ORIGINAL ARTICLE

PATTERN AND SEVERITY OF DIASTOLIC DYSFUNCTION IN OBESE HYPERTENSIVE PATIENTS IN RURAL POPULATION IN SOUTH INDIA

Prashant S. Sidmal¹, Mallikarjun H. P², K. C. Shekarappa³

HOW TO CITE THIS ARTICLE:

Prashant S. Sidmal, Mallikarjun H. P, K. C. Shekarappa. "Pattern and Severity of Diastolic Dysfunction in Obese Hypertensive Patients in Rural Population in South India". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 67, August 20; Page: 11600-11615, DOI: 10.14260/jemds/2015/1675

ABSTRACT: OBJECTIVES: To assess the effect of obesity and hypertension on left ventricular (LV) diastolic function. **BACKGROUND:** Obese and overweight individuals are at increased risk of heart failure. LV diastolic dysfunction is an asymptomatic condition associated with future heart failure. It is unclear whether obesity and overweight are independently associated with LV diastolic dysfunction. Obesity is associated with heart failure, but an effect of weight, independent of comorbidities, on cardiac structure and function is not well established. Severe prolonged obesity in adults results in increased plasma volume, eccentric LV hypertrophy, and diastolic dysfunction. Obese people are at increased risk for the development of heart failure. **METHODS:** A total of eighty subjects of either gender, coming from rural background admitted in a tertiary care hospital in South India, were enrolled in this cross sectional case control study. Patients were enrolled from March 2014 to May 2015. The study sample was divided into three groups: normal weight [body mass index (BMI) <25.0], overweight (BMI 25.0-29.9) and obese (BMI ≥30). Diastolic dysfunction in each category of patients was assessed with standard methods. **RESULTS:** BMI was independently associated with higher E, A, and E/E', an indicator of LV filling pressure (all $p \leq 0.01$). Overweight and obese had lower E' (both $p < 0.01$) and higher E/E' (both $p < 0.01$) than normal weight participants. E/A was lower in obese than normal weight subjects ($p < 0.01$). The risk of diastolic dysfunction was significantly higher in overweight and obese compared to normal weight individuals. Hypertensive patients were found to have worse diastolic function as compared to those having normal blood pressure. **CONCLUSIONS:** Increased BMI was associated with worse LV diastolic function. The increased risk of LV diastolic dysfunction in both overweight and obese individuals may partially account for the increased risk of heart failure associated with both conditions. Overweight subjects without overt heart disease have subclinical changes of LV structure and function. These abnormalities in LV function may have important implications for explaining the myocardial dysfunction that is associated with increased cardiovascular morbidity and mortality caused by obesity. Hypertension adds to the worsening of diastolic dysfunction.

KEYWORDS: Obesity; Overweight; Diastolic dysfunction; Echocardiography; Risk.

INTRODUCTION: The prevalence of obesity is steadily increasing worldwide, and constitutes a major health issue because of its association with morbidity, mortality and cardiovascular diseases.⁽¹⁻³⁾ Obesity is an independent predictor of incident heart failure in the general population, and evidence exists that overweight also carries an increased risk of heart failure, which is intermediate between that of obese and lean individuals.^(4,5) An increase in body size, besides being associated with cardiovascular risk factors such as hypertension, diabetes and hyperlipidemia, directly affects cardiac structure and function. The excess in body fat determines an increase in both preload and afterload due to a hyperdynamic circulation, chronic volume overload and increase in peripheral

ORIGINAL ARTICLE

resistance.^(6,7) In addition, it has been demonstrated that increased adiposity enhances the effect of blood pressure on LV mass growth.⁽⁸⁾ As a result, left ventricular (LV) dilation and increased LV mass are frequent findings in individuals with increased body weight, with both eccentric and concentric LV geometric patterns described in these conditions.⁽⁹⁻¹¹⁾

LV diastolic dysfunction is a condition that reflects an impairment of the filling properties of the LV that has been demonstrated to be a predictor of future development of heart failure in population settings.⁽¹²⁻¹⁵⁾ LV diastolic dysfunction might therefore represent one of the pathophysiological links between an increased body weight and the future occurrence of heart failure. Cardiovascular risk factors and cardiac structural changes associated with obesity/overweight are also major determinants of LV diastolic function.^(16,17) Whether an increased body weight is associated with an impairment of LV diastolic mechanics, independent of associated risk factors, has not been fully established.

The prevalence of obesity (A body mass index [BMI]>30) is increasing in both the developed and developing worlds.⁽¹⁸⁾ Obesity has been associated with heart failure^(19,20) and individuals with severe obesity have long been recognized to have a form of cardiomyopathy attributed to chronic volume overload, characterized by left ventricular (LV) dilation, increased left ventricular wall stress, and compensatory (eccentric) left ventricular hypertrophy.⁽²¹⁾ Impairment of cardiac function has been reported to correlate with BMI and duration of obesity,^(22,23) with most studies reporting abnormal diastolic function^(24,25) without consistent association with systolic dysfunction. Indeed, obesity has been linked to a spectrum of more minor cardiovascular changes, ranging from a hyperdynamic circulation to subclinical cardiac structural changes. These early manifestations may be important, because treatment to reverse the process is most likely to be effective earlier in the disease.

Obesity affects more than 43 million Americans, and the incidence has been increasing markedly in both men and women in recent years.⁽²⁶⁾ Obesity is an independent risk factor for the development of heart failure (HF), even after accounting for other co-morbid conditions that cluster with it, such as diabetes and hypertension. Obese and overweight women are at higher risk than obese and overweight men for developing HF.⁽²⁷⁾ The effects of long-standing obesity on left ventricular (LV) structure and function have been characterized as eccentric LV hypertrophy and diastolic dysfunction and occasionally systolic dysfunction and HF.^(28,29)

One study of adolescents showed obesity to be associated with concentric remodeling rather than the classically described eccentric hypertrophy.⁽³⁰⁾ Regarding the systolic function of young obese people, some studies report that systolic function is normal or increased, whereas others show decreases in systolic function.⁽³¹⁻³⁴⁾ These studies of LV systolic function and past studies of LV diastolic function are confounded by the fact that obesity is associated with an increase in plasma volume and that the evaluation of LV function in these studies was assessed using load-dependent indices, such as the left ventricular ejection fraction (LVEF) and mitral inflow velocities (early diastolic and atrial [E/A] ratios).

Diastolic filling consists of two parts normally: rapid, early diastolic (active) relaxation and late diastolic (passive) filling. The first phase depends on the rate of ventricular relaxation, elastic ventricular recoil, the atrio-ventricular pressure gradient, and the passive elastic features of the left atrium and ventricle.^(35,36) The second phase formed on the basis of the strength of left atrial contraction and the stiffness of the left ventricle. Diastolic dysfunction occurs when the passive elastic traits of the myocardium are reduced to increased myocardial mass and changes in the

ORIGINAL ARTICLE

extracellular collagen secondarily.⁽³⁷⁾ This leads to stiffening and hypertrophy of the left ventricle with decreased compliance and higher diastolic pressures at each diastolic volume. So, relatively small increases in intravascular volume can lead to elevations in diastolic pressures. Shifting this pressure into the left atrium and pulmonary venous system can lead to pulmonary edema.⁽³⁷⁻⁴⁰⁾

Ventricular diastolic compliance and diastolic function can be assessed by measuring the velocity of blood flow from the left atrium to the left ventricle during early diastole (the E wave) and late diastole (the A wave) and calculating the E/A ratio by using the Doppler echocardiography. In other words, determinants of a diastolic dysfunction on a Doppler echocardiogram are decreased E/A ratio- the ratio of early to late (Atrial) phases of ventricular filling and delayed early diastolic transmitral filling with prolonged deceleration and isovolumetric relaxation times.⁽⁴¹⁾ Many studies indicated that some level of diastolic dysfunction exists in most patients with cirrhosis.⁽⁴¹⁻⁴⁶⁾

Diastolic dysfunction can be graded as follows according to the diastolic filling pattern (as shown in figure 1)

- Grade 1= impaired relaxation pattern with normal filling pressure.
- Grade 2= pseudonormalized pattern.
- Grade 3= reversible restrictive pattern.
- Grade 4= irreversible restrictive pattern.

Figure 1: Grading of diastolic dysfunction

METHODS: A total of eighty obese subjects of either gender, coming from rural background admitted in a tertiary care hospital in South India, were enrolled in this cross sectional case control study. Patients were enrolled from March 2014 to May 2015. This study project was approved by the ethics committee. A written informed consent was obtained from each patient. Subjects were counseled and explained about the objectives of the study by a qualified medical doctor.

ORIGINAL ARTICLE

Detailed personal history was taken using a standard questionnaire. Demographic details of age, gender, clinical status, and blood pressures were obtained from standard measurements and questionnaires. Arterial pressure was measured after subjects had rested for 5 minutes, in a supine position in a quiet room. Anthropometric measurements (Weight, height) were obtained, and BMI was calculated (Body weight divided by height in meters squared).

Exclusion Criteria Comprised: 1) any history or findings of cardiovascular disease, including HF, congenital heart disease, and/or had undergone any cardiovascular procedures; 2) major systemic disease (e.g., cancer, lupus); 3) engaged in smoking within 12 months of the study; 4) were pregnant; and 5) were taking any vasoactive medications.

Risk Factors Assessment: Hypertension was defined as systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg at the time of the visit (mean of two readings), or patient's self-reported history of hypertension or of anti-hypertensive medications. Hypercholesterolemia was defined as total serum cholesterol >240 mg/dL, a patient's self-report of hypercholesterolemia or of use of lipid-lowering treatment. The referent group (BMI, 18.5 to 24.9 kg/m²) was recruited from healthy volunteers in the community. Three groups were identified: obese (BMI >30 kg/m²), overweight (BMI, 25 to 29.9 kg/m²), and healthy referent subjects (BMI <25 kg/m²).

Electrocardiography: A 12-lead surface ECG was obtained from all subjects in the supine position. ECG was recorded at a paper speed of 50mm/s.

Echocardiography: Diastolic function of the heart was assessed and recorded. Echocardiographic studies were performed using a HDI 3000 (Philips ATL, Bothell, WA, USA) equipped with 2 to 4 MHz probes allowing M-mode, colour Doppler, two dimensional, and pulsed Doppler measurements. Echocardiography was performed according to the guidelines of American Society of Echocardiography.

Mitral Inflow Patterns: The normal E/A ratio is between 1 and 2.

Grade 1: Diastolic Dysfunction (Impaired Myocardial Relaxation) The E/A ratio is <1 , with a prolonged deceleration time (Dct) (>240 ms). In the tissue doppler assessment, e' is also reduced with a resultant E/e' ratio (Medial) <8 , suggesting a normal LA pressure. The D wave of the pulmonary venous inflow is smaller than the S wave and the AR wave is normal.

Grade 2: Diastolic Dysfunction (Pseudonormalized Pattern) When diastolic LV function deteriorates, LV compliance progressively decreases and there is an increase of LA pressure and the diastolic filling pressure. The transmitral E wave velocity progressively increases and the Dct decreases. As it does so, it goes through a phase that resembles a normal filling pattern. The E/A ratio is between 1 and 2 and the Dct between 160 and 240ms. This pseudo-normal pattern is a transition pattern from impaired relaxation to restrictive filling and is a result of a moderately increased LA pressure superimposed on a relaxation abnormality. The following clues help distinguish this from a normal filling pattern E/e' ratio (medial) >15 . Pulmonary venous flow AR >25 cm/sec and longer than transmitral A wave.

ORIGINAL ARTICLE

Grade 3 and 4: Diastolic Dysfunction (Restrictive Pattern) with more severe diastolic dysfunction, LV compliance reduces and LA pressures rise. The low compliance of the LV causes a rapid increase in the early LV pressure and a shortened inflow and DT. The E/A ratio is >2 . Dct is <160 ms. The high LA pressure manifests as a E/e' ratio >15 at the medial annulus. Forward diastolic pulmonary vein flow stops in mid-late diastole and during atrial contraction there is a significant flow reversal resulting in a prolonged AR. A reversal to grade 1 or 2 on reducing the preload by performing Valsalva manouvre or administering nitroglycerine suggests reversibility of the cardiac restriction and is termed grade 3. Diastolic filling should be graded as irreversible (grade 4) in the absence of such a reversal.

Statistical Analysis: SPSS for Windows, version 16, was used for data analysis. The qualitative data were analyzed by chi-square, Fisher's exact test and the Student's t test for continuous variables. Continuous variables are presented as mean $\pm$ standard deviation (SD); categorical variables are presented as percentages. p value <0.05 was considered significant. The Fisher's exact test was used to test differences between proportions. Multiple linear regressions were used to assess the independent association of BMI with diastolic function parameters.

RESULTS: Study Population: The baseline characteristics of the groups are shown in Table 1. The study population consisted of 80 participants. The study sample was divided into three groups: those with a BMI <25.0 kg/m² (Normal weight group, n=20), those with a BMI between 25.0 and 29.9 kg/m² (over weight group, n=30) and those with a BMI ≥ 30 kg/m² (Obese group, n=30). By definition, the BMI was significantly higher in the obese group; the average duration of obesity was 12 ± 6 years (Range 6 to 22 years).

	Normal weight	Over weight	Obese
	N=20	N=30	N=30
Age	55 $\pm$ 10.4	65 $\pm$ 8.9	72 $\pm$ 8.8
Women n (%)	14(17.5%)	18(22.5%)	19(23.7%)
BMI	22.4 $\pm$ 1.8	28.2 $\pm$ 1.4	34 $\pm$ 3.6
Waist circumference	80.4 $\pm$ 7.5	96.0 $\pm$ 6.6	109 $\pm$ 10.8
Systolic BP	122 $\pm$ 16.2	156 $\pm$ 14.2	166 $\pm$ 16.6
Diastolic BP	70.4 $\pm$ 5.6	92 $\pm$ 9.4	104 $\pm$ 10.6
HTN, n (%)	16(20%)	22(27.5%)	24(30%)
Diabetes, n (%)	4(5%)	6(7.5%)	12(15%)
Hypercholesterolemia, n (%)	13(16.2%)	18(22.5%)	22(27.5%)

Table I: Demographic, and clinical characteristics of the three groups

BMI and Diastolic Function Parameters: The correlation between BMI and echocardiographic diastolic function parameters was tested. (Table II.) Higher BMI was associated with higher peak E wave (p=0.006), higher peak A wave (p <0.001), lower E/A (p=0.01) and higher E/E' ratio (p=0.001). In multivariate comparisons (Table II), peak E was significantly higher in obese than in normal weight subjects (p <0.01). Peak A was significantly higher in the overweight and obese (Both p <0.01) groups compared to the normal weight group.

ORIGINAL ARTICLE

E/A was significantly lower in obese patients compared with normal weight participants ($p<0.01$). Peak E' was significantly lower in overweight and obese compared to normal weight individuals (Both $p<0.01$). E/E' was significantly higher in overweight and obese compared to the normal weight individuals (Both $p<0.01$).

	Normal weight	Over weight	Obese
	N=20	N=30	N=30
Peak E, cm/s	68.2	70.4	76.2
Peak A, cm/s	84.6	90.2	94.6
E/A ratio	0.88	0.82	0.74
Peak E', cm/s	7.6	7	6.6
E/E' ratio	8.9	11.2	12.6

Table II: Diastolic function parameters by BMI categories

	Normal weight	Over weight	Obese
	N=20	N=30	N=30
Normal function	18	0	0
DD I	2	2	1
DD II	0	4	4
DD III	0	11	10
DD IV	0	13	15

Table III: Categories of diastolic dysfunction by level of BMI

Normal diastolic function was seen in 18 normal weight subjects. (Table III). But in remaining all overweight and obese patients diastolic dysfunction was found from grade I to grade IV. First degree diastolic dysfunction was found in normal weight subjects. As the degree of obesity increased, there was worsening of diastolic function. Grade III and IV dysfunction were found more commonly in overweight and obese patients.

Prevalence of LV diastolic dysfunction in the overall sample was 77.5% ($n=62$). Grade I Diastolic dysfunction was present in 2.5% of the normal weight, 2.5% of overweight patients and 1.2% of obese patients. Pseudo-normalized diastolic pattern (grade II) was present in 5% of the overweight and 5% of the obese subjects but none in the normal weight subjects. After adjusting for covariates, both the overweight ($p=0.03$) and the obese ($p=0.02$) groups had a significantly higher risk of diastolic dysfunction compared to the normal weight group.

Diastolic Dysfunction									
Gender	Normal Function	DD I		DD II		DD III		DD IV	
		Number	%	Number	%	Number	%	Number	%
Male	10	3	3.75	5	6.2	14	17.5	18	22.5
Female	8	2	2.5	3	3.7	7	8.7	10	12.5
Total	18	5	6.2	8	10	21	26.2	28	35

Table IV. Distribution of diastolic dysfunction by gender

ORIGINAL ARTICLE

Overall 18 patients had normal diastolic function (Table IV). All grades of diastolic dysfunction was commonly seen in males as compared to females. No significant interaction was found between sex and BMI on LV diastolic dysfunction (p value =0.61).

Diastolic Function									
Age Group	Normal Function	DD I		DD II		DD III		DD IV	
		Number	%	Number	%	Number	%	Number	%
<40	18	0	0	1	1.2	3	3.7	4	5
40-60	0	2	2.5	3	3.7	8	10	8	10
>60	0	3	3.7	4	5	10	12.5	16	20
Total	18	5	6.2	8	10	21	26.2	28	35

Table V: Distribution of diastolic dysfunction in various age groups

As age advances diastolic function worsened as shown in Table V. Higher grade of diastolic dysfunction was seen in patients over age 60 (20% of patients). 10% of patients of the age group 40-60 were found to grade IV diastolic dysfunction. (Figure 2)

Figure 2: Bar diagram showing pattern of distribution of diastolic dysfunction in different groups

Hypertension and LV diastolic function (Table VI): Hypertension was significantly associated with peak A ($p < 0.001$) and with E/ A ($p = 0.05$). Hypertension as a continuous variable was significantly associated with an increased risk of diastolic dysfunction ($p = 0.01$). (Table VI). Although the SBP was significantly higher in the obese group ($p < 0.005$); the heart rate, was similar between the groups.

ORIGINAL ARTICLE

Diastolic Function									
Age Group	Normal Function	DD I		DD II		DD III		DD IV	
		Number	%	Number	%	Number	%	Number	%
HTN -	18	1	1.2	2	2.5	7	8.7	6	7.5
HTN +	0	4	5	6	7.5	14	17.5	22	27.5
Total	18	5	6.2	8	10	21	26.2	28	35

Table VI: Distribution of diastolic dysfunction by hypertension

As compared to those of normal weight subjects, hypertensive patients were found to have worsened diastolic dysfunction. (Figure 3).

DISCUSSION: We analyzed the association between measures of body size and LV diastolic function, measured by traditional Doppler analysis of mitral inflow parameters. Our findings indicate that: 1) the relationship between BMI and diastolic function parameters is continuous and independent of cardiovascular risk factors that cluster with obesity, such as hypertension, and 2) the overweight status is already associated with an impairment of LV diastolic function, close to that observed in obese individuals. In fact, no significant differences were found in most parameters of diastolic function between obese and overweight subjects. This observation was also confirmed by the similar odds ratio for diastolic dysfunction associated with both conditions. Overweight and obese subjects had also higher risk of a pseudo-normalized diastolic pattern.

Furthermore, the use of E/E' ratio, a widely used indicator of LV filling pressure^(47,48) and an independent predictor of cardiac events including heart failure and myocardial infarction⁽⁴⁹⁾ revealed higher LV filling pressures in obese and overweight patients than in normal weight subjects. Cardiovascular risk factors were significantly more prevalent in overweight and obese individuals than in normal weight subjects. It is established that hypertension, diabetes and increased LV mass negatively affect LV diastolic function. However, BMI was still associated with LV diastolic function parameters after controlling for hypertension and diabetes. In fact, there is ample evidence that the accumulation of adipose tissue may determine cardiovascular alterations in several metabolic and

ORIGINAL ARTICLE

neuro-hormonal pathways, causing abnormalities in sodium handling, neuro-endocrine activation, renin-angiotensin-aldosterone system, and increasing myocardial oxidative stress.^(50,51)

Changes in myocardial metabolism have been demonstrated in obese patients, with a shift toward free fatty acid utilization and subsequent cardiac lipotoxicity, resulting in cardiomyocyte apoptosis and reduced cardiac efficiency.^(52,53) In particular, myocardial fatty infiltration in obese patients may affect the cardiac structure and function, leading to the development of severe diastolic dysfunction.^(54,55) Previous reports had shown a relationship between obesity and diastolic function in extremely selected samples of young women,⁽⁵⁶⁻⁵⁸⁾ in subjects without cardiovascular risk factors⁽⁵⁹⁾ or in extremely obese subjects.^(60,61)

In a large study in patients that underwent diagnostic coronary angiography, LV end-diastolic pressure was significantly higher in obese patients than in patients with a BMI <25⁽⁶²⁾ Another study reported that waist circumference, but not BMI, was correlated to lower ventricular filling⁽⁶³⁾ which is in agreement with our findings. The results of this study show changes in the LV structure and function in healthy subjects with excess weight who have no other clinically appreciable cause of heart disease. These changes appear to be related to the degree of obesity, and some are even present with less severe obesity. Moreover, these echocardiographic changes are shown to contribute to reduced exercise capacity.

LV Diastolic Function: However, earlier studies of transmitral flow patterns in obese individuals have reported inconsistent changes in LV filling indexes.⁽⁶⁴⁾ Such disparities in simple flow measures may reflect the sensitivity of transmitral flow indexes to loading conditions as well as the influence of increased LV mass.^(65,66) The interpretation of transmitral flow in relation to tissue diastolic velocity (em) may be a better means of assessing diastolic function-especially given the intravascular volume expansion of obese subjects. Our results are in agreement to a recent study using tissue Doppler imaging that showed depressed diastolic function in young obese women.⁽⁶⁷⁾

Potential Mechanisms: This study provides observational findings that link obesity, and myocardial disturbances. A number of putative mechanisms may underlie these morphological changes. First, increased stroke volume and cardiac output leads to dilatation of the heart chambers with eccentric left ventricular hypertrophy. However, the mechanical advantage conferred by the compensatory reduction of myocardial fiber shortening is offset by a concomitant increase in myocardial oxygen consumption and ventricular wall stress. Second, insulin resistance may mediate the increased LVM in obese subjects.⁽⁶⁸⁻⁷⁰⁾ A recent study on young obese women further supported the notion that insulin resistance and alterations in myocardial substrate metabolism lead to myocardial contractile dysfunction associated with obesity.⁽⁷¹⁻⁷²⁾

It has been proposed that insulin may also exercise its influence on cardiac geometry due to its growth-stimulating, sodium retention and other neuroendocrine effects. Third, adipose tissue may contribute to circulating angiotensin II,⁽⁷³⁾ which promotes myocardial tissue growth as well as influencing aldosterone, which may mediate myocardial fibrosis. Fourth, obstructive sleep apnea is common in obese persons and may contribute to heart failure through several mechanisms. In the general community, obstructive sleep apnea is associated with hypertension, although such patients were excluded from our study. Increases in afterload and wall stress associated with generation of negative intrathoracic pressure during episodes of obstructive apnea, as well as inflammatory cytokines and sympathetic activation are potential mechanisms.⁽⁷⁴⁾

ORIGINAL ARTICLE

In the present study, because increased BMI was predictive of LV functional abnormalities (By use of load-dependent techniques), there may be alterations intrinsic to the myocardium in obesity. Epidemiologic studies have shown that obesity is an independent risk factor for the development of HF, even after accounting for co-morbid conditions, such as diabetes, and that obese and overweight women are at higher risk of developing HF than obese and overweight men,⁽⁷⁵⁾ Specifically, early in the course of obesity there is an increase in blood volume, which leads to increased BP, increased LV wall stress, and compensatory LV hypertrophy.

As obesity becomes more chronic, continual volume and/or pressure overload causes eventual LV enlargement, eccentric LV hypertrophy, and progressive systolic and diastolic dysfunction; the later stages are characterized by dilated cardiomyopathy and HF.^(76,77) Obese subjects have a high incidence of co-morbid conditions that also affect function, such as hypertension. A previous study of obese subjects showed that a relatively load-independent index of contractility, the end-systolic wall stress/end-systolic volume, was decreased in obese subjects compared with normal subjects.⁽⁷⁸⁾

LIMITATIONS: Although the duration of obesity has previously been shown to be a determinant of cardiac changes from obesity, we were unable to demonstrate such a relation in our study. This may reflect dependence on patient recall and the lack of objective measurement of BMI during subjects' earlier life. This is a small observational study and, as such, other variables that could potentially predict alterations in LV structure and function, could not be evaluated. Newer echocardiographic techniques like tissue Doppler imaging which are load independent are found to be better in assessment of diastolic dysfunction.

The mean age of the study cohort was high, and so was the prevalence of cardiovascular risk factors; therefore, our results may not be extrapolated to younger populations with lower cardiovascular risk profiles. In addition, there are particular challenges common to many non-invasive echocardiographic studies of LV function in obesity: i) The ideal way to index ventricular function to body size remains unknown. ii) Some studies have shown that in obesity cardiac output is increased; however, when indexed to body size, the cardiac index is decreased.

CONCLUSION: LV diastolic dysfunction may be one of the pathophysiological link between overweight/obesity and the associated risk of developing heart failure. While in the past attention was paid essentially to obesity, our study demonstrates that subclinical signs of LV diastolic function impairment are present in overweight subjects too. Presence of hypertension worsens diastolic function.

Therapeutic strategies aimed at promoting optimal body weight resulted in improvements in LV diastolic function and might have a beneficial effect in preventing or delaying the future development of heart failure, a hypothesis that deserves further investigation. Increased BMI was associated with worse LV diastolic function. The increased risk of LV diastolic dysfunction in both overweight and obese individuals may partially account for the increased risk of heart failure associated with both conditions. Overweight subjects without overt heart disease have subclinical changes of LV structure and function. Hypertension adds to the worsening of diastolic dysfunction over and above that of obesity.

ORIGINAL ARTICLE

Obesity is an independent risk factor for HF and for subclinical LV dysfunction. These early abnormalities in LV structure and function may have important implications in explaining the myocardial dysfunction associated with obesity and the associated increased cardiovascular morbidity and mortality. Better understanding of the pathophysiology of obesity related LV characteristics will enable us to modify the disease process resulting in regression of subclinical LV changes.

REFERENCES:

1. Whitlock G, Lewington S, Sherliker P, et al. Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. *Lancet*. 2009; 373: 1083-1096.
2. Eckel RH, York DA, Rossner S, et al. Prevention Conference VII: Obesity, a worldwide epidemic related to heart disease and stroke: executive summary. *Circulation*. 2004; 110: 2968-2975.
3. Murphy NF, MacIntyre K, Stewart S, Hart CL, Hole D, McMurray JJ. Long-term cardiovascular consequences of obesity: 20-year follow-up of more than 15 000 middle-aged men and women (the Renfrew-Paisley study). *Eur Heart J*. 2006; 27: 96-106.
4. Kenchiah S, Evans JC, Levy D, et al. Obesity and the risk of heart failure. *N Engl J Med*. 2002; 347: 305-313.
5. Loehr LR, Rosamond WD, Poole C, et al. Association of multiple anthropometrics of overweight and obesity with incident heart failure: the Atherosclerosis Risk in Communities study. *Circ Heart Fail*. 2009; 2: 18-24.
6. Alpert MA. Obesity cardiomyopathy: pathophysiology and evolution of the clinical syndrome. *Am J Med Sci*. 2001; 321: 225-236.
7. Palmieri V, de Simone G, Arnett DK, et al. Relation of various degrees of body mass index in patients with systemic hypertension to left ventricular mass, cardiac output, and peripheral resistance (The Hypertension Genetic Epidemiology Network Study). *Am J Cardiol*. 2001; 88: 1163-1168.
8. Norton GR, Majane OH, Libhaber E, et al. The relationship between blood pressure and left ventricular mass index depends on an excess adiposity. *J Hypertens*. 2009; 27: 1873-1883.
9. Lauer MS, Anderson KM, Levy D. Separate and joint influences of obesity and mild hypertension on left ventricular mass and geometry: the Framingham Heart Study. *J Am Coll Cardiol*. 1992; 19: 130-134.
10. de Simone G, Devereux RB, Roman MJ, Alderman MH, Laragh JH. Relation of obesity and gender to left ventricular hypertrophy in normotensive and hypertensive adults. *Hypertension*. 1994; 23: 600-606.
11. Turkbey EB, McClelland RL, Kronmal RA, et al. The impact of obesity on the left ventricle: the Multi-Ethnic Study of Atherosclerosis (MESA). *JACC Cardiovasc Imaging*. 2010; 3: 266-274.
12. Bella JN, Palmieri V, Roman MJ, et al. Mitral ratio of peak early to late diastolic filling velocity as a predictor of mortality in middle-aged and elderly adults: the Strong Heart Study. *Circulation*. 2002; 105: 1928-1933.
13. Schillaci G, Pasqualini M, Verdecchia P, et al. Prognostic significance of left ventricular diastolic dysfunction in essential hypertension. *J Am Coll Cardiol*. 2002; 39: 2005-2011.

ORIGINAL ARTICLE

14. Redfield MM, Jacobsen SJ, Burnett JC Jr, Mahoney DW, Bailey KR, Rodeheffer RJ. Burden of systolic and diastolic ventricular dysfunction in the community: appreciating the scope of the heart failure epidemic. *JAMA*. 2003; 289: 194-202.
15. Aurigemma GP, Gottdiener JS, Shemanski L, Gardin J, Kitzman D. Predictive value of systolic and diastolic function for incident congestive heart failure in the elderly: the Cardiovascular Health Study. *J Am Coll Cardiol*. 2001; 37: 1042-1048.
16. Alpert MA, Lambert CR, Terry BE, et al. Influence of left ventricular mass on left ventricular diastolic filling in normotensive morbid obesity. *Am Heart J*. 1995; 130: 1068-1073.
17. Russo C, Jin Z, Homma S, et al. Effect of diabetes and hypertension on left ventricular diastolic function in a high-risk population without evidence of heart disease. *Eur J Heart Fail*. 2010; 12: 454-461.
18. Mokdad AH, Bowman BA, Ford ES, et al. The continuing epidemics of obesity and diabetes in the United States. *JAMA*. 2001; 286: 1195-1200.
19. Hubert HB, Feinleib M, McNamara PM, et al. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. *Circulation*. 1983; 67: 968-977.
20. Kenchaiah S, Evans JC, Levy D, et al. Obesity and the risk of heart failure. *N Engl J Med*. 2002; 347: 305-313.
21. Alpert MA. Obesity cardiomyopathy: pathophysiology and evolution of the clinical syndrome. *Am J Med Sci*. 2001; 321: 225-236.
22. Pascual M, Pascual DA, Soria F, et al. Effects of isolated obesity on systolic and diastolic left ventricular function. *Heart*. 2003; 89: 1152-1156.
23. Scaglione R, Dichiaro MA, Indovina A, et al. Left ventricular diastolic and systolic function in normotensive obese subjects: influence of degree and duration of obesity. *Eur Heart J*. 1992; 13: 738-742.
24. Chakko S. Obesity and Ventricular Function in Man: Diastolic Function. In: Alpert MAAJ, ed. New York, NY: Armonk; 1998; 57-76.
25. Zarich SW, Kowalchuk GJ, McGuire MP, et al. Left ventricular filling abnormalities in asymptomatic morbid obesity. *Am J Cardiol*. 1991; 68: 377-381.
26. Allison DB, Fontaine KR, Manson JE, Stevens J, VanItallie TB. Annual deaths attributable to obesity in the United States. *JAMA* 1999; 282: 1530-8.
27. Kenchaiah S, Evans JC, Levy D, Wilson PWF, Benjamin EJ, Larson MG. Obesity and the risk of heart failure. *N Engl J Med* 2002; 347: 305-13.
28. Alpert MA, Lambert CR, Panayiotou H, et al. Relation of duration of morbid obesity to left ventricular mass, systolic function, and diastolic filling, and effect of weight loss. *Am J Cardiol* 1995; 76: 1194-7.
29. Alpert MA. Obesity cardiomyopathy: pathophysiology and evolution of the clinical syndrome. *Am J Med Sci* 2001; 321: 225-36.
30. Mensah GA, Treiber FA, Kapuku GK, Davis H, Barnes VA, Strong WB. Patterns of body fat deposition in youth and their relation to left ventricular markers of adverse cardiovascular prognosis. *Am J Cardiol* 1999; 84: 583-8.
31. Stoddard MF, Tseuda K, Dillon S, Kupersmith J. The influences of obesity on left ventricular filling and systolic function. *Am Heart J* 1992; 124: 694-9.

ORIGINAL ARTICLE

32. Alpert MA, Lambert CR, Terry BE, et al. Interrelationship of left ventricular mass, systolic function, and diastolic filling in normotensive morbidly obese patients. *Int J Obes* 1995; 19: 550-7.
33. Licata G, Scaglione R, Avellone G, et al. Hemostatic function in young subjects with central obesity: relationship with left ventricular function. *Metabolism* 1995; 44: 1417-21.
34. Ferraro S, Perrone Filardi P, Desiderio A, et al. Left ventricular systolic and diastolic function in severe obesity: a radionuclide study. *Cardiology* 1996; 87: 347-53.
35. J. D. Carroll and O. M. Hess, "Assessment of normal and abnormal cardiac function," in *Braunwald's Heart Disease: A Text book of Cardiovascular Medicine*, D. P. Zipes, P. Libby, R. O. Bonow, and E. Braunwald, Eds., vol. 2, p. 498, Elsevier Saunders, Philadelphia, Pa, USA, 7th edition, 2005.
36. R. F. Lee, T. K. Glenn, and S. S. Lee, "Cardiac dysfunction in cirrhosis," *Best Practice and Research: Clinical Gastroenterology*, vol. 21, no. 1, pp. 125-140, 2007.
37. G. P. Aurigemma and W. H. Gaasch, "Clinical practice. Diastolic heart failure," *The New England Journal of Medicine*, vol. 351, no. 11, pp. 1097-1105, 2004.
38. H. Q. Liu, S. A. Gaskari, and S. S. Lee, "Cardiac and vascular changes in cirrhosis: pathogenic mechanisms," *World Journal of Gastroenterology*, vol. 12, no. 6, pp. 837-842, 2006.
39. S. Møller and J. H. Henriksen, "Cardiovascular dysfunction in cirrhosis: pathophysiological evidence of a cirrhotic cardiomyopathy," *Scandinavian Journal of Gastroenterology*, vol. 36, no. 8, pp. 785-794, 2001.
40. M. Torregrosa, S. Aguade', L. Dos et al., "Cardiac alterations in cirrhosis: reversibility after liver transplantation," *Journal of Hepatology*, vol. 42, no. 1, pp. 68-74, 2005.
41. S. S. Lee, "Cardiac abnormalities in liver cirrhosis," *Western Journal of Medicine*, vol. 151, no. 5, pp. 530-535, 1989.
42. H. Kelbaek, J. Eriksen, and I. Brynjolf, "Cardiac performance in patients with asymptomatic alcoholic cirrhosis of the liver," *The American Journal of Cardiology*, vol. 54, no. 7, pp. 852-855, 1984.
43. R. D. Grose, J. Nolan, J. E. Dillon et al., "Exercise-induced left ventricular dysfunction in alcoholic and non-alcoholic cirrhosis," *Journal of Hepatology*, vol. 22, no. 3, pp. 326-332, 1995.
44. S. S. Lee, A. Hadengue, R. Moreau, R. Sayegh, P. Hillon, and D. Lebrec, "Postprandial hemodynamic responses in patients with cirrhosis," *Hepatology*, vol. 8, no. 3, pp. 647-651, 1988.
45. M. R. Lunzer, S. P. Newman, A. G. Bernard, K. K. Manghani, S. P. Sherlock, and J. Ginsburg, "Impaired cardiovascular responsiveness in liver disease," *The Lancet*, vol. 2, no. 7931, pp. 382-385, 1975.
46. M. Pozzi, E. Redaelli, L. Ratti et al., "Time-course of diastolic dysfunction in different stages of chronic HCV related liver diseases," *Minerva Gastroenterologica e Dietologica*, vol. 51, no. 2, pp. 179-186, 2005.
47. Ommen SR, Nishimura RA, Appleton CP, et al. Clinical utility of Doppler echocardiography and tissue Doppler imaging in the estimation of left ventricular filling pressures: A comparative simultaneous Doppler-catheterization study. *Circulation*. 2000; 102: 1788-1794.
48. Nagueh SF, Middleton KJ, Kopelen HA, Zoghbi WA, Quinones MA. Doppler tissue imaging: a noninvasive technique for evaluation of left ventricular relaxation and estimation of filling pressures. *J Am Coll Cardiol*. 1997; 30: 1527-1533.

ORIGINAL ARTICLE

49. Sharp AS, Tapp RJ, Thom SA, et al. Tissue Doppler E/E' ratio is a powerful predictor of primary cardiac events in a hypertensive population: an ASCOT substudy. *Eur Heart J*. 2010; 31: 747-752.
50. Gorzelniak K, Engeli S, Janke J, Luft FC, Sharma AM. Hormonal regulation of the human adipose-tissue renin-angiotensin system: relationship to obesity and hypertension. *J Hypertens*. 2002; 20: 965-973.
51. Vincent HK, Powers SK, Stewart DJ, Shanely RA, Demirel H, Naito H. Obesity is associated with increased myocardial oxidative stress. *Int J Obes Relat Metab Disord*. 1999; 23: 67-74.
52. Zhou YT, Grayburn P, Karim A, et al. Lipotoxic heart disease in obese rats: implications for human obesity. *Proc Natl Acad Sci U S A*. 2000; 97: 1784-1789.
53. Peterson LR, Herrero P, Schechtman KB, et al. Effect of obesity and insulin resistance on myocardial substrate metabolism and efficiency in young women. *Circulation*. 2004; 109: 2191-2196.
54. Iacobellis G, Ribaudo MC, Leto G, et al. Influence of excess fat on cardiac morphology and function: study in uncomplicated obesity. *Obes Res*. 2002; 10: 767-773.
55. De Scheerder I, Cuvelier C, Verhaaren R, De Buyzere M, De Backer G, Clement D. Restrictive cardiomyopathy caused by adipositas cordis. *Eur Heart J*. 1987; 8: 661-663.
56. Peterson LR, Waggoner AD, Schechtman KB, et al. Alterations in left ventricular structure and function in young healthy obese women: assessment by echocardiography and tissue Doppler imaging. *J Am Coll Cardiol*. 2004; 43: 1399-1404.
57. Pascual M, Pascual DA, Soria F, et al. Effects of isolated obesity on systolic and diastolic left ventricular function. *Heart*. 2003; 89: 1152-1156.
58. Kosmala W, O'Moore-Sullivan TM, Plaksej R, Kuliczowska-Plaksej J, Przewlocka-Kosmala M, Marwick TH. Subclinical impairment of left ventricular function in young obese women: contributions of polycystic ovary disease and insulin resistance. *J Clin Endocrinol Metab*. 2008; 93: 3748-3754.
59. Wong CY, O'Moore-Sullivan T, Leano R, Byrne N, Beller E, Marwick TH. Alterations of left ventricular myocardial characteristics associated with obesity. *Circulation*. 2004; 110: 3081-3087.
60. Willens HJ, Chakko SC, Lowery MH, et al. Tissue Doppler imaging of the right and left ventricle in severe obesity (body mass index >35 kg/m²). *Am J Cardiol*. 2004; 94: 1087-1090.
61. Di Bello V, Santini F, Di Cori A, et al. Relationship between preclinical abnormalities of global and regional left ventricular function and insulin resistance in severe obesity: a Color Doppler Imaging Study. *Int J Obes (Lond)*. 2006; 30: 948-956.
62. Powell BD, Redfield MM, Bybee KA, Freeman WK, Rihal CS. Association of obesity with left ventricular remodeling and diastolic dysfunction in patients without coronary artery disease. *Am J Cardiol*. 2006; 98: 116-120.
63. Libhaber CD, Norton GR, Majane OH, et al. Contribution of central and general adiposity to abnormal left ventricular diastolic function in a community sample with a high prevalence of obesity. *Am J Cardiol*. 2009; 104: 1527-1533.
64. Pascual M, Pascual DA, Soria F, et al. Effects of isolated obesity on systolic and diastolic left ventricular function. *Heart*. 2003; 89: 1152-1156.

ORIGINAL ARTICLE

65. Scaglione R, Dichiaro MA, Indovina A, et al. Left ventricular diastolic and systolic function in normotensive obese subjects: influence of degree and duration of obesity. *Eur Heart J*. 1992; 13: 738 -742.
66. Chakko S. Obesity and Ventricular Function in Man: Diastolic Function. In: Alpert MAAJ, ed. New York, NY: Armonk; 1998; 57-76.
67. Peterson LR, Waggoner AD, Schechtman KB, et al. Alterations in left ventricular structure and function in young healthy obese women. *J Am Coll Cardiol*. 2004; 43: 1399 -1404.
68. Stoddard MF, Tseuda K, Thomas M, et al. The influence of obesity on left ventricular filling and systolic function. *Am Heart J*. 1992; 124: 694 - 699.
69. Sasson Z, Rasooly Y, Gupta R, et al. Left atrial enlargement in healthy obese: prevalence and relation to left ventricular mass and diastolic function. *Can J Cardiol*. 1996; 12: 257-263.
70. Karason K, Sjostrom L, Wallentin I, et al. Impact of blood pressure and insulin on the relationship between body fat and left ventricular structure. *Eur Heart J*. 2003; 24: 1500 -1505.
71. Mureddu GF, Greco R, Rosato GF, et al. Relation of insulin resistance to left ventricular hypertrophy and diastolic dysfunction in obesity. *Int J Obes Relat Metab Disord*. 1998; 22: 363-368.
72. Peterson LR, Herrero P, Schechtman KB, et al. Effect of obesity and insulin resistance on myocardial substrate metabolism and efficiency in young women. *Circulation*. 2004; 109: 2191-2196.
73. Engeli S, Negrel R, Sharma AM. Physiology and pathophysiology of the adipose tissue renin-angiotensin system. *Hypertension*. 2000; 35: 1270 -1277.
74. Laaban JP, Pascal-Sebaoun S, Bloch E, et al. Left ventricular systolic dysfunction in patients with obstructive sleep apnea syndrome. *Chest*. 2002; 122: 1133-1138.
75. Kenchaiah S, Evans JC, Levy D, Wilson PWF, Benjamin EJ, Larson MG. Obesity and the risk of heart failure. *N Engl J Med* 2002; 347: 305-13.
76. Alpert MA, Lambert CR, Panayiotou H, et al. Relation of duration of morbid obesity to left ventricular mass, systolic function, and diastolic filling, and effect of weight loss. *Am J Cardiol* 1995; 76: 1194 -7.
77. Alpert MA. Obesity cardiomyopathy: pathophysiology and evolution of the clinical syndrome. *Am J Med Sci* 2001; 321: 225-36.
78. Garavaglia GE, Messerli FH, Nunex BD, Schmieder RE, Grossman E. Myocardial contractility and left ventricular function in obese patients with essential hypertension. *Am J Cardiol* 1988; 62: 594 -7.

ORIGINAL ARTICLE

AUTHORS:

1. Prashant S. Sidmal
2. Mallikarjun H. P.
3. K. C. Shekarappa

PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of General Medicine, Subbaiah Institute of Medical Sciences, NH 13, Purlae, Holehonnur Road, Shimoga-577222, Karnataka, India.
2. Assistant Professor, Department of General Medicine, Subbaiah Institute of Medical Sciences, NH 13, Purlae, Holehonnur Road, Shimoga-577222, Karnataka, India.

FINANCIAL OR OTHER

COMPETING INTERESTS: None

3. Associate Professor, Department of General Medicine, Subbaiah Institute of Medical Sciences, NH 13, Purlae, Holehonnur Road, Shimoga-577222, Karnataka, India.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Prashant S. Sidmal,
Associate Professor,
Department of General Medicine,
Subbaiah Institute of Medical Sciences,
NH 13, Purlae, Holehonnur Road,
Shimoga-577222, Karnataka, India.
E-mail: prashantsidmal@gmail.com

Date of Submission: 31/07/2015.

Date of Peer Review: 01/08/2015.

Date of Acceptance: 13/08/2015.

Date of Publishing: 18/08/2015.