothyroidism, and Cushing’s syndrome. Information regarding onset and duration of obesity and physical activity was obtained with the help of prior photographs and by asking about the patient’s pattern of daily life and whether the patient had been or was under physical training. In 17 of 35 obese patients, biopsy specimens from abdominal subcutaneous fat tissue were obtained with an aspiration needle and the size of the adipocytes was measured by the frozen cut method.19 Thirty nonobese subjects matched for age and height were also studied as a control group. Table 1 shows clinical findings in nonobese control subjects and in obese patients. Each subject gave informed consent.

From the Second Department of Internal Medicine, Osaka University Medical School, Osaka, Japan.

Address for correspondence: Tadahisa Nakajima, M.D., Second Department of Internal Medicine, Osaka University Medical School, Fukushima-ku, Osaka, Japan, 553.

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TABLE 1
Comparison of clinical findings between nonobese control subjects and obese patients

<table>
<thead>
<tr>
<th></th>
<th>Nonobese controls</th>
<th>Obese patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Group 1</td>
</tr>
<tr>
<td>n (male/female)</td>
<td>30 (16:14)</td>
<td>35 (19:16)</td>
</tr>
<tr>
<td>Duration of obesity yr</td>
<td>34.8 ± 8.6</td>
<td>34.5 ± 12.5</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>163 ± 9</td>
<td>165 ± 12</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>57.6 ± 7.5</td>
<td>85.1 ± 16.8&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Percent ideal body weight</td>
<td>102 ± 6</td>
<td>147 ± 19&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>119 ± 9</td>
<td>123 ± 11</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>72 ± 6</td>
<td>73 ± 8</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>65 ± 6</td>
<td>61 ± 6&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Values are mean ± SD.

Statistical comparisons (vs nonobese controls): <sup>a</sup>p < .01; <sup>b</sup>p < .001.

Echocardiograms were obtained with a mechanical sector scan echocardiograph unit (ATL-Mark V) equipped with a 3.0 MHz transducer. The patients were studied in the supine or slightly left lateral decubitus position after a rest of at least 10 min until blood pressure and heart rate had become stable. Figure 1 shows a set of cardiograms from this study. An M mode echocardiogram of left ventricular minor axis dimension was obtained by directing the ultrasonic beam just inferior to the free edge of the mitral valve in conjunction with the two-dimensional echocardiogram, and the recording was made at a paper speed of 50 mm/sec. According to the method of Friedman et al.,<sup>12</sup> left ventricular end-diastolic (Dd) and end-systolic dimensions (Ds) were measured with the leading-edge techniques at the peak of the R wave of the simultaneously recorded electrocardiogram and at the nadir of septal motion, respectively. End-diastolic thickness of the posterior wall and the interventricular septum were measured in the standard fashion<sup>11</sup> by leading-edge techniques, with gain adjustment to minimize the width of epicardial and endocardial signals. An M mode echocardiogram of the mitral valve was recorded with a phonocardio gram, an electrocardiogram, and a carotid arterial pulse tracing at a paper speed of 100 mm/sec with 0.04 sec time lines. Intervals from onset of the Q wave to the aortic second sound (Q-II) and from the aortic second sound to mitral valve opening (isometric relaxation time), and left ventricular ejection time were measured in milliseconds. Only 35 of 48 obese patients were analyzed because good-quality echocardiograms for evaluating left ventricular dimension and wall thickness could not be obtained from the others. Systemic blood pressure and heart rate were recorded every 2 min during the study by a mercury sphygmomanometer and a cuff long enough to fit the obese arm<sup>20</sup> by means of continuous blood pressure monitoring equipment (Nihon-Kohrin Co., Ltd., Tokyo, Japan).

The following indexes were calculated for each patient from the average of measurements from 5 beats:

1. Fractional shortening (FS) derived by (Dd - Ds)/Dd.
2. Mean rate of circumferential shortening (mean Vcf) derived by FS/ejection time.
3. End-diastolic radius/wall thickness ratio (R/Th) derived by Dd/(PW + IVS), where PW and IVS are thickness of left ventricular posterior wall and interventricular septum, respectively.
4. Left ventricular dimension index calculated from (left ventricular dimension)/(BSA)<sup>10</sup> according to the methods of Henry et al.<sup>21</sup> and Gardin et al.<sup>22</sup> where BSA is body surface area.

FIGURE 1. Echocardiogram in a 28-year-old woman who weighed 80.0 kg and whose percent of ideal body weight was 194%, illustrating measurements made during the study. For details see text. CAP = carotid arterial pulse tracing; ET = left ventricular ejection time; IRT = isometric relaxation time; IVS = interventricular septum; PW = posterior wall; Q-II = interval from onset of Q wave to aortic second sound.
surface area calculated according to the formula of DuBois et al. 22a
(5) End-systolic wall stress derived by (systolic pressure) ×
(R/Th); end-systolic pressure was estimated by interpolation
 techniques after the method of Marsh et al. 23 from the
height of the dicrotic notch of the carotid arterial tracing,
with the peak as systolic pressure and nadir as diastolic
pressure. Noninvasive definition of this index has been
validated by several investigators. 24, 25
(6) Stroke volume calculated according to the formula of
Teichholz et al. 26
(7) Cardiac output derived by (stroke volume) × (heart rate).
(8) Preejection period derived by (Q-II) − (ejection time).

Statistics. Results were expressed as mean ± SD. The signi-
ficance of differences between mean values for two
groups was determined by Student’s t test for unpaired data after
an analysis of variance. Independent variables in multiple re-
gression analysis were body weight (kg), duration of obesity
(years), and age (years).

Results

Comparison of nonobese control subjects and obese pa-
tients. Table 2 shows cardiographic values in nonobese
control subjects and obese patients. Obese patients
showed a significant increase in Dd (p < .001), Ds
(p < .001), stroke volume (p < .001), cardiac output
(p < .001), and thickness of interventricular septum
(p < .001) and posterior wall (p < .001) compared
with nonobese subjects. Since heart rate was normal or
low in the obese patients, the high cardiac output proba-
bly resulted from a high stroke volume. Furthermore,
diastolic dimension index (Ddi) (p < .001) and stroke
index (SI) (p < .001) were greater in the obese pa-
tients than in the nonobese subjects. The increase of
Dd was much larger than that of wall thickness. There-
fore, R/Th (p < .01) and end-systolic wall stress
(p < .01) increased significantly in obese patients.
Fractional shortening, mean Vcf, isometric relaxation
time, and preejection period/ejection time were similar
between nonobese control subjects and obese patients.

Effects of duration of obesity. Obese patients were di-
vided into two groups according to the duration of their
obese state (groups 1 and 2, see Methods). There were
no differences in such clinical factors as age, height,
weight, percent of ideal body weight, and blood pres-
sure. In addition, the average size of adipocytes, which
increased markedly in both obese groups, was not sig-
nificantly different between the two groups. This indi-
cated that there was no specific distinction in degree of
obesity and cellularity of adipose tissue between the
two groups. Ddi, SI, and R/Th were larger in group 2
than in group 1 (43.2 ± 1.7 vs 40.9 ± 1.7 mm/m²), p
< .001; 49.1 ± 4.5 vs 41.9 ± 5.6 ml/m², p < .001;
and 2.89 ± 0.09 vs 2.71 ± 0.11, p < .001, respec-
tively), while there was no difference in these indexes
between nonobese subjects and group 1. Therefore the
significant increase in Ddi, SI, and R/Th seen in the
obese patients depended mainly on the findings in

| TABLE 2 |
| Comparison of cardiographic parameters between nonobese control subjects and obese patients |

<table>
<thead>
<tr>
<th>Nonobese controls</th>
<th>Obese patients</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Group 1</td>
</tr>
<tr>
<td>n</td>
<td>30</td>
<td>35</td>
</tr>
<tr>
<td>Dd (mm)</td>
<td>46.4 ± 2.3</td>
<td>52.1 ± 3.6b</td>
</tr>
<tr>
<td>Ddi (mm/m²)</td>
<td>39.6 ± 1.6</td>
<td>42.0 ± 2.1b</td>
</tr>
<tr>
<td>Ds (mm)</td>
<td>29.8 ± 2.4</td>
<td>32.9 ± 2.7b</td>
</tr>
<tr>
<td>Dsl (mm/m²)</td>
<td>25.4 ± 1.8</td>
<td>26.5 ± 1.6b</td>
</tr>
<tr>
<td>Posterior wall thickness (mm)</td>
<td>8.8 ± 0.7</td>
<td>9.5 ± 0.9b</td>
</tr>
<tr>
<td>Septal thickness (mm)</td>
<td>8.5 ± 0.9</td>
<td>9.1 ± 0.6b</td>
</tr>
<tr>
<td>R/Th</td>
<td>2.69 ± 0.13</td>
<td>2.80 ± 0.13b</td>
</tr>
<tr>
<td>End-systolic wall stress (mm Hg)</td>
<td>163 ± 18</td>
<td>177 ± 21b</td>
</tr>
<tr>
<td>Stroke volume (ml)</td>
<td>65.1 ± 6.2</td>
<td>86.9 ± 14.7b</td>
</tr>
<tr>
<td>SI (ml/m²)</td>
<td>40.4 ± 3.0</td>
<td>45.4 ± 6.3b</td>
</tr>
<tr>
<td>Cardiac output (l/min)</td>
<td>4.2 ± 0.5</td>
<td>5.2 ± 0.7b</td>
</tr>
<tr>
<td>Cardiac index (l/min/m²)</td>
<td>2.6 ± 0.3</td>
<td>2.7 ± 0.3</td>
</tr>
<tr>
<td>Fractional shortening</td>
<td>0.36 ± 0.03</td>
<td>0.37 ± 0.03</td>
</tr>
<tr>
<td>Mean Vcf (sec)</td>
<td>1.17 ± 0.11</td>
<td>1.20 ± 0.12</td>
</tr>
<tr>
<td>Preejection period/ejection time</td>
<td>0.29 ± 0.06</td>
<td>0.29 ± 0.06</td>
</tr>
<tr>
<td>Isometric relaxation time (msec)</td>
<td>59 ± 14</td>
<td>62 ± 18</td>
</tr>
<tr>
<td>Size of adipocyte (nl)</td>
<td>0.29 ± 0.07</td>
<td>0.61 ± 0.18b</td>
</tr>
</tbody>
</table>

Values are mean ± SD.

Statistical comparisons: *p < .01, **p < .001 compared with nonobese controls; **p < .01, ***p < .001 compared with group 1.

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group 2. Furthermore, as shown in figure 2, DdI, SI, and R/Th correlated positively with the duration of obesity (p < .001).

**Multiple regression analysis in obese patients.** Multiple regression analyses were undertaken to ascertain whether the duration of obesity had independent correlation with indexes for cardiac performance. Multiple and partial correlation coefficients in multiple regression analysis are summarized in table 3. Dd increased with both body weight and the duration of obesity. Ds and thickness of posterior wall and interventricular septum increased in parallel with body weight but not with the duration of obesity. DdI, SI, and R/Th were not correlated with body weight, as expected. However, these three indexes increased markedly with the duration of obesity. No indexes were correlated with age.

**Discussion**

Recent advances in echocardiographic instrumentation and techniques make it possible to obtain clear echocardiograms even in obese patients. In this study we compared indexes of left ventricular size, wall thickness, and pump function between 35 obese patients and nonobese subjects and assessed the influences of body weight excess and duration of obesity on cardiac performance in obese patients. There are limitations of echocardiographic assessment of left ventricular function, as is well known. Since M mode echocardiography records information from only limited regions of the left ventricle, the ventricle must have a relatively normal geometry and uniform contraction for echocardiographic measurement of internal dimension, wall thickness, and ventricular volume to reflect total ventricular structure. None of the obese patients in this study showed regional abnormalities of left ventricular contraction on two-dimensional echocardiography.

Cardiac output was greater in obese patients than in nonobese subjects and correlated with body weight, in agreement with the results of previous studies, which showed that obese patients were in a high cardiac output state as a result of physiologic adaptation to increased blood flow in increased adipose tissue. In addition to the above data, we found that SI, DdI, and R/Th also increased in obese patients when compared with nonobese subjects, which has not been observed in previous reports.

When we divided obese patients into two groups according to the duration of obesity, there were substantial differences in these indexes. Group 2, with a long duration of obesity (>15 years), had significantly larger values for DdI, SI, and R/Th than group 1 (≤15 years); moreover, multiple regression analysis revealed that these indexes were positively correlated with duration of obesity. These data showed that the duration of obesity played an important role in left ventricular performance and that the morphologic alteration of the left ventricular chamber might progress with long-standing volume overload, even in subjects with relatively mild obesity.

It has been reported that there are two types of adipocytes involved in increases of adipose tissue volume in obese subjects: hypertrophic and hyperplastic. Resting blood flow per unit of adipose tissue has been shown to be significantly greater in adipose tissue with smaller adipocytes than in that with larger ones. We
examed whether the duration of obesity influenced the cellularity of adipose tissue and found that the size of adipocytes was almost identical in groups 1 and 2 (table 2). This suggested that there was no difference in the degree of volume overload between the two groups. Thus the large SI and DdI in group 2 was not explained by differences in cellularity of adipose tissue between two groups but almost solely by the continuing of volume overload per se. The mechanism of the increase of these indexes associated with duration of obesity is not clear. One explanation for this is the following: Alexander reported that the oxygen uptake during exercise was much greater in obese patients than in normal subjects, while the increment in cardiac output per unit increment of oxygen uptake was the same in two groups. This finding suggests that the difference of the degree of volume overload between obese patients and normal subjects for a given level of activity was much greater than that of the degree of volume overload estimated at rest, and that obese patients who are chronically burdened with moving excess weight are similar to athletes under training, who have increased SI and decreased heart rate at rest. Over the long term a mechanism similar to that in the hearts of training athletes may act on cardiac performance in obese patients, although the decrease in heart rate in group 2 was not statistically significant. Another explanation is that the increase in DdI might be an expression of geometric change in the left ventricular chamber, which becomes spheroidal rather than ellipsoidal as the result of chronic volume overload, as seen in the left ventricular chamber of other volume-overloaded hearts. We attempted two-dimensional echocardiographic studies from the apical four-chamber view without success, except in three obese patients (one in group 1 and two in group 2) in whom there was no evident difference from normal subjects in left ventricular minor/long-axis ratio.

The increase in R/Th correlating to the duration of obesity suggests that the hypertrophic reaction of myocardium became inappropriate to the increase in Dd with long-standing obesity. In a pathologic study of 12 patients with chronic obesity whose blood pressure was within normal range, Amad et al. described two cases of fat infiltration between myocardial fibers and four other cases of myocardial fibrosis. The Barnes Hospital Clinicopathologic Conference added a case of interstitial fibrosis of myocardium. These pathologic changes might suggest that coronary perfusion is inadequate for the increased oxygen demand of myocardium, which is caused by volume overload in obese subjects, even without any coronary artery disease. With time, this condition might lead to an impairment of the hypertrophic reaction of myocardium.

The difference in physical activity between groups 1 and 2 might account for the difference in R/Th between these two groups because of the activity-associated increase in afterload. However, there was no difference in estimated degree of physical activity in the two groups, although the informed activity would be subjective in nature. Since systolic wall stress is the product of systolic blood pressure and R/Th, R/Th provides important diagnostic and prognostic information of left ventricular function. The increase in systolic wall stress even in subjects with relatively mild obesity in this study suggests that long-standing obesity becomes a risk factor for heart failure. Fractional shortening, mean Vcf, preejection period/ejec-

### Table 3: Correlation coefficient in multiple regression analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Partial correlation coefficient</th>
<th>Multiple correlation coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>y</td>
<td>BW</td>
<td>DO</td>
</tr>
<tr>
<td>Dd (mm)</td>
<td>0.656&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.605&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>DdI (mm/m&lt;sup&gt;2&lt;/sup&gt;)</td>
<td>0.096</td>
<td>0.667&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Ds (mm)</td>
<td>0.584&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.427</td>
</tr>
<tr>
<td>Posterior wall thickness (mm)</td>
<td>0.754&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.014</td>
</tr>
<tr>
<td>Septal thickness (mm)</td>
<td>0.548&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.085</td>
</tr>
<tr>
<td>Stroke volume (ml)</td>
<td>0.539&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.547&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>SI (ml/m&lt;sup&gt;2&lt;/sup&gt;)</td>
<td>-0.183</td>
<td>0.602&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cardiac output (l/min)</td>
<td>0.634&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.384</td>
</tr>
<tr>
<td>R/Th</td>
<td>-0.298</td>
<td>0.620&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Explanatory variables were body weight (BW), duration of obesity (DO), and age: y = C<sub>0</sub> + C<sub>1</sub> × BW + C<sub>2</sub> × DO + C<sub>3</sub> × age, where C<sub>0</sub>, C<sub>1</sub>, C<sub>2</sub>, and C<sub>3</sub> are partial regression coefficients. The first value for partial correlation coefficient, for example, is the correlation coefficient between Dd and body weight after adjustment for duration of obesity and age.

Statistical comparisons (n = 35): *p < .01; **p < .001.
tion time, and isometric relaxation time were not different between nonobese control subjects and obese patients at rest. However, since these indexes are load-dependent, it might be necessary to evaluate them and/or other indexes of left ventricular contractility that are independent of preload, such as end-systolic pressure/ dimension under loading conditions, to fully clarify the status of left ventricular contractility.

References
Noninvasive study of left ventricular performance in obese patients: influence of duration of obesity.

T Nakajima, S Fujioka, K Tokunaga, K Hirobe, Y Matsuzawa and S Tarui

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