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Original Article

Association and pattern of diastolic dysfunction in metabolic syndrome: Potential for diagnosis and prognosis

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ABSTRACT

Background: There is need to assess left ventricular diastolic dysfunction (LVDD) in metabolic syndrome to effectively implicate and strengthen population-based prevention strategies.

Objectives: To assess the prevalence of LVDD in metabolic syndrome.

Methods: This study was conducted in the Department of Medicine, Guru Gobind Singh Medical College and Hospital, Faridkot on 100 cases (with metabolic syndrome diagnosed on International Diabetic Federation criteria) and 100 age- and sex-matched controls (without metabolic syndrome) between 30 and 60 years of age by echocardiography to assess LVDD. **Results:** Overall prevalence of diastolic dysfunction was 73% in the cases and 14% in controls with an increasing trend with increasing age in both groups showing age an important determinant of diastolic dysfunction; gender-wise difference was not significant in any group. However, increasing trend with increasing body mass index, elevated blood pressure, elevated fasting blood sugar, elevated serum triglyceride, and decreased serum high density lipoprotein was noted showing their risk correlation in the outcome of diastolic dysfunction; participants without metabolic syndrome had lesser diastolic dysfunction (14%).

Conclusions: The diastolic dysfunction in metabolic syndrome was found to be higher that supports the assumption that metabolic syndrome could be correlated to risk of development of LVDD. Holistic prevention of metabolic syndrome has an important role to prevent development of diastolic dysfunction.

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1. Introduction

Globally increased prevalence of diastolic dysfunction has been shown in the metabolic syndrome that results from abnormality in active relaxation of myocardium and an increase in passive stiffness due to metabolic derangements and structural remodeling.^{1,2} Diastolic dysfunction is the key pathophysiologic mechanism responsible for hemodynamic perturbations and symptoms in patients of heart failure with normal ejection fraction also called as diastolic heart failure. Patients with diastolic dysfunction have impaired quality of life because of the deterioration in exercise capacity that limits activities of daily living. Left ventricular diastolic dysfunction (LVDD) with a normal left ventricular ejection fraction is clinically very important because it is responsible for half of all hospital admissions for acute heart failure.^{1,3–5} Researchers working in different parts of the world have noted that metabolic syndrome comprises of a constellation of metabolic abnormalities that confer increased risk of hyperglycemia and dyslipidemia leading to a spectrum of cardiovascular diseases including heart failure with normal ejection fraction.^{1,6–9} National Cholesterol Education Program's Adult Treatment Panel III report identified the metabolic syndrome as a multiplex risk factor for cardiovascular disease that deserves more clinical attention.¹⁰ Asian Indians have double the risk of coronary artery disease characterized by high serum levels of apolipoprotein B, lipoprotein and triglycerides (TGs) and low levels of apolipoprotein A1, and high-density lipoprotein cholesterol leading to metabolic syndrome cases of high prevalence of LVDD.^{11,12} In the above scenario, this study was undertaken to assess the prevalence of LVDD in metabolic syndrome by echocardiography so that we can effectively implicate and strengthen the population-based prevention strategies for prevention of epidemic of obesity and metabolic syndrome.

2. Methods

This study was conducted on consenting participants aged between 30 and 60 years (both genders) among 100 cases [50 males and 50 females fulfilling the criteria of metabolic syndrome of International Diabetic Federation (IDF)] and 100 controls [50 males and 50 females without metabolic syndrome].^{10,12} Patients with known cases of valvular heart diseases, coronary heart disease, cor pulmonale, pulmonary hypertension, primary volume overload, atrial fibrillation, left ventricular ejection fraction less than 55%, left ventricular hypertrophy (LVH), pericardial effusion, and poor transthoracic window were excluded from the study. The parameters of diastolic dysfunction were E/A index [ratio of transmitral flow during early (E) ventricular filling to flow during atrial (A) contraction] <1 or >2, DT <150 or >220 ms, IVRT <60 or >100 ms, E/e' <15, e'/a' <1.0.^{13,14}

Ethical approval from the Institutional Ethics Committee was taken. Each participant was individually counseled following Helsinki declaration and asked to provide informed consent. Detailed history, clinical, and anthropometric evaluation were carried out including body mass index (BMI), blood

pressure, and fundus assessment. Laboratory investigations included complete blood count, liver function test, renal function test, serum electrolytes, and complete urinalysis using standard operating procedures. Pulsed Doppler evaluation of transmitral inflow and Tissue Doppler Imaging, M mode echocardiography, and 2D echocardiography was performed to minimize the errors in assessing the diastolic dysfunction. Pulsed-wave Doppler-derived transmitral inflow velocities were obtained in the apical 4-chamber view with the sample volume placed at the mitral valve leaflet tips. Measurements included the transmitral early diastolic and atrial wave velocities to calculate E/A ratio, IVRT, and deceleration time. For tissue Doppler imaging, mitral annulus velocity was done with a 2 mm sample volume placed at the septal side of the mitral annulus. Data were analyzed to find relations between metabolic syndrome and its various components with diastolic dysfunction.

3. Results

Among the cases (i.e. with metabolic syndrome), 73 out of 100 (73%) had diastolic dysfunction and in the control group (i.e. without metabolic syndrome), 14 out of 100 (14%) had diastolic dysfunction which was statistically significant ($p < 0.0001$) (Table 1).

Diastolic dysfunction was found in 21 cases (60%) in 30–40 years of age group, 24 (70.59%) in 41–50 years of age group, and 28 (90.32%) persons in 51–60 years of age group which was statistically significant ($p = 0.02$). Among controls, diastolic dysfunction was 2.86% in 30–40 years of age group, 3 (9.09%) in 41–50 years, and 10 (31.25%) persons in 51–60 years which was statistically significant ($p = 0.002$) (Table 1).

In the cases, 38 males (76%) and 35 females (70%) were found to have diastolic dysfunction. On the other hand, diastolic dysfunctions were noted more in males (76%) than females (70%). Controls had less diastolic dysfunction which was statistically insignificant (Table 1).

3 out of 4 (75%) participants with overweight category, 23 out of 35 (65.71%) with obesity class I category, 25 out of 37 (67.57%) with obesity class II category, and 22 out of 23 (95.65%) with obesity class III category, had diastolic dysfunction in the study group; diastolic dysfunction increased as BMI increased. It was statistically significant with p value of 0.03.

Among cases with hypertension according to IDF criteria of metabolic syndrome, 82.5% had diastolic dysfunction that was statistically significant ($p < 0.0001$) (Table 1).

In our study, in persons who have fasting blood sugar (FBS) according to IDF criteria of metabolic syndrome, 65 out of 84 (78.57%) were found to have diastolic dysfunction in the study group. It was statistically significant with p value of 0.024 (Table 1).

In participants with high serum TG according to IDF criteria of metabolic syndrome, 69 (75.82%) were found to have significantly higher diastolic dysfunction ($p = 0.043$) (Table 1).

In participants with high serum high density lipoprotein (HDL) according to IDF criteria of metabolic syndrome, 56 (78.87%) had diastolic dysfunction that was statistically significant ($p = 0.038$) (Table 1).

Table 1 – Diastolic dysfunction among metabolic syndrome cases and controls.

	Cases		Controls	
	Present	Absent	Present	Absent
Age groups				
30–40	21 (60%)	14 (40%)	1 (2.86%)	34 (97.14%)
41–50	24 (70.59%)	10 (29.41%)	3 (9.09%)	30 (90.91%)
51–60	28 (90.32%)	3 (9.68%)	10 (31.25%)	22 (68.75%)
Total	73 (73%)	27 (27%)	14 (14%)	86 (86%)
Gender				
Male	38 (76%)	12 (24%)	7 (14%)	43 (43%)
Female	35 (70%)	15 (30%)	7 (14%)	43 (43%)
Body mass index (BMI) (kg/m²)				
Normal (18.5–24.9)	0 (0%)	1 (100%)		
Over weight (25–29.9)	3 (75%)	1 (25%)		
Obese class I (30–34.9)	23 (65.71%)	12 (34.29%)		
Obese class II (35–39.9)	25 (67.57%)	12 (32.43%)		
Obese class III (≥40)	22 (95.65%)	1 (4.35%)		
<i>According to International Diabetic Federation criteria of metabolic syndrome</i>				
Blood pressure (BP)				
Elevated BP	66 (82.5%)	14 (17.5%)		
Normal BP	7 (35%)	13 (65%)		
Fasting blood sugar (FBS)				
Elevated FBS	65 (77.38%)	19 (22.62%)		
Normal FBS	8 (50%)	8 (50%)		
Triglyceride (TG)				
Elevated TG	69 (75.82%)	22 (24.18%)		
Normal TG	4 (44.44%)	5 (55.56%)		
High density lipoprotein (HDL)				
Deceased HDL	56 (78.87%)	15 (21.13%)		
Normal HDL	17 (58.62%)	12 (41.38%)		

4. Discussion

We noted powerful effect of metabolic syndrome on various parameters of diastolic dysfunction. Similar results had also reported significantly higher diastolic dysfunction in metabolic syndrome.^{7,12} Penjašković et al. working on central obesity found at least two of the other four characteristics of metabolic syndrome according to IDF criteria and also found a positive correlation between the number of characteristics of metabolic syndrome and the diastolic dysfunction grade.¹⁵

4.1. Age

The diastolic dysfunction was noted to increase with the increase in age in our study. Patil concluded that metabolic syndrome was significantly higher in 45 years and above irrespective of genders age groups; 73.07% males and 64.58% females with metabolic syndrome had diastolic dysfunction though this difference was insignificant.¹²

4.2. Body mass index (BMI)

In our study, the diastolic dysfunction increased also with increased BMI. Pascual et al. noted subclinical LVDD in all grades of isolated obesity, correlated with BMI, and increased systolic function in the early stages of obesity. Subclinical diastolic dysfunction was significantly more prevalent with

higher BMI.¹⁶ Wong et al. reported correlation of BMI with left ventricular mass and wall thickness; significantly obese subjects (BMI >35) had reduced left ventricular systolic and diastolic function with increased myocardial reflectivity even with normal left ventricular ejection fraction. Among overweight participants, without overt heart disease, subclinical changes were noted on left ventricular structure and function even after adjustment for mean arterial pressure, age, gender, and left ventricular mass.¹⁷ Kenchaiah et al. concluded that increased BMI was associated with an increased risk of heart failure; compared with a normal BMI, obese subjects doubled the risk of heart failure. For women, the hazard ratio was 2.12; for men, the hazard ratio was 1.90.¹⁸ Dwyer et al. reported that, even in the absence of coronary artery disease, diastolic dysfunction (44%) and systolic dysfunction (25%) were common findings as hypertension and obesity were most essential in black patients for development of diastolic dysfunction.¹⁹

Others noted dominant effect of waist circumference on cardiovascular parameters.²⁰

4.3. Hypertension

Evrengul et al. reported that peak A velocity was significantly higher and E/A ratio was significantly lower in hypertensive patients.²¹ Chinali et al. noted that hypertension was most strongly associated with cardiac markers of preclinical disease.²²

4.4. Fasting blood sugar (FBS)

In our study, diastolic dysfunction increased with increased FBS as per IDF criteria. Miyazato et al. noted fasting plasma glucose as a sensitive predictor for LVDD in nondiabetic patients with treated hypertension. FBS and glycated hemoglobin (HbA1c) levels were positively correlated with A/E ratio and the deceleration time of E wave. Since a slight increase in plasma glucose levels was associated with abnormalities in diastolic function independent of LVH, an early stage of impaired glucose metabolism in hypertensive patients might specifically deteriorate cardiac diastolic function.²³

4.5. Insulin resistance

Hwang et al. reported abnormal left ventricular structure and diastolic function with insulin resistance as common findings. Metabolic syndrome and insulin resistance was independently associated with an increased risk for LVDD. Further, with the increase of homeostasis model assessment of insulin resistance (HOMA-IR) value, the cardiac structure and LVDD parameters significantly increased and E/A ratio significantly decreased.²⁴

4.6. Dyslipidemia

Khan reported that several cardiac functional abnormalities, regardless of symptoms, increased progressively with increasing degree of metabolic syndrome and found a positive association between serum TG and diastolic dysfunction.²⁵ Roes et al. showed increased aortic pulse wave velocity and LVDD with metabolic syndrome, regardless of blood pressure but independently associated with HDL cholesterol level.²⁶

4.7. Co-morbidities

Chinali et al. showed correlation of abnormal left ventricular geometry and function with metabolic syndrome; after controlling for confounders, participants with the mitral stenosis had greater left ventricular dimension, mass, relative wall thickness, left atrial diameter, higher prevalence of LVH, with lower ejection fraction, midwall shortening, and mitral E/A ratio in metabolic syndrome. In multiple regression modeling, high blood pressure and abdominal obesity were the only components of mitral stenosis associated with increased left ventricular diameter; only hypertension was associated with increased LV mass and LVH.²²

Diamant observed altered myocardial energy metabolism exaggerated left ventricular diastolic functional changes in recently diagnosed well-controlled uncomplicated type 2 diabetes affecting indexes of diastolic function like early acceleration peak, deceleration peak, peak filling rate, and transmitral early-to-late diastolic peak flow (E/A) ratio.²⁷

Boyer et al. observed LVDD in asymptomatic, normotensive patients with type 2 diabetes without significant coronary artery disease was much higher than previously

suspected. Tissue Doppler imaging (TDI) markedly improved the echocardiographic detection of diastolic dysfunction in asymptomatic patients with type 2 diabetes.²⁸

Ahn showed that degree of metabolic syndrome clustering was strongly correlated with geometric eccentricity of LVH, diastolic dysfunction and arterial changes irrespective of age and blood pressure status, particularly in females.²⁰ Cosson and Kevorkian noted that co-existence of diabetic cardiomyopathy enhanced myocardial dysfunction in diabetic patients in absence of ischemic, valvular, or hypertensive heart disease. Diastolic dysfunction was described as an early sign of this diabetic heart muscle disease preceding the systolic damage.²⁹

Wong et al. noted that systolic and diastolic dysfunctions were common even with normal coronary arteries with hypertension, diabetes, and/or obesity and was frequently severe in black population in whom myocardial disease was more common. Significant and incremental variations in left ventricular systolic and diastolic functions were according to the number of components of metabolic syndrome with reduced systolic and diastolic functions even without LVH. A similar dose-response association was present between the number of components of the metabolic syndrome with exercise capacity and arterial compliance.³⁰

Masugata et al. noted diastolic dysfunction without LVH or systolic dysfunction though E/A and Tei index were significantly altered in metabolic syndrome.³¹ Aijaz et al. reported association of isolated metabolic syndrome with increased left ventricular mass index and LVDD in women as evidence of early ventricular dysfunction. Isolated metabolic syndrome was 21.7% in men and 16.7% in women. Left ventricular mass index was greater and LVDD was more in women with isolated metabolic syndrome but no such difference in men.³²

Gong et al. concluded that left ventricular systolic and diastolic functions were impaired in metabolic syndrome even if they had normal left ventricular ejection fraction. Echocardiographic strain and strain-rate imaging would be a sensitive and feasible method to detect subclinical abnormalities among them.³³

5. Conclusions

To sum up, we observed positive correlation between diastolic dysfunction and metabolic syndrome following characteristics of IDF criteria. Diastolic dysfunction is an intriguing diagnosis in metabolic syndrome patients with a high index of suspicion. There is justified need for careful echocardiographic assessment, aiming to identify individuals at higher risk, so that early intervention measures could be carried out like weight reduction or at least stabilization in overweight for moderately obese people.

Conflicts of interest

The authors have none to declare.

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