

# Obesity cardiomyopathy: a review of literature on clinical status and meta-analysis of diagnostic and clinical management

Aref Albakri\*

St-Marien hospital Bonn Venusberg, Department of Internal Medicine, Bonn, Germany

## Abstract

Obesity cardiomyopathy (OCM) is a recently described form of heart muscle disorder. However, with the prevalence of obesity rapidly rising, research interest on its deleterious effect on cardiac morphology and function has been on the increase. However, with morphological and functional features mimicking those of dilated cardiomyopathy, research on OCM has been reduced to a sub-type or a secondary cause of dilated cardiomyopathy (DCM). Considerable debate also persists as to whether isolated obesity can directly cause cardiomyopathy in humans since its effect on cardiac function and structure cannot be isolated from those of comorbidities such as hypertension, dyslipidemia, glucose intolerance and coronary artery disease. With such extraneous factors, research on IOC has been fragmented and at most inconsistent. The purpose of the present review and meta-analysis is to synthesize current scholarly and practitioner understanding of IOC with a focus on broadening the knowledge on diagnosis and clinical management.

## Introduction

Obesity is fast becoming a major public health burden worldwide. It is a significant risk factor for the development of cardiovascular diseases (CVD) and an important cause of premature death [1]. It has an independent association with the development of heart failure (HF) [2,3] and involved in the development of several comorbid conditions principally atherosclerosis, hypertension and diabetes mellitus (DM) that predispose patients to the development of HF [4]. An extreme consequence of obesity is its involvement in the development of a range of pathological alterations in ventricular morphology and function, a condition clinically termed as obesity cardiomyopathy (OCM). Over the past three decades, the global prevalence of obesity has nearly doubled and the mean body mass index (BMI) has risen by 0.4 kg/m<sup>2</sup> [5]. Current projections predict by 2025, the prevalence of obesity will reach epidemic proportions [6]. The deleterious effect of obesity on cardiac performance vis-à-vis its rapidly rising prevalence warrants a precise understanding of its relationship with ventricular structure and function to guide diagnosis and clinical management. Thus, this review article aggregates current research findings and practitioner knowledge on the clinical status of obesity cardiomyopathy including two meta-analyses of its diagnosis and clinical management methods.

## Description

**Historical context:** Despite the recency of increased research interest in the relationship between obesity and cardiac function, description of obesity-associated heart failure in medical literature dates as far back as the late 1700s [7]. The initial mention of excess deposition of fat involving the heart of obese individuals was in 1783. About two decades later (in 1806), adipose tissue surrounding the heart in obese individuals was suspected to oppress the heart leading to sudden death [8]. In the late 19th Century [9,10] and in the early 20th Century [11] research evidence of the deleterious effect of obesity on cardiac function began to accumulate. However, the initial clinical descriptions

of a pathologic obesity-associated cardiac morphology and dysfunction appeared in 1933. Saphir and Corrigan [12], and Smith and Willis [13] described the deleterious effect of fatty infiltration or adiposity of the heart on cardiac function and structure.

Since then, several subsequent studies have demonstrated cardiomyopathic processes caused by obesity may involve both the left and right sides of the heart, which occur in the absence of other cardiac or extra cardiac conditions associated with morbid obesity [14-18]. These conditions mainly include systemic hypertension, diabetes mellitus and coronary artery disease (CAD) but which on their own could contribute to cardiac decompensation, and as such, they remain significant risk factors accelerating the development of OCM [18-20]. More recently, the Framingham Heart Study (FHS) further reported obesity is an independent risk factor for the development of HF, demonstrating its deleterious effect on the ventricular function [21,22]. Despite the decades-long accumulated evidence of obesity associated heart failure, the recent research interest on OCM is attributable to the rapidly increasing global prevalence of obesity in the general population. Since the 1933 initial clinical description of OCM, more than 57,000 articles whose titles include the term obesity and CVD have been published in PubMed, with the bulk of the studies published towards the end of the 1990s.

Research on the prevalence of obesity in the general population has been extensive. However, a longitudinal systematic epidemiological study by Ng and associates [23] remains the biggest and most powerful.

\*Correspondence to: Aref Albakri, St-Marien hospital Bonn Venusberg, department of internal medicine, Bonn, Germany, E-mail: arefalbakri@yahoo.com

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Spanning over three decades (1980-2013) and recruiting individuals aged between two (2) years and over 80 years old from 188 countries, the study reported the highest prevalence of obesity (defined as BMI  $\geq 30$  kg/m<sup>2</sup>) in Oceania, North Africa and the Middle East, which exceeded 50% of the general population. The prevalence was lower but still very high on other parts of the world. In North America, a third of the population was obese while in Western Europe, a fifth of the population was obese [23]. These extremely alarming global levels and trends of obesity in the general population and its harmful effect on many different physical and mental conditions together with its involvement in cardiac diseases explains the renewed research interest in obesity

**Classification:** Obesity cardiomyopathy has been long recognized as a clinical entity but current morphological-and functional-based classification systems have excluded it as a distinct form of cardiomyopathy. The European Society of Cardiology (ESC) Working Group on Myocardial and Pericardial Diseases [24] does not classify OCM as a type of cardiomyopathy. On the other hand, the 2016 Scientific Statement of the American Heart Association (AHA) classifies OCM as a sub-type of dilated cardiomyopathy (DM) under endocrine or metabolic etiologies of DCM [25]. In support of AHA's classification, Kasper et al. [26] found a higher incidence of idiopathic DCM (77% versus 36%) among obese patients (mean body weight 130 kg) compared with lean patients (mean body weight 71kg). Several other studies have also demonstrated an association between obesity and idiopathic DCM [27-30] with some reporting a direct toxic effect of obesity on cardiac morphology and function [27,29,30].

Classification of OCM as a sub-type or an etiology of DCM adds to the current considerable debate to the existence of a true obesity-induced cardiomyopathy. Although OCM has been documented in rodent models, it is unclear whether isolated obesity can directly lead to cardiomyopathy in humans. Moreover, majorities of obese individuals have concomitant and likely synergistic risk factors for developing cardiac dysfunction, DCM and heart failure [27] [29,31]. In addition, pure obesity in the absence of hypertension, dyslipidemia, glucose intolerance and CAD is very rare, and therefore, difficult to isolate the deleterious cardiac effects of these comorbid disease entities from that caused exclusively by obesity.

## Definition

**Morbid/Extreme Obesity:** The term obesity defines individuals with a body mass index (BMI) of 30 kg/m<sup>2</sup> or higher while overweight defines individuals with BMI of between 25 to 29 kg/m<sup>2</sup>. Morbid or extreme obesity defines individuals with BMI of 35 kg/m<sup>2</sup> or higher [32]. Morbid obese individuals are of particular interest in the study of OCM because of a significantly elevated risk (50 to 100 times) of death from any cause compared to normal-weight individuals as well as are at the greatest risk of developing OCM [20,32].

**Obesity Cardiomyopathy:** Current definitions of obesity cardiomyopathy (OCM) lack a standardized definition. Contributing to the lack of a definitional uniformity is the ongoing controversy surrounding its recognition as a true cardiomyopathy and its varied terminologies, which include fatty heart, fatty infiltration, lipotoxic cardiomyopathy, cardiac steatosis or adiposity of the heart [12,13,33]. One category of definitions emphasize on the cause of cardiomyopathy, defining OCM as a potentially reversible cardiac condition in which an individual develops a form of non-ischemic DCM secondary to direct toxic effects of lipid accumulation in the myocardial cells [34,35]. The other category of definitions emphasize on pathological structural

and functional alterations occurring in the myocardium. In this category, the AHA defines OCM as myocardial disorder characterized by alterations in ventricular morphology and function including left ventricular (LV) dilatation, eccentric or concentric LV hypertrophy, LV systolic and diastolic dysfunction, and right ventricular (RV) dysfunction occurring in the setting of morbid obesity [25]. The 1985 National Institutes of Health Consensus Development Conference [36] and the World Health Organization (WHO) Expert Committee Anthropometric reference data for international use defined OCM as a cardiac condition characterized with clinically demonstrable LV dysfunction not explained by structural heart disease or systemic hypertension [37]. Although the current definitions agree that morbid obesity is the culprit etiology of OCM, the condition lacks pathognomic features to distinguish it from DCM, hence supporting the 2016 AHA guidelines classifying it as a sub-type of DCM.

*Effect on cardiac performance:* Morbid obesity (defined as BMI  $> 35$  kg/m<sup>2</sup>) potentially causes a wide range of alterations in cardiac performance including changes in cardiac hemodynamics, and LV morphology and function (Table 1).

## Pathophysiology

Research interest to clarify the relationship between obesity, and cardiac structure and function began in the 1950s. The initial studies centered on the effect of obesity on cardiac hemodynamics, chamber size, LV wall thickness and mass and ventricular diastolic or systolic function [7]. Recent studies involving animal models expanded the focus to include the effect of obesity-associated neurohumoral activation and metabolic abnormalities on cardiac structure and function [38]. Today, the scientific consensus is that excessive adipose accumulation in myocardial tissues is the primary etiologic agent in the development of OCM through the synergistic effect of five key pathophysiologic mechanisms. (a) Alterations in cardiac hemodynamic, structure and function; (b) metabolic disturbances; (c) myocardial lipotoxicity; (d) neurohumoral derangement (over activation of the renin-angiotensin-aldosterone and sympathetic nervous systems); and

**Table 1.** Impact of Obesity on Hemodynamics and LV Morphology and Function

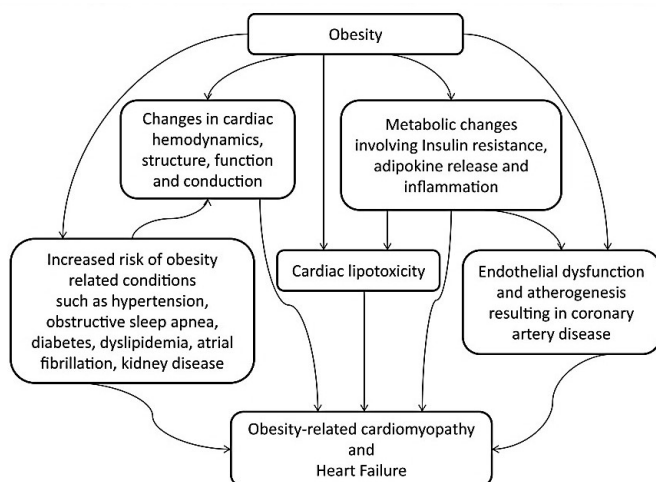
Cardiac Function/Structure	Description of the Effect of Obesity
Hemodynamics	Increased blood volume
	Increased stroke volume/Work
	Increased arterial pressure
	Increased LV wall stress
	Pulmonary artery hypertension
Cardiac Structure	LV concentric remodeling
	LV hypertrophy (eccentric/concentric)
	Left atrial enlargement
	RV hypertrophy
Cardiac Function	LV diastolic dysfunction
	LV systolic dysfunction
	RV failure
Inflammation	Increased C-reactive protein
	Over-expression of tumor necrosis factors (TNF)
Neurohumoral	Insulin resistance and hyperinsulinemia
	Leptin resistance and hyperleptinemia
	Reduced adiponectin
	Sympathetic nervous system over-activation
	Activation of renin-angiotensin-aldosterone system
Cellular	Hypertrophy
	Apoptosis
	Fibrosis

(e) small-vessel disease (microangiopathy and endothelial dysfunction) [38-41] (Figure 1).

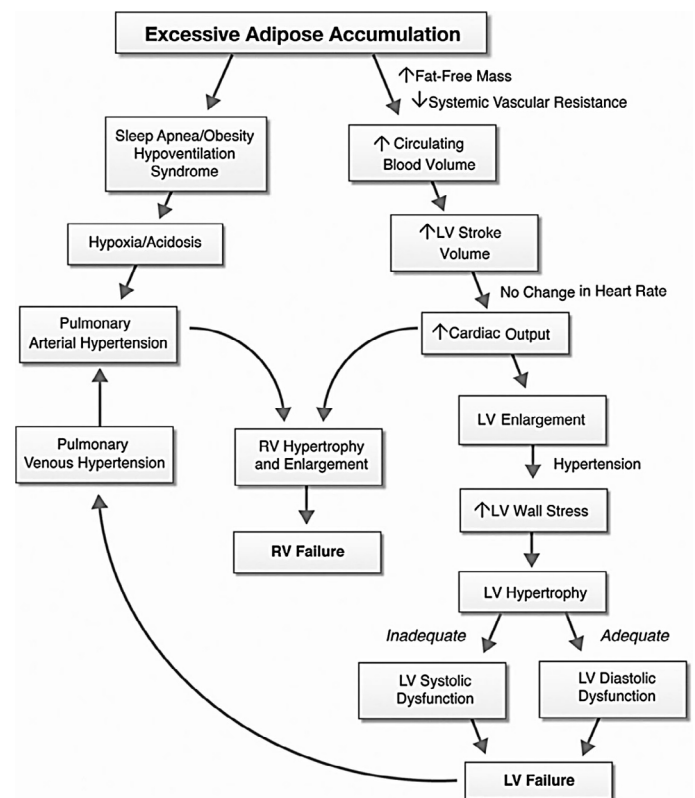
**Changes in Cardiac Performance:** Extensive research evidence has clearly demonstrated an injurious association between adiposity (obesity), and changes cardiac performance (hemodynamics, structure and function) [7,26,43-47]. Systematic involvement of excess adipose accumulation causes alterations in ventricular hemodynamics, structure and function contributing in the pathophysiology of obesity (Figure 2).

**Hemodynamic Changes:** Excessive adipose tissue and increased fat-free mass in obese individuals increases metabolic demands leading to hyperdynamic circulation: increased circulating blood volume (CBV) and increased cardiac output (CO) [48]. The increase in circulating blood volume causes an increase in venous return to the right and left ventricles and a subsequent increase in wall tension and chamber dilatation [49]. In obese individuals, heart rate remains unchanged or is mildly increased but LV stroke volume (volume of blood pumped from the left ventricle per beat) increases relative to the excess body weight leading to increased LV stroke work above that predicted for the ideal body weight [38,50,51]. Obesity widens arteriovenous oxygen difference due to elevated LV pressure and volume, which increases oxygen consumption causing a leftward shift in the Frank-Starling curve [43,44,52]. These changes cause hemodynamic overload, increased LV stroke workload and eventually causes LV failure [50,53]. Obesity increases LV afterload because of increased peripheral vascular resistance and greater aortic stiffness mainly in obese patients with hypertension [48,54]. RV afterload may be increased because of the LV changes, or obstructive sleep apnea (OSA) and/or obesity hypoventilation syndrome (OHS), which may cause hypoxia-induced vasoconstriction and pulmonary arterial hypertension (PAH) [38,54,55].

**Myocardial Remodeling:** Obesity causes myocardial remodeling (structural changes to the heart), which is a key mechanism in the subsequent development of heart failure [38,56,57]. Cardiac weight and body weight have a positive correlation with morbid obese patients. In chronic obesity, especially occurring concomitant with systemic hypertension, LV hypertrophy and dilatation are common,



**Figure 1.** Pathophysiologic Mechanisms of Obesity Cardiomyopathy [39]. In morbid obese patients, cardiomyopathy may result from obesity, which may be potentiated with increased predisposition to other risk factors such as coronary artery disease, diabetes mellitus, hypertension, dyslipidemia, insulin resistance, metabolic syndrome, kidney disease, obstructive sleep apnea and cardiac conduction abnormalities



**Figure 2.** Hemodynamics, Structural and Functional Alterations in Obesity Cardiomyopathy [42]. This diagram schematically represents hemodynamic changes resulting from excessive adipose accumulation in morbid obese patients and their subsequent effect on cardiac morphology and ventricular function and eventually heart failure. LV hypertrophy may be eccentric in normotensive morbid obese patients or concentric in morbid obese patients with chronic systemic hypertension. Neurohormonal and metabolic abnormalities may contribute to the development of LV failure, and pulmonary arterial hypertension due to sleep apnea/obesity may lead to RV failure

and to a lesser extent, RV hypertrophy and dilatation may occur [39,58]. Both eccentric and concentric LV hypertrophy occur in obese individuals. The degree of cardiac remodeling correlates with the severity and duration of obesity [53,54]. Obesity (higher BMI) or waist circumference also correlate with higher LV mass compared to age-matched lean individuals [50]. Increased CBV, LV hypertrophy, LV stiffness and LV-end diastolic pressure may cause left atrial (LA) enlargement [39]. Obesity individuals also have excessive epicardial fat, which correlates with visceral adiposity but not with overall adiposity [58]. Obesity-associated epicardial fat extension into the ventricular and atrial myocardium may result in fatty infiltration in the RV and perivascular regions. Myocardial fibrosis occurring concomitant with tissue regeneration and inflammation is common in obese individuals and corresponds with the severity of obesity. It represents an important change in cardiac morphology preceding the development of LV hypertrophy and a key contributor to cardiac dysfunction [7,26].

**Ventricular Dysfunction:** Excess adipose accumulation in the myocardium has been shown to produce a deleterious effect on diastolic cardiac function. Obesity-associated alterations in LV filling occur in the setting of increased LV mass and abnormal loading conditions, which reduce ventricular compliance [54,59]. Decreased E/A ratio, prolonged isovolumetric relaxation times, decreased mitral annular velocity and myocardial early diastolic velocity are common in obesity [59,60]. The presence of myocardial fat infiltration does not always cause LV systolic dysfunction because it is not always present in obesity.



The initial compensatory LV hypertrophy may normalize LV wall stress and preserves systolic function [21,61,62]. However, increased blood volume may lead to LV dilatation, which in turn may reduce systolic contraction because of reduced myofibril shortening [21]. Moreover, chronic obesity and continued increase in LV blood volume may lead to systolic dysfunction accompanied by LV hypertrophy and fibrosis, cardiomyocytes injury and progressive collagen deposition and subsequent diastolic dysfunction. Persisting LV dysfunction may cause pulmonary edema and pulmonary hypertension, eventually leading into RV dysfunction [32] [39]. However, the assessment of RV dysfunction in obesity is challenging because of a high comorbid rate of obstructive sleep apnea and pulmonary hypertension [32].

## Metabolic Disturbances

**Insulin Resistance:** Insulin resistance is an independent predictor of the incidence of heart failure [63]. Since insulin resistance states correlate highly with obesity, it may potentiate the association between obesity and heart failure [64]. Insulin resistance changes myocardial substrate metabolism through an imbalance between free fatty acid (FFA) oxidation (uptake) and use leading to increased myocardial oxygen demand [65,66]. Decreased myocardial oxidative capacity reduces cardiac contractility and efficiency by altering sarcoplasmic reticular calcium stores and promoting mitochondrial dysfunction ultimately leading to cardiac dysfunction and increased susceptibility to pressure overload and ischemic injury [63,66]. Increased LV stroke work due to changes in hemodynamics further stimulates myocardial metabolism setting up a vicious cycle [66]. Stimulated global insulin resistance in obesity could result in hyperinsulinemia and chronic systemic hyperglycemia and hyperglycemia-induced cardiomyocytes injury or glucotoxicity-induced cardiomyocytes apoptosis [64]. Hyperglycemia is also involved in alterations of cardiac structure and function by producing advanced glycated end-products and modifying extracellular matrix (ECM), which alters the expression and function of intra-myocellular calcium channels. Collectively, insulin resistance mediated changes lead to systolic and diastolic dysfunction [64].

**Adipokines Release:** Adipokines are cytokines (cell signaling proteins) secreted by adipose tissue involved in the regulation of myocardial function. They participate in myocardial metabolism, cardiomyocyte hypertrophy, cardiomyocyte apoptosis, and changes in the structure and composition of the ECM [67]. In vitro and in vivo studies have demonstrated that adipokines directly regulates myocardial remodeling components (matrix metalloproteinase, tissue inhibitor of metalloproteinases and collagens) [67]. Two key adipokines (adiponectin and leptin) are involved in cardiac disease and myocardial remodeling. Adiponectin has cardioprotective effect of decreasing the action of insulin-induced adrenergic receptor-mediated cardiac myocyte hypertrophy. In obese individuals, reduced adiponectin levels and over-expression of tumor necrosis factor (TNF), which suppresses adiponectin, mitigate the cardioprotective effect of adiponectin [68,69]. Leptin on the other hand appear to have an opposite effect to adiponectin. It stimulates cardiac hypertrophy directly through cell signaling mechanisms and indirectly through its effect on hypertension and sympathetic nervous system (SNS) [70,71]. Leptin conveys a cardioprotective effect against ischemic reperfusion injury and limiting cardiac lipotoxicity [72]. Although Shibata et al. [69] reports that obese individuals are insensitive to leptin, it is postulated that, since leptin has an opposite effect to adiponectin, leptin/adiponectin ratio may play a role in myocardial remodeling and heart failure development [72]. The effect of other adipokines such as resistin, apelin, visfatin, vastin,

omentin and chemerin on cardiac function and structure is not well-established [72].

**Inflammation:** Inflammation is involved in the pathophysiology of obesity cardiomyopathy. Obese individuals usually exhibit chronic inflammation with elevated circulating levels of inflammatory markers and increased expression and/or release of inflammation-associated adipokines except adiponectin whose expression is decreased [73]. Interleukin-6, a pro-inflammatory cytokine, modulates hepatic secretion of C-reactive peptide, an inflammatory marker [49]. Interleukin-6, C-reactive peptide and TNF are associated with heart failure and subclinical LV dysfunction. Inflammatory pathways and Interleukin-6 in particular has the strongest prediction for heart failure in obese patients [74]. In addition to adipokines-associated inflammation, FFA in the epicardial adipose tissue may potentiate obesity-associated inflammation by activating inflammatory responses in epicardial macrophages [75]. Chronic inflammation promotes insulin resistance and fibrotic changes in the myocardium, leading to cardiac dysfunction [21,40,75].

**Myocardial Lipotoxicity:** Myocardial lipotoxicity is the deposition of excess FFA and triglycerides (TG) in parenchymal cardiomyocytes through a process called cardiac steatosis leading to cellular dysfunction and apoptosis and ultimately myocardial dysfunction [40,76,77]. In obese rat models, defects in lipid oxidation (mismatch between FFA uptake and use) causes the accumulation of FFA and TG in cardiomyocytes causing ventricular hypertrophy and dysfunction. In humans, cardiac steatosis correlates positively with BMI and the severity of adiposity due to elevated LV mass and suppressed septal wall thickening [68,78]. Although high myocardial TG content is non-toxic, and may initially provide a buffer against FFA toxic pathways [79], cardiomyocytes have limited storage and shunt excess FFA into non-oxidative pathways resulting into lipotoxicity and apoptosis of lipid-filled cardiomyocytes [49,79,80]. Fat in intervening cells may also produce pressure-induced atrophy of adjacent cardiomyocytes leading to restrictive pattern of cardiomyopathy [49].

**Neurohumoral Derangement:** Certain obesity-associated neurohumoral derangements (over-activation of the renin-angiotensin-aldosterone system [RAAS] and increased sympathetic nervous system [SNS] tone) have been linked to the pathogenesis of OCM. The two systems (RAAS and SNS) serve as baseline regulatory signaling cascade controlled by negative feedback to preserve normal hemodynamics and facilitate adequate myocardial perfusion [8,32]. Insulin resistance and hyperinsulinemia (excess levels of insulin circulating in the blood relative to the level of glucose) lead to an increase in angiotensinogen, a component of the renin-angiotensin system [21,81]. Elevated levels of angiotensinogen causes an increase in angiotensin II and aldosterone, which potentiate cardiomyocyte growth factors and promote myocardial and perivascular changes leading to ventricular hypertrophy, fibrosis and ultimately cardiac dysfunction [21,38,57]. Continuous sympathetic activation due to cardiac dysfunction increases and impaired signal transduction due to down-regulation of beta-adrenergic receptors and decreased sarcoplasmic reticular calcium ATPase depresses cardiac contractility and leads to further myocardial dysfunction [21,26,50,57].

**Small-Vessel Disease:** Small vessel disease also contributes to the pathophysiology of OCM. Endothelial dysfunction and inflammation of the small vessel wall are important events in the development of atherosclerosis. Obesity is an independent pathobiological determinant for atherosclerosis and directly contributes to atherogenesis by creating a prothrombotic and proinflammatory state [49,52,82]. Obesity in young

adults accelerates the progression of atherosclerosis decades before the appearance of clinical manifestations [52]. Excessive circulating FFA, TG, and low-density lipoprotein cholesterol are risk factors for the development of lipotoxicity, which may cause injury to vascular tissues or alter their functions [83]. Lipotoxicity causes endothelial dysfunction independently or in concert with hyperglycemia, oxidative stress, over-activated RAAS and elevated levels of proinflammatory cytokines [84].

**Comorbidities:** Besides direct involvement of obesity in the pathophysiology of OCM, it also conveys an indirect involvement. Obesity predisposes to the risk of comorbidities that may potentiate or increase the risk of developing OCM. Hypertension, diabetes mellitus, dyslipidemia, insulin resistance, metabolic syndrome, obstructive sleep apnea and kidney diseases are frequently encountered comorbidities in obese patients [32,39,54]. In the setting of obesity, these comorbidities increase the risk of atherogenesis and heart failure [54]. In addition, obesity hypertension and obstructive sleep apnea are predictors of LV hypertrophy (a risk factor for heart failure) [85], while CAD is involved in the development of LV hypertrophy [86].

**Risk factors:** Several factors have been identified that increase the risk of developing heart failure in OCM patients. In a study of cardiac structure and LV function in normotensive morbidly obese patients with or without congestive heart failure, Alpert and associates [15] identified five factors that increase the risk of heart failure in morbidly obese patients. (a) The duration of morbid obesity; (b) LV internal dimension in diastole; (c) LV end-systolic wall stress; (d) Left atrial (LA) dimension; and (e) RV internal dimension (Table 2).

In subsequent studies, Alpert and associates [15,38] isolated the duration of morbid obesity (BMI > 25 kg/m<sup>2</sup>) as the strongest risk factor for HF in obese patients. They reported that twenty (20) years of obesity conveyed a 66% risk for developing obesity-related HF, which rose to 95% for 25 years duration of morbid obesity. Moreover, obesity cardiomyopathy is now well recognized in the HF community, accounting for about 11% of HF in men and 14% in women [87]. Duration and severity of adverse loading conditions particularly hypertension increases the risk of LV dysfunction and HF in obese patients [39]. The severity of obesity is another risk factor for HF. After controlling for other risk factors, a unit increase in BMI increase the risk of HF by 5% in men and 7% in women [19]. Visceral fat, insulin resistance and increased age are also important risk factors for the development of obesity-associated heart failure [21,88]. Co-occurring diseases such as CAD, diabetes mellitus, hypertension, obstructive sleep apnea, kidney disease and cardiac conduction abnormalities increase the risk of developing HF [39]. In addition to OCM-specific risk factors, classical risk factors for cardiovascular diseases may increase the risk for HF in obese patients. These factors include smoking, glucose dysmetabolism and sedentary lifestyle. However, the extent these classical risk factors contribute to an independent additional risk among morbid obese patients remains unclear [89,90].

## Clinical presentation and diagnosis

**Clinical Presentation:** Obesity cardiomyopathy presents with a similar clinical spectrum of HF symptoms to other forms of

cardiomyopathies. Frequently encountered symptoms are dyspnea, orthopnea, paroxysmal nocturnal dyspnea, wheezing, exercise intolerance and lower extremity edema [21]. These symptoms are attributable to mechanical consequences of the structural remodeling of the heart [21,26,19,91]. Obese patients may also present with reduced exercise time, functional capacity, larger LV mass, worse symptoms and labile obstructive hemodynamics [92]. Obesity may co-occur with hypertension, heart failure, atrial fibrillation, hypercholesterolemia, coronary artery disease, diabetes mellitus, obstructive sleep apnea, asthma, deep vein thrombosis and a variety of other medical conditions [34].

**Clinical Diagnosis:** The 2016 AHA Scientific Statement on Diagnostic and Treatment Strategies for specific forms of dilated cardiomyopathy lacks specific diagnostic criteria for OCM. Classified as a sub-type of DCM, the AHA proposes the diagnosis of OCM should be through the exclusion of other causes of DCM. Patients presenting with HF exclusively or predominantly due to obesity are considered to have OCM, usually with a BMI > 40 kg/m<sup>2</sup> [93,94]. However, diagnosis of OCM remains challenging since obesity produces a wide spectrum of hemodynamic changes predisposing patients to pathologic alterations in cardiac morphology and ventricular functions including LV dilatation, eccentric or concentric LV hypertrophy, LV systolic and diastolic dysfunction, and RV dysfunction. These changes occur in all classes of obesity but more pronounced in morbidly obese patients [8,95].

**Imaging Modalities:** Several studies recent have suggested that non-invasive ejection indices such as LV fractional shortening and LV ejection fraction (LVEF) have been used in the assessment of LV function in obesity [95,96,97] [98,99,100,101]. However, even in studies reporting lower indices of LV systolic function in obese than in lean patients, LV ejection phase remained preserved or mildly impaired in a majority of patients with depressed values [8] [51,95]. Fewer studies report supra-normal LV systolic function in obese patients [96,97]. Despite research support for the concept of a true OCM, severe systolic dysfunction occurs infrequent in obesity alone, such that the presence of LV systolic dysfunction should trigger the exclusion of other potential etiologies before it is diagnosed as OCM [8].

On the other hand, LV diastolic filling due to obesity may mimic that of adverse loading conditions that correlate negatively with LV systolic function such as conditions producing increased afterload [96]. Long-standing obesity are associated with greater decrease in LV systolic function but the severity of obesity inversely relates to LV ejection phase [97]. Tissue Doppler Imaging [TDI] and speckle tracking imaging modalities have been recently reported to reveal significantly lower systolic annular velocities in obese patients compared to lean patients with a progressive decrease as severity of obesity increases. The two imaging modalities also reveal abnormal myocardial systolic deformation and abnormal longitudinal strain and strain rate usually with a compensatory increase in radial strain [8] [95,98,99]. Changes in myocardial function detected by TDI and speckle tracking are frequently observed in the absence of clinical HF and with normal LV ejection fraction, suggesting subclinical LV systolic dysfunction is common in obese patients.

**Cardiac Biomarkers:** In addition to imaging modalities, the AHA recommendations suggest changes in the levels of cardiac markers should provide complementary diagnostic clues. Patients with OCM have depressed levels of B-type Natriuretic Peptide (BNP) and NT-pro B-type Natriuretic Peptide (NT-Pro BNP) compared to lean patients. The levels correlate with the severity of obesity, with levels decreasing

**Table 2.** Risk Factors for Obesity-Related Heart Failure

Risk Factor	Significance (p value)
Duration of morbid obese	< 0.0000002
LV internal dimension in diastole	< 0.00003
LV end systolic wall stress	< 0.00004
Left Atrial dimension	< 0.000001
RV internal dimension	< 0.00004

with increasing severity. However, the assessment of BNP levels are not confirmatory in the diagnosis of OCM since lower levels of BNP can also occur in both acute and chronic state of heart failure as well as in the setting of decompensated HF and elevated filling pressures [102,103]. Since clinical symptoms of dyspnea and edema are non-specific to HF in obese patients, hemodynamic confirmation is required in obese patients more than in lean patients for confirm clinical diagnosis [25].

**Meta-Analysis of Diagnosis Parameters:** Diagnosis of OCM has been challenging because of a frequent association with a wide spectrum of ventricular structural and functional changes. This meta-analysis combines findings from current studies on diagnosis of ventricular dysfunction in OCM patients compared to normal (control) patients. The objective is to identify the most frequently used clinical and imaging parameters in the diagnosis of ICM.

**Search Strategy:** Medical literature was reviewed to identify studies evaluating ventricular dysfunction in obese patients using echocardiographic imaging modalities: conventional and Tissue Doppler Imaging (TDI). A computerized search was performed in PubMed, OVID and EMBASE online databases. Studies were identified using a combination of the following key words: ventricular function, obesity, obese, body mass index (BMI) and echocardiography. Screening of bibliographies from qualifying studies and review articles complemented the online search. The inclusion criteria for studies included: (a) prospective and retrospective trials; (b) used echocardiography imaging for diagnosis of ventricular dysfunction; (c) published outcomes on alterations in both ventricular structure and function; and (d) compared data from obese and controls (lean patients). Data abstracted from the included studies to Microsoft Excel Worksheet included: patient population, mean age, mean BMI, LV structure (LVEDV, LVESV, RWT and LV mass), systolic dysfunction (LV ejection fraction and LV fractional shortening) and diastolic dysfunction (E/A ratio) and IVRT (Table 3).

## Results

Based on the inclusion criteria, five studies [59,104-107] were included in the final review and meta-analysis. Analysis of the included data comprised of 217 obese patients (BMI > 35 kg/m<sup>2</sup>) and 167 control or lean patients (BMI < 30kg/m<sup>2</sup>). The mean age was comparable between the two study cohorts – obese (36 years) and control patients (37 years). The obese group had a significantly higher weighted mean BMI of 40 kg/m<sup>2</sup>, range 37 to 46 kg/m<sup>2</sup>, while the control group had BMI 23 kg/m<sup>2</sup> range 21 to 24 kg/m<sup>2</sup>. All the five included studies used both

conventional echocardiography and Tissue Doppler Imaging (TDI) imaging modalities to assess LV structural changes and LV diastolic/systolic function. The most assessed echocardiographic parameters related to ventricular structure: LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), relative wall thickness (RWT) and LV mass. The most common echocardiographic parameters for assessing alterations in LV systolic function were LV ejection fraction (LVEF) and LV fractional shortening (LVFS) while the most common parameters for assessing changes in LV diastolic function were early diastolic and atria ratios (E/A ratio) and isovolumic relaxation time (IVRT). Parameters such as deceleration time, early diastolic myocardial velocities and late diastolic myocardial velocities, LV end diastolic diameters and left atrial diameter were reported less frequently.

The assessment of obesity-associated changes in LV structure was common in all studies. The mean LV mass was higher in obese patients (199 g, range 161 to 240 g) compared to control (144 g, range 128 to 163 g). LV mass was significantly higher in obese patients in all the five studies. Left ventricular (LV) end-diastolic volume (LVEDV) was also significantly higher in obese patients (104 ml) versus lean patients (82 ml). However, although LVESV was higher in obese patients (42 ml) compared to control (30 ml) the difference was not significant. Differences in RWT between obese patients and control were also not significant. LV ejection fraction (LVEF) and LV fractional shortening (LVFS) were the most common measures of LV systolic function. However, both obese and control patients did not reveal any significant differences in LVEF (67%) compared to control (64%) and LVFS (38% vs. 37%). Altered diastolic function was evident in obese vis-à-vis control patients. The E/A ratio was significantly decreased in obese patients (1.46) compared to control (1.72) while IVRT was significantly prolonged in obese patients (96 ms) compared to control (82 ms).

## Discussion

Morbid obesity-associated pathophysiological changes are injurious to almost all body systems hindering clinical diagnosis and making diagnostic processes challenging. The objective of the present meta-analysis was to describe structural and functional alterations of the LV in morbid obese patients leading to the development of cardiomyopathy. The findings associate morbid obesity with pathological alterations in both LV structure and function. The presence of increased LV mass, end-diastolic and systolic volume (and diameter) suggest enlarged (hypertrophied) LV structure. Decreased E/A ratio and prolonged IVRT are important diagnostic clues for LV diastolic dysfunction common in obese patients. However, LV systolic dysfunction is not always present

**Table 3.** Summary of Findings on Diagnosis of Obesity Cardiomyopathy

1st Author (Year)	Wong et al. (2004) [59]		Peterson et al. (2004) [104]		Pascual et al. (2003) [105]		Morricone et al. (2002) [106]		Iacobellis et al. (2002) [107]	
Parameters	Obese	Control	Obese	Control	Obese	Control	Obese	Control	Obese	Control
Patient No.	46	33	20	31	48	25	28	18	75	60
Mean Age	43±10	46±10	32±4	30±5	28±10	28±8	43±11.9	46±9.5	33±11.9	33±13.2
BMI (kg/m <sup>2</sup> )	46±11	23±1	37±5	24±4	40±3.5	21±2.2	37±5.4	22±1.7	38±5.5	23±1.4
LVEDV (ml)	NS	NS	94±17	85±17	117±31	75±22	101±27.2	87±22.1	NS	NS
LVESV (ml)	NS	NS	33±10	30±8	50±18.1	29±11.4	NS	NS	NS	NS
RWT	0.44±0.08	0.34±0.07	0.40±0.06	0.34±0.05	0.35±0.08	0.37±0.06	NS	NS	0.35±0.05	0.33±0.04
LV mass (g)	229±59	137±40	161±26	128±32	NS	NS	240±85.3	163±37.5	167±50.3	148±26.5
LVEF (%)	66±6.0	66±6.0	65±6	65±5	74±9.1	66±12.8	62±5.8	61±7.3	66±7.6	61±7.3
LV FS (%)	NS	NS	37±5	38±5	37.5±8.0	30.8±7.4	37.8±7.3	36.1±7.0	40±5	43±4
E/A Ratio	1.4±0.4	1.4±0.4	1.76±0.51	2.02±0.55	1.7±0.6	1.7±0.4	1.06±0.29	1.35±0.30	1.38±0.6	2.12±0.4
IVRT (ms)	99±18	86±15	92±13	88±11	72.0±15.8	80±22.1	81±17.8	76±8.9	121±10.4	89±8.8

**FS:** Fractional Shortening; **IVRT:** Isovolumic Relaxation Time; **LVED:** LV End-Diastolic; **LVEF:** LV Ejection Fraction; **LVES:** LV-End Systolic; **E/A:** Early Diastolic and Atria Ratios; **RWT:** Relative Wall Thickness.



or easily demonstrable in morbid obese patients. The two common echocardiography indices – LVEF and LVFS – show similar values with non-obese individuals.

Consistent with the present findings, several authors have already reported a significant association between morbid obesity (BMI > 40 kg/m<sup>2</sup>) and echocardiography-defined alterations in LV structure and function predisposing to obesity-associated cardiomyopathy [38,50,53-57]. The chronic nature of obesity supports the use of non-invasive imaging, which is both safe and effective for repeat assessment of LV performance. Since echocardiography is a well-established modality in the assessment of LV function and morphology and readily available, it is the preferred non-invasive imaging modality for assessing LV performance in OCM patients [108]. Several studies have already reported greater incidences of LV hypertrophy (enlargement) and diastolic dysfunction in morbid obese patients. Left ventricular (LV) hypertrophy occurs in between 62% [109] and 82% [110] of morbid obese individuals while diastolic dysfunction is common in between 55% [110] and 60% [111]. However, unlike LV structural alterations and diastolic dysfunction, systolic dysfunction is uncommon affecting fewer morbid obese individuals estimated at between 11% [110] and 25% [111].

The present analysis also reports fewer diagnosis of LV systolic dysfunction. However, LV systolic dysfunction maybe present in the subclinical phase of OCM but not easily demonstrable using conventional echocardiography. In addition, in the early stages of the developing LV dysfunction, compensatory LV hypertrophy modulates LV wall stress and preserves systolic function, which may explain the slightly reduced or normal LVEF and LVFS values in obese patients [21,61,62]. Prolonged morbid obesity with increased circulating blood volume and LV stroke work may reduce or eliminate compensatory effect of LV hypertrophy to cause systolic dysfunction [38,56,57]. Similar echocardiographic changes may also occur in overweight patients (BMI = 25-29 kg/m<sup>2</sup>) demonstrating subclinical clues of LV diastolic dysfunction even before the development of risk factors such as increased LV mass (hypertrophy) [112].

**Clinical management:** Obesity cardiomyopathy lacks specific clinical management guidelines. Current treatment protocols target the underlying causes of obesity (weight loss) and heart failure. The 2016 AHA Scientific Statement for Diagnostic and Treatment Strategies for Specific DCM recommends management of obesity and comorbidities such as diabetes mellitus, hypertension and metabolic syndrome. For patients with OCM and overt heart failure, the AHA guidelines recommend the inclusion for conventional treatment for LV systolic dysfunction and symptomatic HF as outlined in the 2013 ACCF/AHA Guidelines for the Management of Heart Failure [113].

**Lifestyle Modification:** Lifestyle modification in the form of exercise (increased physical activities) and dietary management (caloric restriction) remains the mainstay of chronic treatment for OCM. The therapeutic target is to cause weight loss and reverse obesity-associated hemodynamic and structural abnormalities. Weight loss has favorable clinical effect in preventing the development of comorbidities that potentiate or accelerate the risk of HF as well as producing long-term improvement of cardiovascular function [114]. The largest exercise intervention trial – Heart failure: A Controlled Trial Investigating Outcomes of Exercise Training (HF-ACTION) reported a non-significant trend towards a reduction in mortality or hospitalization and significant improvement in health status. Exercise intervention also caused a slightly higher degree of weight reduction in obese patients compared to lean patients [115]. Although weight loss changes may be

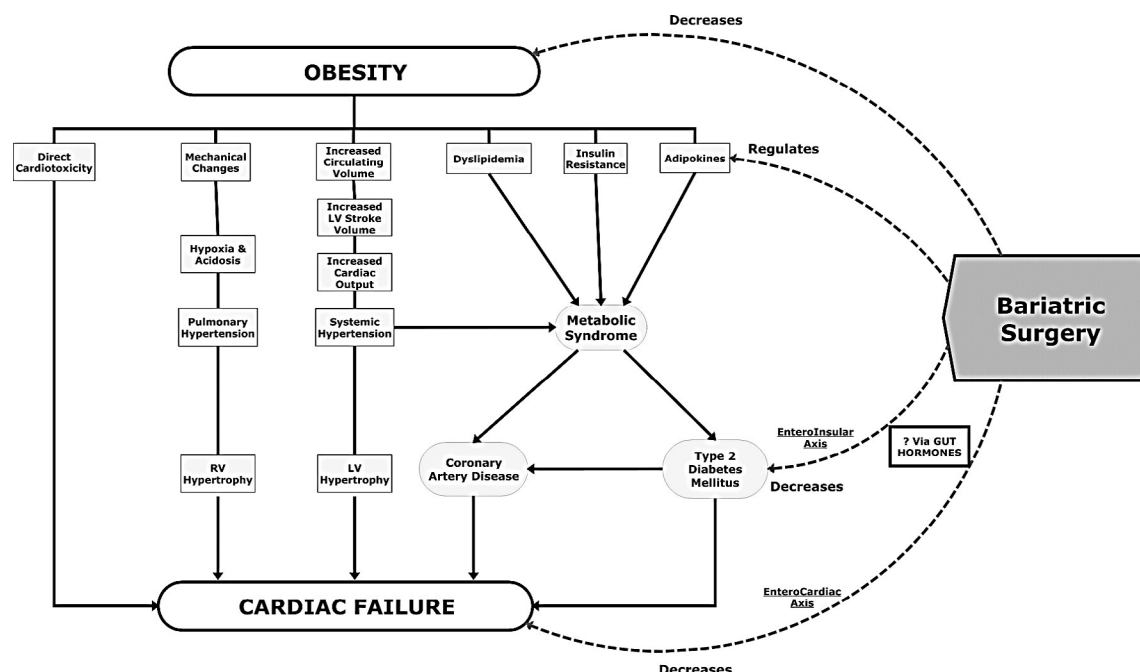
minimal, weight reduction changes as low as 7% sustained for a mean of 2.8 years decreases the risk of diabetes mellitus by 58% in patients with impaired glucose tolerance compared with control group under diabetes management program [116]. Exercise intervention that achieves weight reduction reverses the adverse profile of circulating cytokines leading to favorable profile with increased secretion of adiponectin and reduced secretion of TNF [114]. While weight reduction increases plasma adiponectin, exercise intervention in the absence of weight loss improves insulin sensitivity but does not increase adiponectin [114]. Aerobic exercise further contributes to decreasing systolic blood pressure in both hypertensive and normotensive patients. It should be included as a complementary therapy to exercise intervention [116].

**Bariatric Surgery:** Bariatric surgery refers to all medical procedures utilized to achieve a reduction of excess weight. It is categorized into restrictive, malabsorptive or a combination of the two [117]. The restrictive type refers to surgical reduction of the size of the stomach leading to food intolerance and subsequently weight loss. Malabsorptive type on the other hand refers to operations to bypass segments of bowel to cause malabsorption of nutrients. However, the gold standard of bariatric surgery is a combination of restrictive and malabsorptive surgical procedures [117]. Bariatric surgery is a widely accepted indication for morbidly obese patients with HF and/or clinically pronounced alterations in cardiac hemodynamic and structural or with comorbidities. The primary criteria for indication is the presence of high-risk comorbidities and severe obesity (BMI > 35 kg/m<sup>2</sup>) [32]. The clinical role of bariatric surgery in OCM patients is a reduction of excess weight and subsequently the risk of cardiac failure (Figure 3).

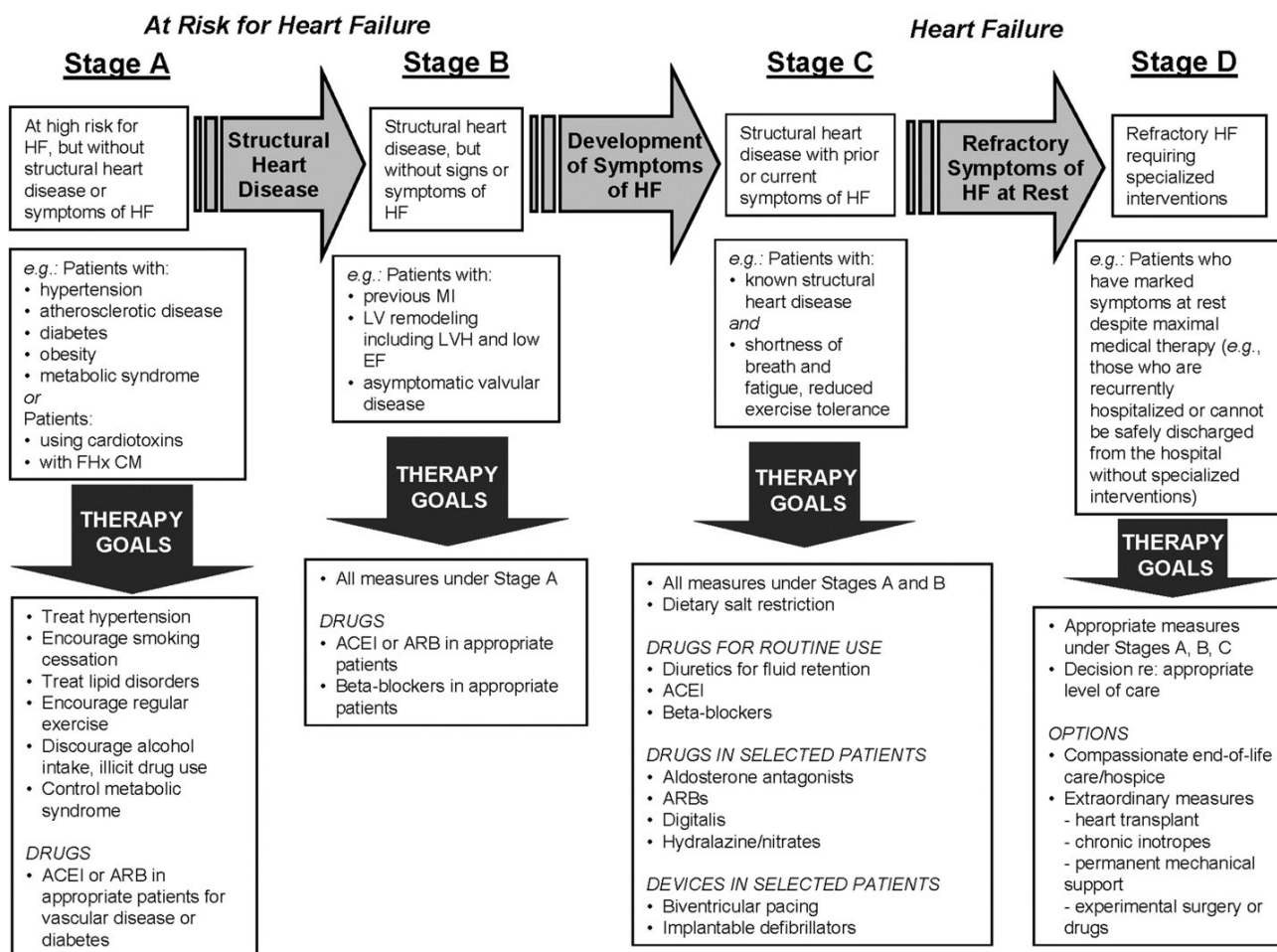
Extensive research evidence has demonstrated the role of bariatric surgery on the management of OCM. The evidence shows bariatric surgery achieves substantial reversal of obesity-associated hemodynamic and structural alterations by leading to a larger magnitude of weight loss compared to exercise or dietary interventions [118-126]. It improves insulin resistance and leads to resolution of diabetes mellitus, improve hyperlipidemia and hypertension and may eliminate obstructive sleep apnea [57,127]. In morbid obese patients with altered ventricular function, bariatric surgery causes a reversal of ventricular remodeling [127,128]. The findings reveal the safety and efficacy of bariatric surgery as a weight loss intervention for OCM patients or a bridge to recovery or to heart transplantation.

**Heart Failure Therapy:** Lifestyle modification and bariatric surgery targets weight reduction as a prophylactic and curative therapy for OCM. However, for OCM patients having significant LV systolic dysfunction and symptomatic heart failure, conventional heart failure therapy as outlined in the 2013 ACCF/AHA Guidelines for the Management of HF should be considered [113]. The guidelines classified HF in to Stages A to D and recommends specific therapy for each stage, which include conventional HF therapy for OCM patients should include prophylactic (healthy living - targeting weight loss), pharmacological support, device therapy, and heart transplantation (Figure 4).

**Meta-Analysis of Bariatric Surgery:** Weight loss interventions remain the mainstay of the treatment of OCM. The clinical target is to reduce myocardial adiposity and consequently achieve a reversal in ventricular remodeling and minimize the risk of developing comorbidities. Current studies and meta-analysis have shown bariatric surgery achieves a greater weight loss in comparison to non-surgical (dietary or pharmacological) interventions. This meta-analysis goes further to combine recent research findings to determine the efficacy



**Figure 3.** Figure 3: Role of Bariatric Surgery in Management of Obesity Cardiomyopathy [32]. Bariatric surgery causes substantial weight loss to directly decrease obesity and cardiac failure as well as indirectly decrease metabolic syndrome and comorbidities, and reverse ventricular remodelling and dysfunction



**Figure 4.** Development Stages of Heart Failure and their Treatment Strategies [113]. The 2013 ACCF/AHA Guidelines for the Management of Heart Failure. HF is classified into Stages A to D, with specific treatment protocols for each stage



of bariatric surgery in reducing BMI and its effect on cardiac structure and function.

**Literature Search:** The search for relevant literature on bariatric surgery was performed on PubMed, EMBASE, Ovid and Cochrane online databases. A combination of search terms were used: 'bariatric surgery' OR 'metabolic surgery' OR 'weight loss surgery' OR 'obesity surgery' AND 'echocardiography' OR 'magnetic resonance imaging' OR 'cardiac imaging' OR 'cardiac dimensions' OR 'ventricular dimensions'. Criteria for inclusion included studies that: (a) were prospective or retrospective cohort clinical trials; (b) recruited obese patients symptomatic of heart failure; (c) followed patients for at least three (3) months; (d) investigated bariatric surgery; and (e) provided quantifiable outcomes including at least one of the following. Pre and post BMI, pre and post LV function (LVEF), and pre and post LV structure (LV mass index). The exclusion criteria included (a) non-human studies; (b) non-surgical weight loss interventions; (c) case reports; (d) letters and comments; and (e) studies with follow-up of less than one month. There was no restriction on publication language or study population (both children and adults were eligible for inclusion). Additional studies identified from screening bibliographies and review articles on bariatric surgery.

Electronic copies of all articles identified in the online search were reviewed against the inclusion/exclusion criteria. All qualifying studies were then screened to determine they had sufficient data for analysis including weight loss and the effect on cardiac function and structure reported as a mean of the sample size. Selected articles were then abstracted and entered into a data abstraction form to extract all the salient information for analysis. Data abstracted included: (a) first author name; (b) publication year; (c) patient sample size; (d) mean age of recruited patients; (e) percentage of female patients; (f) BMI; (g) LVEF; (h) LV mass index; and mean follow-up period. In the case of more than one follow-up period, the longest period was considered (Table 4).

## Results

After reading title, abstract and full article of all qualifying studies, eighteen (18) were identified that fulfilled the inclusion criteria [129-

146]. All the studies used non-invasive cardiac imaging methods – echocardiography or cardiac magnetic resonance (CMR) imaging – for prognostication and assessment of treatment efficacy of bariatric surgery on OCM patients. Fifteen (15) of these studies recruited a prospective cohort while three (3) recruited a retrospective cohort. The 18 studies produced a pooled data set of 872 OCM patients, mean age 41 years, range 16 [144] to 52 [129] [133] years. There was a gender bias, with women accounting for 74% of the combined study population. The high participation of females may be attributed to three studies [136,140,142] recruiting exclusively women (100%). The baseline mean BMI for the 872 patients was 47 kg/m<sup>2</sup>, range 39.7 [141] to 60.0 [144] kg/m<sup>2</sup>.

Bariatric surgery achieved a significant decrease of weighted BMI mean of 12.7 kg/m<sup>2</sup> from 47.0 kg/m<sup>2</sup> to 34.3 kg/m<sup>2</sup> within a mean of 13.8 months follow-up period. The decrease was consistent in all the 18 studies. Pooled data from nine studies [131,138-142,144-146] demonstrated significant alterations in LV structure (LV reverse remodeling). The absolute LV mass in the nine studies reported a significant decrease in LV weighted mean of 9.3g from 52.7g at baseline (presentation) to 43.4g after 13.8 months follow-up. Systolic function measured using LVEF in 15 studies [129-138,141-143,145,146] demonstrated a slight insignificant increase in weighted mean of 2.9% from 56.5% to 59.4%. However, most of the recruited patients had preserved LV systolic function at baseline (LVEF > 45%) except three studies that recruited patients with significant LV dysfunction (LVEF = 21.7% [143] and LVEF = 23.0% [146] and LVEF = 36.2% [129]).

## Discussion

Overall, the present analysis demonstrates bariatric surgery improves both cardiac structure and function in OCM patients. These changes include statistically significant improvement in LV structure and systolic function. The clinically beneficial effects were demonstrated after significant reductions in weight (BMI reduction by 12.7 kg/m<sup>2</sup>) and echocardiography and CMR-defined reduction in LV mass (hypertrophy). Although current research on bariatric surgery in morbid obese patients with or without overt heart failure consist of small size studies, the present findings confirm and extend previous evidence

**Table 4.** Summary of Findings on Bariatric Surgery in Obesity Cardiomyopathy

1 <sup>st</sup> Author Name [Ref]	Year	Study Design	Patient Sample Size	Mean Age (yrs.)	% Female	BMI (kg/m <sup>2</sup> )		LVEF (%)		LV Mass Index (g)		Mean F/U (Months)
						Pre	Post	Pre	Post	Pre	Post	
Vest et al. [129]	2014	Retrospective	42	52	50	48.2	35.5	36.2	41.3	NS	NS	12
Kaier et al. [130]	2014	Prospective	52	44	NS	42.4	31.5	59.0	67.0	NS	NS	6
Graziani et al. [131]	2013	Prospective	51	NS	NS	47.9	35.7	55.9	59.2	55.3	49.4	24
Damiano et al. [132]	2012	Prospective	26	41	50	49.7	39.9	59.0	61.0	NS	NS	8
Koshino et al. [133]	2013	Prospective	28	52	71	51.0	37.0	62.0	62.0	NS	NS	23
Cavarretta et al. [134]	2013	Prospective	16	46	75	44.8	31.2	62.1	64.5	NS	NS	16
Luaces et al. [135]	2012	Prospective	41	40	83	47.4	30.3	65.7	65.1	NS	NS	12
Lin et al. [136]	2011	Prospective	30	44	100	44.0	29.0	61.0	61.0	NS	NS	3
Valezi et al. [137]	2011	Prospective	43	34	72	41.8	28.4	70.2	72.9	NS	NS	12
Owan et al. [138]	2011	Prospective	338	42	81	47.9	32.2	63.0	65.0	44.0	38.0	24
Hsuan et al. [139]	2010	Prospective	66	31	65	43.3	34.1	NS	NS	50.0	39.0	3
Algahim et al. [140]	2010	Prospective	15	49	100	46.7	32.0	NS	NS	50.0	37.0	24
Rider et al. [141]	2009	Prospective	30	44	80	39.7	32.2	69.0	71.0	59.0	58.0	12
Jhaveri et al. [142]	2009	Prospective	17	45	100	44.1	37.1	68.1	63.0	55.0	49.0	17
Ramani et al. [143]	2008	Retrospective	12	41	75	53.0	38.0	21.7	35.0	NS	NS	12
Ippisch et al. [144]	2008	Prospective	38	16	69	60.0	40.0	NS	NS	54.0	42.0	10
Di Bello et al. [145]	2008	Prospective	13	31	85	47.0	36.0	72.0	70.6	56.2	41.8	24
McCloskey et al. [146]	2007	Retrospective	14	NS	29	50.8	36.8	23.0	32.0	50.8	36.8	6

(NS: Not Stated; BMI: Body Mass Index; LV: Left Ventricular; LVEF: Left Ventricular Ejection Fraction; F/U: Follow-up)

of surgical weight loss interventions on LV structure and LV systolic/diastolic function. Studies using CMR imaging demonstrated increased preciseness compared to echocardiography studies but were fewer because of the ready availability and ease of use of echocardiography.

The present results reveal that bariatric surgery for morbid obese patients with cardiomyopathy or overt heart failure are feasible, safe and efficacious. The present findings are consistent and extend those of previous meta-analyses reporting that bariatric surgery achieves significant weight loss in morbid obese patients [147,148]. Another meta-analysis study [149] revealed that bariatric surgery compared with non-surgical weight loss interventions (dietary and pharmacological) achieves a greater weight loss and higher remission rates of Type 2 Diabetes and metabolic syndrome, which are significant risk factors for developing OCM. However, the results on superiority of surgical to non-surgical weight loss interventions were limited to two years follow-up and depended on outcomes of a small number of studies (11 studies) [149]. With increased experience in bariatric surgery, American Society for Bariatric Surgery and the American Society for Bariatric Surgery Foundation report mortality rates as low as 0.5% demonstrating the safety of bariatric surgical procedures [150].

Further, consistent with a review of bariatric surgery in OCM patients, Iyengar and Leier [151] report bariatric surgery causes a reversal in LV remodeling and improves LV function. LV remodeling contributes to the development of LV hypertrophy and LV diastolic dysfunction, which may result in biventricular enlargement and systolic dysfunction. The study also reports bariatric surgery causes a reduction in LV mass and wall stress, improves both diastolic and systolic function and depresses clinical manifestation of heart failure [151]. Further, while the benefits of bariatric surgery on BMI plateaus after sometimes, the effect on metabolism and LV mass remain sustained for longer suggesting it may be mediated by neurohumoral factors. In addition, declining LV mass likely contributes to improved long-term survival of morbid obese patients after bariatric surgery weight loss [148,149]. Moreover, McCloskey et al. [146] report that in addition to the protective effect of bariatric surgery on cardiac morphology and function, it provides a bridge to heart transplantation to patients initially contraindicated due to their morbid obesity.

## Conclusion

Morbid obesity is a leading cause of lifestyle related diseases. Its extreme consequence is obesity cardiomyopathy (OCM), a form of non-ischemic dilated cardiomyopathy occurring in the setting of lipid accumulation in the cardiomyocytes causing alterations in cardiac structure and function not explained by structural heart diseases or systemic hypertension. Although recognized as a disease entity, controversy persists as to whether isolated obesity can cause cardiomyopathy. It is difficult to isolate the effect of obesity on cardiac function from that of other concomitant and synergistic comorbidities. Pathophysiologic mechanisms for the development of OCM include changes in cardiac hemodynamics, myocardial remodeling, ventricular dysfunction; metabolic disturbances; myocardial lipotoxicity, neurohumoral derangement; and small vessel disease. The presence of comorbidities such as hypertension, diabetes mellitus, dyslipidemia, insulin resistance, metabolic syndrome, obstructive sleep apnea and kidney diseases may accelerate or potentiate the development of OCM in morbid obese patients. Clinical presentation of OCM mimics that of other forms of cardiomyopathy and heart failure – dyspnea, orthopnea, paroxysmal nocturnal dyspnea, wheezing, exercise intolerance and lower extremity edema. The mainstay of diagnosis is non-invasive

imaging using echocardiography and speckle tracking to characterize LV structural and functional changes. The assessment of cardiac biomarkers BNP and NT-Pro BNP provide complementary diagnostic clues but are non-specific to OCM. Finally, the cornerstone of clinical management of OCM is weight loss using exercise interventions or bariatric surgery. For OCM patients with significant LV systolic dysfunction and overt heart failure, management consists treatment of heart failure using conventional heart failure therapy.

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