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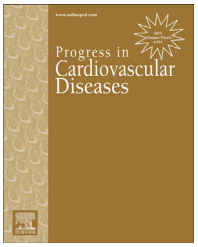

Impact of Obesity and Weight Loss on Cardiac Performance and Morphology in Adults

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ABSTRACT

Obesity, particularly severe obesity is capable of producing hemodynamic alterations that predispose to changes in cardiac morphology and ventricular function. These include increased cardiac output, left ventricular hypertrophy and diastolic and systolic dysfunction of both ventricles. Facilitated by co-morbidities such as hypertension, the sleep apnea/obesity hypoventilation syndrome, and possibly certain neurohormonal and metabolic alterations, these abnormalities may predispose to left and right heart failure, a disorder known as obesity cardiomyopathy.

That obesity is related to abnormal cardiac performance and morphology has been known since Victorian times.[1] Senac was the first to describe excess fat deposition involving the heart of obese persons in 1783.[1] In 1806, Corvisart described adipose tissue surrounding the heart and suggested that in obese people the heart was "oppressed by enveloping fat that sometimes caused sudden death".[1] In 1819, Laennec was the first to establish the fatty heart as an entity, distinguishing between "fatty surcharge on the surface of the heart" and "fatty degeneration in which muscular substance was transformed into fat exhibiting pallor like dead leaves".[1] The latter finding was subsequently found by Quain, Gallavardin and others to be attributable to coronary artery disease (CAD) or to cachexia, anoxemia or other conditions such as severe anemia.[1] In 1847, William Harvey described the autopsy findings of a severely-obese man named Thomas Parr and found that the heart was "large, thick and fibrous, with a considerable quantity of adhering fat, both in its circumference and over its septum".[1] Harvey stated "shortly before his death I had observed that his face was livid and he suffered from difficult breathing and orthopnea".[1] This is thought to be the first clinical description of obesity cardiomyopathy. Smith and Willius published a study of post-mortem cardiac findings of 135 obese adults in 1933.[2] In this study, heart weight was increased in proportion to the degree of obesity up to 105 kg. Heart weight was greater than that predicated for normal weight and height in both men and women and was far greater than expected in extremely obese persons. Almost all subjects had excess epicardial fat, whereas myocardial fat content was normal in most individuals. During the 1950's several case reports and small series described what came to be known as the "Pickwickian syndrome" in severely obese patients.[1] This condition was characterized by biventricular failure, sleep apnea and hypoventilation with marked hypoxia, hypercapnia and polycythemia. It received its informal name from Dickens' description of the "fat boy Joe" in his novel Pickwick Papers.[1]

Beginning in the late 1950s and continuing until the present scientists have attempted to clarify the relation between obesity and cardiac performance and morphology.[1] Such efforts have characterized central and peripheral hemodynamics, cardiac chamber size, left ventricular (LV) wall thickness and mass, and diastolic and systolic function of both ventricles in obese subjects.[1] More recent studies, primarily involving

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Abbreviations and Acronyms

BMI = body mass index

BP = blood pressure

CAD = coronary artery disease

CBV = central blood volume

CO = cardiac output

HF = heart failure

HTN = systemic hypertension

LA = left atrial or left atrium

LV = left ventricular or left ventricle

PVR = peripheral vascular resistance

RAAS = renin–angiotensin–aldosterone system

RV = right ventricular or right ventricle

TG = triglyceride(s)

animal models, have identified a variety of neurohormonal and metabolic abnormalities that may contribute to altered cardiac structure and function in obesity. The purpose of this review is to describe central and peripheral hemodynamic changes associated with obesity, to discuss their impact on cardiac morphology and ventricular function, to describe neurohormonal and metabolic abnormalities that may influence cardiac performance and morphology, and to describe the effects of weight loss on these alterations in adults.

Hemodynamic alterations associated with obesity

Studies by Alexander and others demonstrated that excess adipose accumulation is associated with increased total and central blood volume (CBV) and increased (CO).[3–10] The rise in CO was originally attributed to increased fat mass, but more recent studies suggest that in class I and class II obesity it is predominantly attributable to an increase in fat-free mass.[3–10] Obesity is associated with a reduction in peripheral vascular resistance (PVR) in normotensive obese persons which facilitates the increase in CO.[3–5,8,9] In severely- obese patients, it is not uncommon to observe CO values as high as 10 L/min.[3–5] As heart rate changes little with obesity, the rise in CO is attributable to an increase in LV stroke volume and is associated with increased LV stroke work.[3–5] In the resting state there is a direct positive (virtually linear) correlation between relative body weight and CBV, CO, LV stroke volume and LV stroke work.[3–5] Arteriovenous oxygen difference is usually widened in obesity.[3,4] This is attributable to lower oxygen extraction by adipose tissue than by other organs.[3,4] Thus, blood flow per unit body weight is reduced, particularly in severe obesity.[3,4] Whether the central hemodynamics of patients with central obesity differ from those of subjects with peripheral obesity is uncertain. Early studies suggested that CO was somewhat lower and PVR was slightly higher in patients with central obesity than in those with peripheral obesity.[3–5] Regardless of the distribution of fat mass, it is clear that severe obesity is a high CO state associated with increased CBV and facilitated by a reduction in PVR.

In class II and III obese persons the increase in CBV augments venous return to the right heart and increases LV preload.[3–10] Thus, LV end-diastolic pressure and pulmonary capillary wedge pressure are frequently elevated.[3–10] This contributes to elevated pulmonary artery pressure, right ventricular (RV) end-diastolic pressure and right atrial pressure.[3–10] Hypoxia-induced vasoconstriction and remodeling of small pulmonary arteries may contribute to elevation of right heart pressures and may produce an increase in pulmonary vascular resistance indicating a diastolic pressure gradient across the pulmonary vascular bed.[3–10] In addition to reporting elevated right heart pressures in class II and III obese patients, DiDivitiis et al. reported a decrease in LV Vmax in such patients.[7]

Exercise produces an interesting dichotomy in central hemodynamics.[3,4] At lower workloads (2–3 times the resting level) the increase in CO and its relation with oxygen consumption are appropriate.[3,4] However, at workloads ≥ five times the resting level CO decreases to a low-normal level.[3,4] Increased CO in such subjects is associated with increased LV end-diastolic pressure and pulmonary capillary wedge pressure, and frequently with elevation of right heart pressures.[3,4] In an exercise study of 18 class III obese patients, Kaltman and Goldring reported a 20% increase in CBV, an increase in LV end-diastolic pressure from 21–31 mmHg and a 57% increase in LV dP/dt.[10] Backman and Freyschuss also reported a substantial increase LV end-diastolic pressure with exercise. LV filling pressure rises disproportionately to the increase in stroke work with exercise indicating reduced LV compliance.[6]

Little information exists concerning peripheral hemodynamics in obese subjects. Cerebral blood flow detected using older techniques was reported to be low-normal or mildly reduced.[3] Splanchnic blood flow was slightly higher than that predicted for normal weight. Renal blood flow was considered to be low-normal. Adipose tissue averages blood flow 2–3 ml/min less than that of other parenchymal organs. In total, blood flow attributable to adipose tissue and parenychymal organs, cannot completely account for the increase in observed CO.[3] As previously noted, recent studies indicate that in class I and II obesity, the increase in CO is attributable as much or more to fat-free mass (presumably muscle mass) as to fat mass.[3] Whether this relationship holds true in class III obesity is uncertain.

Cardiac morphology in obesity

Post-mortem studies

The first systematic study to characterize cardiac morphology in obesity was that of Smith and Willius published in 1933.[2] Post-mortem findings were analyzed in 135 patients who were 13%–170% overweight. This study included four severely obese patients who succumbed to heart failure (HF). There was a linear increase in heart weight with increasing body weight up to 105 kg and to a lesser extent above this threshold. The average heart weight was 444 g in men and 345 g in women. Both of these values were greatly in excess of that predicted for normal body weight. Excessive epicardial fat was observed in 95% of patients. Isolated instances of penetration of fronds of epicardial fat into RV myocardium were noted. No such penetration into LV myocardium was