

Diastolic Dysfunction

Gary W. Lewis, M.D.

- Diastolic heart failure (DHF) is a clinical syndrome in which patients have symptoms and signs of HF, normal or near normal left ventricular ejection fraction (LVEF), and evidence of diastolic dysfunction (eg, abnormal left ventricular filling and elevated filling pressures).

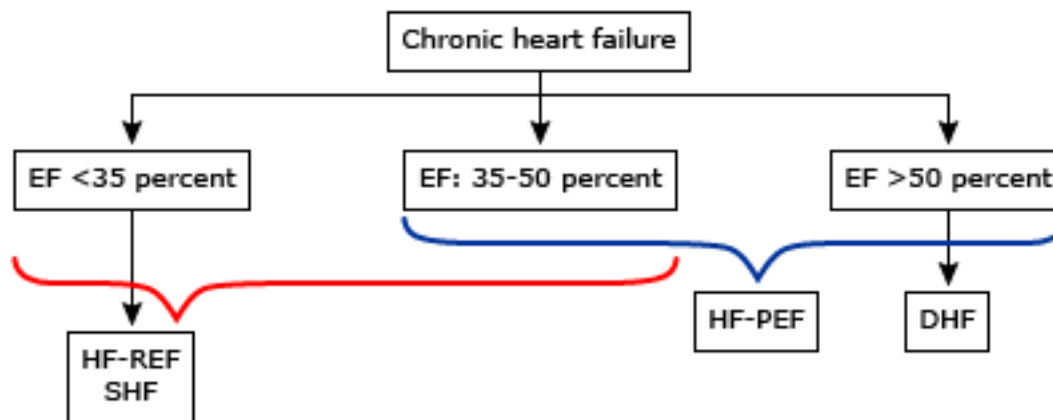
Diastolic dysfunction and diastolic heart failure (DHF) are not synonymous. The term diastolic HF is reserved for patients with clinical HF, in the setting of a normal or near-normal EF, and abnormalities in diastolic function

HFPEF

HFPEF

Heart Failure with
Preserved Ejection Fraction

Types of heart failure



Clinical trials

DIG Ancillary Study EF: EF >45 percent

CHARM-Preserved: EF >40 percent

PEP-CHF: EF >45 percent

I-Preserve: EF >45 percent

SENIORS: EF >35 percent

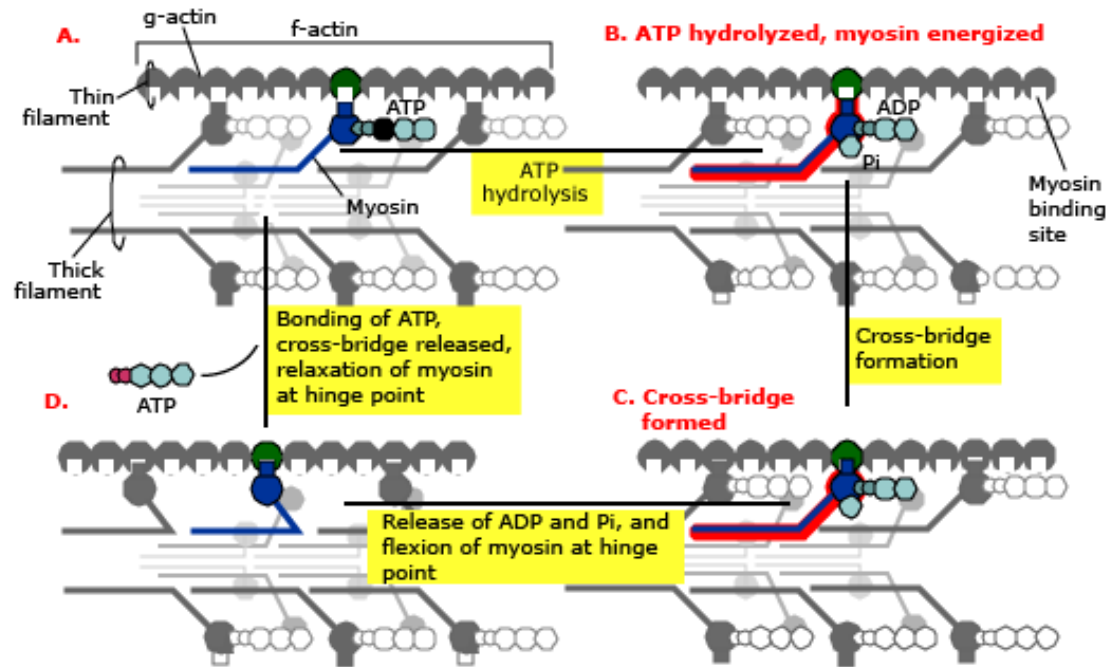
Courtesy of Dr. Michael Zile.

Left ventricular structure and function in chronic heart failure

	Systolic heart failure	Diastolic heart failure
LV remodeling		
End-diastolic volume	↑	Normal
End-systolic volume	↑	Normal
Mass	↑	↑
Geometry	Eccentric	Concentric
Cardiomyocyte	↑ Length	↑ Diameter
Extracellular matrix	↓ Collagen	↑ Collagen
LV systolic properties		
Performance		
Stroke volume	↓ (or normal)	Normal (or ↓)
Stroke work	↓	Normal
Function		
Preload recruitable stroke work	↓	Normal
Ejection fraction	↓	Normal
Contractility		
(+)dP/dt	↓	Normal
End-systolic elastance	↓	Normal (or ↑)
Stress shortening	↓	Normal
Preload reserve	Exhausted	Limited
LV diastolic properties		
End diastolic pressure	↑	↑
Tau	↑	↑
Chamber stiffness	↓	↑
Myocardial stiffness	Normal (or ↑)	↑

Courtesy of Dr. Michael Zile.

Actin-myosin interaction in myocardial contractility



A model of the sliding filament theory of muscular contraction. Panel A shows myosin in the relaxed state having just been bound by ATP. Panel B shows the first step by which myosin is energized via hydrolysis of an ATP high energy phosphate bond, resulting in the formation of ADP and inorganic phosphate (Pi). The myosin head then binds actin at the myosin binding site, forming the actin-myosin crossbridge as shown in Panel C. Panel D shows release of ADP and inorganic phosphate, plus flexion of the myosin molecule at its hinge point, causing the filaments to slide past each other. The cross-bridge remains until myosin is again bound by ATP which allows dissociation of the myosin and actin and relaxation of the myosin molecule. The actin-myosin complex returns to the state in Panel A except that the filaments have now moved relative to each other.

Courtesy of Timothy W Smith, MD, PhD.

DHF is associated with remodeling that affects left ventricular and left atrial chambers, the cardiomyocytes, and extracellular matrix with impact on diastolic as well as systolic function. Nearly all patients with diastolic HF have a normal LV end diastolic volume; most have increased LV wall thicknesses, mass and relative wall thickness

The prevalence of DHF increases with age. DHF is more common in women than in men.

Asymptomatic diastolic dysfunction is much more common than symptomatic disease..

The major causes of DHF are chronic hypertension with left ventricular hypertrophy, hypertrophic cardiomyopathy, coronary heart disease, and restrictive cardiomyopathy.

Diastolic function is determined by two factors: the process of myocardial relaxation (which is an active process that requires metabolic energy) and the elasticity or distensibility of the left ventricle (which is a passive process).

Diastolic and systolic HF have similar symptoms. Exercise intolerance seen in DHF may be caused by elevation in left atrial and pulmonary venous pressures and/or impaired stroke volume leading to dyspnea and fatigue.

In clinical practice, the diagnosis of DHF is typically based upon finding signs and symptoms of HF, normal or mildly abnormal LVEF (LVEF >50 percent), and evidence of diastolic dysfunction on Doppler echocardiography.

DHF is one of several causes of cardiogenic pulmonary edema in patients with a normal LVEF.

Occult coronary heart disease is a potentially reversible cause of DHF.

Plasma BNP and N-terminal pro-BNP
are elevated in patients with DHF
but cannot effectively distinguish
DHF from SHF

The key distinguishing feature between systolic and diastolic HF is whether the ejection fraction is reduced (indicating systolic HF) or preserved, meaning normal or near-normal (indicating diastolic HF). Diastolic dysfunction is not the only cause of HF in patients with preserved LVEF

Differential diagnosis of heart failure with preserved left ventricular ejection fraction

Diastolic heart failure
Hypertensive heart disease
Restrictive cardiomyopathy
Infiltrative cardiomyopathies
Hypertrophic cardiomyopathy
Noncompaction cardiomyopathy
Coronary heart disease
Miscellaneous factors: diabetes mellitus, chronic kidney disease, aging
Valvular heart disease
Valvular stenosis
Valvular regurgitation
Right heart failure
Pulmonary hypertension
Right ventricular infarction
Arrhythmogenic right ventricular cardiomyopathy
Pericardial disease
Cardiac tamponade
Constrictive pericarditis
Effusive-constrictive pericardial disease
Intracardiac mass
Atrial myxoma
Congenital heart disease
High-output heart failure
Episodic or reversible LV systolic dysfunction
Pulmonary vein stenosis

Adapted from: Oh JK, Hatle L, Tajik AJ, Little WC. Diastolic heart failure can be diagnosed by comprehensive two-dimensional and Doppler echocardiography. *J Am Coll Cardiol* 2006; 47:500.

During exercise, physiologic mechanisms normally ensure that cardiac input keeps pace with cardiac output with preservation of a low pulmonary venous pressure.

Since both afterload (systolic pressure) and diastolic load (left atrial diastolic pressure) can affect measurement of diastolic function, these factors must be considered in assessing the intrinsic relaxation rate.

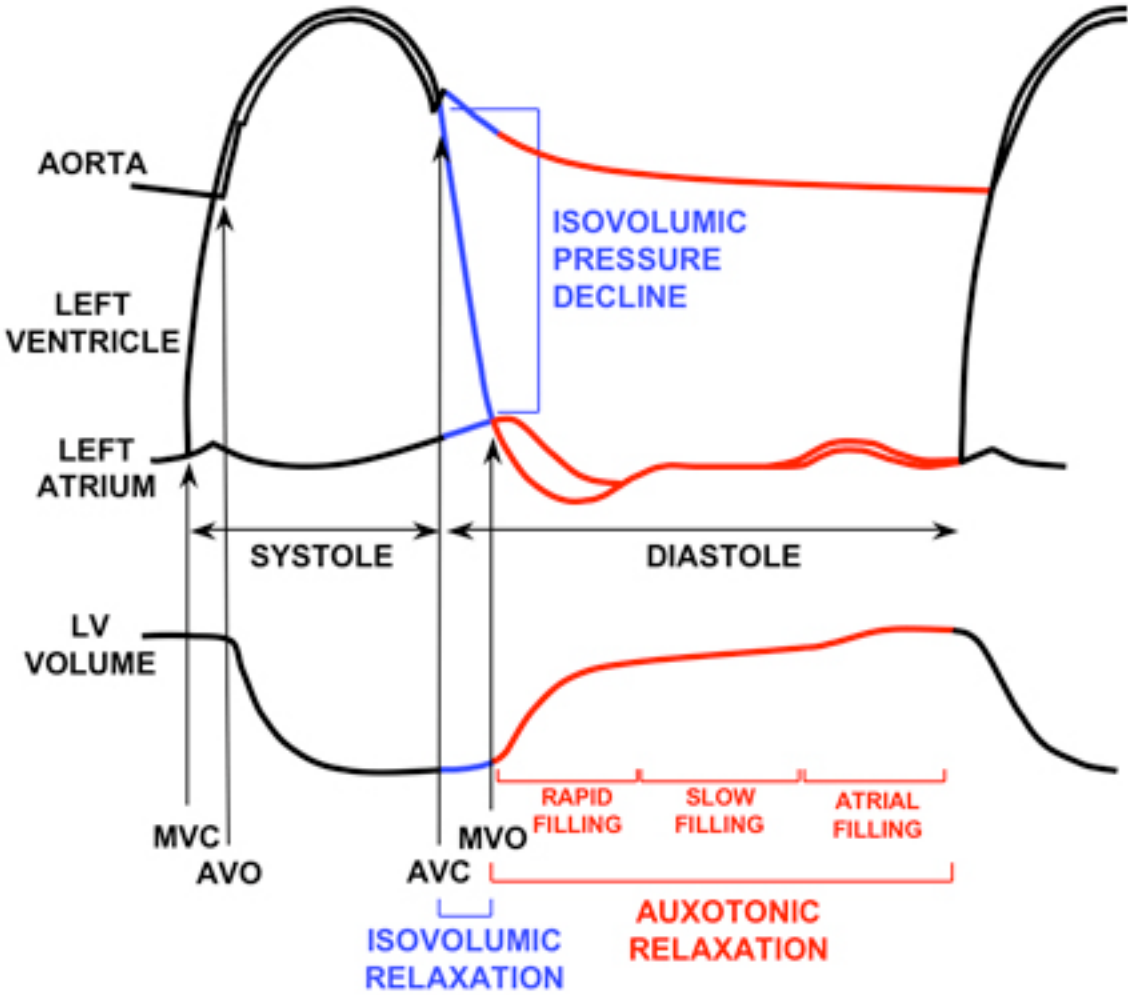
The two most common pathways to DHF are left ventricular hypertrophy and ischemia.

In patients with diastolic heart failure (DHF), certain types of hemodynamic stress including atrial fibrillation; tachycardia; abrupt, severe, or refractory elevations in systemic blood pressure, and myocardial ischemia are associated with worsening of diastolic dysfunction.

Echocardiography is the recommended imaging modality for the assessment of left ventricular (LV) diastolic function.

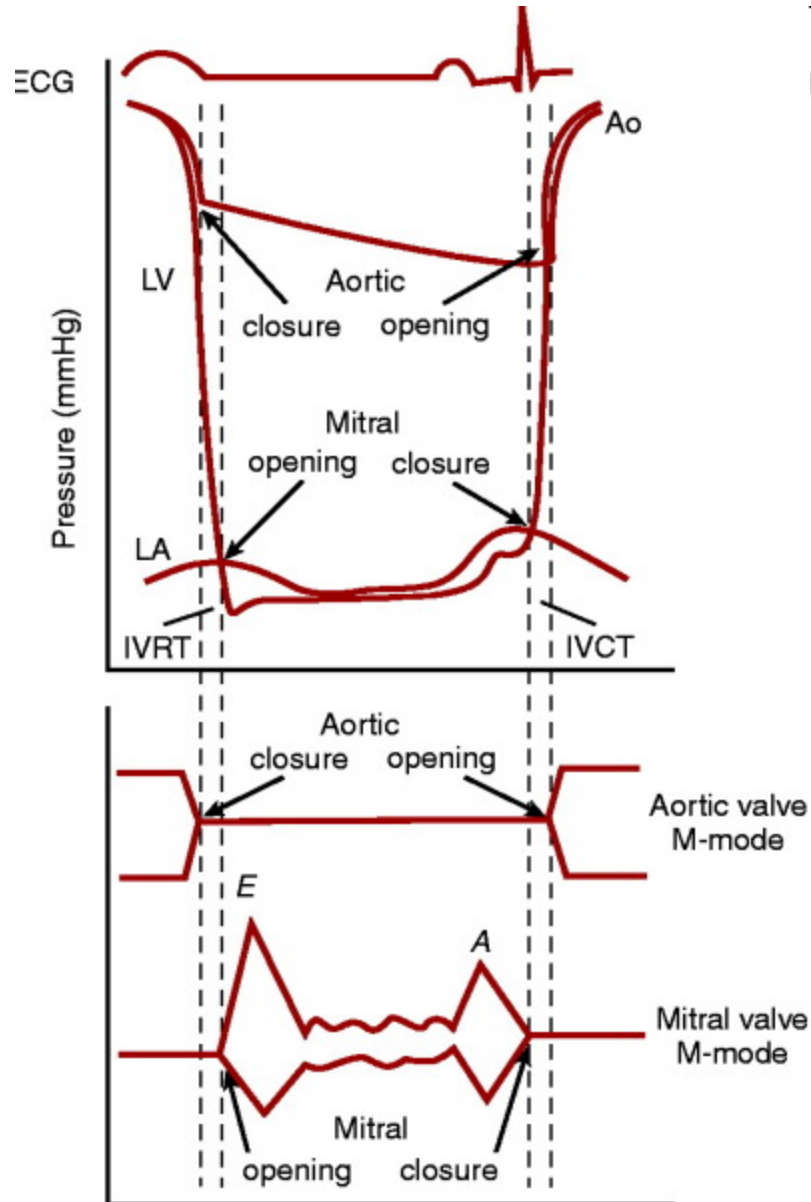
Doppler measurements provide
incremental prognostic information
to clinical and anatomic findings

Phases of diastole

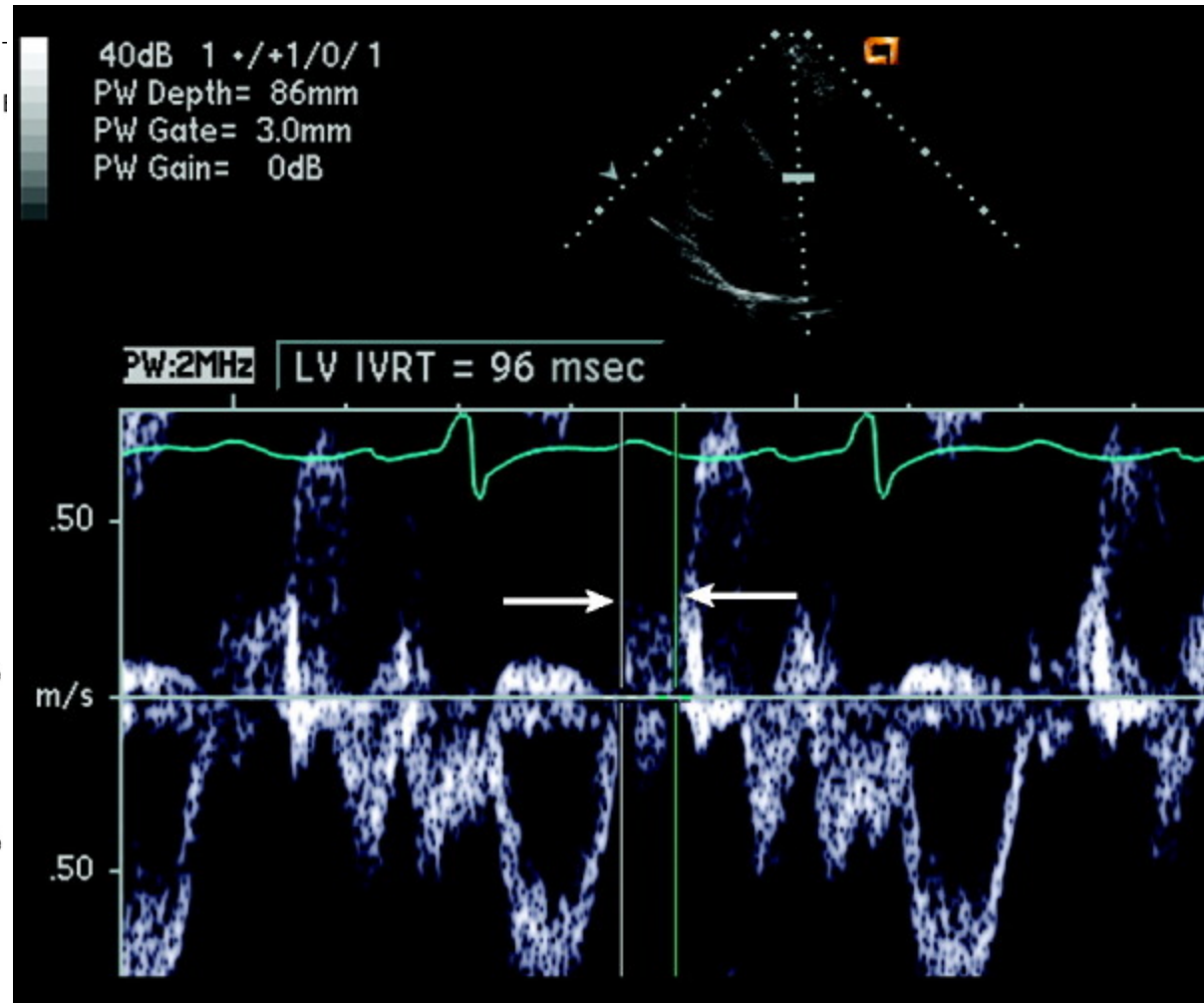
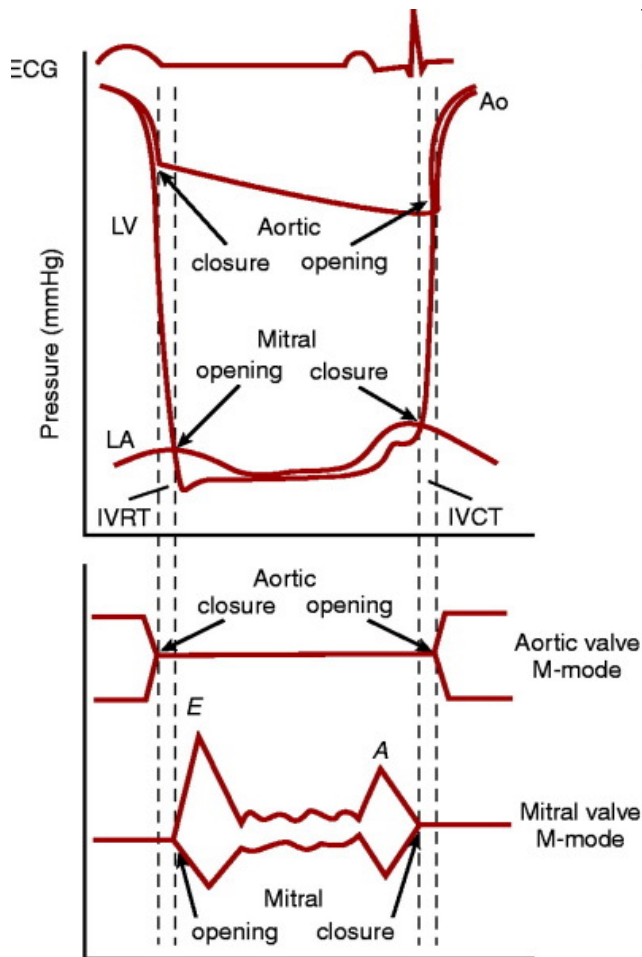


Diastole begins with isovolumic relaxation followed by auxotonic relaxation and continues until atrial contraction is complete. During the later phases of diastolic HF, the LV is readily distensible. Atrial contraction normally contributes 20 to 30 percent to total LV filling volume but usually increases diastolic pressures by less than 5 mmHg.

Diastole



Isovolumic Relaxation Time (IVRT)

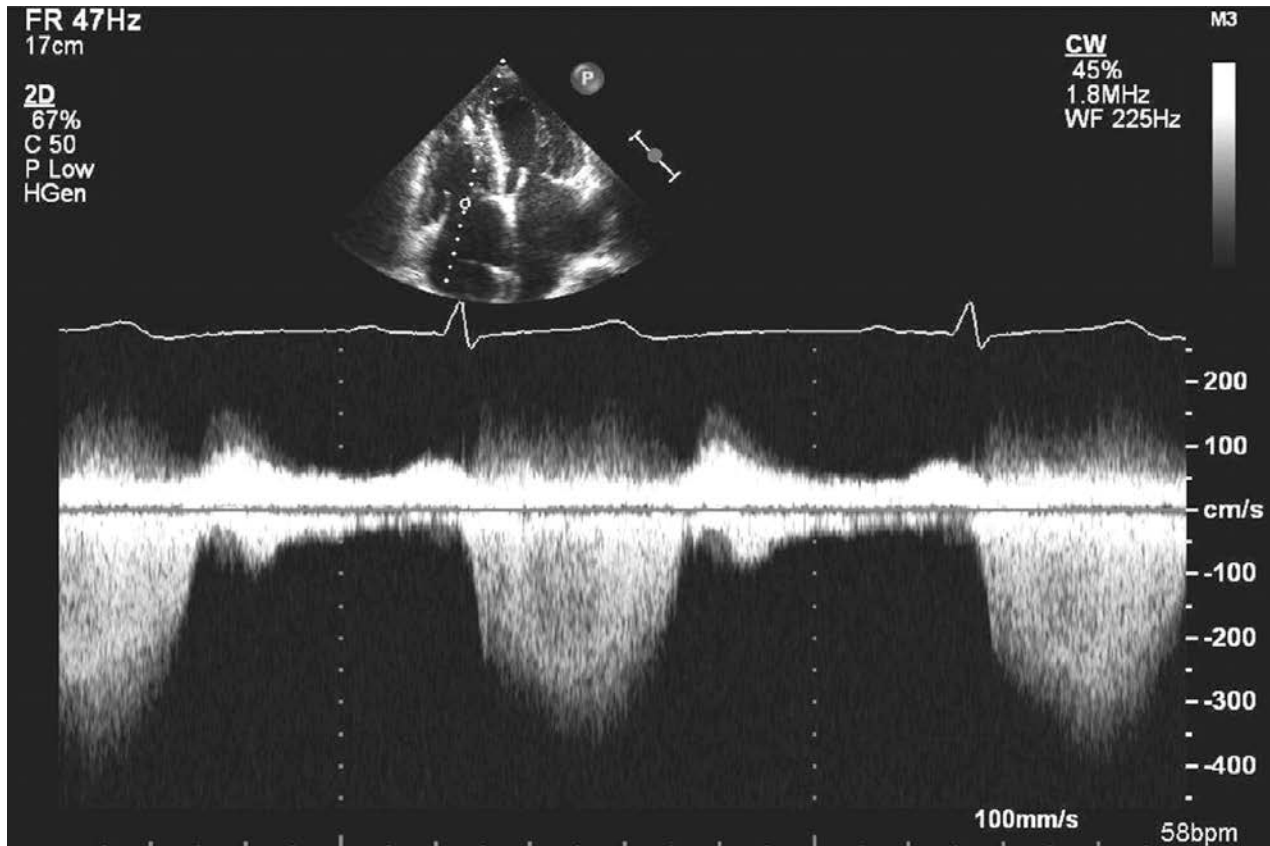


Normal IVRT 70-90ms.

IVRT lengthens w/ impaired LV relaxation and shortens when LV compliance is decreased and LV filling pressures increase.

IVRT varies with HR, preload and ventricular function.

Calculation of PA systolic pressure using the TR jet.



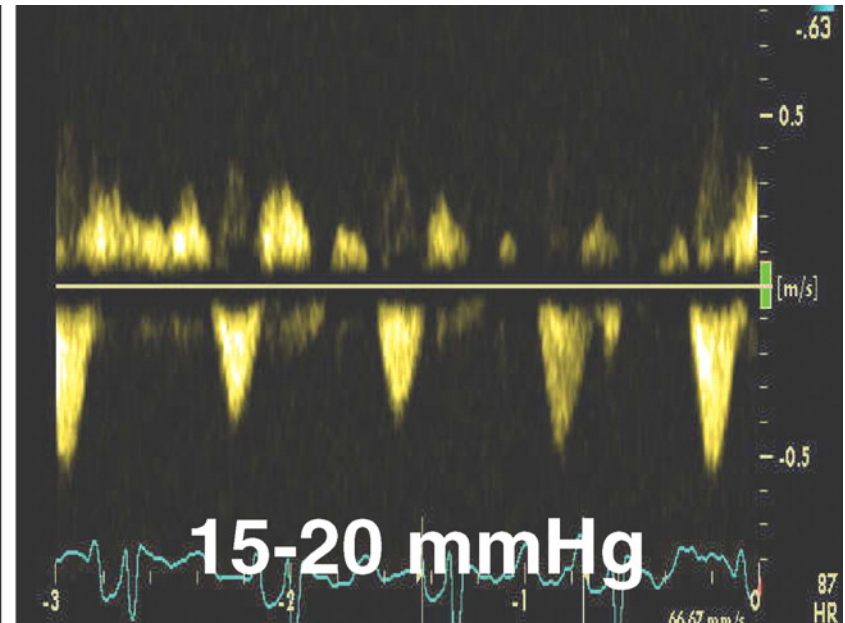
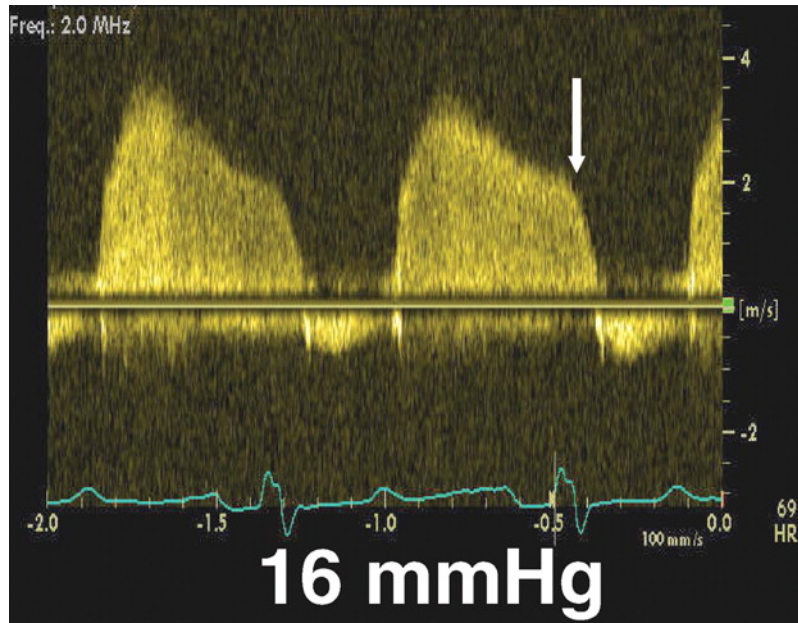
$4 (V)^2$ of peak TR velocity = PAS – RAP

$4 (3.6)^2$ or 52 = PAS - 20

PAS = 52 + 20 = 72 mmHg

Nagueh S F et al. Eur J Echocardiogr 2009;10:165-193

Calculation of PA diastolic pressure using the PR jet (left) and hepatic venous by PW Doppler (right).



$$4 (V)^2 \text{ of end diastolic PR velocity} = \text{PAD} - \text{RAP}$$

$$4 (2)^2 \text{ or } 16 = \text{PAD} - (15 \text{ or } 20)$$

$$\text{PAD} = 16 + (15-20) = 31-36 \text{ mmHg}$$

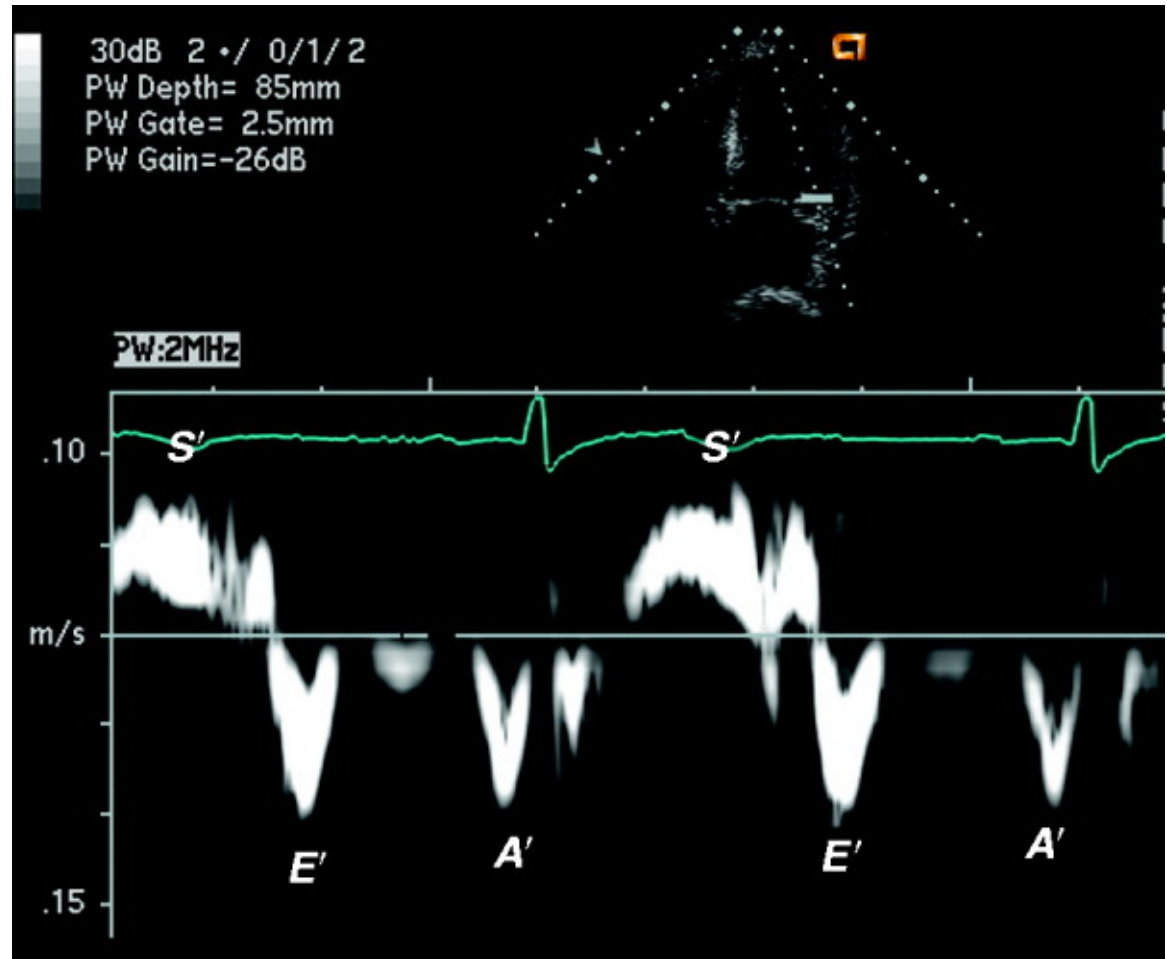
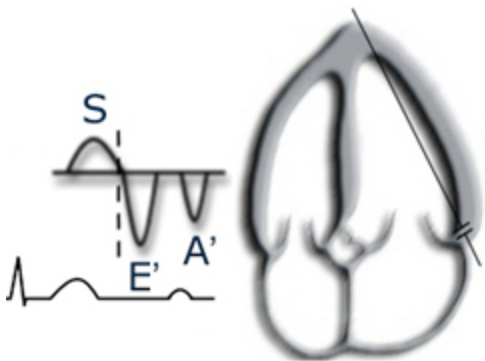
Nagueh S F et al. Eur J Echocardiogr 2009;10:165-193

In patients with normal LV EF,
the initial step is calculating the
E/e' ratio

Tissue Doppler Imaging (e')

- E/e' ratio (combo of transmitral flow velocity and annular velocity) is best parameter for predicting mean LVEDP
- <8 is normal,
- >15 abnormal

Tissue Doppler Imaging (e')



**Septal and lateral
velocities should be
acquired by PW
Doppler**

**Sample volume should be placed at or
1 cm within
septal and lateral insertion sites of
mitral leaflets**

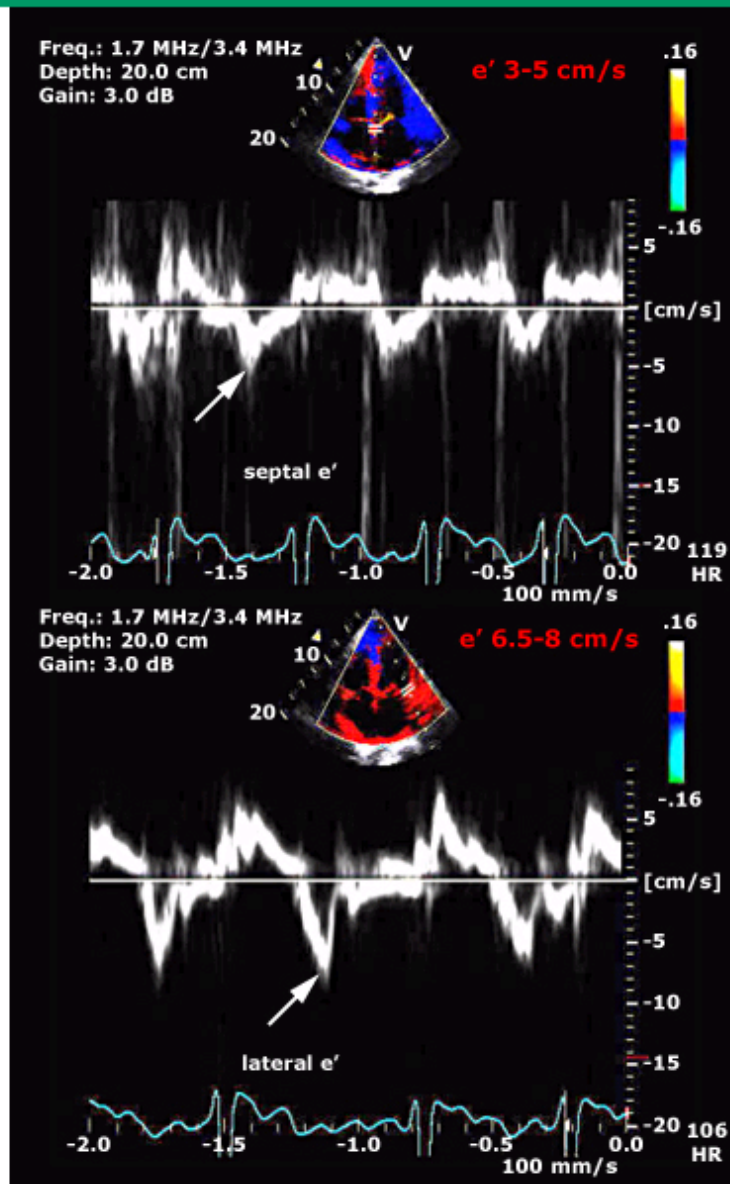
**Identify e' from
Isovolumic Relaxation velocities**

Avoid angulation

**E/e' not accurate in mitral valve
disease, heavy annular
calcification, constrictive pericarditis,
and abnormal
septal motion**

**Average E/e' ratio in
patients with regional
dysfunction**

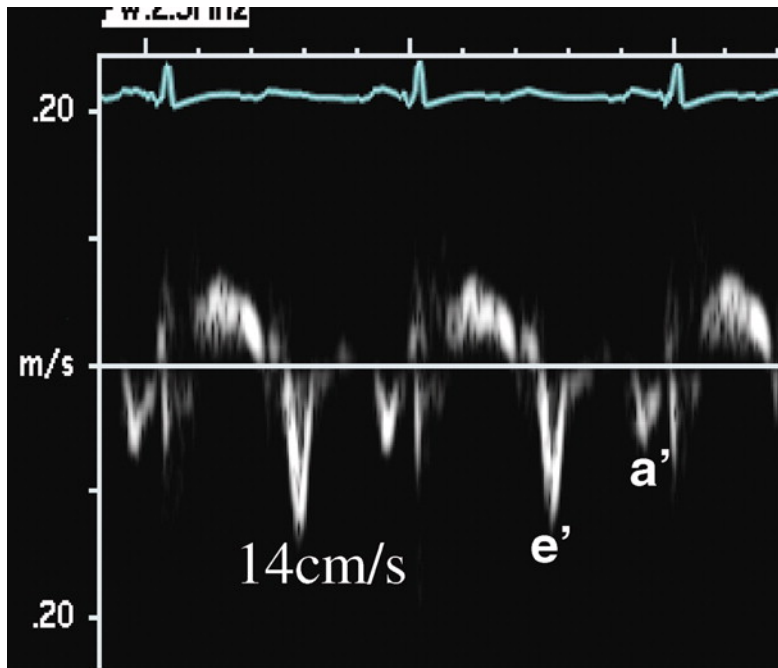
Example of tissue Doppler recordings



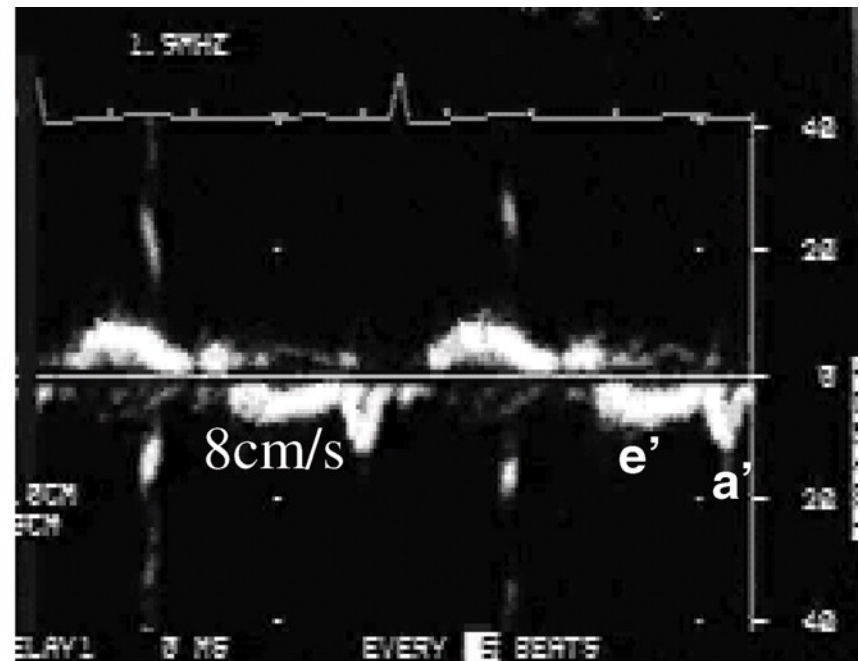
Courtesy of Dr. Sherif F Nagueh.

A ratio <8 is often associated with normal LV filling pressures and a ratio >15 is indicative of elevated LV filling pressures. In patients with a ratio >8 but <15 , other parameters are needed, which include pulmonary venous flow velocities, LA maximum volume index, and PA systolic pressure using the tricuspid regurgitation jet using continuous wave Doppler.

Tissue Doppler (TD) recording from the lateral mitral annulus from a normal subject aged 35 years (left) ($\dot{\epsilon} = 14$ cm/s) and a 58-year-old patient with hypertension, LV hypertrophy, and impaired LV relaxation (right) ($\dot{\epsilon} = 8$ cm/s).



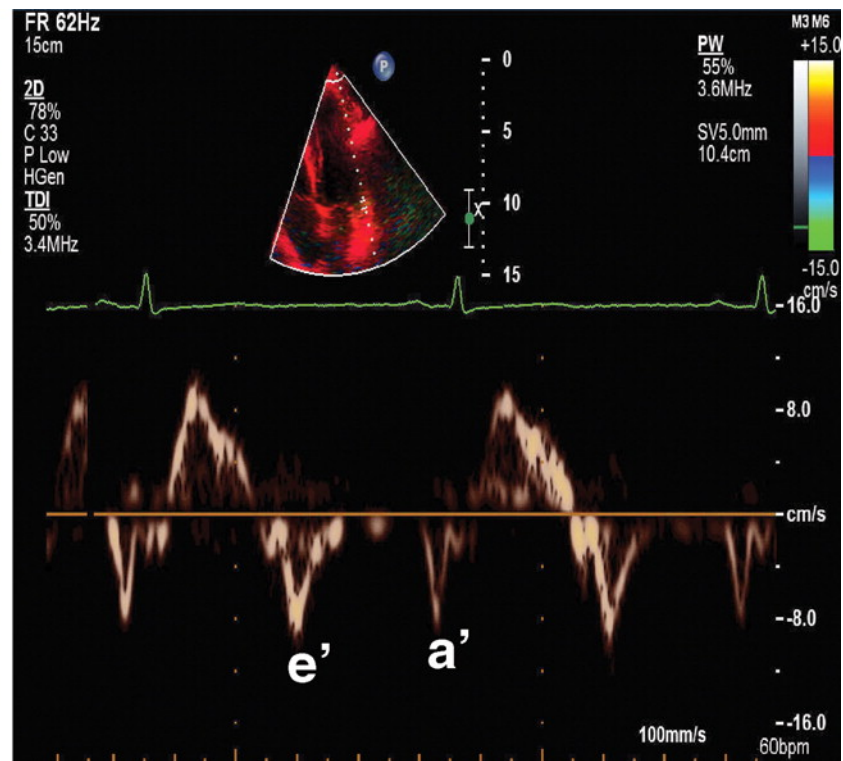
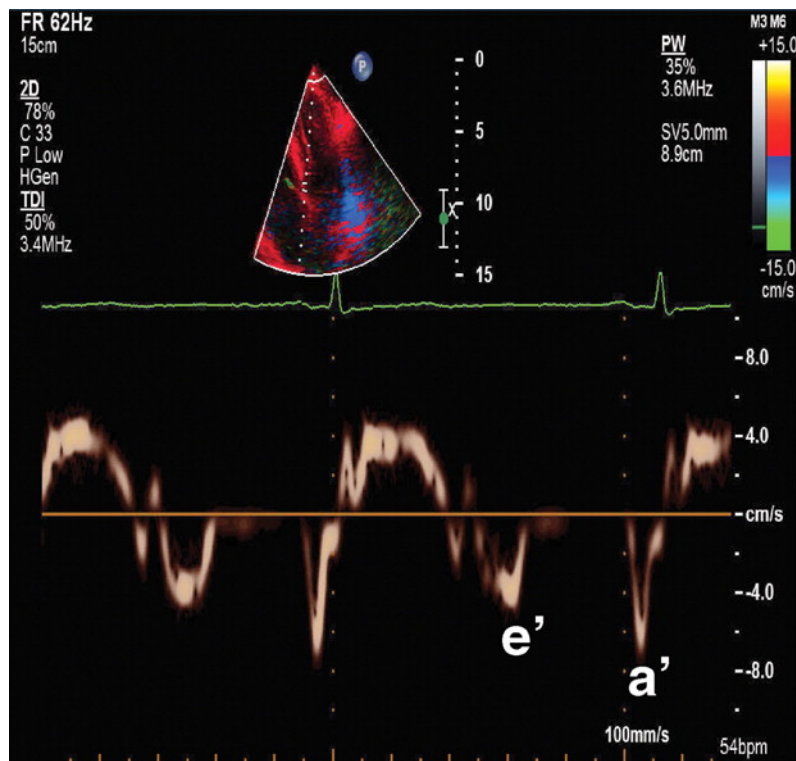
Normal
35 years old



Hypertension with LVH
58 years old

Nagueh S F et al. Eur J Echocardiogr 2009;10:165-193

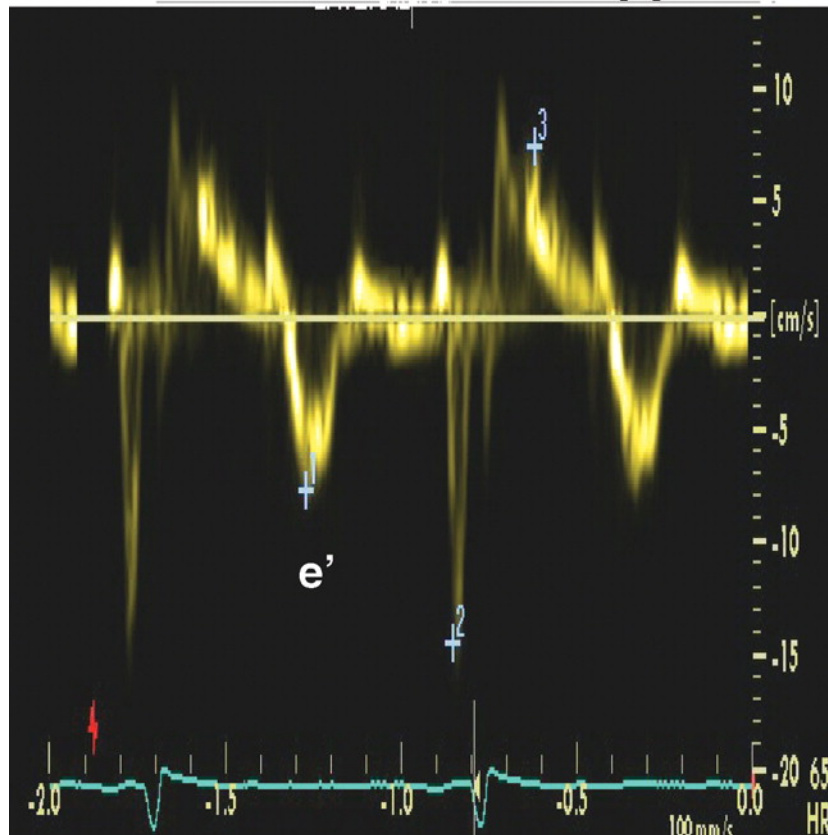
Septal (left) and lateral (right) tissue Doppler recordings from a patient with an anteroseptal myocardial infarction.



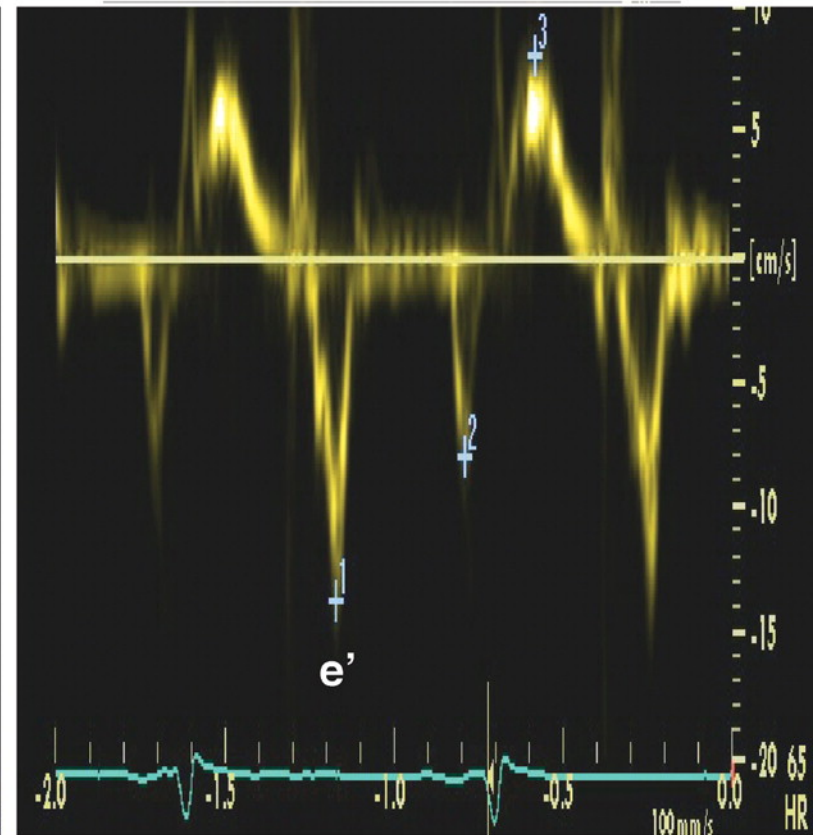
Nagueh S F et al. Eur J Echocardiogr 2009;10:165-193

Lateral (left) and septal (right) TD velocities from a patient with constrictive pericarditis.

Lateral Tissue Doppler



Septal Tissue Doppler

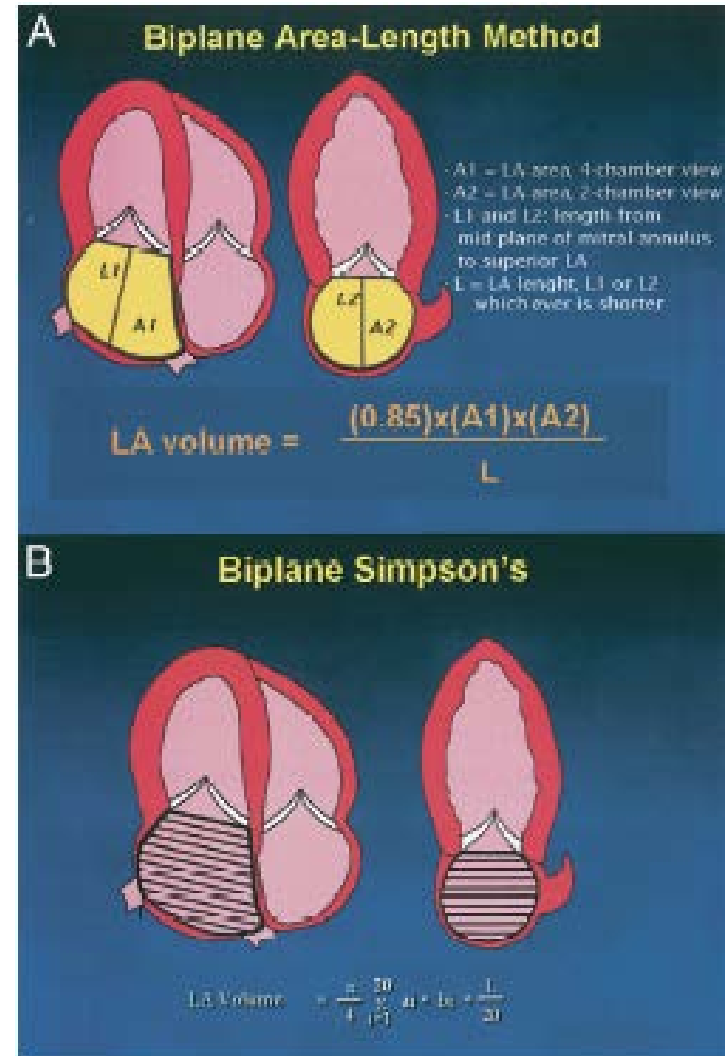


Nagueh S F et al. Eur J Echocardiogr 2009;10:165-193

Two-dimensional (2D) imaging is important to determine LV volumes, mass, and systolic function and left atrial (LA) volume. Patients with diastolic heart failure frequently have left ventricular hypertrophy, LA enlargement and increased PA pressures.

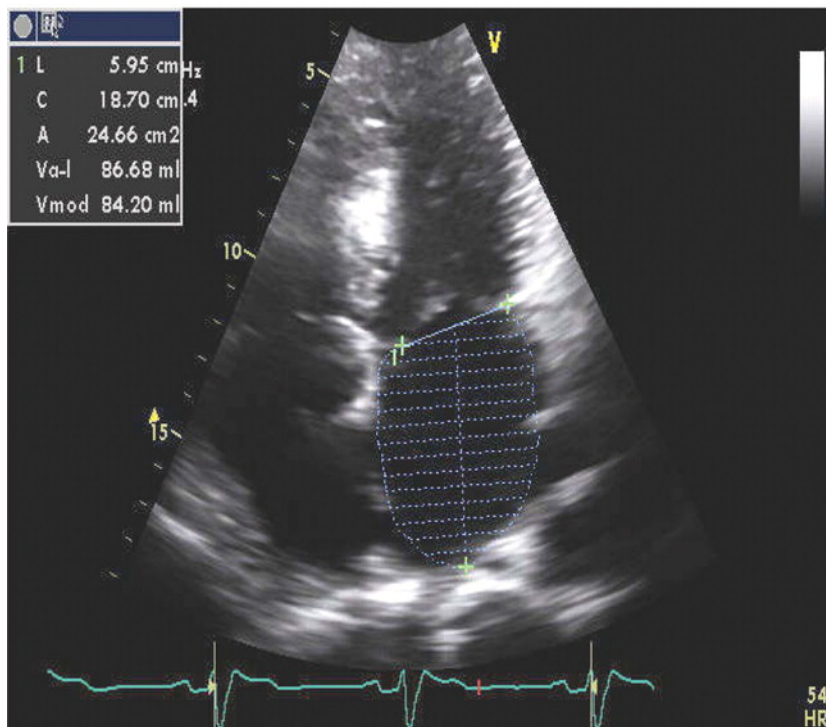
LA Volume

- Barometer (HgA1C) of the chronicity of diastolic dysfunction.
- Should be measured in comparison to body surface area (ml/m²)
- LA volume index
> 34 ml/m² is an independent predictor of death, heart failure, atrial fibrillation and ischemic stroke

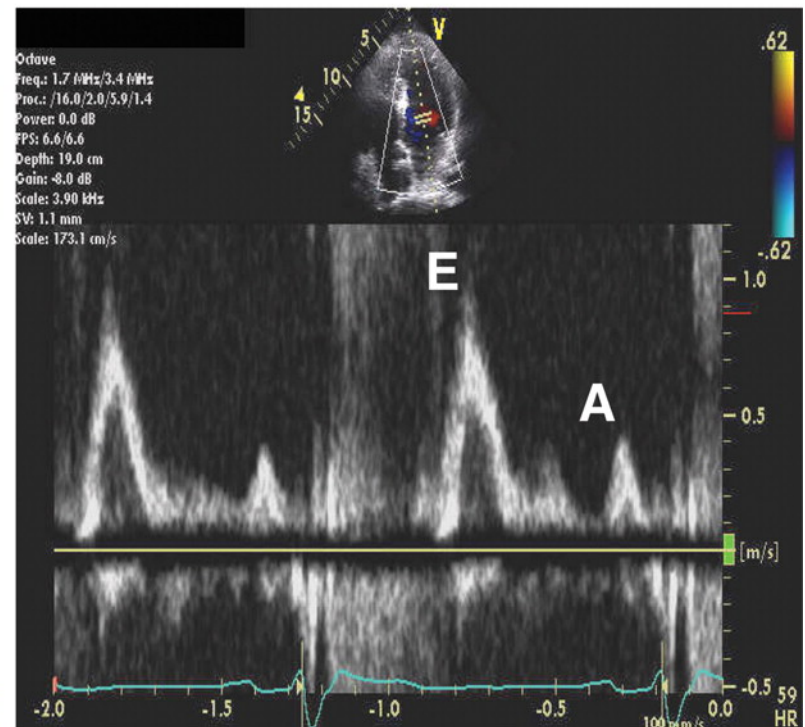


(Left) End-systolic (maximum) LA volume from an elite athlete with a volume index of 33 mL/m².

LA volume in apical 4-chamber view



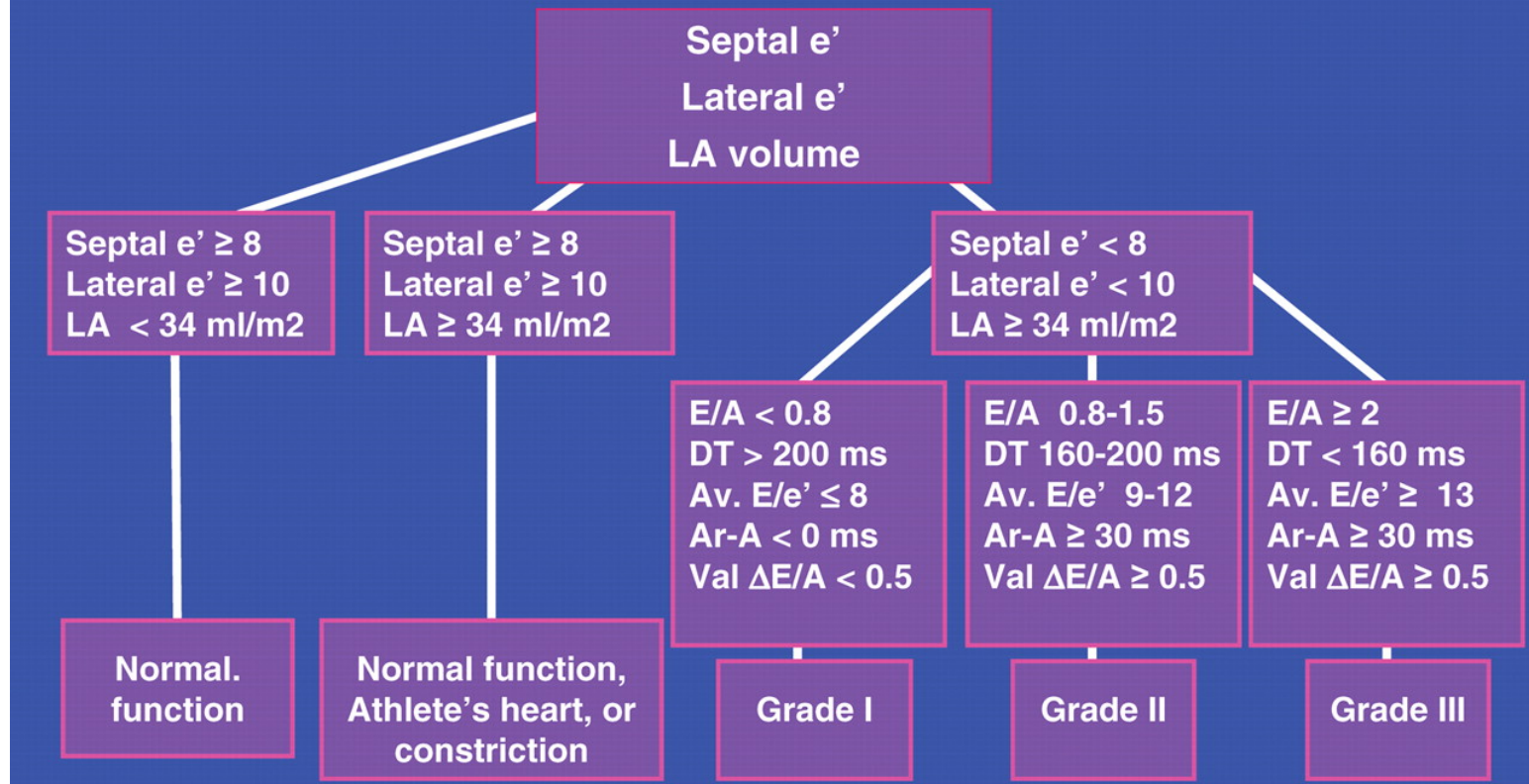
Mitral inflow at tips by PW Doppler



Nagueh S F et al. Eur J Echocardiogr 2009;10:165-193

Scheme for grading diastolic dysfunction.

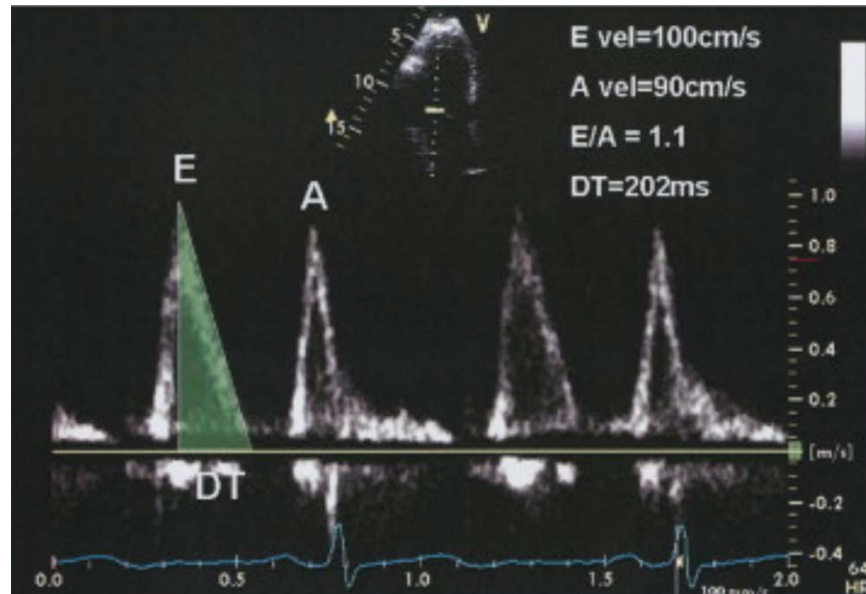
Practical Approach to Grade Diastolic Dysfunction



Nagueh S F et al. Eur J Echocardiogr 2009;10:165-193

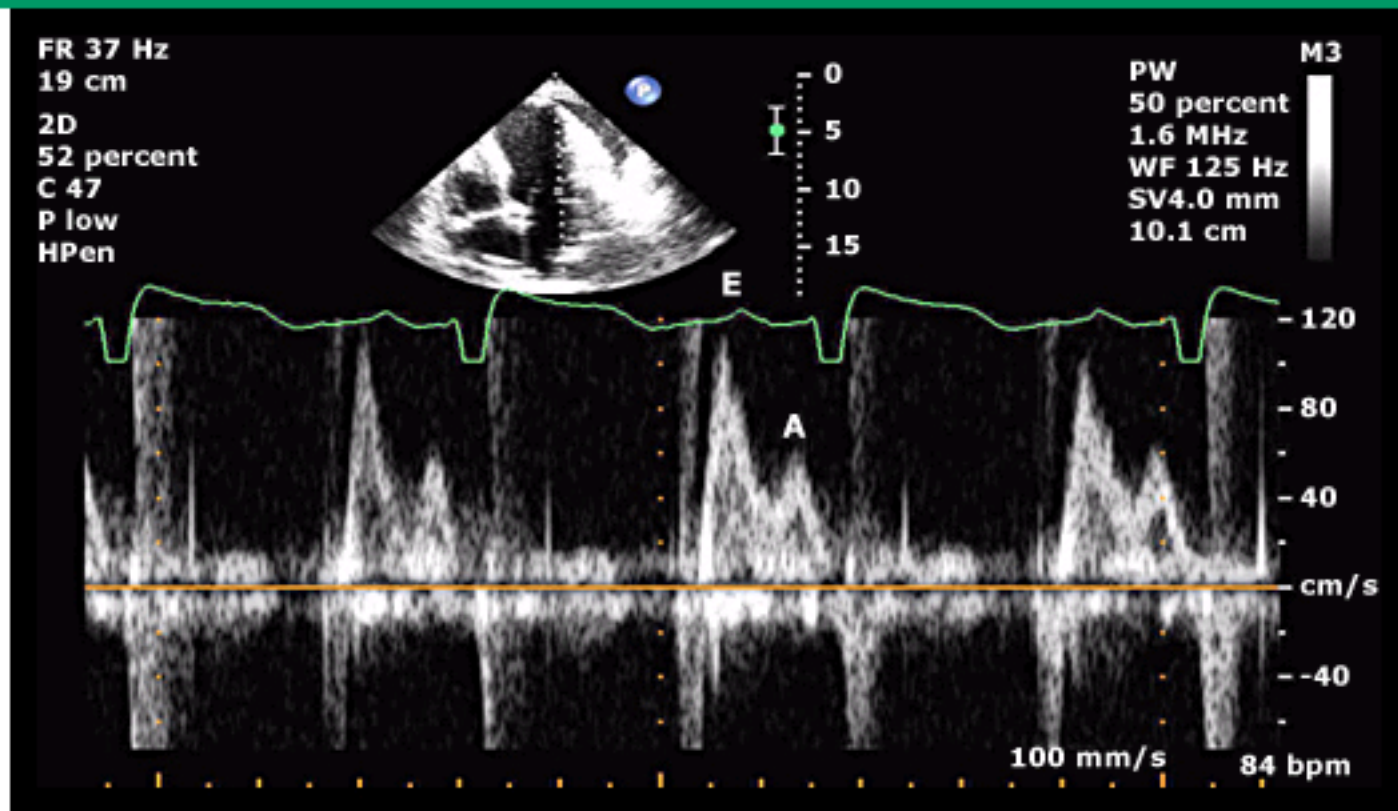
From: Unlocking the Mysteries of Diastolic Function: Title and subTitle BreakDeciphering the Rosetta Stone 10 Years Later

J Am Coll Cardiol. 2008;51(7):679-689. doi:10.1016/j.jacc.2007.09.061



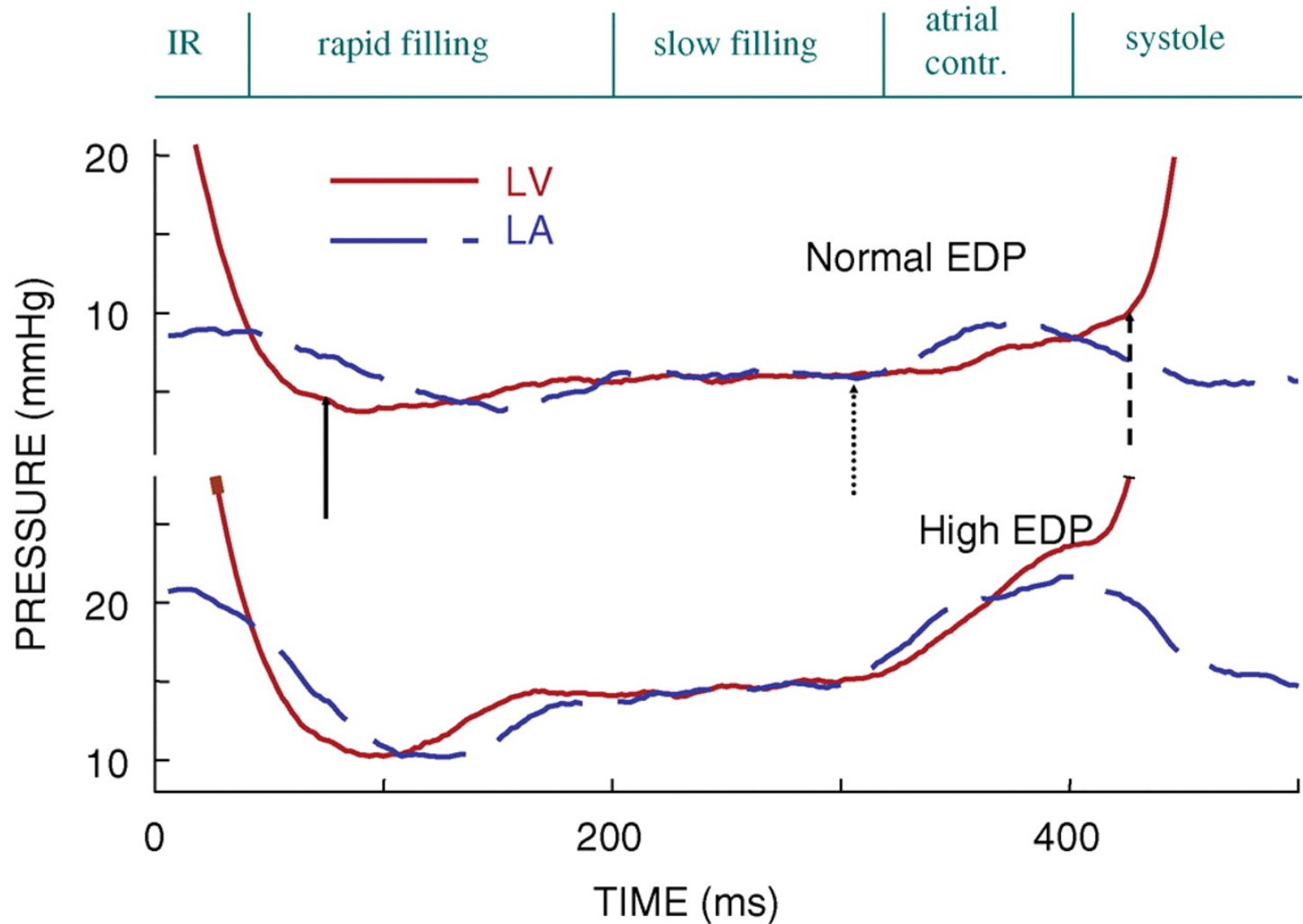
Primary measurements include peak E and A velocities, E/A ratio, DT, and IVRT.

Mitral flow inflow velocities

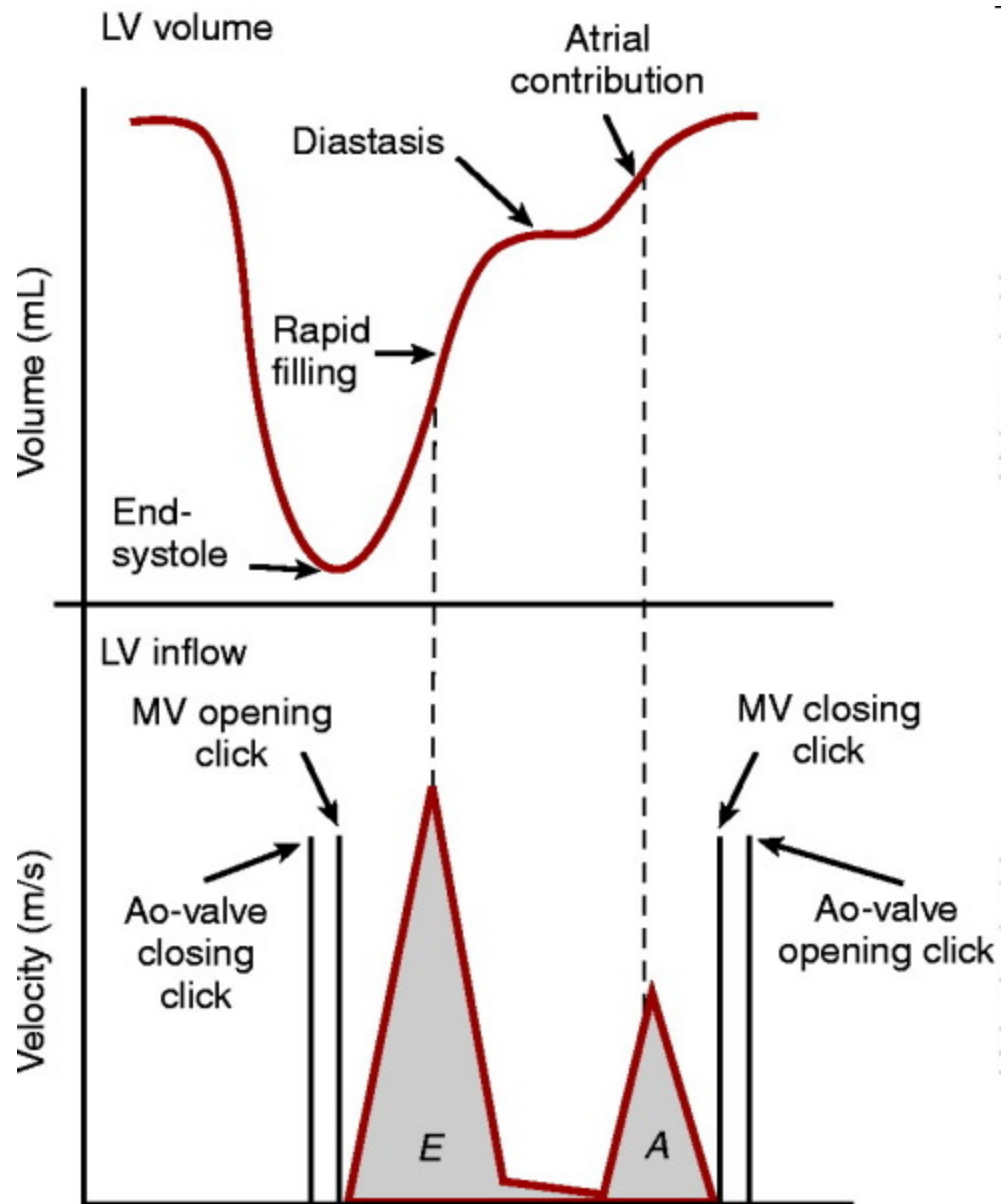


Courtesy of Dr. Sherif F Nagueh.

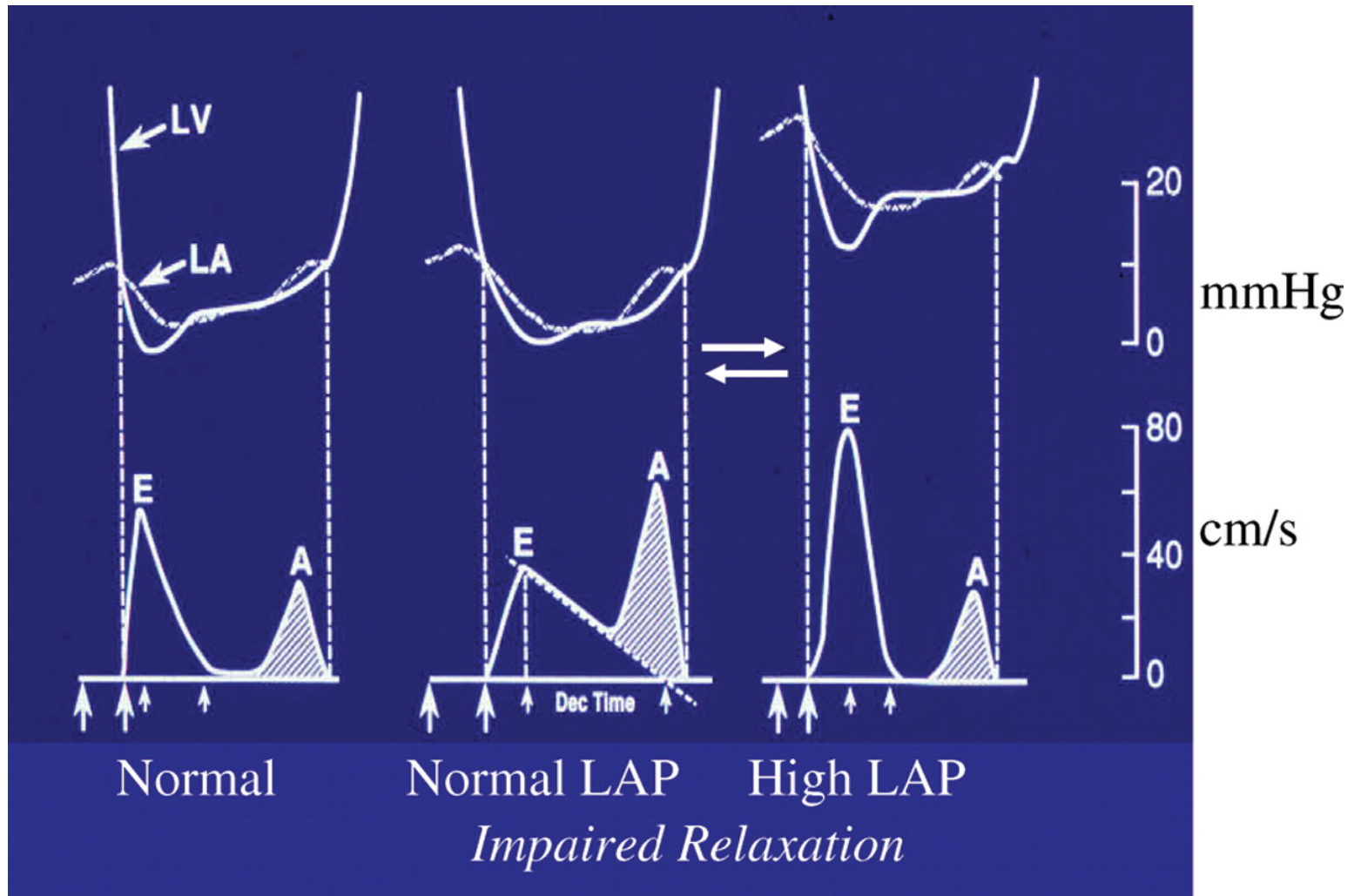
The 4 phases of diastole are marked in relation to high-fidelity pressure recordings from the left atrium (LA) and left ventricle (LV) in anesthetized dogs.



Nagueh S F et al. Eur J Echocardiogr 2009;10:165-193



Schematic diagram of the changes in mitral inflow in response to the transmitral pressure gradient.



Nagueh S F et al. Eur J Echocardiogr 2009;10:165-193

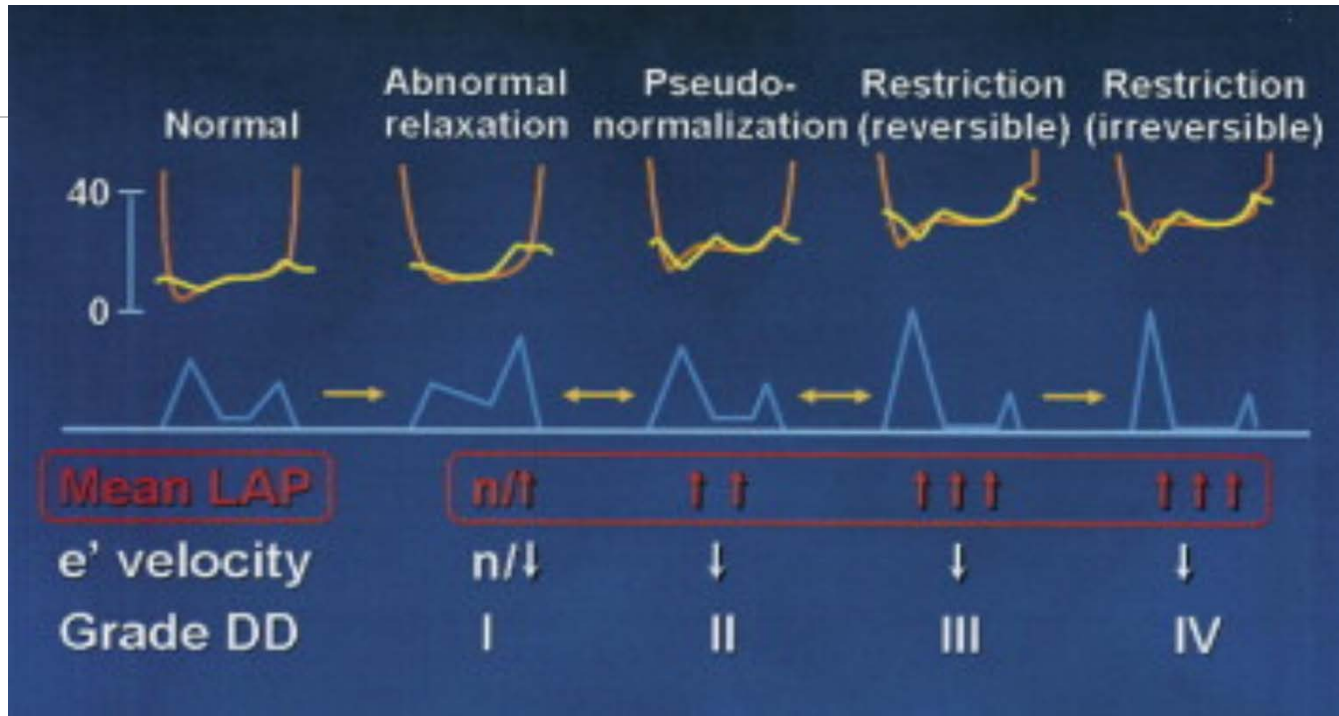


Figure Legend:

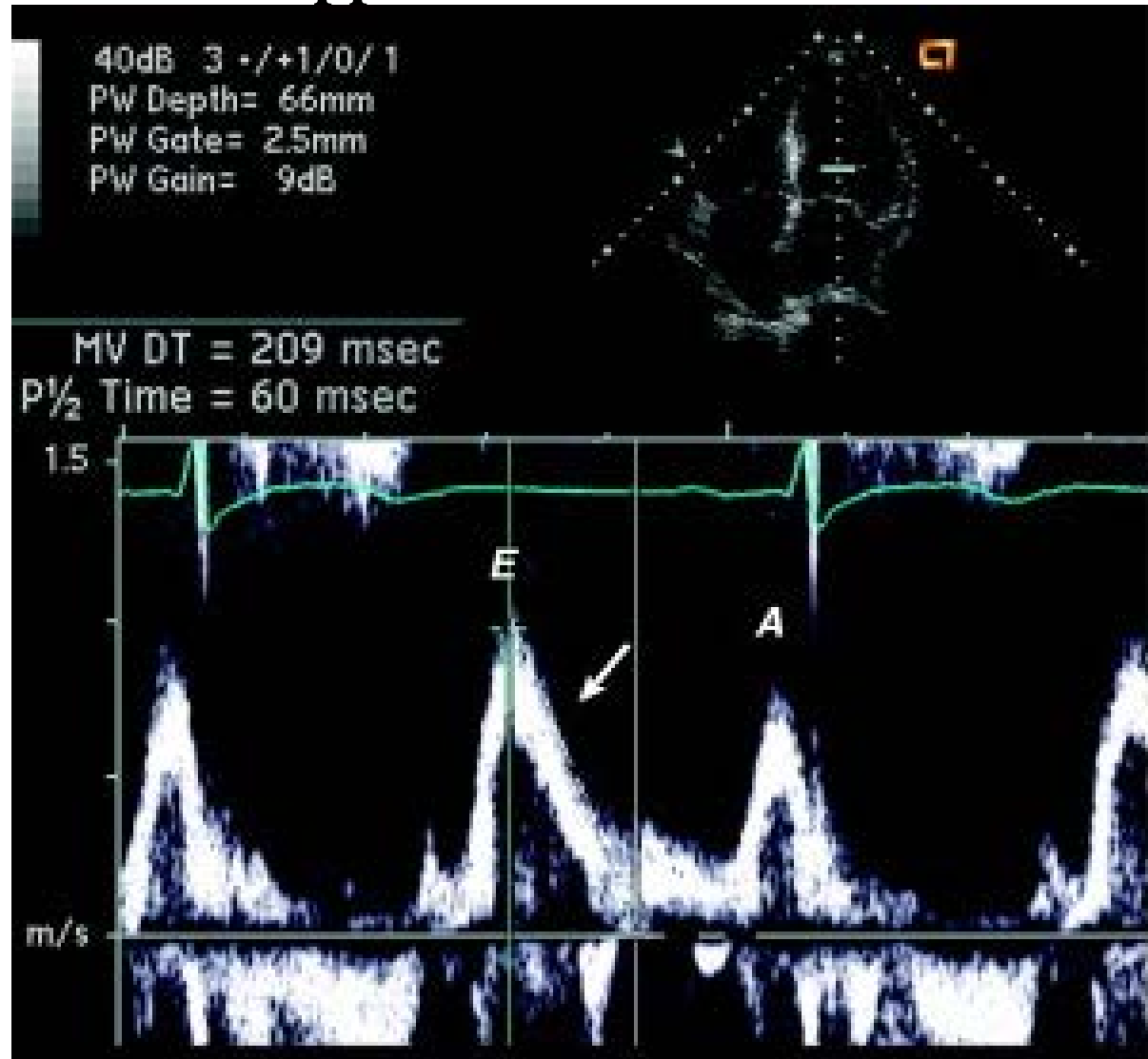
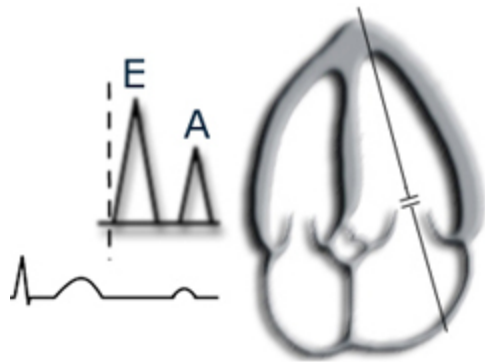
The Natural History of Diastolic Function and LV Filling

DD = diastolic function; e' = early diastolic mitral annular velocity; LAP = left atrial pressure; LV = left ventricular.

Pulsed Wave Doppler is performed in the apical 4 chamber view to obtain mitral inflow velocities to assess left ventricular filling

**1-3 mm sample volume between
tips of the leaflets of the mitral
valve during diastole**

Transmitral Doppler Inflow



**Valsalva maneuver can
be performed to
identify pseudonormal
filling**

The Valsalva maneuver is performed by forceful expiration (about 40 mm Hg) against a closed nose and mouth.

The patient must generate a sufficient increase in intrathoracic pressure, and the sonographer needs to maintain the correct sample volume location between the mitral leaflet tips during the maneuver.

A decrease of 20 cm/s in mitral peak E velocity is usually considered an adequate effort in patients without restrictive filling.

In cardiac patients, $\geq 50\%$
decrease in E/A ratio
has high specificity for increased
filling
pressures, but smaller changes do
not always
indicate normal diastolic function

In Systolic Heart Failure,
mitral velocities and
time intervals
correlate better with
filling pressures, and
prognosis
than Ejection Fraction

In patients with depressed left ventricular systolic function, mitral inflow velocities can be used as the first step in an algorithm to estimate LV filling pressure

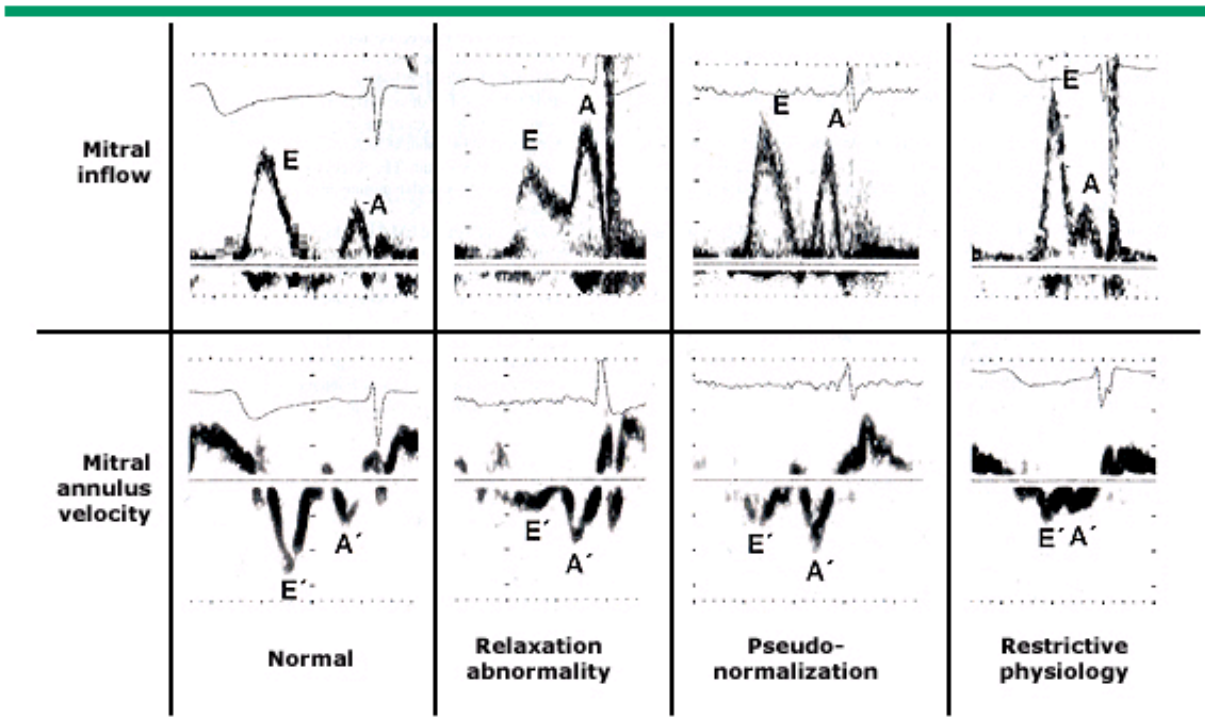
When the E/A ratio is <1 and pulmonary venous flow shows predominant systolic filling, LV filling pressures are usually normal.

On the other hand, a restrictive LV filling pattern (transmitral E/A ratio (≥ 2), IVRT (<70 ms) and DT (<150 ms)) indicates elevated LA pressure. LA pressure elevation can be confirmed with a systolic filling fraction <40 percent.

While most patients with pseudonormal filling have elevated filling pressures, it is preferable to confirm that conclusion by additional Doppler findings. These include the following: change in E/A ratio with Valsalva, E/e' ratio (average >15), E/Vp ratio (≥ 2.5), and PA systolic pressures (>35 mmHg).

In Diastolic Heart Failure,
mitral inflow velocities
do not relate well with
LV filling pressures

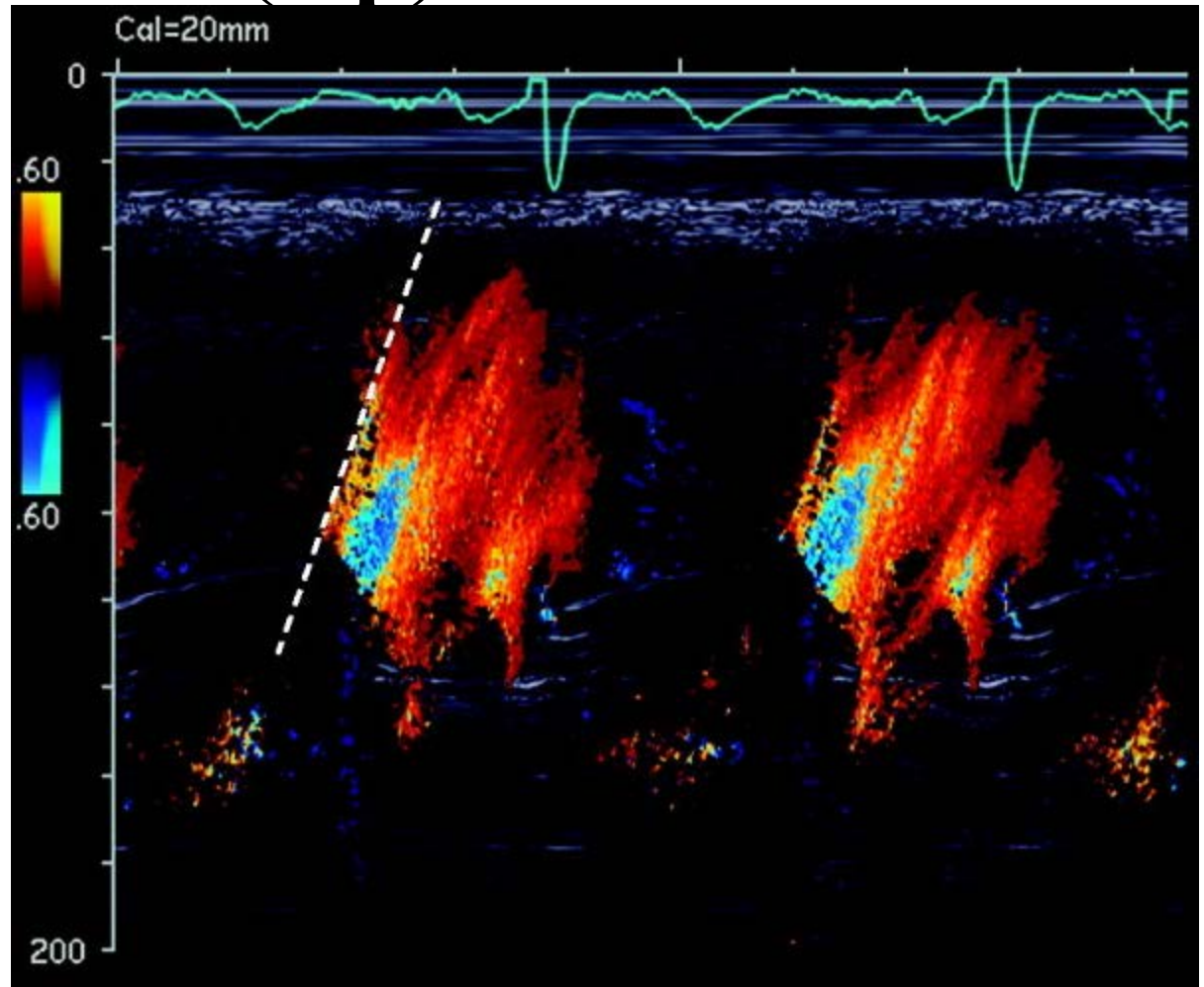
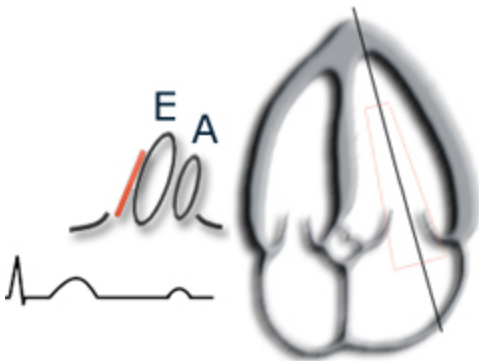
TDE assessment of mitral annulus velocity and diastolic dysfunction



Tissue Doppler echocardiography (TDE) can be used to assess the motion of the mitral annulus during diastole as a method of detecting diastolic dysfunction. The mitral valve ring moves toward the left ventricular apex (upward on the image) during systole. During diastole, there are two phases of motion. An early phase of movement away from the cardiac apex (downward on the image) corresponds to early diastolic filling and is analogous to the E wave on the Doppler profile of mitral inflow; it is marked E'. A late phase of movement in the same direction corresponds to atrial contraction and is analogous to the A wave; it is marked A'. The E' wave is blunted in the presence of either impaired relaxation or diminished compliance (restrictive physiology).

Reproduced with permission from: Sohn DW, Chai IH, Lee DJ, et al. Assessment of mitral annulus velocity by Doppler tissue imaging in the evaluation of left ventricular diastolic function. J Am Coll Cardiol 1997; 30:474. Copyright © 1997 American College of Cardiology.

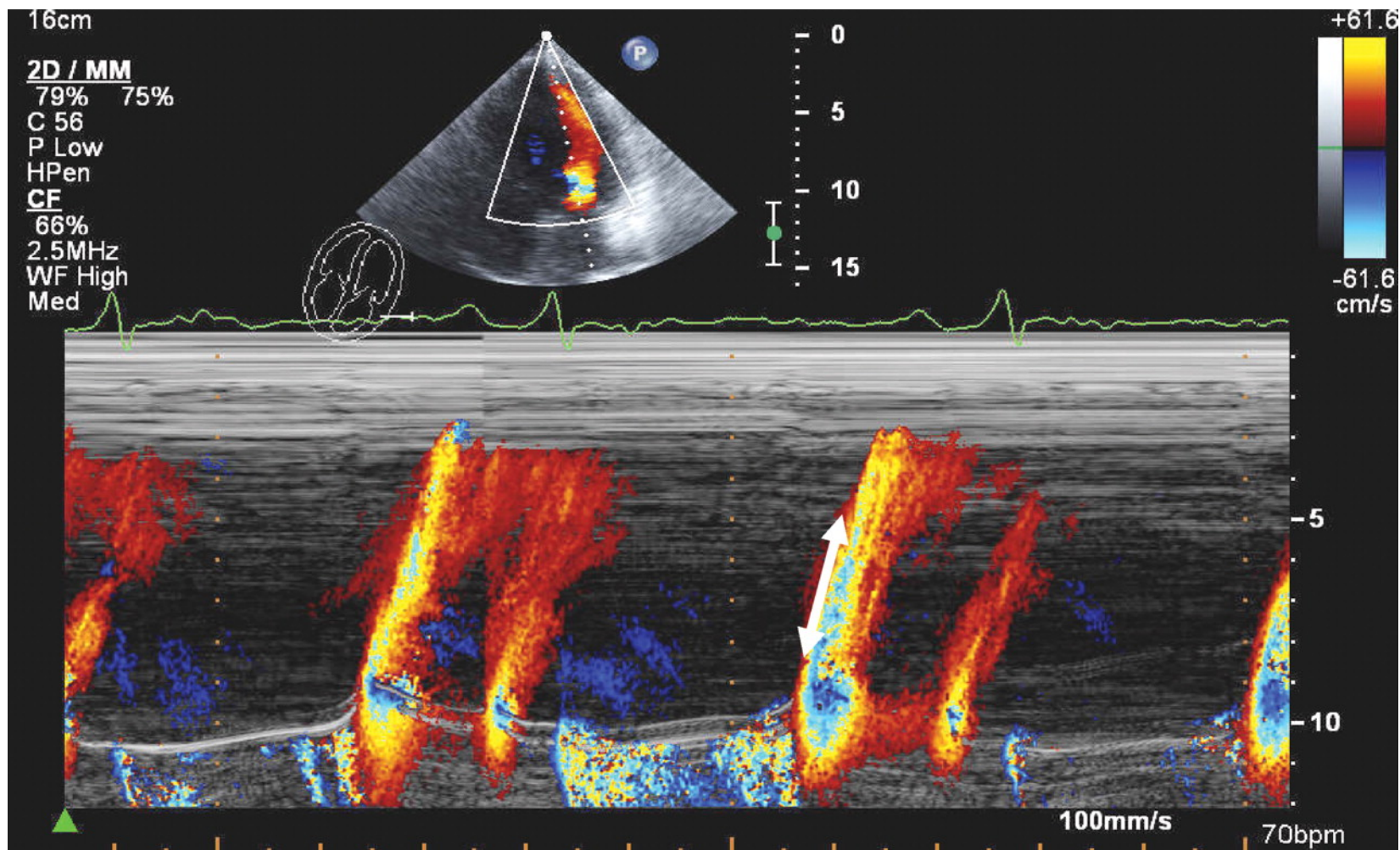
Mitral Inflow Propagation Velocity (V_p)



**M-mode scan line should
be placed in centre
of LV inflow column**

**Baseline shift so central
highest velocity jet is
blue**

Color M-mode Vp from a patient with depressed EF and impaired LV relaxation.



Nagueh S F et al. Eur J Echocardiogr 2009;10:165-193

In Systolic Heart Failure, an

$$\mathbf{E/V_p \geq 2.5}$$

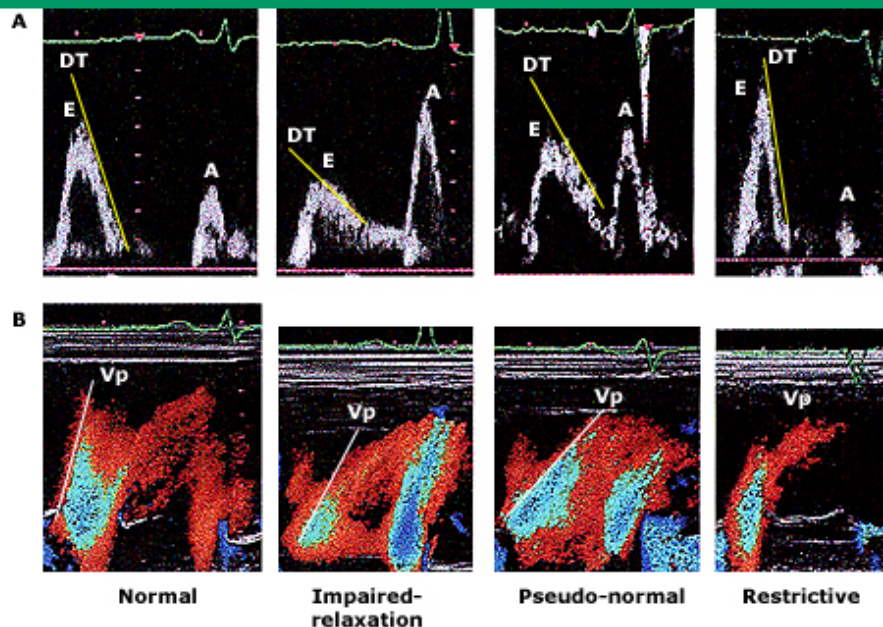
has good accuracy

in predicting

PCWP >15 mmHg

**In normal Ejection Fraction,
caution should be exercised as
 $V_p > 50$ cm/s
despite impaired LV relaxation**

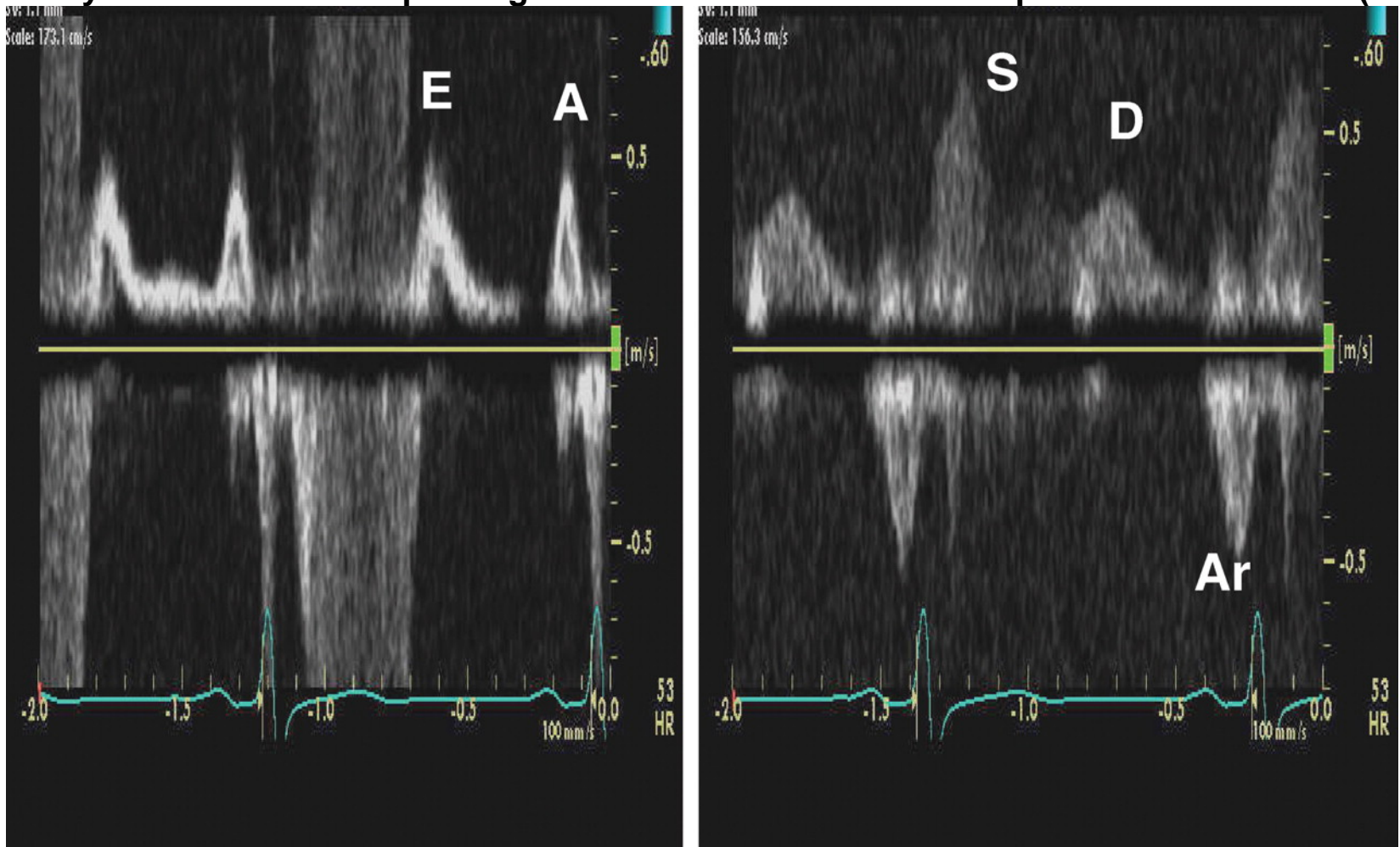
Left ventricular diastolic dysfunction is a predictor of outcome after a myocardial infarction



Pulsed Doppler recordings of transmitral filling (panel A) and color M-mode Doppler echocardiography (panel B) are methods for evaluating left ventricular (LV) diastolic function. In a normal filling pattern, the mitral E-wave deceleration time (DT) is 140 to 240 ms and the M-mode flow propagation velocity (Vp) is ≥ 45 cm/s. In diastolic dysfunction with impaired relaxation the DT is prolonged ≥ 240 ms and Vp is normal or reduced (< 45 cm/s). In a pseudonormal filling pattern the DT may be normal or prolonged, but the Vp is < 45 cm/s. In diastolic dysfunction with a restrictive filling, the DT is < 140 ms and the Vp is normal or < 45 cm/s. Patients with a myocardial infarction who have a restrictive or pseudonormal pattern have an increased incidence of left ventricular dilation and cardiac death.

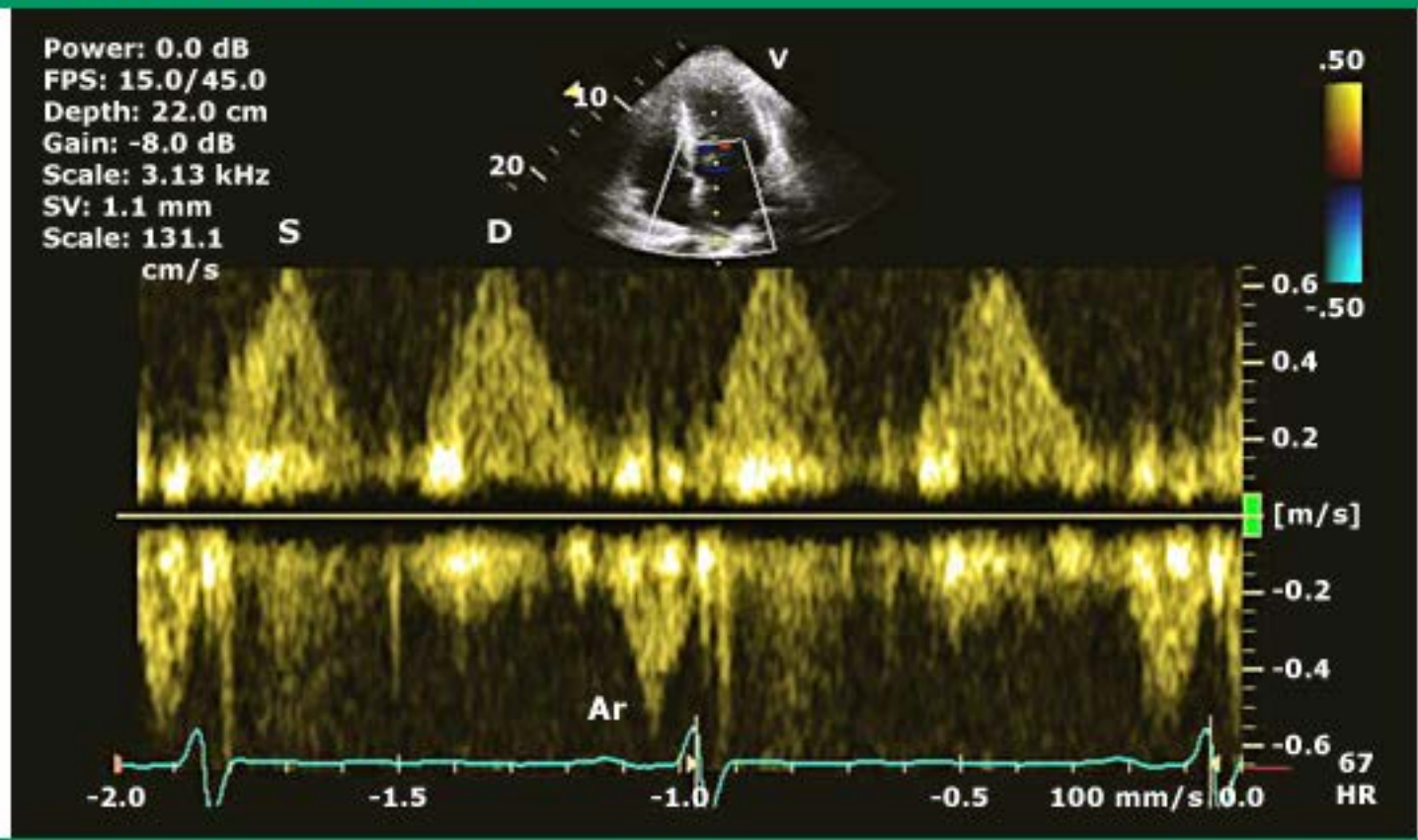
Data from Moller JE, Sondergaard E, Poulsen SH, Egstrup K. *J Am Coll Cardiol* 2000; 36:1841. Reprinted with permission from the American College of Cardiology.

Recording of mitral inflow at the level of the annulus (left) and pulmonary venous flow (right) from a patient with increased LVEDP. Notice the markedly increased pulmonary venous Ar velocity at 50 cm/s and its prolonged duration at >200 ms in comparison with mitral A (late



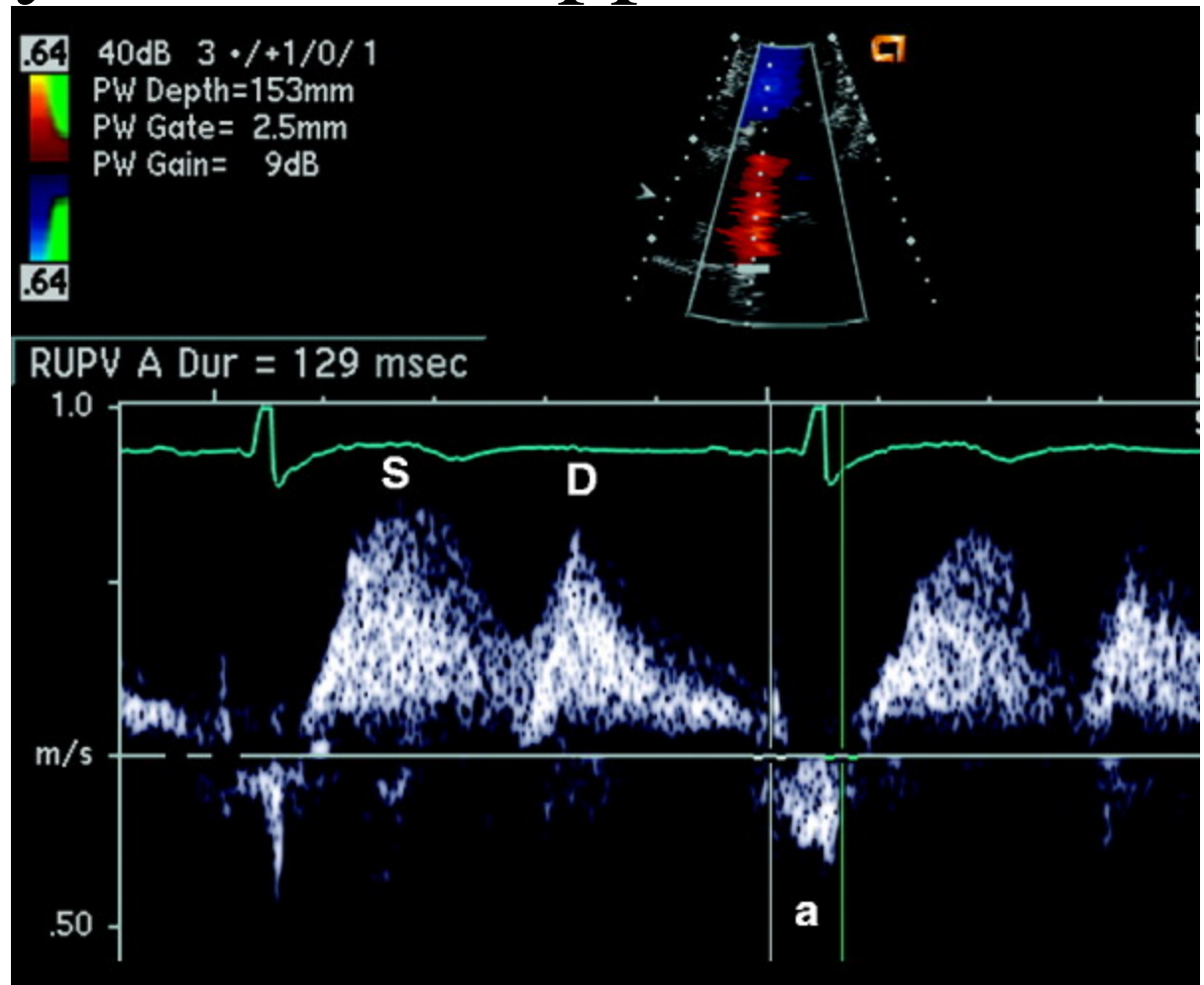
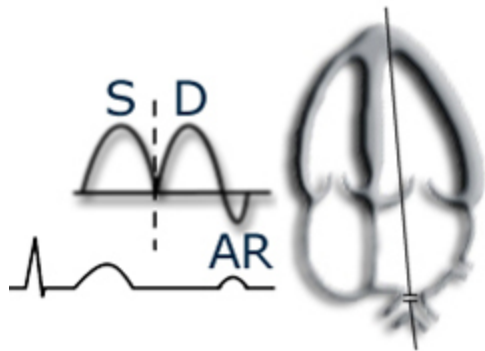
Nagueh S F et al. Eur J Echocardiogr 2009;10:165-193

Pulmonary vein velocities



Courtesy of Dr. Sherif F Nagueh.

Pulmonary Venous Doppler Flow



<http://www.echobasics.de/diastole-en.html>

PW Doppler of pulmonary venous flow is performed in the apical 4-chamber View. A 2-mm to 3-mm sample volume is placed 0.5 cm into the pulmonary vein for optimal recording of the spectral waveforms.

Measurements include peak S and D velocities, the S/D ratio, systolic filling fraction, and peak Ar velocity in late diastole. Another measurement is the time difference between Ar duration and mitral A-wave duration (Ar -A).

With increased LVEDP,
Ar velocity and duration
increase, as well as
Ar-A duration

In Systolic Heart Failure,
a SFF <40% is associated
with increased
LA Pressure

In Diastolic Heart Failure, systolic and diastolic velocities are not reliable predictors of LV filling pressures, but Ar and Ar-A duration can still be applied

Sinus tachycardia and AV block
are major
limitations to the clinical
application of
pulmonary venous flow
to assess
LV diastolic function

Doppler echocardiographic criteria for classification of diastolic function

	Normal diastolic function	Mild diastolic dysfunction	Moderate diastolic dysfunction*	Severe diastolic dysfunction	
		Impaired relaxation	Pseudonormal	Reversible restrictive	Fixed restrictive
Mitral inflow	$0.75 < E/A < 1.5$ DT > 140 ms	$E/A \leq 0.75$	$0.75 < E/A < 1.5$ DT > 140 ms	$E/A > 1.5$ DT < 140 ms	$E/A > 1.5$ DT < 140 ms
Mitral inflow at peak Valsalva Maneuver	$\Delta E/A < 0.5$	$\Delta E/A < 0.5$	$\Delta E/A \geq 0.5$	$\Delta E/A \geq 0.5$	$\Delta E/A < 0.5$
Doppler tissue imaging of mitral annular motion	$E/e' < 10$	$E/e' < 10$	$E/e' \geq 10$	$E/e' \geq 10$	$E/e' \geq 10$
Pulmonary venous flow	$S \geq D$ $ARdur < Adur$	$S > D$ $ARdur < Adur$	$S < D$ or $ARdur > Adur + 30$ ms	$S < D$ or $ARdur > Adur + 30$ ms	$S < D$ or $ARdur > Adur + 30$ ms
Left ventricular relaxation	Normal	Impaired	Impaired	Impaired	Impaired
Left ventricular compliance	Normal	Normal to ↓	↓↓	↓↓↓	↓↓↓↓
Atrial pressure	Normal	Normal	↑↑	↑↑↑	↑↑↑↑

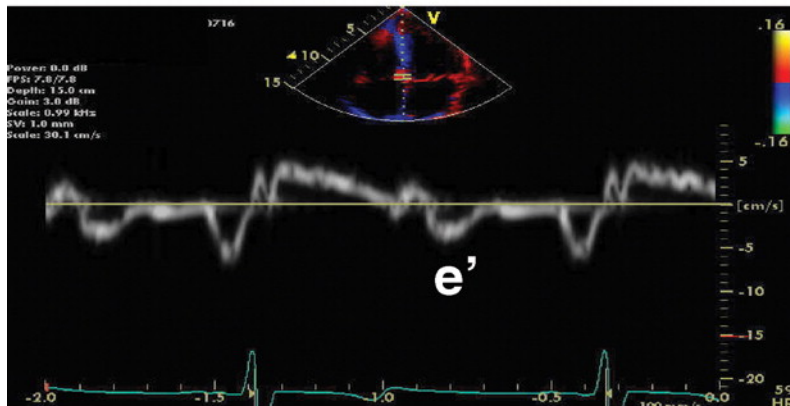
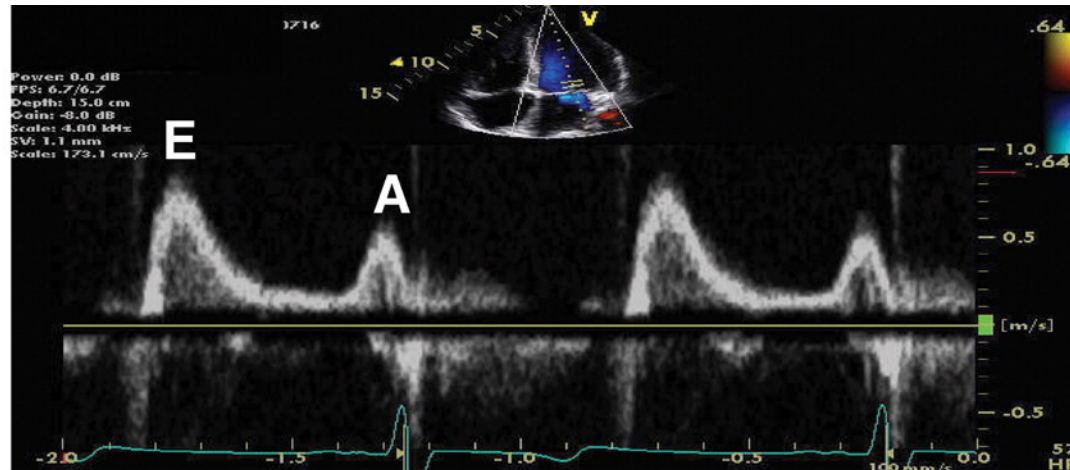
Participants with atrial fibrillation with DT > 140 ms, other arrhythmia, fusion of E and A, or in whom diastolic parameters were not obtained, who had only one criterion suggesting moderate or severe diastolic dysfunction, or in whom diastolic parameters were borderline and suggestive of but not diagnostic of abnormality were classified as having indeterminate diastolic function.

Grade I (mild) diastolic dysfunction is characterized by the impaired relaxation pattern. Grade II (moderate) diastolic dysfunction is characterized by a pseudonormal pattern. Grades III and IV (severe) diastolic dysfunction is characterized by a (irreversible and fixed) restrictive pattern.

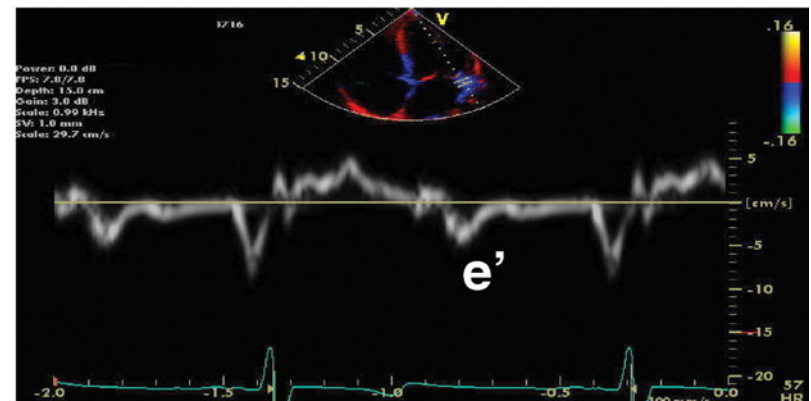
E: peak early filling velocity; A: velocity at atrial contraction; DT: deceleration time; Adur: A duration; ARdur: AR duration; S: systolic forward flow; D: diastolic forward flow; AR: pulmonary venous atrial reversal flow; e': velocity of mitral annulus early diastolic motion; a': velocity of mitral annulus motion with atrial systole; DT: mitral E velocity deceleration time.

Reproduced with permission from: Redfield MM, Jacobsen SJ, Burnett JC Jr, et al. Burden of systolic and diastolic ventricular dysfunction in the community: Appreciating the scope of the heart failure epidemic. JAMA 2003; 289:194. Copyright © 2003 American Medical Association. All rights reserved.

Mitral inflow (top), septal (bottom left), and lateral (bottom right) tissue Doppler signals from a 60-year-old patient with heart failure and normal EF. The E/e' ratio was markedly increased, using e' from either side of the annulus.



Septal $E/e' = 80/4 = 20$

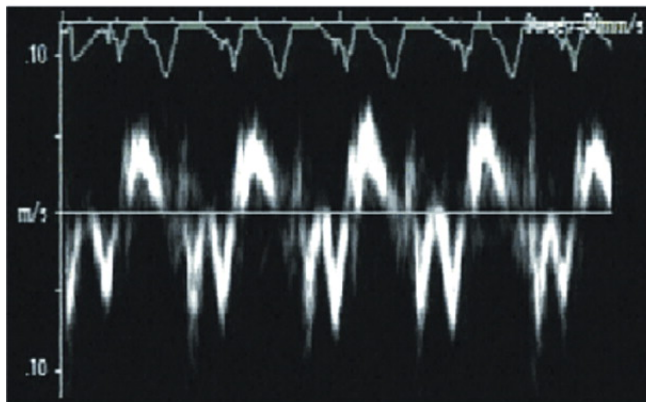
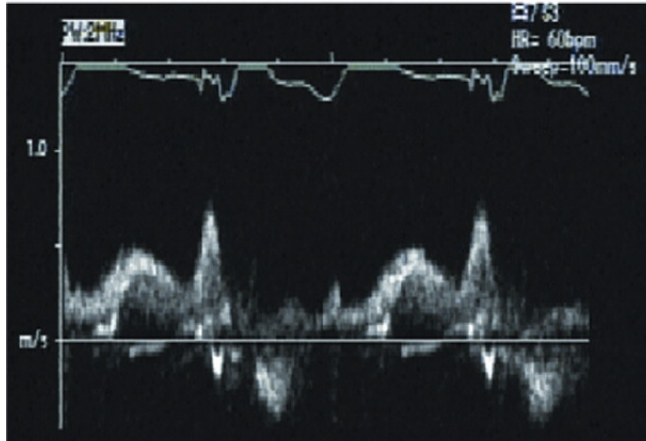


Lateral $E/e' = 80/5 = 16$

Nagueh S F et al. Eur J Echocardiogr 2009;10:165-193

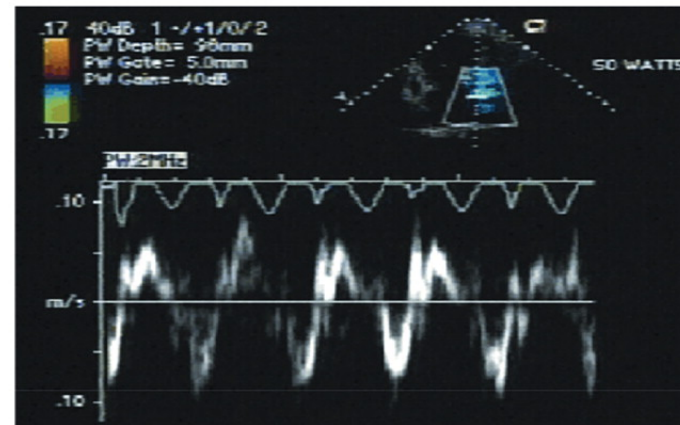
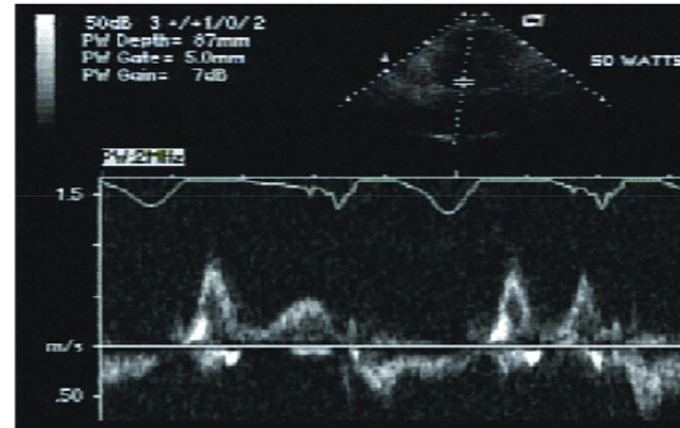
Exercise Doppler recordings from a patient with reduced diastolic reserve.

Baseline



E= 50 cm/s, DT= 250 ms
e' = 7, E/e' = 7
TR = 2.4 m/s

Supine Bike at 50 Watts

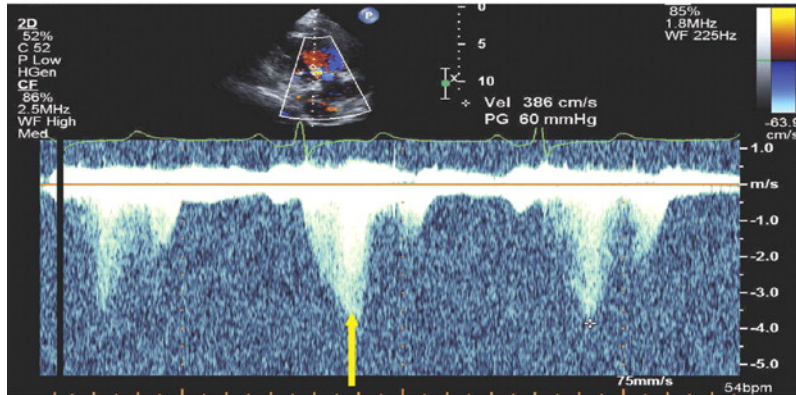


E= 85 cm/s, DT= 140 ms
e' = 8, E/e' = 11
TR = 3.8 m/s

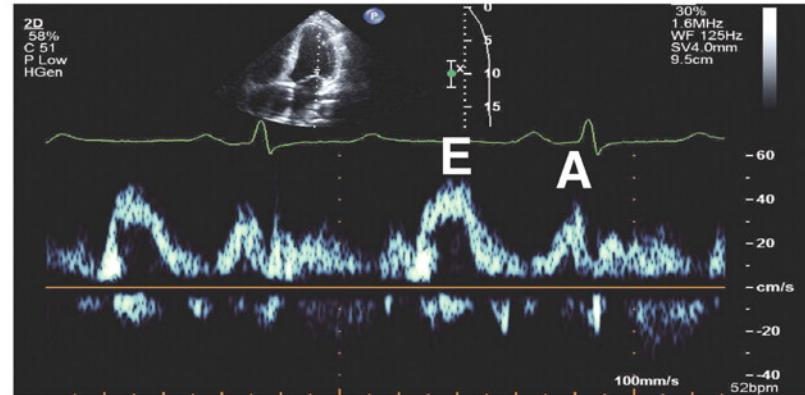
Nagueh S F et al. Eur J Echocardiogr 2009;10:165-193

(Top left) Recording of TR jet by CW Doppler (peak velocity marked by yellow arrow) from a patient with primary pulmonary hypertension.

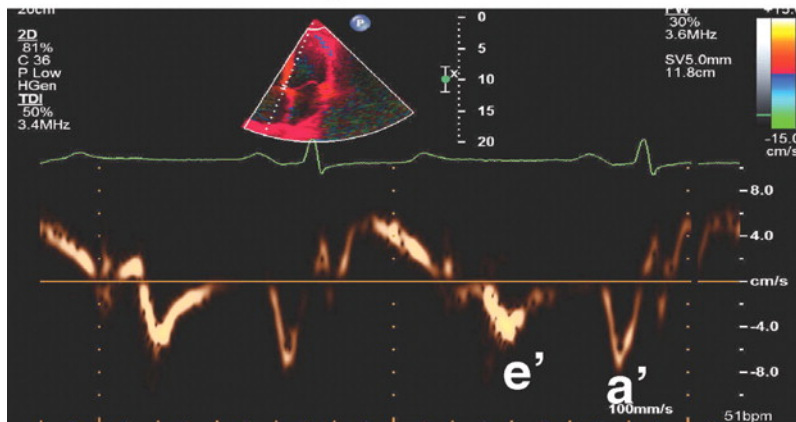
TR by CW Doppler



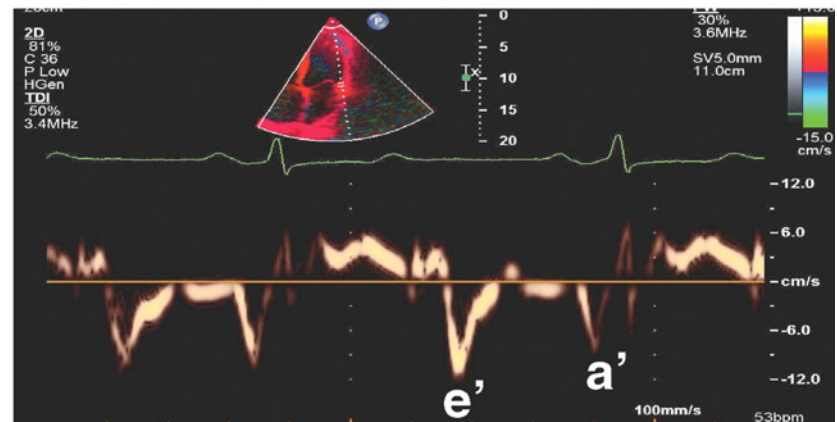
Mitral Inflow



TD at septal annulus



TD at lateral annulus



Nagueh S F et al. Eur J Echocardiogr 2009;10:165-193

Special Populations

- Atrial fibrillation
- Sinus tachycardia
- Hypertrophic cardiomyopathy
- Constrictive pericarditis
- Restrictive cardiomyopathy
- Noncardiac pulmonary hypertension
- Mitral Stenosis
- Mitral Regurgitation

From: Unlocking the Mysteries of Diastolic Function: Title and subTitle BreakDeciphering the Rosetta Stone 10 Years Later

J Am Coll Cardiol. 2008;51(7):679-689. doi:10.1016/j.jacc.2007.09.061

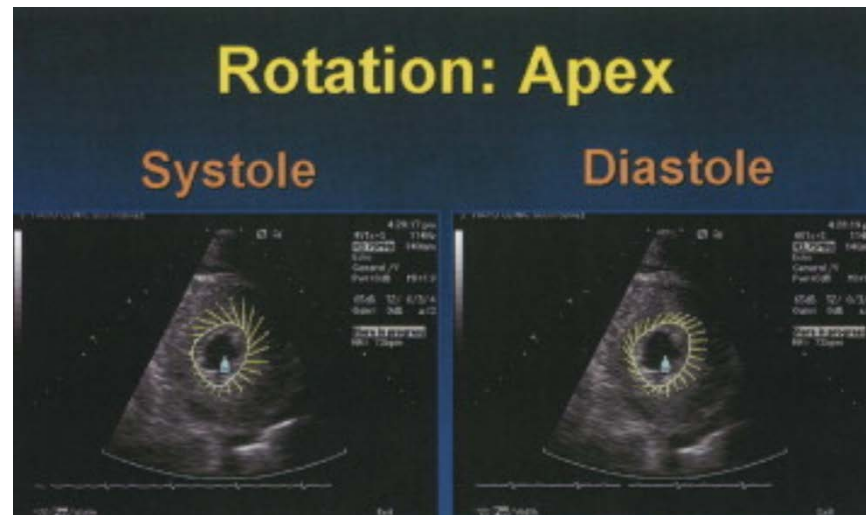
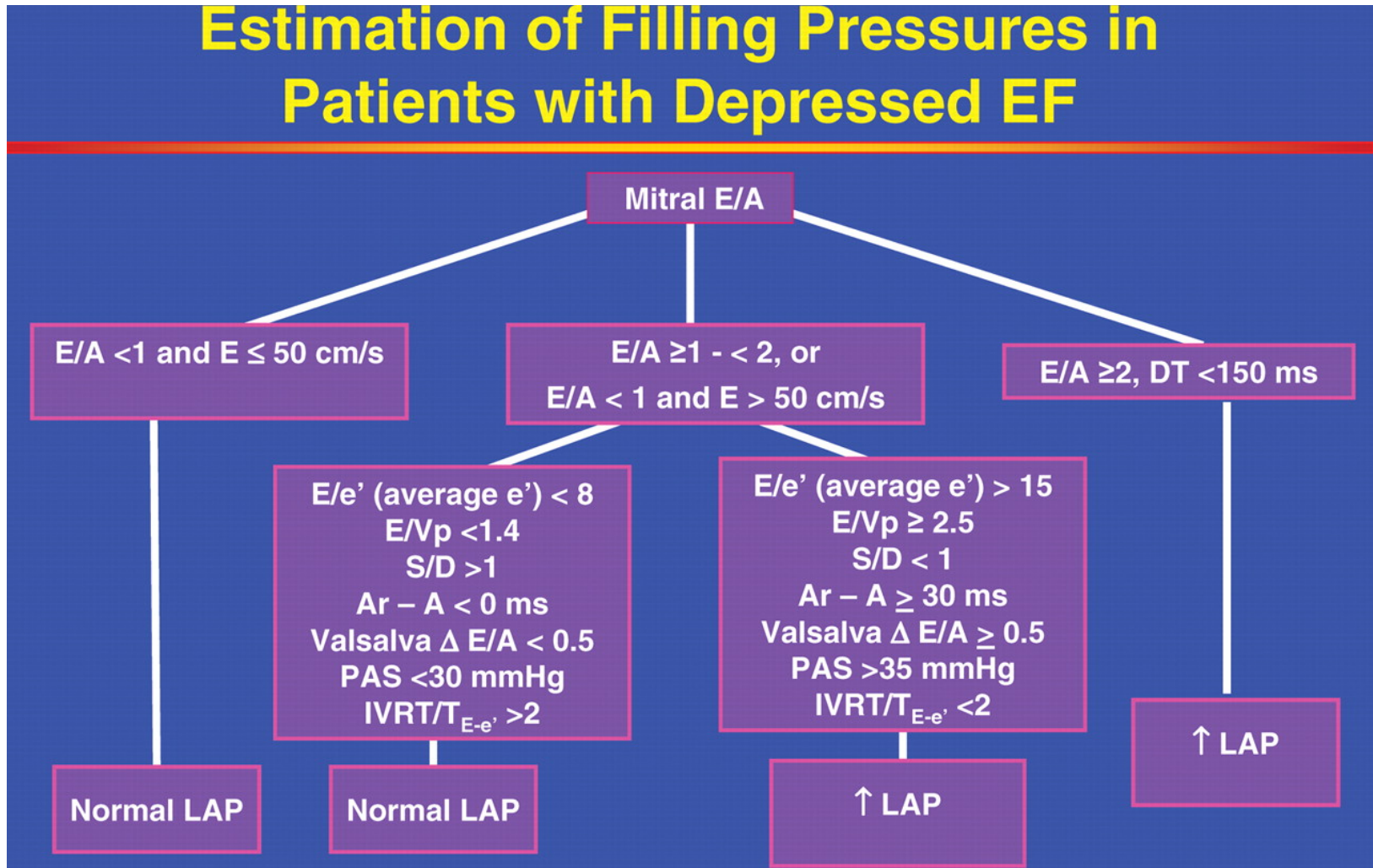


Figure Legend:

VVI Illustrating the Rotation Motion of the LV Apex

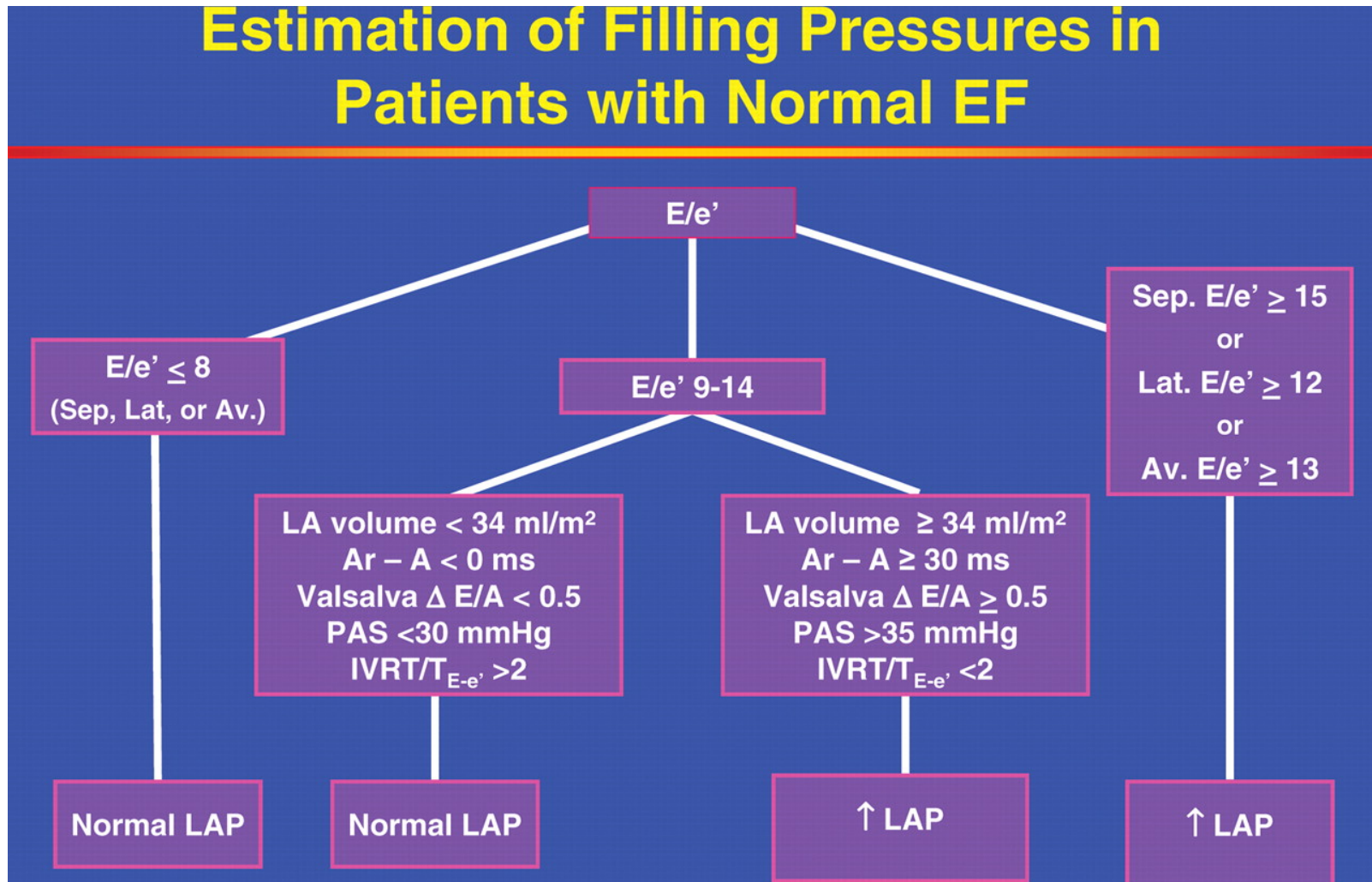
(Left) Systole where the apical rotation is predominantly anticlockwise; (right) systole where the apical rotation (now untwisting) is predominantly in the clockwise direction. LV = left ventricular; VVI = Velocity Vector Image.

Diagnostic algorithm for the estimation of LV filling pressures in patients with depressed EFs.



Nagueh S F et al. Eur J Echocardiogr 2009;10:165-193

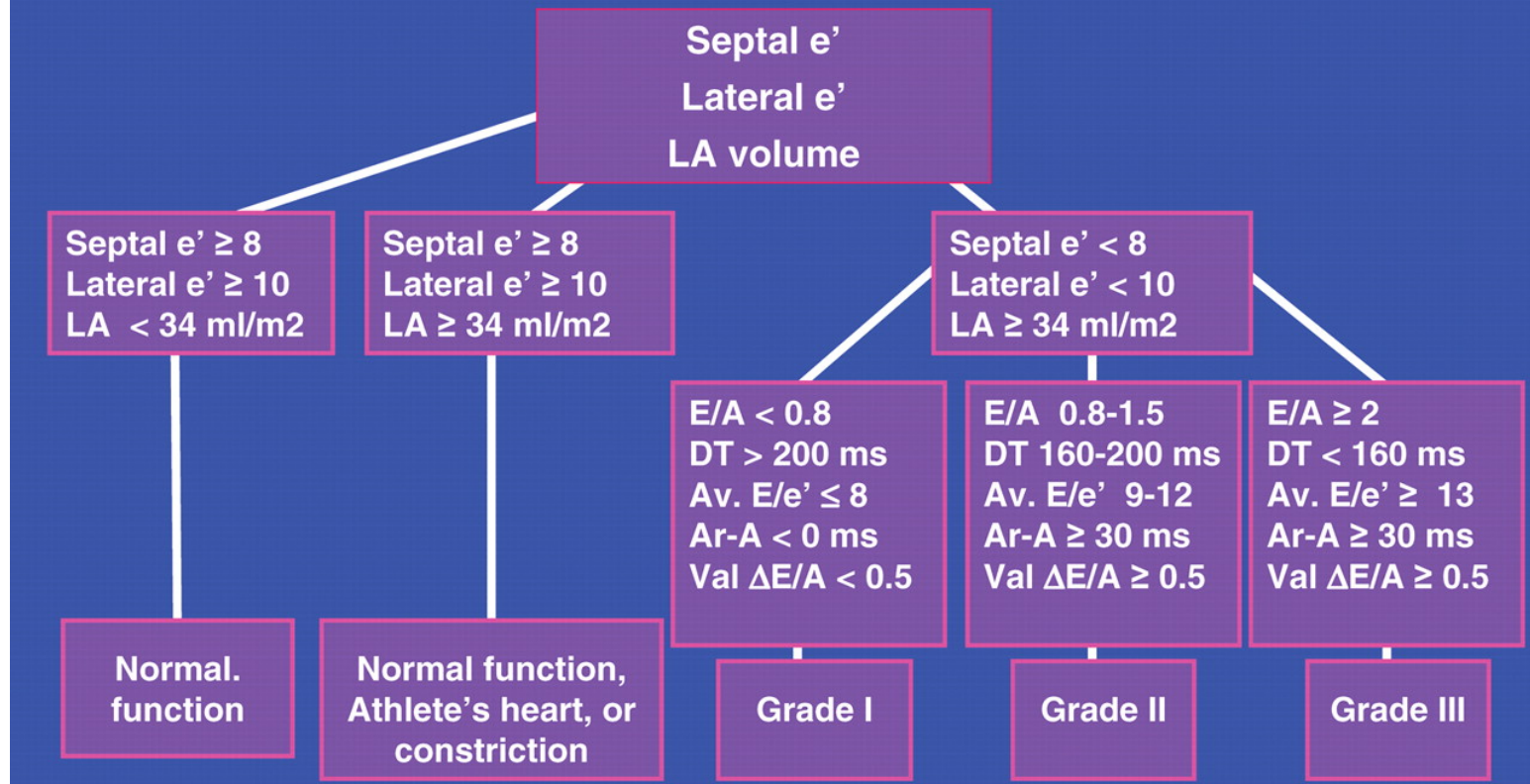
Diagnostic algorithm for the estimation of LV filling pressures in patients with normal EFs.



Nagueh S F et al. Eur J Echocardiogr 2009;10:165-193

Scheme for grading diastolic dysfunction.

Practical Approach to Grade Diastolic Dysfunction



Nagueh S F et al. Eur J Echocardiogr 2009;10:165-193

Treatment

Medications proven to be effective in
the treatment of HFPEF

The RELAX (Phosphodiesterase-5 Inhibition to Improve Clinical Status and Exercise Capacity in Heart Failure with Preserved Ejection Fraction) trial compared the effects of the PDE-5 inhibitor sildenafil with placebo in patients with HFPEF.

Conclusions:

The use of the phosphodiesterase-5 inhibitor sildenafil in patients with HFPEF did not result in significant improvement in exercise capacity or clinical status when compared to placebo.

Redfield MM, Chen HH, Borlaug BA et al. Phodiesterase-5 Inhibition on Exercise Capacity and Clinical Status in Heart Failure With Preserved Ejection Fraction. A Randomized Clinical Trial. JAMA 2013;309:1268-1277.

Asymptomatic LV diastolic dysfunction is a predictor of future cardiovascular morbidity. Symptomatic patients with DHF experience morbidities (eg, hospitalization for heart failure) at a rate that is virtually the same as that seen in patients with SHF. Mortality rates in both DHF and SHF are high; published data on differences in mortality rates are conflicting.

The treatment of DHF remains empiric since trial data are limited. The general principles for treatment of DHF are control of systolic and diastolic hypertension, control of ventricular rate, particularly in patients with atrial fibrillation, control of pulmonary congestion and peripheral edema with diuretics, and coronary revascularization in patients with coronary heart disease with ischemia judged to impair diastolic function.

An important caveat is that the patient who has LV diastolic dysfunction with a small, stiff left ventricular chamber is particularly susceptible to excessive preload reduction, which can lead sequentially to underfilling of the LV, a fall in cardiac output, and hypotension. In patients with severe left ventricular hypertrophy (LVH) due to hypertension or hypertrophic cardiomyopathy, excessive preload reduction can also create subaortic outflow obstruction.

For these reasons, the administration of diuretics or venodilators such as nitrates and dihydropyridine calcium channel blockers must be performed with caution.

Restoration and maintenance of sinus rhythm is preferred when AF occurs in patients with DHF. When this cannot be achieved, rate control becomes important.

ACC/AHA/ESC guideline summary: Management of patients with heart failure (HF) and preserved systolic function

Class I - There is evidence and/or general agreement that the following approaches are effective in the management of HF and preserved left ventricular systolic function

- Control of hypertension, both systolic and diastolic, according to current guidelines.
- Control of ventricular rate in atrial fibrillation.
- Control of pulmonary congestion and peripheral edema with diuretics.

Class IIa - The weight of evidence or opinion is in favor of the usefulness of the following approach in the management of HF and preserved left ventricular systolic function

- Coronary revascularization for symptomatic or asymptomatic myocardial ischemia that is thought to have an adverse effect of cardiac function.

Class IIb - The weight of evidence or opinion is less well established for the usefulness of the following approaches in the management of HF and preserved left ventricular systolic function

- Restoration of sinus rhythm to improve diagnosis in patients with atrial fibrillation.
- Among patients controlled hypertension, use of beta blockers, angiotensin converting enzyme inhibitors, angiotensin II receptor blockers, and calcium channel blockers in an attempt to reduce symptoms of HF.
- Digitalis to reduce symptoms of HF.

Data from: Hunt SA, Abraham WT, Chin MH, et al. ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure): developed in collaboration with the American College of Chest Physicians and the International Society for Heart and Lung Transplantation: endorsed by the Heart Rhythm Society. Circulation 2005; 112:e154.

Management of patients with diastolic heart failure

Control edema

- Low salt diet (eg, <2 g sodium per day)
- Diuretic (eg, furosemide or hydrochlorothiazide)
- ACE inhibitor* (eg, enalapril or lisinopril)
- Angiotensin II receptor blocker* (eg, candesartan, valsartan, or losartan)
- Aldosterone antagonist* (eg, spironolactone)

Rate control

- Calcium channel blocker (eg, diltiazem or verapamil)
- Beta blocker (eg, atenolol, metoprolol)
- Radiofrequency modification of atrioventricular node and pacing

Maintain and restore atrial contraction

- Cardioversion
- Radiofrequency ablation
- Antiarrhythmic therapy

Manage myocardial ischemia

- Medical management
 - Nitrates (eg, isosorbide dinitrate or isosorbide mononitrate)
 - Beta blocker (eg, atenolol or metoprolol)
 - Calcium channel blocker (eg, diltiazem or verapamil)
- Percutaneous coronary intervention
- Coronary artery bypass surgery

Control arterial hypertension•

- Diuretic (eg, chlorthalidone or hydrochlorothiazide)
- Beta blocker (eg, atenolol or metoprolol)
- Calcium channel blocker (eg, amlodipine or felodipine)
- Angiotensin converting enzyme inhibitor (eg, enalapril or lisinopril)
- Angiotensin II receptor blocker (eg, candesartan, valsartan, or losartan)

*The renin-angiotensin-aldosterone system is inhibited by angiotensin converting enzyme inhibitor, angiotensin II receptor blocker, and aldosterone antagonist and thus these agents have a theoretical benefit in promoting regression of left ventricular hypertrophy and preventing myocardial fibrosis. However more data are required to demonstrate whether they improve outcomes in patients with diastolic heart failure. Two of these three agents may be combined in some patients with proper monitoring but use of all three is generally not recommended.

• The list of medications is not comprehensive but rather includes examples that are in common clinical use or have been included in studies of patients with diastolic dysfunction or heart failure. A more exhaustive list of antihypertensive agents can be found in the guidelines of the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.

Courtesy of Dr. William H. Gaasch.