The Cardiac Pathology of Chronic Exogenous Obesity

By Kamel H. Amad, M.D., James C. Brennan, M.B., B.Ch., and James K. Alexander, M.D.

Although the development of congestive heart failure in obese persons without evidence of other heart disease was recognized as early as 1933,1 and an investigation of the circulatory effects of obesity was undertaken in 1932,2 It was not until the description of the so-called “Pickwickian syndrome” in 19563 that significant alteration of cardiopulmonary function occurring in some instances of marked obesity was generally appreciated. Recent investigations of very obese subjects have demonstrated a high incidence of cardiorespiratory symptoms, hemodynamic alterations, and a consistent tendency to cardiomegaly.4,5 In view of these findings, an appraisal of the gross and microscopic anatomy of the heart in very obese subjects seemed desirable. The most specific previous inquiry into this question was that reported by Smith and Willius in 1933.4 They found excess epicardial fat and fatty infiltration of the myocardium in the hearts of obese subjects, and postulated that fatty infiltration interfered with cardiac function. An instance of pronounced cardiac hypertrophy in a grossly obese subject whom we observed suggested the possible importance of other factors, and led to the observations reported here. We believe these studies necessitate some revision of the previous conclusions of Smith and Willius, and point clearly to ventricular hypertrophy as the predominant and most specific alteration in the hearts of grossly obese persons at postmortem examination.

Materials and Methods

The necropsy findings on gross and microscopic anatomic examination of 12 selected obese persons form the basis of this study. Data relative to age, sex, and body height and weight are shown in table 1. Extremely obese subjects were chosen in preference to moderately obese individuals, on the premise that variations from the normal would tend to be more striking and therefore more easily identified and characterized. Six men and six women were studied. In the men, ages ranged from 33 to 64 years, with a mean of 48, and the women’s ages ranged from 35 to 75, with a mean of 53. Height varied from 167 to 179 cm. (mean 174), and body weight from 99 to 225 Kg. (mean 150) in the male group. In the female group, height ranged from 155 to 171 cm. (mean 163), and weight from 108 to 159 Kg. (mean 136). Predicted ideal weight was obtained from the table of the Metropolitan Life Insurance Company,6 based on sex, height, and body frame. Excess body weight was obtained by subtracting the predicted ideal from the observed weight. Amounts of excess body weight ranged from 25 to 159 Kg., representing increments of 34 to 240 per cent above the predicted ideal weights.

In each case review of the clinical record indicated that obesity of considerable degree had been present for many years prior to death, i.e., from 20 to 40 years, dating from puberty in most instances. Since it was desired to obtain information relative to the effects of obesity on the heart in the absence of hypertension or other complicating factors, only patients whose blood pressure recordings had been within the normal range (i.e., less than 150/90 mm. Hg) were chosen for study. Similarly, no patient was included in the study who had clinical signs or pathologic evidences of coronary arteriosclerosis, rheumatic fever, syphilis, myxedema, or other chronic diseases with possible cardiac effects. In most instances death had come about from some intercurrent cause, such as gunshot or stab wound, acute hemorrhage, cerebrovascular accident, or acute fulminating infection. Three subjects, however, (nos. 1, 2, and 10, table 1) died in congestive heart failure, having had symptoms and signs of myocardial insufficiency for several months prior to death.

Heart weight was determined in the usual manner at the time of necropsy, and the findings

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on gross examination were recorded. Representative sections were obtained from each heart for microscopic study, and reviewed with particular attention to the amount of epicardial fat, alterations in the myocardium, the condition of the coronary vessels, and the state of the endocardium. To obtain predicted heart weight at the ideal body weight, the normal mean ratio of cardiac weight to body weight as determined by Smith* (0.43 per cent for men, and 0.40 per cent for women) was multiplied by the ideal weight in kilograms. Gross and microscopic findings in the lungs, liver, kidneys, and adrenal glands ruled out the presence of other chronic disease, one of the criteria for patient selection. The three patients with frank congestive failure were found to have pulmonary edema and visceral congestion.

Results

In table 1 are shown the heart weight and ventricular thickness in the 12 obese subjects studied. In each case the observed heart weight was considerably greater than that predicted at ideal body weight. Similarly, if 350 Gm. is taken arbitrarily as the upper limit of normal in men, and 300 in women, the observed heart weight was greater than normal in all the subjects studied. Mean values for body weight, heart weight, and relationship of the two are shown separately for the male and for the female subjects in table 2. Body weight and heart weight were roughly twice the predicted, and heart weight expressed as grams per kilogram predicted body weight was approximately twice that found when expressed as grams per kilogram observed body weight. The mean cardiac weight in this series was 575 Gm. which taken with the mean body weight of 143/Kg. gives a value of 0.40 per cent for the mean ratio of cardiac weight to body weight (table 1). This is essentially the same as that found by Smith and Willius1 in their series of obese patients. The relationship between heart weight and body weight is displayed graphically in figure 1, indicating a rough proportionality. There was a similar trend in the relationship between the increase in heart weight above that predicted for the ideal body weight* and

*The heights and body frames of these subjects indicated no unusual stature that might render questionable the methods used for estimation of predicted ideal weight and predicted heart weight.
the amount of excess weight, as shown in figure 2.

Table 3 summarizes the microscopic findings referable to the myocardium, epicardium, endocardium, and coronary vessels. Examination of the myocardium revealed the microscopic appearance of diffuse muscular hypertrophy to be present in all cases, of moderate degree in 10, and of marked degree in two. Gross infiltration of the myocardium by fat was not observed. Where small foci of fat cells were found adjacent to the coronary arteries (two cases), or in the outer layers of the right ventricular myocardium (one case), no alteration of adjacent muscle fibers had occurred. In four cases scattered or occasional small foci of fibrosis were found in the myocardium, not large enough to be seen macroscopically. The amount of epicardial fat was estimated to be within the normal range in all cases but three. Two of these demonstrated slight to moderate increase, and the third considerable increase in epicardial fat. The endocardium was histologically normal in all instances. The major coronary vessels were patent in all cases, and were normal on microscopic study in eight cases. Slight intimal thickening or medial hypertrophy was present in four cases. None of the hearts in this group exhibited evidence of valvular abnormality. The aorta and pulmonary artery were normal in all cases.

**Discussion**

Gross and microscopic examination of the hearts of this series indicated clearly that the increases in cardiac weight and ventricular wall thickness were due to changes in muscle mass and not to fatty infiltration. Although modest increase in epicardial fat was present in two cases, a gross excess of epicardial fat

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Body weight, Kg</th>
<th>Predicted ideal weight, Kg</th>
<th>Body weight as per cent predicted</th>
<th>Heart weight, Gm</th>
<th>Heart weight as Gm./Kg. body weight</th>
<th>Heart weight as Gm./Kg. predicted body weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 Men</td>
<td>150</td>
<td>69.8</td>
<td>218</td>
<td>651</td>
<td>4.34</td>
<td>9.39</td>
</tr>
<tr>
<td></td>
<td>±22.2</td>
<td>±1.6</td>
<td>±34.6</td>
<td>±11.4</td>
<td>±0.35</td>
<td>±1.73</td>
</tr>
<tr>
<td>6 Women</td>
<td>136</td>
<td>60.7</td>
<td>225</td>
<td>499</td>
<td>3.69</td>
<td>8.20</td>
</tr>
<tr>
<td></td>
<td>±7.1</td>
<td>±1.9</td>
<td>±11.8</td>
<td>±44.7</td>
<td>±0.33</td>
<td>±0.60</td>
</tr>
</tbody>
</table>

*Values shown represent means and standard errors.

Figure 1

Relation between heart weight and body weight in 12 very obese subjects.

Figure 2

Relation between increment in heart weight and body weight above predicted values in 12 very obese subjects.
<table>
<thead>
<tr>
<th>Subject</th>
<th>Epicardium</th>
<th>Myocardium</th>
<th>Endocardium</th>
<th>Coronary vessels</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Normal amount of fat</td>
<td>Marked hypertrophy of all myocardial fibers with minimal focal perivascular fibrosis</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>2</td>
<td>Large amount of epicardial fat</td>
<td>Mild to moderate hypertrophy; small amount of fat infiltration between peripheral myocardial fibers</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>3</td>
<td>Normal amount of fat</td>
<td>Moderate hypertrophy of myocardial fibers; very small foci of fatty tissue about the major coronary branches; no myocardial fibrosis</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>4</td>
<td>Normal amount of fat</td>
<td>Diffuse hypertrophy; small amount of perivascular infiltrating fat</td>
<td>Normal</td>
<td>Minimal intimal proliferation</td>
</tr>
<tr>
<td>5</td>
<td>Normal amount of fat</td>
<td>Diffuse hypertrophy; no fatty infiltration or fibrosis</td>
<td>Normal</td>
<td>Medial hypertrophy</td>
</tr>
<tr>
<td>6</td>
<td>Slight increase in epicardial fat</td>
<td>Diffuse hypertrophy; no myocardial fibrosis; no fatty infiltration</td>
<td>Normal</td>
<td>Minimal focal intimal thickening by fibrosis</td>
</tr>
<tr>
<td>7</td>
<td>Normal amount of fat</td>
<td>Moderate hypertrophy of myocardial fibers; occasional foci of myocardial fibrosis; no fatty infiltration</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>8</td>
<td>Normal amount of fat</td>
<td>Diffuse hypertrophy; no fatty infiltration or fibrosis</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>9</td>
<td>Normal amount of fat</td>
<td>Diffuse hypertrophy; no fatty infiltration or fibrosis</td>
<td>Normal</td>
<td>Slight medial hypertrophy. No coronary sclerosis</td>
</tr>
<tr>
<td>10</td>
<td>Normal amount of fat</td>
<td>Diffuse hypertrophy; slight patchy interstitial fibrosis; no fatty infiltration</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>11</td>
<td>Moderate increase in epicardial fat</td>
<td>Marked diffuse hypertrophy, occasional small foci of fibrosis; no fatty infiltration</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>12</td>
<td>Normal amount of fat</td>
<td>Diffuse hypertrophy; no fatty infiltration; no fibrosis</td>
<td>Normal</td>
<td>Normal</td>
</tr>
</tbody>
</table>
and fatty infiltration of the myocardium occurred in only one of the 12 cases. Thus, epicardial fat represented no significant contribution to the heart weight in most instances of this series. It may be concluded that although excess epicardial fat and fatty infiltration of the right ventricular myocardium are not uncommon at necropsy examination of the hearts taken from obese subjects, these findings are neither specific for nor characteristic of the heart with obesity. As regards fatty infiltration, this conclusion is supported by the observation of Saphir and Corrigan who, in a survey of 58 cases of myocardial fatty infiltration, found that it occurred without relationship to general nutrition. Since fatty infiltration of the myocardium without other change brings about no increase in heart weight, it does not account for the increased heart weights of obese subjects.

In this study, evaluation of the presence and degree of left and right ventricular hypertrophy was based on measurement of the thickness of the ventricular walls, determination of total cardiac weight, and microscopic examination. It is recognized that measurement of wall thickness is not an entirely satisfactory criterion for the determination of ventricular hypertrophy, because of the wide range of normal variation, the difficulty of making an accurate measurement, and the effect of chamber enlargement. Estimations of normal ventricular wall thickness have been variously recorded as 8 to 15 mm. for the left, and 2 to 5 mm. for the right. To minimize possible error in the diagnosis of hypertrophy by this method, we have arbitrarily chosen the highest values cited in the literature as the upper limits of normal. As regards the relationship between ventricular hypertrophy and cardiac weight, the study of Fulton, Hotchinson, and Jones involving determination of right and left ventricular weight by anatomic dissection, is pertinent. This study indicated that in cases of isolated right ventricular hypertrophy the maximal increment in weight that the right ventricle contributed to the total cardiac weight was of the order of 150 Gm. In general, heart weights in excess of 450 Gm. in men, and 400 Gm. in women, cannot be accounted for on the basis of right ventricular hypertrophy alone. Similarly, in the absence of increased epicardial fat, tumor, or infiltrative lesions, cardiac weights in excess of 600 Gm. in men, and 550 Gm. in women, must involve chiefly an increased left ventricular weight. Since heart weights in excess of 600 Gm. were recorded in four cases of this group, under such circumstances, predominant increase in left ventricular weight clearly occurred in these cases.

Results obtained in this study referable to ventricular wall thickness have been interpreted as consistent with predominant left ventricular or combined left and right ventricular hypertrophy. It is noteworthy that neither the observations on cardiac weight nor on ventricular wall thickness indicated isolated or predominant right ventricular hypertrophy in any case of this series. These findings are in harmony with the clinical and physiologic evidence that chronic exogenous obesity does not give rise to the development of isolated cor pulmonale in the absence of pulmonary embolization.

Although these studies provide no specific information regarding possible mechanisms leading to the development of cardiac hypertrophy, appreciable increases in the work of the heart have been found in very obese subjects, and it is probable that this factor plays a significant role. A recent study of obesity and cardiac performance demonstrated that the work of the heart in very obese subjects at rest was considerably greater than that predicted for normotensive subjects at ideal body weight. This change was effected chiefly by increased left ventricular work, which was roughly correlated with the amount of excess body weight. Because of the need to move excess body weight, at any given level of activity, the cardiac work load was much greater for the obese subjects than for individuals at ideal body weight. Thus the circumstances obtaining in gross obesity may be similar to those under conditions of prolonged or continuous physical exercise. Experimental development of
cardiac hypertrophy under such conditions has been well documented. Cardiac hypertrophy may be produced in rats by daily treadmill exercise or by swimming. Development of congestive heart failure secondary to prolonged physical exertion in otherwise healthy men, or in experimental animals, however, has not been reported. In this respect the situation obtaining with gross obesity differs. This study provides further confirmation of the existence of heart failure in certain very obese persons without evidence of other heart disease.

Summary

Appraisal of the gross and microscopic anatomy of the heart was carried out at necropsy in 12 subjects (six men, six women) with marked chronic obesity. In each case the observed heart weight was considerably greater than that predicted at ideal body weight. Nine of the 12 subjects were found to have increase in left ventricular wall thickness, and two increase in right. The increases in heart weight and ventricular wall thickness were due to muscle hypertrophy involving the left ventricle or both left and right ventricles. Neither isolated nor predominant right ventricular hypertrophy was observed.

It has been concluded that myocardial hypertrophy is a more specific and significant anatomic alteration in the hearts of very obese subjects than are the previously reported findings of excess epicardial fat and fatty infiltration of the myocardium. The relationship between chronic augmentation of the work of the heart in these subjects and the development of cardiac hypertrophy has been discussed. The findings in this study have been interpreted as providing further support for the propositions that manifestations of myocardial insufficiency do occur in very obese subjects without evidences of other heart disease, that these manifestations are those of predominant left ventricular or biventricular failure, and that isolated cor pulmonale does not develop in the absence of pulmonary embolization.

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