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ASSESSMENT OF LEFT VENTRICULAR DIASTOLIC DYSFUNCTION BY TISSUE DOPPLER IMAGING IN ACUTE MYOCARDIAL INFARCTION

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CERTIFICATE

This is to certify that this dissertation entitled Assessment Of Left Ventricular Diastolic Dysfunction By Tissue Doppler Imaging In Acute Myocardial Infarction submitted by **Dr. G.Marimuthu** to The Tamil Nadu Dr. M. G. R. Medical University, Chennai is in partial fulfillment of the requirement for the award of DM Cardiology and is a bonafide research work carried out by him under direct supervision and guidance.

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DECLARATION

I, **Dr.G.Marimuthu** solemnly declare that I carried out this work on **Assessment of Left Ventricular Diastolic Dysfunction by Tissue Doppler Imaging in Acute Myocardial Infarction** at Department of Cardiology, Government Rajaji Hospital during the period of March 2006 –January 2008.

I also declare this bonafide work or a part of this work was not submitted by me or any other for any award, degree, diploma to any university, board either in India or abroad.

This is submitted to the TamilNadu Dr.M.G.R. Medical University, Chennai in partial fulfillment of the rules and regulation for the DM Cardiology Degree examination.

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INTRODUCTION

Coronary artery disease remains the leading cause of mortality and morbidity. Earlier thought to be a disease of the modern world, it has been found to be equally or even more prevalent in underdeveloped and developing countries[1,2]. This disease is, unfortunately, being witnessed in the younger population also. It remains the most common single cause of mortality and morbidity in men below 65 years of age. Diastolic dysfunction is the primary mechanism responsible for dyspnea in patients with heart failure, irrespective of the presence or severity of systolic dysfunction.

Left Ventricular Diastolic Function

Left ventricular diastolic function is recognized as an important contributing factor in the pathophysiology of many common cardiovascular diseases. The clinical manifestations of coronary artery disease are often the result of abnormalities of left ventricular filling. Diastolic dysfunction may be present prior to, or concomitant with, systolic dysfunction. Although treatments are often aimed at improving left ventricular contractile performance, they may conflict with appropriate therapy for diastolic abnormalities. Recently, attention has been increasingly directed toward the diagnosis, evaluation, and treatment of diastolic dysfunction[2,3]Although catheterization measurements of diastolic performance remain the standard, these invasive parameters have proved technically challenging and tedious to acquire. In recent years, a large body of literature has accrued describing various Doppler echocardiographic techniques for assessing diastolic function. These methods have given new insight into the flow dynamics of the left ventricle, mitral valve, and pulmonary veins and have allowed a more practical noninvasive assessment of diastolic function. Several features of Doppler flow patterns have emerged as having important diagnostic and therapeutic implications.

Physiology of Diastole

Definition

Traditionally, diastole has been described as the portion of the cardiac cycle that begins with

aortic closure (S2) and ends with mitral closure (S1). Importantly, this definition includes the isovolumic relaxation phase. Normal diastolic function may be clinically defined as the ability of the left ventricle to accommodate an adequate filling volume to maintain cardiac output while operating at a low pressure. The initial diastolic event is myocardial relaxation, an active energy-dependent process that causes pressure to decrease rapidly in the LV after the end of contraction and during early diastole.

The normal cycle of cardiac contraction and relaxation requires a precise, transient increase and decrease in the intracellular concentration of calcium ions. The sarcoplasmic reticulum helps orchestrate the movement of calcium during each contraction and each relaxation. The contraction of cardiac muscle is initiated by the cellular action potential that causes the opening of L-type sarcolemmal calcium channels through which calcium ions enter the cytosol. This influx of calcium ions results in the release of more calcium ions from the adjacent sarcoplasmic reticulum through ryanodine receptor channels, a process called calcium-induced calcium release. These calcium ions bind to troponin C, which ultimately disinhibits the interaction of actin and myosin and results in the formation of cross-bridges. Myocardial relaxation is accomplished primarily by the removal of calcium ions from troponin C by an enzyme in the sarcoplasmic reticulum, called sarcoplasmic reticulum calcium adenosine triphosphatase ($SERCA_2$), and the sarcolemmal sodium-calcium exchanger. In humans, approximately 75% of calcium ions are removed by $SERCA_2$ and 25% by the sodium-calcium exchanger. The activity of $SERCA_2$ is modulated by phospholamban, a protein located near $SERCA_2$ in the sarcoplasmic reticulum. Through phosphorylation by protein kinase A and other kinases, phospholamban enhances calcium ion uptake by $SERCA_2$. Failure of the mechanisms of reuptake of calcium ions extruded during contraction can result in the slowing of relaxation or the inability of the cytosolic calcium concentration to return to normal diastolic levels. The latter causes diastolic calcium overload and incomplete relaxation that includes excessive diastolic tension or stiffening. An experimental model of senescence has demonstrated that decreased uptake of calcium ions by the sarcoplasmic reticulum during relaxation is associated with a decrease in the concentration and activity

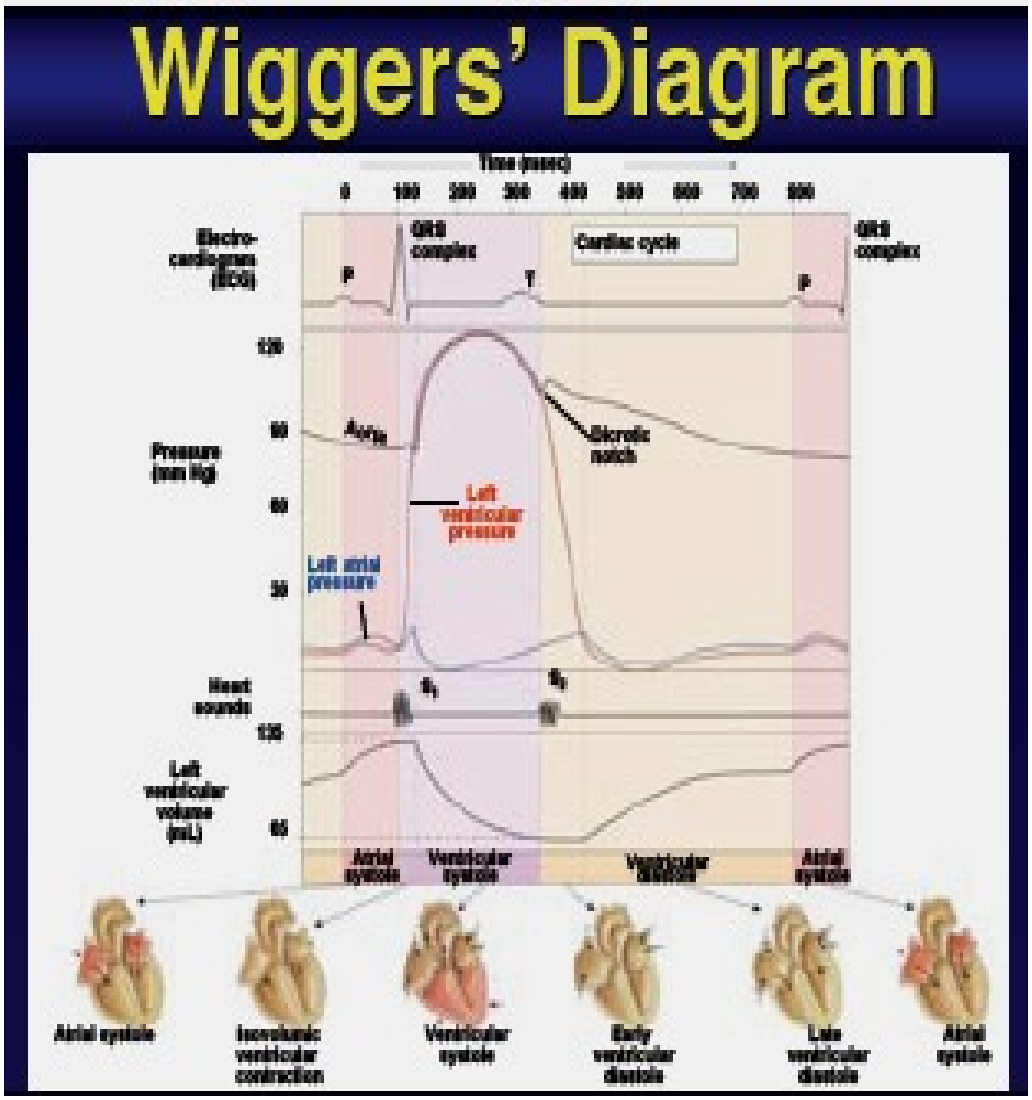
of $SERCA_2$. More recently, $SERCA_2$ levels were found to be greatly decreased in senescent human myocardium (14). This decrease was associated with impaired myocardial function at baseline, and further deterioration occurred during hypoxic conditions. Thus, a decrease in $SERCA_2$ concentration and an associated decrease in uptake of calcium ions by the sarcoplasmic reticulum are thought to influence diastolic dysfunction. Despite normal systolic function, the vulnerability of calcium reuptake is a contributing factor to abnormal LV relaxation early in cardiac disease.

Phases of Diastole

For descriptive purposes, the diastolic period can be divided into four stages after systolic ejection is complete and left ventricular pressure falls below aortic pressure, the aortic valve closes. This marks the beginning of isovolumic relaxation, which subsequently ends at mitral valve opening. During this interval, pressure continues to fall at a rapid rate, while ventricular volume remains constant. Events occurring during this phase have been attributed mainly to myocardial relaxation and have been shown to be an energy-requiring process. At this time, myofibrils return to their resting state from the contracted state. The left ventricular cavity changes in geometry, while volume remains constant[3,4].

Invasive Measures of Diastolic Function

From the description just given, it should be evident that no single parameter can be derived that will adequately describe diastolic performance. Left ventricular filling is the result of a variety of complex forces, including myocardial relaxation, ventricular suction, ventricular stiffness, viscoelastic properties of the myocardium, filling of the coronary arteries, atrial contraction, ventricular interdependence, and pericardial restraint. To understand the role of Doppler echocardiographic information in assessing diastolic function, it is necessary to have a working knowledge of other conventional methods.[5]



Schematic of intracardiac pressures and volumes to define the four stages of diastole. The periods of isovolumic relaxation, rapid filling, slow filling (diastasis), and atrial filling are shown. AVC, aortic valve closure; AVO, aortic valve opening; LV, left ventricle; MVC, mitral valve closure; MVO, mitral valve opening.

(From Zile M: Mod Concepts Cardiovasc Dis 1989;58:67.)

Traditionally, catheterization-based methods for studying diastolic events have focused on evaluation of the relationship between left ventricular pressure and volume. Because of the dynamic nature of

diastole, measurements have been derived to describe the function of the ventricle during its isolated phases. The indices of function have centered on the evaluation of relaxation, filling, or compliance. As shown, these measurements are not interchangeable and, like Doppler descriptors, describe different phenomena during the sequential phases of diastole. They may also be variably influenced by changes in factors such as load or heart rate. Hemodynamic indices describing early diastolic events include peak -dP/dt, the time constant of isovolumic left ventricular pressure decay or tau (τ), the isovolumic relaxation time (IVRT), and the half-time of ventricular pressure decline (T1/2).[6,7]

Chamber Stiffness

Catheterization methods have also been derived for pressure-volume events during filling. The assessment of diastolic mechanics in the catheterization laboratory requires highly accurate determinations of both pressure and volume. The simultaneous recording of these values allows the calculation of compliance as the rate of change in volume per rate of change in pressure, dP/dt. The reciprocal of this value, dP/dV (called chamber stiffness), is usually derived by obtaining pressures at different volumes, measured at end-diastole. Since this relationship is exponential for the left ventricle, the rate of change is calculated from a single point and represents the instantaneous slope of the tangent to this curve. Chamber stiffness values are preload dependent, so that an increase in volume will result in an increase in chamber stiffness. However, when dP/dV is plotted against pressure, a linear relationship exists for a given ventricle. The slope of the line describing chamber stiffness versus pressure is called the modulus of chamber stiffness, or Kv. Although Kv is relatively independent of pressure and volume, comparison between ventricles of different volume must be normalized for chamber stiffness (i.e., VdP/dV). The reciprocal dV/VdP represents specific chamber compliance. Normal values for Kv range from 0.010 to 0.025, and dV/VdP data generally fall between 0.015 and 0.045. Although often difficult to acquire, these values are descriptive of events occurring in late diastole and define the passive components of ventricular filling. The values have not been validated for acute conditions, making comparisons among patients somewhat impractical.[13.14]

Radionuclide Descriptors of Filling

Contrast ventriculography and radionuclide angiography have been used to describe the volume changes that occur with ventricular filling. When volumes are calculated and plotted over time, the resultant curve can readily define the rapid filling, diastasis, and atrial contraction phases of diastole. The first derivative of this time-activity curve (dV/dt) describes the peak filling rate and time to peak filling rate. Other available measurements include the atrial filling fraction and early or rapid filling fraction. In summary, there are a number of time-honored methods for describing left ventricular diastolic function.[15, 16] Catheterization methods have the advantage of combining pressures with volume but are tedious, often define only a single point in time, and are load dependent. Although these elegant indices can provide significant insight regarding the physiology of ventricular diastole, their practical application to individual patients remains limited.

Doppler Echocardiographic Indices of Diastolic Function

Isovolumic Relaxation Time

Dynamic left ventricular relaxation begins at the time of peak systolic pressure. The process continues as ventricular pressure falls below aortic pressure, ejection ceases, and the valve closes. Left ventricular pressure continues to fall even as volume remains constant during the isovolumic phase of diastole but prior to mitral valve opening. M-mode echocardiography with simultaneous phonocardiography traditionally has been used to assess the length of this period between aortic closure and mitral opening. With the aortic closure sound (phono) recorded on a separate channel from but with the same time sweep as mitral leaflet opening (M-mode echo), the aortic closure-mitral opening time interval (representing IVRT) can be readily measured. The IVRT has been described for normal subjects and for subjects in ischemic heart disease. Generally, as relaxation becomes impaired, the IVRT is prolonged, with normal values approximating 65 ± 20 msec. More

recently, the phonocardiographic method has been replaced by a continuous wave Doppler echocardiographic method. In this technique, the continuous wave beam is directed from the apical five-chamber view across the region between the aortic outflow tract and the mitral inflow tract. The Doppler echocardiographic spectrum in this position includes aortic valve flow with valve closure and the onset of mitral inflow, so that the aortic closure-mitral opening interval can be determined.[17,18] Comparisons of Doppler IVRT with catheterization measurements of this time period have shown reasonable correlations. Notably, nuclear scintigraphy conventionally includes the IVRT in the early filling phase, since the volume/count technique is unable to distinguish isovolumic changes. The IVRT has been demonstrated to be shortened in restrictive diastolic dysfunction, probably because of high left atrial pressures resulting in early mitral opening. However, measurement of the IVRT as the sole predictor of diastolic function is limited, since no information on ventricular filling is provided.

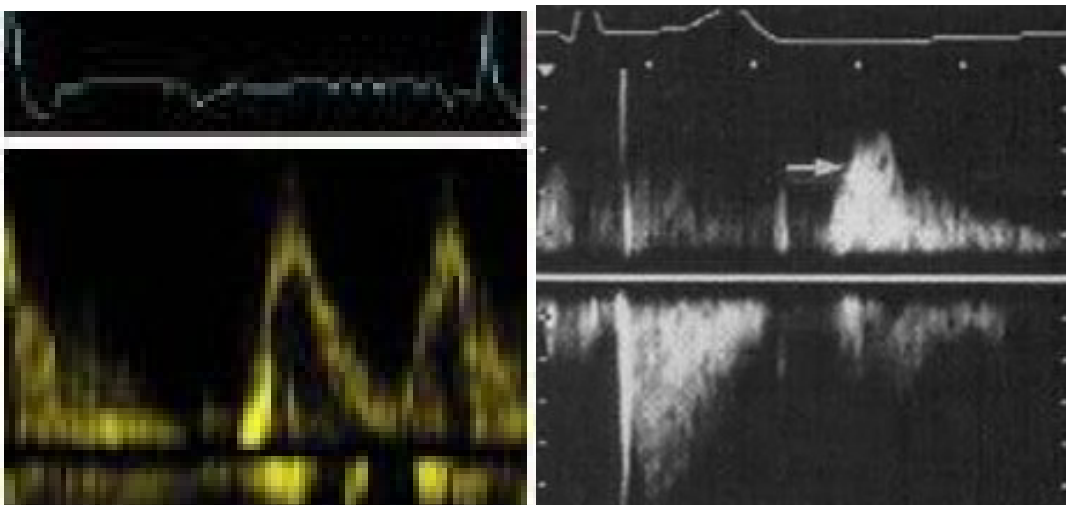
Transmitral Flow

The use of pulsed Doppler echocardiography to describe events of left ventricular filling is based on the assumption that transmitral blood flow velocities are representative of volumetric flow. According to the law of conservation of mass, true volumetric transmitral flow is equal to the velocity of flow times the area of the orifice ($F = A \times V$). Thus, the dynamic nature of the mitral orifice during diastole plays a role in producing the flow profile. Although the mitral cross-sectional area remains relatively constant in size at the annulus level, the diastolic area of flow constantly changes at the leaflet tips. The Doppler velocity profile, therefore, does not represent a direct recording of volumetric flow but is proportional to the atrioventricular pressure gradient, according to the modified Bernoulli equation: $P1 - P2 = 4(V2)$, one of the main determinants of transvalvular blood flow. True volumetric flow rates can be derived when combined with valve area

measurements, although a significant benefit of this step in assessing diastolic function has not been well established. The two phases of forward flow in early diastole and late diastole can be readily identified by their[19,20] triangular shape and are separated by a brief period of diastasis. The early phase, or E wave, represents flow during the rapid filling phase, while the second peak, or A wave, represents transmitral flow occurring as a result of atrial contraction. The E and A waves are two well-defined peaks within the spectrum and usually display a linear upslope and downslope that can be measured as acceleration and deceleration, respectively, in centimeters per second. Other conventional measurements include the peak E and A velocities, as well as the integrated areas within each phase, Ei and Ai. At slower heart rates, the E and A waves are separated by low, flat velocities during diastasis. These velocities are more readily recorded using low wall filter settings and sweep speeds of 50 or 100 mm per second. Occasionally, a separate distinct and positive inflow wave is seen immediately after the E wave; this wave has been designated the L wave. It is thought to represent pulmonary venous flow passing through the left atrium, which acts as a conduit during this period. Studies performed to compare transmitral velocities with ventricular cineangiography have found a significant correlation for both early and late phases.[21,22]

Studies by **Friedman** et al and **Spirito** et al demonstrated similar findings for Doppler versus radionuclide techniques. However, filling time intervals between Doppler and these methods have not correlated well, in part because of the inclusion of IVRT by nuclear methods but not by Doppler echocardiography. Normative data from Doppler transmitral velocities have been reported mainly as control data for studies of various disease states A normal peak E wave velocity is in the range of 70 to 100 cm per second, with a peak A wave of 45 to 70 cm per second, resulting in an E/A ratio of 1.0 to 1.5. The normal deceleration time (DT) for the E wave is 160 to 220 msec . The recording methods and the populations sampled vary considerably among centers. Therefore, normative data should be established for each laboratory using standard examination and measurement techniques so that individual subjects can be evaluated against control

subjects.[23,24]

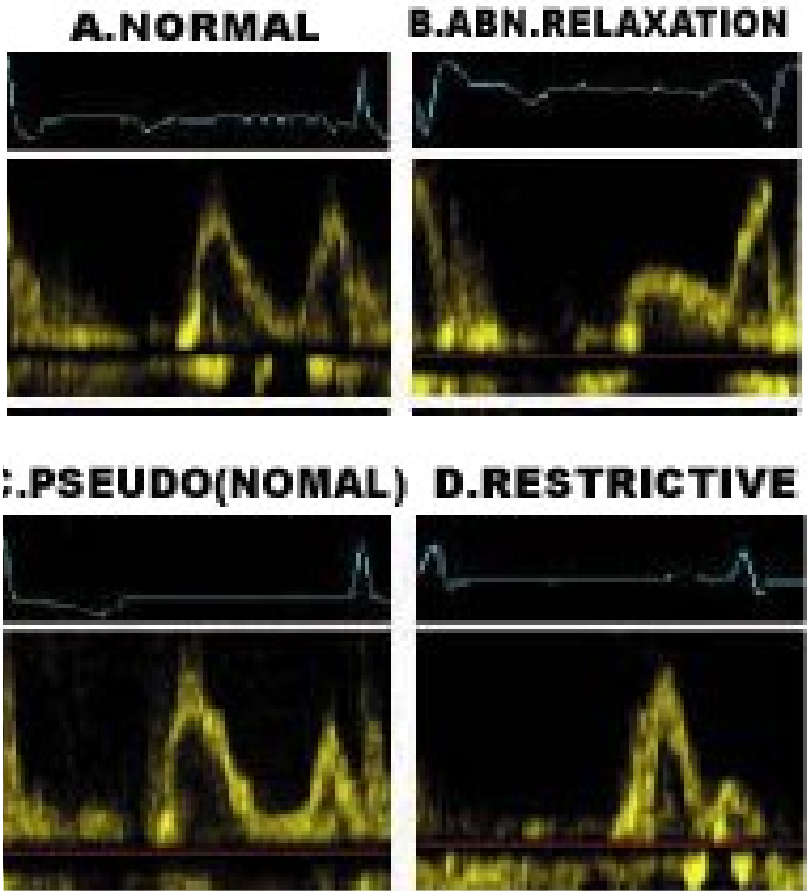


Measurement of isovolumic relaxation time by continuous wave Doppler with the beam directed between the aortic outflow tract and mitral inflow

Abnormal Transmitral Flow Patterns

Although the ranges for normal values are wide and Doppler parameters are affected by a variety of hemodynamic and physiologic factors, patients with proven diastolic dysfunction have been shown to demonstrate characteristic abnormalities in the spectral flow profile. Rarely is a single finding diagnostic of a specific disease process, but constellations of abnormalities tend to be present for a given pathophysiologic condition. Thus, three distinct clinical patterns of abnormal transmitral flow have been described. The first pattern consists of a prolonged IVRT and deceleration time with a reduced peak E and an increased peak A wave velocity. These findings have been associated with normal early diastolic filling pressures and are attributed to impaired left ventricular relaxation[25,26]. The delay in relaxation directly lengthens the IVRT and produces a smaller atrioventricular gradient in early diastole. The effect is a reduced E wave velocity with a more gradual downslope (or prolonged deceleration time). The increased peak A wave velocity and Ai are likely the result of diminished early diastolic flow with a higher left atrial residual volume at the time of atrial contraction. A second transmitral flow

pattern has been termed restrictive. The characteristics of this pattern are a short (or normal) IVRT and reduced deceleration time, along with increased E wave and diminished A wave velocities. Thus, filling is predominantly shifted to the rapid filling phase in early diastole and is thought to be due to a high cross-over pressure at the time of mitral valve opening in the presence of a relatively nondistensible left ventricle. The result is a high early velocity of transmitral flow but with rapid equilibration of the atrioventricular pressures and an abrupt cessation of flow (short deceleration time). Late diastole is characterized by diminished atrial transport caused by high left ventricular pressures, poor atrial function, or both. A third pattern has been termed normalized or pseudonormal.This pattern has characteristics of normal transmitral velocities but results from counterbalancing influences of both abnormal relaxation and restrictive forces. This pattern represents an intermediate pattern between the two ends of the pathologic spectrum and may be viewed as a transition from one pattern to another. An example of a pseudonormal pattern is shown. [27,28] The pseudonormal flow pattern shows nearly equal E and A wave velocities, with a deceleration time that is either normal or shortened. The fact that flow patterns can be seen to change over time within individual patients has caused concern that transmitral doppler tracings alone may not be used to identify diastolic dysfunction. Indeed, it is currently recognized that patients with a pattern of impaired relaxation may convert to "normal" (pseudonormal) as a result of increased mitral regurgitation, hypervolemia, or increased ventricular stiffness resulting from progression of the underlying disease. These physiologic changes can all potentially produce an increased E wave and more rapid deceleration slope. Similarly, the restrictive pattern may be affected by lowering preload. The ability of Doppler flow patterns to mutate as a result of changes in load compromises the use of these recordings from a single examination to assess diastolic function. Thus, serial studies, along with available clinical or direct hemodynamic information, may be beneficial in sorting out findings in individual patients. In addition, studies of Doppler recordings of pulmonary vein flow have contributed to knowledge in this area.



Physiologic Factors Affecting Transmitral Flow

A number of physiologic variables have been shown to influence the pattern of flow across the mitral valve during diastole; these include age, heart rate, heart rhythm, loading conditions, systolic function, atrial function, and phases of respiration. The complex interplay of these parameters results in the final spectral Doppler echocardiographic signal. It is therefore important to consider each of these factors to interpret the clinical relevance of the Doppler echocardiographic findings.

Age

Age has been found to be an important determinant of the transmitral flow profile. In studies of normal populations, the peak E wave and integrated E wave (Ei) velocities have been shown to decrease with advancing age from 20 to 75 years. The peak A and Ai velocities increase with age, resulting in a decreased E/A ratio. Furthermore, the IVRT and deceleration time have been demonstrated to be progressively longer with age. Thus, Doppler examination of normal, young

patients may resemble the restrictive pattern, whereas patients with advanced age often show findings compatible with impaired relaxation. It has been proposed that these changes are due to the development of left ventricular hypertrophy, since wall thickness and mass are known to increase over time in the normal population. An increase in hypertrophyand myocardial stiffness could lead to delayed relaxation and result in prolonged IVRT, decreased E wave, and longer deceleration time. This development of a "physiologic state of hypertrophy" remains hypothetical, since Doppler echocardiographic characteristics were not dependent on blood pressure or left ventricular mass in these studies.[29,30]

Heart Rate

Changes in heart rate affect the resulting transmitral flow pattern by several mechanisms. As heart rate increases and the diastolic interval is shortened, the A wave begins to encroach on the preceding E wave. Studies of patients with dual-chamber pacemakers have shown a decreased E wave peak velocity and Ei, with concomitant increases in A waves with heart rates up to 90 beats per minute. The increase in atrial contribution may be due to a reflex increase in myocardial contractility (the Bowditch phenomenon); a rise in left atrial pressure; or, more simply, the result of higher atrial volume at the onset of atrial systole due to elimination of diastasis. Similarly, in normal volunteers with atrial pacing via a transesophageal electrode, the peak A wave was seen to increase by a mean value of 8 cm per second for each increment of 10 beats per minute in heart rate. Most studies have shown that at rates greater than 100 beats per minute, the E and A waves become fused, making conventional measurements of peak velocities, velocity integrals, and acceleration or deceleration unobtainable in most cases.[31,32]

Heart Rhythm

Changes in atrioventricular synchrony due to alterations in the PR interval, atrial fibrillation, or ectopic rhythms can cause dramatic changes in Doppler transmitral flow. A prolongation of the PR interval usually results in a reduced E wave component, possibly due to more complete atrial emptying

and a reduced diastolic time interval, especially during the rapid filling period. Atrial ectopic rhythms and heart block may provide a variety of E and A wave profiles depending on the timing of atrioventricular dyssynchrony. Atrial fibrillation results in an absence of organized A wave velocities, with variable E waves, depending on the length of the preceding RR interval.

Loading Conditions

Loading conditions have a substantial impact on the Doppler transmitral flow pattern. The most important variable appears to be the left ventricular preload, which can have a profound effect on E wave velocities.

A study by **Choong** et al first demonstrated that the administration of nitroglycerin reduced the peak E, Ei, and deceleration rates of the rapid filling phase without significant changes in A wave parameters. Most importantly, these changes were noted to resemble the pattern of impaired relaxation, even though there was no hemodynamic evidence for diastolic dysfunction. The mechanism for these changes is felt to be related to a decreased left atrium —left ventricle pressure gradient at the time of mitral valve opening ("cross-over pressure"), which results in lower E wave velocities. Other studies using a tilt table or lower body negative pressure have substantiated these findings. Of all hemodynamic parameters evaluated, left atrial pressure was the most significant determinant of peak E wave values.[33,34]

Systolic Function

Left ventricular systolic function also affects the transmitral flow rate during the rapid filling phase. Studies have shown that left ventricular end-systolic volume is indirectly correlated with peak E wave velocity. Thus, in the presence of systolic dysfunction or increased afterload, the early diastolic velocities can be expected to be reduced, with deceleration time prolonged. These important studies

make it clear that one must take volume status and loading conditions into account before classifying patients into categories of diastolic dysfunction. Obviously, patients evaluated in an echocardiographic laboratory may be subject to extremes of load and volume due either to the underlying disease process or to treatment with vasoactive drugs. Careful consideration of these circumstances must be given to individual patients during analysis of the Doppler data.[35]

Atrial Function

The size and functional status of the left atrium itself may contribute to changes in the Doppler transmitral flow profile. For example, it has been noted that the reduced atrial contractility (or "atrial stunning") that occurs after cardioversion of patients with atrial fibrillation or flutter results in a reduced peak A-wave velocity. Thus, despite restoration of sinus rhythm, the atrial transport function (and A wave component) of diastole may remain impaired for weeks after cardioversion. Theoretically, any acute process affecting atrial function (e.g., inflammation, scarring, or infarction) could produce similar abnormalities in transmitral flow.

Respiration

The physiologic intrathoracic pressure changes that occur during normal breathing produce minor changes in transmitral flow. As a result of negative pressures and, consequently, enhanced peripheral venous return—developed during inspiration, right heart and transtricuspid flows predominate[37,38]. Concurrently, the transmitral velocity spectrum yields reduced peak E wave velocities in the range of 5% to 10%. Since little or no change is seen in the corresponding A wave, the E/A ratio may fall slightly under that seen in normal circumstances. These changes are compatible with known physiologic reduction of left ventricular preload during inspiration. However, in situations of acute right heart strain or pericardial tamponade, the effect of respiration on transmitral flow has been shown to be much more dramatic. To minimize respiratory changes, most laboratories record the transmitral spectral Doppler echocardiogram with the patient in held, shallow endexpiration.

Technical Considerations of Transmitral Flow Measurements

Two-Dimensional Imaging Plane

Doppler recordings of transmitral flow must be performed in a standardized fashion for consistency. Since the Doppler equation includes a term for angle of incidence (cos theta), the technique for recording transmitral flow velocities is optimally performed from the apical window (four-chamber, two-chamber, or long-axis views). Most laboratories use the four-chamber view because of its orthogonal relationship to the major diameter of the mitral annulus.[39]

Pulsed Wave versus Continuous Wave Doppler

Because of its superior temporal and range resolution, pulsed wave Doppler echocardiography is the preferred technique for recording transmitral flow. Although the continuous wave method may ensure that the highest velocities are recorded, these signals may arise from other locations along the interrogating beam path (i.e., from aortic insufficiency) rather than via diastolic transmitral flow. In addition, the pulsed wave signal provides a "cleaner" outer border that readily lends itself to tracing peak velocities and slopes. However, the continuous wave Doppler technique is required for obtaining the IVRT, as previously described.[40]

Sample Site

Studies in the literature differ according to optimal location of the pulsed wave sample volume. Some investigators have recommended placing the sample volume near the center of the mitral annulus, just on the ventricular side, using two-dimensional imaging for positioning. This scheme has the advantage of being more reproducible among patient studies and providing a better evaluation of the atrial component. Recordings made between the mitral leaflet tips yield higher velocities of flow and a better assessment of the rapid filling phase. Since no clear consensus currently exists, each laboratory must establish a protocol for recording and analysis, as the spectral profiles often differ at these location, and published studies must be read carefully if the methods are to be reproduced. Flow through the normal mitral orifice with normal cardiac output remains essentially laminar and has a blunt profile. Thus, the border of the pulsed wave velocity spectrum generally exhibits very little

spectral dispersion, since at any given instant the red cell targets within the region of interest are moving at nearly the same speed and direction. However, the border does show a finite width. The darkest portion of this band represents the modal velocity and has been suggested as the best location for tracing or measuring the spectrum, as it should be less susceptible to changes in gain.[41,42]

E and A Wave

At slower heart rates, the early (E) and late (A) contributions to left ventricular filling can be readily identified, as well as the lower velocities occurring during diastasis (if wall filters are kept low). However, at heart rates above 100 beats per minute, the individual E and A waves often become fused, making measurements of Ei and Ai difficult. At higher heart rates (around 130 beats per minute), peak velocities may not be readily discriminated and appear as a single large wave . Various approaches have been taken to this problem. For example, the E and A waves can be measured by extrapolating the descending and ascending slopes, respectively, through the merged portion of velocity spectrum. Another approach involves dropping a perpendicular line from the point of convergence. Our experience suggests that integrated time velocity values may be less reliable in this setting and that perhaps only peak velocity values should be used, since these usually remain distinctly visible. The E wave deceleration time can usually be obtained by extrapolating the visible portions of the downslope to the baseline. If Ei and Ai are to be measured, a convention should be adopted for the laboratory. It should be noted that use of these different methods may account for differences in time-velocity integrals and time intervals between separate examinations and centers.

Diastasis

The velocities recorded between the E and A waves represent the ventricular filling that occurs during diastasis. Normally these velocities are low and represent a very small contribution to overall volume of flow. Indeed, if wall filters are increased to eliminate noise around the baseline, the velocity spectrum during the period may be completely eliminated. Since this portion of the Doppler spectrum may be helpful in understanding pulmonary vein flows, the wall filters should be adjusted as low

as possible to eliminate noise and yet preserve the outer border of the spectrum during this time period.

Deceleration Slope versus Deceleration Time

Measurements of the descending limb of the transmitral E wave have been reported in terms of both deceleration slope (cm per second squared) and time (msec). The slope is defined by the rate of decline from the peak velocity, whereas deceleration time describes the time interval between peak velocity and the point of intercept of the decay slope (or extrapolated slope) with the baseline. Although these parameters have both been used to describe relaxation events in early diastole, they are not equivalent.[43] The deceleration slope is influenced by and directly related to peak E velocity, whereas deceleration time has the advantage of being more independent of the E velocity.

Pulmonary Vein Flow

Normal Patterns

Doppler echocardiographic recordings of flow within the pulmonary venous system have been obtained using both transthoracic and transesophageal windows.These spectral patterns have yielded important insight into the physiology of left ventricular filling and diastolic function. The pattern of flow is largely determined by transmitral flow and left atrial function. The pattern consists of two forward waves and one reverse (below the baseline) wave. One forward wave occurs during systole (S) and coincides with left atrial relaxation immediately after atrial contraction. The systolic wave occasionally demonstrates two separate components at slow heart rates; these may be distinguished by a notch in the upslope. The early component (SE) is thought to result from atrial relaxation, and the late systolic wave (SL) has been described as originating from movement of the mitral annulus toward the apex. The other forward wave occurs during diastole (D) and coincides with the early transmitral flow and ventricular filling but is delayed by approximately 50 msec. In this context, the diastolic flow can be viewed as produced by

ventricular relaxation, resulting in forward pulmonary vein flow, with the left atrium acting as a conduit after mitral valve opening. With short RR intervals, the systolic and diastolic waves may merge, resulting in a single forward-flow wave. Thus, depending on heart rate and rhythm, the pulmonary vein velocities above the baseline may be recorded as monophasic, biphasic, or triphasic. Reverse flow can often be recorded as a small, brief velocity signal below the baseline during atrial contraction (just after the P wave). This wave has been variously designated the pulmonary vein *A* (PVa) or atrial reversal (Ar) wave and represents retrograde pulmonary vein flow. It is usually larger when the atrial afterload is high from left ventricular hypertrophy or restrictive/constrictive processes. Some workers have termed the systolic and diastolic forward waves as *J* and *K waves* or *X* and *Y waves,* respectively. Although labeling of the pulmonary vein velocity has not yet been standardized as for transmitral flow, most recent investigators have used the S and D designations. This format has the advantage of being readily associated with timing within the cardiac cycle. However, the J and K terminology is more easily associated with the L wave of transmitral flow during diastasis and thus is preferred in some laboratories. Other authors have named these as X and Y waves to correspond to the x and y descent of the pulmonary capillary wedge pressure tracings. In this scheme, the atrial reversal velocity is called the Z wave.[44]

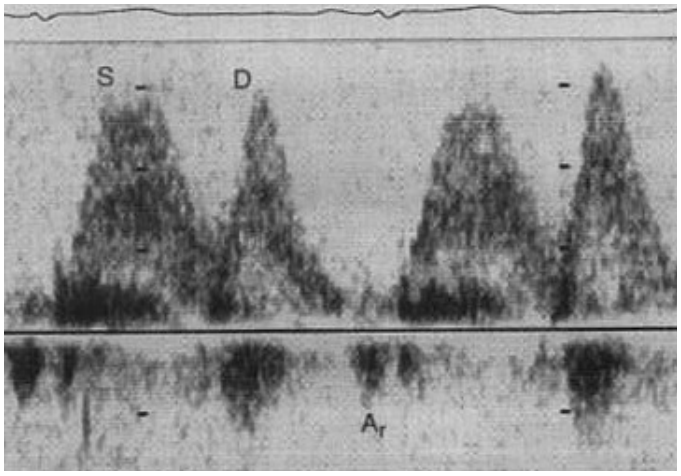
Measurements

As with the transmitral flow, the conventional assessment of pulmonary vein velocity waves has included the measurement of peak velocities, as well as the time velocity integral for S (Si) and D (Di). The ratio of the systolic to diastolic components has also been described by peak S/peak D or expressed as the systolic fraction (percent)

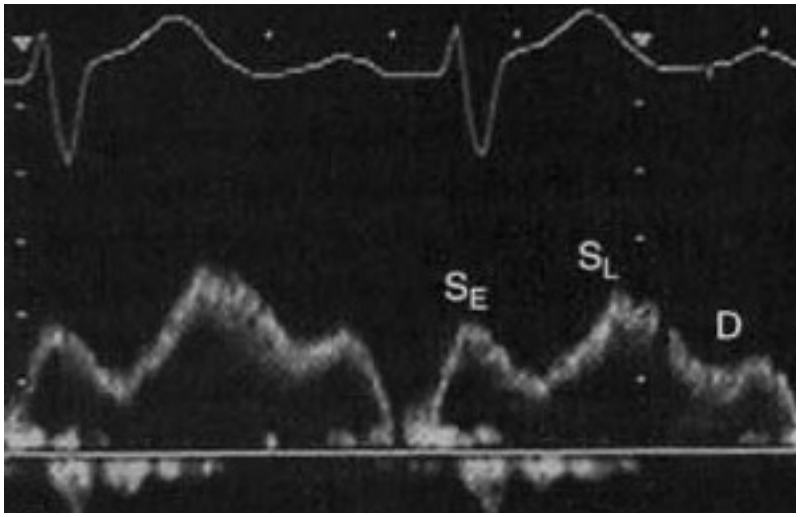
by the following equation

$$\text{Systolic fraction} = \left(\frac{S_i}{S_i + D_i}\right) \times 100\%$$

The peak Ar velocity, velocity time integral, and duration (Adur, in milliseconds) have also been defined. Fewer studies of normative data are available for pulmonary vein flow than for transmitral Doppler data. However, as indicated, some of these investigations were performed in patients undergoing catheterization or elective operations and thus may not reflect values obtained during a routine echocardiographic examination. In general, the S wave is predominant in normal patients, with peak velocities ranging from approximately 40 to 60 (±15) cm per second and time velocity integrals of 15 ± 5 cm. The SE component is usually smaller than SL, with peak velocities of 30 to 40 (±10) cm per second. The diastolic wave has been measured in the range of 35 to 45 (±15) cm per second with a velocity integral of around 7.5 to 9.5 (±4) cm. The ratio of peak S to peak D has been described in normal subjects as 1.3 to 1.5 (±0.3), with a systolic fraction of 60 to 68 (±10%). The peak A wave is normally the smallest of the velocity components at -22 to -32 (±10) cm per second, with integrated values of 2 ± 1 cm. The Ar duration has been found to be helpful in the clinical interpretation of pulmonary vein flow and is approximately 137 ± 31 msec[45,46].



Normal Doppler pulmonary vein flow tracings using transthoracic techniques



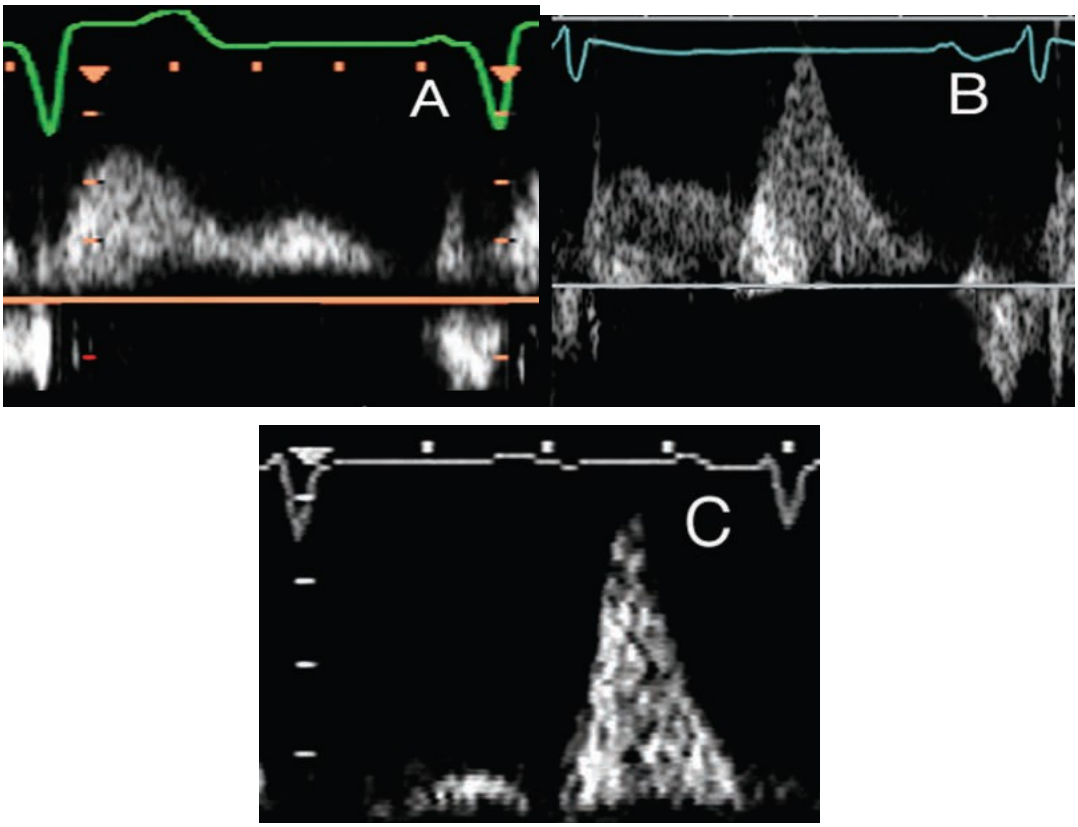
Normal Doppler pulmonary vein flow tracings using Transesophageal techniques

Abnormal Patterns of Pulmonary Vein Flow

The alterations in transmitral waveforms seen in various cardiac disease states and loading conditions and with aging have also been described for pulmonary vein velocities. Since pulmonary vein tracings provide additional information about atrial filling and function, these patterns have been used in conjunction with transmitral flows to better define abnormalities of ventricular filling. In patients with impaired left ventricular relaxation, the pulmonary vein flow during early diastole (D) becomes smaller, corresponding to decreased E wave velocities at the transmitral site, both being related to a slower rate of ventricular relaxation. As a result, pulmonary vein flow is shifted toward the systolic phase (S) and results in a in this category often have had progressive increases in left atrial volume and pressure due to decreasing left ventricular compliance over time. Because atrial compliance often becomes gradually reduced in this setting, the pulmonary venous flow during systole (S) is reduced owing to decreased atrial relaxation. Thus, the diastolic (D) wave may become predominant, with Si /Di less than 1 and systolic fraction less than 50%. A characteristic feature to this pattern is also a larger Ar wave, reflecting reduced ventricular compliance.[47,48]

The features of pulmonary vein velocity waveforms in patients with restrictive physiology are a small S wave and a large D with an abrupt cessation of flow. The Ar wave size and duration are

variable depending on the state of left atrial function. If left atrial contractility is preserved, the pulmonary vein A may be very large and prolonged. However, if left atrial failure has occurred due to chronic dilation, the Ar may become diminutive.



Three patterns of pulmonary venous flow are presented: (A) the pattern of impaired relaxation with a low velocity D wave; (B) this is pseudonormal; and (C) is an example of the restrictive pattern with a high velocity D wave and low velocity S wave.

Estimation of Left Atrial Pressure

A relationship between pulmonary venous flow variables and mean left atrial or left ventricular diastolic pressures has been described.

Kuecherer et al compared pulmonary vein flow variables as well as mitral inflow with mean left atrial pressure (LAP) in 47 consecutive patients undergoing cardiovascular surgery and transesophageal echocardiography. The pulmonary vein systolic fraction correlated best with LAP (r = -.88; SEE = 3.5 mm Hg). The relationship between the two parameters was described by the following equation:

$$\text{LAP} = 35 - 0.39 \times (\text{systolic fraction})$$

The authors believed that the shift from predominant systolic flow to diastolic flow seen with rising left atrial pressure was most likely due to decreased left atrial compliance. Retrospective evaluation of the data also suggested that a systolic fraction less than 55% was 91% sensitive and 87% specific for predicting a mean left atrial pressure of 15 mm Hg or greater.[49]

A similar study using transthoracic pulmonary venous flow recordings was reported by **Brunazzi** et al in 116 consecutive patients undergoing elective catheterization that included measurements of pulmonary capillary wedge pressures (PCWP). The systolic fraction was again noted to correlate best, with r = -.88 and SEE = 3.1 mm Hg. A success rate of 83% was reported in recording pulmonary vein flow from the transthoracic window, and the authors suggested that a systolic fraction of less than 36% percent predicted a mean PCWP of 18 or greater, with a 90% sensitivity and 85% specificity.

Rossvoll and **Hatle** have demonstrated a strong relationship between systolic fraction and the pre-A wave left ventricular end-diastolic pressure (LVEDP). A systolic fraction less than 40% was predictive of LVEDP greater than 18 mm Hg (r = -.70). These investigators also found that the pulmonary A wave duration (Adur) was frequently prolonged, whereas the transmitral A wave was significantly shortened in patients with increased LVEDP. The difference ([PV−Adur] − [M−Adur]) in milliseconds correlated best with LVEDP (r = -.68). A longer duration of the pulmonary vein A wave than transmitral A wave predicted LVEDP greater than 15 mm Hg with a sensitivity of 85% and specificity of 79%. This study was also recorded using the transthoracic approach in 45 patients undergoing diagnostic catheterization.[50]

Factors Affecting Pulmonary Vein Flow

As with transmitral recordings, a number of physiologic factors may affect the pulmonary vein Doppler echocardiographic velocity profile.

Age

Studies of normal subjects with a wide age range have demonstrated that the diastolic

components are diminished and the systolic velocities are increased with advancing age. A trend toward a larger atrial flow reversal wave has also been noted, perhaps reflecting abnormalities of left ventricular diastolic performance as part of the normal aging process.

Loading Conditions

The volume of pulmonary venous flow occurring during systole is dependent on preload—that is, with preserved myocardial contractility and increasing preload (i.e., volume loading), the atrial preload will also increase, resulting in increased pulmonary venous systolic flow. This increase in S and S/D has been observed in human studies in the operating room. A direct correlation between both systolic and diastolic forward flows and cardiac output has also been found.

The effect of afterload was studied by Nishimura et al. Patients given phenylephrine in the operating room exhibited variable responses in pulmonary vein flow patterns. Those with a dramatic rise in PCWP (>50%) showed an increase in diastolic pulmonary vein velocities, and a middiastolic flow wave (L) became apparent.

Mitral Regurgitation

Changes in transmitral and pulmonary vein velocity profiles have been found to be useful clinical markers for the estimation of severity of mitral insufficiency.

Castello et al found a significantly lower peak S/D velocity ratio (0.4 ± 1.3) in patients with moderate to severe regurgitation compared with patients with less regurgitation (1.4 ± 0.5, $P < .0001$). This trend toward "systolic blunting" was more remarkable as regurgitation worsened. In patients with severe mitral regurgitation, the systolic flow was reversed (retrograde) into the pulmonary veins. The presence of reversed systolic flow was identified as a sensitive (90%) and specific (100%) marker for severe regurgitation in the 75 patients evaluated.[51]

Similar results were reported by **Klein** et al. An equally high sensitivity and specificity for reversed systolic flow was noted, and the pattern subsequently returned to normal after operative repair in 22 patients. Thus, significant mitral regurgitation may alter the phasic appearance of pulmonary

venous flow, with a progressive increase in the diastolic (D) wave component for increasing grades of insufficiency.

Technical Considerations in Pulmonary Vein Flow Recordings

Transesophageal versus Transthoracic Methods

The pulmonary vein flow spectrum is generally of superior quality when recorded from the transesophageal window. The transesophageal window has been described as especially helpful in recording reversed flow during atrial contraction (Ar) and in separating the two components of forward systolic flow (SE and SL) Indeed, the transthoracic method may be limited in these areas, yielding Ar recordings of acceptable quality in the minority of patients studied. When the transthoracic four-chamber view is used, the right upper (medial) pulmonary vein is recommended for sampling. Spectral data from this site correlate well with velocities recorded from the same vein using the transesophageal technique. The use of color flow or newly available echocardiographic contrast agents may help in identifying the location of the pulmonary vein orifice and in improving Doppler signal intensity from transthoracic studies. Although the esophageal window normally allows imaging of all four pulmonary veins, the upper veins are preferred for sampling because they provide a more parallel flow angle for Doppler interrogation. The advantages of the transesophageal study must be weighed against those of patient discomfort to determine the need for this procedure in each clinical instance.

Sample Position

The ideal position for sampling pulmonary vein velocities and analyzing waveforms is 0.5 to 1 cm from the pulmonary vein orifice into the left atrium. Sampling at greater depths results in spectral broadening, decreased diastolic flow velocities, and loss of phasic characteristics of systolic flow.

Pulmonary Vein Size

One potential factor affecting reproducibility of pulmonary vein inflow velocities is variation of

the vein orifice size during the cardiac cycle. Studies of vein dimensions and flow humans have not demonstrated this to be a substantial factor under physiologic conditions. However, in comparisons between mitral and pulmonary vein flow velocities, this factor must certainly be considered.[52]

Clinical Applications of Doppler Techniques for Assessing Diastolic Function

Transmitral and Pulmonary Vein Recordings: A Combined Approach

From the preceding discussion, it should be clear that no single noninvasive or catheterization-derived parameter can be used to describe the complex nature of diastolic function. As with systolic measures of performance, there are general descriptors (e.g., ejection fraction) and more specific measurements (e.g., Vmax , dP/dt, and mean velocity of circumferential fiber shortening [Vcf]) that define the process of contractility in greater detail. Each measurement must be evaluated in the context of the clinical situation so that modifiers such as age, loading conditions, and volume status can be included. Since the 1980s, diastolic dysfunction has become increasingly recognized as an important part of many clinical syndromes.Consequently,Doppler echocardiography has been recognized as a readily available tool for evaluating left ventricular filling and has given the clinician a method for better understanding these events. However, it must be recognized that the diagnosis of diastolic abnormalities is not routine and requires significant effort and knowledge, even for the experienced echocardiographer. In specific disease states, Doppler variables have provided a conceptual framework for understanding pathophysiology without necessitating cardiac catheterization. Recordings of transmitral and pulmonary vein flows, along with isovolumic relaxation time, should be evaluated in context with other two-dimensional echocardiographic information to best apply these techniques. For example, in the assessment of left ventricular filling, the thickness, cavity size, and systolic function, as well as left atrial size, should be assessed. In other settings, the Doppler data may provide more subtle clues that are helpful in distinguishing restrictive from constrictive processes. Thus, although the Doppler information represents a significant advance in the field, its use for detecting abnormal hemodynamics may still be considered part of the "art of medicine." More recent studies also suggest

that these noninvasive indices may give insight regarding the prognosis of various heart diseases.[53]

Characteristic Doppler Findings in Various Stages of Diastolic Dysfunction

	Normal (young)	Normal (older)	Delayed Relaxation	Pseudonormal Filling	Restrictive Filling
E/A	>1	≥1	<1	1–2	>2
DT, msec	<220	<220	>220	150–200	<150
IVRT, msec	<100	<100	>100	60–100	<60
S/D	<1	≥1	≥1	<1	<1
AR, cm/sec	<35	<35	<35	≥35	≥25
V_p, cm/sec	>55	>45	<45	<45	<45
E_m, cm/sec	>10	>8	<8	<8	<8

Modified from Garcia MJ, Thomas JD, Klein AL: J Am Coll Cardiol 1998;32:872

Newer Doppler Echocardiographic Approaches to Diastolic Function

Two-Dimensional Left Ventricular Volume Methods

Echocardiographic methods have been described to assess the time course of diastolic changes in left ventricular volume and dimension. M-mode methods are limited by the need for geometric assumptions to calculate volume and inaccuracies introduced by regional wall motion differences. Traditional two-dimensional techniques require off-line manual tracing of imprecise borders from multiple stillframe images. The frame rate produced at usual scanning depths (around 30 per second) is also slow relative to the instantaneous changes that occur during the isovolumic time period. As a result of these problems, alternative methods have been developed. Research in this area has led to the development of computer-assisted automated border detection algorithms. By differentiating between ultrasound backscatter from myocardium and low-energy reflectances from blood within the left ventricular cavity, these systems can track the motion of the endocardial edge throughout the cardiac cycle. Commercially available programs currently include a real-time assessment of area, volumes, and rate of change within a region of interest . The accuracy of this method compares well with manual edge tracing and has been validated in studies using radionuclide and cineangiography standards. The main advantage of these methods of quantitation is the on-line availability of data. Comparisons

between Doppler and acoustic quantitation in diastolic measurements of the rapid filling and atrial filling phases have shown significant correlations[54]. Therefore, this method has potential uses in evaluating left ventricular filling. However, the technique is gain dependent and requires significant operator experience to acquire reproducible data, especially in patients with characteristics that lead to less than ideal image quality.[55]

Color M-Mode Doppler Echocardiography

Several investigators have described a new method for relating ventricular inflow velocities to left ventricular relaxation. This method uses color M-mode Doppler echocardiography from apical windows, directed along the longitudinal axis of inflow from mitral valve to apex. The recording typically shows the two waves (early filling and atrial contraction) of flow propagation from the base toward the apex. The slope of the early filling wavefront has been shown to represent the presence of intraventricular gradients produced from active recoil (suction) of the ventricular myocardium. The velocity of streamlined flow propagation into the ventricle (Vp) is therefore described along the M-mode line by the slope of the color wavefront, in centimeters per second. Measurements of Vp have now been successfully obtained using either the leading edge (transition from black to color) or by tracing along any isovelocity line.

More reproducible measurements can be obtained by

(1) adjusting the color scale or baseline shift to produce color aliasing,

(2) tracing the slope of the first aliasing velocity line,

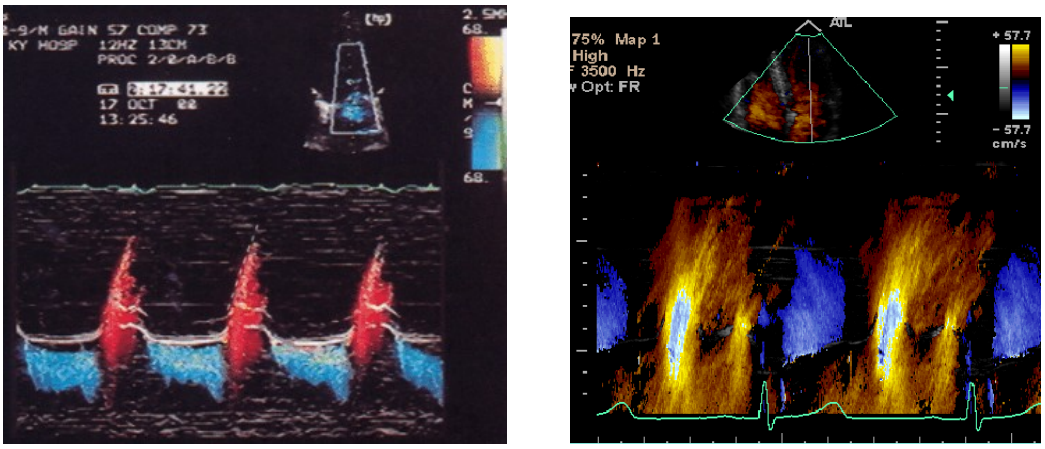
(3) tracing the slope from the mitral leaflet tips to a position 4 cm distally into the left ventricle, and

(4) avoiding intracavity flow originating before mitral opening.

The method may not be applicable to patients with tachycardia, arrhythmia, or heart block. Young, healthy individuals generally have Vp greater than 55 cm per second, whereas older people have Vp greater than 45 cm per second. Patients with abnormal transmitral filling patterns such as delayed relaxation, restrictive or pseudonormal, will generally have Vp less than 45 cm per second.

Thus, when combined with other Doppler parameters, measurement of early filling by color M-mode may be useful in distinguishing pseudonormal from normal patterns. This method appears to be less affected by preload than transmitral or pulmonary vein flow. For example, a "pseudonormal" transmitral flow pattern can be produced by increased left atrial pressure in otherwise normal patients. A blunted S wave is commonly seen in young people (especially athletes) in whom the left atrium is functioning as a "passive conduit" and can masquerade as restrictive filling pattern. These situations may be clarified by examining the color M-mode slope during the early filling phase.[56]

- PCWP = 4.5 Ã— [10^3/(2 Ã— IVRT) + Vp] - 9
- PCWP = (5.27 Ã— E/Vp) + 4.6



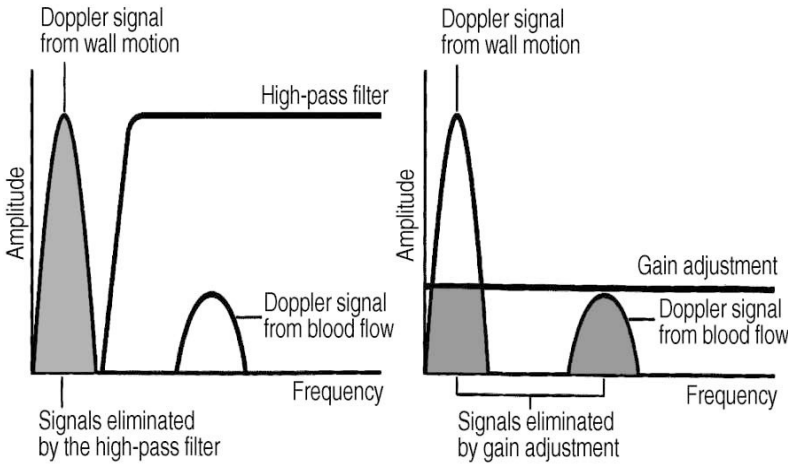
Color M-mode Doppler recording of diastolic flow toward the apex from the four-chamber view.

Tissue Doppler imaging (TDI)

TDI is a new ultrasound technique that is based on color Doppler imaging principles and allows quantification of intramural myocardial velocities by detection of consecutive phase shifts of the ultrasound signal reflected from the contracting myocardium. Doppler tissue imaging uses the same principles as colour flow Doppler mapping, applying standard autocorrelation processing but reversing high velocity and low amplitude filters such that the high amplitude/low velocity motion of tissue is displayed in preference to blood flow. [58]

Principles of Tissue Doppler Imaging

Unlike conventional Doppler signals that are typified by high velocity and low amplitude, myocardial motion is characterized by relatively low velocity and high amplitude signals. To record low wall motion velocity, gain amplification is reduced and high pass filters are bypassed with the tissue signal directly entered into the autocorrelator. The thresholding and filtering algorithms are changed to reject the low-amplitude echoes from the blood pool. As cardiac structures move in a velocity range 0.06 to 0.24 m/s, some 10 times slower than myocardial blood flow, and have an amplitude approximately 40 decibels higher, it is possible to obtain images of tissue Doppler motion of high resolution without significant artifact originating from the blood pool. During image acquisition, it is important to optimise the frame rate using an image sector as narrow as possible and to select the appropriate velocity scale.



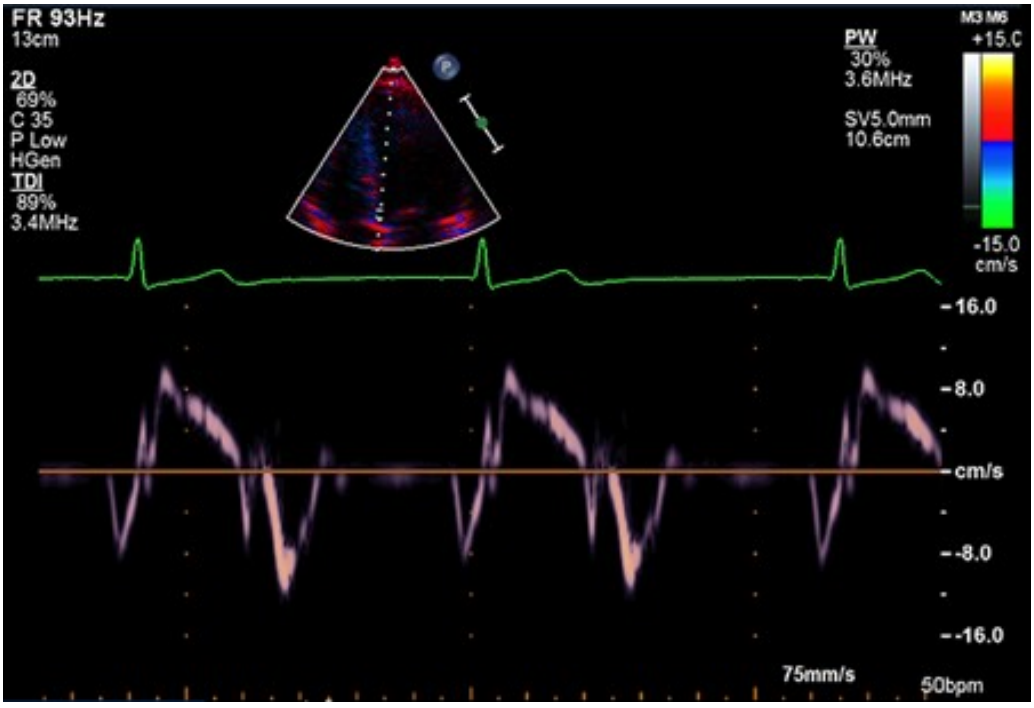
Principle of conventional Doppler. High amplitude myocardial wall signals are eliminated by high pass filter. Right: Doppler signals from myocardial wall are extracted, blood flow signals are eliminated

Modalities of Tissue Doppler Imaging

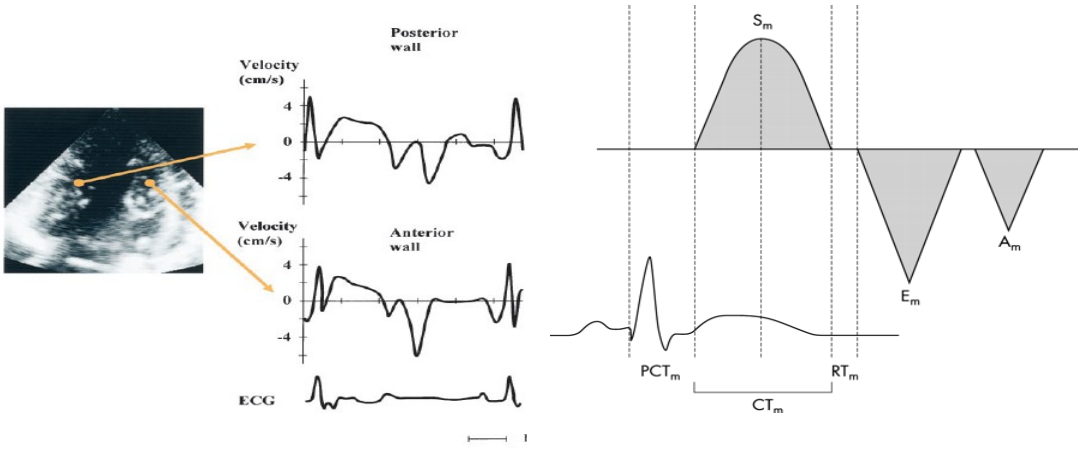
TDI has three modalities: spectral pulsed wave Doppler, two dimensional, and M mode colour Doppler.

Pulsed Spectral Doppler

Spectral pulsed TDI has the advantage of online measurements of velocities and time intervals and an excellent temporal resolution (8 ms). According to the Doppler principle[8], tissue velocities moving toward the transducer are positive, whereas velocities moving away from the transducer are negative. The spectral PW-TDI method provides higher temporal resolution and resolves all peak velocities. With this modality a sample volume is placed within the myocardium (either in the endocardium or the epicardium) and the low Doppler shift of frequencies recorded from the heart wall moving through the sample volume during the cardiac cycle is recorded. The pattern can be divided into two parts systolic and diastolic, from which several measurements can be obtained: 1. The systolic phase is characterized by a positive wave (S) preceded by the time taken for regional isovolumic contraction (RIVCT); 2. The diastolic phase, which is complex, is composed of 4 periods: a) regional isovolumic relaxation (RIVRT); b) the rapid filling period characterized by a negative wave (Ea); c) diastasis, and d) filling due to atrial contraction, represented by a second negative wave (Aa). [59]



Schema of the tissue Doppler imaging pattern of the left ventricular mitral annulus. A_m, late diastolic wave; CT_m, myocardial contraction time; E_m, early diastolic wave; PCT_m, myocardial precontraction time; RT_m, myocardial relaxation time; S_m, myocardial systolic wave.

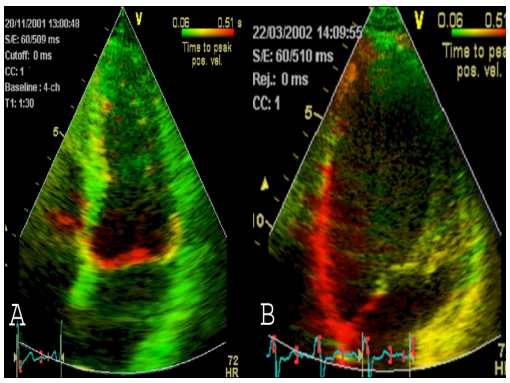


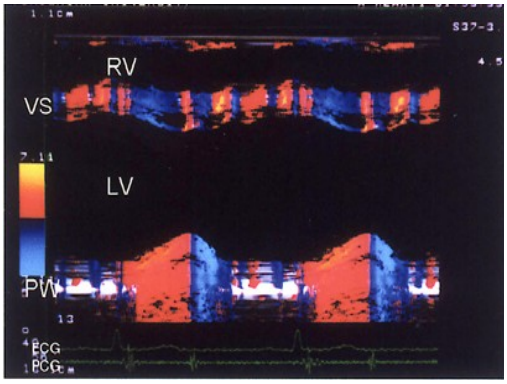
Colour Doppler and M Mode

In colour TDI, red encodes wall motion towards the transducer (positive velocities), whereas blue encodes wall motion away from the transducer (negative velocities). On each side of the scale, the brightest shades correspond to the highest velocities. Colour images require digital acquisition and storage for off-line post-processing analysis. In contrast to spectral Doppler, endocardial and epicardial layers can be separately analyzed. Peak and mean velocities, time velocity integral, and regional time intervals can be measured in each myocardial segment, in each myocardial layer, and in each phase of the cardiac cycle. [60,61]

M mode colour encoded TDI has a high temporal resolution (5–10 ms). Colour two dimensional imaging has been limited by a slow frame rate, but parallel processing and advances in beam formation technology have increased the frame rate to a level adequate for analysis of most cardiac events (temporal resolution 10–100 ms)

Color Doppler **M- Mode**

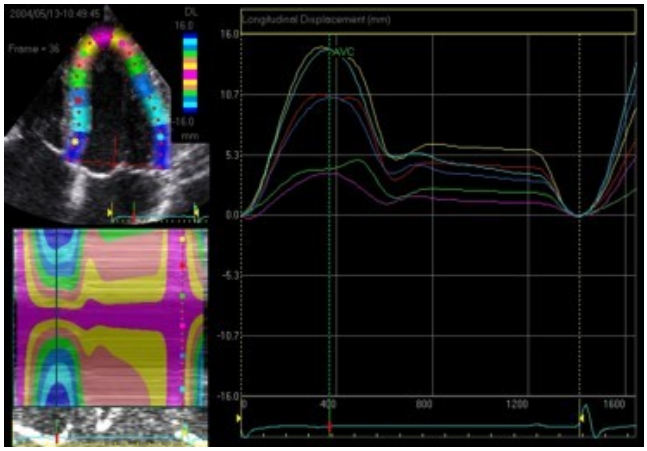




Strain and Strain Rate Echocardiography

Strain and strain rate are TDI derived modalities that are now available in real time. Strain rate measures the rate of deformation of a tissue segment. Peak systolic strain rate represents the maximal rate of deformation in systole. An algorithm calculates spatial differences in tissue velocities between neighbouring samples within the myocardium aligned along the Doppler beam. A sample distance of 5 to 11 mm has been previously used. Strain is obtained by integrating strain rate over time and represents deformation of a tissue segment over time. Strain is expressed as the per cent change from the original dimension. Systolic strain represents the magnitude of deformation between end diastole used as a reference point and end systole. [62]

Systolic strain is positive and blue encoded when there is regional expansion. This is thickening in parasternal views and lengthening in apical views. Negative systolic strain is yellow to red encoded to denote regional compression, which is thinning in parasternal views and shortening in apical views. Infarcted myocardial tissue does not demonstrate shortening or lengthening activity and shows no or minimal systolic strain rate or strain, which is displayed as green. The technique of raw data storage and reconstruction permits the measurement of tissue velocity, peak systolic strain rate, peak early and late diastolic strain rate, and peak systolic strain from the same sample volume within the same cardiac cycle. Simultaneous interrogation of multiple myocardial segments and curved M mode colour display are also applicable to strain and strain rate[63].



Strain and Strain Rate Imaging

Detection of Ischemia Using TDI

Experimental and clinical studies have shown that during acute ischemia, myocardial peak systolic velocity and strain rate were notably reduced or reversed within 5 seconds after coronary occlusion and were delayed. In addition, there was positive velocity after the end of ejection [Post systolic velocity]. Post-systolic shortening or thickening can be easily recognised by pulsed tissue doppler imaging and high velocity, strain rate or strain occurring during the isovolumic relaxation period, often extending into the early filling period.[64,65]

REVIEW OF LITERATURE

Myocardial Ischemia

Several studies have demonstrated that acute coronary occlusion results in diastolic dysfunction. Most studies have used Doppler indices recorded before and during angioplasty in patients with angina as the clinical model for evaluating the effects of ischemia on diastolic function.

Wind et al reported an increased proportion of left ventricular filling during late diastole and a decreased E/A ratio in 34 patients with normal global systolic function who underwent Doppler echocardiographic examination 1 day before and 1 day after coronary angioplasty for angina. These findings were thought to be consistent with impaired relaxation, as previously reported from radionuclide scans in coronary angioplasty patients. The authors provided indirect evidence that the abnormal diastolic indices were due to a prolongation of IVRT, although this was not directly measured.

Labovitz et al investigated 32 patients during coronary angioplasty and found that evidence of diastolic left ventricular dysfunction was the earliest change during coronary occlusion with the balloon, preceding electrocardiographic changes, chest pain, or systolic wall motion abnormalities. Impaired relaxation was the pattern most often exhibited and occurred within 15 seconds of balloon inflation but returned to baseline by 15 seconds after deflation.

Masuyama et al also found a reduction in peak E-wave velocities and E/A ratio in serial Doppler echocardiographic studies of patients undergoing percutaneous transluminal coronary angioplasty to be a strong predictor of significant coronary restenosis. [66,67]

The most complete comparison of hemodynamic and Doppler indices of diastolic function in patients with coronary disease has been performed by **Stoddard et al.** Their study evaluated the relationship of chamber stiffness and relaxation (tau) to the traditional transmitral indices in 35 patients undergoing diagnostic catheterization for chest pain. Subjects without coronary artery disease and with normal relaxation were found to have a direct correlation between increasing chamber stiffness and enhanced early filling velocities. Conversely, the group with coronary disease showed a significant indirect correlation between impaired relaxation and decreased peak E velocity. Although their findings

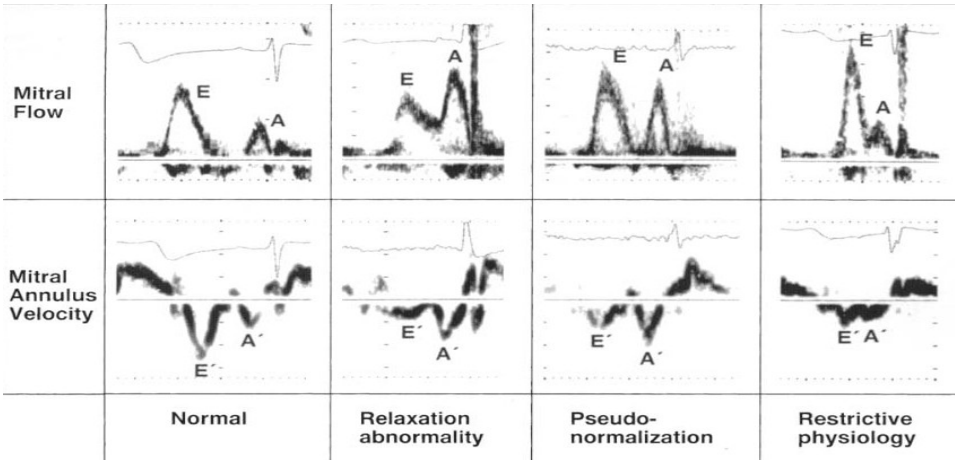
differ from those of previous studies in that a variety of patterns of transmitral flow were found, they are consistent with early observations by other investigators. The authors concluded that chamber stiffness has a greater influence than relaxation on the pattern of diastolic filling in patients without coronary disease. In contrast, abnormal relaxation appears to be the predominant factor influencing the Doppler pattern in patients with coronary disease and an abnormal tau value.[68,69]

El-Said et al studied the effects of ischemia on left ventricular filling using Doppler transmitral flow recordings during dobutamine stress echocardiography. Their data showed marked decreases in peak E velocities (-22%) and time to peak E acceleration (-28%) in ischemic subjects, whereas 10 control subjects had an increase in both values (+33% and +75%, respectively; $P < .0001$). There was no overlap in the percentage change from baseline to peak dobutamine stress values between normal subjects and patients who had documented singlevessel coronary disease. The authors also found diastolic abnormalities to be more sensitive than induction of wall motion abnormalities for detecting coronary stenoses. Thus, the transmitral Doppler pattern of impaired relaxation appears to be the type most often seen in association with acute (or induced) myocardial ischemic syndromes.[70]

Fujii et al showed a reduced E/A ratio and prolonged deceleration time to be common in patients with a history of infarction, regardless of location. Other studies comparing inferior with anterior infarct patients have suggested that transtricuspid Doppler echocardiographic recordings may be more sensitive in demonstrating abnormal filling and high right ventricular end-diastolic pressures. One study also suggests a significant relationship among infarct size, degree of systolic dysfunction, and restrictive transmitral flow patterns. This pattern is seen more often in coronary artery disease patients with a worse functional class and poorer prognosis. However, larger studies specifically designed to assess the clinical applicability of Doppler filling patterns in this population are currently not available.[71]

A recent study by **Sohn et al** has shown Em values from tissue Doppler echocardiograms to

correlate well with tau as measured during catheterization and to be relatively unaffected by preload changes induced by volume infusion and nitroglycerin. Patients with pseudonormal filling were separated from normal by an Em velocity of less than 8.5 cm per second and an Em/Am ratio less than 1, with a sensitivity of 88% and a specificity of 67%. Thus, the combination of transmitral flow patterns and color M-mode and tissue Doppler measurements may be helpful in distinguishing patients in various stages of diastolic dysfunction.



Patterns of mitral annulus velocity as recorded by Doppler tissue imaging, with sampling of the septal side of the mitral annulus from the apical view.

Estimation of Left Ventricular Filling Pressures

As described previously, various Doppler echocardiographic indices of transmitral and pulmonary vein flow have been combined to predict left atrial pressure. Similarly, by combining transmitral E wave velocities with a preload-independent parameter such as the velocity of motion of the lateral mitral annulus (Ea), a reasonable estimate of left atrial pressure can be obtained.

Nagueh et al found that an E/Ea ratio of greater than 10 correlated well with a mean pulmonary capillary wedge pressure of greater than 15 mm Hg. The correlation coefficient was 0.87 in 60 patients who had hemodynamic measurements, with the relationship described by the following equation:

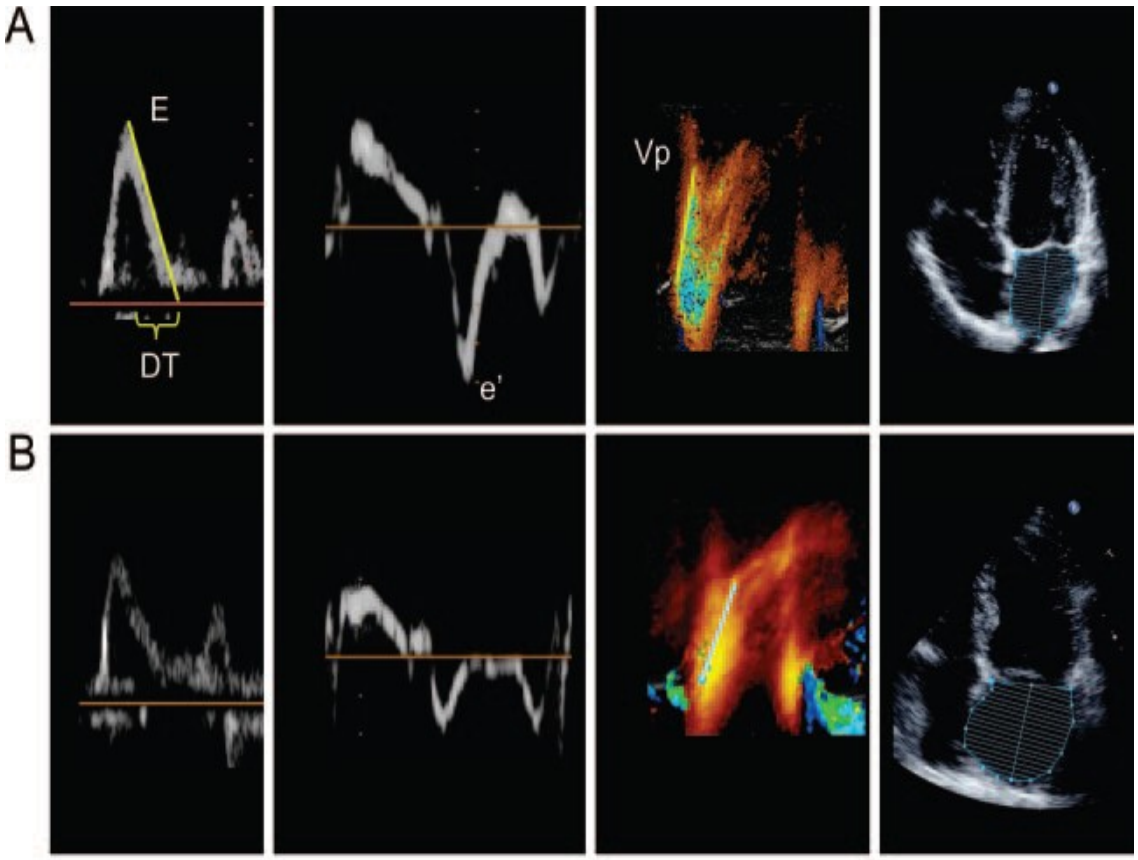
$$PCWP\ (mm\ Hg) = 1.24[E/Ea] + 1.9$$

The authors proposed that left ventricular filling pressure can be estimated (with a 95%

confidence level of ± 7.6 mm Hg) from these two simple Doppler measurements.

These findings have recently been confirmed by **Ommen et al**. Their study consisted of 100 consecutive patients who underwent catheterization with micromanometer-tipped catheters and simultaneous Doppler measurements. A ratio of E/E' (or E/Ea) greater than 15 identified patients with elevated LVEDP greater than 12 mm Hg, whereas an E/E' ratio less than 8 accurately predicted normal pressures. Patients with ratios between 8 and 15 had widely variable ventricular diastolic pressures. The authors also noted that, in their experience, adequate signals were more often obtained from the medial or septal portion of the annulus. Although there are currently few such data available, these early and well conducted investigations are highly suggestive that the combination of tissue Doppler and mitral inflow velocities can be used to noninvasively estimate left ventricular filling pressures.[72]

Acute myocardial infarction (AMI) is characterized by regional myocardial damage that may lead to systolic and diastolic dysfunction with a subsequent risk of left ventricular (LV) remodeling, local and systemic neurohormonal activation, and vascular dysfunction. The pathophysiology and prognosis of LV systolic dysfunction after AMI have been the focus of research for several decades. Insights from these studies have led to several therapeutic interventions that improve outcome. In addition to depressed systolic function, clinical or radiographic evidence of heart failure is a consistent and powerful predictor of outcome in patients after AMI. Pulmonary congestion after infarction reflects raised LV filling pressures but is frequently seen after what appears to be only minor myocardial damage. The pathophysiological mechanism for this is incompletely understood but may involve impaired active relaxation of the myocardium and increased LV chamber stiffness and hence abnormalities in diastolic function. If these are to be determined directly, cardiac catheterization with assessment of pressure volume relationships with the use of high-fidelity micromanometer catheters is required. This highly specialized approach is not suitable for daily clinical practice.



	PW mitral inflow	Tissue Doppler	Color M - mode	LA volume
	Normal	Grade 1	Grade 2	Grade 3
PW-Doppler	DT 140-240 ms E/A 0.75-1.5	DT >240 ms E/A <0.75	DT 140-240 ms E/A 0.75-1.5	DT <140 E/A >1.5
Color M-mode	Vp >0.45	Vp ≤0.45	Vp ≤0.45	Vp ≤0.45
Tissue Doppler	E/e´ <15	E/e´ <15	E/e´ ≥15	E/e´ ≥15
LA pressure	Normal	Normal	Moderately increased	Severely increased

Likewise, although direct measurements of LV end-diastolic pressure are important predictors of adverse outcome after AMI in selected populations, the risk of complications precludes routine use of indwelling catheters in all patients. There has therefore been considerable interest in using noninvasive estimates of diastolic function, particularly Doppler echocardiographic assessment of LV filling dynamics and, more recently, the volume of the left atrium (LA), to predict outcome in patients with AMI.[74]

The objective of this review is to summarize the current understanding of abnormal LV filling in the early phase after AMI with focus on the complementary prognostic information that may be gained by assessment of LV filling dynamics and LA volume with the use of 2-dimensional and Doppler echocardiography.

After an AMI, myocardial ischemia, cell necrosis, microvascular dysfunction, and regional wall motion abnormalities will influence the rate of active relaxation. In addition, interstitial edema, fibrocellular infiltration, and scar formation will directly affect LV chamber stiffness. Thus, abnormalities in LV filling are common in this setting.

Spectral Pulsed-Wave

Doppler Echocardiography

The pulsed-wave Doppler technique allows assessment of flow velocities (2 m/s) at a distinct spatial position, making the technique suitable for assessment of changes in inflow velocities across the mitral valve during diastole. With mitral valve opening, the early inflow velocity will be determined largely by ventricular suction and the pressure gradient between the LA and LV.5–7 This is followed by a steady decrease in inflow velocity, with a normal duration of 140 to 240 ms (early mitral deceleration time [DT]). After a period of diastasis, atrial contraction will cause a new increase in inflow velocity less than that of the early inflow; thus, the ratio of early to atrial inflow velocities (E/A ratio) will usually be 1 to 1.5. If active relaxation is impaired, the early mitral inflow velocity will

decrease, increasing the atrial contribution to filling, resulting in a reversal of the E/A ratio and a prolonged DT. This “impaired relaxation” pattern, indicative of grade 1 diastolic dysfunction, is usually associated with normal LV filling pressure With worsening of diastolic dysfunction, LA pressure increases, and the gradient between the LA and LV at mitral valve opening increases; hence, the velocity of early inflow will increase even though relaxation is impaired. Because of rapid equilibration, early ventricular filling is terminated abruptly, causing a shortening of the time period during which early filling occurs; hence, DT returns to normal. Therefore, the combination of delayed relaxation and elevated LA pressure may create an apparently normal transmitral inflow pattern that has been termed pseudonormal (grade 2 diastolic dysfunction) . With further deterioration, early filling will terminate abruptly because of the increase in LV stiffness. The DT will be abnormally short and the E/A ratio will be high, a pattern termed restrictive (grade 3 diastolic dysfunction) .The restrictive filling pattern can be subdivided further as reversible, if preload reduction, accomplished either by treatment or by the Valsalva maneuver, causes reversal of the filling pattern to the nonrestrictive pattern, or irreversible, if preload reduction causes no reversal of the filling pattern. In patients with previous AMI, short DT (<140 ms) is associated with elevated LV filling pressures, even in the presence of atrial Fibrillation and irrespective of the severity of mitral regurgitation. In contrast, DT >140 ms, especially in patients with preserved LV systolic function, correlates poorly with filling pressures. Although transmitral filling patterns are fundamental to the assessment of LV diastolic function, they have several limitations. They may change rapidly with variations in preload. Pseudonormalization of the inflow pattern despite moderate elevation of filling pressures is a further major shortcoming. To overcome this, less load-dependent indices of LV filling can be used, usually in combination with transmitral parameters. These may include assessment of the pulmonary venous flow pattern. This, however, is difficult to obtain in all patients18 and is greatly affected by heart rhythm. Thus, other techniques have been developed. The most extensively validated of these are the determination of blood flow propagation within the LV with the use of color M-mode and tissue

Doppler assessment of mitral annulus motion during diastole[75]

Spectral Pulsed-Wave Tissue

Doppler Echocardiography

The motion of myocardium during the cardiac cycle can be displayed as a spectral pulsed-wave Doppler image, in which the signal will reflect the movement of myocardium parallel with the Doppler cursor. Because the apex of the LV is relatively fixed throughout the cardiac cycle and the motion of the LV base is nearly parallel with the long axis, assessment of the movement of the basal LV segments reflects the longitudinal vector of contraction and relaxation. Early diastolic mitral annulus velocity (Ea) is a useful indicator of LV relaxation. Invasive studies have demonstrated that Ea correlates inversely with invasive indices of relaxation. In the presence of low (<0.1 m/s) velocities, Ea is less affected by changes in preload and may be used to identify pseudonormal LV filling. Using the ratio of peak mitral E-wave velocity to early mitral annulus velocity (E/Ea), numerous studies have demonstrated a good approximation of LV filling pressures. This relationship has been validated in the presence of atrial fibrillation, sinus tachycardia, preserved or depressed LV systolic function, secondary mitral regurgitation, and LV hypertrophy.

Ommen et al demonstrated that E/Ea -15 accurately detects elevated filling pressures, and E/Ea -8 accurately detects normal LV filling pressures. However, because the Doppler method tracks the velocity of movement, tissue Doppler cannot separate active contraction from passive tethering. Annular velocities vary depending on the location sampled, with the velocity of the lateral annulus usually higher than that of the septal annulus. This has led to controversy about which site should be used. Local myocardial damage may affect the mitral annular velocity, which may be a theoretical disadvantage of this measurement in AMI.

E/Ea = 18 ± 12 (cm/s) in the Anterior AMI group;

E/Ea = 16 ± 10 (cm/s) in the Posterior AMI group;

E/Ea = 8 ± 2 (cm/s) in the control group.

Tissue Doppler or Color M-Mode for Assessment of LV Filling?

Although different in methodology, both tissue Doppler and color M-mode are relatively preload insensitive, allow estimation of filling pressures with reasonable accuracy, and facilitate identification of the pseudonormal LV filling pattern. In patients with small LV cavities due to hypertrophy, tissue Doppler is preferred because of pseudonormalization of Vp. Although Vp has a good reproducibility for distinguishing normal from abnormal, the reproducibility of Ea is superior. In assessment of filling pressures and detection of pseudonormal LV filling, most studies but not all that have compared the techniques have favored E/Ea. Thus, the better reproducibility and lesser dependence on LV geometry make tissue Doppler echocardiography Ea measurement the preferred technique.

Relation between LV Filling Pattern/LA Size and Prognosis after AMI

The prognostic importance of a restrictive filling pattern after AMI was initially reported by **Oh et al** in 1992. In a cohort of 62 patients, a restrictive filling pattern was associated with a high occurrence of in-hospital congestive heart failure.

This was confirmed by **Poulsen et al** 52 in an age-selected population with a first AMI in which Doppler echocardiography was performed within 1 hour of hospital admission.

In 1997, **Nijland** et al reported in a study of 95 patients with first AMI those DT <140 ms was associated with a 22% survival rate at 3 years compared with 100% in the nonrestrictive group. Although the study was limited by a small number of deaths (n=8), this finding has subsequently been confirmed in several studies. In these studies, patients with a restrictive filling pattern have been characterized by higher age, more advanced LV systolic dysfunction, and a high risk of in-hospital heart failure. A restrictive filling pattern seems to have the same prognostic importance in Stand non–ST-segment elevation AMI and in patients treated with thrombolysis or primary angioplasty. Although

the results of those studies have been strikingly similar, many have been limited by small populations and few events. However, in 799 patients with assessment of LV filling within 6 days of AMI, DT <140 ms was a predictor of all-cause mortality. However, a large study among 520 patients with ST-segment elevation AMI treated with fibrinolysis enrolled in the ATTenuation by Adenosine of Cardiac Complications (ATTACC) study failed to find an independent prognostic importance of restrictive filling. Restrictive filling was defined by either DT <140 ms or E/A ratio >2. Data on the number of patients screened for possible enrollment in this study were not provided. However, in the group in which echocardiography was performed between day 2 and 10, 1-year mortality rate was only 6.2%, lower than the 10.5% among all 608 patients enrolled in the study. Thus, selection bias, with exclusion of patients at highest risk, may account for the discrepant result. This is underscored by a relatively small percentage (10%) of patients with DT <140 ms. Although the impact of a restrictive filling pattern on outcome after AMI has been studied extensively, less is known about milder forms of abnormal filling. In a previous prospective study of 125 post-AMI patients, pseudonormal filling was diagnosed when DT appeared normal (140 to 240 ms) and Vp was decreased < 45 cm/s.Those patients with an apparently pseudonormal filling pattern were characterized by a high occurrence of in-hospital heart failure and poor outcome. Although these patients were older and frequently had complicating heart failure, LV systolic function assessed by LV ejection fraction (LVEF) was relatively preserved (mean 0.50). In contrast to the restrictive and pseudonormal patterns, there is little evidence that mild diastolic dysfunction is an independent risk factor after AMI. In some studies, univariate analysis has suggested increased mortality among patients with impaired relaxation; however, this has not remained the case in multivariate analysis after adjustment for age, LV systolic function, and Killip class. Because filling pressures are generally normal in patients with impaired relaxation, this suggests that it is the elevation of filling pressure that is the important link between diastolic dysfunction and prognosis.

ASSESSMENT OF LEFT VENTRICULAR DIASTOLIC DYSFUNCTION BY TISSUE DOPPLER IMAGING IN ACUTE MYOCARDIAL INFARCTION

AIM

The aims of this study were;

1. To assess the left ventricular diastolic dysfunction by tissue doppler imaging in acute myocardial infarction
2. To assess the clinical correlation with the tissue doppler imaging

METHODS

Selection of the study group

This was a prospective study done between May 2006-September 2007 at the Department of Cardiology, Government Rajaji hospital, Madurai. We had enrolled 100 patients who were referred to our department for the management of acute myocardial infarction

Patients with chest pain with features of acute myocardial infarction were eligible for the study if they did not meet any of the following excluding criteria: hemodynamically significant valvular heart disease, congenital heart disease, previous myocardial infarction, unstable angina, pressure or volume right ventricular overload, permanent pacemaker and abnormal atrioventricular pathways. (Table.1)

The study group consisted of 100 patients with acute myocardial infarction including 78 males

and 22 females after informed consent for study and approval of institutional ethical committee.

Mean age of the patients was 54.07±5.5 (27 to 74), 78(78%) were males, 22(22%) were females in this study. Totally 72 patients were thromb olysed including 46 patients with anterior wall infarction and 26 patients with inferior wall infarction.Of the 28 non-thrombolysed patients,19 patients were with anterior wall infarction and 9 patient were with inferior wall infarction. Totally there were 65 anterior wall infarction and 35 inferior wall infarction.Median delay of thrombolysed patients was 7±1.5 hrs (5.5 to 8.5 hrs).Most common cause for non-thrombolysis was median delay more than 12 hrs.

All the selected patients underwent standard Doppler and TD echocardiography and TEE of pulmonary veous flow.All patients were classified into thrombolysed and not thrombolysed

Standard Doppler echocardiography and Tissue Doppler Imaging.

Standard Doppler echocardiograms and pulsed TD were performed with the subjects in partial left decubitus, using the Aloka SSD-4000 model equipped with a variable-frequency phased-array transducer, TEE probe and TD capabilities. Two D-guided, M-mode LV analysis and Doppler recording of the LV transmitral diastolic inflow was performed as previously described. The LV mass was calculated using the criteria of the American Society of Echocardiograph and normalized for body height. The two-dimensional LV end-diastolic and end-systolic volumes were calculated using the Simpson method and the LV ejection fraction was calculated using the following formula: **end-diastolic volume end-systolic volume/end-diastolic volume x 100.**

Pulsed TD was performed at transducer frequencies of 3.5-4.0 MHz, adjusting the spectral pulsed Doppler signal filters to obtain the Nyquist limits of 15 and 20 cm/s, and using the minimal optimal gain. In the apical 4-chamber view, the pulsed Doppler sample volume was subsequently placed septal side mitral annulus.

The apical 4-chamber view and parasternal short axis views were chosen to obtain the quantitative assessment of the regional myocardial wall motion. The apical 4-chamber view was used to measure transmitral flow velocity parameters and tissue Doppler mitral annulus

velocity parameters. The continuous wave beam is directed from the apical five-chamber view across the region between the aortic outflow tract and the mitral inflow tract to measure the IVRT. The Doppler echocardiographic spectrum in this position includes aortic valve flow with valve closure and the onset of mitral inflow, so that the aortic closure-mitral opening interval can be determined The following TD measurements were determined as indexes of regional myocardial function: myocardial systolic peak velocity (Sa, m/s), and myocardial early (Ea m/s) and atrial (Aa m/s) peak velocities (m/s) and their ratios, as diastolic measurements by placing the sample volume in the septal aspect of mitral annulus .Our TDI methods and reproducibility have been previously described.Transpulmonary venous flow pattern parameters were obtained from TEE at 45-65^0 short axis view placing the sample volume 1 cm within the left upper pulmonary vein for better delineation of waveforms.

Patient's clinical data were analyzed in relation to the Doppler data in routine transmitral flow parameters, transpulmonary flow parameters and mitral annulus tissue doppler velocity parameters.

Filling Pattern in Diastolic Dysfunction – Appletion and Hatle et al

Pattern	E/A ratio	Deceleration time (ms)	IVRT (ms)	S/D	AR (cm/sec)
Normal	2 : 1	180	76	1.0	19
Age > 50 years	1 : 1	210	90	1.7	23
Impaired relaxation	<1.2	>220	>100	>1.0	<35
Pseudo Normal	1.0 – 2.0	150 – 200	60 – 100	<1.0	>35
Restriction	>2.0	<150	60	<1.0	>35

Statistical analysis

Variables were presented as mean ± 1 SD. Analysis of variance was performed to estimate intergroup differences. Linear regression analyses and partial correlation testing using Pearson's method were used to assess univariate relations. The null hypothesis was rejected for $p < 0.05$.

Results:

In this study there were 59% smokers, 28% type 2 DM, 31% systemic hypertension,11% family history of CAD and 28% dyslipidaemia. The demographic characteristics of the groups are listed in

table 2. There were no differences in gender, age, body mass index, heart rate and blood pressure. The results of Doppler echocardiographic analysis are reported in table 3.

Table 3.Doppler echocardiographic analysis and ejection fraction

Parameters	Impaired relaxation Pattern (n =17)	Pseudonormal Pattern (n=38)	Restrictive pattern (n=45)
E(cm/s)	52±4	84±6	96±7
A(cm/s)	76±3	62±5	48±6
E/A	0.68±0.16	1.39±0.14	1.99±0.15
DT(msec)	234±12	166±14	135±11
IVRT(msec)	116±9	84±8	56±7
Ps/Pd	1.3±0.2	0.74±0.3	0.68±0.2
Pa(cm/s)	–32±3	–43±5	–48±6
(Pa-dur)—(Ma-dur) (msec)	–32±6	+36±4	+40±5
EF %	48±13	45±15	40±14

Conventional transmitral and pulmonary venous flow showed impaired relaxation filling pattern in 17 patients, pseudonormal filling pattern in 38 patients and restrictive filling pattern in 45 patients. There was no linear relationship between ejection fraction and severity of pattern abnormality. Even the patients with normal EF had severe form of diastolic dysfunction.

The DT value less than 140 msec was significantly associated with increased morbidity and mortality with hazard ratio of 2.4 (95% CI 1.2 to 3.6). Likewise the IVRT value less than 60 msec was also a marker for increased morbitity and mortality with relative risk of 2.1(95% CI 1.5 to 2.7). Totally there were 25 symptomatic patients due to diastolic dysfunction. Most of symptomatic patients had restrictive pattern of diastolic filling, 15out of 25 symptomatic patients had restrictive pattern of filling with E/Ea value more than 15(60%)$p<0.005$.

Transpulmonary venous flow doppler pattern in TEE showed impaired relaxation in 17 patients, pseudonormal pattern in 38 patients and restrictive pattern in 45 patients. In patients with pseudonormal pattern in transmitral and transpulmonary flow pattern, diffentiation from normal pattern was consistently and reproducibly possible with the tissue doppler imaging .If Ea value was less than

that of Aa value, the absolute Ea value less than 8 and if E/Ea more than 15 then the pseudonormal pattern was confirmed.

Table 4.Tissue Doppler annular velocities parameters: n=100

Parameters	Impaired relaxation pattern (n=17) 17%	Pseudonormal filling pattern (n=38) 38%	Restrictive filling pattern (n=45) 45%
Ea(cm/s)	7.2±2.2	6.3±1.7	5.2±1.6
Aa(cm/s)	9.1±3.1	7.3±2.8	4.4±1.8
Ea/Aa	0.78±0.2	0.86±0.3	1.25±0.28
E/Ea	7.43±2.3	14.2±2.6	18.4±3.3
Sa(cm/s)	8.1±3.4	6.3±2.7	6.1±1.3

The absolute Ea , Aa and Sa values did not correlate with degree of diastolic dysfunction. E/Ea ratio was very much reliable indicator of elevated PCWP/LVEDP. It was well correlated with clinical features, morbidity and mortality of the patients with diastolic dysfunction as in other studies. If the E/ Ea value was more than 15 then it showed features increased LV filling pressures in the form of breathlessness, orthopnea, brank pulmonary edema, S3, S4, wheezing and bilateral lung crepitatation.Severe degree of restrictive pattern of diastolic dysfunction.

Table 5.Morbidity and mortality associated with diastolic dysfunction in correlation with E/Ea value

	E/Ea <8 n=14	E/Ea 8-15 n=33	E/Ea >15 n=50
Breathlessness	2	8	15
S3	0	7	10
S4	1	3	4
LUNG SIGNS LOWER 1/3	2	7	6
>LOWER 1/3	0	3	12
CARDIOGENIC SHOCK	0	4	9
MORTALITY	0	4	11

There were totally 15 deaths in this study during the hospital stay of 10 days. Eleven death were occurred in patients with E/Ea more than 15(30%), 4 death were occurred in patients with E/Ea less than 15(12%) p< o.003.

Patients with anterior wall myocardial infarction had more patients with E/Ea more than 15 and patients with restrictive pattern of filling. Out of 65 patients with anterior wall infarction 33 (51%)

had restrictive pattern of filling with E/Ea more than 15 $p<0.03$.The average E/Ea value in anterior wall infarction was 15.60.

The patients with inferior wall infarction showed 34% (n=12) with restrictive pattern, 46 % (16) with pseudonormal pattern and 20% (n=7) with impaired relaxation .The average E/Ea value in patients with inferior wall infarction was 12.31.When compared with anterior wall infarction this value significantly lower $p<0.04$.

Table 5. Diastolic filling pattern in Anterior Wall Myocardial Infarction. n=65

Parameters	Impaired relaxation pattern (n=10) 15%	Pseudonormal filling pattern(n=22) 34%	Restrictive filling pattern(n=33) 51%
E(cm/s)	48±5	88±7	97±6
A(cm/s)	72±7	58±6	49±4
E/A	0.67±0.3	1.48±0.28	1.97±0.25
DT(msec)	226±12	158±14	132±11
IVRT(msec)	118±9	76±8	48±7
Ps/Pd	1.18±0.2	0.71±0.3	0.65±0.2
Pa(cm/s)	–33±3	–45±5	–53±6
(Pa-dur)—(Ma-dur) (msec)	–30±6	+38±4	+43±5
Ea(cm/s)	8.3±3.2	6.2±2.5	5.4±2.6
Aa(cm/s)	9.2±3.1	8.1±2.8	4.3±1.8
Ea/Aa	0.89±0.3	0.75±0.4	1.25±0.38
E/Ea	6.2±1.3	14.7±1.6	19.3±2.3
Sa(cm/s)	8.2±3.4	6.3±2.7	5.2±1.3
EF%	46±11	40±13	38±14

Table 6.Diastolic filling pattern in Inferior Wall Myocardial Infarction n=35

Parameters	Impaired relaxation pattern (n=07) 20%	Pseudonormal filling pattern(n=16) 46%	Restrictive filling pattern(n=12) 34%
E(cm/s)	68±6	85±8	90±5
A(cm/s)	79±6	55±6	47±4
E/A	0.67±0.3	1.48±0.28	1.91±0.25
DT(msec)	218±12	156±14	134±11
IVRT(msec)	112±9	78±8	54±7
Ps/Pd	1.3±0.2	0.76±0.3	0.68±0.2
Pa(cm/s)	–35±3	–40±5	–51±6
(Pa-dur)—(Ma-dur) (msec)	–29±6	+34±4	+42±5

Ea(cm/s)	**9.3±3.2**	**7.2±2.5**	**6.1±2.6**
Aa(cm/s)	**11.1±3.1**	**9.2±2.8**	**5.4±1.8**
Ea/Aa	**0.82±0.4**	**0.78±0.5**	**1.20±0.5**
E/Ea	**7.56±1.3**	**12.4±1.6**	**15±2.3**
Sa(cm/s)	**9±3.4**	**8±2.7**	**6±1.3**
EF%	**50±14**	**51±13**	**45±14**

Table 7. Diastolic filling pattern in male patients n=78

Parameters	Impaired relaxation pattern (n=12) 15%	Pseudonormal filling pattern(n=31) 40%	Restrictive filling pattern(n=35) 45%
E(cm/s)	**65±6**	**82±8**	**92±5**
A(cm/s)	**73±6**	**56±6**	**47±4**
E/A	**0.89±0.3**	**1.46±0.28**	**1.96±0.25**
DT(msec)	**222±12**	**164±14**	**130±11**
IVRT(msec)	**116±9**	**74±8**	**52±7**
Ps/Pd	**1.4±0.2**	**0.72±0.3**	**0.63±0.2**
Pa(cm/s)	**–32±3**	**–39±5**	**–48±6**
(Pa-dur)—(Ma-dur) (msec)	**–33±6**	**+38±4**	**+46±5**
Ea(cm/s)	**8.1±3.2**	**6.2±2.5**	**5.3±2.6**
Aa(cm/s)	**10.1±3.1**	**8.3±2.8**	**4.3±1.8**
Ea/Aa	**0.80±0.4**	**0.75±0.5**	**1.25±0.5**
E/Ea	**8.13±1.3**	**13.67±1.6**	**18.4±2.3**
Sa(cm/s)	**8.2±3.4**	**6.1±2.7**	**5.2±1.3**
EF%	**48±14**	**45±13**	**40±14**

There was no much difference in filling pattern between male female patients but there was slight increase in the average E/Ea value in female patients .The average E/Ea value in male patients was 14.94 and in female patients was 15.10p<0.08 statistically not significant.

Table 8. Diastolic filling pattern in female patients n=22

Parameters	Impaired relaxation pattern (n=05) 23%	Pseudonormal filling pattern(n=07) 32%	Restrictive filling pattern(n=10) 45%
E(cm/s)	**60±4**	**88±7**	**96±6**
A(cm/s)	**76±6**	**59±6**	**45±4**
E/A	**0.79±0.29**	**1.49±0.26**	**2.13±0.3**
DT(msec)	**230±12**	**158±14**	**128±11**
IVRT(msec)	**112±9**	**74±8**	**54±7**
Ps/Pd	**1.3±0.2**	**0.73±0.3**	**0.65±0.2**
Pa(cm/s)	**–31±4**	**–41±5**	**–46±7**
(Pa-dur)—(Ma-dur) (msec)	**–32±6**	**+36±4**	**+44±5**
Ea(cm/s)	**8.2±3.2**	**6.2±2.5**	**5.3±2.6**
Aa(cm/s)	**9.1±3.1**	**9.2±2.8**	**4.2±1.8**
Ea/Aa	**0.89±0.4**	**0.67±0.5**	**1.25±0.5**

E/Ea	**7.5±1.3**	**14.67±1.6**	**19.20±2.3**
Sa(cm/s)	**8.1±3.4**	**6.3±2.7**	**5.2±1.3**
EF%	**48±16**	**45±13**	**40±12**

There were 27 patients with normal left ventricular ejection fraction above 50%.They have showed restrictive pattern in 30 % (n=08), pseudonormal pattern in 44% (n=12) and impaired relaxation pattern in 26% (n=7) patients. This shows the importance of the assessment diastolic dysfunction patients with normal left ventricular ejection fraction in acute myocardial infarction patients.

Table 9. Diastolic filling pattern in patients with normal ejection fraction (>50%) n=27

Parameters	Impaired relaxation pattern (n=07) 26%	Pseudonormal filling pattern(n=12) 44%	Restrictive filling pattern(n=08) 30%
E(cm/s)	**68±6**	**85±8**	**96±6**
A(cm/s)	**79±6**	**55±6**	**48±4**
E/A	**1.27±0.3**	**1.48±0.28**	**1.99±0.3**
DT(msec)	**218±12**	**156±14**	**128±11**
IVRT(msec)	**112±9**	**78±8**	**54±7**
Ps/Pd	**1.3±0.2**	**0.76±0.3**	**0.65±0.2**
Pa(cm/s)	**–35±3**	**–40±5**	**–46±7**
(Pa-dur)—(Ma-dur) (msec)	**–29±6**	**+34±4**	**+44±5**
Ea(cm/s)	**9.2±3.2**	**7.3±2.5**	**5.2±2.6**
Aa(cm/s)	**10.1±3.1**	**9.1±2.8**	**4.3±1.8**
Ea/Aa	**0.90±0.4**	**0.78±0.5**	**1.25±0.5**
E/Ea	**7.56±1.3**	**12.4±1.6**	**19.20±2.3**
Sa(cm/s)	**9.2±3.4**	**8.2±2.7**	**5.1±1.3**
EF%	**>50**	**>50**	**>50**

Thrombolysis definitely improves diastolic function in acute myocardial infarction patients. In this study ,there was significant increase in E/Ea value in non thrombolysed patients. The average E/Ea value in thrombolysed patient was 14.8 and in non-thrombolysed patients was 17.1 $p<0.004$.

Table 10 . Diastolic filling pattern in thrombolysed patients n=72

Parameters	Impaired relaxation pattern (n=12) 16%	Pseudonormal filling pattern(n=30) 42%	Restrictive filling pattern(n =30) 42%
E(cm/s)	**58±6**	**83±8**	**91±5**
A(cm/s)	**76±6**	**54±6**	**45±4**
E/A	**0.76±0.3**	**1.54±0.28**	**2.02±0.25**
DT(msec)	**222±12**	**164±14**	**130±1 1**
IVRT(msec)	**112±9**	**72±8**	**53±7**

Ps/Pd	1.3±0.2	0.73±0.3	0.65±0.2
Pa(cm/s)	–33±3	–38±5	–45±6
(Pa-dur)—(Ma-dur) (msec)	–33±6	+38±4	+46±5
Ea(cm/s)	8.2±3.2	5.8±2.5	5.1±2.6
Aa(cm/s)	9.8±3.1	8.7±2.8	4.5±1.8
Ea/Aa	0.89±0.4	0.67±0.5	1.13±0.5
E/Ea	7.02±1.3	14.37±1.6	18.4±2.3
Sa(cm/s)	8.2±3.4	6.1±2.7	5.2±1.3
EF%	49±13	45±12	40±12

Table 11 . Diastolic filling pattern in non-thrombolysed patients n=28

Parameters	Impaired relaxation pattern (n=5) 18%	Pseudonormal filling pattern(n=8) 29%	Restrictive filling pattern(n=15) 54%
E(cm/s)	56±6	88±8	98±5
A(cm/s)	76±6	48±6	45±4
E/A	0.76±0.3	1.54±0.28	2.02±0.25
DT(msec)	223±12	174±14	130±11
IVRT(msec)	108±9	68±8	50±7
Ps/Pd	1.2±0.2	0.72±0.3	0.64±0.2
Pa(cm/s)	–32±3	–39±5	–44±6
(Pa-dur)—(Ma-dur) (msec)	–30±6	+37±4	+43±5
Ea(cm/s)	7.8±3.2	5.4±2.5	4.8±2.6
Aa(cm/s)	9.5±3.1	9.2±2.8	4.5±1.4
Ea/Aa	0.89±0.4	0.67±0.5	1.13±0.5
E/Ea	7.1±1.3	16.30±1.6	20.42.4±2.3
Sa(cm/s)	8.2±3.4	6.1±2.7	5.2±1.3
EF%	44±13	41±12	39±2

DISCUSSION

In the absence of direct measurements of filling pressures, noninvasive estimation of filling pressures with the use of E/Vp or E/Ea could prove useful. This was demonstrated in a retrospective study of 250 patients with AMI; an increased (>15) E/Ea ratio was found to be an important predictor of all-cause mortality incremental to LVEF, age, and a restrictive filling transmitral filling pattern. Importantly, E/Ea allowed risk stratification among patients with preserved as well as depressed LV systolic function. This supports the finding of an adverse outcome in patients with pseudonormal filling (moderate increase in filling pressures) despite preserved LV systolic function and concurs with the results of studies in which the E/Vp ratio was used. When LV filling is assessed with the use of transmitral, color M-mode, and tissue Doppler echocardiography, an instantaneous assessment of filling dynamics will be obtained.

In a recent study of postinfarction patients with left ventricular ejection fraction less than 35%, a mitral deceleration time of less than 120 msec was highly predictive of a pulmonary capillary wedge pressure of greater than 20 mm Hg. In a second study of patients with systolic dysfunction after infarction (ejection fraction >40%), there was an increased rate of adverse events in two years of follow-up in patients with higher mitral E/A ratios and shorter deceleration times. This finding has been confirmed in subsequent studies. Several new parameters of diastolic function have been studied in postinfarction patients. The deceleration time of the diastolic component of pulmonary venous flow has a better correlation with wedge pressure in post patients with myocardial infarction than does the mitral deceleration time. The sensitivity and specificity of a pulmonary venous deceleration time less than 160 msec in predicting greater than or equal to 18 mm Hg in pulmonary capillary wedge pressure were 97% and 96%, respectively, compared with 86% and 59%, respectively, for a mitral deceleration time of less than 130 msec. The propagation velocity of mitral inflow measured on M-mode color Doppler echocardiography also has prognostic significance.

The prognostic importance of a restrictive filling pattern after AMI was initially reported by **Oh et al** in 1992. In a cohort of 62 patients, a restrictive filling pattern was associated with a high occurrence of in-hospital congestive heart failure.

This was confirmed by **Poulsen et al** 52 in an age-selected population with a first AMI in which Doppler echocardiography was performed within 1 hour of hospital admission.

In 1997, **Nijland** et al reported in a study of 95 patients with first AMI those DT <140 ms was associated with a 22% survival rate at 3 years compared with 100% in the nonrestrictive group. Although the study was limited by a small number of deaths (n=8), this finding has subsequently been confirmed in several studies. In these studies, patients with a restrictive filling pattern have been characterized by higher age, more advanced LV systolic dysfunction, and a high risk of in-hospital heart failure. A restrictive filling pattern seems to have the same prognostic importance in Stand non–ST-segment elevation AMI and in patients treated with thrombolysis or primary angioplasty. Although the results of those studies have been strikingly similar, many have been limited by small populations and few events. However, in 799 patients with assessment of LV filling within 6 days of AMI, DT <140 ms was a predictor of all-cause mortality, with a hazard ratio of 2.1 (95% CI, 1.5 to 3.1), after adjustment for various clinical variables including in-hospital heart failure and LV systolic function. This has recently been replicated in 2 other large studies. These studies of 2500 patients have shown that an abnormally short DT is an independent predictor of adverse outcome after AMI and is incremental to conventional indicators of poor outcome such as age, Killip class, enzymatic infarct size, ejection fraction, wall motion score index, and end-systolic volume.

In this study also results were in concurrence with the finding in previous other study.So the tissue doppler study gives reproducible results not affected by preloading conditions that affects the conventional transmitral and transpulmonary flow doppler pattern.E/Ea value more than 15, IVRT less than 60 msec and DT less than140 were the reliable predictors of morbidity and mortality following acute myocardial infarction.Thrombolysis was associated with improvement in the diastolic function.

This study was simple noninvasive assessment diastolic function in acute myocardial infarction to prognosticate the patients with normal or low left ventricular ejection fraction.

The correlation between the left atrial size as marker of diastolic dysfunction to prognosticate the patients with acute myocardial infarction was well documented in various studies in comparisons with the conventional doppler method and tissue doppler method. The doppler E/Ea value was in linear relationship with the left atrial size in prognosticating the patients' acute myocardial infarction.

LIMITATIONS OF THE STUDY

1. This noninvasive method of pulmonary capillary wedge pressure measurement not compared with the invasive measurement method.
2. The patients were followed up for 2 weeks only. This is insufficient to prognosticate on long term basis.
3. Not compared with the left atrial size.
4. Other compounding factors that affect the diastolic function could not be separated to measure the diastolic dysfunction caused by acute myocardial infarction such as systemic hypertension, diabetes mellitus ,chronic renal failure,hypothyroidismand pericardial diseases
5. Role of previous angina, stunned myocardium and hibernating myocardium in producing the diastolic dysfunction could not be quantified.

CONCLUSIONS

1. Thrombolysed patients showed average E/Ea value 14.8 and non-thrombolysed patients showed average E/Ea 17.1.
2. This study showed increased morbidity and mortality in patients with E/Ea value more than 15.
3. Tissue doppler imaging is a simple noninvasive investigation to diagnose the diastolic dysfunction and prognosticate the patients with acute myocardial infarction.
4. Pulsed Tissue Doppler imaging for myocardial velocities is far more practical, as the analysis can be performed on-line and does not require sophisticated time-consuming post-processing and which makes the method useful for daily clinical practice.
5. The proposed method is technically simple and can be easily performed using any echo machine equipped with conventional pulsed Doppler myocardial imaging.
6. Pulsed TD derived echocardiographic methods are quantifiable, reproducible, and noninvasive techniques for assessing the presence of diastolic dysfunction in acute myocardial infarction.

APPENDIX-I

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PPENDIX-III

LIST OF ABBREVIATIONS

2-D	**Two-dimensional**
Am	**Late diastolic mitral annulus velocity**
A dur	**Late diastolic mitral flow wave duration**
A dur	**Late diastolic mitral annulus velocity duration**
A-wave	**Late diastolic mitral flow wave**
DT	**E Wave deceleration time**
ECG	**Electrocardiogram**
ECHO	**Echocardiography**
EF	**Ejection fraction**
E-wave	**Early diastolic mitral flow wave**
Em	**Early diastolic mitral annulus velocity**
IVCT	**Isovolumic contraction**
IVRT	**Isovolumic relaxation**
LA	**Left atrium / atrial**
LV	**Left ventricle / ventricular**
LAD	**Left anterior descending coronary artery**
M-mode	**Motion mode**
Ps	**Pulmonary venous peak systolic velocity**
Pd	**Pulmonary venous peak diastolic velocity**
Pa	**Pulmonary venous atrial reversal velocity**
PSV	**Peak systolic velocity**
Sm	**Systolic Mitral annulus Velocity**
TDI	**Tissue Doppler imaging**

APPENDIX-II

PROFORMA

ASSESSMENT OF LEFT VENTRICULAR DIASTOLIC DYSFUNCTION BY TISSUE DOPPLER IMAGING IN ACUTE MYOCARDIAL INFARCTION

SERIAL NO: **IP NO:** **CD NO:**

NAME : **AGE :** **SEX :** **OCCUPATION:**

ADDRESS:

DIAGNOSIS:

COMPLAINTS:

CHEST PAIN YES / NO, BREATHLESSNESS YES / NO, SYNCOPE YES / NO

PAST HISTORY: SHT / DMT2 /ANGINA / MI / TIA /PVD /SIMILAR ILLNESS

PERSONAL HISTORY: SMOKING / ALCOHOLIC /TOBACCO USE

VITALS ON ADMISSION:

HT WT BM I WAIST HIP RATIO

PR: BP: JVP DYSPNEA YES / NO

CYANOSIS YES / NO PALLOR YES /NO PEDAL EDEMA YES /NO

CARDIOVASCULAR SYSTEM :API

S1 S2 S3 S4 THRILL M URM U R

RESPIRATORY SYSTEM :

ABDOMEN

CENTRAL NERVOUS SYSTEM:

INVESIGATIONS:

HB% **BL.UREA** **mgs%** **BL.SUGAR** **mgs%** **Sr.CREATININE** **mgs%**

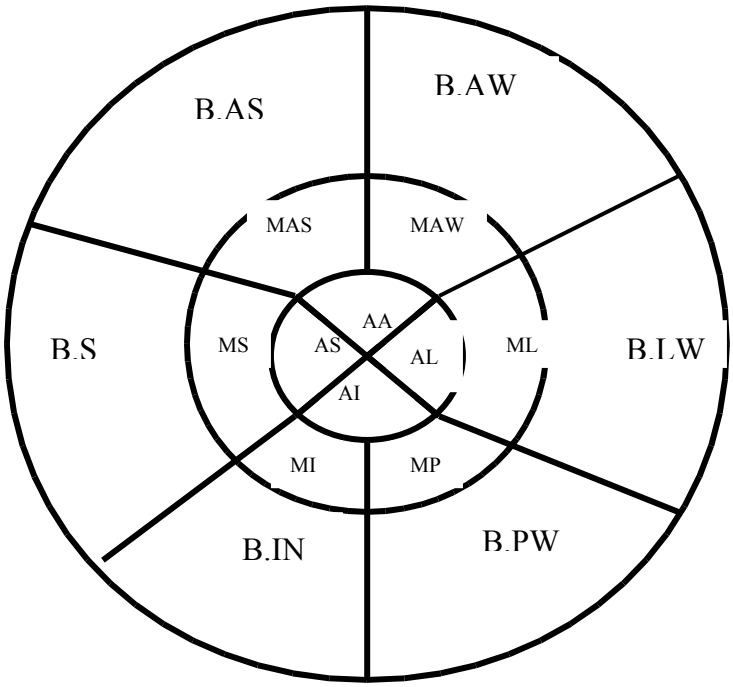
LIPID PROFILE : TCL **LDL** **HDL** **VLDL** **TGL**

THROMBOLYSED	**NONTHROMBOLYSED**
MEDIAN DELAY	**CONTRAINDICATION**

ECG

RATE	**RHYTHM**	**INTERVAL**		**AXIS**		**Q WAVE**	**ST-SEGMENT**	**T-WAVE**
		PR	**QTc**	**P**	**QRS**			

TTE RWMA



M-MODE

	DIASTOLIC	SYSTOLIC	EDV	SV
LVID				
IVS			**ESV**	**LVEF**
PW				

PULSE DOPPLER TRANSMITRAL PARAMETERS

E cms/s	A cms/s	E/A	DT	IVRT	A dur

TISSUE DOPPLER MITRA SNNULAR PARAMETERS

	S' cms /s	E' cms /s	A' cms /s	E/E'	E'/A'
SEPTAL					

PULMONARY VENOUS FLOW PARAMETERS

Ps cms/s	Pd cms/s	Pa cms/s	Pa dur