Impact of metabolic syndrome on global left ventricular function: As evaluated by the myocardial performance index

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Background: Metabolic syndrome is associated with the development of diabetes mellitus and cardiovascular disease. The impact of metabolic syndrome on the progression of atherosclerosis has been well documented. This study was designed to evaluate the impact of metabolic syndrome on global left ventricular function by using left ventricular myocardial performance index (LV MPI).

Methods: The diagnosis of metabolic syndrome was made as per the criteria of the International Diabetes Federation. Echocardiography was performed with a Philips IE33 machine using a 1–5 MHz transthoracic probe. LV MPI was calculated by adding isovolumic contraction time with isovolumic relaxation time and dividing it by ejection time.

Results: The mean LV MPI value in metabolic syndrome was 0.64 ± 0.09, while that in controls was 0.48 ± 0.06 (p < 0.001). Metabolic syndrome was seen to have more significant influence on LV MPI.

Conclusions: Metabolic syndrome is a strong predictor of sub-clinical myocardial dysfunction in subjects free of clinically apparent heart disease.

Keywords: Metabolic syndrome, Myocardial performance index, Isovolumic relaxation time, Isovolumic contraction time

Introduction

Metabolic syndrome (MetS) constitutes a constellation of metabolic abnormalities that confer an increased risk of cardiovascular disease and diabetes mellitus (DM). Although the impact of MetS on the progression of atherosclerosis has been well documented, its effects on left ventricular function have not been extensively evaluated [1–3]. Metabolic syndrome is considered to be an independent risk factor for heart failure.

At least one third of patients with heart failure have both systolic and diastolic dysfunction. A
Doppler-derived index of myocardial performance (Tei index), combining both systolic and diastolic time intervals was introduced in 1995 [4,5]. This index, represented by the sum of isovolumic relaxation time (IVRT) and isovolumic contraction time (IVCT) divided by left ventricular ejection time (ET), is reported to be a sensitive measure of global left ventricular performance. Myocardial performance index can be determined easily using conventional Doppler echocardiography.

Hence, this study was designed to evaluate the impact of MetS on global left ventricular function by using left ventricular myocardial performance index (LVMPI) and to compare it with healthy controls.

Materials and methods

We recruited 50 consecutive patients with MetS attending to the Cardiology Out-patient Department of Sri Venkateswara Institute of Medical Sciences into this prospective case-control study. The diagnosis of MetS was made as per the International Diabetes Federation (IDF) criteria [6]. According to this criteria, diagnosis of MetS was performed with waist circumference ≥90 cm for men or ≥80 cm for women (for South-Asian ethnic group) along with any two of the following: triglyceride (TGL) levels ≥150 mg/dL or treatment for elevated TGL, HDL Cholesterol (HDL-C) levels ≥40 mg/dL for men or ≥50 mg/dL for women; blood pressure ≥130/85 mmHg or undergoing antihypertensive treatment, and fasting glucose levels ≥100 mg/dL or treatment for DM.

The study excluded patients aged above 60 years, patients with structural heart disease, including valvular and ischemic heart disease, patients with atrial fibrillation, atrial flutter and AV blocks, patients with other secondary causes of hyperlipidemia like hypothyroidism and renal insufficiency. Thirty age- and sex-matched healthy controls were recruited into the control cohort. Informed consent was obtained from each of the patients and controls following ethical guidelines of the 1975 Declaration of Helsinki. This study was approved by the Institutional Ethical Committee of Sri Venkateswara Institute of Medical Sciences, Tirupati, Andhra Pradesh, India.

Baseline assessment in all patients included a detailed history, physical examination, and cardiovascular examination. Risk factors like diabetes mellitus, hypertension and obesity were assessed. Anthropometric evaluation included waist circumference which was measured to the nearest centimeter, just above the iliac bones, with the subject standing using a flexible and non-distensible tape. Waist circumference >90 cm was considered as abdominal obesity. Blood pressure was measured twice with a three-minute interval after a 10-min rest with no tight clothes. The mean of the two measurements was recorded. Obesity was defined as body mass index (BMI) greater than 30 kg/m². Plasma glucose, serum triglycerides and serum HDL cholesterol levels were measured using commercially available kits on auto analyzer (Synchron CX9 from Beckman, USA).

Echocardiography was performed with a Philips IE33 (Philips, The Netherlands) machine using a 1–5 MHz transthoracic probe, according to the guidelines of the American Society of Echocardiography [7]. A parasternal long axis view approximately at the level of the mitral valve leaflet tips was used to measure LV wall thickness, end systolic and end diastolic dimensions. The mitral inflow velocity pattern was recorded in the apical 4-chamber view with the pulsed wave Doppler sample volume positioned at the tip of mitral leaflets during diastole. The left ventricular outflow velocity pattern was recorded in the apical 5-chamber view with the pulse wave Doppler volume positioned just below the aortic valve [8].

Both ventricular inflow and outflow patterns were recorded at 100 mm/s sweep speed. Doppler measurements were obtained by an average of five consecutive beats as described by Quiñones et al. [8]. Doppler time intervals were measured from the mitral inflow and left ventricular outflow velocity time intervals. The interval between mitral valve closure and opening corresponds to the time from cessation to onset of mitral inflow and is equal to the sum of IVCT, ET, and the IVRT. Left ventricular ejection time was measured as the duration of the left ventricular outflow velocity profile. Then, myocardial performance index
(MPI) was calculated as the sum of IVCT and IVRT, dividing it by ET. In Doppler tissue imaging, the sample volume was positioned at the medial end of the mitral annulus. Isovolumic contraction time (IVCT) was calculated from mitral valve closure to the aortic valve opening (end of Am to onset of Sm). Ejection time (ET) was calculated from onset of Sm to end of Sm. Isovolumic relaxation time (IVRT) was calculated from aortic valve closure to mitral valve opening (end of Sm to onset of Em). LVMPI was calculated by adding IVCT + IVRT, and dividing it by ET. The LVMPI was then compared with the controls of the non-MetS group [9,10].

**Statistical analysis**

Data was expressed as mean ± SD for continuous variables and numbers with percentages for categorical variables. For quantitative variables, Student’s t-test was used to compare the difference in mean values in the two groups. The association between categorical variables and the outcome was evaluated by χ² test or Fisher’s exact test as appropriate. Results with p < 0.05 were considered to be significant. Stepwise linear regression analysis was used for studying the relationship of LVMPI with the study variables. The correlation between LVMPI derived from tissue Doppler imaging (TDI) and the conventional pulse wave Doppler (PWD) imaging was studied. Statistical analysis was performed with SPSS 20.0 (IBM Corporation, Chicago, IL, USA).

**Results**

Mean age of cases was 40.84 years and that of controls was 44.03 years, with no significant difference (p = 0.089). Thirty-eight percent of cases (19/50) were obese in comparison to 13.3% (4/30) of controls. Mean BMI value in cases was 29.05 ± 4.81, while in controls it was 24.75 ± 4.02 (p = 0.0001). BMI was higher in cases than in controls as obesity is an exogenous risk factor for MetS. All the cases had abdominal obesity as per the inclusion criteria while 60% of the controls (18/30) had abdominal obesity (p < 0.0001).

Incidence of hypertension in cases was 52% (26/50), while in controls it was 3.3% (1/30) (p < 0.0001). In cases, 48% (24/50) were normotensives. In cases, 68% (34/50) were hyperglycemic in contrast to 10% (3/30) in controls (p < 0.0001). Among the cases, 10% (5/50) had impaired fasting glucose (IFG). Comparison of all demographic and clinical characteristics of the study population are summarized and compared with and without MetS groups in Table 1.

Seventy-four percent of cases (37/50) had hypertriglyceridemia, whereas only 10% of controls (3/30) had higher triglyceride values. The mean value of triglycerides in cases was 259.04 ± 208.97 mg/dl, and in controls it was 130.50 ± 89.71 mg/dl (p = 0.002).

Eighty-two percent of cases (41/50) had low HDL-C levels, whereas 46.7% of controls (14/30) had low HDL-C levels. The mean value of HDL-C in cases was 36.92 ± 4.98 mg/dl, and was 40.70 ± 7.70 mg/dl (p = 0.009) in controls. The influence of each studied variable on LVMPI in the study population is summarized in Table 2.

**Distribution of LVMPI by tissue Doppler imaging in the study population**

The mean LVMPI value in cases was 0.64 ± 0.09, while in controls it was 0.48 ± 0.06 (p < 0.0001). In

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**Table 1. Comparison of Demographic and Clinical characteristics.**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>MetS group</th>
<th>Control group</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (M/F)</td>
<td>28/22</td>
<td>18/12</td>
<td>0.90</td>
</tr>
<tr>
<td>Age (years)</td>
<td>40.84 ± 6.58</td>
<td>44.03 ± 9.95</td>
<td>0.09</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>159.09 ± 21.46</td>
<td>164.40 ± 9.04</td>
<td>0.20</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>76.25 ± 13.62</td>
<td>67.07 ± 12.77</td>
<td>0.004*</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.05 ± 4.81</td>
<td>24.75 ± 4.02</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Waist circumference (inch)</td>
<td>99.42 ± 13.63</td>
<td>87.10 ± 10.47</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>259.04 ± 208.97</td>
<td>130.50 ± 89.71</td>
<td>0.002*</td>
</tr>
<tr>
<td>HDLC (mg/dL)</td>
<td>36.92 ± 4.98</td>
<td>40.70 ± 7.71</td>
<td>0.009*</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>132.00 ± 13.48</td>
<td>112.00 ± 9.81</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>88.50 ± 9.98</td>
<td>73.36 ± 6.86</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>FBS (mgs%)</td>
<td>112.84 ± 16.71</td>
<td>84.03 ± 13.37</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>LVMPI-TDI</td>
<td>0.64 ± 0.09</td>
<td>0.48 ± 0.06</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>LVMPI-PWD</td>
<td>0.63 ± 0.08</td>
<td>0.48 ± 0.05</td>
<td>&lt;0.0001*</td>
</tr>
</tbody>
</table>

MetS: metabolic syndrome; M: male; F: female; BMI: Body mass index; HDLC: high density lipoprotein cholesterol; SBP: systolic blood pressure; DBP: diastolic blood pressure; FBS: fasting blood sugar; LVMPI: left ventricular myocardial performance index; TDI: tissue Doppler imaging; PWD: pulse wave Doppler.

* Indicates a significant p-value (p < 0.05).
our study, the components of MetS were seen to have significant influence on LVMPI. The important influencing parameters on LVMPI were identified with the help of Stepwise Multiple Linear Regression analysis. With the Stepwise Multiple Linear Regression analysis model, high waist circumference, high triglycerides and fasting blood sugars were found to be the most influencing variables and were associated with an increased LVMPI (Table 3).

### LVMPi by conventional pulse wave Doppler method

Mean LVMPi with conventional pulse wave Doppler imaging in cases was 0.63 ± 0.08, while in controls, it was 0.48 ± 0.05. Mean LVMPi by conventional pulse wave Doppler method was significantly high in cases when compared to controls ($p < 0.0001$).

Comparison of means of LVMPi obtained by conventional pulse wave Doppler and tissue Doppler imaging is shown in Table 4. There was no significant difference in the mean LVMPi between the two methods ($p = 0.08$). The correlation between the two methods for measuring LVMPi was also good ($r = 0.941$).

### Discussion

The main finding of the present study is that MetS is associated with abnormal myocardial per-

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**Table 2. Influence of each variable on the LVMPI in the study population.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>LVMPI</th>
<th>p-Val for effect of each variable on the study population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obese ($n = 23$)</td>
<td>0.617 ± 0.11</td>
<td>0.101</td>
</tr>
<tr>
<td>Non-obese ($n = 57$)</td>
<td>0.572 ± 0.11</td>
<td></td>
</tr>
<tr>
<td>Visceral obesity ($n = 68$)</td>
<td>0.606 ± 0.103</td>
<td></td>
</tr>
<tr>
<td>Non-visceral obesity ($n = 12$)</td>
<td>0.466 ± 0.064</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Hypertension ($n = 27$)</td>
<td>0.634 ± 0.074</td>
<td></td>
</tr>
<tr>
<td>Normotensives ($n = 53$)</td>
<td>0.561 ± 0.12</td>
<td>0.005*</td>
</tr>
<tr>
<td>IFG/Diabetes ($n = 37$)</td>
<td>0.629 ± 0.096</td>
<td></td>
</tr>
<tr>
<td>Normoglycemics ($n = 43$)</td>
<td>0.548 ± 0.11</td>
<td>0.0008*</td>
</tr>
<tr>
<td>Hypertriglyceridemia ($n = 40$)</td>
<td>0.635 ± 0.088</td>
<td></td>
</tr>
<tr>
<td>Normal triglycerides ($n = 40$)</td>
<td>0.535 ± 0.108</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Decreased HDL-C ($n = 55$)</td>
<td>0.598 ± 0.102</td>
<td></td>
</tr>
<tr>
<td>Normal HDL-C ($n = 25$)</td>
<td>0.558 ± 0.125</td>
<td>0.134</td>
</tr>
</tbody>
</table>

LVMPi: left ventricular myocardial performance index; IFG: impaired fasting glucose; HDL-C: high density lipoprotein cholesterol.

* Indicates a significant $p$-value ($p < 0.05$).

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**Table 3. Stepwise Multiple Linear regression analysis.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unstandardized coefficient</th>
<th>Standardized coefficient Beta</th>
<th>t</th>
<th>p-Val</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist circumference</td>
<td>0.0029 (.001)</td>
<td>.376</td>
<td>2.120</td>
<td>.040*</td>
</tr>
<tr>
<td>BMI</td>
<td>0.000 (.003)</td>
<td>-.009</td>
<td>-0.052</td>
<td>.959</td>
</tr>
<tr>
<td>SBP</td>
<td>-.0007 (.021)</td>
<td>-.065</td>
<td>-0.410</td>
<td>.691</td>
</tr>
<tr>
<td>DBP</td>
<td>-.0009 (.030)</td>
<td>-.072</td>
<td>-0.614</td>
<td>.322</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>0.0002 (.000)</td>
<td>.322</td>
<td>3.417</td>
<td>.001*</td>
</tr>
<tr>
<td>HDL-C</td>
<td>-.003 (.003)</td>
<td>-.169</td>
<td>-1.168</td>
<td>.249</td>
</tr>
<tr>
<td>FBS</td>
<td>-.104 (.043)</td>
<td>-.317</td>
<td>-2.342</td>
<td>.024*</td>
</tr>
</tbody>
</table>

LVMPi as dependent variable and other variables as independent variables.

BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL-C: High density lipoprotein cholesterol; FBS: fasting blood sugar.

* Indicates a significant $p$-value ($p < 0.05$).

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**Table 4. Comparison of LVMPi by Pulse wave Doppler and tissue Doppler imaging:**

<table>
<thead>
<tr>
<th></th>
<th>Mean LVMPI (PWD)</th>
<th>N</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVMPi (PWD)</td>
<td>0.575</td>
<td>80</td>
<td>0.1029</td>
<td>.0115</td>
<td></td>
</tr>
<tr>
<td>LVMPi (TDI)</td>
<td>0.583</td>
<td>80</td>
<td>0.1124</td>
<td>.0126</td>
<td></td>
</tr>
</tbody>
</table>

LVMPi: left ventricular myocardial performance index; PWD: pulse wave Doppler; TDI: tissue Doppler imaging.

* Indicates a significant $p$-value ($p < 0.05$).
formance as assessed by the Tei index in the Asian-Indian population.

The mean value of BMI was 29.05 ± 4.81 in our study cases, while in the study by Turhan et al. [11] it was 30 ± 4, both of which are comparable. Twenty-nine percent of the study population had obesity (BMI > 30 kg/m²) with higher mean LVMPI values than in non-obese cases (0.62 ± 0.11 vs 0.57 ± 0.11, p = 0.121). This is in accordance with a study published by Dayi et al. where weight loss was associated with a decrease in LVMPI values [12]. Using a cutoff value of BMI ≥ 30 kg/m², 38% of cases and 13.3% of controls were obese. In their recent guidelines, the Indian Council of Medical Research (ICMR) lowered the BMI threshold for Indians due to the higher incidence of insulin resistance than their western counterparts [13]. According to this classification, BMI of less than 18.4 kg/m² is underweight, 18.5–22.9 kg/m² is normal, 23–24.9 kg/m² is overweight, and more than or equal to 25 kg/m² is considered obese. Using this new classification, 76% of cases and 44% of controls were obese.

We also found that visceral obesity assessed by waist circumference is more predictive of MetS than obesity assessed by BMI. This was explained by the fact that among our cases all had abdominal obesity by definition and only 38% were obese (BMI > 30 kg/m²). This is in accordance with the finding that increased intra-abdominal fat is associated with worse metabolic profile and elevated pro-inflammatory cytokines, as in the study published by Després and Limieux in Nature in 2006 [14]. The same finding was also noted in the study by Voulgari et al. [15].

In the present study, 66% of the study population were normotensives with higher LVMPI values (0.561 ± 0.12). This shows that MetS per se, irrespective of hypertension, is associated with changes in cardiac function. This is in accordance with the study by Voulgari et al., which found that 18% of cases were normotensives with higher LVMPI values [15]. The Strong Heart Study reported worse left ventricular function in subjects with MetS, and a history of hypertension was the strongest predictor of changes in left ventricular geometry followed by other components of MetS [16].

In our present study, MetS as a whole was seen to have a more significant influence on LVMPI than each of its individual components. In Women’s Health Study, cardiovascular mortality was found to increase linearly as the number of components of MetS increased [3].

In the evaluation of left ventricular function it is important to use the parameters that reflect both systolic and diastolic dysfunction, as approximately one-third of heart failure patients have impairment of both systolic and diastolic function. In the assessment of the Tei index, left ventricular systolic dysfunction shortens ejection time and prolongs IVCT, while left ventricular diastolic dysfunction prolongs IVRT. The Tei index has proved to be more effective for analysis of global myocardial performance than systolic or diastolic indices alone [17]. Additionally, data have shown that a higher value of the Tei index is associated with increased cardiovascular risk [18].

Although the impact of obesity and diabetes on left ventricular function has been studied extensively, there are a few studies that demonstrate the effects of MetS on left ventricular function. Further, it was found that patients with idiopathic dilated cardiomyopathy have high prevalence of insulin resistance, suggesting a possible link with MetS [19]. In this regard, we evaluated left ventricular function in MetS with the Tei index.

Previous studies have shown abnormal myocardial performances in MetS. A study by Chinali et al. has shown significant alteration in diastolic function using echocardiographic examination in American Indians with MetS [20]. Wong et al. showed impairment of both systolic and diastolic dysfunction in MetS using global strain rate [21]. Dutta et al. evaluated the impact of insulin resistance on cardiomyocyte function in sucrose fed rats and showed that contraction and relaxation are prolonged with insulin resistance. They hypothesized that alteration in matrix proteins caused by the accumulation of advanced glycation end products can lead to increased stiffening of the heart [22]. Rutter et al. in the Framingham Heart sub study on the impact of insulin resistance on cardiac function found significant shortening of ET in patients of insulin resistance. This shortening of ET is mainly related to left ventricular systolic dysfunction and can lead to an increase in LVMPI values. In the Framingham off spring study, progressively increasing glucose intolerance is associated with increasing left ventricular mass and wall thickness [23].

The present study has a higher mean Tei index value in its study population (0.64 ± 0.09 vs 0.48 ± 0.06, p < 0.001) than previous studies done by Turhan et al. (0.55 ± 0.06 vs 0.38 ± 0.04, p < 0.001); and Voulgari et al. (0.41 ± 0.04, p < 0.001) [11,15]. This can be explained by the fact that the incidence of metabolic risk factors like hypertension, diabetes and dyslipidemia were higher in a
study population with poorly controlled risk factors.

In the multivariate analysis of the present study, variables of MetS which were shown to have a strong association with the Tei index are waist circumference, and high TGL and FBS levels. In the study by Voulgari et al. [15] variables shown to have a strong association with the Tei index were high blood glucose, hypertension, and low HDL-C levels. The regression analysis of our study implies that patients can have abnormal myocardial performance values based on the performance of these three variables.

Our study also found that the Tei index is more sensitive than conventional systolic or diastolic indices. Left ventricular systolic function as assessed by LVEF was normal in the entire study population, and diastolic function as assessed by E/A ratio and Em was also normal in a significant number of study participants. In a prospective study by Tei et al. LVMPI better correlated with the TAU index (left ventricular relaxation time constant) assessed invasively, than conventional diastolic indices [24].

With the above findings, it is apparent that diagnosis of abnormal myocardial performance in patients of MetS can be made with the help of LVMPI when most of the conventional systolic and diastolic indices are normal. Left ventricular myocardial performance index (LVMPI) is useful not only for evaluating ventricular function but also the impact of the therapeutic approach on myocardial function.

Mean LVMPI as estimated by conventional pulse wave Doppler imaging was significantly increased in cases than in controls (0.63 vs 0.48, p < 0.001). LVMPI, as estimated by conventional pulse wave Doppler, correlated well with that estimated by tissue Doppler imaging (r = 0.941). A study by Tekten et al. [10] shows that LVMPI by both methods had good correlation.

Evidently, MetS adds important prognostic information in terms of cardiovascular risk prediction. Additionally, recent data demonstrate that MetS is associated with a twofold increased risk of heart failure irrespective of established risk factors including myocardial infarction [25]. The recent guidelines for the management of hypertension suggest that blood pressure levels of more than 130/85 mmHg in these patients should be treated [26].

Conclusions

Metabolic syndrome is a strong predictor of myocardial dysfunction in subjects free of clinically apparent heart disease. Strategies should aim at prevention of MetS to reduce the cardiovascular burden and risk of heart failure.

Limitations

1. Load dependency of the Tei index: This is important in critically ill patients who have acute changes in pre load and after load. But the majority of our patients were hemodynamically stable. Further, measurement of the Tei index by tissue Doppler is independent of load changes.
2. Pseudo normalization of the Tei index: As diastolic pressures increase to restrictive filling states the Tei index decreases due to decrease in IVRT. However, the majority of our patients were in Grade I diastolic dysfunction.
3. The Tei index, determined by tissue Doppler imaging, takes into consideration only myocardial fiber shortening along its long axis. Circumferential fiber shortening is not taken into consideration.
4. Open label study.
5. Possibility of sub clinical coronary artery disease in the study population.

Acknowledgement

None.

References


