RESEARCH PAPER | Medical science | Volume : 6 | Issue : 6 | June 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

Obesity and Associated Cardiovascular Morbidity – A Study in a Tertiary Care Hospital of North India

KEYWORDS: Systolic function; Diastolic function; Echocardiography, Body mass index, LV mass

Dr. Ajay Kumar
Asso. Professor, Department of Medicine, Teerthanker Mahaveer Medical College & Research Centre Moradabad, UP-244001

Dr. B. Kumar
Professor, Department of Medicine, Teerthanker Mahaveer Medical College & Research Centre Moradabad, UP-244001

Dr. Vishvanayak
223B, pocket-A, Mayur Vihar Ph-2, New Delhi- 91

Dr. Sanjeet Kumar Pandit
Asst. Professor, Department of Medicine, Teerthanker Mahaveer Medical College & Research Centre Moradabad, UP-244001

ABSTRACT *Obesity is an independent factor implicated in left ventricular (LV) hypertrophy and increased left ventricular mass. Early detection of increased LV mass in obese patients has prognostic and therapeutic implications. Obesity and high BMI is associated with increased cardiovascular morbidity and mortality. A direct effect of isolated obesity on cardiac function is not well established. The study was designed to determine the direct effect of various grades of isolated obesity on echocardiographic indices of systolic and diastolic left ventricular function. Two Hundred obese and 25 normal weight, personnel without any other pathological condition were studied. Group I (n=25) consisted of subjects with normal weight and body mass index (BMI <25kg/m2), Group II (n=100) of overweight subjects (BMI 25-29.9 kg/m2) and Group III (n=100) of obese subjects (BMI >30 kg/m2). Echocardiographic indices of systolic and diastolic function were obtained and dysfunction was assumed when at least two values differed by ≥ 2 SD from the normal weight group. Ejection fraction, fractional shortening were increased (p<0.05) in Group II and III. Left ventricular dimensions were increased (p< 0.001) but relative wall thickness was unchanged. Systolic dysfunction was not observed in any of the obese patients. The mitral valve pressure half time (p< 0.01), left atrial diameter (p < 0.01) and the deceleration time were increased (p< 0.01) in obese subjects, while other diastolic variables were unchanged. No difference were found between obesity subgroups. Subclinical diastolic dysfunction was more prevalent among obese subjects. BMI correlated significantly with indices of left ventricular systolic and diastolic function.*

INTRODUCTION

Obesity is associated with cardiomyopathy resulting in heart failure in severe obesity cases. This has been attributed to chronic volume overload characterized by left ventricular (LV) dilation, increased left ventricular wall stress and compensatory (eccentric) left ventricular hypertrophy. Impairment of cardiac function has been reported to correlate with degree of obesity i.e. body mass index (BMI) and duration of obesity. Abnormal diastolic function is the most important component of the impaired cardiac function, while systolic dysfunction is not so common. Obesity has also been linked to a spectrum of minor reversible cardiovascular changes, ranging from a hyper dynamic circulation to subclinical cardiac morphological changes in the form of greater aortic root and left atrial enlargement. Abnormal cardiac functions are noted in individuals even with slight or mild obesity. The abnormal cardiac function in association with obesity may reflect the role of co-morbidities like hypertension, diabetes, coronary artery disease and obstructive sleep apnea. However individuals with isolated obesity have altered loading of the ventricles due to increased stroke volume and cardiac output leading to cardiac dysfunction. Echocardiography has consistently been the most accurate non-invasive method of assessing the left ventricular function. The relation between obesity (assessed by BMI) and alterations in cardiac function, as well as the impact of different grades of obesity on cardiac structure and function is less well documented. The aim of this study was to determine the direct effect of different grades of isolated obesity on echocardiographic indices of systolic and diastolic left ventricular function. Obese and overweight persons are at increased risk of heart diseases and constitute an important public health problem because of associated increased risk of cardiovascular (CV) morbidity and mortality. A world health organization (WHO) consultation described obesity as a chronic disease that is prevalent in developed and developing countries. Body mass index (BMI) is recognized and widely used for identifying overweight or obesity. The cut-off points of BMI for Asians were: in overweight BMI >25.0 kg/m2 and in obesity BMI >30.0kg/m. BMI was calculated by the formula: BMI=Wt. (kg)/Ht (m^2). Obesity also Influences blood pressure (BP) and left ventricular hypertrophy (LVH). The degree of increased myocardial muscle mass (LVH) is also a strong and independent risk factor for cardiac morbidity and mortality.

MATERIAL AND METHODS

Healthy non-diabetic, normotensive male reporting for medical examination constituted the study population. Informed consent was obtained from all the volunteers. After taking medical history, a detailed physical examination was conducted for all participants which included recording of height and weight. BMI was calculated by dividing the bodyweight (in kilograms) by the square of height (in meters). A 12-lead electrocardiogram (ECG) was obtained. Hematological and biochemical variables were determined from fasting blood samples. This included glucose, total cholesterol, triglycerides, high density lipoprotein cholesterol, low density lipoprotein cholesterol, urea, uric acid and full blood count. Obesity was defined as a BMI of ≥ 30kg/m^2, with clear evidence on physical examination of

Volume : 6 | Issue : 6 | June 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

excessive subcutaneous adipose tissue. The participants in the study were classified into three groups based on the BMI: a normal weight (control) group had a BMI of < 25 kg/m^2, an overweight group was classified as a BMI between 25–29.9 kg/m^2 , and an obese group was classified as BMI ≥ 30 kg/m^2. Patients suffering from hypertension, diabetes mellitus, coronary artery disease or dyslipidemia were excluded. Patients with normal ECG without any chronic or acute disease, not on medication that could affect heart and those not involved in competitive sports were included. A cross sectional echocardiogram was obtained on all participants (Sonos 5500, Hewlett-Packard, Palo Alto, California, USA). Echocardiograms included cross sectional, M mode and Doppler studies. The following indices of cardiac function were evaluated: Left ventricular systolic function : Left ventricular end diastolic (EDD), end systolic diameter (ESD) and fractional shortening (FS) were obtained in the parasternal long axis views using M mode. Pre ejection period (PEP) and ejection period (EP) was also recorded in all patients. The relative wall thickness (RWT) was calculated from the posterior wall thickness (PWT) and the EDD, as (2 x PWT)/ EDD. Left ventricular diastolic function : Pulsed doppler measurements were obtained in the apical four chamber view. The doppler beam was aligned perpendicular to the plane of the mitral annulus and a 5 mm pulsed wave doppler sample volume was placed between the tips of the mitral leaflets during diastole. The following variables were calculated: maximum velocity of passive mitral filling (E), maximum velocity of active mitral filling (A), ratio of passive to active velocity (E/A), mitral valve pressure half time (MVPHT), deceleration time (DT) and isovolumic relaxation time (IVRT). The left atrial diameter was measured using M mode in the parasternal long axis view. A difference of more than 2 SD from the mean values of the normal weight group, was used to estimate the prevalence of cardiac functional abnormalities. Subclinical dysfunction was assumed when two or more indices of altered diastolic or systolic function were present. Descriptive statistics were done on each of the variables to obtain the frequency distributions. Quantitative variables were described as mean. Comparisons between the obese group and the normal weight group were analyzed by t tests. Analysis of variance (one way ANOVA) was used to compare obese subgroups. Correlations between clinical variables and left ventricular function were determined by linear regression analysis. Probability values of p < 0.05 were considered significant. Patients with current coronary artery disease, current/prior angina, or myocardial infarction, current/prior history of arrhythmia, cardiovascular co-morbidity (prior cerebrovascular accidents and/or peripheral vascular disease), current therapy with vasoactive drugs, statins or fibrates, active smoking, creatinine >2 mg/dl, presence of neoplasia and/or systemic disease, and suboptimal echocardiographic window were also excluded from the study. Participants provided information on age, family history, personal habits (alcohol intake, tobacco consumption, type and level of physical exercise, drugs ingestion). Routine measurements of blood pressure, height in centimetres (cm), and weight in kilograms (kg) were recorded.

Table 1

Baseline characteristic of study population				
	Group I	Group II	Group III	
	Normal (n=25)	Over weight (n=100)	Obese (n=100)	p value (overall)
Age (years)	35.3 ± 10.0	35.3 ± 10.5	35.28 ± 9.5	NS
Weight (kg)	69.3 ± 7.3	78.1 ± 10.1[a]	93.5 ± 13.5[b,c]	< 0.001
Height (m)	1.62 ± 0.07	1.64 ± 0.07	1.62 ± 0.05	NS
BMI (kg/m^2)	22.9 ± 1.2	27.1 ± 1.2[a]	32.2 ± 2.6[b,c]	< 0.001
BMI (range)	16.7 - 24.7	25.8 - 29.9	30.1 - 35.9	-
HR (beats/ minute)	78 ± 10	75 ± 9	80 ± 9	NS

a: Group I vs Group II, b: Group I vs Group III, c: Group II vs Group III, *p < 0.05; for differences between subgroups BMI: body mass index, HR: heart rate, NS: non significant

Table 2

Indices of left ventricular systolic function						
	Group I		Group II		Group III	
	Normal (n=25)		Over weight (n=100)		Obese (n=100)	p value (overall)
EDD (cm)	43.4 ± 5.61		45.7 ± 4.5 [a]		51.1 ± 3.5 [b,c]	< 0.001
ESD (cm)	25.2 ± 5.1		27.9 ± 3.7 [a]		28.1 ± 3.8 [b]	0.002
FS (%)	40.8 ± 18.1		38.6 ± 7.7		44.9 ± 6.3 [b,c]	< 0.001
EF (%)	65.7± 12.8		73.4± 9.1		74.6 ± 9.8 [b]	0.001
PEP/EP	0.31 ± 0.07		0.35 ± 0.07		0.38 ± 0.08	0.58
RWT	0.38 ± 0.05		0.39 ± 0.04		0.40 ± 0.08	0.60

a: Group I vs Group II, b: Group I vs Group III, c: Group II vs Group III, *p < 0.05; for differences between subgroups BMI: body mass index, EDD: end diastolic diameter; ESD: end systolic diameter; FS: fractional shortening; EF: ejection fraction; EP: ejection period;

PEP: pre-ejection period; RWT: relative wall thickness.

Table 3

Indices of left ventricular diastolic function						
	Normal (n=25)		Over weight (n=100)		Obese (n=100)	p value (overall)
E (cm/s)	77.6 ± 13.9		78.0 ± 15.3		79 ± 16.1	0.92
A (cm/s)	52.6 ± 9.93		56.4 ± 10.2		58.0 ± 12.5	0.58
E/A	1.51 ± 0.3		1.43 ± 0.4		1.35 ± 0.3	0.15
DT (ms)	173.6 ± 13.9		191.0 ± 19.4 [a]		202.2 ± 25.3 [b,c]	< 0.01
MVPHT (ms)	63.7 ± 7.8		63.2 ± 11.0		70.0 ± 14.8 [b,c]	< 0.01
LAD (cm)	2.9 ± 0.4		3.3 ± 0.4 [a]		3.6 ± 0.42 [b,c]	< 0.01

a: Group I vs Group II, b: Group I vs Group III, c: Group II vs Group III, *p < 0.05; for differences between subgroups, E: maximum velocity of passive mitral filling; A: maximum velocity of active mitral filling; DT: deceleration time; MVPHT: mitral valve pressure half-time; LAD: left atrial diameter

RESULTS

We studied 200 over weight and obese men with mean age of 35.3 ± 10.6years, (range 26–52 years) and 25 normal weight controls with mean age of 35.3 ± 10.2 years (range 25–52 years). The characteristics of the patients

Volume : 6 | Issue : 6 | June 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

studied are presented in Table 1. Only weight and BMI were significantly different within the obese subgroups, with respect to the normal weight group. The measured indices of left ventricular systolic function are presented in Table 2. A left ventricular diameter was significantly increased in obese personnel, though relative wall thickness was similar to control group. The contractility indices (ejection fraction and fractional shortening) were significantly higher in the obese personnel than in the controls. In the prevalence analysis, no obese patient met the criteria for systolic dysfunction. The measured indices of left ventricular diastolic function are presented in Table 3. In obese subjects, MVPHT, left atrial diameter and deceleration time were significantly increased. Subgroup analysis showed significant differences among the over weight and obese subgroups for these variables. The values of E, A, and E/A ratio, were similar in all the three subgroups. In the prevalence assessment, subclinical diastolic dysfunction was significantly more prevalent among obese patients (p = 0.002) than in the control group. It was found in seven (20.5%) individuals in the over weight group and eight (47%) individuals in the obese group. The correlations between clinical variables and left ventricular function are shown in Table 4. Among the indices of systolic function, BMI correlated positively with %FS and PEP/EP while EP correlated positively with age. Among the indices of diastolic function, BMI correlated positively with MVPHT, left atrial diameter and deceleration time. Similarly, age correlated positively with left atrial diameter and negatively with E and E/A. Echocardiograms of 200 patients to assess left ventricular mass was obtained. Mean age of the patients was 42.42±6.10 years [range 24–50], while BMI was in the range of 19–45 with mean of 28.42±5.54. LV Mass was in the range of 76.198 with mean of 136.05±29.118. There were 59 (59%) male patients and 41 (41%) female patients. * Linear correlation coefficient r was used to examine the relation between LVM measurements and BMI. The value of r=0.6. Our data showed significant correlation between LVM and BMI with *p* value of (*p*=0.00).

Table 4
Correlations between the clinical variables and left ventricular function

Variable	BMI	Age
LV systolic function		
EF	0.23	- 0.05
FS	0.26*	0.00
PEP	0.25	0.00
E P	- 0.14	0.25*
PEP/EP	0.30*	- 0.14
LV diastolic function		
E	0.06	- 0.28*
A	0.02	0.20
E/A	0.01	- 0.38**
D T	0.32**	0.14
MVPHT	0.27**	- 0.13
IVRT	- 0.19	0.13
LAD	0.42**	0.34*

*p < 0.05; **p < 0.01; ***p < 0.001, EF: ejection fraction; FS: fractional shortening; PEP: pre-ejection period; EP: ejection period; E: maximum velocity of passive mitral filling; A: maximum velocity of active mitral filling; DT: deceleration time; MVPHT: mitral valve pressure half-time; IVRT: isovolumetric relaxation time; LAD: left atrial diameter.

DISSCUSSION

Overweight and obesity are the most common nutritional disorders influences left ventricular muscle thickness structure, function and this has heightened our concern given the strong association between obesity and cardiovascular morbidity . In the present study we have made an attempt to assess the effect of different grades of obesity on the left ventricular function. No patient with isolated obesity presented with subclinical systolic dysfunction. On the contrary, there was a significant increase in the ejection fraction and in the percentage of fractional shortening, but this only reached significance in obesity groups compared with the controls. The ejection fraction is a reliable index but is relatively insensitive to left ventricular contractile function, so its value may be maintained within normal limits even when there is substantial compensatory modification of the contractile state. However, the normality of the ejection fraction was in accordance with the normal relative wall thickness in our obese groups, which indicates that systolic function was preserved. These findings imply that in the groups with lesser degrees of obesity there is a compensatoryincrease in systolic function, which has not yet reached the stage of cardiac deterioration. Most echocardiographic studies using measurements of the ejection phases to evaluate systolic function in obese subjects have shown normal results. Left ventricular systolic function is affected late in the course of obesity and more so in patients with considerabledegree of obesity. Alterations in the left ventricular diastolic function were more frequent with increasing obesity. The MVPHT was found to be significantly prolonged in the obese personnel and correlated directly with the grade of obesity. Similar finding has been noted in other studies and suggests an abnormal relaxation of the left ventricle and there is increased dependency on left atrial contraction for normal filling. Similarly, the deceleration time was significantly prolonged in the obese subjects and correlated inversely with BMI. IVRT was similar in obese subjects and in controls, and did correlate with BMI, this is in contrast to previously published data in which this variable has been found to be prolonged in both moderate and gross obesity. The E,A and E/A values did not differ across the spectrum of obesity. The associations of these indices with obesity reported in previous studies have been variable. Some studies have reported a decrease in the maximum velocity of passive mitral filling (E) in obese individuals, while others have found no significant change in it. However in both these studies E/A ratio was decreased, in the former due to decrease in the E velocity and in later study due to increase in the active mitral filling (A) velocity with unchanged E velocity. Doppler method is a good way of assessing diastolic function but when volume overload is present, as seen in obesity, normal values may result, as the increase in left atrial pressure caused by intravascular volume can mask the alterations observed in the early phases of abnormal diastolic relaxation. In contrast to systolic function, we found that alterations in diastolic function were common, not only in the severely obese personnel but also in overweight subjects. These alterations in diastolic function correlated strongly with BMI. In obesity, cardiac adaptation to chronic volume overload is associated with eccentric hypertrophy and abnormalities of diastolic function from the initial stages, indicating that structural changes and an obesity cardiomyopathy are present in all obese individuals. In the present study LV mass and LV geometry was not assessed hence it is difficult to say whether the alteration of the diastolic function is due to morphological change or represents a mere functional change. A greater awareness of weight control is required to induce beneficial changes in cardiac

Volume : 6 | Issue : 6 | June 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

function. The alterations that occur in obesity can be reversed easily and quickly by weight loss, to the long term benefit of the patient. Obesity was measured using only BMI, and no measurements of body fat distribution were made. In view of higher prevalence of abdominal obesity in our country correlating the echocardiographic variables with anthropometric markers of abdominal obesity could have provided additional information. Conventional measures of LV function assessment (mitral inflow velocities, isovolumetric ventricular relaxation times and ejection fraction) used in the present study are load dependent and hence may show inconsistent changes. Newer echocardiography technique such as tissue doppler which is less load dependent may be better tool for assessing LV function in obese individuals . Overweight and obesity influences left ventricular muscle thickness, structure and function. WHO Western Pacific Region in 2000 recommended lower cut-off for overweight (Body Mass Index-BMI ≥23.0) and obesity (Body Mass Index-BMI ≥25.0) in Asians. However, studies considering the new recommendations of BMI are lacking. The finding that BMI is the driving factor behind increased LV mass was not totally unexpected but has never been specifically tested before, especially in the context of non-diabetic and normotensive patients and in patients without co-morbidities. Left ventricular mass plays an essential role in determination of left ventricular hypertrophy (LVH). The degree of hypertrophy indicates the severity of volume overload of the systemic circulation. Electrocardiogram is relatively non-sensitive and infrequently predicts LVH, especially in obese persons due to decrease in surface voltage. M-mode echocardiography provides an accurate assessment of LVM that is more sensitive and specific than the electrocardiogram for detecting LVH which is an important prognostic finding to evaluate the high risk of subsequent cardiovascular morbidity and mortality.

CONCLUSION

All patients with isolated obesity have subclinical left ventricular diastolic dysfunction, which correlates with BMI and is associated with an increased in systolic function in the early stages of obesity. BMI is significantly correlated with left ventricular mass, even after controlling for confounding variables as diabetes mellitus, renal failure, blood pressure and other co-morbidities mentioned earlier. The increase in left ventricular mass associated with increasing BMI reflects increase in both left ventricular wall thickness and left ventricular internal dimension.

REFRENCES

1. Hirayama H, Suganon M, Abe N, Yonemechi H, Makino N. Determination of left ventriculation mass by echocardiography in normotensive diabetic patients. Jpn Circ J 2000;64:921–4.
2. Hubbard VS. Defining overweight and obesity: what are the issues? Am J Clil Nutr 2000;72:1067–8.
3. WHO Expert Consultation. Appropriate body mass index for Asian population and its implication for policy and intervention strategies. Lancet 2004;363:157–63.
4. Okosun IS, Prewitt TE, Cooper RS. Abdominal obesity in the United States: prevalence and attributable risk of hypertension. J Hum Hypert 1999;13:425–30.
5. Celentano A, Palmieri V, Esposito ND, Pietropaolo I, Crivaro M, Mureddu GF *et al.* Inappropriate left ventricular mass in normotensive and hypertensive patients. Am J Cardiol 2001;87:361–3.
6. Lorber R, Gidding SS, Daviglus ML, Colangelo LA, Liu K, Gardin JM. Influence of systolic blood pressure and body mass index on left ventricular structure in healthy African- American and white young adults. J Am Coll Cardiol 2003;41:955–60.
7. Devereux RB, Alonoso DR, Lutas EM, Gottlieb GJ, Combo E, Sachs I, *et al.* Echocardiographic assessment of left ventricular hypertrophy. Am J Cardiol 1986;57:450–8.
8. Scott D. Solomon D, Bulwer, Janardhanan R. Echocardiographic assessment of left ventricular Systolic function. In:Scott D, editor. Essential Echocardiography. Totowa, N.J: Humana press; 2007.101–2.
9. Hashemi M, Sartaj R. Left ventricular mass in diabetic patients. J Res Med Sci 2004;9(4):182–5.
10. Brian P. Griffin, Eric J. Nonlipid Cardiovascular Risk Factors. In: Grasso AW, editor. Manual of Cardiovascular medicine. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2009.p. 589–90.
11. Badeer HS. Biological significance of cardiac hypertrophy. Am J Cardiol 1964;14:133.
12. Sasayama S, Ross J Jr, Franklin D, Bloor CM, Bishop S, Dilley RB. Adaptations of the left ventricle to chronic pressure overload. Circ Res 1976;38:172–8.
13. AJ. Hypertrophy, hyperplasia and structural dilatation of the human heart. Adv Cardiol 1976;18:1–13.
14. Kannel WB, Gordon T, Castelli WP, Margolis JR. Electrocardiographic left ventricular hypertrophy and risk coronary heart disease. The Framingham Study. Ann Intern Med 1970;72:813–22.
15. Reichek N, Devereux RB. Left ventricular hypertrophy: relationship of anatomic echocardiographic and electrocardio-graphic findings. Circulation 1981;63:1391–8.
16. Rackley CE, Dodge HT, Cable YD Jr, Hay RE. A method for determining left ventricular mass in man. Circulation 1964;24:666–71.
17. Kathrotia RG, Paralikar SJ Rao PV Oommen ER. Impact of different grades of body mass index on left ventricular structure and function. Indian J Physiol Pharmacol 2010;54(2):149–56.
18. Rodrigues SL, Angelo LC, Pereira AC, Krieger JE, Mill JG. Determinants of left ventricular mass and presence of metabolic risk factors in normotensive individuals. Int J Cardiol 2009;135:323–30.
19. Sivanandam S, Sinaiko AR, Jacobs DR Jr, Steffen L, Moran A, Steinberger J. Relation of increase in adiposity to increase in left ventricular mass from childhood to young adulthood. Am J Cardiol 2006;98:411–5.