Role Of Tissue Doppler Imaging And Strain/Strain Rate Imaging In The Assessment Of The Effect Of Obesity On Left Ventricular Structure And Myocardial Systolic Function

Thesis
Submitted for Partial Fulfillment of MD Degree In Cardiology
By
Hany Hassan Ahmed Ebaid
(M.Sc Cardiology)

Under Supervision Of

Prof. Dr. Heba Abd Elkader Mansour
Professor of Cardiology
Benha Faculty of Medicine

Prof. Dr. Reda Baiomy Bastawisy
Assistant Professor of Cardiology
Benha Faculty of Medicine

Prof. Dr. Neama Ali Elmeligy
Ass consultant of Cardiology
Benha Faculty of Medicine

Dr. Mohamed Hassan Ibraheem
Lecturer of Cardiology
Benha Faculty of Medicine

Benha Faculty of Medicine
Benha University
(2014)
## Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>List of Abbreviations</td>
<td>II</td>
</tr>
<tr>
<td>List of Tables</td>
<td>IV</td>
</tr>
<tr>
<td>List of Figures</td>
<td>VI</td>
</tr>
<tr>
<td>Introduction</td>
<td>1</td>
</tr>
<tr>
<td>Aim of the work</td>
<td>4</td>
</tr>
<tr>
<td>Review of Literature</td>
<td>5</td>
</tr>
<tr>
<td>Chapter I: Tissue Doppler imaging</td>
<td>5</td>
</tr>
<tr>
<td>Chapter II: Obesity</td>
<td>54</td>
</tr>
<tr>
<td>Section I: Obesity</td>
<td>54</td>
</tr>
<tr>
<td>Section II: Obesity and cardiovascular system</td>
<td>65</td>
</tr>
<tr>
<td>Patients and Methods</td>
<td>80</td>
</tr>
<tr>
<td>Results</td>
<td>87</td>
</tr>
<tr>
<td>Discussion</td>
<td>108</td>
</tr>
<tr>
<td>Conclusion</td>
<td>116</td>
</tr>
<tr>
<td>Limitations</td>
<td>117</td>
</tr>
<tr>
<td>Recommendations</td>
<td>118</td>
</tr>
<tr>
<td>Summary</td>
<td>119</td>
</tr>
<tr>
<td>References</td>
<td>122</td>
</tr>
<tr>
<td>Arabic Summary</td>
<td></td>
</tr>
</tbody>
</table>
**List of abbreviations**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A’</td>
<td>Atrial contraction mitral annular velocities</td>
</tr>
<tr>
<td>AF</td>
<td>Atrial fibrillation</td>
</tr>
<tr>
<td>Am</td>
<td>Myocardial end diastolic wave</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>BSA</td>
<td>Body surface area</td>
</tr>
<tr>
<td>CHD</td>
<td>Coronary heart disease</td>
</tr>
<tr>
<td>CRT</td>
<td>Cardiac resynchronization therapy</td>
</tr>
<tr>
<td>CRP</td>
<td>C-reactive protein</td>
</tr>
<tr>
<td>CVD</td>
<td>Cardiovascular disease</td>
</tr>
<tr>
<td>DSE</td>
<td>Dobutamine stress echocardiography</td>
</tr>
<tr>
<td>DT</td>
<td>Deceleration time</td>
</tr>
<tr>
<td>ECG</td>
<td>Electrocardiography</td>
</tr>
<tr>
<td>EF</td>
<td>Ejection fraction</td>
</tr>
<tr>
<td>E’</td>
<td>Early diastolic mitral annular velocities</td>
</tr>
<tr>
<td>Em</td>
<td>Myocardial early diastolic wave</td>
</tr>
<tr>
<td>HDL-C</td>
<td>High density lipoprotein cholesterol</td>
</tr>
<tr>
<td>HTN</td>
<td>Hypertension</td>
</tr>
<tr>
<td>IVCT</td>
<td>Isovolumic contraction time</td>
</tr>
<tr>
<td>IVRT</td>
<td>Isovolumic relaxation time</td>
</tr>
<tr>
<td>LA</td>
<td>Left atrium</td>
</tr>
<tr>
<td>LAD</td>
<td>Left anterior descending</td>
</tr>
<tr>
<td>LDL-C</td>
<td>Low density lipoprotein cholesterol</td>
</tr>
<tr>
<td>LV</td>
<td>Left ventricle</td>
</tr>
<tr>
<td>LVEF</td>
<td>Left ventricular ejection fraction</td>
</tr>
<tr>
<td>LVH</td>
<td>Left ventricular hypertrophy</td>
</tr>
<tr>
<td>LVM</td>
<td>Left ventricular mass</td>
</tr>
<tr>
<td>LVMI</td>
<td>Left ventricular mass index</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>MVG</td>
<td>Myocardial velocity gradient</td>
</tr>
<tr>
<td>NO</td>
<td>Nitric oxide</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>PCWP</td>
<td>Pulmonary capillary wedge pressure</td>
</tr>
<tr>
<td>PW TDI</td>
<td>Pulsed wave tissue Doppler imaging</td>
</tr>
<tr>
<td>RV</td>
<td>Right ventricle</td>
</tr>
<tr>
<td>Sm</td>
<td>Myocardial systolic wave</td>
</tr>
<tr>
<td>SR</td>
<td>Strain rate</td>
</tr>
<tr>
<td>TDI</td>
<td>Tissue Doppler imaging</td>
</tr>
<tr>
<td>TG</td>
<td>Triglycerides</td>
</tr>
<tr>
<td>TNF-α</td>
<td>Tumor necrosis factor alpha</td>
</tr>
<tr>
<td>WC</td>
<td>Waist circumference</td>
</tr>
<tr>
<td>W/H ratio</td>
<td>Waist hip ratio</td>
</tr>
</tbody>
</table>
## List of Tables

<table>
<thead>
<tr>
<th>Table</th>
<th>Subject</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)</td>
<td>Normal values for systolic velocities of the right and left ventricle.</td>
<td>11</td>
</tr>
<tr>
<td>(2)</td>
<td>Color coded TD velocity values.</td>
<td>16</td>
</tr>
<tr>
<td>(3)</td>
<td>Advantages and disadvantages of TDI derived techniques strain and strain rate.</td>
<td>23</td>
</tr>
<tr>
<td>(4)</td>
<td>Advantages and the disadvantages Non-Doppler 2D-strain imaging.</td>
<td>25</td>
</tr>
<tr>
<td>(5)</td>
<td>Normal values for strain and strain rate.</td>
<td>26</td>
</tr>
<tr>
<td>(6)</td>
<td>Normal values of peak pulsed TDI diastolic velocities for basal segments of the left ventricle recorded in the apical views.</td>
<td>46</td>
</tr>
<tr>
<td>(7)</td>
<td>Classification of BMI for people aged 18 and over BMI (kg/m2)</td>
<td>81</td>
</tr>
<tr>
<td>(8)</td>
<td>The approximate normal values for LV diastolic function</td>
<td>83</td>
</tr>
<tr>
<td>(9)</td>
<td>Normal values of left ventricular mass and mass index in females.</td>
<td>84</td>
</tr>
<tr>
<td>(10)</td>
<td>Normal values of left ventricular mass and mass index in males.</td>
<td>84</td>
</tr>
<tr>
<td>(11)</td>
<td>Demographic data of the three groups</td>
<td>88</td>
</tr>
<tr>
<td>(12)</td>
<td>Demographic data of the obese versus non obese groups</td>
<td>88</td>
</tr>
<tr>
<td>(13)</td>
<td>Echocardiographic data in the obese versus non obese groups.</td>
<td>89</td>
</tr>
<tr>
<td>(14)</td>
<td>Echocardiographic data in the morbid obese versus non obese groups</td>
<td>91</td>
</tr>
<tr>
<td>(15)</td>
<td>Echocardiographic data in the mild obese versus non obese groups</td>
<td>92</td>
</tr>
<tr>
<td>(16)</td>
<td>Left ventricular mass &amp; left ventricular mass index in the obese versus non obese groups.</td>
<td>93</td>
</tr>
<tr>
<td>(17)</td>
<td>Left ventricular mass &amp; left ventricular mass index in morbid obese versus non obese groups</td>
<td>94</td>
</tr>
<tr>
<td>(18)</td>
<td>Left ventricular mass &amp; left ventricular mass index in mild obese versus non obese groups</td>
<td>95</td>
</tr>
<tr>
<td>#</td>
<td>Description</td>
<td>Page</td>
</tr>
<tr>
<td>-----</td>
<td>-----------------------------------------------------------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>19</td>
<td>Global diastolic diameters of obese versus non obese groups</td>
<td>96</td>
</tr>
<tr>
<td>20</td>
<td>Global diastolic diameters of morbid obese versus non obese groups</td>
<td>97</td>
</tr>
<tr>
<td>21</td>
<td>Global diastolic diameters of mild obese versus non obese groups</td>
<td>98</td>
</tr>
<tr>
<td>22</td>
<td>Mean systolic velocity &amp; mean systolic strain/strain rate in obese versus non obese in the six selected segments</td>
<td>100</td>
</tr>
<tr>
<td>23</td>
<td>Mean systolic velocity &amp; mean systolic strain/strain rate in morbid obese versus non obese in the six selected segments</td>
<td>102</td>
</tr>
<tr>
<td>24</td>
<td>Mean systolic velocity &amp; mean systolic strain/strain rate in mild obese versus non obese in the six selected segments</td>
<td>104</td>
</tr>
<tr>
<td>25</td>
<td>Correlation between BMI &amp; variables among the three groups</td>
<td>106</td>
</tr>
<tr>
<td>26</td>
<td>Correlation between BMI &amp; color coded TDI of the six selected segments (Peak systolic velocity, strain &amp; strain rate) among the three groups</td>
<td>107</td>
</tr>
</tbody>
</table>
List of Figures

<table>
<thead>
<tr>
<th>Figure</th>
<th>Subject</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)</td>
<td>Principle of conventional Doppler and TDI.</td>
<td>8</td>
</tr>
<tr>
<td>(2)</td>
<td>Example of pulsed wave TDI.</td>
<td>12</td>
</tr>
<tr>
<td>(3)</td>
<td>Schematic representations of the strain and strain rate parameters</td>
<td>22</td>
</tr>
<tr>
<td>(4)</td>
<td>Oil red O staining for lipids of hearts from an obese and a nonobese human.</td>
<td>78</td>
</tr>
<tr>
<td>(5)</td>
<td>Demographic data of the three groups</td>
<td>87</td>
</tr>
<tr>
<td>(6)</td>
<td>Echocardiographic data in the the obese versus non obese groups</td>
<td>90</td>
</tr>
<tr>
<td>(7)</td>
<td>Echocardiographic data in the obese versus non obese groups</td>
<td>90</td>
</tr>
<tr>
<td>(8)</td>
<td>Echocardiographic data in the morbid obese versus non obese groups</td>
<td>91</td>
</tr>
<tr>
<td>(9)</td>
<td>Echocardiographic data in the mild obese versus non obese groups</td>
<td>92</td>
</tr>
<tr>
<td>(10)</td>
<td>Left ventricular mass &amp; left ventricular mass index in obese versus non obese groups</td>
<td>93</td>
</tr>
<tr>
<td>(11)</td>
<td>Left ventricular mass &amp; left ventricular mass index in morbid obese versus non obese groups</td>
<td>94</td>
</tr>
<tr>
<td>(12)</td>
<td>Left ventricular mass &amp; left ventricular mass index in mild obese versus non obese groups</td>
<td>95</td>
</tr>
<tr>
<td>(13)</td>
<td>Global diastolic diameters of obese versus non obese groups</td>
<td>97</td>
</tr>
<tr>
<td>(14)</td>
<td>Global diastolic diameters of morbid obese versus non obese groups</td>
<td>98</td>
</tr>
<tr>
<td>(15)</td>
<td>Global diastolic diameters of mild obese versus non obese groups</td>
<td>99</td>
</tr>
</tbody>
</table>
Introduction

The prevalence of obesity is increasing in both the developed and developing worlds, with about 20% of the US adult population being reported as obese (Mokdad et al., 2001).

Obesity is a major contributor to the global burden of disease and disability because it is a risk factor for numerous medical conditions such as heart disease, diabetes, hypertension, stroke, pulmonary emboli, certain cancers, osteoarthritis, gallbladder disease, and respiratory abnormalities (Poirier & Eckel 2000):

Obesity is associated with a substantial reduction in life expectancy. Data from the United States suggest that a severe level of obesity (BMI > 45) during early adulthood (aged 20–30 years) may reduce a man’s life expectancy by up to 13 years and a woman’s by up to 8 years (Fontaine et al. 2003).

Obesity is associated with increased cardiac output. The increased cardiac output in obese patients is to meet the metabolic demand of the adipose tissue and is achieved mainly through an increase in stroke volume. The left ventricular chamber dilates to accommodate the increased venous return and, in turn, develops an eccentric type of hypertrophy to keep the wall stress normal (Kaltman & Goldring, 1976).

The left atrium also enlarges in obese individuals and is initially caused by the increased blood volume and venous return. Later, other factors like left ventricular hypertrophy and diastolic dysfunction may also be responsible for increased left atrial size (Ku, et al., 1994).

However, in the Strong Heart Study cohort (Collis, et al., 2001), it was observed that increases in stroke volume, cardiac output, and left ventricular mass
were more closely related to the associated increase in lean body mass than to the amount of fat in obese patients.

Obesity is accepted as an independent risk factor for the development of heart failure (He, et al., 2001), (Kenchaiah, et al., 2002).

Impairment of cardiac function has been reported to correlate with the degree of obesity, body mass index and duration of obesity (Tumuklu et al., 2007). Abnormal diastolic function is the most important component of the impaired cardiac function, while systolic dysfunction is not so common (Abhayaratna et al., 2006).

Although the mechanisms leading to heart failure in obese patients have not been clarified, severe obesity has long been recognized to cause a form of cardiomyopathy characterized by chronic volume overload, left ventricular (LV) hypertrophy, and LV dilatation. The effects of longstanding obesity on LV structure and function have been characterized as eccentric LV hypertrophy, diastolic dysfunction, and occasionally systolic dysfunction (Alpert, 2001). Some studies have also revealed a spectrum of more minor cardiovascular changes, ranging from hyperdynamic circulation to subclinical cardiac structural changes in obesity (Wong et al., 2004).

The early detection of these subclinical manifestations may be important from the standpoint of earlier effective treatment to reverse the process, which may end with heart failure. Echocardiography has consistently been the most accurate non-invasive method of assessing the left ventricular function (Pirat et al., 2007). However, conventional echocardiographic modalities are often suboptimal for detailed evaluation of cardiac structures and for detection of subtle functional changes associated with obesity. Newer echocardiographic techniques such as tissue Doppler imaging (TDI) (Palka et al., 1995) and TDI-derived techniques—
strain imaging/strain rate imaging (SRI) (Pellerin et al., 2003), could better characterize these possible cardiac abnormalities associated with obesity.

Tissue doppler which is less load dependent may be better tool for assessing LV function in obese individuals (Tanalp et al., 2008). This new modality allows detection of subtle anomalies of global LV systolic and diastolic function, and regional subendocardial function (Hashimoto et al., 2003).

However conventional and TDI-derived echocardiographic systolic parameters may not be able to detect early abnormalities in longitudinal systolic function (Willens et al., 2004). TDI derived echocardiographic techniques may be new tools for early detection of subclinical cardiac functional and structural changes and to evaluate their natural history and the efficacy of therapeutic interventions over time (Peterson et al., 2004).
Aim of the Work

The aim of this work is to assess the effect of obesity on left ventricular structure & myocardial systolic function using tissue Doppler imaging (TDI) and TDI-derived techniques—strain imaging/strain rate imaging (SRI).
Chapter One

Tissue Doppler Imaging

Evaluation of LV systolic function is one of the most common indications for performing echo in an outpatient or inpatient basis (Schiller et al., 1989).

For 30 years, the non-invasive ultrasonic assessment of myocardial function has relied on grey scale echocardiography and Doppler examination of intracardiac flow velocities. However, standard methods are often limited by technical problems, inaccuracy and sometimes significant inter-observer and intra-observer discrepancies (Picano et al., 1990).

Routine echocardiographic assessment of regional LV wall motion is subjective because it is determined by visual determination of endocardial excursion and wall thickening. The percent fractional shortening of the LV based on M-mode echocardiography and the LV ejection fraction determined by two-dimensional echocardiography are indices of LV pump function, and therefore cannot accurately evaluate LV myocardial contractility. On the other hand, TDI offers the promise of a new objective measure to quantify regional and global LV function (Nikitin and Witte, 2004).

Tissue velocity imaging (TVI) is an ultrasound technique that provides quantitative information on the velocity of the tissue. Traditionally, Doppler techniques have mainly been used to measure blood flow, and the signal component from tissue was considered noise that needed to be removed. There were early studies in the 1960s and 1970s using the pulsed-wave (PW) Doppler method to detect
myocardial motion (Kostis et al., 1972). However; the method has had widespread use only since the late 1980s.

Isaaz et al were the first to introduce the concept of tissue Doppler echocardiography (TDE) to assess myocardial velocity using the pulsed Doppler technique (Isaaz et al., 1989). The use of colour TDE was subsequently reported by Sutherland et al (Sutherland et al., 1994) and Yamazaki et al (Yamazaki et al., 1994).

Heimdal et al introduced real time strain rate calculation in the longitudinal axis in 1998 (Heimdal et al., 1998). TDE is now available on most modern cardiac ultrasound systems and can be used during a routine echo examination to assess global and regional left ventricular function. This color TVI provides the possibility of extracting other parameters through spatial and temporal processing of the velocity data. Displacement, strain, and strain rate are examples of such parameters (Pan et al., 2001), (D’hooge et al., 2000).

Strain rate echocardiography has been available and has been developed by estimating the spatial gradients in myocardial velocities. It is independent of overall heart motion, cardiac rotation, or motion induced by contraction in adjacent myocardial segments. Therefore, it is accepted as a true measure of local deformation (Stoylen et al., 1999). This new modality allows detection of subtle anomalies of global LV systolic and diastolic function, and regional subendocardial function (Hashimoto et al., 2003).

Therefore, this noninvasive, rapidly evolving and expanding technique appears promising for quantification of regional myocardial contraction (Gondi and Dokainish., 2007).
**Principles of Tissue Doppler:**

Classic Doppler echocardiography measures the high-frequency, low-amplitude signals from rapidly moving red blood cells, enabling quantification of blood flow velocities. The high frequency signal contained Doppler shift data describing the flow of red blood cells, which travel through the cardiovascular system at normal velocities as high as 150 cm/s in arterial circulation and 10 cm/s in venous circulation.

Unlike conventional Doppler signals that are typified by high velocity and low amplitude, in TDI, myocardial motion is characterized by relatively low velocity and high amplitude signals (*Yamazaki et al., 1994*).

The technique is based on the Doppler principle of velocity estimation of structures moving with respect to the ultrasound transducer. An instrumentation feature common to both pulsed and color-coded TDI involves removal of the high-pass filter used for routine Doppler to assess blood flow in order to focus on the lower velocity values of myocardial motion (*Miyatake et al., 1995*). In addition, thresholding is used to enhance low-velocity myocardial signals and eliminate the blood flow signals within the cardiac chambers (*Sutherland et al., 1999*).

In the 1980s, color flow mapping was designed to filter out signals reflected from slow moving structures such as the myocardium (*Kasai et al., 1985*). In 1989, Isaaz, McDicken and Sutherland adapted this technique to visualize tissue velocities (*Sutherland et al., 1994*).

So to summarize, Doppler signal from ventricular wall motion differ from signals of blood flow in two major aspects,

1. Ventricular wall motion velocity is approximately 10 times slower than red blood cells with a velocity ranging from 0.06 to 0.24 m/s (*Lange et al., 1997*).
2. Doppler shifts obtained from myocardial tissue motion of high amplitudes, about 100 times greater than that of blood flow signal, so it is possible to display regional myocardial velocities by using thresholding and filtering algorithms that reject the echoes originating from the blood pool (Lange et al., 1997).

Fig. (1): Left: Principle of conventional Doppler. High amplitude myocardial wall signals are eliminated by high pass filter. Right: Doppler signals from myocardial wall are extracted; blood flow signals are eliminated (Erbel et al., 1995).

Modalities of TDI:

Tissue Doppler imaging Display:

TDI can be displayed as:
1- Color-coded 2-D or 2-D guided M-mode tracing.
2- PW-TDI velocity curves.
3- Intramyocardial velocity Gradient (MVG).
4- Strain and strain rate imaging (SRI).
[1] Pulsed-wave TDI:

PW TDI is an online, live measurement, while color-coded TDI requires post-processing of data. It is similar to routine pulsed-Doppler, with adjustments of the scale and sweep speed to optimize the spectral display similar to pulsed-Doppler of blood flow.

PW TDI measures instantaneous peak myocardial velocities. It has a very high temporal resolution: the sampling rate is 250–300 samples/s equivalent to a temporal resolution of 3–4 ms. For routine clinical use, a sample volume of 6–8 mm is generally used. It should be positioned in the center of the region of interest. To prevent velocity aliasing, the velocity range should be set at approximately 24 cm/s. It has been suggested that the data are collected during a short breath hold in order to exclude respiratory variation.

Pulsed-wave TDI is used to measure peak myocardial velocities and is particularly well suited to the measurement of long-axis ventricular motion because the longitudinally oriented endocardial fibers are most parallel to the ultrasound beam in the apical views. Because the apex remains relatively stationary throughout the cardiac cycle, mitral annular motion is a good surrogate measure of overall longitudinal left ventricular contraction and relaxation (Vinereanu et al., 1999).

Normal pattern of PW-TDI:

To analyze the normal patterns of PW-TDI velocities it is important to understand the normal myocardial architecture and fiber orientation. Heart muscle fibers are organized in 3 ways: longitudinal, circumferential and oblique, being the longitudinal the most important in shortening and relaxation of LV.

Longitudinal fibres with a right-handed helical arrangement predominate within the subendocardium (Sengupta et al., 2006), moving to a more circumferential orientation in the midwall and becoming longitudinal again, with a
left-handed helical arrangement in the subepicardium. However, due to the relatively small longitudinal muscle mass, it has been suggested that systolic function may be more dependent on circumferential fibre shortening (*Waggoner and Bierig, 2001*).

If reductions in cardiac function occur, it may follow that the smaller muscle mass of the longitudinal fibres are more prone to these changes. Indeed, within pathological models, longitudinal dysfunction precedes circumferential dysfunction (*Brecker, 2000*), (*Poulsen et al. 2007*).

PW-TDI has the advantage of online measurements of velocities and time intervals and an excellent temporal resolution and resolving all peak velocities. According to Doppler principle, tissue velocities moving towards the transducer are positive, whereas velocities moving away from the transducer are negative.

**From the velocity curve we can identify the following velocity waves:**

**Waves recorded during systole are:**

1. **The first systolic wave (S1 wave)** corresponding mainly to the longitudinal shortening during IVC which lasts from the Q wave of the QRS complex until the onset of the inward motion of the ventricular wall (*Oki et al., 1999*). The IVC has another negative wave and then it can be called IVC-\(b\) and the positive S1 wave is called IVC-\(a\).

2. **The second systolic wave (S2 wave)** corresponding mainly to transverse shortening during the rapid ejection phase of the cardiac cycle. It occurs after the R wave and extends to the end of T wave of the ECG (*Oki et al., 1999*).

Table (1) shows normal values for systolic velocities of the right and left ventricle from the HUNT study
**Table (1):** Normal values for systolic velocities of the right and left ventricle from the HUNT study.

<table>
<thead>
<tr>
<th></th>
<th>Left ventricle, mean of 4 walls (cm/sec)</th>
<th>Right ventricle (free wall) (cm/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S' (pw TDI)</td>
<td>S' cTDI</td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 40 years</td>
<td>8.9 (1.1)</td>
<td>7.2 (1.0)</td>
</tr>
<tr>
<td>40 - 60 years</td>
<td>8.1 (1.2)</td>
<td>6.5 (1.0)</td>
</tr>
<tr>
<td>&gt; 60 years</td>
<td>7.2 (1.2)</td>
<td>5.7 (1.1)</td>
</tr>
<tr>
<td>All</td>
<td>8.2 (1.3)</td>
<td>6.6 (1.1)</td>
</tr>
<tr>
<td>Males</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 40 years</td>
<td>9.4 (1.4)</td>
<td>7.6 (1.2)</td>
</tr>
<tr>
<td>40 - 60 years</td>
<td>8.6 (1.3)</td>
<td>6.9 (1.3)</td>
</tr>
<tr>
<td>&gt; 60 years</td>
<td>8.0 (1.3)</td>
<td>6.4 (1.2)</td>
</tr>
<tr>
<td>All</td>
<td>8.6 (1.4)</td>
<td>6.9 (1.3)</td>
</tr>
</tbody>
</table>

Values are mean (SD). pwTDI: Pulsed Tissue, c TDI: colour TDI.

*(Dalen et al., 2010)*
Fig. (2). Example of pulsed wave tissue Doppler imaging (Citro et al., 2008).

**Waves recorded during diastole are:**

1) *Isovolumic relaxation time period:* It starts with the end of the S2 wave and lasts until the beginning of the outward motion of early diastolic relaxation velocity (e wave). The best method to analyze this time is to measure the time interval from the aortic component of the second heart sound to the beginning of the early diastolic relaxation velocity; it is formed of initial small positive and a second larger negative wave of variable amplitude and duration. The initial component is termed IVR-a and the second termed IVR-b (Garcia et al., 1996).

2) *Early diastolic relaxation (e wave):* Corresponding to the rapid filling phase and it follows the T wave of the ECG and occurs after IVR period. It is mostly negative wave except for the anterior wall and septum in the parasternal short axis and parasternal long axis views respectively. It coincides with the mitral valve opening and corresponds to the E-wave of Doppler trans-mitral flow (Zamorano et al., 1997).
(3) **Diastasis:** Following this early relaxation wave an intermediate period without myocardial wall motion can be observed. It corresponds to diastasis during which there is no wall motion and no trans-mitral pressure gradient is present (Garcia et al., 1999).

(4) **Rapid diastolic wave (a wave):** It corresponds to the atrial contraction and it follows the P wave of the ECG. It corresponds to the A-wave of doppler trans-mitral flow (Francesco et al., 1998). Relationship between both diastolic waves (e/a wave) is normally grater than one (Zamorano et al., 1997).

It was found that the (e) wave along the short axis was greater than that along the long axis, whereas (a) wave along the long axis was greater than that along the short axis, thus during diastole the circumferential fibers predominated in LV wall expansion at early diastole, whereas longitudinal fibers predominated at atrial systole (Takatsuji et al., 1997).

[2] **Color-coded TDI (2-D or M-mode)**

Color-coded TDI system is a modification of the conventional color Doppler, by bypassing the high pass filter and the low frequency Doppler shifts of cardiac tissue motion. Color-coded blood velocity data are then superimposed on conventional gray scale two-dimensional images in real time.

The operation of color-coded TDI is similar to operation of routine color flow Doppler instrumentation. Variables include:

- **Color gain** — TDI color gain should be maximized to below the level of color noise artifact.

- **Velocity range** — since the most common application of TDI is to interrogate myocardial velocities; a velocity range should be selected to maximize the sensitivity of displaying lower velocity values, without limiting the ability to measure higher velocity values. Velocities that exceed
the upper limits of the selected range can be displayed as a saturated value at that highest velocity value in some systems. Selected velocity ranges of ± 9 to ± 20 cm/sec appear to be useful to assess myocardial velocity by TDI.

As in conventional color Doppler, the color determines the direction of movements (red towards and blue away from the transducer) and the hue of color determines the velocity (higher velocities are depicted in brighter colors and slower velocities in darker ones) (Miyatake et al., 1995). Several velocity maps may be used, but usually, yellow-red and white-blue are used to display higher velocities (Gorscan et al., 1996).

According to the movement direction and velocity, each cardiac wall shows different types and intensity of colors during the different phases of the cardiac cycle (Zamorano et al., 1997). Timing can be done non-invasively by ECG and phonocardiography to define phase of the cardiac cycle (Gorscan et al., 1996). The color-coded TDI images are usually saved in digital format. To view the myocardial velocity curves, post-processing is needed, either on the echocardiographic platform itself, or using a dedicate workstation.

Two-dimensional and color gain settings, filters and pulse repetition frequency should be adjusted to optimize color saturation. The data should be acquired at as high frame rate as possible. A frame rate of at least 100 frames/s is recommended. To reach the highest possible frame rate, sector size and depth should be reduced. If necessary, data should be recorded from each wall separately to ensure adequate frame rate. This is often needed in large, dilated ventricles in which attempts to include all LV walls cause unacceptably low frame rates. Ideally three consecutive heart beats may be recorded from each view and five heart beats are recommended in case of atrial fibrillation or frequent extra-systoles.

This information can be displayed as a standard 2-D image or as a M-mode TDI, where temporal resolution is enhanced. Differences in myocardial velocity
from endocardium to epicardium are thus displayed, leading to the recognition of myocardial velocity gradients (Uematsu et al., 1995).

A) **Color-coded 2-D TDI:**

Color two dimensional imaging has been limited by a slow frame rate, but parallel processing and advances in beam formation technology have increased the frame rate to a level adequate for analysis of most cardiac events. It allows a rapid visual qualitative assessment of the dynamics of the wall, provides a good spatial resolution that permits differentiation of the velocity profile between subendocardial and subepicardial layers and allows simultaneous analysis of various myocardial regions but is limited by its poor temporal resolution. Table (2) shows color coded TDI velocity values.

**Table (2):** Color coded TDI velocity values
<table>
<thead>
<tr>
<th>Color</th>
<th>Velocity (cm/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bright yellow</td>
<td>30</td>
</tr>
<tr>
<td>Yellow</td>
<td>25.7</td>
</tr>
<tr>
<td>Yellow/orange</td>
<td>21.4</td>
</tr>
<tr>
<td>Bright orange</td>
<td>17.1</td>
</tr>
<tr>
<td>Orange</td>
<td>12.9</td>
</tr>
<tr>
<td>Red/orange</td>
<td>8.6</td>
</tr>
<tr>
<td>Red</td>
<td>4.3</td>
</tr>
<tr>
<td>Black</td>
<td>0.0</td>
</tr>
<tr>
<td>Dark blue</td>
<td>-4.3</td>
</tr>
<tr>
<td>Blue</td>
<td>-8.6</td>
</tr>
<tr>
<td>Blue/turquoise</td>
<td>-12.9</td>
</tr>
<tr>
<td>Turquoise</td>
<td>-17.1</td>
</tr>
<tr>
<td>Turquoise/green</td>
<td>-21.4</td>
</tr>
<tr>
<td>Green</td>
<td>-25.7</td>
</tr>
<tr>
<td>Bright green</td>
<td>-30</td>
</tr>
</tbody>
</table>

*(Gorscan et al., 1996)*
Analysis of velocity vectors according to the imaging view:

1- Apical 2-, 4-and 5—chamber views:

From this view, the basal segments of all LV and RV walls can be obtained where both velocity components are in the same direction towards the transducer and chest wall in systole and away in diastole, the velocity will be the sum of both components, but the apex is moving in opposite direction to the direction of the cardiac motion during both systole and diastole. The net motion will be equal to intrinsic contraction and relaxation velocities minus the whole cardiac motion (Garcia et al., 1996).

Using the color coded velocity maps from the apical 2, 4 and 5 chamber views, all the basal and mid segments will be colored red during systole and blue during diastole but the apical segments will be colored blue during systole (away from transducer) and red during diastole (Garcia et al., 1996).

2- Parasternal views:

a) Parasternal long axis view:

From this view the septum is moving towards the center of gravity and away from the chest wall and transducer during systole. During diastole the opposite occur, so that the septal velocities derived from this view will be displayed in blue color during systole and in red color during diastole. The opposite occur in the posterior wall. So it can be noticed that the transitional movement (anterior displacement of the whole heart towards the chest wall and transducer during systole, and away during diastole) will be added to the motion of the posterior wall and subtracted from that of the septum. This why the systole and diastole velocities of the posterior wall are higher than that of the septum in this view (Fleming et al., 1994).

b) Parasternal short axis view:
In this view, velocities from the septum and anterior wall are displayed in blue color during systole and colored red during diastole. The opposite occurs in the posterior and inferior. The velocity of the anterior and septal wall will be lower than that of the posterior and inferior walls. This can be explained by the fact that the translation movement of the whole heart will be added to the posterior and inferior walls and subtracted from the anterior and septal walls during systole and diastole. During isometric phase the only force present is the whole cardiac motion, so the all cardiac segments move in the same direction and displayed as red in systole and blue in diastole (Garcia et al., 1996).

B) Color-coded M-mode TDI:

This mode was found to have two main advantages over the 2-D mode. Firstly, the high frame rate allows better temporal resolution (5-10 ms) of systolic and diastolic velocities and difference in myocardial velocity from endocardium to epicardium can usually be appreciated. Secondly, from the same image it is possible to determine both systolic and diastolic velocities. As with the 2-D color TDI, tissue velocities directed towards the transducer are color-coded red and those away from the transducer are coded blue. Higher velocities are depicted in brighter colors and slower ones are depicted in darker colors (yellow-red and white-blue) (Galiuto et al., 1998).

Differences between PW TDI and color-coded TDI:

Regional peak myocardial velocities of PW TDI are usually around 10–20% higher than color-coded TDI peak mean velocities derived from the same segment (Kukulski et al., 2000). However, the ability of color-coded TDI to collect full sector image data of various LV segments significantly reduces the scanning time compared with the segment by segment sampling when PW TDI is used. As with color Doppler, the velocities from color TDI are mean velocities whereas those from pulsed TDI are peak velocities.
So, during assessment of longitudinal velocities by TDI in the apical views, several factors must be taken into account when using reference values:

**First**, velocities obtained by color-coded TDI will be on average 10–20% lower than velocities obtained by PW TDI (*Kukulski et al., 2000*).

**Second**, normal values for longitudinal velocities depend on the position of the sample area within the wall. Systolic and diastolic velocities measured in the lateral wall will be higher than velocities measured in the septum. Also, when considering myocardial velocities within one region, a gradient of peak velocities exists with apical segments which have a lower peak velocity than more basal segments.

**Third**, velocities obtained from apical views are age-dependent. Most studies, using PW or color-coded TDI have documented a small decrease with age of systolic velocities of the left and right ventricle. More importantly, diastolic velocities show profound changes with age. All studies, using PW TDI or color-coded TDI, have shown that early diastolic mitral annular Velocities (E’) decrease with age while atrial contraction velocities (A’) increase with age. Similar findings have been documented for tricuspid annular velocities (*Nikitin et al., 2003*).
Deformation Imaging:

Strain and Strain Rate

Strain and strain rate deformation parameters based on Color Doppler myocardial imaging, and more recently on two-dimensional gray scale images, have evolved as important methods for the quantification of myocardial function. However, the visual estimation of wall motion usually used is very subjective and therefore highly operator dependent. It also has high interobserver and intraobserver variability and additionally it allows only limited evaluation of radial displacement and deformation, without the possibility of assessing myocardial shortening and twisting *(Perk G et al., 2007).*

Tissue velocities do not discriminate between actively contracting muscle and passive motion due to heart translation and tethering effects *(Derumeaux et al., 1998).* To separate this two-typed motion, strain and strain rate have been proposed as measures of regional contractility *(Garcia-Fernandez et al., 2003).*

Strain and strain rate assess function in heart segments. Strain is directly related to fiber shortening and strain rate is the speed of fiber shortening, which is a measure of contractility *(Pavlopoulos and Nihoyannopoulos., 2008).*

**Strain** is the amount of deformation is usually expressed in percent %. Negative strain values describe shortening, positive values describe thickening of a given myocardial segment related to the original length. During myocardial contraction, as the wall shortens it also thickens and thus assessment of all parameters, radial thickening (positive strain), circumferential shortening (negative strain) and longitudinal shortening (negative strain), is useful for the evaluation of contractile function.

**Strain rate** is the rate at which deformation changes (change of strain per unit of time ‘dt’). It is the temporal derivative of strain and describes the rate of
shortening or lengthening of a part of the heart. As strain rate describes the speed of deformation, its measurement unit is (1/s). Myocardial fibers shorten in the longitudinal and circumferential directions and thicken in the radial direction. By convention, shortening is indicated by negative SR and lengthening by positive SR values.

In principle, the superiority of deformation parameters for assessing cardiac function compared to motion-velocity-displacement parameters is related to the basic strain-algorithm, which subtracts the motion due to the contraction of neighboring segments (tethering effect). Strain parameters on the other hand, are referred to as motion-deformation between two points in the myocardial wall, which is unrelated to the motion towards the transducer, and this fact discriminates the actual passive movement from true contraction in any myocardial region. In cardiac muscle physiology, strain is directly related to fiber shortening and SR to the speed of shortening, which is a measure of contractility. Several groups of investigators have demonstrated the superiority of SR and strain and better site specificity, over tissue Doppler velocity data for tracking local systolic function (Voigt et al., 2000).
Myocardial deformation imaging initially became possible using Tissue Doppler. More recently it has also become possible with myocardial Speckle Tracking using 2D echocardiography. Although the feasibility of both TDI derived strain and speckle tracking derived strain are comparable, the inter- and intra-observer reproducibility is generally better with 2D speckle tracking (Hanekom et al., 2007).

(1) Tissue Doppler-derived strain and strain rate imaging:

TDI measurements allow the reconstruction of strain and strain rate curves and color coded images. Thus, the transmural velocity gradient (difference in endocardial and epicardial velocities divided by the instantaneous wall thickness) is equal to the transmural strain rate (rate of wall thickening), whereas the longitudinal velocity gradient over a segment with a fixed distance is a measure of longitudinal strain rate. So assessing tissue movement in relation to the transducer...
rather than relative to adjacent segments is a fundamental limitation of tissue velocity imaging, which can also affect tissue Doppler-derived strain and strain rate imaging (Cheuk-Man et al., 2007). Table (3) shows the advantages and disadvantages of TDI derived techniques strain and strain rate.

Table (3):  Advantages and disadvantages of TDI derived techniques strain and strain rate.

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>● High temporal resolution.</td>
<td>● 1-dimension measurements.</td>
</tr>
<tr>
<td>● Image quality less important.</td>
<td>● Tissue movement assessment in relation to the transducer.</td>
</tr>
<tr>
<td></td>
<td>● Measurement dependent on angle between ultrasound beam and direction of myocardial movement.</td>
</tr>
<tr>
<td></td>
<td>● Limited spatial resolution.</td>
</tr>
<tr>
<td></td>
<td>● Highly sensitive to signal noise; reduced signal-to-noise ratio.</td>
</tr>
<tr>
<td></td>
<td>● Higher interobserver variability in comparison with 2D-strain imaging.</td>
</tr>
<tr>
<td></td>
<td>● Time consuming steps for data acquisition and processing.</td>
</tr>
<tr>
<td></td>
<td>● Important learning curve; necessity of expert readers.</td>
</tr>
</tbody>
</table>

(International Journal of Cardiology, 2009)
(2) Non-Doppler 2D-strain imaging

It is derived from speckle tracking which is a newer echocardiographic technique for obtaining strain and SR measurements (Uematsu et al., 1995). It analyzes motion by tracking speckles (natural acoustic markers) in the 2D ultrasonic image. Thus, the motion pattern of myocardial tissue is reflected by the motion pattern of speckles.

Rapid events during the cardiac cycle such as isovolumetric phases may not appear on images and peak SR values may be reduced due to undersampling in isovolumetric phases and in early diastole. Using higher frame rates could reduce the under-sampling problem, but this will result in a reduction of spatial resolution and consequently less optimal region of interest tracking (Teske et al., 2007). With too low a frame rate the speckle pattern could be outside the search area, again resulting in poor tracking (Korinek et al., 2007). Table (4) shows the advantages and the disadvantages Non-Doppler 2D-strain imaging.
Table (4): Advantages and the disadvantages Non-Doppler 2D-strain imaging.

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Deformation analysis in 2 dimensions.</td>
<td>● Temporal resolution limited in comparison to the TDI-based technique.</td>
</tr>
<tr>
<td>● Tissue movement assessment relative to adjacent segments.</td>
<td>● Dependent on high-resolution image quality.</td>
</tr>
<tr>
<td>● Angle independent.</td>
<td>● The lower optimal frame rate for speckle tracking (compared to TDI-derived) technique limits the reliability of measurements in patients with tachycardia.</td>
</tr>
<tr>
<td>● Better spatial resolution in comparison to the TDI-based technique.</td>
<td></td>
</tr>
<tr>
<td>● Less sensitive to signal noise.</td>
<td></td>
</tr>
<tr>
<td>● Better measurement reproducibility in comparison to the TDI-based technique.</td>
<td></td>
</tr>
<tr>
<td>● In comparison to the TDI-based technique, less time consuming data acquisition and easy data processing.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>● The automated tracking system allows accurate measurements even for inexperienced observers.</td>
</tr>
</tbody>
</table>

*(International Journal of Cardiology, 2009)*

Although speckle tracking derived 2D-strain and TDI derived strain calculations do not give the same values (2D-strain imaging gives lower SR
values), strain and SR measurements obtained by these two different imaging techniques correlate well (Perk et al., 2007). Table (5) shows the normal values for strain and strain rate from the HUNT study.

Table (5): Normal values for strain and strain rate from the HUNT study.

<table>
<thead>
<tr>
<th></th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>End systolic</td>
<td>Peak systolic</td>
</tr>
<tr>
<td></td>
<td>strain (%)</td>
<td>strain rate</td>
</tr>
<tr>
<td>&lt; 40 years</td>
<td>-17.9% (2.1)</td>
<td>-1.09 s⁻¹ (0.12)</td>
</tr>
<tr>
<td>40 - 60 years</td>
<td>-17.6% (2.1)</td>
<td>-1.06 s⁻¹ (0.13)</td>
</tr>
<tr>
<td>&gt; 60 years</td>
<td>-15.9% (2.4)</td>
<td>-0.97 s⁻¹ (0.14)</td>
</tr>
<tr>
<td>Over all</td>
<td>-17.4% (2.3)</td>
<td>-1.05 s⁻¹ (0.13)</td>
</tr>
</tbody>
</table>

Values are mean (SD).

(Dalen et al., 2010)
Measurements of strain and strain rate by echocardiography have been validated using microcrystals and magnetic resonance. Non-Doppler 2D-strain measurements correlated well with data obtained by magnetic resonance imaging, both in normal myocardial segments and infarcted areas (*Amundsen et al., 2006*). Strain and strain rate measurements appeared to be sensitive indicators for sub-clinical diseases, including arterial hypertension, diabetes, systemic sclerosis, myocardial ischemia, isolated mitral regurgitation and non-ischemic cardiomyopathies.

**In Heart Failure:** It was very useful for the assessment of myocardial damage after myocardial infarction, evaluation of myocardial revascularization efficiency and prediction of patient outcome with heart failure. In a study on 137 consecutive patients with suspected congestive heart failure of different etiologies it was also shown that mean longitudinal LV strain is closely related to plasma brain-type natriuretic peptide levels, in patients with both systolic and diastolic heart failure (*Yoneyama et al., 2008*). Experimental work performed on adult dogs showed that global diastolic strain rate can be useful for the assessment of ventricular relaxation and estimation of filling pressures (*Wang et al., 2007*).

**Detection of LV myocardial ischemia:** The validity of non-Doppler 2D-strain imaging for identification and quantification of myocardial ischemia was proved experimentally in pigs with occlusion of the LAD and in rat ischemia reperfusion models with temporary LAD occlusion (*Sun et al., 2007*). Also it was experimentally shown that speckle tracking 2-Dstrain imaging correctly identifies segmental LV dysfunction induced by the scarring that follows myocardial infarction in rats (*Popovic et al., 2007*). Comparing the accuracy of 2D-strain imaging derived from speckle tracking with TDI-derived strain imaging in 150 patients undergoing DSE and coronary angiography, Hanekom et al. found similar accuracy of these two methods during DSE in the anterior coronary circulation (*Hanecom et al., 2007*).
Monitoring LV function after Aortic valve replacement: Tissue Doppler-derived strain and strain rate measurements are also useful for the monitoring of LV function during the reverse remodeling processes after aortic valve replacement in patients with aortic stenosis (Poulsen et al., 2007).

In Amyloidosis: Longitudinal strain may be useful to identify accurately cardiac amyloidosis at various stages in the disease process. It cannot distinguish between the different types of amyloidosis. A study has demonstrated that Doppler derived longitudinal strain, averaged for the 16 segments of the LV as well as a simpler average of the 6 basal segments, can distinguish biopsy proven cardiac amyloidosis patients with normal 2D and Doppler echocardiograms from healthy controls (Bellavia et al., 2008).

Detection of doxorubicin induced cardiac injury: It was found that 2D-strain imaging is highly sensitive for the early detection of doxorubicin induced cardiac injury, and radial strain reduction in patients who underwent chemotherapy with doxorubicin appeared to be associated with histologic markers of doxorubicin cardiomyopathy (Migrino et al., 2008).

Patient selection for surgical ventricular restoration (SVR): 2D-strain imaging is also the method of choice for patient selection for SVR. It was also found that systolic dyssynchrony and the end-systolic dyssynergy indexes, calculated from regional strain values are highly sensitive for evaluations of myocardial functional changes during the postoperative reverse remodeling processes after SVR (Knosalla et al., 2007).

In Sport medicine: Strain and strain rate assessment appear to be useful in sports medicine for the quantification of LV systolic function in athletes and the differentiation of athletes' hearts from asymptomatic non-obstructive hypertrophic cardiomyopathy and hypertensive cardiac hypertrophy. Kato et al. confirmed that the regional heterogeneity of LV systolic function detected by SR imaging was in
part, due to heterogeneity of LV hypertrophy and may be linked to impaired global LV relaxation in hypertrophic cardiomyopathy (*Kato et al., 2008*).

**Evaluation of RV function:** It was shown that strain and strain rate imaging is useful for the evaluation of RV function in pulmonary hypertension and RV diseases of different etiologies (RV infarction, arrhythmogenic RV dysplasia/cardiomypathy) (*Sevimli et al., 2007*).

**Early detection of acute rejection:** Systolic and diastolic global strain rate reduction appeared to be more sensitive for the early detection of acute rejection than the reduction of systolic and diastolic global strain values. 2D-strain imaging is useful for the evaluation of anti-rejection treatment efficacy (*Dandel et al., 2007*).

**Early detection of post-transplant coronary artery disease:** In patients without visible alterations in LV kinetics, 2D-strain imaging appeared reliable for noninvasive prediction of posttransplant coronary artery disease with and without focal stenoses. Eroglu et al. found that strain and SR imaging in combination with DSE is useful for early detection of posttransplant coronary artery disease before the development of relevant stenoses detectable with conventional angiography (*Eroglu et al., 2008*).

**Detection of intraventricular dyssynchrony:** 2D-strain imaging by speckle tracking and TDI-derived strain imaging are well suited to detecting and defining intraventricular dyssynchrony and they have already proved to be useful for both the selection of patients who might benefit from CRT and the evaluation of CRT efficiency (*Nagueh., 2008*). Arita et al. found radial strain by speckle tracking to be more accurate than TDI velocity to detect cardiac dyssynchrony (*Arita et al., 2007*). An important aspect for CRT effectiveness is its dependency on the LV lead position. To find out the optimal LV lead position is therefore a major goal, and
recent studies have shown that 2D-strain imaging is a useful tool for this purpose (Becker et al., 2007).

In patients with *idiopathic dilated cardiomyopathy* who were accepted for heart transplantation it was found that systolic and diastolic LV dyssynchrony and dyssynergy, which were detectable by 2D-strain imaging in all investigated patients, were more closely related to hemodynamic alterations, exercise intolerance and patient outcome than LVEF. It was also found that 2D-strain imaging provides prognostic information, which can be useful for patients' selection for heart transplantation. Thus, in patients with similar LVEF, those with rapid worsening toward inotropic support dependence showed higher dyssynchrony and lower global strain rate values than those who remained clinically stable (Dandel et al., 2007).

**In pediatric medicine:** Heart rate changes in healthy children during growth have an important impact on both systolic and diastolic myocardial strain and also on late diastolic SR calculated from color Doppler myocardial imaging (Boettler et al., 2005).

**Diagnosis of ventricular noncompaction:** An isolated case report now describes the use of SR in the diagnosis of LV noncompaction by demonstrating alternating regions of compression and expansion during systole and diastole (Williams et al., 2003).

Myocardial velocity gradient
Systolic MVG is an indicator of regional myocardial contraction that is independent of the translational motion of the heart. It is also little affected by the Doppler angle of incidence (Bach et al., 1996). It was defined as the slope of the regression line between myocardial velocities and wall thickness. It can also be calculated as the difference between endocardial and epicardial velocities, divided by wall thickness (Palka et al., 1996).

\[
\text{MVG} = \frac{(\text{Vend} - \text{Vepi})}{L}
\]

Vend=endocardial velocity, Vepi=epicardial velocity, L=wall thickness.

MVG can be measured either by velocity measurements across the thickness of the myocardium at the time of visually selected maximal color brightness (thickness-plot method) or by continuous velocity measurements throughout the cardiac cycle in two sites, the subendocardium and the subepicardium (time velocity plot method). Pellerin et al. have demonstrated that the two methods enable similar interpretation of dobutamine effects on LV wall motion, but the time-velocity plot method provides automatic detection of peak velocity, timing, and duration of wall velocity changes over time (Pellerin et al., 1999).

By contrast with diastolic velocity measurements, it has been shown that myocardial peak systolic velocity gradients are independent of age (Palka et al., 1996).

Normal segmental variability of different velocities

Normally there is heterogeneous pattern of velocities among different myocardial segments and this was proved in different studies as Galiuto et al who used the apical window to measure the longitudinal velocities from 12 segments. Lower velocities were found in the septum compared to other walls as longitudinal fibers are abundant in these walls while deficient in the septum. Also there is higher base to mid wall difference in systolic and diastolic velocities although the
E/A ratio remain the same. The highest systolic velocities in the longitudinal axis are observed in the mitral annulus and basal segments of the anterior and lateral free walls and the highest peak early diastolic velocities were in the lateral and posterior walls while the lowest systolic and diastolic velocities were in the septum. All velocities are higher in the basal than mid segments. The E’/A’ ratio are similar to the E/A ratio of mitral inflow velocities and were normally ≥ 1 (Galiuto et al., 1998).

Clinical applications of Tissue Doppler Imaging
These methods for the assessment of global cardiac functions might be valuable for the early diagnosis of diseases affecting systolic function, for monitoring disease progression and for evaluating the effect of various treatments.

- **Assessment of systolic and diastolic cardiac functions:**

  Will be discussed later.

- **Diagnosis of acute heart failure:**

  In an attractive prospective study, the authors conclude that the measurement of the tissue Doppler-derived E/E’ ratio is able to provide accurate diagnostic information in patients presenting with acute dyspnea in emergency departments. It was first reported the additional role of bedside TDI as a noninvasive Swan-Ganz catheter for the emergency diagnosis of congestive heart failure in 70 consecutive patients with acute dyspnea and preserved LV systolic function, a condition that requires the assessment of LV filling pressures for differentiating acute heart failure from non-cardiac cause of acute dyspnea (Arques et al., 2005).

  The study of Huang et al support the interest of a wide spread of bedside TDI as a diagnostic complement to inconclusive clinical, radiographic and biochemical data in the emergency care of acute dyspnea (Huang et al., 2006).

- **Detection of ischaemia:**

  In an animal model, Derumeaux et al studied TDI velocity curves during different severities of ischaemia. Within 5 seconds of occlusion of the LAD artery, significant reductions in systolic and early diastolic velocities were seen. At 30 seconds, the systolic velocities became negative and peaked at 1 minute. Simultaneously, early diastolic velocities decreased and late diastolic velocities increased. A good correlation was observed between the decrease of systolic velocities and regional myocardial blood flow. In patients with chronic coronary
artery obstruction, abnormalities of longitudinal shortening have been observed using TDI (Derumeaux et al., 1998).

TDI has been used during stress echocardiography to investigate whether it can provide more objective and numeric information on regional contractility. Von Bibra et al showed that a reduction of early diastolic velocities during DSE was more accurate than peak myocardial systolic velocities for detection of coronary artery stenosis (Von Bibra et al., 2000).

Evaluation of TDI myocardial velocities during low-dose DSE has been investigated for its ability to differentiate between viable myocardium and scar tissue. Bountioukos et al reported at low-dose dobutamine challenge, highly significantly higher systolic velocities in viable regions than in non-viable regions (Bountioukos et al., 2004).

Some studies have shown that pulsed Doppler TDI in apical views demonstrates reduced myocardial systolic longitudinal velocities in ischemic or infarcted segments (Alam et al., 2000). Investigators have suggested that TDI may be used to evaluate regional myocardial response to pharmacologic or exercise stress for the diagnosis of ischemic heart disease (Pasquet et al., 2000).

- **Differentiating constrictive pericarditis from restrictive cardiomyopathy:**

  Since restrictive cardiomyopathy is a disease of the myocardium, E’ is blunted, whereas constrictive pericarditis is a disease of the pericardium and E’ velocity is preserved, and septal E’ velocity is usually higher than lateral E’ velocity, and the E/E’ ratio is inversely related to LV filling pressures (Ha et al., 2001).

  Although experience is limited to a small number of patients, general guidelines are that an E’ less than 10 cm/s by pulsed-TDI and less than 7 cm/s by color-coded TDI are supportive of restrictive pathophysiology (Garcia et al., 1996).
PW TDI can also distinguish between them by measuring the MVG. One study evaluated this approach in 15 patients with restrictive cardiomyopathy, 10 with constrictive pericarditis, and 30 age-matched normal controls. The Doppler MVG, as measured from the LV posterior wall in early diastole and during ventricular ejection, was significantly lower in patients with a restrictive cardiomyopathy compared to those with constrictive pericarditis and normal controls (Palka et al., 2000). Recent studies have also noted that the presence of a reduced annular systolic velocity is of value in borderline cases as they identify patients with primarily myocardial disease (Choi et al., 2007).

These initial results were confirmed by Ha et al who compared the E' values of 23 patients with constrictive pericarditis, 38 patients with cardiac amyloidosis and 14 patients with restrictive cardiomyopathy. The E' was significantly higher in patients with constrictive pericarditis and a cut-off value of 8 cm/s resulted in 95% sensitivity and 96% specificity for the diagnosis of constrictive pericarditis (Ha et al., 2004).

● Early detection of cardiomyopathies:

Next to genetic testing, PW TDI appears to be an attractive diagnostic tool for preclinical diagnosis of hypertrophic cardiomyopathy since it enables detection of myocardial contraction and relaxation abnormalities, irrespective of the presence of LV hypertrophy. So TDI has emerged as a sensitive and non-invasive technique for detecting the early stage of a cardiomyopathy (De Backer et al., 2005).

● Use in evaluating chronic aortic valve disease:
TDI may be helpful for identifying subclinical LV dysfunction in patients with chronic severe aortic regurgitation who are asymptomatic but may be candidates for surgery. In one study of 21 asymptomatic patients, reduced long axis contraction, as measured by mitral annular excursion and systolic velocity, were indicators of subclinical LV dysfunction established by impaired exercise capacity and a reduction in ejection fraction with exercise. A systolic annular excursion <12 mm and a resting mitral annular velocity <9.5 cm/sec were the best indicators of subclinical LV dysfunction (Vinereanu et al., 2001).

In asymptomatic patients with moderate–severe aortic stenosis a lower than normal increase in Sm after treadmill exercise is a marker of early LV systolic dysfunction (Van Pelt et al., 2007).

- **Differentiation of hypertrophic cardiomyopathy from left ventricular hypertrophy:**

  Although the echocardiographic findings of systolic anterior movement of the mitral valve and asymmetrical septal hypertrophy are useful for diagnosing hypertrophic cardiomyopathy, these findings may also be present in patients with LV hypertrophy secondary to hypertension or vigorous exercise. TDI may help to distinguish among these disorders; together with Doppler mitral inflow velocity can be used to determine whether left ventricular filling pressures are elevated in patients with hypertrophic cardiomyopathy.

  Palka et al. showed that systolic MVG measured by color M-mode TDI at the level of LV posterior wall was lower in patients with hypertrophic cardiomyopathy than in athletes and normal subjects (Palka et al., 1997).

  Athletes typically have highly compliant ventricles with brisk E’ velocities, in contrast to the reduced E’ velocities in individuals with hypertrophic cardiomyopathy (Cardim et al., 2003).
• **Evaluation of mechanical dyssynchrony by TDI:**

  Determination of asynchrony by TDI seems to be the best predictor for improvement after biventricular pacing. Some authors evaluated LV dyssynchrony by comparing the septal and lateral segments of the LV allowing for prediction of clinical response and reverse remodelling after CRT (*Bax et al.*, 2004). Others proposed a 12-segment LV model to measure the extent of LV dyssynchrony (*Yu CM et al.*, 2002).

  One study using the time difference between the septal and the lateral LV wall showed the value of tissue synchronization imaging for evaluation of mechanical dyssynchrony and prediction of clinical response and LV remodelling after CRT (*Van de Veire et al.*, 2007).

  Mechanical dyssynchrony can also be evaluated using the triplane TDI modality (*Van de Veire et al.*, 2008). The triplane technique permits simultaneous comparison of various LV segments during the same heartbeat. If the triplane technique is combined with tissue synchronization imaging, a three-dimensional LV volume can be constructed allowing visual appreciation of activation times. Real-time, three-dimensional echocardiography has been proposed as an alternative modality to TDI for assessment of intraventricular dyssynchrony. However, in patients with ischaemic cardiomyopathy, TDI and real-time, three-dimensional echocardiography show poor agreement for evaluating the magnitude of intraventricular dyssynchrony and the site of maximal mechanical delay. This may be explained by their respective assessment of longitudinal versus radial timing (*Burgess MI et al.*, 2007).

• **Routine monitoring after heart transplantation:**
Studies proved TDI’s reliability for early detection of acute rejection and posttransplant coronary artery disease and showed that serial TDI can spare patients unnecessary and distressing routine invasive examinations (Yu et al., 2007).

TDI also appeared reliable for prognostic estimations after heart transplantation and for the evaluation of rejection severity and guidance of anti-rejection therapy (Dandel et al., 2003).

Also it was showed that TDI can also be helpful in evaluations of myocardial recovery during mechanical unloading after ventricular assist device implantation (Dandel et al., 2005).

- **Assessment of right ventricular function**

  The intrinsic limitations of standard echocardiography does not allow for an examination of a heart chamber with such complex anatomy as that of the RV. The problem becomes more evident in obese patients, chronic bronchopneumopathy and patients in intensive care. PW TDI seems to have this potential more than other methods; In experimental studies, myocardial acceleration during isovolumetric contraction has been shown to be a load-independent parameter that correlates with telesystolic elasticity of the RV, and if this is verified in clinical practice, it could become a useful and interesting parameter to measure RV systolic function (Vogel et al., 2002).

  Peak systolic pulsed TDI of the tricuspid annular velocity provides a simple, rapid, and non-invasive tool for assessing RV systolic function in patients with heart failure (Meluzin et al., 2001).

- **Assessment of atrial mechanical function:**
TDI and strain methods have been applied in the study of atrial mechanical function. Strain indices have been shown to be capable of identifying those patients with higher probability to maintain sinus rhythm after electrical cardioversion of atrial fibrillation (Weidemann et al., 2003).

- **Other applications of TDI:**

  Change of velocity and patterns of velocity propagation along the heart walls can be easily observed using the 2-D TDI image sequences. The application in electrophysiology enables recognition of the site of pre-exitation in the Wolff-Parkinson-White syndrome and detecting the origin of other rhythm abnormalities (Eder et al., 2000).

  Also, Bartel et al. demonstrated that using TDI patterns increases the detection of vegetation in infective endocarditis as well as of thrombus formations (Bartel et al., 1999).
Role of tissue Doppler in assessment of cardiac functions

TDI can be used to measure tissue velocities in different segments of the myocardium, both in systole and in diastole. Moreover, TDI can also be applied for measurement of velocities at different sites of the mitral valve annulus. These latter velocities reflect the longitudinal vector of shortening and lengthening of myocardial segments. The diastolic velocities decrease more with age than do systolic velocities (Sun et al., 2004).

However, the velocities of the mitral flow are influenced by several factors, such as age, heart rate and preload. On the other hand, new echocardiographic indices obtained at the tissue Doppler have shown to be less preload-dependent (Barberato and Pecoits., 2006).

Assessment of LV functions:

1. Systolic function:

A- Global LV function:

This has been quantified by measuring the displacement distance of the mitral annulus by M mode echocardiography and correlates with LVEF. Measurement is made at several sites; lateral, septal, inferior and anterior aspects of the mitral annulus to derive an average figure for mitral annular displacement velocity, mean velocity is more likely to reflect global LV function, it provides significant incremental prognostic value compared with clinical information and mitral DT of the E wave. However, mitral annular velocity measurement cannot be used in patients with prosthetic ring or prosthetic mitral valve or severe mitral annular calcification; Soeki et al has shown that severe mitral annular calcification is associated with elevated transmitral inflow velocities in the absence of significant valvular stenosis, and low E’ velocities (Soeki et al., 2002).
Also Gulati et al compared the descent velocity of the mitral annulus by TDI with the standard of radionuclide ventriculographic EF. They applied TDI to 6 points around the annulus and found that the 6-site average compared linearly with EF. An average mitral annular descent velocity of > 5.4 cm/s was 88% sensitive and 97% specific for EF > 50% (Gulati et al., 1996).

Mitral annular peak systolic velocity is also a sensitive indicator of alterations in LV contractility induced by low dose dobutamine infusion at 1, 2, 3, and 5 mg/kg/min. Mitral annular systolic velocity significantly increased with only 1 mg/kg/min of dobutamine and further incremental increases occurred with each subsequent dose. A linear dose to response relation was demonstrated within this narrow dosage range. Routine measures of LVEF by Simpson’s rule did not detect increases until the 3 mg/kg/min dose. Another report showed that mitral annular systolic velocity can detect abnormal systolic function in patients with heart failure and a normal EF (Yip et al., 2002).

Tricuspid annular velocity can be used as an index of RV function in patients with heart failure. There was a good correlation between tricusped systolic annular velocity and RV ejection fraction assessed by radionuclide ventriculography. A systolic annular velocity, 11.5 cm/s predicted RV ejection fraction 45% with a sensitivity of 90% and a specificity of 85% (Meluzin et al., 2001). Myocardial acceleration during isovolumic contraction has recently been validated in experiments as a novel noninvasive index of right and left ventricular contractile function (Vogel et al., 2003).

B-Regional LV function:

Postionning a sample volume within the myocardium equidistant from endocardial and epicardial borders allows measurement of segmental myocardial velocities. The color coded 2D tissue velocity map also assist regional function, as
deviation from the normal pattern of LV motion and color changes throughout the cardiac cycle.

Areas of akinesia are shown by darker hues of color representing low velocity of motion, and dyskinetic segments may be seen to exhibit colors opposite to those of adjacent normal segments, particularly during systole. Analysis of the intramyocardial velocity gradients also aids detection of regional dysfunction but this technique is restricted to only a few myocardial segments and this reduces its utility as a practical tool.

Because TDI facilitates quantitative evaluation of regional wall motion abnormalities, many studies have tried to determine LV myocardial viability during DSE using pulsed TDI and color-coded TDI. There is a possibility that ischemic and nonischemic segments interact with each other (tethering), resulting in a decrease in systolic motion velocity in the nonischemic segment (Yamada et al., 1998). However, Sw1 along the long axis during the isovolumic contraction phase is more sensitive than systolic parameters during the ejection phase in detecting myocardial viability (Matsuoka et al., 2002).

Strain and SR also diminish significantly with regional ischemia and can differentiate infarcted and ischemic from normal myocardium. They can identify the extent of transmural infarction (Weidemann et al., 2006).

In the normal subject, regional differences in systolic and diastolic myocardial velocities exist between individual wall segments (Alam et al., 1999).

In the parasternal view, velocities are lower in the anteroseptal wall than in the posterior wall. In a series of 24 normal volunteers, Garcia et al, who used pulsed TDI in the parasternal short-axis view, found an average value of 4.5 ± 1.6 cm/s for peak systolic velocity at the anteroseptal wall and 7 ± 1.5 cm/s for the posterior wall (Garcia et al., 1996). In the apical view, myocardial systolic velocities recorded by TDI are higher at the base than at the mid left ventricle or at
the apex (Pai et al., 1998), and velocities at the lateral margin of the tricuspid annulus are higher than those on the left side (Isaaz et al., 1993).

Lateral E’ velocity is usually higher than septal E’ velocity (Nagueh et al., 1997). This difference can be exaggerated or reversed in patients with hypertrophic cardiomyopathy (Nagueh et al., 1999), septal infarction (Rivas-Gotz et al., 2003), or those with primary pulmonary hypertension (Ruan et al., 2007).

2. LV diastolic function:

Conventional Doppler measures LV filling derived from mitral inflow velocities reflect only global diastolic function, TDI offers the ability to measure regional diastolic function. PW TDI has enabled characterization of the normal pattern of early and late diastolic velocity peaks, with highest values at the mitral annulus, decreasing progressively towards the apex (Galuito et al., 1998).

The standard criteria for LV diastolic dysfunction is characterized by impairment of LV relaxation during the IVC time in cardiac catheterization. However, routine invasive cardiac catheterization is not always feasible, and therefore, there is need to a simple noninvasive modalities to replace catheterization (Daneshvar et al., 2010).

Two main velocity waves (Em and Am), directionally opposite to the major systolic wave can be recorded by TDI during early and late diastole, respectively. As for systolic velocities, studies in healthy subjects show that Em recorded in the short-axis view are higher at the level of posterior wall than at the anteroseptal wall. Garcia et al., found an average value of 6.3 ± 1.7 cm/s for Em at the anteroseptal wall versus 9.3 ± 3 cm/s at the posterior wall (Garcia et al., 1996). In the apical view, myocardial diastolic velocities recorded by TDI are higher at the base than at the mid LV or at the apex, which is almost stationary (Galuito et al., 1998).
The early diastolic tissue velocity, $E'$, correlates with the invasive measure of diastolic function (Ommen et al., 2000). Though somewhat preload dependant in hearts with normal systolic functions, it is much less preload dependant than the early transmitral Doppler wave ($E$) (Nagueh et al., 1997). This decrease in preload dependency allows $E'$ to differentiate a normal and pseudonormal pattern on the transmitral Doppler flow trace (Sohn et al., 1997). The $E/E'$ ratio can predict LV filling pressures (Nagueh et al., 1997). In patients with EF < 50%, $E' < 3$ cm/s is a powerful predictor of mortality (Wang et al., 2005), whereas $E/E' ≥ 15$ is an independent predictor of future heart failure (Liang et al., 2006).

Early works had already shown that pulsed TDI is able to detect abnormal myocardial diastolic velocities pattern at the level of the LV posterior wall in patients with heart disease characterized by a decreased $E_m$ with a decreased ratio $E_m/A_m$ (Isaaz et al., 1993).

More studies have reported reduced $E_m$ and $E_m/A_m$ ratio in ischemic or infarcted segments with the use of pulsed Doppler TDI in apical views (Alam et al., 2000). Thus, TDI allows quantitation of the critical mass of myocardium with abnormal regional diastolic function that leads to abnormal global diastolic function as assessed by standard transmitral flow analysis.

Myocardial diastolic velocities recording by TDI may provide a sensitive method for detecting transient myocardial ischemia. Bach et al., using quantitative color two-dimensional TDI in their patients undergoing percutaneous coronary angioplasty, showed that TDI peak diastolic velocities decrease like systolic velocities during balloon inflation in the myocardium subtended by the angioplasty vessel with a rebound increase after reperfusion (Bach et al., 1996). Derumeaux et al., in their animal study showed that $E'$ measured by pulsed TDI at the base in the apical view decreased within 5 seconds after coronary artery occlusion (Derumeaux et al., 1998).
Data showed that age is one of the strongest determinants of both the E’ and the E/E’ values. This may suggest that in clinical practice, a single cut-off value for E/E’ for the evaluation of diastolic function or raised LV filling pressures should not be used but that age-dependent normal values should be acquired (De Sutter et al., 2005).

Late diastolic velocity of the mitral anulus at the time of atrial contraction increases during early diastolic dysfunction, as is the case for the mitral inflow A wave, but decreases as atrial function deteriorates. A’ has been correlated with LA function (Khankirawatana et al., 2004). Table (6) presents normal values of peak pulsed TDI diastolic velocities for basal segments of the left ventricle recorded in the apical views.

<table>
<thead>
<tr>
<th></th>
<th>Em (cm/sec)</th>
<th>Am (cm/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lateral (Isaaz K et al., 1993)</td>
<td>16.3 ± 2.9</td>
<td>17.3 ± 4.4</td>
</tr>
</tbody>
</table>

Table (6): Normal values of peak pulsed TDI diastolic velocities for basal segments of the left ventricle recorded in the apical views.
Assessment of LV filling pressures

In the absence of direct measurements of filling pressures, non-invasive estimation of filling pressures with E/E’ could also provide useful prognostic information. In a retrospective study comprising 250 patients with acute MI, E/E’ independently predicted all-cause mortality incremental to LVEF, age and a restrictive transmitral filling pattern (Hiller et al., 2004). Also, in patients with non-valvular atrial fibrillation, E/E’ is a powerful predictor of clinical outcome (Okura et al., 2006).

A simple tool for the non-invasive evaluation of LV filling pressures is the ratio of transmitral early peak flow velocity (E) over early diastolic mitral annulus velocity (E’). Nagueh et al demonstrated that the E/E’ ratio correlated well with PCWP measured invasively. An E/E’ ratio, 10 detected a mean PCWP equals 15 mm Hg with a sensitivity of 97% and a specificity of 78%. Ommen et al suggested...
a higher cut-off value of 15 for E/E’, which is now commonly used. The different cut-off values can be explained by the fact that Nagueh et al used the lateral mitral valve annulus whereas Ommen et al used the medial mitral valve annulus (Nagueh et al., 1997,(Ommen et al., 2000). 

It is usually not critical to use TDI in predicting LV filling pressures in patients with depressed EF. However, in patients with normal EF, TDI is the most reliable method for the assessment of LV relaxation and filling pressures. Importantly, two studies have shown the lateral velocity to be more accurate in that regard (Kasner et al., 2007). However, if the average of septal and lateral E’ is used, a ratio < 8 identifies patients with normal filling pressure, whereas a ratio >13 identifies those with increased filling pressures. When the ratio falls between these cutoffs, other echocardiographic measurements are needed (Rivas-Goetz et al., 2003).

The conclusion made by McCulloch et al that estimation of LV filling pressure by color tissue Doppler could lead to significant errors when compared with estimation by spectral tissue Doppler is misleading and is not supported by the data presented. The authors did not demonstrate that the estimate of LV filling pressure by the ratio of mitral inflow early diastolic velocity to early mitral annular diastolic velocity (E/E’) using spectral Doppler is more accurate than estimates using validated cut-off values for color tissue Doppler (McCulloch et al., 2006).

Huang et al evaluated the diagnostic accuracy of E/E’ in patients with acute dyspnoea who are visiting the emergency department. The E/E’ value was found to be a useful supplementary diagnostic tool for patients with inconclusive blood B-type natriuretic peptide level (Huang et al., 2006). Another study validated the use of E/E’ for the estimation of LV filling pressures during semisupine exercise testing (Burgess et al., 2006). European Society of Cardiology Guidelines have included TDI-derived E/E’ in the diagnostic flow chart on how to diagnose heart failure with normal LV EF (Paulus et al., 2007).
**Estimation of myocardial relaxation:**

In patients with early diastolic dysfunction, E'/A’ ratio is reduced. With progressive diastolic dysfunction, A’ velocity decreases, and E'/A’ ratio is less than 1. Recently, E'/A’ ratio was reported to identify well patients with diastolic heart failure as determined by high fidelity LV pressure/volume measurements (*Kasner et al., 2007*).

Em is generally thought to be related to the myocardial process of relaxation, and some works have suggested that Em recorded by pulsed TDI at the cardiac base in the apical views is less preload dependent than early transmitral velocity. Sohn et al. showed that in patients with relaxation abnormality as assessed by transmitral velocity variables, saline loading led to a pseudonormalized transmitral pattern whereas Em and Em/Am remained unchanged; similarly, unloading with nitroglycerin infusion in patients with baseline normal transmitral pattern led to a decreased early to late transmitral velocities ratio without any changes in Em and Em/Am. In 38 consecutive patients undergoing catheterization simultaneously with noninvasive measurements, the authors showed that the time constant Tau was better linearly related to Em and Em/Am than to transmitral velocity variables. A value of Em less than 8.5 cm/s with a ratio Em/Am less than 1 identify a pseudonormalized transmitral velocity pattern with a 88% sensitivity and a 67% specificity (*Sohn et al., 1997*).

Also Nagueh et al. confirmed that pulsed TDI Em at the mitral annulus behaves as a preload-independent index of relaxation. They studied 3 groups of patients: 34 normal subjects, 40 asymptomatic patients with normal EF and transmitral E/A less than 1, and 51 patients with congestive heart failure and a E/A ratio greater than 1(pseudonormal); they found that Em was lower with a decreased Em/Am in both impaired relaxation and pseudonormal compared with normals; the ratio E/Em was similar between normals and patients with impaired relaxation but
was significantly higher in the patients with pseudonormal transmitral pattern; in 60 patients in whom mean PCWP was measured, the authors found a very good correlation between the ratio E/Em and mean PCWP, a ratio E/Em greater than 10 indicated a PCWP greater than 12 mm Hg with a 91% sensitivity and a 81% specificity (Nagueh et al., 1997).

Advantages of Tissue Doppler Imaging

The use of TDI has been a clear advantage and which are incontrovertible are listed below.

1. TDI detects and measures the motion of weaker and more complex echoes from within the layers of the myocardial wall. Velocity gradients are known to exist in different layers of the myocardium, which are altered in diseased states, and can be detected by TDI. (Waggoner et al., 2001).

2. Use of TDI and SR imaging have already been shown to be superior to conventional real-time B-mode imaging for the interpretation of regional wall motion abnormalities (Fathi et al., 2001). Distinguishing hypokinesis and akinesis or dyskinesis by conventional echocardiography has wide interobserver variability. Routine use of TDI and SR imaging makes this job simple and quantitative. (Pislaru et al., 2002).

3. Longitudinal motion of the mitral valve annulus by M-mode has been used for assessing systolic and diastolic LV function. This information is now readily available by pulsed Doppler TDI and SR imaging (Pislaru et al., 2002).

4. Very high temporal resolution (<4 ms) have provided an insight into a number of physiologic and pathologic short-lived events during the cardiac cycle, particularly in myocardial ischemia and its detection. Assessment of segmental
viability by post-systolic thickening or strain is now an invaluable tool in clinical practice (Edvardsen et al., 2002). Similarly, estimation of regional and global isovolumic phases, ejection and filling periods is possible within a single cardiac cycle from a single point of sample volume, even without the use of an ECG. This is the only technique that provides temporal data of both phases of the cardiac cycle simultaneously.

5. TDI is a valuable tool for the assessment of diastolic dysfunction, and can easily differentiate normal from pseudonormal patterns of diastolic dysfunction. Compared to hemodynamic flow Doppler parameters, it is relatively load-independent and does not fuse even at high heart rates (Waggoner et al., 2001).

6. SR imaging data obtained from Doppler ultrasound has good agreement with that obtained from magnetic resonance tagging. (Edvardsen et al., 2002).

7. TDI has a distinct advantage with regard to the assessment of RV function, which is difficult otherwise because of the complex geometry (Frommelt et al., 2002).
Limitations of TDI

- Apical velocity are not so accurate in comparison to velocities measured from other segments as the apex is in the near field of the echo transducer with high signal to noise ratio, with consequent suboptimal image quality. Also the apex is virtually fixed in respect to longitudinal movement (Galiuto et al., 1998).

- The measured velocity includes two components; the intrinsic myocardial velocity and whole cardiac motion during contraction and relaxation. The last component modifies the color of wall motion. The potential for these problems is more apparent in patient with cardiac translation movement such as RV volume overload, LBBB and after cardiac surgery (Gorscan et al., 1996). This may be overcame by calculation of MVG (Uematsu et al., 1995).

- It is angle dependant so the recorded peak velocities may not be the true peak velocities so multiple planes must be acquired.

- Velocity resolution, although the assessment of the wall motion velocity is gain independent, it can be affected by intensified noise. Therefore attempts should be made to visualize ventricular wall as clearly as possible (Miyatake et al., 1995).

- Velocity saturation, the relatively narrow range selected by investigators to maximize sensitivity of low velocities makes velocities exceeding this limit saturated at that value and always displayed as white color whatever its value, this appear to occur in normal segments especially in early diastole. Accordingly, the values reported by such technique may likely represent under estimation of peak velocities for normal subjects (Gorscan et al., 1996).
• Low frame rate, it is important limitation especially with 2-D leading to missing some subtle changes, it is less significant in M-mode due to relatively higher frame rate.

• Absent color coding, indeed, in some patients a part of the myocardium particularly in either the septal or lateral wall is not encoded by color although wall motion is maintained. It is sometimes difficult to distinguish between lack of color encoding due to akinesia and that due to technical factors.

• Effect of heart rate may influence the quantification regional function.

• The RV shape changes may influence LV translation assessed by TDI.
Chapter Two

Obesity

Section 1: Obesity

**Background:**

The spread of obesity has been declared a worldwide epidemic by the World Health Organization (WHO). In fact, a new term, globesity, has been coined to describe the recent upsurge of overweight and obesity throughout the world’s population. How severe is the problem? According to WHO, worldwide obesity has more than doubled since 1980. In 2008, 1.5 billion adults, 20 years and older, were overweight. Of these, more than 200 million men and 300 million women were obese. Sixty-five percent of the world’s population live in countries where overweight and obesity kills more people than underweight. Furthermore, nearly 43 million children under the age of five were overweight in 2010.

Obesity is a leading preventable cause of death worldwide, with increasing prevalence in adults and children, and authorities view it as one of the most serious public health problems of the 21st century (*Barness et al., 2007*).

It is a medical condition in which excess body fat has accumulated to the extent that it may have an adverse effect on health, leading to reduced life expectancy and increased health problems. It increases the likelihood of various diseases, particularly heart disease, type 2 diabetes, breathing difficulties during sleep, certain types of cancer, and osteoarthritis (*Haslam and James, 2005*). Central obesity is also highly correlated to the risk of cardiovascular disease (*Gustafson et al., 2010*).
Conclusion

On average, obesity reduces life expectancy by six to seven years, a BMI of 30–35 reduces life expectancy by two to four years, while severe obesity (BMI > 40) reduces life expectancy by 10 years (Whitlock et al., 2009).

Overweight and obesity in early adulthood combines with the difficulty of sustained weight loss after becoming obese to portend a major demographic scenario of chronic obesity. The 2007 Wanless report highlights the ever increasing problem of obesity and the consequent health problems. Despite many attempts to develop interventions to prevent obesity, little success has been reported (Wanless et al., 2007).

Obesity is most commonly caused by a combination of excessive food energy intake, lack of physical activity, and genetic susceptibility, although a few cases are caused primarily by genes, endocrine disorders, medications or psychiatric illness. Evidence to support the view that some obese people eat little yet gain weight due to a slow metabolism is limited; on average obese people have a greater energy expenditure than their thin counterparts due to the energy required to maintain an increased body mass (Kushner and Robert, 2007).

In adults, early age at menarche is a strong risk factor for increased risk of obesity in women. However, the causal direction and mechanism behind this association are debatable, as girls with earlier menarche are more likely to be overweight even before the onset of puberty (Must et al., 2005).

Obesity in children and adolescence:

Obesity clusters in families, and parental obesity is the most important risk factor for obesity in children (Shalitin et al., 2003). Weight, height and recumbent length of children are measured routinely in most clinics. In one prospective cohort, increased weight gain during the first 3 years of life was associated
independently with higher BMI, fat mass, and waist circumference at 17 years of age (Ekelund et al., 2006).

Pediatric obesity is associated with increased risks of concomitant psychological or psychiatric problems, cardiovascular risk factors, chronic inflammation, type 2 diabetes mellitus, and asthma (Danials et al., 2005).

For an understanding of developmental patterns, mean body fat percentages derived from bioelectrical impedance analyses are available for US children >12 years of age (Chumlea et al., 2002), and percentile curves have been published for British children 5 to 18 years of age (McCarthy et al., 2006).

In 1994, the Expert Committee on Clinical Guidelines for Overweight in Adolescent Preventive Services recommended that children who’s BMI exceeds 30 kg/m² or is ≥95th percentile for age and gender should be considered overweight. In 2005, the Institute of Medicine consciously departed from the previously described terminology and elected to define children with BMI of ≥ 95th percentile for age and gender as obese, rather than overweight (Koplan et al., 2005). Olshansky and colleagues have reported the results of mathematical modeling, which suggests that because of obesity in children, this current generation of children is likely to have a shorter average lifespan than their parents (Olshansky et al., 2005).

**Assessment of obesity:**

In the clinical setting, obesity is typically evaluated by measuring BMI, waist circumference, and evaluating the presence of risk factors and comorbidities.

1. **Body mass index [BMI]:**
Conclusion

The most frequently used measure is weight in relation to height, usually represented by the BMI which defined as weight (kg)/height squared (m$^2$) ([Sweeting, 2007]).

Obesity can be measured directly using dual energy X-ray absorptiometry and isotopic dilution techniques ([Goodpaster, 2002]). However, these are costly and their limited availability makes it difficult to perform such measurements in large numbers of subjects. In some studies, fat mass has been measured indirectly using bioelectrical impedance or skin-fold thickness both of which correlate reasonably well within the normal range but less so in the very lean or the obese. The most commonly used marker of adiposity is BMI which is a measure of heaviness that can be performed in large epidemiological studies and correlates reasonably well with body fat content. Several expert have recommended BMI as the preferred measure for evaluating obesity among children and adolescents 2 to 19 years of age ([Koplan et al., 2005]).

In adults, overweight is defined as a BMI 25 to 29.9 kg/m$^2$ and obesity as BMI $\geq$ 30 kg/m$^2$. Other indexes that have been used less commonly but possibly with more predictive power include body fatness, WC, W/HR, and weight-to-height ratio ([Litwin, 2008]). A recent study of nearly 360,000 participants from 9 European countries showed that both general obesity and abdominal adiposity are associated with risk of death and support the importance of WC or WHR in addition to BMI for assessing mortality risk ([Pischon, 2008]).

BMI-for-age gender-specific reference charts with recommended cut-offs defining obesity have been developed in a number of countries. In addition, the International Obesity task Force (IOTF) has produced charts based on pooled international data using percentile curves based on the recommended definitions of adult overweight and obese, aiming to compare across populations and employ a consistent definition throughout the lifespan ([Chinn, 2006]).
Conclusion

The correlation between the BMI number and body fatness is fairly strong; however the correlation varies by sex, race, and age. These variations include the following examples; women tend to have more body fat than men, older people tend to have more body fat than younger adults and highly trained athletes may have a high BMI (Prentice and Jebb, 2001).

In an important study, Katzmarzyk et al assessed the validity of BMI and WC criteria for overweight and obesity for identifying correctly youths 5 to 18 years of age who had ≥3 of 6 risk factors (low HDL cholesterol levels, high LDL cholesterol levels, high triglyceride levels, high plasma glucose levels, high plasma insulin levels, or high blood pressure) (Katzmarzyk et al., 2004).

2. Waist Circumference (WC):

Unfortunately, a BMI-based definition fails to take body fat distribution into account. Although weight reduction is not recommended for patients with a BMI < 25, some patients in this category clearly have risks related to body fat distribution. WC has attracted much recent attention as an indicator of fatness and health risks in children and adults. The interest in WC stems from research linking accumulated visceral adipose tissue to increased health risks and metabolic disorders in children and adults (Katzmarzyk et al., 2004).

Compared with BMI, WC in children provides a better estimate of visceral adipose tissue measured with MRI at the level of the fourth lumbar vertebra, whereas BMI is better at estimating subcutaneous adipose tissue (Brambilla et al., 2006). In multivariate regression models, WC is significantly more efficient than BMI in predicting insulin resistance, blood pressure, serum cholesterol levels, and triglyceride levels (Lee et al., 2006). A WC of greater than 102 cm in men and greater than 88 cm in women is consistent with abdominal obesity and provides a substantial increased risk for metabolic complications (Aronne, 2002).

3. Waist to hip ratio (W/HR):
The W/HR has been used to identify subjects with abdominal fat accumulation (W/HR of greater than 1.0m in men and greater than 0.85m in women) as has WC alone, which is a convenient and simple measurement and correlates well with BMI, W/HR and most importantly with risk factors for cardiovascular disease. Body measurements, such as the W/HR and WC, seem to predict the risk of mortality better than the BMI (Haffner et al., 2007).

4. Skinfold Thickness:

It was considered attractive research tools because measurements are noninvasive and specific to subcutaneous fat. There is little evidence that, once BMI is known, skinfold thickness categories increase the accuracy of identifying those with the most total body fat or other risk factors. Moreover, when skinfold measurements are included in regression models, they provide unique information beyond height and weight in accounting for variations in risk indicators, including blood lipid levels, lipoprotein levels, blood pressure, plasma glucose levels, plasma insulin levels, insulin resistance, and inflammation (Vikram et al., 2004).
Clinical types of obesity:

Types of obesity:

1- Overall obesity:

Overall obesity is reflected by BMI and central adiposity reflected by WC is designated by the American Heart Association as major risk factors associated with an increased risk of CHD. It has been well-established that men and women exhibit different styles of obesity; upper body obesity is more prevalent among men while lower body obesity is more prevalent among women. Overall obesity, as measured by BMI, is an independent risk factor for CVD and increased mortality (Mora et al., 2005).

2- Central obesity:

Recently, particular attention has been given to patterns of body fat distribution and their comparative impact on CVD risk. Central obesity, commonly measured by W/HR, is increasingly recognized as a more powerful predictor of obesity related cardiovascular risk factors and death than is overall obesity (Nicklas et al., 2006).

In general, anthropometric measurements [WC, W/HR, or skinfold thickness] have been used to estimate central or upper body obesity. These provide useful estimates of the proportion of abdominal fat but they do not distinguish between accumulations of deep abdominal fat and subcutaneous abdominal fat. Imaging techniques such as CT or MRI provide more accurate data, but are costly and infeasible for use in large studies. The American Heart Association in 1992 and the US Department of Agriculture in 1990 recommend a WC threshold of 102 cm and 88 cm for men and women, respectively, and a WHR threshold of 95 cm and 88 cm for men and women, respectively. WHO has accepted the proposed
lowest health risk WC values of below 94 cm and below 88 cm for men and women, respectively (Zhu et al., 2002).

**Causes of Obesity:**

At an individual level, a combination of excessive food energy intake and a lack of physical activity are thought to explain most cases of obesity (Lau et al., 2007). A limited number of cases are due primarily to genetics, medical reasons, or psychiatric illness (Bleich et al., 2008). In contrast, increasing rates of obesity at a social level are felt to be due to an easily accessible and palatable diet (Drewnowski and Specter., 2004), increased reliance on cars, and mechanized manufacturing (James., 2008).

A 2006 review identified ten other possible contributors to the recent increase of obesity: (1) insufficient sleep, (2) endocrine disruptors (environmental pollutants that interfere with lipid metabolism), (3) decreased variability in ambient temperature, (4) decreased rates of smoking, because smoking suppresses appetite, (5) increased use of medications that can cause weight gain (e.g., antipsychotics), (6) proportional increases in ethnic and age groups that tend to be heavier, (7) pregnancy at a later age, (8) epigenetic risk factors passed on generationally, (9) natural selection for higher BMI, and (10) assortative mating leading to increased concentration of obesity risk factors (Keith et al., 2006).

Obesity runs in families as much through habit as genetics. More than 41 such genetic sites have been identified and in their presence obesity will develop only if there is a favorable environment. These genes control different processes, such as regulation of fat distribution, metabolic rate, response to exercise and diet, control of feeding, and food preferences, etc. But the striking rise in the incidence of obesity, which has happened in the last few decades, is not because of changes in the genetic background of the human race, since these changes take thousands of
years to evolve. This epidemic is mainly caused by rapid lifestyle changes involving eating habits and exercise (Grundy et al., 2004).

**Prevalence of obesity:**

The prevalence of overweight and obesity is increasing at a very high rate, affecting an estimated 300 million individuals worldwide. A number of studies carried out in developing countries report an approximate 20% prevalence of obesity (Marquezine et al., 2008).

Obesity has now become a critical problem in the United States, with the prevalence among adults increasing by nearly 50% during the 1980s and 1990s. In 2007–2008, obesity in the United States was reported to affect 32.21% of male adults and 35.5% of female adults (Flegal et al., 2010). Additionally, the distribution of BMI in the U.S. has shifted in a skewed fashion such that the proportion of the population with morbid obesity has increased by a greater extent than overweight and mild obesity (Poirier et al., 2006).

It has been reported that the prevalence of obesity in adults is very high in Egypt, particularly among women. Generalized obesity in Egypt and its association with certain chronic diseases has been reported in many studies including hypertension and CVD risk in men and women (Tawfik et al., 2003).

Unlike Europe and North America, obesity in the Eastern Mediterranean Region is more prevalent in women, urban areas and those of higher socioeconomic status. In Egypt the prevalence of obesity was 56% in urban areas compared with 44% in rural areas (Musaiger et al., 2003). Egyptian females have the highest proportion of overweight (31.7%), as well as the highest proportion of obesity in the Eastern Mediterranean countries (20.1%) (Martorell, 2000).

**Prevalence of obesity in children:**
The prevalence and severity of childhood obesity are both increasing. Childhood obesity increases the risk of obesity in adulthood tenfold and pediatric patients that persistently remain at the 99th BMI percentile are at very high risk for severe adult obesity. Current estimates are that 4% of children and adolescents have a BMI above the 99th percentile for BMI, a level that is associated with an even more dramatic increase in cardiovascular risk factors in young individuals (Freedman et al., 2007).

Considering the standard definition for overweight and obesity in the pediatric population, 11.9% were at or above the 97th percentile of the BMI, 16.9% were at or above the 95th percentile and 31.7% were at or above the 85th percentile (Ogden et al., 2010).

Study noted particularly high prevalence in countries in North America, Great Britain and south-western Europe. A review of surveys conducted within Europe during the 1990s, suggested higher levels of childhood overweight and obesity in southern countries and lower levels in the central and eastern countries which experienced political and economic transition over that period. Within developing countries, high prevalence is found in the Middle East (Kelishadi, 2007).

**Pathophysiology of Obesity:**

The adipocyte acts as an endocrine organ, and plays a substantial role in the pathogenesis and complications of obesity (Martin et al., 2008). Obesity is a low-grade systemic inflammatory condition. Studies have revealed that adipose tissue is not only a passive reservoir for energy storage but also produces and secretes a variety of bioactive molecules called adipocytokines, including tumor necrosis factor, leptin, resistin ... etc. Dysregulated production of adipocytokines is associated with the pathophysiology of obesity-related metabolic diseases (Trayhurn, 2005).
Adipose tissue is inflamed in obesity, with decreased expression of the anti-inflammatory adipokine adiponectin and increased secretion of a variety of proinflammatory cytokines, e.g., tumor necrosis factor alpha (TNF-α), interleukin (IL)-6, and prothrombotic factors such as plasminogen activator inhibitor-1 (PAI-1) \((\text{Lehrke and Lazar, 2004})\). Infiltration of adipose tissue by macrophages is in part responsible for this inflammatory process associated with obesity \((\text{Xu et al., 2003})\).

Increased levels of leptin may be also particularly related with CVD. CRP may play a role in the development of leptin resistance, which is important because endogenous hyperleptinemia does not reduce appetite or increase energy expenditure \((\text{Enriori et al., 2006})\). Several studies have already shown that elevated TG impair the transport of leptin to the brain, thereby preventing the brain from responding to the leptin \((\text{Shapiro et al., 2008})\).

Recently, increased concentrations of both CRP and leptin were associated with an increased risk of major cardiovascular events, but leptin seems to be a more robust predictor \((\text{Romero-Corral et al., 2008})\). In a multivariate model, leptin was an independent predictor of cardiovascular events, whereas CRP was not. In fact, the increase in inflammatory markers is associated with insulin resistance, obesity, and cardiovascular events \((\text{Lavie et al., 2008})\).
Section 2

Obesity and Cardiovascular System

**Background:**

There are numerous adverse effects of obesity on general, and especially, cardiovascular health. It has a major impact on CVD and is associated with reduced overall survival.

**Cardiovascular Consequences of Obesity:**

**Obesity and atherosclerosis:**

Obesity results in increased deposition of perivascular fat around the heart and its major branches. This increased adipose tissue surrounding the blood vessels causes the overproduction of proinflammatory and profibrotic cytokines, leading to inflammation and atherosclerosis, with a consequent increase in intima-media thickness and decrease in arterial distensibility (Gustafson, 2010).

Obesity directly contributes to atherogenesis via the effects of some of the adipokines that adipose tissue generates. Specifically, interleukin-6 (IL-6), tumor necrosis factor (α-TNF), angiotensin-II, and leptin, are all proinflammatory and are secreted by adipose tissue. IL-6 induces vascular cell adhesion molecule (VCAM-1) expression and monocyte chemoattractant protein-1 (MCP-1) secretion by endothelial cells, both of which encourage monocytes to attach to and infiltrate into the subendothelial space of the artery wall (Rott, 2003).

Adipokine, α-TNF, also stimulates VCAM-1 expression, LDL uptake by macrophages, and promotes plaque destabilization. Angiotensin II also stimulates VCAM-1 and MCP-1 expression, monocyte infiltration, and smooth muscle cell proliferation in the vessel wall (Libby, 2002). Leptin also promotes atherosclerosis
because leptin increases the accumulation of cholesterol esters in foam cells and promotes oxidative stress (*Beltowski, 2006*).

*Adiponectin*, an anti-inflammatory adipokine, on the other hand, is thought to stabilize atherosclerotic plaques via tissue inhibitor of metalloproteinase-1 (TIMP-1), inhibit transformation of macrophages to foam cells, and inhibit cell proliferation stimulated by oxidized LDL. Thus, the relative adiponectin deficiency associated with obesity also would promote atherogenesis and plaque formation. Inflammation and oxidative stress also appear to play a role in the vascular calcification that often is a relatively late finding in atherosclerosis (*Towler., 2007*).

**Obesity and dyslipidemia:**

High TG and low levels of HDL are commonly seen with obesity. Although there is more controversy regarding the cardiovascular risk associated with high TG, there are several large trials suggesting that they are a risk factor for CVD, particularly in women (*Nordestgaard, 2007*).

Childhood obesity is also associated with dyslipidemia (*Freedman et al., 2001*). It may adversely affect LDL-cholesterol. It has also been found to be associated with endothelial dysfunction and increased carotid intima-media thickness, both of which are recognized to be associated with atherosclerotic CVD and increased risk of adverse CVD outcomes in adults (*Freedman et al., 2004*).

**Obesity and thrombosis:**

Obesity is considered a prothrombotic condition due to increased activity of the coagulation cascade, which is not fully compensated by increased activity of the fibrinolytic cascade. Several studies have shown that the plasma concentrations
of many prothrombotic factors are higher in obese compared with normal weight individuals (Darvall, 2007). Plasma concentrations of antithrombotic factors are also increased, but not enough to counteract the increase in prothrombotic factors (Abdollahi., 2003).

Leptin, resistin, plasminogen activator inhibitor-1 (PAI-1), angiotensin II, α-TNF, β- transforming growth factor, and IL-6 are all secreted by adipose tissue and are all implicated in thrombosis. The general pathway through which these adipokines are thought to increase thrombotic potential is via inflammation and reactive oxygen species, which are known to lead to platelet activation and thrombosis (Darvall, 2007).

PAI-1 is the primary inhibitor of fibrinolysis. It is secreted mainly by platelets and vascular endothelium and is also produced by adipocyte cells. It is elevated in individuals with obesity and plays a key role in promoting thrombus formation following the rupture of atherosclerotic plaque (Bray et al., 2009).

The increased thrombotic potential accompanying obesity is related to insulin resistance. Insulin resistance is associated with inflammation and oxidative stress, both of which are implicated in the generation of components of the thrombotic cascade. Resistance to insulin leads to thrombosis promotion because insulin is antithrombotic and profibrinolytic (Dandona, 2005).

**Obesity and endothelial dysfunction:**

Endothelial dysfunction is associated with a large number of clinical conditions and laboratorial alterations, including diabetes mellitus, hypercholesterolemia, hypertension, insulin resistance, advanced age and obesity (Meyers et al., 2007). Unfortunately, the association between excess weight and endothelial dysfunction can present as early as childhood (Pena, 2006).
An excessive amount of lipid stored in adipocytes leads to functional abnormalities of the endoplasmic reticulum and mitochondria, which, in turn, contribute to intracellular and systemic disorders such as the stimulation of a proinflammatory state, insulin resistance, and high production of free fatty acids (de Ferranti and Mozaffarian, 2008). Fat in the liver also represents a site beyond adipose tissue that independently contributes to the synthesis of inflammatory mediators such as CRP, IL-6 and PAI-1, which are increased in nonalcoholic fatty liver disease (Lucero et al., 2011).

CRP levels are positively correlated with BMI and visceral fat accumulation. It inhibits the formation of NO by endothelial cells. The lack of NO promotes vasoconstriction, leukocyte adherence, platelet activation, oxidation, and thrombosis, thereby leading to endothelial dysfunction and arterial hypertension (de Ferranti and Mozaffarian, 2008). High levels of CRP are also predictive of atherothrombotic events (Cornier et al., 2008).

Obese patients have elevated levels of endogenous leptin which have been linked to vasculopathy via obesity associated with HTN (Hutley and Prins, 2005).

TNF-α is mainly produced from macrophages within the adipose tissue as well as adipocytes themselves (de Ferranti and Mozaffarian, 2008). It also plays a role in stimulating the expression of other inflammatory mediators, such as IL-6, and reduces the expression of anti-inflammatory mediators, such as adiponectin (Hutley and Prins, 2005).

TNF-α also plays a role in this process as it inhibits endothelium-dependent vasorelaxation by increasing the generation of reactive oxygen species, which activate nuclear factor kappa beta NF-κβ, a transcription regulator of molecular adhesion important to the control of inflammatory and oxidative states of vascular endothelial cells (Pierce et al., 2009).
Reduced synthesis of NO is also an early inducer of obesity. Insulin resistance and the chronic rise in plasma glucose enhance the expression of glutamine fructose 6-phosphate transaminase, which in turn stimulates the production of glucosamine, thereby favoring oxidative stress in endothelial cells (Wu and Meininger, 2009).

Adiponectin levels are significantly lower in obese individuals in comparison to nonobese individuals and have been negatively correlated with percentage of body fat, WHR and abdominal fat. This contributes to a variety of obesity-related diseases, including diabetes, vascular abnormalities, and heart disease, and is inversely associated with CRP and TNF-α levels (Hopkins et al., 2007).

The main effects of adiponectin are the regulation of glucose metabolism, the improvement of sensitivity to insulin, the reduction in atherosclerotic lesions, the inhibition of monocyte adhesion to endothelial cells, the suppression of macrophage transformation into foam cells, and the decrease in the proliferation and migration of smooth muscle cells (Wassink et al., 2007). It also increases endothelial NO production. Nonalcoholic fatty liver disease has been also associated to low serum levels of adiponectin (Lucero et al., 2011).

**Obesity and myocardial metabolism:**

Alterations in myocardial metabolism may also play a role in the development of cardiac dysfunction. Animal studies suggest that alterations in myocardial metabolism contribute to cardiac dysfunction in obesity (Chiu, 2005).

However, it appears that if excessive FA delivery to the myocardium persists, it will lead to increased FA storage. Although much of this excess lipid may be stored in a relatively neutral form such as triglycerides, some of the FAs that enter the cell may contribute to apoptosis, via lipotoxicity (Zhou et al., 2000). Studies in
animal models of lipotoxicity, the myocardial metabolic abnormalities precede cardiac dysfunction and are thought to contribute to it (Chiu, 2005).

In addition, LV biopsies from human hearts demonstrate that patients with obesity or diabetes and heart failure have more accumulation of lipid within the myocardium than those with heart failure from other causes (Sharma, 2004).

Excessive myocardial FA metabolism may also contribute to cardiac dysfunction via increased free radical production. In obesity, with its inherent increase in FA oxidation, there is increased myocardial oxidative stress. In animal studies free radicals appear to impair both vascular and LV systolic and diastolic function since decomposition of free radicals leads to improvement of these parameters (Radovits, 2007).

Lastly, increasing BMI is an independent predictor of increasing myocardial oxygen consumption and decreasing efficiency both in animal models and in a recent study in young obese women (Boudina. 2007).

**Effects of Obesity on Hemodynamics and CV Structure and Function:**

Obesity has been linked to a spectrum of more minor cardiovascular changes, ranging from a hyperdynamic circulation to subclinical cardiac structural changes (Haque et al., 2008).

**Effects of Obesity on Hemodynamics:**

Obesity increases total blood volume, cardiac output, and cardiac workload. Obese patients have a higher cardiac output but a lower level of total peripheral resistance at any given level of arterial pressure. Most of the increase in cardiac
output with obesity is caused by stroke volume, although because of increased sympathetic activation, heart rate is typically mildly increased as well.

**Effects of Obesity on cardiovascular Structure:**

With increased filling pressure and volume, overweight and obese individuals often develop LV chamber dilatation. Even independent of arterial pressure and age, obesity increases the risk of LV hypertrophy, as well as other structural abnormalities, including concentric remodeling and concentric LV hypertrophy *(Lavie et al., 2007)*.

Concentric LV hypertrophy is thought to develop into eccentric hypertrophy with increased duration of obesity, and consequent increased duration of LV volume overload. Studies, using modern techniques to evaluate cardiac structure suggest that obesity even in the absence of hypertension, first leads to concentric LV remodeling, characterized by increased LV wall thickness relative to the LV end-diastolic dimension. This is best expressed as an increase in relative wall thickness and can be seen even in adolescents with obesity *(Mensah et al., 1999)*.

Using standard echocardiography techniques, Kosar and colleagues found that obese patients without CVD exhibit enlargement of LA *(Kosar et al., 2008)*.

**Effects of Obesity on cardiovascular function:**

Initially there is LV diastolic dysfunction with hyperkinetic systole but with longer duration of obesity diastolic dysfunction progressively worsens and gradually systolic dysfunction also sets in. The effects of obesity on LV systolic function are less clear-cut, with some studies demonstrating decreased, some showing increased, and some showing no effect on LV systolic function *(Peterson et al., 2004)*.
Indeed, the risk of developing clinical heart failure is estimated to increase by 5% –7% for every 1 kg/m\(^2\) BMI increase. Consistent with this there are several studies using load dependent measures demonstrating the detrimental effects of excess body weight on diastolic function as measured using traditional echocardiographic Doppler imaging (Gates, 2003).

Thus, the mechanisms responsible for the obesity-related impairment in heart function appear due to both alterations in load as well as load-independent alterations. There is an increase in load through an increase in plasma and blood volume via activation of the renin-angiotensin-aldosterone system (Alpert, 2001).

In addition to alterations in chamber size, obese patients demonstrate increased tissue density, evidenced by increased calibrated myocardial backscatter. Previous studies with this modality have shown that moderate and severe myocardial fibrosis is a frequent autopsy finding in obese subjects (Ahmed et al., 1997).

**Effect of obesity on pericardial fat:**

Epicardial fat was found to be positively associated with the mass of the LV, implicating these fat depots in heart hypertrophy in obesity, it is characterized by a high rate of FFA release. The study by Greif et al, in the issue of *Arteriosclerosis, Thrombosis, and Vascular Biology* highlighted the association between pericardial adipose tissue and the number of atherosclerotic plaques evaluated concomitantly by Dual source CT scan. This measurement was qualitatively interpretable in 264 consecutive patients with a large range of age, a normal or moderately increased BMI, and no a prior coronary disease. An estimated volume of pericardial fat more than 300 cm\(^3\) provided an incremental value for the presence of coronary atherosclerosis independently of well known risk factors. Ninety-five percent of patients with pericardial adipose tissue volume >300 cm\(^3\) had one or more atherosclerotic plaques (Greif et al., 2009).
Obesity and Cardiovascular Diseases:

The mass of fat in the visceral area associates independently of obesity with the development and progression of CVD in a series of clinical and epidemiological studies (Despres et al., 2008).

This led to the concept of a pathophysiological link between abdominal obesity and metabolic syndrome. More recently, fat depots localized around the heart, highly variable among individuals, were proposed to contribute to the pathogenesis of coronaryopathy independently of other visceral depots (Iacobellis et al., 2008).

A. Coronary artery disease:

Obesity is an independent predictor of coronary artery disease. Among men aged less than 50 years, obese individuals have twice the risk of coronary disease and obese women of a similar age have a 2.4-fold greater risk (Mathew et al., 2008).

Experimental studies have demonstrated that, even in the early stage of obesity, there is a reduction in coronary endothelium-dependent vasorelaxation (Galili et al., 2007).

Recently, Bibbins-Domingo et al. reported the results of a computer simulation to estimate the impact of adolescent obesity on adult CHD. In this analysis, they estimated the prevalence of obesity in 35-year-olds in 2020 based on the prevalence of overweight in adolescents in 2000. They then used the CHD Policy Model, a computer simulation of U.S. residents who are over 35 years of age, to predict the annual excess incidence and prevalence of CHD. They also evaluated the effect of treating obesity-related increases in hypertension and dyslipidemia on subsequent outcome. They found that the incidence of CHD and
the total number of CHD events and deaths would be expected to increase in young adulthood as a result of ongoing obesity (Bibbins-Domingo et al., 2007).

Additionally, excess adiposity has been strongly related to first non-ST-segment myocardial infarction occurring at a younger age (Madala et al., 2008).

B. Congestive Heart failure:

Obesity has been associated with systolic and diastolic heart dysfunction. In a cross-sectional study, Ammar and colleagues found a strong correlation between LV systolic and diastolic dysfunction and central obesity, as measured by the W/HR (Ammar et al., 2008). For each increment of one above 30 on the BMI, the risk of developing heart failure increases 5% in men and 7% in women (Mathew et al., 2008).

Kapoor and Heidenreich have recently reported that the mortality rate in cardiac events is increased in obese patients with a BMI of 45 or more in comparison to lean persons (Kapoor and Heidenreich, 2010).

Accumulation of TG in non fat cells like myocytes can also directly cause cell dysfunction because of lipotoxicity (Poirier et al., 2006).

Changes in the right heart also occur in obesity. The pathophysiology is related to OSA and/or the obesity hypoventilation syndrome, which produce pulmonary hypertension and right ventricular hypertrophy, dilatation, progressive dysfunction, and finally failure. However, RV dysfunction can also occur as a consequence of LV dysfunction, and the heart failure that develops is often biventricular (Alpert et al., 1993).

C. Hypertension:
Conclusion

Hypertension is three to five times more common in obese subjects in comparison to individuals within the ideal weight range, and the risk of death among obese individuals is two to three times higher than nonobese individuals and the severely obese individuals have a 5-to-20-year decrease in life expectancy in comparison to nonobese individuals matched for age and gender (Cannon, 2008).

Chiolero and colleagues conducted a prevalence study on hypertension and found that this condition was attributed to overweight or obesity in 37% of cases (Chiolero et al., 2007).

In Switzerland, Maggio and colleagues found an association between obese children and systolic hypertension in 47.6% of patients as well as an increase in LV mass partially caused by high systemic blood pressure (Maggio et al., 2008). One study reports that 10 kg of excess body weight is associated with a 3.0-mmHg higher systolic and 2.3-mmHg higher diastolic blood pressure (Poirier et al., 2006). Stabouli and colleagues reported that obese adolescents have higher blood pressure and greater carotid artery intima-media thickness in comparison to nonobese pairs (Stabouli et al., 2005).

Obese children have a ten fold greater risk of developing hypertension as young adults than nonobese children and a continuous relationship between BMI and arterial pressure has been reported (Ippisch et al., 2008).

Obese patients have increased systemic blood volume. The normal compensatory response to an elevated cardiac output, which should be a drop in peripheral vascular resistance, is hindered in obese patients with hypertension, exhibiting an inappropriately normal total peripheral resistance (Reisin and Jack, 2009).

The activation of the rennin–angiotensin–aldosterone system also significantly contributes to hypertension in obese patients. In this regard, the
formation of angiotensin II in the adipose tissue enhances the production of proinflammatory and profibrotic cytokines (Wassink et al., 2007).

D. Arrhythmia:

*Obesity and ventricular dysrhythmias:*

Obesity is associated with abnormalities in sympathovagal balance, leading to higher heart rate and reduced heart rate variability, known factors related with increased risk of sudden cardiac death (Lavie et al., 2008).

Various tissues of heart, like the sinus node, atroventricular node, right bundle branch, and the myocardium near the atroventricular ring, are replaced by fat cells in obesity. These can occasionally cause conduction defects like sinoatrial block, bundle branch block, and rarely atrioventricular block (Zhou, 2000).

*Obesity and AF:*

The prevalence of AF is increasing in obesity, and is expected to increase 2.5-fold by 2050. Recently, Wanahita et al. reviewed 16 studies enrolling 123,000 patients to assess the impact of obesity on AF. In the subgroup of 5 population-based studies enrolling 78,602 patients, obese patients had a nearly 50% increased risk of developing AF that escalated with increasing BMI. On the other hand, post-cardiac surgery studies enrolling 44,647 patients failed to show an increased risk of AF in obesity (Wanahita et al., 2008).
Myocardial Steatosis:

Obesity is related with a pathologic condition, known as Adipositas Cordis wherein the myocardium is so filled with lipid. The lipid in the heart can be from an infiltrative process, with adipocytes strands streaming in from the epicardial fat, and/or a metaplastic process in which myocardial cells are replaced by adipocytes (*Poirier et al., 2006*).

Fat is a direct cardiotoxin. The original autopsy studies suggested that fatty degeneration of the heart is a common consequence of obesity and a possible cause of dilated cardiomyopathy in humans. Intramyocardial fatty infiltration also appears in normal myocardium with greater prevalence reported in the RV myocardium than in the LV (*Raney et al., 2008*).

Because the interindividual variability is quite high, adiposity is not the sole determinate of lipid deposition in the human myocardium. Recently, a study of patients with heart failure who underwent cardiac biopsies demonstrated that patients who are obese or have type 2 diabetes have intramyocardial lipid levels that are 5 to 6 times higher than those of healthy controls (*Sharma et al., 2004*).

An increased amount of fatty infiltration is also reported in subjects with a large amount of epicardial fat, as the excess adipose tissue infiltrates the RV myocardium and atrial septum. In normal hearts, fat is commonly seen in the insertion of inferior RV (*Raney et al., 2008*) and in the atroventricular groove. It is also not uncommon to find adipose tissue in the intraatrial septum (*O’Connor et al., 2006*). Figure (4) shows Oil red O staining for lipids of hearts from an obese and a nonobese human.
Figure (4): Oil red O staining for lipids of hearts from an obese (body mass index, 42) and a nonobese human (body mass index, 28). Adapted by permission of the Federation of American Societies for Experimental Biology (Unger & Orci, 2001).

Quantification of lipids in human myocardium:

Fat-water–separated imaging in the heart by MRI is a sensitive means of detecting intramyocardial fat and characterizing fibrofatty infiltration. It is also useful in characterizing fatty tumors and delineating epicardial and/or pericardial fat, and in distinguishing pericardial disease (Kellman et al., 2009).

Single-voxel magnetic resonance spectroscopy techniques have been used to quantify intracellular lipid levels and may discriminate between TG in adipocytes and droplets in the cardiomyocytes based on a small chemical shift (Meer et al., 2007).

Unlike the liver and muscle, however, quantification of lipid in the myocardium is difficult because the heart is perpetually in motion and is surrounded by a large depot of adipocytes (epicardial fat pad) that could interfere with the measurements. To overcome these limitations, the sample volume is placed in the interventricular septum because it is the portion of the myocardium most distal from the large epicardial fat pad that envelops the heart. Furthermore,
samples are obtained only during end-systole (when the heart is at its thickest diameter) and end-exhalation (when heart–lung interaction is minimal).

**Pathophysiology of myocardial steatosis:**

Not surprisingly, a cross-sectional study performed on a small cohort of healthy men has shown an association between circulating FFA acids levels and myocardial fat (*Kankaanpaa et al.*, 2006).

Free fatty acids enter the myocardial cell via diffusion or via fatty acid–specific transporters like fatty acid translocase. Fatty acid uptake seems critical because fatty acid translocase deficiency is sufficient to reverse the lipotoxic phenotype in myosin heavy chain α–peroxisome proliferator-activated receptor α–(PPAR) mice (*Yang et al.*, 2007). Because the heart has a very limited capacity to store TG and because increased fatty acid supply results in increased fatty acid uptake, the heart is subject to increased susceptibility to spillover of toxic lipid byproducts (*Muoio & Newgard.*, 2007).

Overexpression of long-chain acyl-CoA synthetase, a key enzyme involved in TG synthesis, produces an example of cardiac-restricted steatosis. Increased protein expression of acyl-CoA synthetase in the myocardium disrupts the balance between lipid import and export in the myocardium, which results in diffuse lipid accumulation and a greater than 2-fold increase in heart mass (*Chiu et al.*, 2001). Of note, early administration of thiazolidinedione therapy is effective in attenuating myocardial TG accumulation and normalizing LV contractile performance (*Zhou, 2000*).
Patients and Methods

- **Study Design:**
  The present study is a prospective single centre study that was conducted at “Benha University hospital.

- **Patients:**
  This study included 100 patients selected during the period from July 2012 to July 2013 & divided into two groups:

  - **Group I:** It included 50 obese patients {body mass index (BMI) > 30 kg/m\(^2\)} aged 35 years or older, referred for routine cardiovascular assessment in the out-patient clinic with no obvious cardiovascular disease.

  Group I was subdivided into two subgroups:

  I. Group A: Included 25 morbidly obese patients {body mass index (BMI) > 35 kg/m\(^2\)}.

  II. Group B: Included 25 mildly obese patients {body mass index (BMI) 30-35 kg/m\(^2\)}.

  - **Group II:** Included 50 Age- and sex-matched healthy normal volunteers {body mass index (BMI) < 25 kg/m\(^2\)} and considered as the control group.

- **Exclusion Criteria:**
  1) Patients with any history or findings of cardiovascular disease (Previous myocardial infarction, heart failure, valvular heart disease, overt cardiomyopathy, etc.).

  2) Patients with Diabetes mellitus or Hypertension

  3) Patients with impaired renal or liver functions.

  4) Patients with malignancy, Thyroid disease or anemia.

  5) Patients receiving vasoactive drugs or anti-obesity agents.
Methods:
The following data were collected in all patients in the studied groups after obtaining informed consent from all participants:

Detailed medical history: to exclude co-morbid conditions other than obesity (e.g. DM, Hypertension, etc.).

A) Full physical examination: including biometric measurements (height, weight) and blood pressure readings.

BMI was calculated by dividing an individual’s weight in kilograms (kg) by the square of height in meters (m).

\[
\text{BMI} = \frac{\text{weight (kg)}}{\text{height}^2 (\text{m}^2)} \quad (\text{Palombo et al., 1981})
\]

Table (7): Classification of BMI for people aged ≥ 18 Y

<table>
<thead>
<tr>
<th>BMI (kg/m²)</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 18.5</td>
<td>Underweight</td>
</tr>
<tr>
<td>18.5–24.9</td>
<td>Healthy weight range</td>
</tr>
<tr>
<td>≥ 25</td>
<td>Overweight</td>
</tr>
<tr>
<td>25.0–29.9</td>
<td>Pre-obese</td>
</tr>
<tr>
<td>≥ 30</td>
<td>Obese</td>
</tr>
<tr>
<td>30.0–34.9</td>
<td>Class I obesity</td>
</tr>
<tr>
<td>35.0–39.9</td>
<td>Class II obesity</td>
</tr>
<tr>
<td>≥ 40</td>
<td>Class III obesity</td>
</tr>
</tbody>
</table>

(WHO 2000), (NHDC 2003).

B) Lab investigations: including: fasting blood glucose, serum creatinine level, and complete blood count.

C) Echocardiography:

- Echocardiography was done using VIVID 7 EG cardiac ultrasound scanner, which included software for the acquisition of both standard cardiac ultrasound and Doppler myocardial imaging data using 2.5-MHz
transducer. All measurements were analyzed by the same experienced echocardiographer on an average of three cardiac cycles.

- Data were obtained with the patients at rest, lying in lateral decubitus position at end-expiration. Standard echocardiography analysis include two-dimensional, m-mode, and Doppler flow measurements performed according to American Society of Echocardiography recommendations (Sahn et al., 1978).

The study included conventional echocardiography and tissue Doppler imaging.

A. **Conventional echocardiography:**

1) **Assessment of LV dimensions:**

- M-mode measurements were obtained from the left parasternal and apical views with special attention to exclude overlying trabeculations in the ventricular septum or posterior wall measurements, which may overestimate thickness.

- Measurements were taken at the end diastole –defined as the beginning of the QRS complex –but preferably using the widest LV cavity diameter, and at the end systole -using the narrowest LV cavity diameter.

- The diastolic measurements obtained were the interventricular septal wall thickness, the LV internal diameter at end diastole and posterior wall thickness. In systole, the LV systolic diameter was measured.

2) **Assessment of LV systolic function:**

- **LV ejection fraction** was estimated according to biplane Simpson’s method (55-75%).

- **Fractional shortening** was calculated as percent change in LV internal dimension between systole and diastole.

**LV internal volumes** were derived from LV internal dimension by Teicholz’s formula (Teicholz et al., 1976)

- **Stroke volume** was obtained as the difference between end-diastolic and end-systolic volumes.

3) **Diastolic function assessment:**
Conclusion

- **Pulsed Doppler LV inflow** recordings were performed in the apical four-chamber view, within the sample volume at the tips of the mitral valve. **Peak E** (peak transmitral flow velocity in early diastole), **peak A** (peak transmitral flow velocity in late diastole); **E/A ratio**, and **mitral deceleration time** (from peak E-wave to baseline) were measured.

**Table (8)** The approximate normal values for LV diastolic function

<table>
<thead>
<tr>
<th>Normal ranges for measures of diastolic function</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral valve E (cm/s)</td>
<td>44–100</td>
</tr>
<tr>
<td>Mitral valve A (cm/s)</td>
<td>20–60</td>
</tr>
<tr>
<td>E:A ratio</td>
<td>0.7–1.8</td>
</tr>
<tr>
<td>Mitral E deceleration time (ms)</td>
<td>139–219</td>
</tr>
</tbody>
</table>

(Ashley & Niebauer 2004).

4) **Assessment of LV mass:**

- **Left ventricular mass (LV mass)** was calculated by Devereaux’ equation:

\[
LVM = 1.04 [(LVEDD+PWD+IVSD)^3 - LVEDD^3] \times 0.8 + 0.6
\]

Where **LVEDD** is the left ventricular end diastolic dimension, **PWD** is the posterior wall thickness, **IVSD** is the interventricular septal thickness in diastole, **1.04** is the specific gravity of the myocardium, and **0.8** is the correction factor (Devereux et al., 1986).

5) **Assessment of LV mass index:**

- **Left ventricular mass index (LVMI)** was calculated by dividing LV mass by the BSA.

\[
LVMI = \frac{LVM}{BSA}
\]
Conclusion

Where the BSA are calculated by a variation of DuBois and DuBois (*DuBois and DuBois, 1916*) that gives virtually identical results is:

\[
\text{BSA (m}^2\text{)} = 0.007184 \times \text{Height(cm)}^{0.725} \times \text{Weight(kg)}^{0.425}
\]

Normal values of LVM and LVMI values in both sexes are shown in table (9), (10).

**Table (9):** Normal values of left ventricular mass and mass index in **females** (*Lang et al., 2005*)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Reference Range</th>
<th>Mildly Abnormal</th>
<th>Moderately Abnormal</th>
<th>Severely Abnormal</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV M(g)</td>
<td>67-162</td>
<td>163-186</td>
<td>187-210</td>
<td>≥211</td>
</tr>
<tr>
<td>LVMI (g/m²)</td>
<td>43-96</td>
<td>97-108</td>
<td>109-121</td>
<td>≥122</td>
</tr>
</tbody>
</table>

**Table (10):** Normal values of left ventricular mass and mass index in **males** (*Lang et al., 2005*)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Reference Range</th>
<th>Mildly Abnormal</th>
<th>Moderately Abnormal</th>
<th>Severely Abnormal</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV M(g)</td>
<td>88-224</td>
<td>225-258</td>
<td>259-292</td>
<td>≥293</td>
</tr>
<tr>
<td>LVMI (g/m²)</td>
<td>49-115</td>
<td>116-131</td>
<td>132-148</td>
<td>≥149</td>
</tr>
</tbody>
</table>

**B. Tissue Doppler Imaging and Strain/Strain Rate Imaging:**

The settings of the apparatus were turned to tissue Doppler imaging application. For data acquisition, three complete cycles from each 2D echo views were collected.

- It was used to assess the following:

Color-coded Doppler myocardial velocity data were obtained from parasternal short axis view at papillary muscle level, apical four-chamber and apical two-chamber views.

Regional velocity analyses were performed for six LV myocardial segments:

- Basal lateral, mid lateral and mid posterior septum segments from apical four chamber view.
Conclusion

- Mid anterior segment and mid inferior segment from apical two chamber view.
- Posterior wall at papillary muscle level from parasternal short axis view.

Maximum systolic velocities were measured. Strain and strain rate data were also processed from the color Doppler myocardial imaging. By using apical four- and two-chamber view, in mid septum, mid lateral, basal lateral, mid anterior, and mid inferior strain and strain rate profiles were retrieved. From parasternal short axis view, posterior wall radial strain rates and strain profiles were obtained.

From the strain rate curve, peak systolic strain rate (PSSR) was measured. From the strain curve, peak systolic strain (PSS) was measured.

In all study subjects, global systolic contraction amplitude (glsca) and averaged peak systolic strain (apss) were computed, as global longitudinal LV indices by dividing sum of each longitudinal peak strain and peak strain rate values to the number of the used segments.

**N.B:**

- **glsca** = The ratio of the sum of measured peak strain values from LV basal lateral, mid-lateral, mid posterior septum, mid-anterior, and mid-inferior regions to number of measured segments.

**Averaged peak systolic strain rate (apss)** = The ratio of the sum of measured peak systolic strain rate values from LV basal lateral, mid-lateral, mid posterior septum, mid anterior, and mid inferior regions to number of measured segments.
Statistical Analysis:

- All data were collected, tabulated and analyzed using SPSS (statistical program for social science version 12).

- Quantitative variables were described as mean, SD for continuous variables. The values for obese subjects and controls were compared using Student’s unpaired 2-tailed $t$-test.

- Chi-square test was used to compare qualitative variables of two groups.

- Unpaired $t$-test was used to compare quantitative variables, in parametric data (SD<50% mean)

- Pearson’s correlation coefficient test was used to test univariate relations between TDI-derived indexes of LV systolic function and selected clinical, demographic, and standard Doppler echocardiographic parameters and rank different variables against each others positively or inversely.

  P value >0.05 insignificant

  P <0.05 significant

  P <0.01 highly significant

(Box et al., 1978).
Results

This prospective single center study was conducted at Benha University Hospital from the period between July 2012 to July 2013 and included 100 persons who were divided into two groups, group (1) represented the obese subjects. It was subdivided into group A (Morbidly obese patients) & group B (Mildly obese patients) and group (2) represented the non-obese (control) group.

I. The Demographic data:

The mean age of group (1A) was 42.5±2.9 years, group (1B) was 42.8±3 years and group (2) was 41.8±2.3 years. They were 11 males and 14 females in group (1A), 12 males and 13 females in group (1B), and 25 males and 25 females in group (2). The mean BMI was 38.6±1.6 in group (1A), 32.3±1.4 in group (1B) and 23.8±0.5 in group (2). The mean BSA was 2.14±0.1 in group (1A), 1.95±0.1 in group (1B) and 1.72 ± 0.12 in group (2). These data are shown in tables (11 & 12) & figure (5).

![Bar chart showing demographic data of three groups.](image)

**Figure (5):** Demographic data of the three groups.
Conclusion
Table (11): Demographic data of the three groups.

<table>
<thead>
<tr>
<th>variables</th>
<th>Group (1A)</th>
<th>Group (1B)</th>
<th>Group (2)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years (M±SD)</td>
<td>42.5±2.9</td>
<td>42.8±3</td>
<td>41.8±2.3</td>
<td>(P&gt;0.05)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male n(%)</td>
<td>11 (44%)</td>
<td>12 (48%)</td>
<td>25 (50%)</td>
<td>(P&gt;0.05)</td>
</tr>
<tr>
<td>Female n(%)</td>
<td>14 (56%)</td>
<td>13 (52%)</td>
<td>25 (50%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>25</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>BMI(KG/m2) (M±SD)</td>
<td>38.6±1.6</td>
<td>32.3±1.4</td>
<td>23.8±0.5</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>BSA (m2) (M±SD)</td>
<td>2.14±0.1</td>
<td>1.95±0.1</td>
<td>1.72±0.12</td>
<td>(P&lt;0.05)</td>
</tr>
</tbody>
</table>

Table (12): Demographic data of the obese versus non obese groups.

<table>
<thead>
<tr>
<th>variables</th>
<th>OBESE 1</th>
<th>NON OBESE 2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years (M±SD)</td>
<td>42.7±3</td>
<td>41.8±2.3</td>
<td>(P&gt;0.05)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male n(%)</td>
<td>23</td>
<td>25</td>
<td>(P&gt;0.05)</td>
</tr>
<tr>
<td>Female n(%)</td>
<td>27</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>BMI(KG/m2) (M±SD)</td>
<td>35.51±3.53</td>
<td>23.86±0.58</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>BSA (m2) (M±SD)</td>
<td>2.05±0.15</td>
<td>1.73±0.12</td>
<td>(P&lt;=0.001)</td>
</tr>
</tbody>
</table>
II. **Echocardiographic Data:**

1- **Conventional echocardiography**

   **A. Systolic function:**

   In comparing the obese versus non obese groups regarding conventional echocardiographic parameters, there was significant increase in ejection fraction & stroke volume in group 1A & 1B in comparison to group 2. Inter ventricular septal diameter & posterior wall thickness was larger in group 1A &1B in comparison with group 2. This was evident also for left ventricular end diastolic diameter, left ventricular end systolic diameter & left atrial diameter which were higher in group 1A &1B in comparison with group 2 (Table (13), & figure (6) & (7).

   These changes were evident when comparing the morbidly obese group versus non obese group, but when comparing mild obese group versus non obese group, there was significant increase in ejection fraction, stroke volume, left ventricular end diastolic diameter & left atrial diameter in group 1B in comparison to group 2, while other parameters showed no significant difference. (Table (14) & Table (15)), & figure (8) & (9).

   **Table (13):** Echocardiographic data in the obese versus non obese groups

<table>
<thead>
<tr>
<th>M-mode</th>
<th>OBESE 1A+1B</th>
<th>NON OBESE 2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF%</td>
<td>72.9±3.6</td>
<td>69.5±4.1</td>
<td>(P&lt;0.05)</td>
</tr>
<tr>
<td>FS%</td>
<td>42.08±3.12</td>
<td>39.04±3.43</td>
<td>(P&gt;0.05)</td>
</tr>
<tr>
<td>SV ml</td>
<td>75.17±6.7</td>
<td>60.3±8.2</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>IVSD mm</td>
<td>0.99±0.09</td>
<td>0.85±0.10</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>LVPWD mm</td>
<td>0.99±0.08</td>
<td>0.85±0.10</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>LVEDD mm</td>
<td>4.71±0.17</td>
<td>4.37±0.17</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>LVESD mm</td>
<td>2.73±0.19</td>
<td>2.66±0.12</td>
<td>(P&lt;=0.05)</td>
</tr>
<tr>
<td>LAD mm</td>
<td>3.50±0.30</td>
<td>3.15±0.15</td>
<td>(P&lt;=0.001)</td>
</tr>
</tbody>
</table>

   N.B : EF% : ejection fraction, FS: fractional shortening, SV: stroke volume, IVSD : interventricular septum in diastole. LVPWD, left ventricular posterior wall thickness in diastole, LVEDD: left ventricular end diastolic dimension, LVESD: left ventricular end systolic dimension, LAD : left atrial diameter.
Conclusion

Figure (6): Echocardiographic data in the obese versus non obese groups

Figure (7): Echocardiographic data in the obese versus non obese groups
**Conclusion**

Table (14): Echocardiographic data in the morbidly obese versus non obese groups

<table>
<thead>
<tr>
<th>M-mode</th>
<th>Group 1A</th>
<th>Group 2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF%</td>
<td>72.9±4</td>
<td>69.5±4.1</td>
<td>(P&lt;0.05)</td>
</tr>
<tr>
<td>FS%</td>
<td>42.1±3.4</td>
<td>39±3.4</td>
<td>(P&gt;0.05)</td>
</tr>
<tr>
<td>SV ml</td>
<td>78.4±5.8</td>
<td>60.3±8.1</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>IVSD mm</td>
<td>1.03±0.07</td>
<td>0.85±0.1</td>
<td>(P&lt;=0.05)</td>
</tr>
<tr>
<td>LVPWD mm</td>
<td>1.02±0.08</td>
<td>0.86±0.1</td>
<td>(P&lt;=0.05)</td>
</tr>
<tr>
<td>LVEDD mm</td>
<td>4.79±0.1</td>
<td>4.36±0.17</td>
<td>(P&lt;=0.05)</td>
</tr>
<tr>
<td>LVESD mm</td>
<td>2.77±0.17</td>
<td>2.66±0.12</td>
<td>(P&lt;=0.05)</td>
</tr>
<tr>
<td>LAD mm</td>
<td>3.75±0.13</td>
<td>3.15±0.15</td>
<td>(P&lt;=0.001)</td>
</tr>
</tbody>
</table>

N.B : EF% : ejection fraction, FS: fractional shortening, SV: stroke volume, IVSD : interventricular septum in diastole. LVPWD, left ventricular posterior wall thickness in diastole, LVEDD: left ventricular end diastolic dimension, LVESD: left ventricular end systolic dimension, LAD : left atrial diameter.

**Figure (8):** Echocardiographic data in the morbid obese versus non obese groups
**Conclusion**

**Table (15):** Echocardiographic data in the mild obese versus non obese groups

<table>
<thead>
<tr>
<th>M-mode</th>
<th>Group 1B</th>
<th>Group 2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF%</td>
<td>72.9±3.3</td>
<td>69.5±4.1</td>
<td>(P&lt;0.05)</td>
</tr>
<tr>
<td>FS%</td>
<td>41.9±2.8</td>
<td>39±3.4</td>
<td>(P&gt;0.05)</td>
</tr>
<tr>
<td>SV ml</td>
<td>71.9±6</td>
<td>60.3±8.1</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>IVSD mm</td>
<td>0.96±0.09</td>
<td>0.85±0.1</td>
<td>(P&gt;0.05)</td>
</tr>
<tr>
<td>LVPWD mm</td>
<td>0.96±0.08</td>
<td>0.86±0.1</td>
<td>(P&gt;0.05)</td>
</tr>
<tr>
<td>LVEDD mm</td>
<td>4.62±0.18</td>
<td>4.36±0.17</td>
<td>(P&lt;=0.05)</td>
</tr>
<tr>
<td>LVESD mm</td>
<td>2.68±0.2</td>
<td>2.66±0.12</td>
<td>(P&gt;0.05)</td>
</tr>
<tr>
<td>LAD mm</td>
<td>3.75±0.19</td>
<td>3.15±0.15</td>
<td>(P&lt;=0.001)</td>
</tr>
</tbody>
</table>

N.B: EF% : ejection fraction, FS: fractional shortening, SV: stroke volume, IVSD: interventricular septum in diastole. LVPWD, left ventricular posterior wall thickness in diastole, LVEDD: left ventricular end diastolic dimension, LVESD: left ventricular end systolic dimension, LAD: left atrial diameter.

**Figure (9):** Echocardiographic data in the mild obese versus non obese groups
Conclusion

It was also shown that obese persons have a highly significant larger left ventricular mass and left ventricular mass index. This was also evident when comparing morbid obese & mild obese group versus non obese group separately, details are shown in tables (16), (17) and (18), & figures (10), (11) & (12).

Table (16): Left ventricular mass & left ventricular mass index in obese versus non obese groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>OBESE 1A+1B</th>
<th>NON OBESE 2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVM gm</td>
<td>164.09±20.07</td>
<td>118.28±19.39</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>LVMI gm/m2</td>
<td>80.41±9.6</td>
<td>68.82±12.2</td>
<td>(P&lt;=0.001)</td>
</tr>
</tbody>
</table>

N.B: LVM :left ventricular mass, LVMSI: left ventricular mass index.

Figure (10): Left ventricular mass & left ventricular mass index in obese versus non obese groups
Table (17): Left ventricular mass & left ventricular mass index in morbidly obese versus non obese groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group 1A</th>
<th>Group 2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVM gm</td>
<td>176.4±15.2</td>
<td>118.3±19.4</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>LVMI gm/m2</td>
<td>82.69±7.3</td>
<td>68.82±12.2</td>
<td>(P&lt;=0.05)</td>
</tr>
</tbody>
</table>

N.B: LVM :left ventricular mass, LVMSI: left ventricular mass index.

Figure (11): Left ventricular mass & left ventricular mass index in morbid obese versus non obese groups
Table (18): Left ventricular mass & left ventricular mass index in mild obese versus non obese groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group 1B</th>
<th>Group 2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVM gm</td>
<td>147.6±23.4</td>
<td>118.3±19.4</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>LVMI gm/m2</td>
<td>78.11±11.1</td>
<td>68.82±12.2</td>
<td>(P&lt;=0.05)</td>
</tr>
</tbody>
</table>

N.B: LVM: left ventricular mass, LVMSI: left ventricular mass index.

Figure (12): Left ventricular mass & left ventricular mass index in mild obese versus non obese groups
B. Diastolic function:

The measured indices of left ventricular diastolic function by the conventional methods showed significant higher values of E, A, and deceleration time in obese patients versus non obese patients. E/A ratio were significantly lower in obese group versus non obese groups (Table (19) & figure (13)).

These values were the same when comparing morbidly obese group versus mild obese group, while mild obese group showed significant increase of E, A & significant reduction in E/A ratio versus control group, while no significant difference noticed in deceleration time. This is shown in tables (20) & (21) & figures (14) & (15).

Table (19): Global diastolic diameters of the obese versus non obese groups:

<table>
<thead>
<tr>
<th>Doppler</th>
<th>OBESE 1A+1B</th>
<th>NON OBESE 2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>E M± SD</td>
<td>0.81±0.7</td>
<td>0.71±0.05</td>
<td>(P&lt;=0.05)</td>
</tr>
<tr>
<td>A M± SD</td>
<td>0.69±0.10</td>
<td>0.51±0.06</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>E/A M± SD</td>
<td>1.19±0.10</td>
<td>1.39±0.09</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>DT M± SD</td>
<td>224.94±8.71</td>
<td>214.1±6.18</td>
<td>(P&lt;=0.05)</td>
</tr>
</tbody>
</table>

N.B: E: peak E (Peak transmitral flow velocity in early diastole), A: peak A Peak transmitral flow velocity in late diastole), E/A: E/A ratio, DT: mitral deceleration time (From peak E wave to baseline).


**Conclusion**

**Figure (13):** Global diastolic diameters of obese versus non obese groups

**Table (20):** Global diastolic diameters of morbidly obese versus non obese groups:

<table>
<thead>
<tr>
<th>Doppler</th>
<th>Group 1A</th>
<th>Group 2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>E M± SD</td>
<td>0.85±0.05</td>
<td>0.71±0.04</td>
<td>(P&lt;0.05)</td>
</tr>
<tr>
<td>A M± SD</td>
<td>0.78±0.04</td>
<td>0.51±0.06</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>E/A M± SD</td>
<td>1.09±0.03</td>
<td>1.39±0.09</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>DT M± SD</td>
<td>231.2±5.9</td>
<td>213.9±6.1</td>
<td>(P&lt;0.05)</td>
</tr>
</tbody>
</table>

N.B: E: peak E (Peak transmitral flow velocity in early diastole), A: peak A Peak transmitral flow velocity in late diastole), E/A: E/A ratio, DT: mitral deceleration time (From peak E wave to baseline).
**Conclusion**

**Figure (14):** Global diastolic diameters of morbid obese versus non obese groups

<table>
<thead>
<tr>
<th>Doppler</th>
<th>Group 1B</th>
<th>Group 2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>E M± SD</td>
<td>0.77±0.05</td>
<td>0.71±0.04</td>
<td>(P&lt;0.05)</td>
</tr>
<tr>
<td>A M± SD</td>
<td>0.60±0.04</td>
<td>0.51±0.06</td>
<td>(P&lt;=0.05)</td>
</tr>
<tr>
<td>E/A M± SD</td>
<td>1.28±0.05</td>
<td>1.39±0.09</td>
<td>(P&lt;=0.01)</td>
</tr>
<tr>
<td>DT M± SD</td>
<td>218.7±6.2</td>
<td>213.9±6.1</td>
<td>(P&gt;0.05)</td>
</tr>
</tbody>
</table>

N.B : E: peak E (Peak transmitral flow velocity in early diastole), A: peak A Peak transmitral flow velocity in late diastole), E/A: E/A ratio, DT: mitral deceleration time (From peak E wave to baseline).
Conclusion

Figure (15): Global diastolic diameters of mild obese versus non-obese groups
2. Tissue Doppler Imaging:

Tissue Doppler imaging was used to assess the regional function of the selected six segments of the left ventricle {basal lateral, mid lateral, mid posterior septum, mid anterior, mid inferior, and posterior wall segments}, using color-coded tissue Doppler imaging and assessed by the strain and the strain rate. These data were illustrated in table (20), (21), and (22).

Comparing obese versus control groups, it showed significant reduction in the mean systolic velocity of the six selected segments in the obese group versus non-obese groups.

Mean systolic strain was significantly lower in the obese group versus non-obese groups in mid lateral, mid posterior septum, mid anterior & mid inferior segments.

Mean systolic strain rate was significantly lower in obese group versus non-obese groups in the six selected segments except the basal lateral segment & posterior segment where there was no statistically significant difference.

Global longitudinal strain & average peak systolic strain rate was significantly lower in obese versus non-obese groups.

Table (22): Mean systolic velocity & mean systolic strain/strain rate in the obese versus non-obese groups in the six selected segments:

<table>
<thead>
<tr>
<th>Tissue Doppler imaging</th>
<th>OBESE 1A+1B</th>
<th>NON OBESE 2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal lateral seg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Mean systolic velocity cm/sec</td>
<td>6.55±0.5</td>
<td>7.87±0.3</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>-Mean systolic strain%</td>
<td>-21.22±2.1</td>
<td>-23.52±1.9</td>
<td>(P&gt;0.05)</td>
</tr>
<tr>
<td>-Mean systolic strain rate 1/s</td>
<td>-1.68±0.6</td>
<td>-1.8±0.1</td>
<td>(P&gt;0.05)</td>
</tr>
<tr>
<td>Mid lateral seg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Mean systolic velocity cm/sec</td>
<td>5.10±0.9</td>
<td>6.53±0.2</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>-Mean systolic strain%</td>
<td>-13.72±1.4</td>
<td>-20.48±2.4</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>-Mean systolic strain rate 1/s</td>
<td>-1.17±0.13</td>
<td>-1.46±0.13</td>
<td>(P&lt;0.05)</td>
</tr>
</tbody>
</table>
## Conclusion

<table>
<thead>
<tr>
<th>Tissue Doppler imaging</th>
<th>OBESE 1A+1B</th>
<th>NON OBESE 2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mid posterior septum seg</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Mean systolic velocity cm/sec</td>
<td>4.6±0.4</td>
<td>6.1±0.2</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>-Mean systolic strain%</td>
<td>-16.78±1.9</td>
<td>-21.64±2</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>-Mean systolic strain rate 1/s</td>
<td>-1.33±0.12</td>
<td>-1.68±0.13</td>
<td>(P&lt;0.05)</td>
</tr>
<tr>
<td><strong>Mid anterior seg</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Mean systolic velocity cm/sec</td>
<td>4.5±0.4</td>
<td>6.1±0.2</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>-Mean systolic strain%</td>
<td>-14.42±1.5</td>
<td>-20.34±2.7</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>-Mean systolic strain rate 1/s</td>
<td>-1.26±0.16</td>
<td>-1.77±0.13</td>
<td>(P&lt;0.05)</td>
</tr>
<tr>
<td><strong>Mid inferior seg</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Mean systolic velocity cm/sec</td>
<td>4.6±0.38</td>
<td>5.7±0.22</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>-Mean systolic strain%</td>
<td>-15.5±1.3</td>
<td>-21±1.7</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>-Mean systolic strain rate 1/s</td>
<td>-1.2±0.14</td>
<td>-2±1.8</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td><strong>Posterior wall seg</strong> (Radial strain)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Mean systolic velocity cm/sec</td>
<td>4.1±0.2</td>
<td>5.2±0.3</td>
<td>(P&lt;0.05)</td>
</tr>
<tr>
<td>-Mean systolic strain%</td>
<td>26.28±1.6</td>
<td>28.38±2.6</td>
<td>(P&gt;0.05)</td>
</tr>
<tr>
<td>-Mean systolic strain rate 1/s</td>
<td>1.5±0.15</td>
<td>1.8±0.12</td>
<td>(P&gt;0.05)</td>
</tr>
<tr>
<td><strong>Global longitudinal systolic indices:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Global longitudinal strain (glsca)</td>
<td>17.99±0.7</td>
<td>22.56±1.1</td>
<td>(P&lt;=0.01)</td>
</tr>
<tr>
<td>-Average peak systolic strain rate</td>
<td>1.37±0.3</td>
<td>1.77±0.3</td>
<td>(P&lt;=0.05)</td>
</tr>
</tbody>
</table>
Conclusion

When comparing morbid obese versus non obese group, mean systolic velocity showed significant reduction in six selected segments in the morbid obese group versus non obese groups.

Mean systolic strain was significantly lower in the six selected segments except for the basal lateral segment in morbidly obese versus non obese patients.

Mean systolic strain rate was significantly lower in the six selected segments in morbidly obese versus non obese patients.

Global longitudinal strain & average peak systolic strain rate was significant lower in morbid obese versus non obese groups.

Table (23): Mean systolic velocity & mean systolic strain/strain rate in morbidly obese versus non obese groups in the six selected segments:

<table>
<thead>
<tr>
<th>Tissue Doppler imaging</th>
<th>Group 1A</th>
<th>Group 2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal lateral seg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Mean systolic velocity cm/sec</td>
<td>6.11±0.19</td>
<td>7.87±0.30</td>
<td>(P&lt;0.001)</td>
</tr>
<tr>
<td>-Mean systolic strain%</td>
<td>-21.76±2.3</td>
<td>-23.52±1.9</td>
<td>(P&gt;0.05)</td>
</tr>
<tr>
<td>-Mean systolic strain rate 1/s</td>
<td>-1.4±0.10</td>
<td>-1.81±0.08</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>Mid lateral seg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Mean systolic velocity cm/sec</td>
<td>4.27±0.24</td>
<td>6.53±0.21</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>-Mean systolic strain%</td>
<td>-13.36±1.22</td>
<td>-20.48±2.38</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>-Mean systolic strain rate 1/s</td>
<td>-1.09±0.09</td>
<td>-1.46±0.13</td>
<td>(P&lt;0.05)</td>
</tr>
<tr>
<td>Mid posterior septum seg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Mean systolic velocity cm/sec</td>
<td>4.24±0.21</td>
<td>6.06±0.21</td>
<td>(P&lt;0.001)</td>
</tr>
</tbody>
</table>
## Conclusion

<table>
<thead>
<tr>
<th>Tissue Doppler imaging</th>
<th>Group 1A</th>
<th>Group 2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean systolic</td>
<td>Mean systolic</td>
<td>(P&lt;0.01)</td>
</tr>
<tr>
<td></td>
<td>strain%</td>
<td>strain rate 1/s</td>
<td>(P&lt;0.01)</td>
</tr>
<tr>
<td>Mid anterior seg</td>
<td>-16.88±1.54</td>
<td>-21.64±2.04</td>
<td></td>
</tr>
<tr>
<td></td>
<td>-1.26±0.09</td>
<td>-1.68±0.13</td>
<td></td>
</tr>
<tr>
<td>Mid inferior seg</td>
<td>4.19±0.16</td>
<td>6.09±0.15</td>
<td>(P&lt;=0.01)</td>
</tr>
<tr>
<td></td>
<td>-13.52±1.23</td>
<td>-20.34±2.72</td>
<td>(P&lt;0.001)</td>
</tr>
<tr>
<td></td>
<td>-1.17±0.13</td>
<td>-1.77±0.13</td>
<td>(P&lt;0.01)</td>
</tr>
<tr>
<td>Posterior wall seg (Radial strain)</td>
<td>3.94±0.16</td>
<td>5.19±0.27</td>
<td>(P&lt;=0.01)</td>
</tr>
<tr>
<td></td>
<td>25.56±1.56</td>
<td>28.38±2.65</td>
<td>(P&lt;0.01)</td>
</tr>
<tr>
<td></td>
<td>1.46±0.13</td>
<td>1.83±0.12</td>
<td>(P&lt;0.01)</td>
</tr>
<tr>
<td>Global longitudinal systolic indices:</td>
<td>17.72±0.53</td>
<td>22.53±1.2</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td></td>
<td>1.26±0.05</td>
<td>1.76±0.32</td>
<td>(P&lt;=0.001)</td>
</tr>
</tbody>
</table>
Comparing mild obese group versus non obese group, mean systolic velocity showed significant reduction in six selected segments in the mild obese group versus non obese groups.

Mean systolic strain was significantly lower in the six selected segments except for the basal lateral segment in mild obese versus non obese patients.

Mean systolic strain rate was significantly lower in mid posterior septum, mid anterior & mid inferior segments in mild obese versus non obese patients.

Global longitudinal strain & average peak systolic strain rate was significant lower in mild obese versus non obese groups.

**Table (24):** Mean systolic velocity & mean systolic strain/strain rate in mild obese versus non obese in the six selected segments:

<table>
<thead>
<tr>
<th>Tissue Doppler imaging</th>
<th>Group 1B</th>
<th>Group 2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal lateral seg</td>
<td>6.98±0.29</td>
<td>7.87±0.30</td>
<td>(P&lt;0.001)</td>
</tr>
<tr>
<td>-Mean systolic velocity cm/sec</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Mean systolic strain%</td>
<td>-20.68±1.8</td>
<td>-23.52±1.9</td>
<td>(P&gt;0.05)</td>
</tr>
<tr>
<td>-Mean systolic strain rate 1/s</td>
<td>-1.96±2.30</td>
<td>-1.81±0.08</td>
<td>(P&gt;0.05)</td>
</tr>
<tr>
<td>Mid lateral seg</td>
<td>5.93±0.42</td>
<td>6.53±0.21</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>-Mean systolic velocity cm/sec</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Mean systolic strain%</td>
<td>-14.08±1.44</td>
<td>-20.48±2.38</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>-Mean systolic strain rate 1/s</td>
<td>-1.25±0.12</td>
<td>-1.46±0.13</td>
<td>(P&gt;0.05)</td>
</tr>
<tr>
<td>Mid posterior septum seg</td>
<td>4.94±0.24</td>
<td>6.06±0.21</td>
<td>(P&lt;0.001)</td>
</tr>
<tr>
<td>-Mean systolic velocity cm/sec</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Mean systolic strain%</td>
<td>-16.68±2.24</td>
<td>-21.64±2.04</td>
<td>(P&lt;0.01)</td>
</tr>
<tr>
<td>-Mean systolic strain rate 1/s</td>
<td>-1.40±0.10</td>
<td>-1.68±0.13</td>
<td>(P&lt;0.05)</td>
</tr>
</tbody>
</table>
### Conclusion

<table>
<thead>
<tr>
<th>Tissue Doppler imaging</th>
<th>Group 1B</th>
<th>Group 2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mid anterior seg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Mean systolic velocity cm/sec</td>
<td>4.88±0.27</td>
<td>6.09±0.15</td>
<td>(P&lt;=0.01)</td>
</tr>
<tr>
<td>-Mean systolic strain%</td>
<td>-15.32±1.25</td>
<td>-20.34±2.72</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>-Mean systolic strain rate 1/s</td>
<td>-1.35±0.15</td>
<td>-1.77±0.13</td>
<td>(P&lt;0.01)</td>
</tr>
<tr>
<td>Mid inferior seg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Mean systolic velocity cm/sec</td>
<td>4.94±0.20</td>
<td>5.73±0.22</td>
<td>(P&lt;0.05)</td>
</tr>
<tr>
<td>-Mean systolic strain%</td>
<td>-15.72±1.4</td>
<td>-21±1.69</td>
<td>(P&lt;0.001)</td>
</tr>
<tr>
<td>-Mean systolic strain rate 1/s</td>
<td>-1.30±0.12</td>
<td>-2.05±1.87</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>Posterior wall seg (Radial strain)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Mean systolic velocity cm/sec</td>
<td>4.19±0.24</td>
<td>5.19±0.27</td>
<td>(P&lt;=0.05)</td>
</tr>
<tr>
<td>-Mean systolic strain%</td>
<td>27±1.19</td>
<td>28.38±2.65</td>
<td>(P&lt;=0.05)</td>
</tr>
<tr>
<td>-Mean systolic strain rate 1/s</td>
<td>1.62±0.13</td>
<td>1.83±0.12</td>
<td>(P&gt;0.05)</td>
</tr>
<tr>
<td>Global longitudinal systolic indices:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Global longitudinal strain (glsca )</td>
<td>18.21±0.81</td>
<td>22.53±1.2</td>
<td>(P&lt;=0.001)</td>
</tr>
<tr>
<td>-Average peak systolic strain rate (apss)</td>
<td>1.47±0.39</td>
<td>1.76±0.32</td>
<td>(P&lt;=0.01)</td>
</tr>
</tbody>
</table>
There was a significant direct relation between BMI and left ventricular mass, left ventricular mass index, body surface area & left ventricular end diastolic dimension among the groups.

**Table (25):** Correlation between BMI & variables among the three groups:

<table>
<thead>
<tr>
<th>BMI</th>
<th>variables</th>
<th>r</th>
<th>variables</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVM</td>
<td></td>
<td>0.783</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVMI</td>
<td></td>
<td>0.450</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEDD</td>
<td></td>
<td>0.741</td>
<td></td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Table (26) shows a significant inverse relation between BMI and the peak systolic velocity, peak systolic strain & peak systolic strain rate of the six selected segments except for systolic strain rate of basal lateral segment.

Table (26): Correlation between BMI & color coded TDI of the six selected segments (Peak systolic velocity, strain & strain rate) among the three groups:

<table>
<thead>
<tr>
<th>Tissue Doppler imaging</th>
<th>TDI r</th>
<th>TDI P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal lateral seg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- systolic velocity</td>
<td>-0.92</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>- systolic strain</td>
<td>-0.40</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>- systolic strain rate</td>
<td>-0.13</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Mid lateral seg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- systolic velocity</td>
<td>-0.89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>- systolic strain</td>
<td>-0.82</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>- systolic strain rate</td>
<td>-0.80</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mid posterior septum seg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- systolic velocity</td>
<td>-0.95</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>- systolic strain</td>
<td>-0.69</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>- systolic strain rate</td>
<td>-0.82</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mid anterior seg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- systolic velocity</td>
<td>-0.95</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>- systolic strain</td>
<td>-0.65</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>- systolic strain rate</td>
<td>-0.76</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mid inferior seg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- systolic velocity</td>
<td>-0.93</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>- systolic strain</td>
<td>-0.67</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>- systolic strain rate</td>
<td>-0.28</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Posterior wall seg (Radial strain)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- systolic velocity</td>
<td>-0.89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>- systolic strain</td>
<td>-0.46</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>- systolic strain rate</td>
<td>-0.74</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Global longitudinal systolic indices:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Global longitudinal strain</td>
<td>-0.87</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>-Average peak systolic strain rate</td>
<td>-0.58</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
According to the results of the study we concluded that:

- Otherwise-healthy obese subjects (with no other co morbidities) had a significant increase in LVMI when compared with non-obese subjects.

- Although Ejection fraction was normal in both groups, healthy obese subjects exhibit alterations in LV structure and function manifested by eccentric LV remodeling and decreased global LV systolic function and also regional LV function, together with alteration in diastolic function.

- 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.

- TDI derived echocardiographic techniques used in this study may be new tools for early detection of subclinical cardiac functional and structural changes and to evaluate their natural history and the efficacy of therapeutic interventions over time.
Limitations

The current study had the following limitations:

- We did not have complete data on sleep apnea and measurements for insulin, insulin resistance, cytokines, leptin, sympathetic nervous system activity, and renin–angiotensin–aldosterone system activity. All these could have added information about the underlying mechanisms on myocardial alterations related with obesity.

- The results are from a single medical center (Benha University Hospitals).

- The sample size was relatively small.

- The study did not cover all the types of obesity, obesity was measured using only BMI, and no measurements of body fat distribution were made as waist circumference.

- The study did not determine the duration of obesity which is the factor that determines the likelihood of developing systolic dysfunction and heart failure.

- Technical limitations of SR imaging include its load dependence, angle dependence and low signal-to-noise ratio. Adequate echocardiographic image quality is required for SR imaging, which may be suboptimal in many obese subjects.

- Lack of follow-up of obese subjects in the present study, to document the development of heart failure, or other adverse outcomes associated with obesity.


Recommendations

Based on the results of the current study it is recommended that:

1) Early detection of subclinical pathological cardiac changes associated with obesity would be important to potentially influence the initiation of treatment and to prevent progression to heart failure.

2) Promotion of optimal body weight in children and adults through lifestyle measures such as adequate exercise and proper nutrition may be the best measure to prevent the cardiomyopathy of obesity.

3) Doppler echocardiography is one of the most useful clinical tools for the assessment of left ventricular diastolic function; Tissue Doppler imaging has an emerging role in the study and assessment of systolic function.

4) Further study is recommended to compare between the different types of obesity (overall obesity and central obesity) & to detect improvement of cardiac function with substantial weight reduction.

5) Larger trials should be done for more accurate assessment of LV remodeling and hypertrophy in obese patients and the effect of weight reduction on these changes, also to follow up the development of heart failure in obese patients with early structural changes.
Discussion

Overweight and obesity are the most common nutritional disorders and this has heightened the concern regarding the association between obesity and cardiovascular morbidity. It is associated with cardiomyopathy resulting in heart failure in morbid obesity cases (Haque et al., 2008). Abnormal cardiac functions are noted in individuals even with slight or mild obesity (Ammar et al., 2008).

This has been attributed to chronic volume overload characterized by left ventricular dilatation, increased left ventricular wall stress and compensatory eccentric left ventricular hypertrophy. Impairment of cardiac function has been reported to correlate with degree of obesity i.e. body mass index and duration of obesity (Tumuklu et al., 2007).

Obesity has also been linked to a spectrum of minor reversible cardiovascular changes, ranging from a hyper dynamic circulation to subclinical cardiac morphological changes in the form of greater aortic root and left atrial enlargement (Haque et al., 2008). These early manifestations may be important, because treatment to reverse the process is most likely to be effective earlier in the disease.

The present study was performed to evaluate the effect of obesity on left ventricular structure and myocardial systolic function using conventional echocardiography, tissue Doppler imaging and strain\strain rate imaging.

The results of this study showed that obese subjects who have no other clinically appreciable cause of heart disease exhibit abnormalities in LV structure in addition to subtle but significant alterations in systolic functions of the left ventricle. These alterations include a pattern of LV eccentric hypertrophy and decreased subclinical systolic and diastolic function, as
determined with the help of TDI, strain/strain rate imaging which are load independent indices of LV and RV functions.

In this study it was found that, obesity was associated with elevated LV end-systolic dimension, elevated LV end-diastolic dimension, left atrial enlargement, increased septal wall thickness, posterior wall thickness in diastole, with increased LV mass, and LV mass index. This was obviously related to the severity of obesity as LV mass, and LV mass index were increased in morbidly obese persons versus mild obese persons. BMI was found to be a robust, independent predictor of these functional alterations even after adjusting other clinical variables (Tables (13-18), figures (6-12)).

LV eccentric hypertrophy was considered to be from increased LVMI. The finding of eccentric hypertrophy in the present study is supported by previous studies in which obesity was associated with eccentric rather than concentric LV remodeling (Krisha et al., 2005). Alpert et al also stated that 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 (Alpert 2001). However, this finding is in contrast with those of other studies in which obesity indexes significantly correlated with increased LVM and relative wall thickness (Mensah et al., 1999). These contradictory results may be explained by such differences between subjects enrolled in different studies: age, gender or duration of obesity.

In the present study obese persons had a highly significant larger left ventricular mass and left ventricular mass index (Tables (16-18), figures (10-12)).
These results are in agreement with Masaidi et al., They found that the prevalence of left ventricular hypertrophy in obese individuals was significantly higher (4-5 fold) as compared to their lean counterparts (Masaidi et al., 2009).

LV end diastolic cavity dimensions and LVMI were suggested to be early markers of LV dysfunction in morbidly obese individuals preceding development of an increased LV wall thickness (Messerli et al., 1981).

The association between obesity and increased LV mass has been well established in many studies (Morricone et al., 2002). Piercarlo Ballo et al, found a significant association between obesity and left ventricular hypertrophy; where a higher BMI was associated with greater LV mass (Piercarlo Ballo et al., 2007).

The likely causes of the increased LV mass in obese persons include increase in the total blood volume as a result of an increase in the size of the vascular bed in the excess adipose tissue, cardiac output, and resultant increased afterload (Peterson, 2004), hyperinsulinemia and insulin resistance (Wong et al., 2004), changes in respiratory workload, and other metabolic mechanisms such as renal sodium retention, oxidative stress, and inflammatory cytokines (Otto et al., 2004). As each of these changes may occur in obesity, they induce cardiac hypertrophy and play a part in LV morphologic alterations.

Thus, even if the EF is normal as in this study, myocardial function is often reduced when it is measured with more sensitive methods such as midwall LV fractional shortening, systolic velocity measured with tissue Doppler, or systolic strain rate. Indeed, obese subjects have generally been found to have subclinical contractile abnormalities when assessed with the forementioned techniques (Avelar et al., 2007).
Our results are compatible with Wong et al. who identify subclinical depression of LV function with obesity (*Wong et al., 2004*).

In this study, regional mean systolic velocities were found to be reduced in the obese group in all six selected segments, this was obvious when comparing either morbid obese or mild obese versus control group (Tables 22, 23 & 24).

This is supported by Ammar and his colleagues who found a strong correlation between LV systolic and diastolic dysfunction and central obesity, as measured by the waist-to-hip ratio (*Ammar et al., 2008*).

In a cross-sectional study, Orhan et al found that the obese subjects with no comorbidities have left and right ventricular systolic and diastolic dysfunction (*Orhan et al., 2010*). Additionally, Di Salvo et al also studied 150 healthy obese children (percentile > 97th for sex and age) with no comorbidities and they found systolic dysfunction in both right and left ventricle (*Di Salvo et al., 2006*).

Another study performed by Tumuklu et al showed that systolic left ventricular dysfunction is found in healthy obese subjects with no comorbidities (*Tumuklu et al., 2007*), and Sürücü et al demonstrated that obese adults have right and left ventricular systolic and diastolic dysfunction using tissue Doppler technique (*Sürücü et al., 2008*).

Tissue velocities do not discriminate between actively contracting muscle and passive motion due to heart translation and tethering effects (*Derumeaux et al., 1998*). To separate this two-typed motion, strain and strain rate have been proposed as measures of regional contractility (*Garcia-Fernandez et al., 2003*).

Strain and strain rate assess function in heart segments. Strain is directly related to fiber shortening and strain rate is the speed of fiber shortening, which is a measure of contractility (*Pavlopoulos and Nihoyannopoulos, 2008*).
Strain rate imaging, which reflects the rate of myocardial deformation, has been developed by estimating the spatial gradients in myocardial velocities. It is independent of overall heart motion, cardiac rotation, or motion induced by contraction in adjacent myocardial segments. Therefore, it is accepted as a true measure of local deformation (Stoylen et al., 1999). Therefore, it would have been expected an increase in peak systolic strain rate in obese subjects who may have a tendency for volume overload. However, a significant reduction in systolic myocardial deformation properties was found in obese subjects in the absence of comorbidities. This suggests that obesity may significantly influence regional myocardial systolic function. Other investigators have reported variable results of LV function in obese subjects (Wong et al., 2004).

The concept of strain is complex. It is a dimensionless index, and reflects the total deformation of the myocardium during cardiac cycle relative to (or as percent of) its initial length. Whereas Strain rate is the rate by which the deformation occurs (deformation or strain per unit time). The unit of strain rate is s−1 and the local rate of deformation or strain per unit time equals velocity difference per unit length.

Mean systolic strain in the present study was found to be reduced in mid lateral, mid posterior septum, mid anterior & mid inferior segments,. The mean systolic strain rate was reduced in the six selected segments except the basal lateral segment & posterior segment, where there was significant reduction in the strain rate in the six selected segments in morbidly obese group versus non obese group. Mildly obese group showed reduction in systolic strain rate in mid posterior septum, mid anterior & mid inferior segments versus control group (Tables 22, 23 &24).

These results are supported by a prospective study involving healthy and obese individuals aged between 10 to 18 years, Lorch and Sharkey found a
decrease in systolic strain in the obese group in comparison to the lean group (Lorch et al., 2007).

This is confirmed by a study performed by Wong et al who found that patients with isolated obesity showed alterations in RV and LV systolic function, when assessed by SR imaging (Wong et al., 2006). Also using strain and strain rate to study myocardial function, it was found that overweight subjects have reduced systolic and diastolic function, even after adjustments for mean arterial pressure, age, gender, and LV mass (Wong et al., 2004).

Gong and colleagues also studied 200 patients with metabolic syndrome using strain and strain rate to evaluate cardiac function in comparison to lean controls and demonstrated left ventricular systolic and diastolic dysfunction in the obese group. In their study, multiple regression analysis revealed that the waist-to-hip ratio was an independent predictor of systolic dysfunction and that the waist-to-hip ratio and high-density lipoproteins cholesterol were independent predictors of diastolic dysfunction (Gong et al., 2009).

Di Salvo et al. used SR imaging to evaluate LV systolic function in obese children and found that obesity is associated with significant reductions in systolic myocardial deformation properties (Di Salvo et al., 2006).

The measurement of regional strain rate and strain can be performed in either the longitudinal or radial direction for a myocardial segment, and each direction reflects different aspects of regional myocardial function. One of the aims of this study was to define the effect of obesity on these different aspects of LV myocardial function. The present study showed that obesity affected LV systolic function in global, regional longitudinal and also in radial aspects.

The results of a recent study showed that LV systolic dysfunction may begin with a reduction in longitudinal shortening in the early stage that is compensated by an augmentation of circumferential shortening. Consequently,
radial thickening may be preserved to some degree, maintaining the LV ejection fraction (Yukio et al., 2008). This support the finding of the present study which showed a significant reduction in the strain rate of LV segments (longitudinal fibers) without reduction noted in the posterior wall (circumferential fibers). This change was lost with morbidly obese patients who showed reduction in systolic strain rate in both longitudinal & circumferential fibers.

The results of the present study are in agreement with those reported by Fang et al who showed that systolic radial strain rates in the anterior and posterior LV walls are increased in diabetic obese patients compared with controls (Fang et al., 2004).

The present study compared two mean indices as global longitudinal LV systolic indices: global systolic contraction amplitude and averaged peak systolic strain rate. Averaged peak strain and strain rate value was significantly lower in obese subjects. In addition, BMI was found to be strongly correlated with global systolic contraction amplitude and averaged peak strain rate values of different regions of left ventricle showing inverse relation. Recently, Ingul and colleagues have reported an improvement in cardiac function, as evaluated by strain and strain rate, in obese adolescents after a training program (Ingul et al., 2010). They reported that impaired cardiac function in obese adolescents can be improved by 3 months of aerobic interval training, almost to the same level as lean counterparts.

Regarding left ventricular diastolic function, the present study showed significantly higher values of E, A, and deceleration time in morbid obese patients versus mild obese & control groups. E/A ratio was significantly lower in morbid obese group versus mild obese & non obese groups.

This is against the results of other studies that showed decreased E velocity with obesity, but these studies supported our results of decreased E/A ratio with obesity (Peterson et al., 2004).
Summary

- Obesity is a chronic metabolic disorder associated with cardiovascular disease and increased morbidity and mortality. It is apparent that a variety of adaptations/alterations in cardiac structure and function occur as excessive adipose tissue accumulates.

Overt systolic and diastolic dysfunction has been described in obesity. New findings, indicating the occurrence of pre-clinical systolic and diastolic dysfunction, even in young obese patients, suggest that obese patients should be carefully monitored in order to detect incipient dysfunction.

Since traditional echocardiographic measurements of ventricular function, such as ejection fraction, fractional shortening and mitral inflow are load-dependent, the investigation of right and left ventricle subclinical dysfunction in obesity by sensitive newer echocardiographic techniques, such as tissue Doppler imaging, myocardial strain and strain rate looks like very promising. These techniques permit a quantitative assessment of both global and regional function and timing of myocardial events as well as the assessment of early changes in systolic and diastolic function.

Early detection of cardiovascular abnormalities is very important because the control of this process seems to be more effective during the initial stages of the disease.

The current study was conducted on 100 subjects were divided into two group without comorbidities, fifty subjects with BMI more than 30 representing the obese group, which were subdivided into two subgroups: group A which represents morbidly obese patients with BMI more than 35 & group B which represents mild obese patients with BMI more than 30 and fifty subjects with BMI less than 25 representing the control group referred to the echocardiographic lab at Benha University Hospital for echocardiographic
The candidates were subjected to the following:

1- History taking.
2- Clinical examination.
3- Laboratory examination.
4- Echocardiography (conventional echocardiography and tissue Doppler imaging) : with assessment of left ventricular dimensions, left ventricular systolic and diastolic function, left ventricular mass, left ventricular mass index. Tissue Doppler indices including systolic velocity, strain & strain rate were done for all patients.

This current study concluded that obese subjects had a significant increase in LVM and LVMI when compared with non-obese subjects.

It also concluded that healthy obese subjects exhibit alterations in LV structure and function manifested by eccentric LV remodeling, decreased global LV systolic function and also regional LV function and increased left atrial dimension.

Regional left ventricular systolic function showed significant reductions in systolic myocardial velocity and deformation properties among the obese subjects in the left ventricular selected segments in this study (longitudinal fibers) without reductions noted in strain rate of the posterior wall (circumferential fibers) as the reduction in longitudinal shortening in the early stage is compensated by an augmentation of circumferential shortening.

A highly significant direct relation was found in the present study between BMI versus left ventricular mass and left ventricular mass index, significant inverse relation between BMI and the peak systolic velocity of strain and strain rate.
- So we concluded that TDI derived echocardiographic techniques used in this study may be new tools for early detection of subclinical cardiac functional and structural changes and to evaluate their natural history and the efficacy of therapeutic interventions over time.
References


10. **Arita T, Sorescu GP, Schuler BT, et al.** Speckle-tracking stain echocardiography for detecting cardiac dyssynchrony in a canine model of

11. **Aronne LJ.** Classification of obesity and assessment of obesity-related health risks. *Obes. Res. 10(Suppl. 2) 2002, 105S–115S.*


17. **Barberato SH and Pecoits FR.** Influence of preload reduction on Tei index and other Doppler echocardiographic parameters of left ventricular function. *Arq Bras Cardiol. 2006; 86: 425-31.*


44. Citro et al. *Journal of Cardiovascular Ultrasound;* 2008 6;54.


80. Frommelt PC, Ballweg JA, Whitstone BN, et al. Usefulness of Doppler tissue imaging analysis of tricuspid annular motion for determination of right
ventricular function in normal infants and children. *Am J Cardiol* 2002; 89: 610–613


90. **Gorcsan J III, Gulati VK, Mandarino WA, et al.** Colorcoded measures of myocardial velocity throughout the cardiac cycle by tissue Doppler imaging to quantify regional left ventricular function. *Am Heart J 1996; 131:1203-13.*


115. **Journal of the American Society of Echocardiography** Volume 21, Issue 10, Pages 1138-1144, authors; Yukio Mizuguchi, MD, Yoshifumi Oishi, MD, Hirokazu Miyoshi, MD, Tokushima, Japan October 2008


138. **Lang RM, Bierig M, Devereaux RB, et al.:** Recommendation for chamber quantification: A report from American society of Echocardiography’s Guidelines and standards committee and the chamber quantification writing group, developed in conjugation with the European


159. **McCulloch M, Zoghbi WA, Davis R, et al.** Color tissue Doppler myocardial velocities consistently underestimate spectral tissue Doppler


171. **Musaiger AO:** Socio-cultural factors affecting obesity in the Arab countries. Bahrain, *Bahrain Centre for Studies and Research, 2003 (Technical report).*


204. **Peterson LR, Waggoner AD, Schechtman KB, et al.** Alterations in left ventricular structure and function in young healthy obese women: assessment


الملخص العربي

المقدمة:

السمنة بوجه عام وإن كان لا يصاحبها أمراض أخرى، يصاحبها زيادة في أمراض القلب والأوعية الدموية، وقد وصف في السمنة القصور الظيفي بعضة عضلة القلب الإقياعية والإنساطية.

وقد أكدت بعض الدراسات الحديثة حدوث هذا الخلل الظيفي ببعضة القلب بدون أعراض طبية ظاهرة ويتضمن ذلك الشباب البديناء مما يستدعي ضرورة الكشف المبكر عن حدوث هذا الخلل الظيفي والعمل على وقفه.

و تعتبر قياسات الموجات الصوتية لقلب المعتذدة مثل قياس كفاءة عضلة القلب، مقدار القصر الجنسي والمحيطي للبيضة العضلية وتدفق الدم عبر الصلام المبترالي تعتزم على مقدار الضغط على عضلة القلب و لذلك تعتبر غير دقيقة، وقياس القصور الظيفي للبطينين الأيمن والأيسر غير ظاهر المصاحب للبدانة عن طريق طرق أحدث في تصوير القلب بالموجات الصوتية مثل ديلر لأنسجة الضغط ومعدل الضغط، يكون أكثر دقة في تقييم الخلل الظيفي الغير ظاهر.

كما أن هذه الطرق الحديثة تسمح بتقييم كمي للوظيفة الكلية والجزئية لعضلة القلب ومعرفة توقيت كل حدث بدوره القلب وتقييم التغيرات الطفيفة المبكرة في وظيفة عضلة القلب الإقياعية والإنساطية.

كما أن الكشف المبكر عن التغيرات التي حدثت في القلب والجهاز الدورى يعتبر هام جداً وذال ذلك للتحكم في هذه التغيرات و الذي يكون أكثر تأثيراً في مراحلها المبكرة.
الهدف من البحث:

- تعريف التغيرات التي تحدث بالشكل الوراثي و الوظيفي للبطين الأيسر المساحية

للحيدا باستخدام الموجات فوق الصوتية على القلب و تقنية دوقلر الأنسجة و الضغط و معدل الضغط.

المرضى و الوسائل:

الدراسة تمت مائة فرد تم تقسيمهم إلى مجموعتين متساويتين كل منهما تضمنت خمسين فردًا

maholin عمل فحص موجات فوق صوتية على القلب.

1- المجموعة الأولى: تم تقسيمها إلى مجموعتين

- مجموعة أ: وتشمل المرضى ذوي السمنة المفرطة
- مجموعة ب : وتشمل المرضى ذوي السمنة البسيطة

2- المجموعة الثانية: وتشمل المرضى غير المصابين بالسمنة

أشمل البحث على:

- أخذ التاريخ المرضي
- الفحص الإكلينيكي
- الفحص العملي
- موجات فوق صوتية على القلب و تقنية دوقلر الأنسجة و الإجهاد و معدل الإجهاد لقيم المشكل الوراثي و الوظيفي لعضلة القلب و أبعاد البطين الأيسر و كتلة و معدل كتلة البطين الأيسر.

216
النتائج التي أثبتهما البحث:

أثبتت الدراسة أن الأفراد البدناء يتميزون بزيادة في كتلة و معامل كتلة البطين الأيسر مقارنة بالأفراد الغير بدناء.

و تضمنت الدراسة أيضا وجود تغيرات في شكل ووظيفة البطين الأيسر متمثلة في تضخم غير مركزي في البطين الأيسر و قصور في وظيفة القلب الكلية و الجزئية مع زيادة في أبعاد الأذين الأيسر.

وفي هذه الدراسة وجد علاقة طردية ملموسة بين مؤشر كتلة الجسم و كتلة و معامل كتلة البطين الأيسر و أيضا علاقة عكسية ملموسة بين مؤشر كتلة الجسم و معدل الإجهاد لعضة القلب.

و قد خلصت الدراسة إلى أن المرضى ذوي السمنة والذين لا يعانون من أمراض عضوية أخرى يحدث لهم تغيرات في شكل ووظيفة البطين الأيسر وأن الكشف المبكر عن هذه التغيرات يساهم بشكل فعال في العلاج المبكر لهذه التغيرات وحماية عضلة القلب من التدهور وكذلك أوصت الدراسة بأن استخدام التقنيات الحديثة لدبوير الأنسجة يساهم بشكل أدق لتحديد هذه التغيرات مبكراً.
دراسة استخدام دوبلر الأنسجة وخصائص الاجهاد و معدل الاجهاد في تقييم تأثير السمنة على بنية البطين الأيسر ووظائف عضلة القلب الانقباضية

رسالة مقدمة

توطنة

لحصول على درجة الدكتوراة

في القلب والأوعية الدموية

مقدمة من الطبيب

هاني حسن أحمد عبيد

(ماجستير القلب والأوعية الدموية)

تحت إشراف

أ.د/ هبة عبد القادر منصور

أستاذ القلب والأوعية الدموية

كليه الطب - جامعة بنها

أ.د/ رضا بيومي بسطويسي

أستاذ م القلب والأوعية الدموية

كليه الطب - جامعة بنها

أ.د/ نعمة علي المليجي

استشاري مساعد القلب والأوعية الدموية

كليه الطب - جامعة بنها

د/ محمد حسن إبراهيم

مدرس القلب والأوعية الدموية

كليه الطب - جامعة بنها

كلية طب بنها

جامعة بنها

(2014)