Editorial

Left Ventricular Morphology and Diastolic Function in Severe Obesity: Current Views

Morfología ventricular izquierda y función diastólica en la obesidad grave: perspectivas actuales

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Early observations of cardiac morphology in obesity focused primarily on the prominence of epicardial fat.[1,2] These include anecdotal descriptions by such luminaries as René Laennec, William Harvey, and Jean Nicholas Corvisart.[1] In 1933, Smith and Willius reported autopsy findings on 135 obese patients including 4 who were severely obese.[1–3] In this study heart weight increased in proportion to the degree of obesity up to 105 kg and to a lesser extent thereafter.[1–3] Heart weight was greater than predicted for normal weight and height in both men and women and was far greater than expected in severely obese persons. Nearly all patients had excess epicardial fat and the authors ascribed increased heart weight to this phenomenon. In 1957, Lillington reported biventricular hypertrophy in a severely obese man who died of pulmonary embolism, thus raising the question of left heart involvement in obesity.[1,2] In 1962, Alexander reported the results of a retrospective survey of autopsy studies of extremely obese patients previously cited as having cor pulmonale. Left ventricular hypertrophy (LVH) and pulmonary congestion had been present in each case.[1,2] In 1965, Amad et al. reported the results of postmortem studies of 12 severely obese patients.[1,2] They confirmed that heart weight was increased in all individuals, but demonstrated that it was largely due to LVH. The left ventricle (LV) wall thickness was increased in 11 of the 12 patients and myocyte hypertrophy on microscopic examination was present in all 12. Right ventricular wall thickness was increased in 1 patient and epicardial fat was increased in 6. A later study of 12 severely obese patients by Warnes and Roberts reported increased heart weight, LV wall thickness, microscopic LVH, and excess epicardial fat in all cases and increased right ventricular wall thickness in 4 patients.[1,2] Complicating these observations was the fact that systemic hypertension and/or coronary artery disease were present premortem in many of the subjects in these studies.

The advent of echocardiography permitted premortem assessment of cardiac structure in morbidly obese patients. In a study of 62 normotensive severely obese subjects, Alpert et al. reported LV enlargement in 40%, increased LV wall thickness in 56%, increased LV mass in 64%, left atrial enlargement in 50%, and right ventricular enlargement in 32%.[1,2] Multiple studies have compared LV morphology in obese patients to that of lean subjects.[2–4] LV mass, mass index, mass/height index, or mass/height[2–7] were significantly greater in obese than in lean patients in all of these studies regardless of the severity of obesity.[2–4] The LV internal dimension in diastole was significantly larger in mildly, moderately, and severely obese patients compared to lean subjects.[2–4] Interventricular septal thickness and LV posterior wall thickness were significantly greater in obese than in lean patients regardless of severity of obesity.[2–4] Calculated LV radius to thickness ratios were elevated in most but not all of these studies, suggesting that LVH in obese patients, when present, is usually eccentric.[2] It is notable that not all of these studies excluded hypertensive patients. A study by Kasper and coworkers of 409 lean and 43 severely obese patients with heart failure showed a higher prevalence of dilated cardiomyopathy in obese than in lean patients.[4] A specific cause was identified in 64% of lean and only 23% of obese patients, thus supporting the existence of a cardiomyopathy of obesity. Myocyte hypertrophy was present in 67% of biopsies of obese patients. Based on postmortem and echocardiographic studies reported during the 1980s and 1990s the following cardiac structural abnormalities were identified in obese subjects: increased heart weight, LV enlargement, increased LV wall thickness, an increased LV radius to thickness ratio, increased LV mass, microscopic LVH, left atrial enlargement, right ventricular enlargement and hypertrophy, and excessive epicardial fat.

With the exception of excessive epicardial fat, the aforementioned abnormalities associated with obesity evolve from altered hemodynamics.[5–7] Obesity, particularly severe obesity, produces hemodynamic alterations that predispose to changes in cardiac structure and function.[5–7] Excessive adipose accumulation together with increased fat-free mass combine to increase central blood volume. In the absence of systemic hypertension a reduction in systemic vascular resistance facilitates augmentation of cardiac output.[5–7] Since heart rate changes little if at all with increasing fat mass, the rise in cardiac output is due entirely to increased LV stroke volume. Augmentation of cardiac output leads to dilatation of the LV, left atrium, and right ventricle. The increase in LV chamber size (and therefore radius) causes LV wall stress to rise in accordance with the law of LaPlace.[5–7] This in turn is thought to

predispose to eccentric LVH in the absence of systemic hypertension.[5–7] Studies by Alpert and colleagues have demonstrated that LVH in normotensive severely obese individuals is due at least in part to adverse loading conditions (preload and afterload).[7] Eccentric LVH is a mechanism for normalizing LV wall stress, but predisposes to LV diastolic dysfunction.[5–7] If hypertrophy fails to keep pace with dilatation, wall stress remains high and LV systolic dysfunction may ensue.[5–7] The coexistence of high cardiac output, LVH, and LV diastolic dysfunction (and in some cases systolic dysfunction) may lead to left heart failure with resultant pulmonary venous hypertension, pulmonary arterial hypertension and right heart failure.[5–7] Duration of severe obesity has been identified as an important determinant of alterations of cardiac performance and structure in severe obesity as well as the development of heart failure.[7] Comorbidities such as systemic hypertension and the sleep apnea-obesity hypoventilation syndrome, which are commonly encountered in severely obese patients, may further alter cardiac structure and function and contribute to cardiac decompensation.[5–7] Systemic hypertension further augments cardiac output and increases systemic vascular resistance.[5–8] In such patients, a hybrid form of LVH (so-called eccentric-concentric hypertrophy) may develop.[8] With this form of hypertrophy, LV diastolic chamber size is smaller than with eccentric hypertrophy and diastolic wall thickness is more increased.[8] The LV mass in such individuals is greater than that associated with LV eccentric or concentric hypertrophy alone.[8] The major cause of right heart failure in morbid obesity is left heart failure.[7] However, this may be facilitated by pre-existent right ventricular dilation associated with high cardiac output and by hypoxia-driven pulmonary arterial hypertension resulting from sleep apnea and obesity hypoventilation.[5–7]

During the past decade several studies have challenged the notion that LVH is typically eccentric in the setting of obesity.[9–12] These studies have identified the presence of concentric LV remodeling and concentric LVH in a substantial percentage of obese patients including severely obese patients.[9–12] Concentric LV remodeling and hypertrophy have been reported in up to 50% of obese patients with abnormal LV geometry.[9–12] In several studies, concentric LV remodeling/hypertrophy has occurred more frequently than eccentric LVH.[9–11] Still other recent studies, including the one reported by Luaces et al. in the article published in *Revista Española de Cardiología*, have identified eccentric LVH as the predominant form of hypertrophy in obese patients.[12,13] Why then is there such variation in LV geometry in obese patients? Part of the explanation lies with the newer classification of LV geometry. The current classification is based on relative wall thickness or the LV mass to volume ratio. Eccentric LVH is defined as a relative wall thickness or mass-to-volume ratio of <0.45 in the presence of increased LV mass. Concentric LV remodeling is defined as relative wall thickness or a mass to volume ratio ≥0.45 in those with normal LV mass. Concentric LVH is said to be present when the relative wall thickness or mass to volume ratio is ≥45% in those with increased LV mass. Thus, what was once classified as eccentric-concentric LVH is now classified as concentric LVH. The authors of the study published in *Revista Española de Cardiología* utilized the newer classification.[13] Another reason for the reported variation in LV geometry in obese subjects is the failure to adequately account for systemic hypertension. Many of the studies reporting a high incidence of concentric LV remodeling or hypertrophy in obese patients did not exclude those with systemic hypertension.[9,11] While some of those studies adjusted for the presence of systemic hypertension, they did not take into account the relative severity of obesity and hypertension, nor did they adjust for duration of these variables.[9,11] This is potentially important. For example, a patient with longstanding severe obesity and mild hypertension might be expected to develop eccentric

LVH, whereas a patient with grade 1 obesity and longstanding, poorly controlled hypertension might be expected to develop concentric LV remodeling or hypertrophy. Nevertheless, several studies of patients with uncomplicated obesity have shown high incidence of concentric LVH remodeling and hypertrophy and indeed, re-analysis of older studies suggests that these geometric patterns have always been present to some extent.[2,3,6,10,12] Possible reasons for the development of concentric LV remodeling or hypertrophy in such patients include underdiagnosis of systemic hypertension, activation of the sympathetic nervous system and renin-angiotensin-aldosterone system (both of which occur commonly in obesity), stimulation of growth factors such as insulin-derived growth factors, and altered metabolism of adipokines (eg, leptin and adiponectin).[2,3,7] The predominance of eccentric LVH in the present study probably reflects the fact that all patients were severely obese and that systemic hypertension, when present, was relatively modest in severity.[13]

Multiple studies have assessed the effects of weight loss on LV morphology.[2,3,6,14] In patients with grades 2 and 3 obesity substantial weight loss has consistently produced significant reduction of LV mass.[2,3,6,14] Alpert et al. showed that the reduction in LV mass occurred predominantly in those with LVH prior to weight loss.[2] Older studies demonstrated significant reduction in the LV internal dimension in diastole with weight loss, whereas LV wall thickness failed to change significantly in most instances.[2] In the current study weight loss produced significant decreases in LV mass, interventricular septal thickness, and LV posterior wall thickness, but no significant change in the LV internal dimension in diastole.[13] This observation is consistent with the results of recent studies assessing the effect of weight loss on LV morphology.[3,14] The reasons for the disparity between older and newer studies with regard to reverse remodeling are uncertain. In the current study 70.7% of patients had some form of LV remodeling prior to weight loss.[13] Following weight loss 58.8% of patients exhibited normal LV geometry.[13] This remarkable reversal extends our knowledge concerning the positive impact of substantial weight loss on LV morphology in severely obese patients.

Hemodynamic studies of severely obese patients have consistently reported elevated LV end-diastolic or pulmonary capillary wedge pressure values.[4–7] Exercise significantly increases LV filling pressure, often to levels sufficient to produce pulmonary edema.[5] Thus, it is not surprising that even modest exertion causes dyspnea in such individuals. Multiple studies of obese patients have assessed LV diastolic filling noninvasively using indices derived from echocardiography, transmitral cardiac Doppler flow evaluation, tissue Doppler evaluation, radionuclide techniques, and magnetic resonance imaging.[6,7,10,15–18] Virtually all studies comparing grades 1, 2 and 3 obese patients with lean subjects have shown significantly greater impairment of LV diastolic filling in obese patients than in lean controls.[6,7,15–18] Alpert et al. have demonstrated that impaired LV diastolic filling in severely obese patients occurs predominantly in those with increased LV mass and is related to duration of severe obesity and adverse loading conditions that predispose to LVH.[7,15] Studies assessing the effect of substantial weight loss on LV filling pressure in severely obese patients have reported conflicting results.[5–7] That is, LV end-diastolic or pulmonary capillary wedge pressure does not always decrease or normalize following weight reduction.[5,7] In contrast, several studies of severely obese patients employing noninvasive assessment of LV diastolic function have reported improved LV diastolic filling following substantial weight loss.[6,7,14,15,18] In one study, LV diastolic filling improved in those with increased LV mass, but not in those with normal LV mass.[7] The study reported by Luaces et al. in *Revista Española de Cardiología* showed improvement of load-dependent indices of LV diastolic filling following weight loss, but no significant change in tissue Doppler indices of

LV diastolic function that presumably are load independent.[13] The authors suggest that failure of load-independent LV diastolic function to improve despite regression of LV following substantial weight loss in severely obese patients may be due to myocardial fibrosis.[13] That may well be the case and may explain disparate LV filling pressure responses to weight reduction in severely obese patients. It would have been of interest to compare and contrast LV diastolic function in patients with and without LVH in this study.

The preceding discussion has focused on obesity-related changes in cardiac morphology and performance in adults. An increasing body of evidence suggests that similar LV remodeling occurs in overweight and obese children and adolescents.[2,3]

In conclusion, the study by Luaces et al.[13] published in *Revista Española de Cardiología* demonstrates that LV remodeling occurs commonly in severely obese patients. Although eccentric LVH predominated, concentric LVH or remodeling was noted in a substantial percentage of patients. Substantial weight loss from bariatric surgery had a beneficial effect on LV geometry. At 1 year nearly 60% of patients demonstrated normal LV geometry. However, LV diastolic function assessed by tissue Doppler did not significantly change following substantial weight loss despite a decrease in LV mass. This suggests that nonmodifiable factors such as fibrosis may contribute to LV diastolic dysfunction in severe obesity and may prevent improvement in LV diastolic function following weight loss despite regression of LVH.

CONFLICTS OF INTEREST

None declared.

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