A Dissertation on

ECHOCARDIOGRAPHIC EVALUATION OF LEFT VENTRICULAR DIASTOLIC FUNCTION IN POST – MYOCARDIAL INFARCTION PATIENTS

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CERTIFICATE

This is to certify that **Dr. T. ARUN,** Post -Graduate Student (July. 2003 to September 2006) in the Department of Medicine, Kilpauk Medical College, Chennai- 600 010, has done this dissertation on **"ECHOCARDIOGRAPHIC EVALUATION OF LEFT VENTRICULAR DIASTOLIC FUNCTION IN POST – MYOCARDIAL INFARCTION PATIENTS"** under my guidance and supervision in fulfillment of the regulations laid down by the Tamilnadu Dr.M.G.R. Medical University, Chennai, for M.D. (General Medicine), Degree Examination to be held in September 2006.

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CONTENTS

INTRODUCTION

From a physiological point of view the heart is a muscle – pump system. The term diastole is interpreted as a division, notch, or separation between two contraction – relaxation cycles (Brutsaert 1984). In this interpretation its meaning is restricted to the passive properties of the heart (Gillebert 1994). Diastole of the left ventricle starts when active relaxations have been completed and include the diastasis and the trial contraction phase. In the English medical literature diastole has however come to mean "the dilatation or period of dilatation of the heart, especially that of the ventricles, coinciding with the interval between the second and first heart sounds" (Brutsaert 1984). In this interpretation it is part of the cardiac cycle which starts with the isovolumetric relaxation phase and ends with cessation of mitral inflow (Arrighi 1995). In the present thesis the latter, clinical definition of diastole will be used.

Ebstein extensively discusses the history of views on diastole in 1904 (Ebstein 11904). Mackenzie divides the heart cycle in a presphygmic period with rising ventricular pressure between closure of the atrio – ventricular valves and opening of the aortic valves, a sphygmic or pulse period with opened aortic valves, and a post sphygmic period after aortic valve closure and before atrio – ventricular valve opening where ventricular pressure is falling (Mackenzie 1914). Wiggers subdivided the cardiac cycle into

smaller phases (Wigger 1921). In his view, diastole is preceded by protodiastole, the period between end of ventricular contraction and closure of the semilunar valves. The period of diastole then begins with closure of the semilunar valves and isometric relaxation. After opening of the trio – ventricular valves a period of diastasis is recognized in addition. Wiggers subdivided the period of auricular systole in a period in which auricular contraction exerts effect on ventricular filling or ventricular tension, and a period of auricular filling by venous return form the pulmonary circulation (Wiggers 1921).

In 1978 new interest arose on relaxation and diastole, since symptoms of cardiac disease could be successfully related to pathophysiology of diastole (Meijler).

Heart failure cab be defined as "the pathophysiological state in which an abnormality of cardiac function is responsible for failure of the heart to pump blood at a rate commensurate with the requirements of the metabolizing tissues, or to do so only from an elevated filling pressure" (Braunwald 1992). As a consequence, in diastolic failure increased resistance to ventricular filling leads to elevated ventricular filling pressures or inadequate cardiac output. Accordingly, an increase in pulmonary wedge pressure may lead to symptoms of congestion. It is clear that within this definition many cardiac diseases may result eventually in diastolic failure, including reduced systolic performance, pericardial and valvular

disease. The main causes of diastolic failure can be divided into relaxation abnormalities, decreased compliance and inappropriately high heart rates (Brutseart 1993). All three causes can contribute separately to diastolic failure, but in many conditions they act together.

AIM OF THE STUDY

The aim of the study was to observe the prevalence of diastolic dysfunction in post myocardial infarction patients.

And frequent identification of the diastolic elements in myocardial dysfunction may prove helpful in directing therapy and gauging its benefits.

REVIEW OF LITERATURE

DIASTOLIC FUNCTION

Diastolic Phases

The four phase into which diastole is divided (isovolumic relaxation, rapid filling, diastasis and trial systole) will be discussed briefly. Relaxation of the heart is a dynamic process of isovolumic relaxation and early rapid filling. Rapid filling still continues after relaxation has been completed. A relatively small volume portion is shifted into the left ventricle during diastasis. In the atrial contraction phase intraventricular blood volume increases again.

Isovolumic relaxation. Relaxation is a catecholamine dependent energy consuming process in which large portions of adenosine triphosphate (ATP) are used. The dissociation of actin – myosin cross bridges results from an allosteric action of TP, i.e. a reaction of ATP with a site at the myosin head other than the binding site of actin causing the actinomyosin "rigor complex" to dissociate (Figueredo 1993, Apstein 1994). This process is called the "plasticizing effect" of ATP. Further relaxation is assured by rapid resequestration of cytosolic calcium in the sarcoplasmic reticulum by sarcoplasmic reticulum calcium ATPase, which is activated by phosphorylation of phospholamban, a regulatory subunit of the calcium pump of the sarcoplasmic reticulum. The affinity of the

calcium receptor site on the troponin – tropomyosin complex for calcium is decreased by phosphorylation, thereby increasing the rate of dissociation of calcium from troponin C and enhancing relaxation (Morgan 1991). This process of relaxation starts in late systole and ends in mid – diastole, causing the intraventricular pressure to decline (Brutsaert 1984).

Left ventricular pressure first falls below the pressure in the aortic root, which causes the aortic valve to close. Pressure continues to decline until below left atrial pressure, so that the mitral valve will open, and rapid filling begins. The decline of pressure in time approximates and exponential curve, but in the non – filling heart the left ventricular pressure frequently reaches a negative asymptote due to elastic recoil (Yellin 1986, Yellin 1994). The rate of myocardial relaxation is influenced by several independent factors in the intact heart (Brutsaert 1980, Brutsaert 1984): (1) Pre – and afterload, (2) inactivation (which itself is influenced by neurohumoral factors, the coronary circulation, and the use of drugs), and (3) regional nonuniformity (of load and inactivation). Furthermore, impaired relaxation, whether incomplete or slow, must be discerned conceptually from prolonged systolic contraction, which is a physiologic and compensatory situation merely leading to delayed or retarded relaxation

(Brutsaert 1993). In prolonged contraction, which can be seen in acute and chronic systolic pressure or volume loading, the early phase of hypertrophy and increased contractility, an upward shift of the diastolic part of the pressure – volume loading, the early phase of hypertrophy and increased contractility, an upward shift of the diastolic part of the pressure – volume relation which is seen in impaired relaxation, is not observed.

Summary of condition in which left ventricular diastolic dysfunction may be involved, their pathophysiology and mechanisms (Vasan 1996, Grossman 1991).

Hypertension

- Myocardial ischemia
- Myocardial infarction

Valvular heart disease

- Aortic stenosis
- Mitral stenosis
- Aortic regurgitation
- Mitral regurgitation Hypertrophic cardiomyopathy

Restrictive cardiomyopathy

Constrictive pericarditis

Dilating cardiomyopathy

Mechanism Pathophysiology

- Atrial ventricular pressure. resistance to atrial emptying /
- Afterload – (- contraction load)
- Nonuniformity (regional variation in
- Coronary reserve
- Myocardial compliance (fibrosis)
- Altered chamber geometry
- Coronary turgor
- Retarded inactivation (diastolic calcium nonuniformity (regional variation in myocardial compliance (altered
- Retarded inactivation
- Contraction load
- Nonuniformity (regional variation in regional fibrosis
- Regional myocardial compliance
- Pressure overload concentric hypertrophy
- Relaxation
- Chamber compliance
- Nonuniformity (regional variation)
- Coronary reserve
- Relaxation load
- Contraction load (obstruction)
- Myocardial compliance
- Altered chamber geometry

- Myocardial compliance (deposits,
- Deposits (e.g. Sarcoid)
- Altered collagen matrix
- Diastolic calcium overload
- Retarded inactivation
- Altered collagen matrix
- End – diastolic volume

DIASTOLIC FUNCTION

Rapid filling: When left ventricular pressure falls below left atrial pressure the mitral valve will open. The left ventricle will then be filled by the blood which is accumulated in the left atrium in the previous systole. The rate of early left ventricular filling determined uniquely by the atrioventricular pressure gradient and the impedance of the mitral valve (Ishida 1986, Yellin 1990, Yellin 1992, Yellin 1994). The atrioventricular pressure difference, in turn, is determined by the active and passive properties (relaxation and compliance) of both the left atrium and left ventricle. Thus, factors which determine these properties, like e.g. loading conditions, conditions, contractility, and heart rate influence the early diastolic filling pattern by means of their influence on the pressure difference.

In experimental canine models in which left ventricle were withheld from filling by end-systolic volume clamping, the left

ventricular pressure frequently fell below zero (Yellin 1986, Sabbah 1981). This diastolic suction of the left ventricle is caused by the storage of potential energy generated by preceding systolic contraction to below the “equilibrium volume”, i.e. the volume that the left ventricle exhibits when there is no transmural pressure negativity after volume clamping was increased when contractility was increased (Hori 1982). Evidence was provided by Udelson et al. that elastic recoil and restoring forces are also operative in the intact human heart during b-adrenergic stimulation (Udelson 1990). When, in this experiment, end – systolic volume was further reduced below the equilibrium volume, minimal diastolic pressure was also reduced. This probably resulted from and augmentation of internal restoring forces and elastic recoil, which in turn may result in negative transmural pressure and diastolic suction. So, the fall in left ventricular pressure at the time of opening of the mitral valve is not only resulting from left ventricular relaxation, it is also caused by elastic recoil.

The atrioventricular pressure gradient, the driving force of left ventricular filling, is also determined by left atrial pressure. In experiments by Ishida et al. increased left atrial pressures by volume loading of mongrel dogs resulted in increased peak rapid filling rtes induced by increased atrioventricular pressure gradients, despite decreased rate of left ventricular relaxation induced by increased loading conditions (Ishida 1986). Left atrial

compliance will also affect the peak atrioventricular pressure difference (Keren 1985, Suga 1974). In early diastolic filling, blood leaves the left atrium faster than it is filled by the pulmonary veins, and its pressure will fall (y-descent). At first, left ventricular pressure will continue to decline despite early left ventricular filling, thus accelerating blood into the left ventricle. With increasing left ventricular volume, left ventricular pressure will rise according to the passive filling characteristics, that are determined by viscoelastic properties of the myocardium, myocardial thickness, and external constraints, e.g. pericardium, right ventricle and lungs (Yellin 1990, Little 19990, Jancki 1990, Little 1995). Once relaxation and elastic recoil are completed, left ventricular filling will continue because of inertia, i.e. the mass of flowing blood (Yellin 1990). Early left ventricular filling rate, i.e. the first derivative of volume – versus – time curve, will diminish when atrioventricular pressure is reversed (Courtois 1988). This "deceleration" of rapid left ventricular filling deceleration time decreases as left ventricular chamber stiffness increases (Little 1995). Conversely early diastolic filling deceleration time may increase in the presence of mitral stenosis as a consequence of increased impedance of the mitral valve with prolonged atrioventricular pressure difference associated with elevated left atrial pressure (Meisner 1991).

Diastasis

This stage of ventricular filling is generally addressed as being the phase of passive filling in which the filling rate is slow, the rise in ventricular pressure is moderate, and the pressures of the left atrium and ventricle have reached equilibrium (Arrighi 1995). Some authors however observed a mid diastolic inflow peak into the left ventricle, arising from a reestablishment of a positive atrioventricular gradient due to left atrial filling via the pulmonary veins (Keren 1986, Yellin 1992, Biasucci 1990). Mid diastolic inflow may contribute more than 20% of total filling of the left ventricle in dogs but is absent in the dilated heart and in mitral stenosis (9biasucci 1990, Yellin 1992) Atrial systole. The last phase of ventricular filling is dominated by the contraction of the atria, which causes atrial pressure to rise again above ventricular pressure and induce a new blood flow into the left ventricle. This phase is influenced by left atrial function loading, and heart rate (Wang 1995, Courtois 1994, Udelson 1994). Atrial dysrhythmia, hypertrophy, and dilatation may alter this phase considerably (Rowlands 1967, Bonow 18\983a Kono 1992).

Diastolic Dysfunction in Cardiac Disease

Normal systolic function: An increasing number of studies have reported on the presence of congestive heart failure in patients with normal systolic function (Cohn 1990, Bonow 1992, Vasan 1995). The prevalence of normal systolic function among patients with congestive heart failure varies widely between 13% to

74%. The majority of studies suggest a prevalence of about 40% (Vasan 1995). The criteria used for identification of congestive heart failure, age, and the ratio between acute and chronic reported prevalence (Vasan 1995). Patients with congestive heart failure and normal systolic function at rest are often presumed to have heart failure on the basis of left ventricular diastolic dysfunction (Vasan 1995). However, the presence of diastolic dysfunction needs to be substantiated where possible, although uniform criteria for order to come to standardization of diagnostic criteria for diastolic heart failure, the European study group on diastolic heart failure proposed guidelines for the diagnosis of diastolic heart failure (European study group on heart failure 1998). According to these guidelines, diagnosis of diastolic stiffness (European study group on heart failure 1998). Radionuclide angiographic abnormalities are only described for PFR : < 2.0 EDV / s (Age < 30 year), PFR < 1.8 EDV /s (age 30 – 50 year), PFR < 1.6 EDV/s (Age > 50 year) based on a study performed by Bonow 1988). In isolated diastolic dysfunction the left ventricle is unable to fill adequately at normal diastolic pressure (Grossman 1991). Exercise intolerance is one of the important early symptoms of patients with diastolic heart failure (Kitzman 1991). In the genesis of acute pulmonary edema diastolic dysfunction can play an important role (Grossman 1990). Identification of patients with diastolic left ventricular dysfunction is important because pathophysiology and therapy differ from that of patients with primarily systolic dysfunction.

Congestive heart failure with normal systolic function may be seen in a variety of disorders (Grossman 1991). These disorders include structural abnormalities 1997, Janicki 1994). Valvular heart disease (primarily mitral and tricuspid stenosis) may cause elevated atrial pressure without systolic dysfunction. In Chronic left ventricular volume overload, e.g. in aortic and mitral regurgitation, diastolic dysfunction expressed by increased slope of the end – diastolic pressure volume relation may be present without Diastolic Function: force on the present thesis 15 systolic dysfunction (Grossman 1976). An acute increase of volume load however causes elevated diastolic filling pressures without primary myocardial dysfunction (Arrighi 1995). In the presence of right ventricular dilatation, left ventricular diastolic dysfunction may be present due to ventricular interdependence (Janikcki 1990). In left ventricular hypertrophy diastolic dysfunction may be present as a result of increased myocardial fibrosis and altered myocardial relaxation. Finally, dynamic disorder resulting in relaxation abnormalities, e.g. pressure overload in hypertension with or without left ventricular hypertrophy, and myocardial ischemia may result in diastolic dysfunction.

The Prognosis of patients with congestive heart failure and normal systolic function is variable and depends on the underlying pathophysiological mechanism responsible for the diastolic filling abnormalities. Reported annual mortality rates are lower than that

of systolic heart failure, and range between 1.3% and 17.5% depending on aetiology of diastolic dysfunction and age (Vasan 1995).

The define diagnosis of diastolic congestive heart failure is based on the evaluation of systolic performance showing elevated left ventricular filling when non- invasive techniques show abnormalities of the left ventricular filling pattern with normal systolic function (Arrighi 1995).

Depressed systolic function: Signs and symptoms of cardiac failure in patients with depressed systolic function may partly be due to concomitantly altered diastolic properties of the myocardium (Grossman 1976). In patients with heart failure and depressed systolic left ventricular function the severity of systolic dysfunction correlates with prognosis, but not with exercise capacity or symptom status. (Franciosa 1981, Rihal 1994). Diastolic function parameters are found to correlate significantly to symptom status in such patients (Franciosa 1985, Szlachcic 1985, Rihal 1994). An early sign of systolic heart failure is diminished exercise tolerance (Packer 1990). Recent studies on chronic tachycardia – induced cardiomyopathy leading to marked systolic dysfunction demonstrate that this is associated with an impairment of intrinsic dysfunction the common finding of diastolic dysfunction, a restrictive filling pattern in particular, appears in addition to left

ventricular ejection fraction to be correlated with increased cardiac mortality (Pinamonti 1993, Rihal 1994, Nijland 1997).

Coronary artery disease: Myocardial ischemia may cause transient abnormalities of left ventricular diastolic filling (Arrighi 1995). The majority of patients with coronary artery disease have abnormal diastolic parameters at rest resulting in decreased early diastolic filling and increased atrial transport function (Mahmarian 1990). After coronary artery bypass grafting and percutaneous transluminal coronary angioplasty abnormalities of diastolic filling appear to normalize (Bonow 1982, Lawson 1988).

Impaired relaxation is caused by increased myocardial cytosolic calcium ion concentrations arising from decreased calcium sequestration or increased calcium entry (Bonow 1990). In patients with coronary artery disease left ventricular asynchrony due to regional ischemia affects global left ventricular filling (Perrone – Fillardi 1992). Regional left ventricular nonuniformity can be present in ischemia, after myocardial infarction, but also in other cardiac conditions e.g. hypertrophic cardiomyopathy and the normal ageing process (Bonow 1990). After myocardial infarction a restrictive filling pattern is indicative of diastolic dysfunction due to initial myocardial stiffness or myocardial failure (Algom 1995). Impaired diastolic filling is a constant pathological finding in patients with previous myocardial infarction, and is more severe in patients with concomitant heart failure (Baries 1990). In a recent

study with Doppler echocardiography, a restrictive left ventricular filling pattern was a good predictor of cardiac death (Nijiland 1997).

Tachycardia

Left ventricular diastolic dysfunction may emerge in the presence of inappropriately high heart rats and chronic tachycardia (Brutsaert 1993, Zile 1996). In the presence of chronic tachycardia left ventricular diastolic dysfunction coincides with systolic abnormalities (Shinbane 1997). In the experimental setting of chronic pacing induced cardiomyopathy, the nature of diastolic dysfunction has not been made exactly clear. Generally, in chronic tachycardiomyopathy impaired left ventricular relaxation, increased left ventricular diastolic wall stress, and decreased compliance have been found (Komamura 1992, Zile 1995, Ohno 1994). Administration of inotropic agents could however normalize decreased early left ventricular relaxations, and decreasing loading conditions could normalize increased left ventricular end – diastolic wall stress by relaxation t (Sasayama 1991, Komamura 1992). After cessation of pacing in chronic pacing induced tachycardiomyopathy the normalization of left ventricular systolic function which may occur, is accompanied by development of left ventricular hypertrophy with persistent diastolic dysfunction, consisting of decreased relaxation and decreased compliance (Tomita 1991).

In humans with chronic atrial fibrillation with rapid ventricular response, intrinsic tachycardiomyopathy characterized by decreased systolic left ventricular function normalizes after restoration of sinus rhythm or adequate rate control (Morris JR 1993). In chronic atrial fibrillation also the atria itself are dilated (Davies 1972). Most authors however agree on (partial) functional recovery of atrial function after chemical and electrical cardioversion, and the maze procedure (Mannig 1989, Jovic 1997, Yashima 1997). The increase in Doppler echocardiographic A wave velocity, and decreased E/A ratio after cardioversion of atrial fibrillation may also indicate (Transient impairment of left ventricular relaxation (Xiong 1995).

Other cardiovascular disease

Impairment of diastolic function s the most characteristic pathophysiological abnormality in patients with Hypertrophic cardiomyopathy, leading to decreased early diastolic filling and increased atrial filling due to diminished relaxation and increased chamber stiffness (Hess 1993, Posma 1994). Also hypertension and secondary left ventricular hypertrophy are manifested by such diastolic abnormalities (Hoit 1994). Patients with cardiac syndrome X also have impaired resting left ventricular diastolic filling which improves after the beta blocker atenolol (Fragasso 1997). The normal ageing process is generally associated with structural and functional changes in the heart, leading to decreased early diastolic

filling and increased atrial filling (Nixon 1994). A recent study addressed the changes of left ventricular relaxation with age to presence of coronary artery disease, systemic hypertension, left ventricular systolic dysfunction or hypertrophy (Yamakado 1997). In addition, restrictive cardiomyopathy including cardiac amyloidosis and sarcoidosis is associated with impaired ventricular filling (Kushwaha 1997).

Alteration in Diastolic Properties

Approximately one-third of patients with congestive heart failure have dominant diastolic heart failure, which may be defined as pulmonary (or systemic) venous congestion, and the symptoms consequent thereto, in the presence of normal or almost normal systolic function. Another third have impairment of both systolic and diastolic function, and the remainder primarily disordered systolic function.

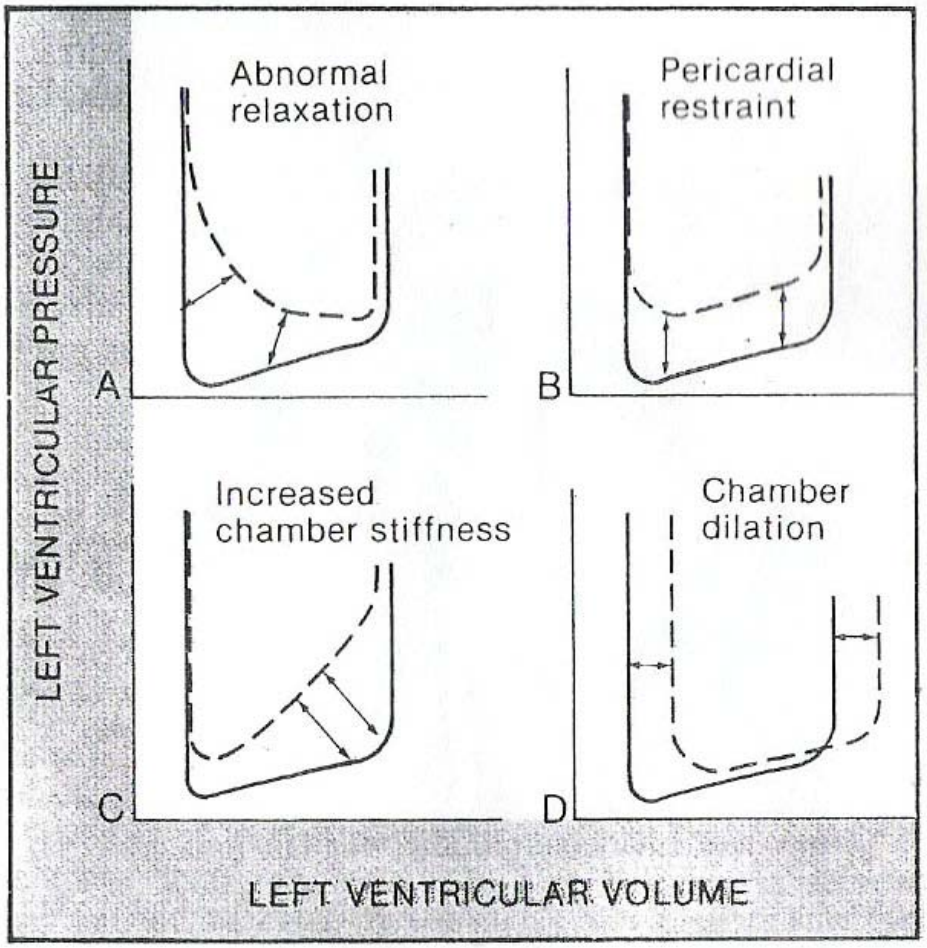


Fig. 1

Mechanisms that cause diastolic dysfunction. Only the bottom half of the pressure-volume loop is depicted. Solid lines represent normal subjects; dashed lines represent patients with diastolic dysfunction.

Altered Ventricular Relaxation

While two aspects of the heart's diastolic characteristics, i.e., relaxation and wall stiffness, are often considered together, they actually describe two different properties. Relaxation (inactivation of contraction) is a dynamic process that begins at the termination of contraction and occurs during isovolumetric relaxation and early ventricular fills . The rate of ventricular relaxation is controlled primarily by the uptake of Ca^{++} by the sarcoplasmic reticulum, but also by the efflux of Ca^{++} from the myocyte. These processes are regulated by the sarcoplasmic reticulum calcium ATP ase, as well as by sarcolemmal calcium pumps. Because these Ca^{++} movements are against concentration gradients, they are energy- consuming. Therefore, ischemia-induced ATP depletion interferes with these processes and slows myocardial relaxation. On the other hand, beta – adrenergic receptor stimulation, by increasing cyclic AMP and cyclic AP – dependent protein kinase activity causes the phosphorylation of phospholamban which accelerates $Ca^{++\ uptake}$ by the sarcoplasmic reticulum and thereby enhances relaxation.

An acute increase in ventricular afterload has also been shown to slow myocardial relaxation. Thus, when pressure overload is applied (before compensatory hypertrophy has normalized after load), ventricular relaxation is slowed. Myocardium isolated from patients with Hypertrophic cardiomyopathy and from ferrets with pressure – overload hypertrophy exhibits a prolonged calcium

transient (i.e., a prolonged elevation of myoplasmic Ca^{++}), associated with a prolonged tension decay, findings consistent with delayed uptake of Ca^{++} by the sarcoplasmic reticulum.

Altered Ventricular Filling

During early ventricular filling the myocardium normally lengthens rapidly and homogeneously. Regional variation in the onset, rate, and extent of myocardial lengthening is referred to as ventricular heterogeneity, or diastolic asynergy; temporal dispersion of relaxation, with some fibers commencing to lengthen later than others, is referred to as asynchrony. Both diastolic asynergy and asynchrony interfere with early diastolic filling. In contrast to these early diastolic events, myocardial elasticity, i.e., the change in muscle length for a change in force, ventricular compliance, i.e., the change in ventricular stiffness, the inverse of compliance, are generally measured in the relaxed ventricle at end-diastole.

These diastolic properties of the ventricle are described by its curvilinear pressure – volume relation. The slope of a tangent to this curvilinear relation (dp/dT) defines the chamber compliance at any level of filling pressure. An increase in chamber stiffness may occur secondary to any one or a combination of these three mechanisms: (1) a rise in filling pressure, i.e., movement of the ventricle up along its pressure – volume overload secondary to

acute valvular regurgitation and in acute left ventricular failure due to myocarditis.

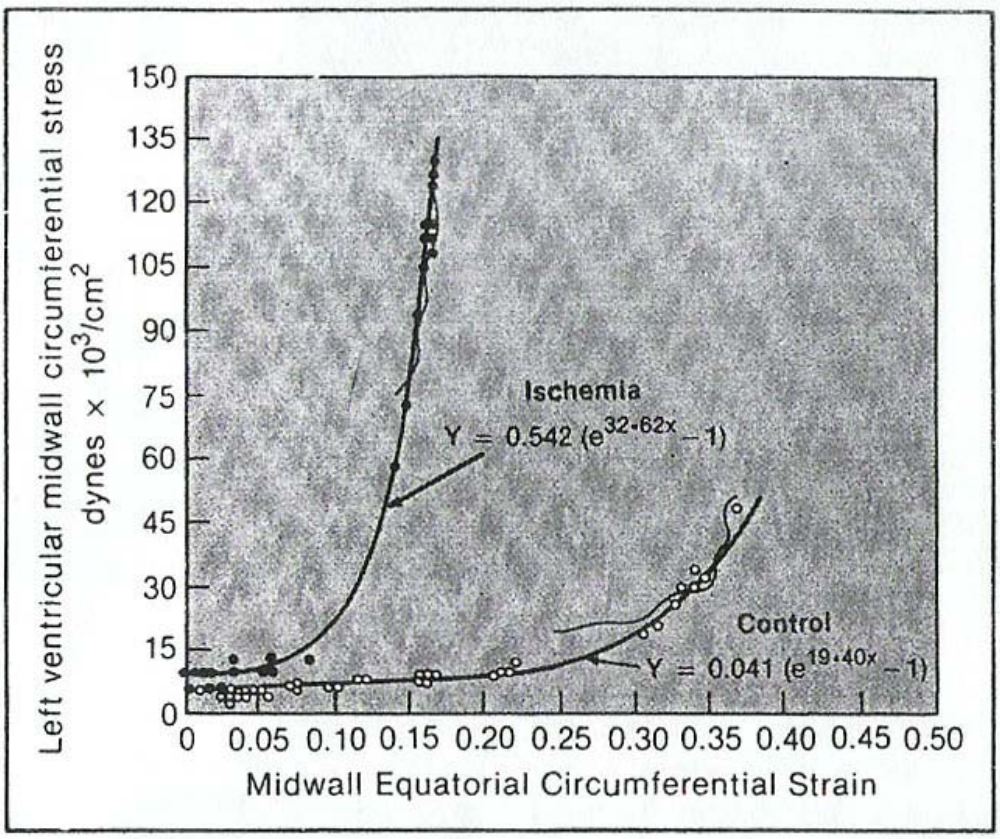


Fig. 2

Diastolic pressure-strain and stress-strain relationships constructed from observations during control period and during ischemia.

(2) A shift to a steeper ventricular pressure-volume or stress-strain curve. This results most commonly from an increase in ventricular mass and wall thickness. Thus, while hypertrophy constitutes a principal compensatory mechanism to sustain systolic emptying of the overloaded ventricle, it may simultaneously interfere with the ventricle's diastolic properties and impair ventricular filling. This shift to a steeper pressure – volume curve can also be caused by an increased in intrinsic myocardial stiffness (the stiffness of a unit of the cardiac wall regardless total mass or thickness of the myocardium), as occurs with disorders in which there is myocardial infiltration (e.g., amyloidosis), endomyocardial fibrosis, or myocardial ischemia A parallel upward displacement of the diastolic pressure – volume curve, generally referred to as a decrease in ventricular dispensability, usually caused by extrinsic compression of the ventricles .

Chronic Changes in Ventricular Diastolic Pressure – Volume Relationships

The compliance of the left ventricle, reflected in the end diastolic pressure – volume relationship, is altered in a variety of cardiac disorders. Substantial shifts in the diastolic pressure – volume curve of the left ventricle can be demonstrated during sustained volume overload. For example, dogs with large chronic arteriovenous fistulas exhibit a rightward displacement of the entire diastolic pressure-volume curve, whereby ventricular volume

is greater at any end-diastolic pressure but the slope of this curve is steeper, indicating increased chamber stiffness. Patients with severe volume overloading due to chronic aortic and / or mitral regurgitation demonstrate similar shift of the diastolic left ventricular pressure – volume relationship. Similar changes frequently occur in patients with dilated or ischemic cardiomyopathy or following large transmural myocardial infarction.

In contrast, concentric left ventricular hypertrophy, as occurs in aortic stenosis, hypertension, and Hypertrophic cardiomyopathy, shifts the pressure-volume relation of the ventricle to the left along its volume axis so that at any diastolic volume ventricular diastolic pressure is abnormally elevated. In contrast to the changes in the diastolic properties of the ventricular chamber, the stiffness of each unit of myocardium may or may not be altered in the presence of myocardial hypertrophy secondary to pressure overload.

In the presence of concentric left ventricular hypertrophy, there is an inverse relationship between the thickness of the posterior wall of the ventricle and its peak thinking rate during early diastole; a higher-than normal diastolic ventricular pressure is required to fill the hypertrophied ventricle. Patients with hypertension have demonstrated slowing of ventricular filling by radionuclide angiography and echocardiography, even when systolic function is normal.

Ischemic Heart Disease

Marked changes in the diastolic properties of the left ventricle can occur in the presence of ischemic heart disease. First, as already pointed out, acute myocardial ischemia slows ventricular relaxation and increases myocardial wall stiffness. Myocardial infarction causes more complex changes in ventricular pressure-volume relationships, depending on the size of the infarct and the time following infarction at which the measurements are made. Infracted muscle tested very early exhibits reduced stiffness. Subsequently, the development of myocardial contracture, interstitial edema, fibrocellular infiltration, and scar contribute to stiffening of the necrotic tissue and thereby to increase chamber stiffness, with a steer ventricular pressure – volume curve (a greater increase in pressure for any increase in pressure for any increase in volume). Later still, in the case of large infarcts, left ventricular remodeling and dilatation cause a rightward displacement of the pressure – volume curve, resembling that observed in volume overload. The subendocardial ischemia that is characteristic of severe concentric hypertrophy (even in the presence of a normal coronary circulation intensifies the failure of relaxation, and when coronary artery obstruction accompanies severe hypertrophy, this abnormality may be particularly severe. Tachycardia, by reducing the duration of diastole and thereby intensifying ischemia, exaggerates this diastolic abnormality and may raise ventricular diastolic pressure even while reducing diastolic ventricular volume, whereas bradycardia has the opposite effect. Successful treatment of ischemia improves diastolic relaxation and lowers ventricular diastolic and pulmonary venous pressures, thereby reducing dyspnoea.

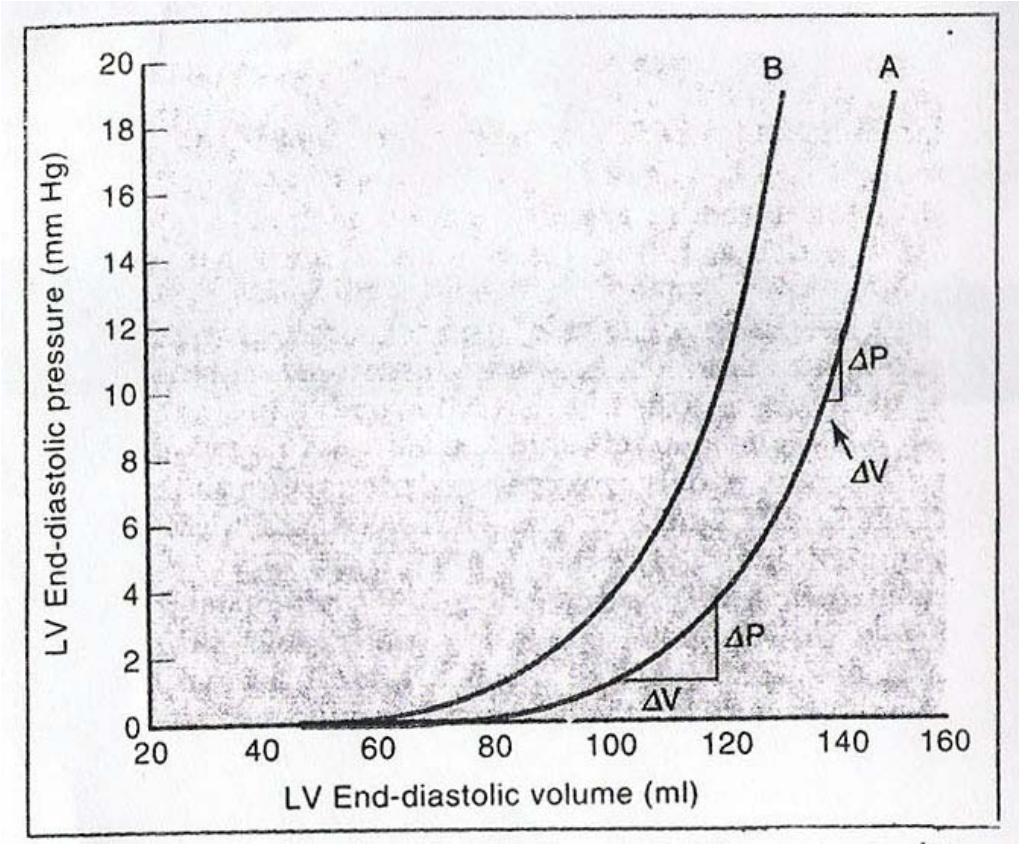


Fig. 3

The slope of the LV end-diastolic pressure-volume relation indicates the passive chamber stiffness. Since the relation is exponential in shape, the slope (ΔP/ΔV) increases s the end-diastolic pressure increases.

Evaluation of Diastolic Performance

The indices of diastolic function can be organized into three groups; measures of isovolumetric relaxation, indices of passive left ventricular characteristics derives from the diastolic left ventricular pressure – volume relations, and measurements of the pattern of left ventricular diastolic filling, which are obtained from Doppler echocardiography or radionuclide angiography.

Isovolumetric Relaxation

Isovolumetric relaxation can be quantified by measuring its duration or by describing the time course of the fill in left ventricular pressure. The duration of isovolumetric relaxation, or the time form aortic valve closure to mitral valve opening, can be measured by M-mode echocardiography. A similar interval, the time from aortic valve closure to the onset of mitral valve flow, can be measured by combining phonocardiography and Doppler echocardiography. Unfortunately, the duration of isovolumetric relaxation depends not only on the rat of left ventricular relaxation but also on the difference in pressures between the aorta at the time of aortic valve closure and the left atrium at mitral valve opening. Thus, the duration of isovolumetric relaxation can be increased by an elevation of aortic pressure. The time from minimum left ventricular volume to peak left ventricular filling rate can

be measured using radio nuclear angiography. Because this time

Table - 1

Normal values of LV diastolic function parameters by Doppler

	N	Age(yr)	E	A	F/A	M sec IRP
Appletoo et al 1988a	30	Adults	PS ± 16	60 + 16	1.5 ± 0.4	71 ± 14
Spirito et al 1988	35	20 – 29	69 ± 12	27 ± 7	2.7 ± 0.7	72 ± 12
	33	30 – 34	62 ± 14	33 ± 7	2.0 ± 0.6	80 ± 12
	18	50 - 74	59 ± 14	36 ± 13	1.2 ± 0.4	84 ± 12
Fuji et al 1985	18	Adults	61 + 7	40 ± 11	1.5 ± 0.18	

E : early diastolic peak velocity, A : late diastolic peak velocity IRP – isovolumic relaxation period

interval spans both isovolumetric relaxation and part of early filling, the interpretation is even more complicated than the duration of isovolumetric relaxation alone.

The time course of isovolumetric pressure decline has been quantitatively described by the peak rate of pressure fall (dp/dt_{min}) and the time constant of an exponential fit of the time course of isovolumetric pressure decline. Each of these requires the measurement of left ventricular pressure using a micro manometer. dp/pt_{min} is strongly influenced by the pressure at the time of aortic valve closure and is not a good measure of the rate of isovolumetric relaxation.

After aortic valve closure, left ventricular pressure declines in an exponential manner during isovolumetric relaxation. The rate of pressure decline can be quantified by the time constant of the exponential decline. The time constant (τ) is increased by processes such as ischemia or other causes of myocardial depression that slow ventricular relaxation. It is shortened by acceleration of the rate active relaxation, as caused by an increase n heart rate or sympathetic stimulation. The time constant of isovolumetric pressure decline can also be altered by changes in loading conditions. An increase in arterial pressure or end-diastolic volume can increase the time constant, although changes in the preload at a constant arterial pressure may have less effect.

Calculation of the time constant of left ventricular isovolumetric pressure decline has several technical limitations. Data are analyzed from the time of minimum dp/dt to a pressure 5 or to mm Hg above end – diastolic pressure. Even if pressure is measured every 2 msec, there are only a limited number of data points. This contributes to a large beat-to-beat variability of τ .

If mitral in-flow is prevented, left ventricular pressure will decline to subatmospheric levels. Thus, it has been suggested that the data should be fit to an exponential function with an asymptote (P_S):

$$P(t) = P_o e^{-t/\tau} + P_S.$$

This is usually done by differentiating both sides and then using the linear least squares technique to fit the equation:

$$dp(t) / dt = (1/\tau)(P - P_S)$$

The normal range of values of τ calculated using this method is 37 to 67 msec.

The use of an asymptote to calculate τ is particularly important when the external pressure of the left ventricle may be changing. However, τ determined form a nonfiling beat in an experimental animals in which the full time course of left ventricular relaxation is available correlates most closely with --- calculated from a normal beat without the use of an asymptote (i.e.,

$P=P_o{}^{-t}/_r$).. To avoid the computational properties of nonlinear fitting in the calculation on --- without an asymptote, the relation is linearised using a natural logarithm transformation to result in:

$$\text{In } P = \text{In } P_o - {}^{t}/_{r}$$

The data are then fit to this equation using the linear least squares technique to determine ---. When calculated using this method, the normal range of values for – is 28 to 45 msec.

Recently, the time course of LV pressured using isovolumetric relaxation has been characterized using noninvasive Doppler measurement of the velocity of a Regurgitant jet across the mitral or aortic valve. In this method the modified Bernoulli equation is used to approximate LV pressure during isovolumetric relation allowing calculation of the maximum rate of left ventricular pressure decline and the exponential time constant.

Passive Diastolic Characteristics of the Left Ventricle

The passive characteristics of the left ventricle can be described as the diastolic pressure –volume relation. Optimally the passive left ventricular diastolic pressure volume relation should be ventricular diastolic pressure volume relation should be constructed from points that are obtained after relaxation is complete and at slow filing rates, so that viscous effects are not present. Practically, this can be approximated using points

obtained late in diastole, when relaxation is assumed to be complete, or from variously loaded beats at end diastole. However, it is important to correct for the effect of respiratory changes in intrathoracic pressure.

The slope of the end –diastolic pressure –volume relation is the Chamber stiffness. Since the pressure-volume relation is nonlinear, the chamber stiffness depends on the point on the curve in which it is measure; stiffness increases with increasing volume . Several techniques have been proposed to correct for this effect by normalizing chamber stuffiness. One approach is to approximate the pressure-volume relation by an exponential function. Another technique is to compare the chamber stiffness at a common pressure or volume. However, the analysis of chamber stiffness does not account for shifts in the pressure-volume relation that can occur from the alternation of load, diseases, or pharmacological agents. The position of the diastolic pressure-volume relation indicates the distensibility of the left ventricle, an upward shift indicating a less distensible ventricle.

The diastolic pressure- volume relation represents the net passive characteristics of the left ventricular chamber. To derive information concerting the properties of the myocardium alone, the effects of wall thickness, ventricular configuration, size, and external pressure must be removed. This can be accomplished by deriving the myocardial stress-strain relation from the chamber

transmural pressure-volume relation that assesses the amount of ventricular chamber distension under pressure, the stress-strain relation represents the resistance of the myocardium influenced by the configuration of the left ventricle. However, calculation of stress requires the use of a geometrical model of the left ventricle, and calculation of strain requires assumption of the unstressed left ventricular volume. In addition to these potential theoretical limitations, these calculations require accurate measurements over a wide range of left ventricular pressures and volumes. Measurements made during rapid filling may be inappropriately influenced by active myocardial relaxation and viscoelastic effects. Observations during diastasis and atrial systole do not have this problem, but they may not supply a wide enough range of data points. The theoretical problems and the technical difficulties in determining myocardial stress-strain relations have limited their clinical applications.

Pattern of Left Ventricular Diastolic Filling

Recently there has been interest in assessing quantified diastolic left ventricular performance by analysis the pattern of left ventricular filling. Such information can be obtained by determining the left ventricular volume or dimension throughout the cardiac cycle, using contrast or radionuclide angiography, M-mode or two-dimensional echocardiography, or by measuring the left ventricular in-flow velocity using a Doppler determination of

mitral valve flow velocities. The most widely used methods today are radionuclide angiography and Doppler mitral valve flow-velocity determination.

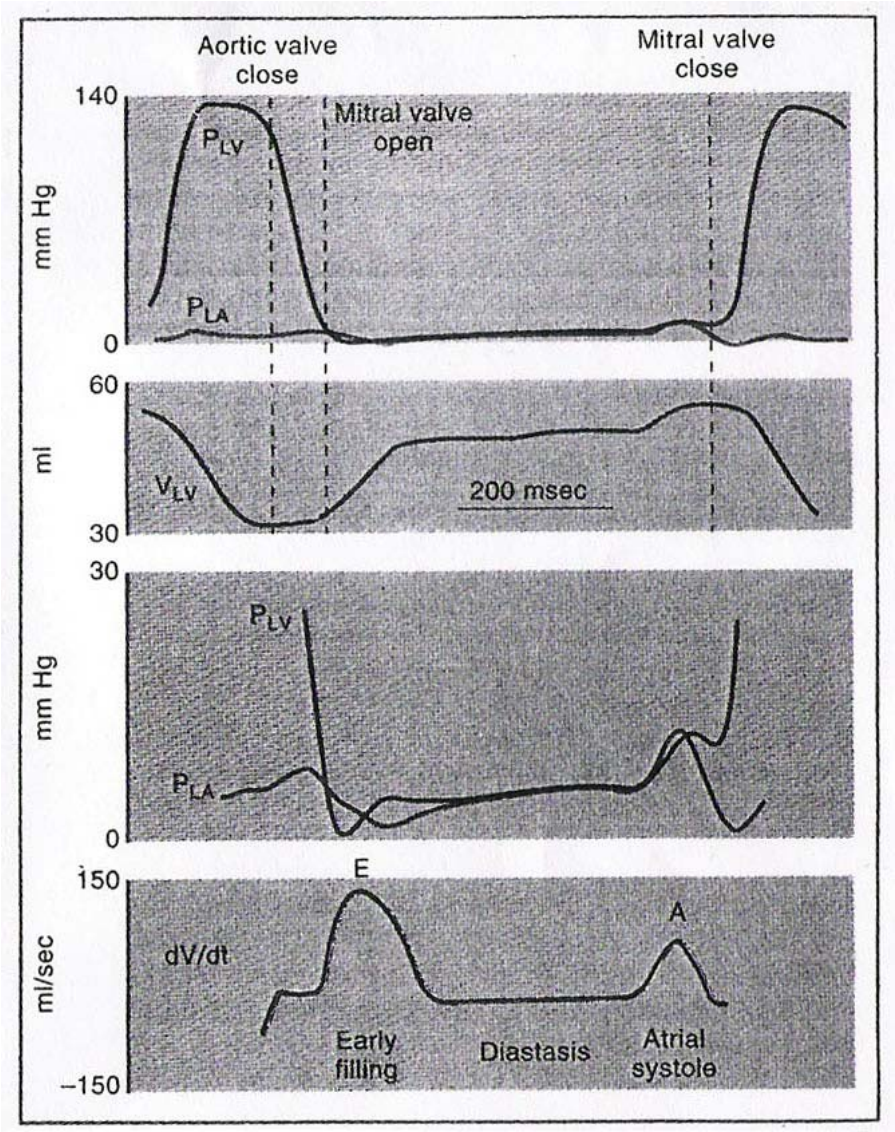


Fig. 4

Recording of left ventricular pressure (P_{LV}), left atrial pressure (P_{LA}), left ventricular volume (V_{LV}), and the rate of change of left ventricular volume (dV/dt), which indicates the rate of left ventricular filling.

Mechanisms of Diastolic filling

To understand the significance of the patterns of left ventricular filling, it is important to consider the mechanisms of normal left ventricular filling. From the time of aortic valve closure until metal valve opening, the left ventricle is normally a closed chamber with a constant volume. Myocardial relaxation begins in the latter part of systole and causes a steep, exponential fall in intraventricular pressure as elastic elements of the left ventricle that compressed and twisted during ejection are allowed to recoil. Although no filling occurs during isovolumetric relaxation, the processes that determine the rate of decline of the isovolumetric pressure influence ventricular filling following opening of the mitral valve. For the first 30 to 40 msec after mitral valve opening, decline of left ventricular wall tension is normally rapid enough to cause left ventricular volume. This fall in left ventricular pressure produces a pressure gradient that accelerates blood from the left atrium into the left ventricle, resulting in rapid early diastolic filling. The rate of early left ventricular filling is determined by the mitral valve pressure gradient. Left atrial pressure-left ventricular pressure. Although peak filling occurs after the peak pressure gradient, the two are closely related. Two major factors (myocardial relaxation and LA pressure) determine the early diastolic mitral valve pressure gradient and the rate of left ventricular filling.

Under normal circumstances more than two-thirds of the stroke volume enters the left ventricle during early diastole.

After filling of the left ventricle begins the metal valve pressure gradient decreases and then transiently reverses. This occurs because left ventricular relaxation is nearing completion and the flow of blood from the left atrium fills the left ventricle, raising the left ventricular pressure. This reversed mitral valve pressure gradient decelerates and then stops the rapid flow of blood into the left ventricle early in diastole. The pressures in the left atrium and left ventricle equilibrate as mitral flow nearly ceases; thus, little left ventricular filling occurs during the midportion of diastole, termed diastasis.

Atrial contraction increases atrial pressure late in diastole producing a left atrium-to-left ventricle pressure gradient that grain propels blood into the left ventricle pressure decreases below left ventricular pressure, causing the mitral valve to begin closing. The onset of ventricular systole produces a rapid increase in left ventricular pressure that seals the mitral valve and ends diastole.

Normal Pattern of left ventricular filling

The normal pattern of left ventricular filling is characterized by rapid filling early diastole with some additional filling during atrial contraction. This normal filling pattern can be quantified by measuring the peak early diastolic filling rate or mitral flow

velocity (E), the integral of the early diastole filling or flow velocity, and the peak filling rate or mitral flow velocity during atrial (a). The relative contribution of early and late (atrial) filling is commonly expressed as the E/A ratio. Normally the E/A ratio are greater than 1. The time required for deceleration of the early diastolic flow and the rates of this deceleration (E/t) are two other important parameters of the filling pattern. A variety of other measures have also been proposed. Table contains a list of the ranges of normal values for these measures of left ventricular filling. The wide range of normal values is probably caused by variations in the technique of performing the observation, in the technique of performing the observations, which are both operator and equipment sensitive. Further-more, the measures can be altered by many physiological factors.

Abnormal pattern of left ventricular filling

The normal pattern of left ventricular filling is altered in many patients with cardiac disease. By means of Doppler mitral flow velocity, three abnormal patterns (in the absence of mitral stenosis) have been identified indicating progressively greater impairment of diastolic function.

The first abnormal pattern of filling has been termed delayed relaxation. In this pattern there is reduced peak rate and amount of early left ventricular filling, and the relative importance of atrial

filling is enhanced. This results in a reversed E/A ratio of less than 1.

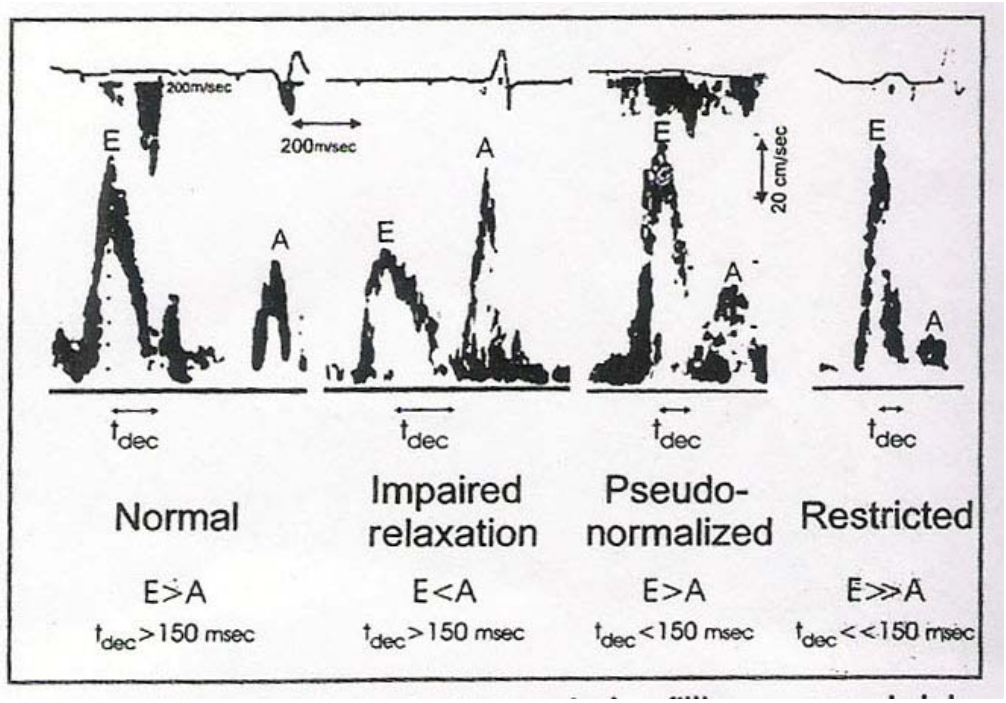


Fig. 5

Patterns of left ventricular filling as recorded by diastolic Doppler mitral flow velocities. In the normal pattern there is a large E wave and a small A wave. There are three abnormal patterns of mitral filling representing progressively worsening left ventricular diastolic performance. With "delayed relaxation" the E wave is less than the A wave. The left ventricular deceleration (t_{dec})is normal or prolonged. In the "pseudonormalized" pattern the E wave is larger than the A wave; however, t_{dec} is shortened.

In the restricted filling pattern E is much larger than A with a very short t_{dec}.

The reduced peak rate of early filling is due to a decreased early diastolic left atrial-to-left ventricular pressure gradient, resulting from a slowed rate of left ventricular relaxation. A delayed relaxation pattern can be seen in patients with left ventricular hypertrophy, arterial hypertension, and coronary artery disease and in normal elderly subjects. In many of these patients, mean left atrial pressure is within the normal range at rest and the patients are asymptomatic. In this situation the vigorous atrial contraction compensates for the reduced early filling due to impaired left ventricular relaxation while maintaining a normal mean left atrial pressure.

A second pattern of abnormal filling has been termed pseudonormalized. This pattern, in which the E/A ratio is greater than 1 (as occurs in normal persons), is seen in patients with more severe impairment of diastolic performance than the pattern is due to restoration of the normalized early diastolic left ventricular pressure gradient due to an increase in left atrial pressure that compensates for the slowed rate of left ventricular relaxation. The pseudonormalized pattern of filling is distinguished from normal by a more rapid rate of early diastolic left ventricular relaxation. The pseudonormalized pattern of filling is distinguished from normal by a more rapid rate of early diastolic flow deceleration and faster

decelerations time. The deceleration time is proportional to the inverse of the square root of the left ventricular chamber stiffness.

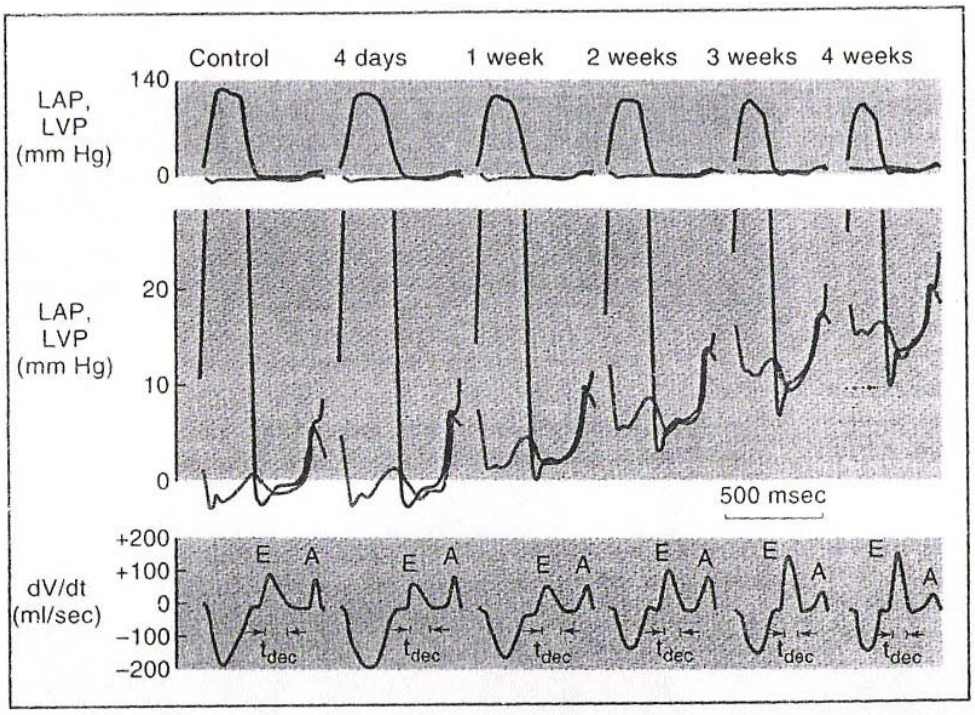


Fig. 6

Recording of left ventricular (LVP) and left atrial pressures (LAP) and the rate of change of left ventricular volume (dV/dt) during control and serially during the development of pacing-induced heart failure in an experimental animal.

Thus, the faster deceleration time indicates increased left ventricular diastolic chamber stiffness.

A third abnormal pattern of left ventricular filling indicating a severe diastolic abnormality has been termed the restrictive pattern. In this pattern the early filling is increased above the control level and greatly exceeds the filling that occurs during atrial contraction and the E/A ratio is usually greater than 2. In fact, there may be litter or no filling during atrial contraction. The deceleration time is much less than 150 msec. This pattern is seen in patients with severe diastolic dysfunction and pulmonary congestion. The enhanced early filling in the restrictive pattern results from markedly elevated LA pressure that more than offsets the slowing of left ventricular relaxation. In this situation, in which left ventricular stiffness is increased, the early flow deceleration time is very short, and the deceleration rate of early flow is rapid. The restrictive filling pattern is seen in patients with severe pulmonary congestion, constrictive pericarditis, and restrictive cardiomyopathies such as cardiac amyloidosis.

The three abnormal patterns of left ventricular filling represent a continuum of increasing severity of diastolic abnormalities. The pattern of delayed relaxation may be observed in asymptomatic patients with only impaired diastolic reserve, while the pseudonormalized and restrictive patterns occur in patients with progressively more severe diastolic dysfunction who almost always have pulmonary congestion.

Pulmonary Venous Flow patterns

The pattern of blood flow in the pulmonary veins provides additional information on diastolic filling. The velocity of pulmonary venous flow can be measured by transthoracic Doppler in some patients and by transesophageal Doppler in most patients. The pulmonary venous flow velocity has three waves the s Wave, indicating antegrade flow into the left atrium during ventricular systole, (@) the D wave, indicating antegrade flow early in diastole just following the peak of the E wave mitral valve flow, and (3) the AR wave of retrograde flow out of the left atrium during atrial systole. The S and D waves correspond to the x and y descents in the left atrial pressure, while the pulmonary venous AR wave corresponds to the left atrial a wave. When left ventricular end-diastolic stiffness is increased, the AR wave is augmented and prolonged, unless atrial systolic failure or atrial fibrillation is present. Thus, pseudonormalized and restricted mitral flow patterns are associated with large, prolonged AR waves with a peak flow velocity > 35 cm/sec.

Echo- Doppler evaluation of left ventricular diastolic dysfunction during acute myocardial infarction: methodological, clinical and prognostic implications.

Left ventricular (LV) diastolic dysfunction has been reported in the sub acute and late phase after myocardial infarction and it is

becoming increasingly clear that abnormalities of diastolic function during acute myocardial infarction (AMI) have a major role in affecting the prognosis. However, until recent years the study of patients with diastolic dysfunction has suffered from the substantial difficulties inherent in diagnosing, measuring, quantitation and in following it over time. Moreover, the complexity of events encompassed by diastole, which are often difficult to control in the clinical arena, and the lack of data available to guide therapy, have hampered the widespread application to guide therapy, have hampered the widespread application of diastole in the clinical setting of AMI. The advent of Doppler echocardiography and its complementary techniques have provided a bedside tool which yields reliable and useful measures of diastolic performance during AMI, placing such as assessment well within the grasp of every clinical echocardiography laboratory. Determination of the pattern of LV filling by Doppler echocardiography provides important information about LV diastolic function in AMI patients. Clinical data gathered so far demonstrate that Doppler – derived LV filling, specifically the restrictive filling pattern, is a powerful independent predictor of late LV dilation and, most importantly, of cardiac death in patients with AMI and clearly indicate the need for evaluating and monitoring LV diastolic function in these patients. Large scale studies, utilizing simple and easy to measure Doppler indexes of LV filling are needed to assess the efficacy of

medical therapy in patients with acute LV diastolic dysfunction during AMI.

Diastolic dysfunction (DD) is very common. In 2042 adults over 45, randomly selected from the general population in Minnesota (by the Mayo Clinic), 21% had mild and 7% had at least moderate diastolic dysfunction! In contrast, only six percent of all people examined had some systolic dysfunction. Of the thirteen people with severe DD, only six had a history of congestive hear failure. (JAMA2003 Jan; 289:194-202) DD is particularly common in the elderly [Cardiovasc Res 2000 Mar; 45 (4):813-25].

Diastolic dysfunction appears to cause a lot of morbidity from heart failure. Up to 40% of heart failure patients have DD [Eur J heart Fair 2002 Agu; 4(4):419-30]. In addition, DD appears early on post acute myocardial infarction, and may predict poor outcomes. IN one study (Am Hear J 137(5): 910-918, 1999), E deceleration time was predictive of subsequent hear failure or death, and in hospital heart failure correlated well with diastolic dysfunction; those who had normal filling were free of heart failure.

Some would argue that in those who have signs and symptoms of heart failure, but have preserved LV systolic function, diastolic function will be found. Zile et al (circulation 2001 Aug 14; 104(7) :779-82] examined 63 such patients with clinical heart failure and preserved systolic function, all of whom were found to

have at least one feature of DD (abnormal time constant of LV relaxation, E/A ratio, or E wave deceleration).

What is DD?

Note the two (poorly distinguished) components to DD:

Poor relaxation (impaired lusiotrophy)

Decreased compliance

The literature is very confusing (and perhaps confused) in this regard- few seem to distinguish adequately between these components!

Diagnosis

We commonly diagnose DD based on the presence of:

Clinical features of heart failure, particularly left heart failure;

A normal ejection filling pressure.

The first two are relatively easily identified, but what about the third?

Invasive intervention seems pretty aggressive, so other measures have been proposed as an indicator of diastolic pressures. People have, looked at :

Isovolumic relaxation time (IVRT, IRT) – this (the time from aortic valve closure to mitral valve opening) is measured by simultaneous Doppler and M-mode echo, or better still by simultaneous phonocardiogram and transmitral Doppler

(Roelandi). If it's prolonged, it indicates poor myocardial relaxation. A normal IRT is about 70 ± 12 ms, perhaps about 10ms longer in those over forty. With abnormal relaxation, the value is usually in excess of 110ms, with restrictive filling, under 60. Transmitral inflow (E/A; E wave deceleration) The E wave occurs related to LV suction and LA pressure – the E wave acceleration will be higher with high LA pressure, and lowered with impaired LV relaxation. Deceleration of inflow of the E wave is measured by deceleration time (DT), which shortens with decreasing LV compliance. DT is rather complex, as higher LA pressures shorten it. A normal DT is about 200±32 ms; values over 240ms indicate impaired relaxation, and under 150ms suggest restriction. There are a lot of problems with relying on E/A ratios, as the effects of impaired relaxation and restriction counter balance one another, resulting in 'Pseudonormalisation'. Pulmonary venous inflow (atrial flow reversal) Pulmonary vein Doppler is easily imaged using TOE, but may even be performed on TTE using a foreshortened apical cross-section (RUPV). The normal pattern is to see a systolic (S) wave, a diastolic (D) wave, with perhaps some retrograde flow during atrial contraction. The last wave is sometimes called the AR wave-it normally has an amplitude of under 25 cm/s, and a shorter duration than the transmitral A wave. Velocity and duration of AR increase with worsening diastolic dysfunction.

E:A Ratio

Normally, early filling exceeds the atrial component of filling, and so the mitral inflow velocity profile shows a bigger E than A wave. With impaired relaxation, the E component will be reduced, resulting in a lower. Conversely, with a restrictive pattern, the E component is said to be increased, resulting in an abnormally high E: A.

The whole assessment of diastolic dysfunction seems bedeviled assessment of diastolic dysfunction seems bedeviled by classifications that assume a progression from: mild dysfunction (E/A under 1, IVRT over 100ms, normal E wave deceleration, atrial reversal of pulmonary venous inflow < 0.35 m/s), to mild.. moderate diastolic dysfunction (similar E/A and IVRT, but atrial reversal over 0.35, and over 20ms greater than mitral A wave duration) moderate disease ("Pseudonormalisation" – apparently normal E/A , atrial reversal over 0.35) severe dysfunction ("restrictive"—large E and small A, short E deceleration of under 120ms, short IVRT, reduced pulmonary systolic wave?

Now, the above progression may be common, but is by no means in inevitable in some conditions, either impaired (e.g. hypertrophic cardiomyopathy) or restriction (restrictive cardiomyopathies, for example) may prevail. With impaired relaxation, early filling is impaired; conversely, with a restrictive pattern, the E/A ratio increases, as early filling are favored! If both are present. then we have the dreaded "Pseudonormalisation".

Note that, with Pseudonormalisation, a method of bringing out abnormality is to alter loading patterns, with Valsalva, glyceryl trinitrate, or even nitroprusside.

Tissue Doppler imaging (TDI, DTI)

TDI of the mitral apparatus is said to be less load – dependent than mitral in flow parameters. an E' and A' wave are seen, corresponding to the E and A waves on mitral in flow. Apart from providing an assessment of LV dp/dT, TDI has been proposed as a way of determining whether a 'normal' mitral inflow is actually 'pseudo normal'. With a pseudo normal pattern, restriction and impaired relaxation are balanced, and the E/A ratio looks normal because of the high LA pressure. E' will velocity will still be abnormal as it's relatively load independent.

TDI may even be of value in the presence of atrial fibrillation, where there's no A wave. Diastolic dysfunction may well be present with a DT under 150ms, E/E' ratio over 15 using TDI, and Pv under 40cm/s on Colour M-mode, provided one looks at cycles corresponding to a rate of 60 – 80 / min.

Colour M-mode transmitral flow. This is said to provide a rapid screening tool for diastolic inflow abnormality. An M-mode cursor is placed parallel to the mitral inflow, and adjusted to maximize the length of the column of Colour flow into the LV. During early filling, the 'slope along a distinct isovelocity line" is

measured. The normal value is under 40cm/s. Those who find terms such as "isovelocity line" unintelligible should take comfort from the likelihood that even these fancy techniques may not be incredibly reliable. (See the note on strain rate imaging below).

Invasive assessment

If one looks at the time constant of the exponential pressure decay during isovolumic relaxation, this should be an indicator of lusiotrophy. Passive elastic properties should be evaluable from the slope of the diastolic pressure volume curve, and "stress-strain relationship" Strain rate imaging. A new buzz – word. A wave of myocardial stretch propagates from the base of the heart to its apex, and this wave is slowed with impaired myocardial relaxation. Unfortunately, the propagation of flow doesn't correlate awfully well with propagation of strain rate. The flow propagation depends not only on relaxation, but also on flow velocity. (See [Cardiovasc Ultrasound. 2003; 1(1): 3. Stoylen A, Skjelvan G, Skjaerpe T]).

Management

It should be clear from the above that accurate diagnostic of DD is non-trivial. On a practical note, if the size of the left atrium is normal, then diastolic dysfunction is said to be extremely unlikely. If someone has preserved systolic function and clinical heart failure, it is reasonable to assume the presence of diastolic dysfunction. Such patients may respond to 'classical' therapy of

heart failure such as diuretics, but such intervention may impair cardiac output more than would be expected with LV systolic dysfunction. More reasonable is to administer agents that will treat the diastolic dysfunction! The following agents may be of value:

Calcium channel blockers (but beware of some with associated ischemic heart disease)

ACE inhibitors and AT-II receptor antagonists: Where there are other co-morbidities (such as severe respiratory disease) that could the clinical picture, diagnosis of heart failure may be normal, DD is likely. If available, B-type natriuretic peptide levels may be invaluable in making the diagnosis in such circumstances. High levels of BNP are equally common in systolic heart failure and diastolic failure.

The big question is "What about those who have both diastolic dysfunction and impaired systolic function"? It may well turn out that the most important predictor of efforts tolerance in patients with systolic dysfunction is in fact diastolic dysfunction! There is emerging evidence that myocardial remodeling (and consequent diastolic dysfunction) is far more important in the pathogenesis of heart failure, is systolic function. Just because systolic function is relatively easily assessed doesn't mean that it's important!

Doppler echocardiographic pattern of left ventricular filling in patients after acute myocardial infarction. Adrian chenzbraeen \MS, Andre Keren MD, American Journal of Cardiology 1992 : 70; 711 – 714 revealed no correlation was found between hypertension left ventricular end diastolic pressure were low to normal in patients with an F/E ration <1 and were usually > 15 mm Hg in those with normal or abnormally increased (>2) F/A ratio thus an apparently normal F/A ratio in patients after myocardial infarction patient may identify those with more severe left ventricular filling pressure.

Non invasive measurement of left ventricular filling pressure by mean of transmitral pulsed Doppler – ultrasound. Thomas v start MD American journal of cardiology 1989; 04 : 655 – 660 reveals L.V. Filling parameters obtained by meant of transmitral pulsed Doppler echocardiography provide a reliable non – invasive measurement of left ventricular end diastolic and pulmonary wedge pressure.

Non invasive assessment of left and right ventricular filling in myocardial infarction with two dimensional Doppler Echocardiography journal of American college of cardiology, 1985: 5 : 1155 – 1160

Fujji J. Yazaki, Y. Sawada et al noted that patient suffering by myocardial infarction had reduced F/A ratio and reduced acceleration and deceleration of the F wave.

Brutscert et al 1984 showed many parameters have now been used in clinical indices as indices of diastolic function" but if should be realized that many interacting factors which as independent of the intrinsic myocardial properties influence the transmitral velocity pattern.

Dougherby et al 1984, souter et al 1985 showed that abnormalities of left ventricular diastolic function may co exit with normal systolic performance. Their diagnosis is important since the proper treatment of patients with predominant diastolic dysfunction considerable different from that for patients with systolic dysfunction.

Practical Points

Principles of Doppler assessment of diastolic left ventricular function.

- Left ventricular diastolic dysfunction is a common pathophysiological mechanism of congestive heart failure that can co – exist with normal systolic function.
- Pulsed wave Doppler transmitral flow velocity recording from within the apical 4 – chamber or apical long – axis view are a

reliable method of evaluating diastolic function measurements must be mode with the same sample volume in the same position in any given patients, usually at the tip of the mitral value leaflets.

- A series of 6 – 9 consecutive beats should be analyzed and mean values calculated to minimize random error and the effects of respiratory variation.

- A prolonged isovolumic relaxation period, defined as the time interval between aortic value closure and the onset of mitral inflow, is a sensitive marker of abnormal left ventricular relaxation.

- The deceleration time, represented by the time interval between the E – peak and the point of the baseline intercepted by the decelerating wave form is a measure of how rapidly early diastolic filling stops.

- Peak atrial filling velocity, represented by the area under the A – wave, reflect the contribution of atrial contraction to left ventricular diastolic filling and is an important index of diastolic function.

- The ratio between peak E and A velocities (the E/ A. ratio) is commonly used to describe diastolic filling.

- Pseudonormalisation of the mitral in flow velocity pattern can occur at a result of increased diastolic filling pressure. In

this situation there will also be prominent reversal of pulmonary venous flow during atrial systole.

- Left ventricular diastolic function in complex and multi factorial affected by age, heart rate and filling conditions in addition to myocardial disease.

FACTORS INFLUENCING DIASTOLIC FUNCTION

Intrinsic Factors (Myocardial)

- Myocardial Relaxation
- Non – uniform Relaxation
- Atrial Contraction
- Visco – elastic properties
- Diastolic Suction (recoil)
- Myocardial elasticity / stiffen

Extrinsic factors (Loading)

- Pre load and after load
- Vascular volume
- Ventricular Interaction
- Pericardial Pressure

Table 2

Conditions associated with congestive heart failure to diastolic dysfunction

Myocardial Hypertrophy

- Hypertension
- Hypertrophic cardiomyopathy
- Aortic Stenosis

Coronary Artery disease

- Chronic stable angina
- Acute myocardial ischemia
- Myocardial infarction

Constrictive / restrictive cardiomyopathy

- Volume overload
- Renal Failure

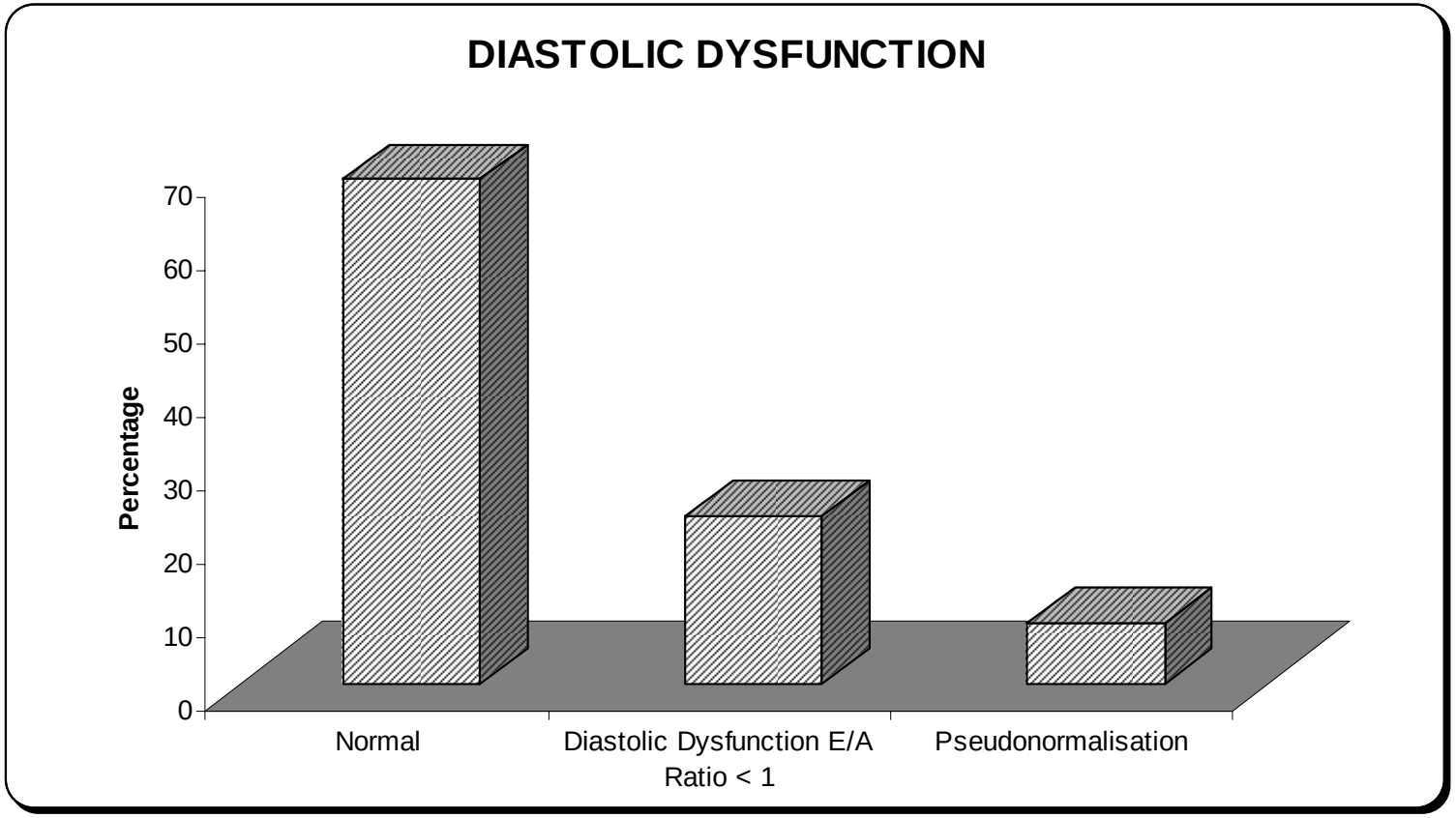
Myocardial ageing

Mechanical obstruction

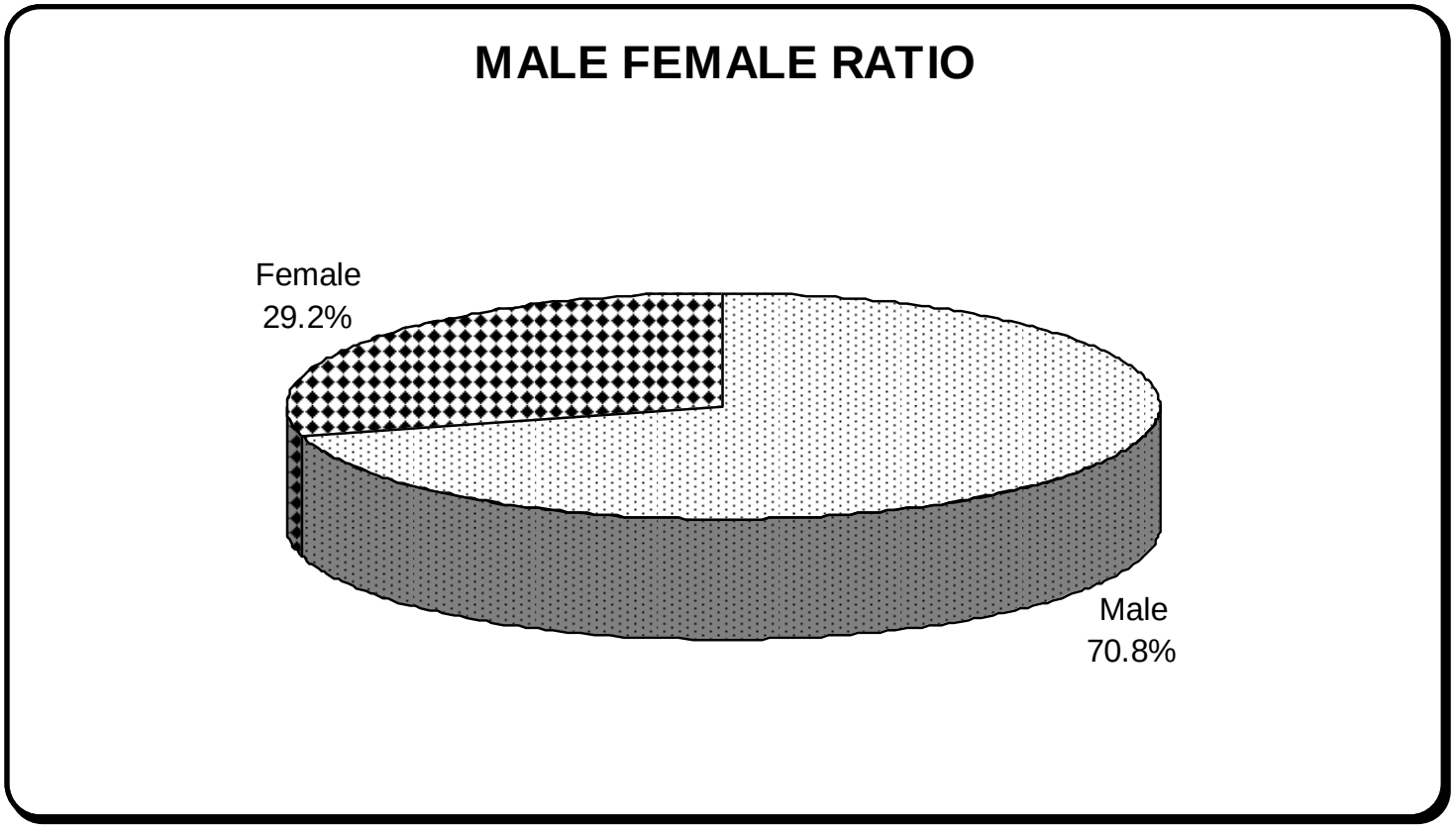
- Mitral or Tricuspid value stenosis
- Atrial myxoma

High cardiac output states.

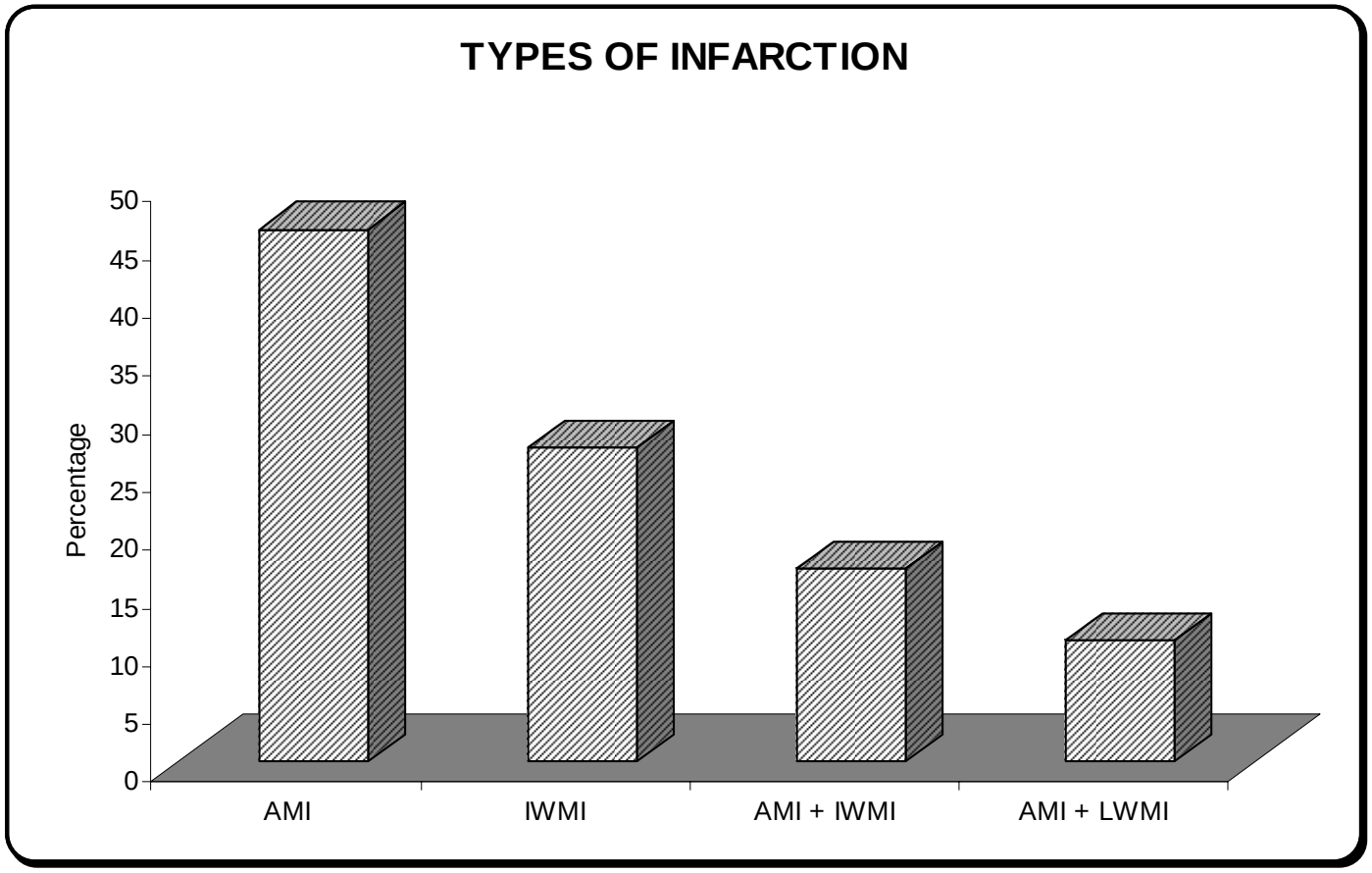
GRAPH - 1


DIASTOLIC DYSFUNCTION
Percentage
70
60
50
40
30
20
10
0
Normal
Diastolic Dysfunction E/A Ratio < 1
Pseudonormalisation

GRAPH - II



GRAPH - III


TYPES OF INFARCTION
Percentage
50
45
40
35
30
25
20
15
10
5
0
AMI
IWMI
AMI + IWMI
AMI + LWMI

MATERIALS AND METHODS

2D Targeted Doppler ultrasound recording were obtained with an Irex meridian echo Doppler system. HEWLETT PACKARD 77020A Equipped with 3.5 MHz and 5 MHz phased array transducer.

This system has a pulsed Doppler capacity with a movable cursor and adjustable sample depth. It was examined in left lateral portion using standard parasternal short axis and bus chamber apical view.

Pulsed Doppler echocardiogram was obtained from the standard apical four chamber view. Mitral in flow velocity were recorded with the sample volume at the submitted annular level.

The transducer was then manipulated to obtain the minimum how signed as assessed by the auditor and spectral output Doppler measurement were made on at least 3 cardiac cycles using the darkest part of spectral recording and was then averaged.

The following measurement were obtained

1. A peak cm / sec (peak rapid filling velocity)

2. A peal cm /sec (peak atrial filling velocity)
3. IRP is msec (Isovolumic relaxation period)
4. DT msec (deceleration time).
5. E : A ratio

And patient included in the study are in the age group 30 -55 satisfying an ECG criteria / enzyme study / h/o chest pain or 2 among the 3 criteria above with duration of more than 3 months.

Exclusion criteria excludes patients with DM, HT, obesity, elderly patients >55 years, any patient with valvular heart disease and any patients with a ECG or Echocardiogram evidence of left ventricular hypertrophy (IVS > 1.0 cm) are also not included..

Also patients with ECG evidence of conduction disturbance are also excluded.

DISCUSSION

In this study seventy five patients were enrolled and only forty eight patients are taken for study. Remaining twenty seven patients are left out since they had diabetes, hypertension and excess age group i.e. more than fifty five years.

Among forty eight patients, thirty four are male (70.8% of study) and fourteen are female (29.2%) of study age group included was forty to fifty five.

Anterior wall myocardial infarction (AMI) occurred in twenty two patients (45.8% of study), Inferior wall myocardial infarction in thirteen (27% of study). Anterior wall myocardial infarction (IWMI) and inferior wall myocardial infarction (AMI+IWMI) together in eight patients (16.6% of study), anterior wall myocardial infarction and lateral wall myocardial infarction (AMI+LWMI) in five patients (10.4%) of study. Twenty two patients were smokers, hypercholestermia occurred in fourteen patients.

Among forty eight patients eleven patients (22.91% had on E/A ratio less than I and four patients (8.33%) has Pseudonormalisation pattern. All the other patients had E/A ratio more than one upto 2.86.

All the eleven patients with E/A ratio < 1 had prolonged isovolumic relaxation period indicating a co relation between the E/A ratio and IRP.

And four patients with E/A ratio > 1 but had a Pseudonormalisation pattern probably due to reversal of blood flow into pulmonary veins.

And studies have shown Pseudonormalisation pattern associated with high filling pressure as confirmed with cardiac catheterization.

A strong co-relation been found by adrien chensbrain, the higher E/A ratio was found in the patient with highest left ventricular end diastolic pressure. The lowest or pathologic E/A ratio (0.5) associated with lowest left ventricular end diastolic pressure.

A correlating study with the Doppler finding to left ventricular end diastole pressure could not be done for want of catheterization lab in our hospital.

A Co-relation is size of infarct to the diastolic dysfunction also made in this study. But johanseen et al found that because

infarction were associated with reduced peak fully rate by radionuclide angiography but with increase E/A ratio by Doppler.

There the result of the effect of impaired myocardial relaxation and increased left ventricular stiffen in complex and result in E/A ratio varying for < 1 to a restrictive pattern of with a ratio > 1 and shortened IRP in patient with stiff ventricular.

Finally the abnormality of diagnostic filling pattern is an in of cardiac evolvement in post infarction facture patients.

Left ventricular diastolic filing abnormality reflects abnormalities is left ventricular compliance it could be an easy indication of the syndrome of congestive heart failure what may occur in the presence of normal systolic function and may suggest specific lies of treatment of the syndrome contrary to congestive heart failure with systolic dysfunction this syndrome must respond to other form of therapy including drugs that enhance left ventricular relaxation, such as ACEI, CCB and those that industry improve relaxation by prolonging the diastolic filling rate as reducing myocardial oxygen consumption such et all beta blocker.

Diuretics should be given very cautiously is these patients.

There are apparently normal E/A ratio in patients after MI may identify those with more severe left ventricular diastolic dysfunction.

And the information provided by these simple and non invasive measurement was nearly equivalent that obtained by measuring pulmonary wedge pressure.

CONCLUSION

From our study we conclude that diastolic dysfunction is present in 22.91% of patient of MI after excluding HT, DM and elderly.

It is also noted that diastolic dysfunction correlate with size of infarction.

Despite the limitations discussed above the results of this study indicate that left ventricular diastolic filling analyzed by pulsed wave Doppler mitral inflow is an important prognostic tool in patients who have MI.

And presence of left ventricular diastolic dysfunction may alter treatment in a better way with ACEI, CCB and BB.

PROFORMA

1. Name :

2. Age :

3. Sex :

4. Type of Infarct :

5. Duration of infarction

6. Killip's Class :

7. Streptokinase given or not

8. Risk Factors :

Echo Study

9. Isovolumic Relaxation Period m Sec

10. E Peak :

11. A Peak :

12. E/A Ratio :

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MASTER CHART

S.No.	Name	Sex	Age in Yrs	Type of infarct	Duration of infarction in months	killips class	SK given or not	Risk factors	IVRT msec	E cm/sec	A cm/sec	E/A ratio
1	Marimuthu	M	54	IWI	1	I	+	-	70	62	48	1.29
2	Kamala	F	48	AMI + IWI	6	II	-	-	84	67	40	1.67
3	Manoj	M	41	AMI	8	I	-	S + HCL	82	58	25	2.32
4	Venkaiyya	M	44	AMI + LWMI	24	II	-	-	94	37	43	0.86
5	Venugopal	M	48	AMI	18	II	-	-	70	59	40	1.47
6	Saroja	F	52	IWI	14	II	-	-	71	70	41	1.7
7	Pappa	F	42	AMI + IWI	3	I	+	HCL	88	66	28	2.35
8	Govindhan	M	54	AMI	18	III	-	-	82	64	49	2.2
9	Rajamani	M	50	AMI	7	III	-	S	97	45	60	0.75
10	Chinnathai	F	49	AMI + IWI	16	I	-	-	84	62	33	1.87
11	Marimuthu	M	49	IWI	12	II	-	S	79	70	34	2.05
12	Munusamy	M	52	AMI	18	I	-	S	81	52	38	1.36
13	Mumtaz	F	49	AMI	4	I	+	-	80	45	60	0.7
14	Mohna	M	48	AMI	1	I	+	S	80	54	32	1.68
15	Bharath	M	55	IWI	4	II	-	-	82	58	38	1.52
16	Valliammal	F	52	AMI	3	II	-	HCL	102	32	64	0.5
17	Vasantha	F	42	AMI + IWI	18	III	+	-	72	70	40	1.75
18	Kondiah	M	43	AMI	2	III	+	S	78	69	28	2.46
19	Naser	M	45	AMI + LWMI	14	II	-	S	98	33	58	0.56
20	Mariam Bee	F	48	IWI	24	II	-	HCL	89	66	29	2.27
21	Joseph	M	45	AMI	22	I	-	-	80	32	33	1.87
22	Manjula	F	41	AMI + LWMI	11	II	+	HCL	99	38	48	0.7
23	Ravi	M	48	AMI	18	I	+	S + HCL	81	65	32	2.03
24	Kialiaperumal	M	53	IWI	12	I	-	S	82	66	38	1.73
25	Pandurangan	M	54	AMI	11	I	-	S	77	70	39	1.79
26	Pungalendi	M	50	AMI	4	I	+	S	70	68	25	2.72
27	Karthikeyan	M	52	IWI	3	II	+	S	84	52	28	1.85
28	Abbas	M	55	AMI	5	II	-	S	82	54	40	1.35
29	Ismail sharif	M	48	AMI	16	III	-	-	74	58	41	1.41
30	Munusamy	M	42	AMI	7	I	+	S + HCL	92	45	60	0.75
31	Rajammal	F	43	IWI	8	II	+	-	89	70	38	1.84
32	Saravanan perumal	M	40	AMI + IWI	18	II	+	HCL	78	66	27	2.44
33	Meena	F	48	IWI	16	I	-	-	98	40	72	0.55
34	Sangeetha	F	52	AMI	4	I	-	HCL	90	63	22	2.86
35	Manickam	M	42	AMI	3	II	-	S	72	63	24	2.62
36	Maheswaran	M	48	IWI	12	II	+	S	102	38	55	0.69
37	Zafirunissa	F	45	AMI	11	III	-	HCL	78	62	38	1.63
38	Mayandi	M	48	AMI + IWI	8	III	-	HCL	82	61	33	1.84
39	Malliga	F	49	AMI	14	I	+	-	81	60	31	1.93
40	Mohammad	M	51	IWI	11	II	-	S + HCL	83	62	42	1.47
41	Arumugam	M	53	AMI + IWI	18	III	-	S	108	43	62	0.69
42	Ramanpillai	M	54	AMI	14	I	+	HCL	84	74	40	1.85
43	Velusamy	M	48	AMI +LWNI	18	II	-	-	71	65	42	1.54
44	Surendran	M	42	AMI	22	II	-	-	78	67	44	1.52
45	Palanichamy	M	43	IWI	14	I	+	HCL	104	48	64	0.75
46	Ismail	M	48	IWI	3	I	+	S	89	68	28	2.42
47	Manimaran	M	52	AMI + IWI	1	I	-	S	80	62	39	1.58
48	Mylsamy	M	51	AMI + LWMI	2	I	-	S	81	55	44	1.25
49	-	-	-	-	-	-	-	-	-	-	-	-
50	-	-	-	-	-	-	-	-	-	-	-	-

AMI - Anterior wall MI , IWI - Inferior wall MI , LWMI - lateral wall MI , HCL - hypercholesteremia, S - smoker, E - peak rapid filling velocity, A - peak atrial filling velocity.