INTRODUCTION

Some of the greatest problems in chronic heart failure (CHF) are to categorize the degree of the impairment of cardiac performance and of cardiovascular disability in order to follow the clinical status of patients over time, to assess the effects of therapeutic interventions and to compare patients with each other ***(Cohn and Rector, 1988).***

A number of methods has been suggested to categorize CHF patients including subjective methods which are not sensitive enough to reflect small but sometimes important clinical changes and so gave rise to the need for more objective methods with the most accepted recently, the measurement of maximal or peak oxygen consumption which offers an objective evaluation of cardiovascular function, providing a high prognostic value in severe heart failure ***(Mancini et al., 1991).***

Recently, it has been proposed that diastolic dysfunction may contribute to significant impairment of exercise tolerance in patients with CHF. Echocardiographic Doppler assessment of left ventricular (LV) filling is the mainstay of our evaluation of myocardial diastolic function (DF) and dysfunction (DD) ***(Pepi et al., 1999 and Zile et al., 2002).***

Trans mitral flow propagation velocity (Vp) is a recently described parameter of the assessment of the rapid filling phase (Active Relaxation Component) of the diastole; (Vp) correlates with intra-ventricular pressure gradients and is a largely preload independent index of ventricular diastolic performance ***(Khouri et al., 2004).***

It is proposed that VO2peak correlated significantly with the LV filling pattern estimated by velocity flow propagation and so Trans mitral flow propagation velocity (Vp) as an index of diastolic function is an important determinant of exercise capacity in CHF patients and holds a substantial diagnostic potential.

AIM OF THE WORK

To compare the relationship between Trans mitral flow propagation velocity (Vp) as an index of diastolic function and exercise capacity in patients with CHF.

Chapter One
DIASTOLIC FUNCTIONS IN HEART FAILURE

Physiology of diastole

Although in normal hearts the transition from contraction to relaxation begins much more before LV end-systole, i.e., at 16% to 20% of the ejection period and even prior to aortic valve opening when LV contractility is severely impaired, the traditional definition of diastole (in ancient Greek language the term διαστολε means "expansion"), includes the part of the cardiac cycle starting at the aortic valve closure – when LV pressure falls below aortic pressure – and finishing at the mitral valve closure.

A normal LV diastolic function may be clinically defined as the capacity of the left ventricle to receive an LV filling volume able in its turn to guarantee an adequate stroke volume, operating at a low pressure regimen. In merely descriptive terms, diastole can be divided in 4 phases:

1. Isovolumetric relaxation, period occurring between the end of LV systolic ejection (= aortic valve closure) and the opening of the mitral valve, when LV pressure keeps going its rapid fall while LV volume remains constant. This period is mainly attributed to the active LV relaxation, with a lower, variable contribution of elastic recoil of the contracted fibers.

2. LV rapid filling, which begins when LV pressure falls below left atrial pressure and, the mitral valve opens. During this period the blood has an acceleration which achieves a maximal velocity, direct related to the magnitude of atrio-ventricular pressure, and stops when this gradient ends. This period represents a complex interaction between LV suction (= active relaxation) and visco-elastic properties of the myocardium (= compliance);

3. Diastasis, when left atrial and LV pressures are almost equal and LV filling is essentially maintained by the flow coming from pulmonary veins – with left atrium representing a passive conduit – with an amount depending of LV pressure, function of LV "compliance".

4. Atrial systole, which corresponds to left atrial contraction and ends at the mitral valve closure. This period is mainly influenced by LV compliance, but depends also by the pericardial resistance, by the atrial force and by the atrioventricular synchronicity (= ECG PR interval) ***(Galderisi, 2005).***

Definition of diastolic dysfunction

Diastolic dysfunction refers to a condition in which abnormalities in mechanical function are present during diastole. It is defined as functional abnormalities that exist during LV relaxation and filling, diastolic dysfunction occurs when these processes are prolonged, slowed, or incomplete. the measurements that reflect changes in this normal function generally depend on the onset, rate, and extent of ventricular pressure decline and filling and the relationship between pressure and volume or stress and strain during diastole. Moreover, if diastolic function is truly normal, these measurements must remain normal both at rest and during the stress of a variable heart rate, stroke volume, end-diastolic volume, and blood pressure ***(Zile et al., 2002).***

Whereas the diastolic pressure-volume relationship may reflect a more compliant chamber, increased diastolic pressure and abnormal relaxation reflect the presence of abnormal diastolic function.

Definition of heart failure

Heart failure is a clinical syndrome characterized by symptoms and signs of increased tissue/organ water and decreased tissue/organ perfusion. Standardized criteria to diagnose heart failure have been developed. Definition of the mechanisms that cause this clinical syndrome requires measurement of both systolic and diastolic function. In patients with systolic heart failure, there are abnormalities in the pressure-volume relationship during systole, that include: decreased EF, stroke volume, and stroke work. In addition, there are changes in the diastolic portion of the pressure-volume relationship. These changes result in increased diastolic pressures in symptomatic patients, which indicate the presence of combined systolic and diastolic heart failure ***(Zile et al., 2002)***.

Diastolic heart failure is a clinical syndrome characterized by the symptoms and signs of heart failure, a preserved ejection fraction (EF), and abnormal diastolic function. From a conceptual perspective, diastolic heart failure occurs when the ventricular chamber is unable to accept an adequate volume of blood during diastole, at normal diastolic pressures and at volumes sufficient to maintain an appropriate stroke volume. These abnormalities are caused by a decrease in ventricular relaxation and/or an increase in ventricular stiffness. Diastolic heart failure can produce symptoms that occur at rest (New York Heart Association [NYHA] class IV), symptoms that occur with less than ordinary physical activity (NYHA class III), or symptoms that occur with ordinary physical activity (NYHA class II) ***(Zile et al., 2002).***

Diastolic heart failure can occur alone or in combination with systolic heart failure. In patients with isolated diastolic heart failure, the only abnormality in the pressure-volume relationship occurs during diastole, when there are increased diastolic pressures with normal diastolic volumes. When diastolic pressure is markedly elevated, patients are symptomatic at rest or with minimal exertion (NYHA class III to IV) ***(Zile et al., 2002).***

In the clinical setting the coexistence of systolic and diastolic dysfunction in patients with symptomatic HF occurs very often. In fact, LV stiffness (or compliance) is related to the length of myocardial fibers, reflecting in its turn on LV end-diastolic dimensions. LV diastolic function, through the influence on left atrial and capillary wedge pressures, determines the onset of symptom in patients with prevalent LV systolic dysfunction too. The clinical progression of HF may follow two different routes. In the first one, as it happens after acute myocardial infarction, post infarction LV dilation (= remodeling) leads to systolic dysfunction and/or systolic heart failure. In the second one, LV structural abnormalities (= LV concentric geometry) induce functional alterations of DD. When diastolic dysfunction becomes symptomatic – that is, when dyspnea occurs diastolic heart failure rises.

The majority of patients affected by isolated diastolic HF show symptoms not at rest but in relation to stress conditions (II NYHA class). Symptoms can be induced or worsened by, firstly, physical exercise but also by events as anemia, fever, tachycardia and some systemic pathologies. In particular, tachycardia reduces the time needed for global LV filling, thus inducing an increase of left atrial pressure and consequent appearance of dyspnea, because of accumulation of pulmonary extravascular water ***(Galderisi, 2005).***

Cardiac performance during exercise depends on an adequate LV diastolic filling and compliance. Therefore, it can be hypothesized that LV diastolic dysfunction might be responsible for reduced systolic performance observed in many patients ***(Spinelli et al., 2003).***

Diagnosis of diastolic dysfunction

Echocardiographic Doppler assessment of left ventricular (LV) filling is the mainstay of our evaluation of myocardial diastolic function (DF) and dysfunction (DD). Due to its insight into LV filling, pulse wave Doppler (PWD) has been termed as the "clinician's Rosetta stone" for simplifying our understanding of this complex process. An understanding and appreciation of DF has introduced clinicians to a new paradigm of a "comprehensive ventricular assessment", i.e., systolic as well as diastolic function ***(Mahmood et al., 2009).***

The diagnostic importance of this tool rises from the high feasibility of trans mitral Doppler indexes of diastolic function, such to be suitable and accurate also for serial evaluations over time. To date, standard Doppler indexes may be efficaciously supported by the evaluation of pulmonary venous flow and by new ultrasound technologies as Tissue Doppler and color M-mode derived flow propagation rate.

The application of maneuvers (Valsalva, leg lifting) to Doppler trans mitral pattern and/or different combination of standard trans mitral Doppler with the new tools (ratio between atrial reverse velocity duration and trans mitral A velocity duration, ratio between trans mitral E peak velocity and Tissue Doppler derived E of the mitral annulus or flow propagation velocity [Vp]) are sufficiently reliable to predict capillary wedge pressure and to distinguish accurately variations of LV end-diastolic pressure ***(Galderisi, 2005).***

Quantification of left atrial size

The LA fulfills 3 major physiologic roles that impact on LV filling and performance. The LA acts as a contractile pump that delivers 15% to 30% of the LV filling, as a reservoir that collects pulmonary venous return during ventricular systole, and as a conduit for the passage of stored blood from the LA to the LV during early ventricular diastole.87 Increased LA size is associated with adverse cardiovascular outcomes ***(Spencer et al., 2001).***

An increase in atrial size most commonly is related to increased wall tension as a result of increased filling pressure. Although increased filling volumes can cause an increase in LA size, the adverse outcomes associated with increased dimension and volume are more strongly associated with increased filling pressure ***(Tsang et al., 2002 and Kizer et al., 2005).***

Relationships exist between increased LA size and the incidence of atrial fibrillation and stroke, risk of overall mortality after MI, and risk of death and hospitalization in patients with dilated cardiomyopathy. LA enlargement is a marker of both the severity and chronicity of diastolic dysfunction and magnitude of LA pressure elevation ***(Benjamin et al., 1995).***

The LA size is measured at the end-ventricular systole when the LA chamber is at its greatest dimension. While recording images for computing LA volume, care should be taken to avoid foreshortening of the LA. The base of the LA should be at its largest size indicating that the imaging plane passes through the maximal short-axis area ***(Simek et al., 1995 and Appleton et al., 1993).***

The LA length should also be maximized ensuring alignment along the true long axis of the LA. When performing planimetry, the LA, the confluences of the pulmonary veins, and LA appendage should be excluded.

LA Linear Dimension:

The LA can be visualized from multiple echocardiographic views from which several potential LA dimensions can be measured. However, the large volume of prior clinical and research work used M-mode or 2D antero-posterior (AP) linear dimension obtained from the parasternal long-axis view, making this the standard for linear LA measurement. The convention for M mode measurement is to measure from the leading edge of the posterior aortic wall to the leading edge of the posterior LA wall (Figure 1). However, to avoid the variable extent of space between the LA and aortic root, the trailing edge of the posterior aortic is recommended ***(Di Tullio et al., 1999; Flaker et al., 1995; Vaziri et al., 1994 and Beinart et al., 2004).***

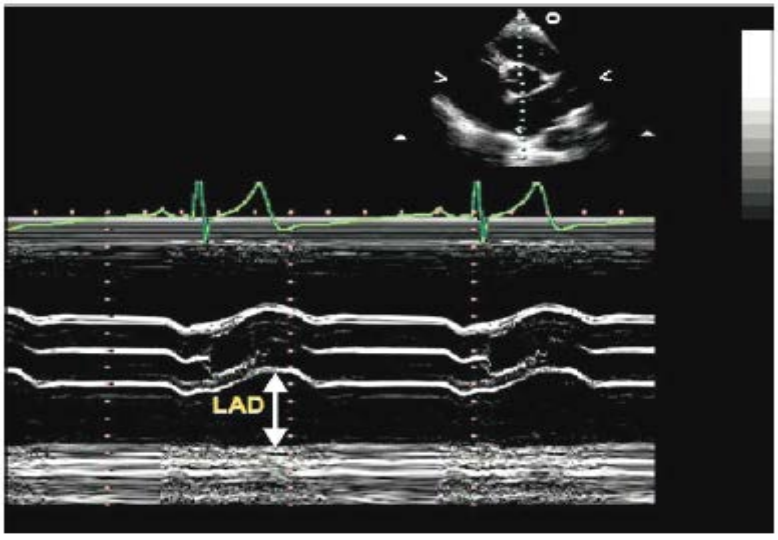
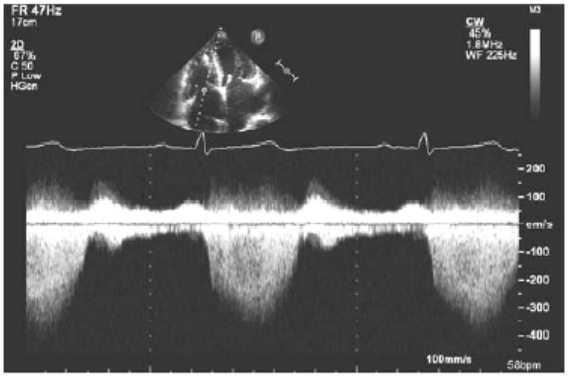


Figure (1): Measurement of left atrial diameter (LAD) from M-mode, guided by parasternal short-axis image at level of aortic valve.

Pulmonary artery systolic and diastolic pressures:

Symptomatic patients with diastolic dysfunction usually have increased pulmonary artery (PA) pressures. Therefore, in the absence of pulmonary disease, increased PA pressures may be used to infer the presence of elevated LV filling pressures. Indeed, a significant correlation was noted between PA systolic pressure and noninvasively derived LV filling pressures ***(Bouchard et al., 2008).***

The peak velocity of the tricuspid regurgitation (TR) jet by continuous-wave (CW) Doppler ***(Figure 2)***, together with systolic right atrial (RA) pressure, are used to derive PA systolic pressure. In patients with severe TR and low systolic right ventricular–RA pressure gradients, the accuracy of the PA systolic pressure calculation is dependent on the reliable estimation of systolic RA pressure. Likewise, the end-diastolic velocity of the pulmonary regurgitation (PR) jet can be applied to derive PA diastolic pressure ***(Quin˜ones et al., 2002).***



4 (V)² of peak TR velocity = PAS – RAP
4 (3.6)² or 52 = PAS - 20
PAS = 52 + 20 = 72 mmHg

Figure (2): Calculation of PA systolic pressure using the TR jet. In this patient, the peak velocity was 3.6 m/s, and RA pressure was estimated at 20 mm Hg ***(Nagueh et al., 2009).***

Pulmonary Venous Flow:

Pulsed wave (PW) Doppler of pulmonary venous flow is performed in the apical 4-chamber view and aids in the assessment of LV diastolic function (Figure 3).

Color flow imaging is useful for the proper location of the sample volume in the right upper pulmonary vein. A 2-mm to 3-mm sample volume is placed.0.5 cm into the pulmonary vein for optimal recording of the spectral waveforms ***(Appleton et al., 1997).***

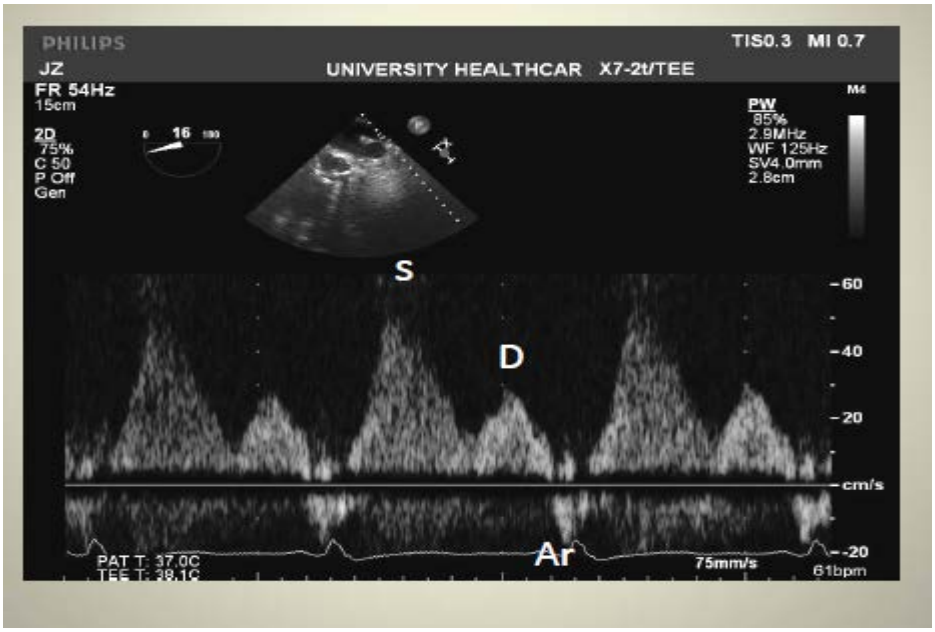


Figure (3): Pulmonary venous flow ***(Nagueh et al., 2009).***

Mitral flow:

Pulsed wave (PW) Doppler is performed in the apical 4-chamber view to obtain mitral inflow velocities to assess LV filling (Figure 4). Color flow imaging can be helpful for optimal alignment of the Doppler beam, particularly when the left ventricle is dilated. Performing CW Doppler to assess peak E (early diastolic) and A (late diastolic) velocities should be performed before applying the PW technique to ensure that maximal velocities are obtained. A 1-mm to 3-mm sample volume is then placed between the mitral leaflet tips during diastole to record a crisp velocity profile.

Primary measurements of mitral inflow include the peak early filling (E-wave) and late diastolic filling (A-wave) velocities, the E/A ratio, deceleration time (DT) of early filling velocity, and the IVRT, derived by placing the cursor of CW Doppler in the LV outflow tract to simultaneously display the end of aortic ejection and the onset of mitral inflow. Secondary measurements include mitral A-wave duration (obtained at the level of the mitral annulus), diastolic filling time, the A-wave velocity-time integral, and the total mitral inflow velocity-time integral (and thus the atrial filling fraction) with the sample volume at the level of the mitral annulus ***(Appleton et al., 1997).***