ASSESSMENT OF LEFT VENTRICULAR STRUCTURES AND FUNCTIONS IN PATIENTS WITH METABOLIC SYNDROME BY TRANSTHORACIC ECHOCARDIOGRAPHY AND TISSUE DOPPLER STUDY

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ABSTRACT:

Background and Aim

Metabolic syndrome is a multiplex risk factor that arises from insulin resistance accompanying abnormal adipose deposition and function. It is a risk factor for coronary heart disease, as well as diabetes, fatty liver, and several cancers. The clinical manifestations of this syndrome may include hypertension, hyperglycemia, hypertriglyceridemia, reduced high-density lipoprotein cholesterol (HDL-C), and abdominal obesity.

Aim of the study: This study aimed to evaluate the effects of the metabolic syndrome and the individual components of the metabolic syndrome on LV structures and functions by transthoracic echocardiography and tissue Doppler study.

Patients And Methods Selected 60 persons were included. All of them underwent echocardiographic assessment at Echocardiography Unit, Al-Azhar University Hospital (Assiut). Those patients were classified into three groups:

1-Control Group (A): 20 persons with absent (0) any criteria of metabolic syndrome.
2-Study Group (B): 20 persons with pre-metabolic syndrome (1-2 criteria).
3-Study Group (C): 20 persons with metabolic syndrome (≥3 criteria).

Results:

As regard LV MPI by PWD there was statistically significant difference between the three groups. As regard LV MPI by TDI there was statistically significant difference between the three groups. As regard LV global S wave by TDI there was statistically significant difference between the three groups. As regard MV E/A ratio there was statistically significant difference between the three groups. As regard MV E/E' ratio there was statistically significant difference between the three groups. As regard IVRT there was statistically significant difference between the three groups. As regard LVM/Ht2.7 there was statistically significant difference between the three groups. As regard LV RWT there was statistically significant difference between the three groups.

Conclusion:

1-MetS associated with more tendency to increase in LV mass and so more tendency to LVH, and the same thing about RWT.  
2-There was strong relationship between number of criteria and impairment of LV function and increased LV mass; so, persons who have more criteria of metabolic syndrome were more impaired in LV function and with greater number of LVH.  
3-In evaluation of LV functions by echocardiography some methods tend to be more accurate in early diagnosis of impairment of LV functions; for example: MPI by TDI is better than MPI.
by PWD in assessment of systolic function, on other hand in assessment of diastolic function both MV E/E’ and IVRT are preferred than other methods.

Key word : Metabolic Syndrome Met S, Tissue Doppler Imaging TDI,Myocardial prefermance Index ,MPI ,Pulsed Wave Doppler ,PWD

I. INTRODUCTION

Metabolic syndrome is a multiplex risk factor that arises from insulin resistance accompanying abnormal adipose deposition and function. It is a risk factor for coronary heart disease, as well as diabetes, fatty liver, and several cancers. The clinical manifestations of this syndrome may include hypertension, hyperglycemia, hypertriglyceridemia, reduced high-density lipoprotein cholesterol (HDL-C), and abdominal obesity [1]. The metabolic syndrome represents a clustering of cardiovascular risk factors affecting approximately 22% of the adult population in industrialized countries and over 40% of the those aged 50 and older [2]. Under current guidelines, revised in 2005 by the National Heart, Lung, and Blood Institute (NHLBI) and the American Heart Association (AHA), metabolic syndrome is diagnosed when a patient has at least 3 of the following 5 conditions: 1-Fasting glucose ≥100 mg/dL (or receiving drug therapy for hyperglycemia)

2-Blood pressure ≥130/85 mm Hg (or receiving drug therapy for hypertension)

3-Triglycerides ≥150 mg/dL (or receiving drug therapy for hypertriglyceridemia) 4-HDL-C < 40 mg/dL in men or < 50 mg/dL in women (or receiving drug therapy for reduced HDL-C) 5-Waist circumference ≥102 cm (40 in) in men or ≥88 cm (35 in) in women; if Asian American, ≥90 cm (35 in) in men or ≥80 cm (32 in) in women (The international diabetes federation [IDF] criteria allow the use of a body mass index [BMI] >30 kg/m2 in lieu of the waist circumference criterion.) [3].

Abundant data suggest that patients meeting these diagnostic criteria have a greater risk of significant clinical consequences, the 2 most prominent of which are the development of diabetes mellitus and of coronary heart disease (Hanley, et al. 2005). Pooled data from 37 studies involving more than 170,000 patients have shown that metabolic syndrome doubles the risk of coronary artery disease [4]. It also increases risk of stroke, fatty liver disease, and cancer [5].LV hypertrophy (LVH) imparts increased risk of cardiovascular morbidity and mortality, including development of systolic and diastolic dysfunction, and progression to heart failure [6]. Although the progressive addition of metabolic syndrome risk factors, such as obesity, diabetes, and/or dyslipidaemia, is associated with increased LV mass, independent of hypertension, the effects of the metabolic syndrome and of each of its component criteria on cardiac structure and function has not been well characterized [7].

Aim of the study: This study aimed to evaluate the effects of the metabolic syndrome and the individual components of the metabolic syndrome on LV structures and functions by transthoracic echocardiography and tissue Doppler study.

Patients And Methods Selected 60 persons were included. All of them underwent echocardiographic assessment at Echocardiography Unit, Al-Azhar University Hospital (Assiut), Those patients were classified into three groups:

1-Control Group (A): 20 personswith absent (0) any criteria of metabolic syndrome.

2-Study Group (B): 20 personswith pre-metabolic syndrome (1-2 criteria).

3-Study Group (C): 20 personswith metabolic syndrome (≥3 criteria).

Inclusion Criteria: Metabolic syndrome is diagnosed when a patient has at least 3 of the following 5 conditions:

A. Fasting glucose ≥100 mg/dL (or receiving drug therapy for hyperglycemia).

B. Blood pressure ≥130/85 mm Hg (or receiving drug therapy for hypertension).

C. Triglycerides ≥150 mg/dL (or receiving drug therapy for hypertriglyceridemia).D. HDL-C < 40 mg/dL in men or < 50 mg/dL in women (or receiving drug therapy for reduced HDL-C). E. Waist circumference ≥102 cm (40 in) in men or ≥88 cm (35 in) in women; if Asian American, ≥90 cm (35 in) in men or ≥80 cm (32 in) in women (The international diabetes federation [IDF] criteria allow the use of a body mass index [BMI] ≥30 kg/m2 in lieu of the waist circumference criterion.) [8].
Exclusion Criteria: -History or findings of cardiovascular disease include heart failure symptoms or systolic dys-
duction (LVEF < 55%). -Coronary artery disease. -Significant valvular heart disease (i.e. greater than mild valvu-
lar insufficiency or stenosis). -Hypertrophic cardiomyopathy. -Pregnancy or lactating. - Major systemic illness
(e.g. advanced liver disease and renal disease).

II. METHODS

All patients underwent the following:

1- Informed consent.

2- History taking: with emphasis on the following: Age & sex Presence of other risk factors for CAD.

3- Clinical Assessment: Full clinical examination was carried out on every patient with special emphasis on the
following data: Pulse: rate and rhythm. Blood pressure. Head and neck examination. Upper and lower limb ex-
amination. Chest and heart examination, for heart sounds, additional heart sounds and murmur and the back for
lung congestion.

4- Resting 12 lead Electrocardiography.

5- Echocardiographic evaluation: A Vivid 7 phased array system equipped were used, complete Transthoracic
Echocardiographic examination including Conventional Echocardiography and Tissue Doppler Echocardiography.
All echocardiographic examinations were performed after 20–30 min of rest with the patient in quiet respiration in
the partial left lateral decubitus position, using a 2–4 MHz transducer, and were accompanied by recording resting
electrocardiography. All measurements were obtained online and echocardiographic parameters were measured ac-
cording to the American Society of Echocardiography Values with each parameter was obtained by averaging measurements from three successive cardiac cycles. Assessment of left ventricular systolic function: By conventional echocardiography and pulsed wave Doppler: By calculating Ejection Fraction (EF) using: M-mode method: Measuring the dimension of left ventricle, from the leading edge of septal endocardial echo to the leading edge of posterior wall of endocardium By using Ticehol’s equation: Ejection Fraction (EF) (%) = (LVIDd³ – LVISd³) / LVIDd³ × 100 [9].

Biplane method Done by manual tracing of the endocardial border of LV in the apical four chambers and apical
two chambers views for detecting LVEDV, LVESV in both views for calculating EF[10]. Pulsed Wave Myocar-
dial Performance Index (PW-MPI): Mitral inflow and left ventricular outflow velocity-time intervals were used to
measure Doppler time intervals: The interval ‘A’ from the cessation to the onset of mitral inflow was equal to the
sum of Isovolumetric Contraction Time (IVCT), Ejection Time (ET), and Isovolumetric Relaxation Time
(IVRT). Left ventricular ET ‘B’ was the duration of the left ventricular Ejection during systole. Thus, the sum of
IVCT and IVRT was obtained by subtracting ‘B’ from ‘A’, The MPI was calculated as (A - B)/B [11].

The normal myocardial performance index is about 0.4 with higher values, typically ranging from 0.6 to >1.0,
indicating ventricular dysfunction [12].
By Tissue Doppler Imaging (TDI):

By activating the TDI function in the echocardiography machine the mitral annular velocities were recorded using the pulsed-wave TDI. A variable frequency phased array transducer (2.0-4.0 MHz) was used. The filter settings were kept low (50 Hz) and gains were adjusted at the optimal level for good quality velocity. From the apical 4-chamber view, the following was calculated:

The longitudinal mitral annular velocities were recorded from Septal, lateral, anterior and inferior LV sites:

i. The positive peak systolic velocity when the mitral ring moved toward the cardiac apex due to longitudinal contraction of the LV (S wave). Two negative diastolic velocities when the mitral annulus moved toward the base away from the apex, one during the early phase of diastole (E’) and the other in the late phase of diastole (A’)[12].

- Average S Wave
- The mitral annular positive peak systolic velocities were recorded from Septal, lateral, anterior and inferior LV sites. A mean value for the above four sites was used to assess global systolic function. Normal value of average S wave considered between 6.8 and 12.2 cm/s,[14].
- Myocardial performance index by TDI (MPI-TDI).
- This was done by TDI velocity time intervals were measured from the sites at mitral annulus at the septal & lateral segments:

  TDI isovolumetric contraction time (IVCT) was measured between cessation of A’ wave and onset of S’ wave.
  TDI ejection time (ET) was obtained between onset and cessation of S’ wave.
  TDI isovolumetric relaxation time (IVRT) was obtained between cessation of S wave and onset of E’ wave.

MPI-TDI was calculated as (IVCT+IVRT)/ (ET)[15]. As mentioned above; MPI from 0.6 to >1.0, indicating ventricular dysfunction.

Assessment of LV diastolic function:

This was done as the following:
Transmitral LV inflow measurements:

The Doppler beam was aligned to the direction of flow and a 1- to 2-mm sample volume placed between the tips of the mitral leaflets during diastole, in the apical 4 chamber view for detecting:

Transmitral early velocity wave (E wave)

Transmitrallate velocity wave (A wave).

Deceleration Time(DT); measured along the descending slope of mitral flow A wave.DT between 150 and 200 msec. considered normal (Otto, 2013).

E/A ratio; ( normally>0.8 ) [16].

Isovolumic Relaxation Time:

Measured by TDI-PWD at left ventricular basal lateral wall from the end of systolic velocity wave (S wave) to the onset of early diastolic wave (E’ wave). Normal range of IVRT is between 60 and 100 msec[12].

MV E/E’ ratio:

Measured by TDI-PWD to obtain mitral inflow early diastolic velocity wave E’ then calculating E/E’ ratio.

E/E’ relates to left atrial pressure. E/E’ <8 suggests normal left atrial pressure and E/E’ > 15 suggests elevated left atrial pressure [9].

Assessment of LV mass index and RWT:

The relative wall thickness (RWT) was calculated as follows: (2×posterior wall thickness / LV internal diameter). The LV mass was determined by the M-mode-derived cubed method and indexed to height2.7 (LVM/Ht2.7) to correct for body habitus; LVH was defined as LVM/Ht2.7 ≥ 51 g/m2.7 for men and ≥ 49.5 g/m 2.7 for women [17].

A. Statistical analysis of data

Statistics were done by computer using Graph Pad Instat& Med-Calc software, word processing data base and statistics programs.

(Mean)X (standard deviation) SD (to measure the central tendency of data and the distribution of data around their mean).

Data were described as mean ± standard deviation (SD) for quantitative (Numerical) variables to measure the central tendency of data & the distribution of data around their mean and as frequency& percentage for qualitative (Categorical) variables.

\[
\text{Mean} = \frac{\sum x}{n} \quad \text{(Where } \sum = \text{sum } n= \text{ number of observations)}
\]

\[
\text{Standard Deviation [SD] :} \quad SD = \sqrt{\frac{\sum (x - \bar{x})^2}{n - 1}}
\]

\[
\text{Standard Error [SE]:} \quad SE = \frac{SD}{\sqrt{n}}
\]

The tests used were:
1-Unpaired t test: used to compare different variables between both groups:
- Significant statistical results were considered if P value <0.05.
- Highly significant results were considered if P value < 0.01.
- Extremely significant results were considered if P value < 0.001.

2- F’ analysis of variance` (or ANOVA test) to test statistical significant difference (P-value) between variable means at the same time:
Significant result is considered if P < 0.05.
Highly significant result is considered if P < 0.005.
Very high significant result is considered if P < 0.001.

3- Chi-square test was used for comparison of distribution of qualitative variables among different group.

4- Pearson Correlation = r- value has:
Strong correlation if > 0.7
Average correlation if between 0.4 - 0.7
Weak correlation if < 0.4
Positive values have direct correlations and negative values have inverse correlations.

III. RESULTS

I-Comparison between the two groups according to patient’s demographic characteristics:

1-Age:
As shown in table (2) the mean age of group A was 35.15 years ± 11.18 while the mean age of group B was 44.55 years ±10.93, and in group C was 46.35 years±7.37 there was statistically significant difference between the three groups as regard Age (P-value = 0.0016).

<table>
<thead>
<tr>
<th>Group</th>
<th>AGE</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>± SD</td>
</tr>
<tr>
<td>Group A</td>
<td>35.15</td>
<td>11.18</td>
</tr>
<tr>
<td>Group B</td>
<td>44.55</td>
<td>10.93</td>
</tr>
<tr>
<td>Group C</td>
<td>46.35</td>
<td>7.37</td>
</tr>
</tbody>
</table>

Figure 15. Comparison between the three groups according to Age.

2- Gender:
There was no statistically significant difference between the three groups as regard sex. (P-value = 1.0).

Table 3. comparison between the three groups according to sex.

<table>
<thead>
<tr>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
</table>

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II-Comparison between the three groups according to patient’s Echocardiographic data:

1-MPI Obtained by PWD:

As regard MPI by PWD:

In group A: MPI by PWD (mean ± SD) was 0.41± 0.02.
In group B: MPI by PWD (mean ± SD) was 0.44 ± 0.03.
In group C: MPI by PWD (mean ± SD) was 0.48± 0.08.

MPI by PWD difference between the three groups was extremely significant (P value = 0.0010).

Table 4. Comparison between the three groups according to MPI by PW doppler.

<table>
<thead>
<tr>
<th>Group</th>
<th>MPI by PWD</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td></td>
</tr>
<tr>
<td>Group A</td>
<td>0.41 ± 0.02</td>
<td>0.0010</td>
</tr>
<tr>
<td>Group B</td>
<td>0.44 ± 0.03</td>
<td></td>
</tr>
<tr>
<td>Group C</td>
<td>0.48 ± 0.08</td>
<td></td>
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</tbody>
</table>

II-Comparison between the three groups according to gender:

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Males</td>
<td>10</td>
<td>50%</td>
<td>8</td>
</tr>
<tr>
<td>Females</td>
<td>10</td>
<td>50%</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
<td>100%</td>
<td>20</td>
</tr>
</tbody>
</table>

Figure 16. Comparison between the three groups according to gender.

2-MPI Obtained by TDI:

By analysis of values of MPI by TDI we found:

In group A: MPI by TDI (mean ± SD) was 0.47± 0.02.
In group B: MPI by TDI (mean ± SD) was 0.44 ± 0.03.
In group C: MPI by TDI (mean ± SD) was 0.55 ± 0.12.

MPI by TDI difference between the three groups was extremely significant (P value < 0.0001).

Table 5. Comparison between the three groups according to MPI by TDI.

<table>
<thead>
<tr>
<th></th>
<th>MPI by TDI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
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Figure 18. Comparison between the three groups as regard MPI by TDI.

3-S wave by TDI:

Results of analysis of S wave by TDI were as follow:

In group A: S wave by TDI (mean ± SD) was 12.4 ± 1.46.
In group B: S wave by TDI (mean ± SD) was 10.1 ± 1.23.
In group C: S wave by TDI (mean ± SD) was 9.3 ± 2.08.

S wave difference between the three groups was extremely significant (P value < 0.0001).

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean ± SD</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>0.47 ± 0.02</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Group B</td>
<td>0.44 ± 0.03</td>
<td></td>
</tr>
<tr>
<td>Group C</td>
<td>0.55 ± 0.12</td>
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</table>

Table 6. Comparison between the three groups according to S wave by TDI.

4-Comparison between the three groups according to MV E/A:

When comparing E/A ratio between the three group we found:

In group A: MV E/A (mean ± SD) was 1.35 ± 0.13.
In group B: MV E/A (mean ± SD) was 0.95 ± 0.22.
In group C: MV E/A (mean ± SD) was 0.83 ± 0.20.

Figure 19. Comparison between the three groups as regard S wave by TDI.
E/A difference between the two groups was extremely significant (P value < 0.0001).

<table>
<thead>
<tr>
<th>Group</th>
<th>E/A</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>1.35 ± 0.13</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Group B</td>
<td>0.95 ± 0.22</td>
<td></td>
</tr>
<tr>
<td>Group C</td>
<td>0.83 ± 0.20</td>
<td></td>
</tr>
</tbody>
</table>

5-Comparison between the three groups according to MV E/E':

MV E/E' ratio revealed the following:

In group A: MV E/E' (mean ± SD) was 5.32 ± 1.09.

In group B: MV E/E' (mean ± SD) was 10.11 ± 4.72.

In group C: MV E/E' (mean ± SD) was 13.29 ± 3.92.

E/ E' difference between the two groups was extremely significant (P value < 0.0001).
6-Comparison between the three groups according to IVRT:

Results of IVRT:

In group A: IVRT (mean ± SD) was 74.65±4.91ms.
In group B: IVRT (mean ± SD) was 90.45±25.78ms.
In group C: IVRT (mean ± SD) was 100.55±24.91ms.

IVRT difference between the three groups was extremely statistically significant (P value < 0.0001).

<table>
<thead>
<tr>
<th>Group</th>
<th>IVRT (mean ± SD)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>74.65 ± 4.91</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>B</td>
<td>90.45 ± 25.78</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>100.55 ± 24.91</td>
<td></td>
</tr>
</tbody>
</table>

7-Comparison between the three groups according to LV mass indexed to Ht2.7:

When LV mass indexed to Ht2.7:

In group A: LVMI to Ht2.7 (mean ± SD) was 24.45± 9.28 g/m2.7.
In group B: LVMI to Ht2.7 (mean ± SD) was 40.91 ± 8.40 g/m2.7.
In group C: LVMI to Ht2.7 (mean ± SD) was 41.78 ± 10.57 g/m2.7.

LVMI to Ht2.7 difference between the three groups was extremely statistically significant (P value < 0.0001).

<table>
<thead>
<tr>
<th>LVMI to Ht&lt;sup&gt;2.7&lt;/sup&gt;</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Comparison of LV RWT revealed:

In group A: LV RWT (mean ± SD) was 0.36 ± 0.03.
In group B: LV RWT (mean ± SD) was 0.38 ± 0.08.
In group C: LV RWT (mean ± SD) was 0.48 ± 0.09.

LV RWT difference between the three groups was extremely statistically significant (P value < 0.0001).

Table 11. Comparison between the three groups as regard RWT

<table>
<thead>
<tr>
<th>Group</th>
<th>LV RWT</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td></td>
</tr>
<tr>
<td>Group A</td>
<td>0.36 ± 0.03</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Group B</td>
<td>0.38 ± 0.08</td>
<td></td>
</tr>
<tr>
<td>Group C</td>
<td>0.48 ± 0.09</td>
<td></td>
</tr>
</tbody>
</table>

Figure 23. Comparison between the three groups as regard LVMi to Ht2.7

8-Comparison between the three groups according to LV Relative Wall Thickness

Figure 24. Comparison between the three groups as regard LV RWT.
9-Correlation Number of criteria of MetS and Left ventricular MPI by TDI:

There was strong positive correlation between number of criteria of MetS and Left ventricular MPI by TDI, \( r = 0.58 \) and \( P \) value \(< 0.0001 \), considered extremely significant.

Figure 25. Correlation between number of criteria of MetS and Left ventricular MPI by TDI.

10-Correlation Number of criteria of MetS and MV E/E':

There was strong positive correlation between number of criteria of MetS and MV E/E', \( r = 0.67 \) and \( P \) value \(< 0.0001 \), considered extremely significant.

Figure 26. Correlation between number of criteria of MetS and E/E'.

11-Correlation Number of criteria of MetS and LVM/Ht2.7:

There was strong positive correlation between number of criteria of MetS and LVM/Ht2.7, \( r = 0.56 \) and \( P \) value \(< 0.0001 \), considered extremely significant.

Figure 27. Correlation between number of criteria of MetS and LVM/Ht2.7.

From these data we found that:

A) There is statistically significant difference between the three groups according to:

- LV systolic function parameter as: PWD MPI, TDI MPI or S wave by TDI.
- LV diastolic function parameter as: MV E/A, MV E/E’ or IVRT.
- LVM/Ht2.7 and LV RWT.

B) There is strong relationship between affection of these parameters and number of MetS criteria.

Selected Cases

Case No. (47)
Figure 28 (A&B). Shows measurement of MPI by pulsed TDI on MV annulus; IVRT=111 ms, IVCT=82 ms and ET=244 ms (TDI MPI=0.79).

Figure 29. Shows measurements of LVIDd, IVS and LVPW by M-mode in left parasternal long axis view (concentric LVH; LVMl/HT2.7=93.9 g/m2.7 and RWRT=0.65).
Figure 30. Shows pulsed tissue Doppler at lateral MV annulus for measurement of systolic velocity (S wave=5 cm/s).

Case No(57)

Figure 31. Shows measurement of IVRT, IVCT and ET by TDI on septal MV annulus (IVRT=107 ms, IVCT=115 ms and TDI MPI= 0.83).
Figure 32. Shows measurement of MV deceleration time (DT) from apical 4-chambers by PWD by placing sample volume on tips of MV leaflets (DT=152 ms).

Figure 33. Shows measurement of MV E/A ratio from apical 4-chambers by PWD by placing sample volume on tips of MV leaflets (pseudonormal pattern E/A=1.15).
IV. DISCUSSION:

Metabolic syndrome (MetS) is a complex disorder with high socioeconomic cost that is considered a worldwide epidemic. MetS is defined by a cluster of interconnected factors that directly increase the risk of coronary heart disease (CHD), other forms of cardiovascular atherosclerotic diseases (CVD), and diabetes mellitus type 2 (DMT2). Its main components are dyslipidemia (elevated triglycerides, and low high-density lipoproteins (HDL)), elevation of arterial blood pressure (BP) and dysregulated glucose homeostasis, while abdominal obesity and/or insulin resistance (IR) have gained increasing attention as the core manifestations of the syndrome. Recently, other abnormalities such as chronic proinflammatory and prothrombotic states, non-alcoholic fatty liver disease and sleep apnea have been added to the entity of the syndrome, making its definition even more complex. Besides the many components and clinical implications of MetS, there is still no universally accepted pathogenic mechanism or clearly defined diagnostic criteria. Furthermore, there is still debate as to whether this entity represents a specific syndrome or is a surrogate of combined risk factors that put the individual at particular risk. A main evolving aspect of MetS is its increasing prevalence in both childhood and young adulthood and the future implications to the global health burden this may confer [18].

The quantification of cardiac chamber size and function is the cornerstone of cardiac imaging, with echocardiography being the most commonly used noninvasive modality because of its unique ability to provide real-time images of the beating heart, combined with its availability and portability [19], so that it is a good tool to evaluate LV function and structure in MetS.

While until now heart failure had been usually considered in terms of systolic failure with a reduced ejection fraction, there is growing appreciation that diastolic dysfunction, which has been relatively neglected in comparison with abnormalities in systolic function, may also play a significant role. Approximately half the patients presenting with signs and symptoms of heart failure have a normal left ventricular ejection fraction but an abnormality in the diastolic properties of the left ventricle, and a history of hypertension is common in such patients [20]. Left ventricular diastolic dysfunction usually precedes systolic dysfunction [21], characterized by abnormal relaxation in the early stages [22].

Diastolic dysfunction can be assessed by tissue Doppler imaging (TDI), which allows the determination of myocardial systolic and diastolic velocities in the myocardium [23].

The aim of this study is to evaluate impact of metabolic syndrome on LV function and structure.

For this purpose left ventricular function and structure were assessed by Echocardiography (Conventional Doppler & Tissue Doppler Imaging) in sixty persons referred to our Echocardiography unit in Cardiology department, Al-Azhar Assuit University Hospital.

This study includes three groups;
Group A (Normal); 20 persons have no criteria of metabolic syndrome.

Group B (Pre metabolic); 20 persons have one or two of criteria of metabolic syndrome.

Group C (Metabolic); 20 persons have three or more of criteria of metabolic syndrome.

This study show the following:

There was strong relationship between number of criteria and impairment of LV function and increased LV mass; so, persons who have more criteria of metabolic syndrome were more impaired in LV function and with greater number of LVH.

1- Left Ventricular Systolic Function;

All patients included in this study show normal LV systolic function as assessed by either by EF- Simpson method and EF-M mode method but when using MPI (Tei index) either by PWD method or TDI method there was statically significant different between three groups with higher values in patients with metabolic syndrome.

As regard MPI by PWD (mean ± SD ): In group(A) was 0.41± 0.02 and in group (B) was 0.44 ± 0.03 while in group (C) MPI by PWD was 0.48 ± 0.08 ( P value = 0.0010).Results for MPI by TDI were 0.47± 0.02 for group (A), 0.44 ± 0.0 for group (B) and 0.55 ± 0.12 for group (C) ( P value < 0.0001).

This came in agreement with Sreenivasa, et al., 2014 who found that Metabolic syndrome is a strong predictor of sub-clinical myocardial dysfunction in subjects free of clinically apparent heart disease. The study included 50 patients with MetS and 30 in control group who were assessed by echocardiography to calculate MPI (Tei index). Mean LVMI 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) [24].

As regard S wave (Vs global) by TDI: In group (A) S wave by TDI (mean ± SD ) was 12.4± 1.46 and in group (B) was 10.1 ± 1.23 and in group( C) S wave by TDI was 9.3 ± 2.08.

This came partially in agreement with Lisa, et al., 2007, Although the LVEF was similar among the three groups, the TDI-derived septal S wave, but not global S wave, (measures of longitudinal systolic myocardial contractility) was significantly lower in the metabolic syndrome group compared with the normal group (P = 0.006) [25].

2- Left Ventricular Diastolic Function;

There was statically significant difference between the three groups as regard diastolic function by different echocardiographic parameters. Persons with MetS were more liable for diastolic dysfunction.

As regard E/A: (mean ± SD ):In group(A) was 1.35± 0.13 and in group (B) was 0.95 ± 0.22while in group (C) E/A was 0.83 ± 0.20 ( P value < 0.0001).

When comparing MV E/ E': (mean ± SD ):In group(A) was 5.32± 1.09and in group (B) was 10.11 ± 4.72 while in group (C) MV E/ E’ was 13.29 ± 3.92 ( P value < 0.0001).

As regard IVRT: (mean ± SD ):In group(A) was 74.65±4.91 ms and in group (B) was 90.45± 25.78 ms while in group (C) IVRT was 100.55±24.91 ms ( P value < 0.0001).

This results came in agreement with Lisa, et al., 2007, which reveals measurements of LV diastolic function worsened progressively from the absent to the pre-metabolic syndrome and metabolic syndrome groups, indicating impairment in diastolic function with increasing burden of metabolic syndrome. This study consisted of 607 subjects, aged 21 and older meeting study criteria and devided in three groups normal, pre-metabolic and metabolic. Results of the study exhibited a stepwise decrease in E/A ratio from the Absent to the pre-metabolic Syndrome to the Metabolic Syndrome groups, primarily a result of increased A-wave velocity; the DT and IVRT were significantly longer in the metabolic syndrome group. The TDI-derived Veseptal and Ve global were significantly lower in both the metabolic syndrome and pre- metabolic syndrome than in the absent group (P =0.0002 for all). These findings suggest that there is a progressive impairment in LV relaxation as the number of metabolic syndrome criteria increase. The prevalence of LV diastolic dysfunction by PWD- and TDI-derived indices ranged from 7–9% in the Absent group to 17–18% in the Pre-Metabolic Syndrome group and 29–35% in
the Metabolic Syndrome group. In the Pre-Metabolic Syndrome group, the odds ratio for detecting LV diastolic dysfunction were 2.6 (95% CI: 1.2–5.6, P = 0.01) by PWD and 2.2 (95% CI: 1.1–4.5, P = 0.03) by TDI; in the Metabolic Syndrome group the odds ratio were 5.2 (95% CI: 2.4–11.4, P < 0.0001), and 5.5 (95% CI: 2.7–11.3, P < 0.0001), respectively [25].

3- Left Ventricular Mass and Relative Wall Thickness;

In this study left ventricular mass was calculated from this equation: LVmass= 0.8 (1.04 ([LVIDD + PWTD + IVSTD])^3- [LVIDD]^3)+ 0.6 g, then indexed to height^2.7 (LVM/Ht2.7). It was found that there is increasing in LVM/ Ht2.7 and RWT in MetS and pre-metabolic than normal persons. As regard LVM/Ht2.7 (mean ± SD ) in group(A)24.45±9.28 , while it was40.91±8.40 in group(B) and 41.78±10.57 in group(C) P value < 0.0001.

When comparing RWT in the three groups we found extremely statically significant relationship between MetS and increase RWT values , (mean ± SD ) in group(A)0.36 ±0.03, while it was0.38±0.08 in group(B) and 0.48±0.09 in group(C) while P value < 0.0001.

This results came in agreement with LA Ferrara, et al., 2007. a study included 707 subjects; 153 (21.6%) of the study population were found to have MetS. The study found that subjects with MetS had a greater LV mass and, accordingly, a higher prevalence of left ventricular hypertrophy LVH (83/153 subjects with MetS, 54.2% (mean±SD) 41.47±11.3 vs 141/554 subjects without MetS, 25.4%; (mean±SD) 49.07±12.0 (P<0.001).

Regarding the geometrical pattern of the left ventricle, concentric hypertrophy was present in 5.0% of the non MetS group and in 8.5% of the MetS group, eccentric hypertrophy in 20.4 and 45.7% respectively.

Moreover 8.3% of non MetS group and 4.4% of MetS had concentric remodelling. The differences in the prevalence of the geometrical patterns of the left ventricle between subjects with and without MetS were statistically significant ,RWT (Mean±SD) was (37.37±7.7) for non MetS and (39.87±7.7) for MetS group (P<0.001).[26].

In Mahmoud, et al., 2009, who studied 160 persons (aged 46±1 years [mean ±SD], 53% male)underwent 2-dimensional echocardiography and tissue Doppler imaging and evaluation for MetS to test the hypothesis that the cardiac structural and functional abnormalities of the MetS are independent of body mass index (BMI), although LV mass was higher with MetS (Mean±SD) 164±7 in MetSvs 149±4 in non MetS (p <0.05), there was no statistically significant difference between 2 groups when LV mass was indexed either to height or height , the LVM/ hieght^2.7 (Mean±SD) was 39±2 in MetS vs 37±1 in non MetS (p non-significant), this may be due to age, sex and BMI was similar in the two groups [27].

These results were not only restricted to adults but also in children. Alkholy , et al., 2016 found that LVMI in obese children was significantly higher when compared to control group and also more significant in MetS obese children when compared to non-MetS obese children. Moreover, a significantly positive correlation was detected between LVMI and parameters of MetS and also with those of insulin resistance. This study included 82 obese children. Their mean age was 10.2 ± 2.8 years; they were divided into 25 obese children with MS and 57 obese children without MS, and 40 healthy age- and sex-matched children were also included in the study as a control group. All children were subjected to clinical assessment and received an echocardiographic examination (2-dimensional, M-mode, Doppler, and tissue Doppler echocardiography) and laboratory assessment, Results. The LVMI were increased in the obese compared to the control group (p < 0.001). There was a significant positive correlation between both LVMI and serum leptin level in comparison to BMI, WC, fasting glucose, fasting insulin, homeostatic model assessment for insulin resistance, triglycerides, and low-density lipoprotein in all obese children, especially the MS group. However, there was a significant negative correlation between both LVMI and serum leptin level in comparison to high-density lipoprotein,[28].

Because hypertension is considered as one of the most common risk factors for development of LVH and increasing LV mass; Al Naggar and Al-Daydakony, 2015 had studied the effect of components of MetS other than hypertension on LVMI and found that even in the absence of hypertension, MetS patients had significantly more, LV wall thickness, more LV mass and mass index, and more incidence of LVH than control subjects in their study that included 50 metabolic syndrome patients without hypertension and 50 healthy subjects. In contrast to our study, there was no significant difference between the two groups regarding some parameters of diastolic function as E/A ratio [29].
Another study was done by Wang, et al., 2015 that included 1733 metabolic syndrome patients and 2373 non-MetS hypertension patients. They found that LV mass and LV mass index were higher in the MetS group than in the non-MetS group. LV mass index, LV mass, interventricular septum, and post wall were raised with the increased number of MetS disorders. MetS was associated with increased LV hypertrophy risk (unadjusted OR 1.38; 95% CI 1.21-1.57); age, sex, and blood pressure (BP; adjusted OR 1.39; 95% CI 1.22-1.59). MetS was also associated with increased risk of eccentric hypertrophy in male and female patients. Mets was only associated with increased risk of concentric hypertrophy in female patients; and MetS was not associated with concentric remodeling[30].

We can say now that MetS can lead to both diastolic dysfunction and LVH. But dose diastolic dysfunction is dependent on LVH or not?. Ayalon, et al., 2014 sought to examine whether preclinical LV diastolic dysfunction can occur independent of LV hypertrophy in MetS. They recruited 90 consecutive participants with MetS and without cardiovascular disease (mean age 46 years, 78% women), and 26 controls (no risk factors for MS; mean age 43 years, 65% women). Participants underwent echocardiography with tissue Doppler imaging. In age- and sex-adjusted analyses, MetS was associated with higher left atrial (LA) diameter, higher LV mass, lower E/A ratio, and lower mean e' (P<0.001 for all). These associations remained significant after further adjusting for blood pressure, anti-hypertensive medication use, and body-mass index. After adjusting for LV mass, MS remained independently associated with higher LA diameter, lower E/A ratio and lower mean e' (P≤0.01 for all). In conclusion, MS was associated with preclinical LV diastolic dysfunction independent of LV mass, as reflected by higher LA diameter, lower E/A ratio, and lower mean e'. This suggests that MS can lead to the development of diastolic dysfunction via mechanisms independent of hypertrophy. Differences in diastolic function were more pronounced at younger ages[31].

V. SUMMARY:

Metabolic syndrome is a multiplex risk factor that arises from insulin resistance accompanying abnormal adipose deposition and function. It is a risk factor for coronary heart disease, as well as diabetes, fatty liver, and several cancers. The clinical manifestations of this syndrome may include hypertension, hyperglycemia, hypertriglyceridemia, reduced high-density lipoprotein cholesterol (HDL-C), and abdominal obesity.

The metabolic syndrome represents a clustering of cardiovascular risk factors affecting about 22% of the adult population in industrialized countries and over 40% of those aged 50 and older.

This study aimed to evaluate the effects of the metabolic syndrome and the individual components of the metabolic syndrome on LV structures and functions by transthoracic echocardiography and tissue Doppler study.

In this study 60 subjects were enrolled and classified according to metabolic syndrome diagnostic criteria into three groups:

1-Group A: 20 patients with absent (0) any criteria of metabolic syndrome.

2-Group B: 20 patients with pre-metabolic syndrome (1-2 criteria).

3-Group C: 20 patients with metabolic syndrome (≥3 criteria). All subjects had been subjected to:- Informed consent, full history taking, clinical examination, resting twelve leads ECG, complete routine laboratory investigations and transthoracic echocardiography (including 2-D, M-mode, Doppler and pulsed wave tissue Doppler imaging) with standard views taken to assess LV functions and dimensions, all data were collected, revised, verified and analyzed statistically. The results revealed the following:

As regard LV MPI by PWD there was statistically significant difference between the three groups.

As regard LV MPI by TDI there was statistically significant difference between the three groups.

As regard LV global S wave by TDI there was statistically significant difference between the three groups.

As regard MV E/A ratio there was statistically significant difference between the three groups.

As regard MV E/E’ ratio there was statistically significant difference between the three groups.

As regard IVRT there was statistically significant difference between the three groups.
As regard LVM/Ht2.7 there was statistically significant difference between the three groups.

As regard LV RWT there was statistically significant difference between the three groups.

There was strong positive correlation between number of criteria of MetS and parameters of LV functions as MPI and E/E’ or LV structures as LVMI/Ht2.7 and RWT.

VI. CONCLUSIONS

1-Individuals with the metabolic syndrome (MetS) and normal LV EF frequently show abnormalities in LV diastolic function and to some extent LV systolic function by other methods.

2-MetS associated with more tendency to increase in LV mass and so more tendency to LVH, and the same thing about RWT.

3-There was strong relationship between number of criteria and impairment of LV function and increased LV mass; so, persons who have more criteria of metabolic syndrome were more impaired in LV function and with greater number of LVH.

4-In evaluation of LV functions by echocardiography some methods tend to be more accurate in early diagnosis of impairment of LV functions; for example: MPI by TDI is better than MPI by PWD in assessment of systolic function, on other hand in assessment of diastolic function both MV E/E’ and IVRT are preferred than other methods.

Recommendations 1-Assessment of LV systolic function using MPI by TDI to detect early impairment of systolic function. 2-Assessment of LV diastolic function using MV E/E’ and IVRT to detect early impairment of diastolic function. 3-Further studies are recommended to assess effect of each criteria of metabolic syndrome on LV functions and structures and determining if these criteria are controlled; a difference will be found about their effect on LV or not. 4-Further studies are recommended to assess LV function in metabolic syndrome patients by many methods as echocardiography, MRI, cardiac catheterization, and radionuclide imaging then making a correlation between these methods.

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