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Obesity and cardiovascular disease

Giacinta Guarini, MD, PhD
Cardiovascular Medicine Division, Cardio Thoracic and Vascular Department, University of Pisa, Italy

Correspondence: Dr Giacinta Guarini, Cardiovascular Medicine Division, Cardio Thoracic and Vascular Department, University of Pisa, Via Paradisa, 2, 56100 Pisa, Italy
E-mail: stefano.delprato@med.unipi.it

Abstract

Obese patients are at increased risk of developing cardiac disease and especially heart failure. Recent studies suggest the existence of a specific cardiac phenotype, called "obesity cardiomyopathy." However, in what is referred to as the "obesity paradox," there is evidence that obesity can confer a beneficial effect on prognosis in patients with heart failure or after acute coronary syndromes. This case report presents the follow-up of one patient with heart failure with preserved ejection fraction, whose only risk factor for cardiovascular disease on admission was a body mass index of 30, the lower cutoff value indicating obesity. The discussion goes on to highlight current data regarding the opposing features in obesity—obesity cardiomyopathy and the obesity paradox—and points out the paucity of data on the impact of weight loss in obese heart failure. ■ *Heart Metab*. 2016;69:31-33

Keywords: heart failure; obesity cardiomyopathy; obesity paradox

A 72-year-old woman was admitted to the emergency department due to shortness of breath (New York Heart Association [NYHA] functional class III), chest oppression on exertion (Canadian Cardiovascular Society functional class II [CCSII]), and fatigue. She reported that all symptoms had become exacerbated within the past 6 months. The patient reported no previous cardiovascular disease, and the only risk factor she had was a body mass index (BMI) of 30.

Her blood pressure was in the upper limit range (140/90 mm Hg), and persistent resting tachycardia was documented (daytime heart rate [HR] range of 90-150 beats per minute [bpm]). Blood analysis excluded anemia and thyroid disorder as the main cause of her symptoms, while showing an elevated level of B-type natriuretic peptide (BNP; 250 pg/mL). Blood gas analysis revealed the presence of mild hypoxia (Po_2, 68 mm Hg; So_2, 90%) with normal pH, which was correlated to the presence of sleep apnea disorder. Normal chest X-ray and spirometry excluded the presence of a chronic lung disorder. Electrocardiography showed diffuse repolarization abnormalities, with the following features recorded: left atrium enlargement; stage III diastolic dysfunction with increased left ventricular (LV) filling pressure; and concentric remodeling of the left ventricle (normal chamber size with mild increase in wall thickness), which exhibited preserved global and regional systolic function (ejection fraction [EF], 60%). The right atrium was mildly enlarged and the right ventricle, normal; a mild increase in estimated systolic pulmonary arterial pressure was recorded. No valve abnormalities or signs of pericardial disease were documented. At this stage of the evaluation, based on the patient's signs and symptoms, a diagnosis of heart failure (HF) with preserved EF (HFpEF) was made.

To further investigate if concomitant ischemic heart disease (IHD) was present (the patient complained of chest oppression on exertion), the patient underwent dobutamine stress echocardiography. The stress test ruled out IHD (no ischemic electro-

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Abbreviations

ACE: angiotensin-converting enzyme; **BMI:** body mass index; **BNP:** B-type natriuretic peptide; **BP:** blood pressure; **bpm:** beats per minute; **EF:** ejection fraction; **HF:** heart failure; **HFpEF:** heart failure with preserved ejection fraction; **HR:** heart rate; **IHD:** ischemic heart disease; **LV:** left ventricular; **LVH:** left ventricular hypertrophy; **NYHA:** New York Heart Association

cardiogram changes, no symptoms, no wall motion abnormalities), therefore medications to treat HFpEF, including angiotensin-converting enzyme (ACE) inhibitors (initially perindopril), β-blockers (initially nebivolol), and diuretics (initially indapamide), were started. On discharge, noninvasive ventilation with continuous positive airway pressure (CPAP) at night (for sleep apnea), measurements of body weight loss, and daily aerobic activity were also recommended.

One month later, the patient was evaluated during an ambulatory visit. She reported that her symptoms had improved a little, but there were no significant changes in NYHA functional class. She had normal blood pressure (130/80 mm Hg) with a resting heart rate of 80 bpm. Blood gas analysis indicated little improvement ($Po_{2,}$ 79 mm Hg; $So_{2,}$ 93%; and normal pH). Electrocardiography indicated no relevant changes, with persistence of stage III diastolic dysfunction. Although somewhat reduced, the BNP level was still elevated, measuring 200 pg/mL. The ACE inhibitor perindopril was switched to enalapril, the β-blocker nebivolol was further uptitrated to 10 mg/day, and a more potent diuretic (furosemide 25 mg/day) was initiated, replacing indapamide. Recommendations for weight loss were strengthened.

Three months later, the patient was hospitalized for recurrent HF symptoms, with further limitation of daily activity and orthopnea. Electrocardiography on admission recorded tachycardia/atrial fibrillation, but spontaneous cardioversion was observed later on in the day. Holter monitoring documented several self-limiting episodes of atrial fibrillation, therefore anticoagulation and antiarrhythmic therapy with amiodarone, in combination with β-blocker therapy (now shifted to carvedilol 6.25 mg twice a day), was introduced. Diuretic therapy was further augmented. Despite the recommendations for lifestyle modifications, the patient had gained more weight. There were no changes on echocardiography, which still showed left ventricle EF to be 60% as well as persistent stage III diastolic dysfunction. Hemodynamic parameters at discharge were as follows: blood pressure (BP), 125/80 mm Hg; HR, 75 bpm; $So_{2,}$ 94%; BMI, 31; and BNP level, 180 pg/mL.

The patient was then evaluated four weeks later, and again at three months and six months. Despite increasing diuretic doses and uptitration of the β-blocker, no further improvement was observed. Her NYHA functional class oscillated between class III and class II and three other episodes of hospitalizations for worsening HF occurred in the same year.

HF therapy was augmented by further introducing ivabradine (5 mg twice a day) in order to potentiate the HR-reducing efficacy of the β-blocker without affecting blood pressure. On top of the β-blocker (carvedilol 25 mg/day), ACE inhibitor (enalapril 10 mg/day), diuretic (furosemide 100 mg/day), and oral anticoagulant (dabigatran 150 mg twice a day), antiarrhythmic prophylaxis with amiodarone 200 mg was deemed necessary in order to maintain the atrial contribution to cardiac output. Moreover, spironolactone 25 mg/day—as a potassium-sparing drug—was added to the daily medication regimen. All medications were maximally uptitrated, with final doses reported in *Table I*.

Medication regimen	
Enalapril	10 mg/day
Carvedilol	25 mg/day
Ivabradine	10 mg/day
Amiodarone	200 mg/day
Spironolactone	25 mg/day
Furosemide	100 mg/day
Omega-3	1 g/day
Dabigatran	300 mg/day

Table I *Daily medication regimen (at maximum tolerated doses when appropriate).*

However, despite the pharmacological and non-pharmacological (nocturnal noninvasive ventilation for sleep apnea) strategies adopted, the NYHA functional class remained high (class III), and quality of life, poor. The patient was hospitalized several times without real clinical benefit. She continued to gain body weight despite adoption of all the recommendations, and was therefore referred for bariatric surgery. Unfortunately, sudden cardiac death occurred before bariatric surgery could be performed.

Discussion

Obese patients are recognized to be at increased risk for developing HF. Indeed, the prevalence of HF changes according to BMI, with a 5% increase in HF prevalence in men and a 7% increase in HF prevalence in women for every 1 kg/m^2 increase in BMI. As compared with subjects with a normal BMI, obese subjects had double the risk of HF, with women being at higher risk.[1] Functional and structural modifications have been recognized in this population and in experimental models of obesity. Clearly, obesity is associated with eccentric LV hypertrophy (LVH) and systolic and diastolic abnormalities, along with a propensity for more ventricular arrhythmias and sudden cardiac death.[2-5] Indication of a specific cardiac pattern in these patients suggests the existence of an obesity-related cardiomyopathy,[6] although this is still debated. Obese patients are more prone to develop signs and symptoms of HF despite preservation of cardiac systolic function.[7] Several mechanisms have been implicated in the development of these modifications, including lipid accumulation in the heart (lipotoxicity theory), a chronic inflammatory state, volume overload, and neurohormonal activation.[8] Moreover, often, patients with obesity suffer from sleep apnea disorders, further aggravating the effect of obesity on cardiac metabolism and general hemodynamics.[9] Interestingly, once HF has developed, it seems that obesity confers a beneficial influence on prognosis in what has been termed the "obesity paradox."[10] There is little evidence regarding the impact of weight loss in obese HF and whether or not this is beneficial. Only a few studies have investigated the cardiovascular effects of both dietary weight loss and bariatric surgery, with few specifically including HF patients or animal models.[11] Accordingly, the existence of the obesity paradox raises the question of whether or not obesity should be treated.[12,13] Inconsistent results have also been obtained in clinical trials investigating patients with HFpEF. Moreover, mortality rates and rates of rehospitalization are not significantly different between HFpEF and HF with reduced LV function. This may be partially attributed to the multiple mechanisms responsible for HF development. Therefore, therapeutic pharmacological and nonpharmacological strategies should be tailored to patient needs. ■

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