

Physiology of Diastolic Function Made Easy

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Bluhm Cardiovascular Institute
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Chicago, Illinois

Conflicts of interest: GE, Abbott, Edwards (honoraria)
Spouse employment: Bay Labs

Diastole is Not a Single Entity

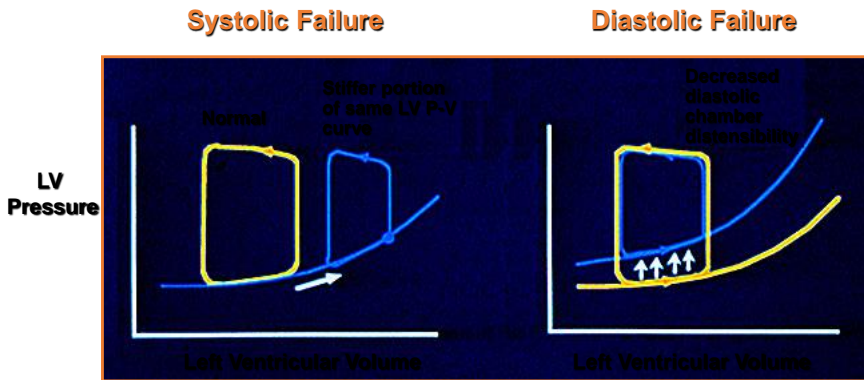
Four Components of Diastolic Dysfunction

1. Fill on a stiff pressure-volume loop
2. Delay LV relaxation
3. Lose diastolic suction
4. Suffer atrial systolic failure

These rarely occur in isolation but considering them separately helps to understand diastole

How to Get Diastolic Dysfunction

1) Fill on Stiff P-V Loop



Lorell BH. Ann Rev Med 1991;42:411-37

Medical Physiology
Lectures

Sources of Passive Elasticity

Collagen	++++
Titin	++++
Actin	++
Intermediate	+
Microtubules	-

Passive Tension in Cardiac Muscle: Contribution of Collagen, Titin, Microtubules, and Intermediate Filaments
Granzier HL, Irving TC Biophysical Journal 1995; 68: 1027-1044

Medical Physiology
Lectures

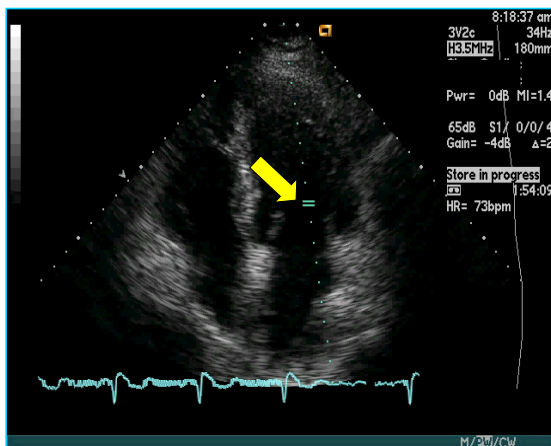
Diastology 2018

Available Echocardiographic Methods

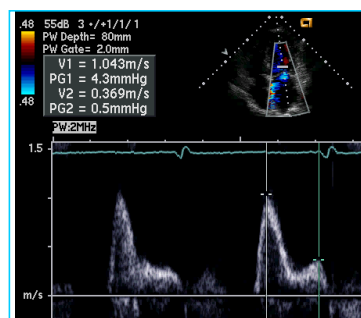
- *Transmitral velocity profiles*
- *Pulmonary venous profiles*
- *Doppler tissue imaging*
- *Color Doppler M-mode*
- *Future directions*

NYC Department of Health
NYC Medicine

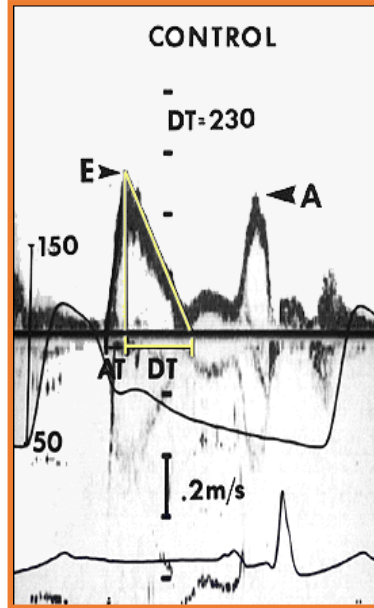
Mitral Inflow: E/A Velocity



SV at MV Leaflet Tips



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NYC Medicine

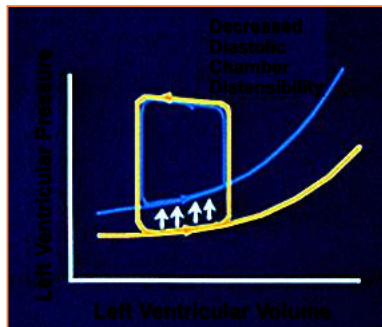
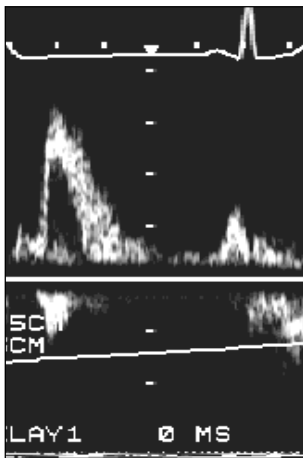


Key parameters of the mitral inflow pattern:

- E velocity
- Decel time
- A velocity
- A Duration
- E/A ratio

MV Deceleration

Physical Determinants

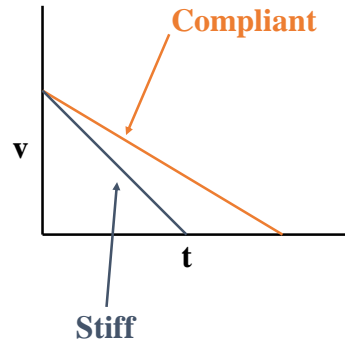
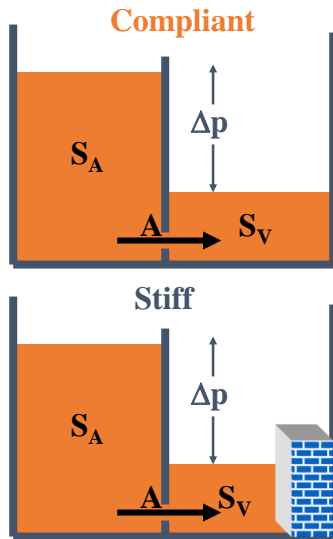


The stiffer the ventricle, the more rapid the pressure rise and reversal of Δp and the more rapid the deceleration

$$dv/dt \approx -MVA/(LA-LV \text{ Compliance})$$

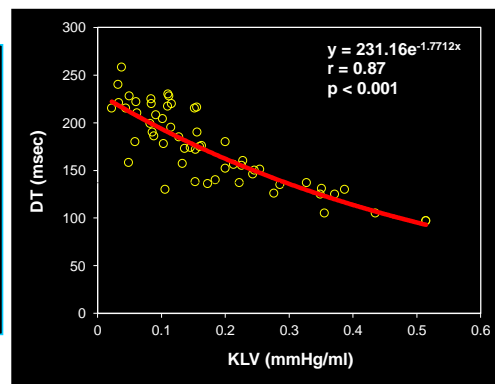
Physical Determinants of Deceleration

Stiffer Ventricle = Shorter Decel Time



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 University of Michigan

$$DT \propto 1/LV \text{ stiffness}$$



- $DT \sim 140 \text{ msec} \Rightarrow \text{stiffness} \sim 0.3 \text{ mmHg/ml}$

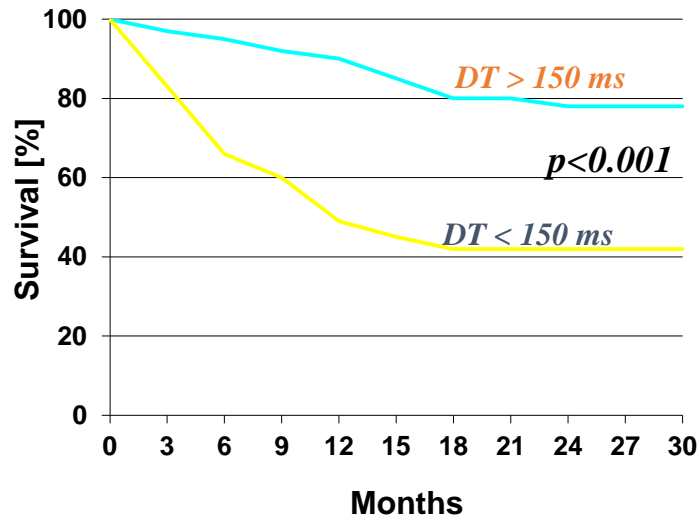
Little et al. *Circulation* 1995;92:1933

Garcia et al. *Am J Physiol* 2001;280:H554

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Transmitral Flow and Prognosis

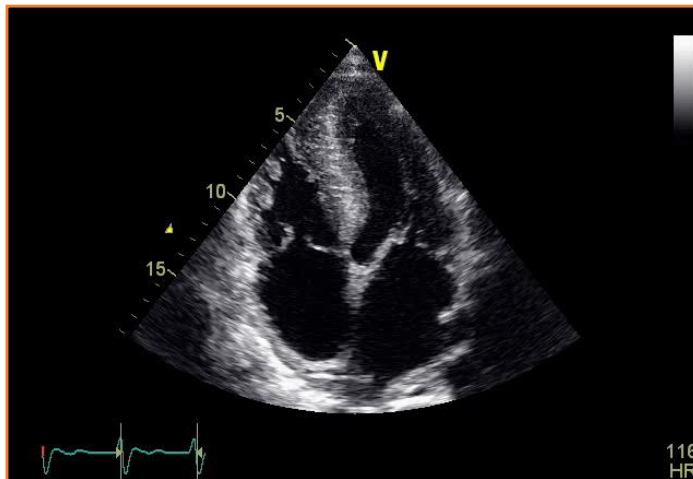
Restrictive Cardiomyopathy



Klein et al., Circ 1991; 83: 808-815

Medical
Medicine

Some Ventricles LOOK Like Amyloid

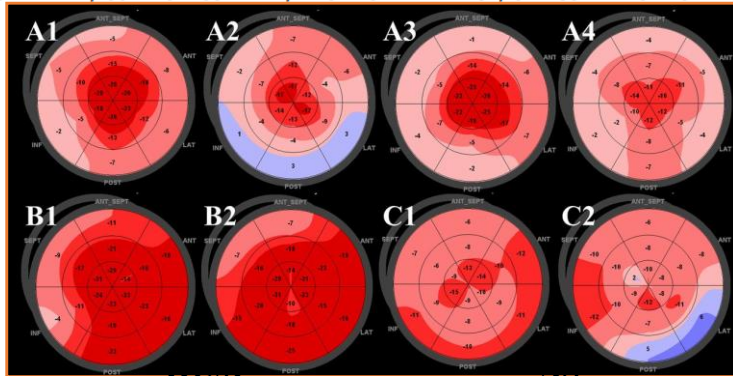


Are there new diagnostic methods for less obvious ones?

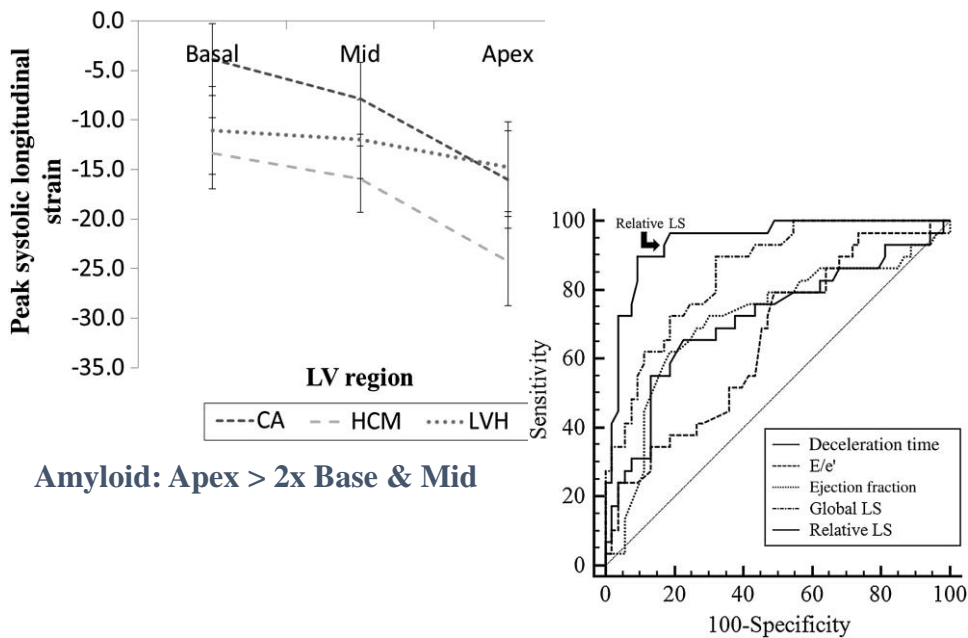
Medical
Medicine

Relative 'apical sparing' of longitudinal strain using two-dimensional speckle-tracking echocardiography is both sensitive and specific for the diagnosis of cardiac amyloidosis

Dermot Phelan, Patrick Collier, Paaladinesh Thavendiranathan, Zoran B Popović, Mazen Hanna, Juan Carlos Plana, Thomas H Marwick, James D Thomas



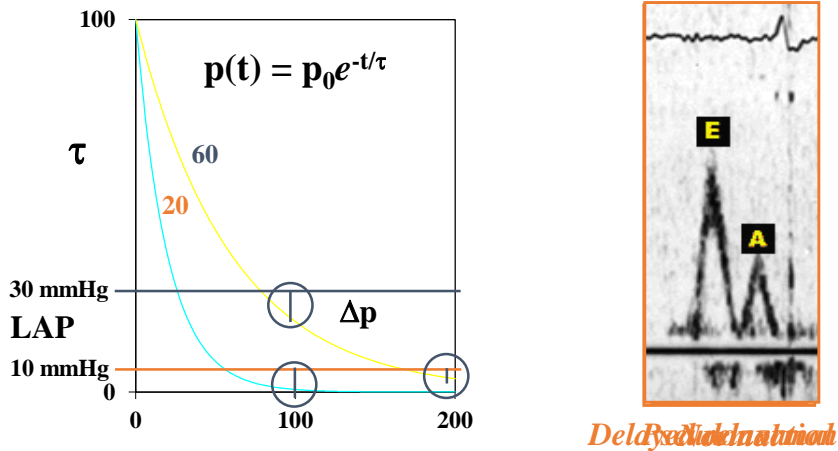
Phelan, Collier et al. Heart 2012; 98: 1442-1448



Phelan, Collier et al. Heart 2012; 98: 1442-1448

How to Get Diastolic Dysfunction

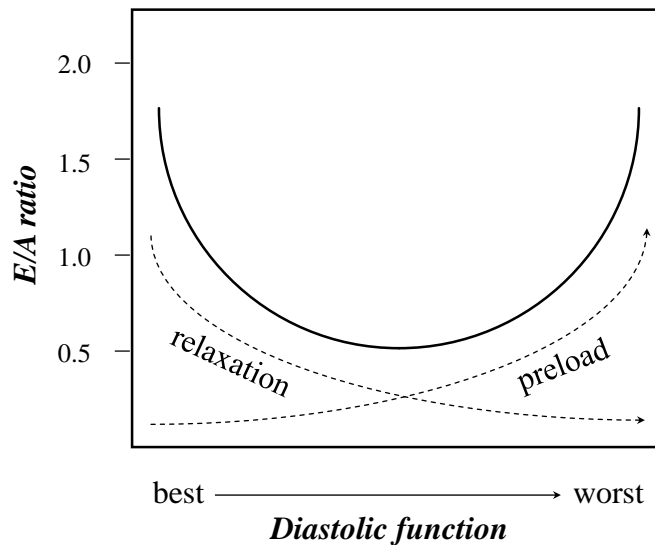
2) Delay relaxation



Rate of rise is proportional to growth of transmural pressure gradient, Δp , and $d\Delta p/dt = LAP/\tau$

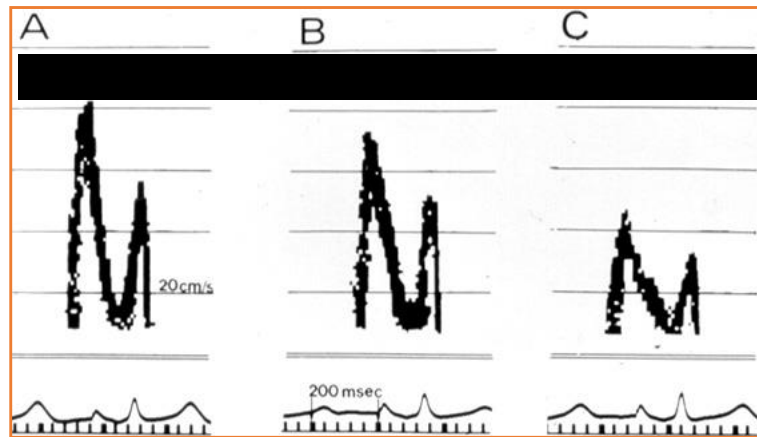
Preload vs Relaxation

Confounding Effects



Garcia et al, JACC 1998;32:865

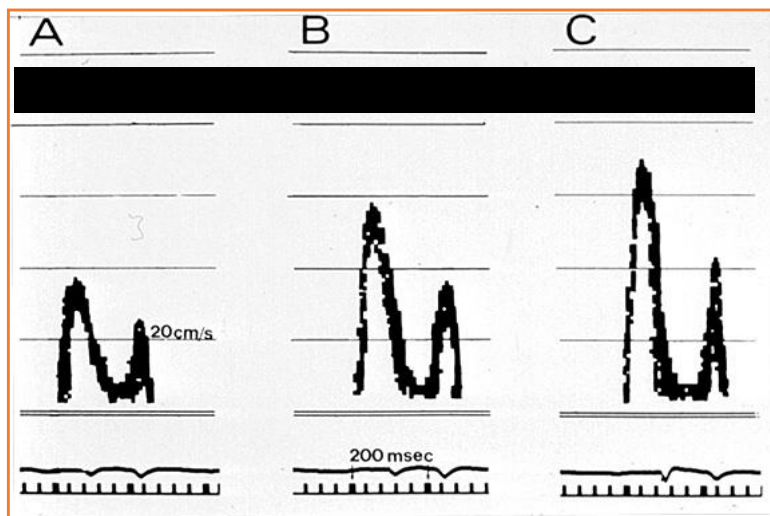
Effect of Relaxation on LV Inflow



With delayed relaxation, acceleration is slowed and E peak is lower.

Choong, et al, Circ 1987

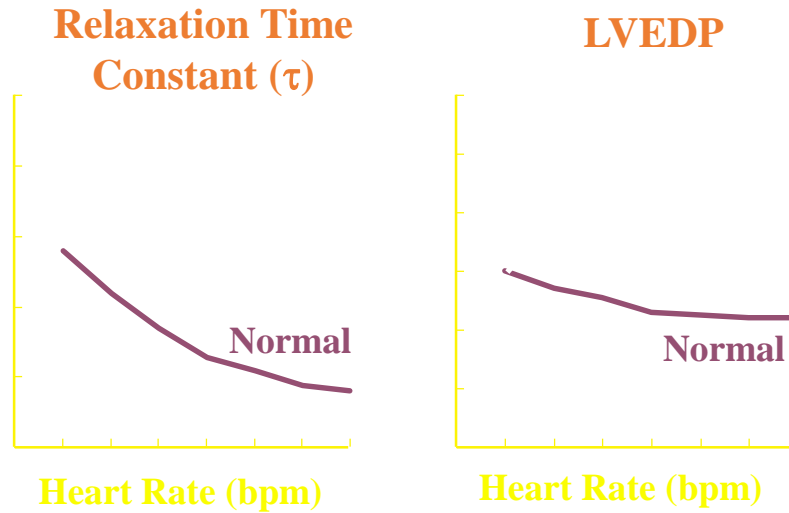
Effect of LAP on LV Inflow



With rising LA pressure, acceleration is faster and E peak is higher.

Choong, et al, Circ 1987

Exercise Can Unmask Delayed Relaxation



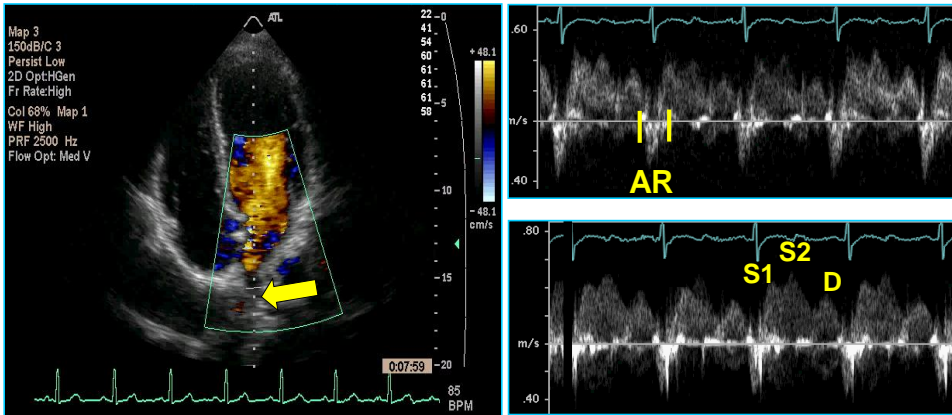
Diastology 2018

Available Echocardiographic Methods

- *Transmitral velocity profiles*
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- *Doppler tissue imaging*
- *Color Doppler M-mode*
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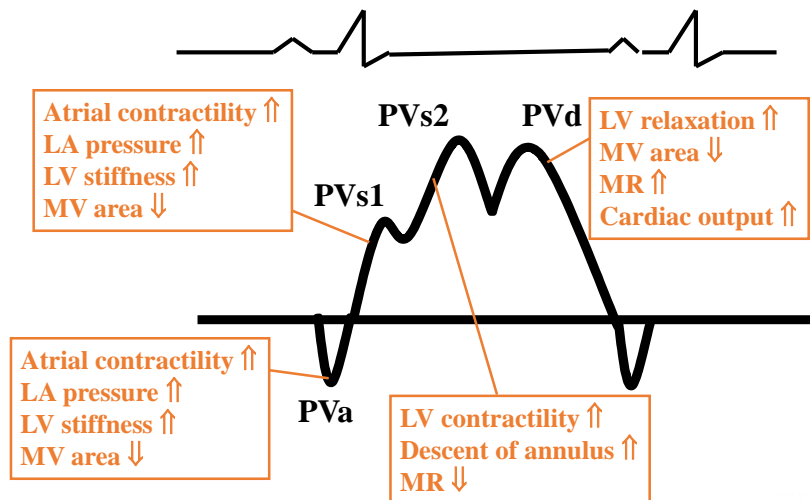
Pulmonary Vein Doppler

Acquisition



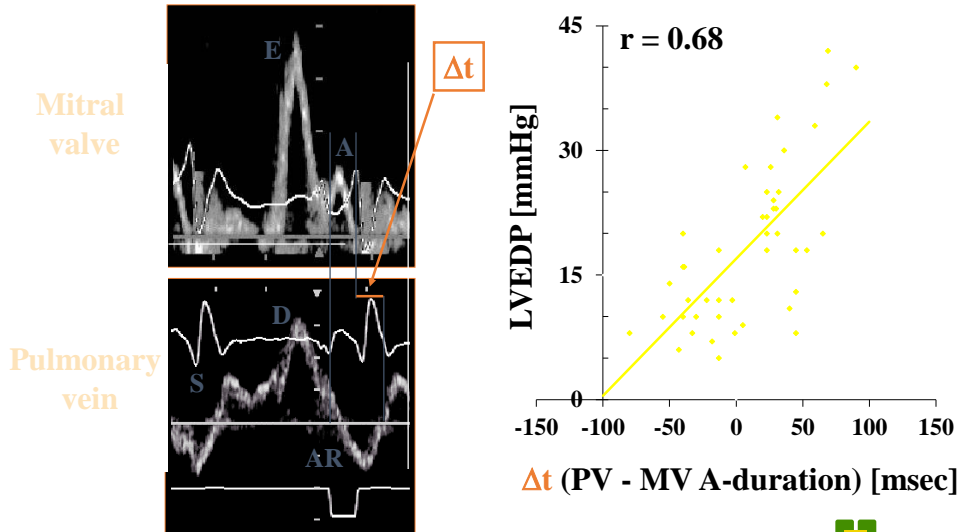
Pulmonary Vein Doppler

Determinants of Waves



Predicting LVEDP

From Mitral and PV A-wave Duration

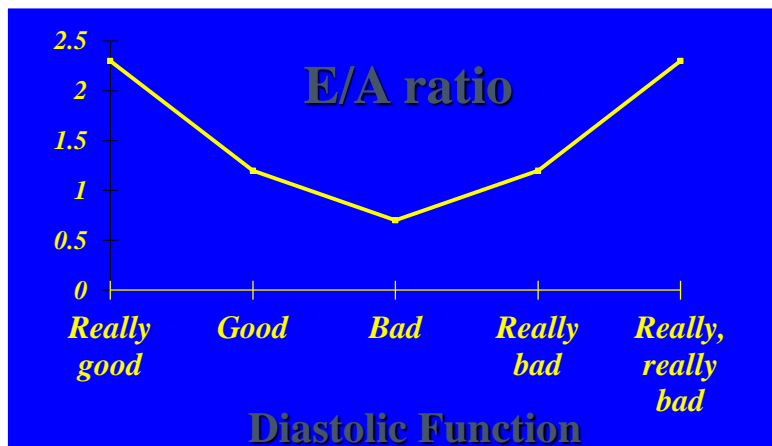


Rossvoll & Hatle, et al., JACC 1993; 21: 1687-1696



The Problem with All Flow-Based Indices of Diastolic Function

Preload Sensitivity



Needed: measures of LV systolic and diastolic function that are less dependent on preload

Diastology 2018

Available Echocardiographic Methods

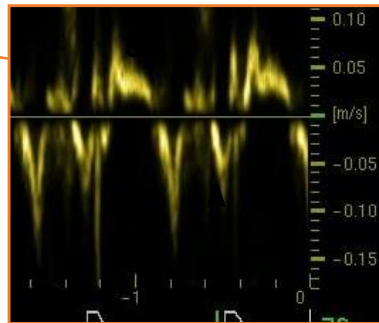
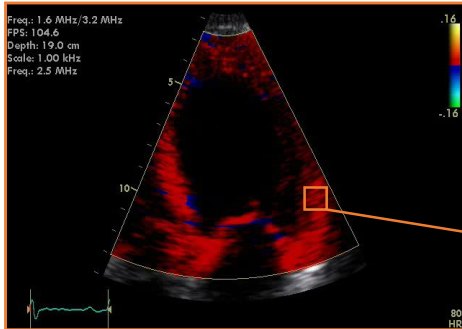
- *Transmitral velocity profiles*
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Tissue Doppler Imaging

Blood: High velocity, low amplitude



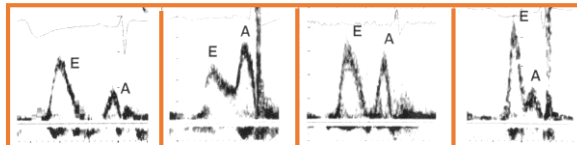
Tissue: Low velocity, high amplitude



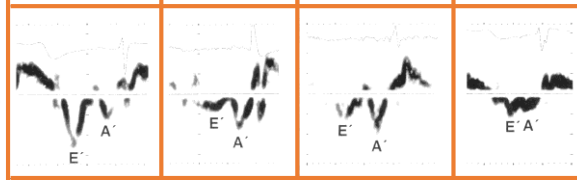
Myocardial Wall Velocities

Do not pseudonormalize

Mitral inflow



Mitral annulus



Normal

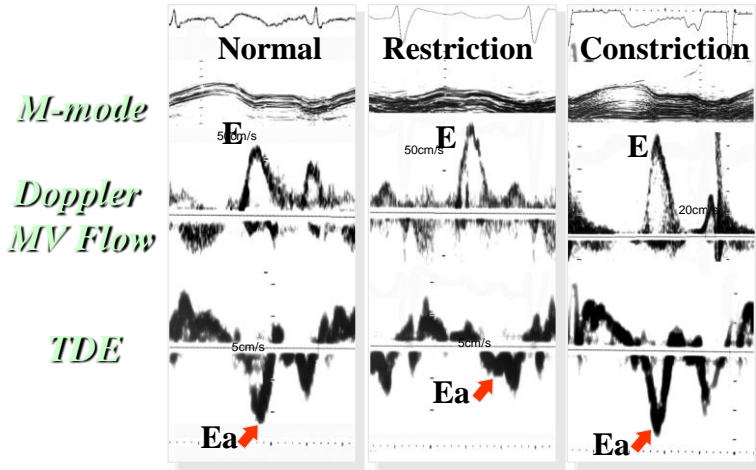
Delayed relaxation

Pseudo-normal

Restrictive

Sohn et al., JACC 1997; 30: 474-80

Constriction vs Restriction



Garcia et al., JACC 1996; 27: 108-114

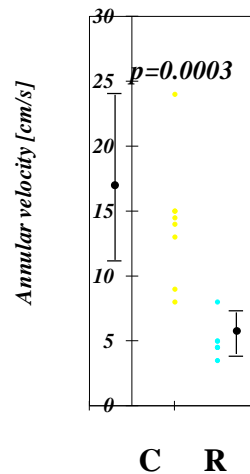
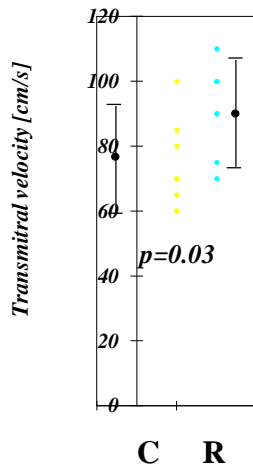
Journal of Intensive
Cardiovascular Medicine

Constriction vs Restriction

Doppler Differentiation

Mitral Pulsed Doppler

Annular DTI

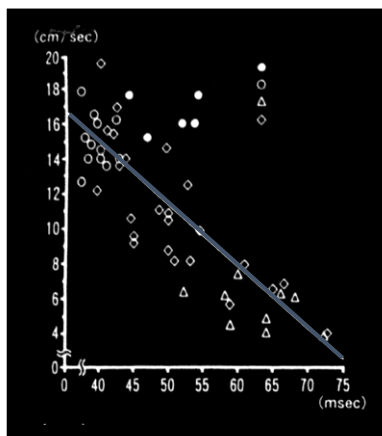


Garcia et al., JACC 1996; 27: 108-114

Journal of Intensive
Cardiovascular Medicine

Assessment of LV Relaxation

DTE E-wave Inversely Related to τ



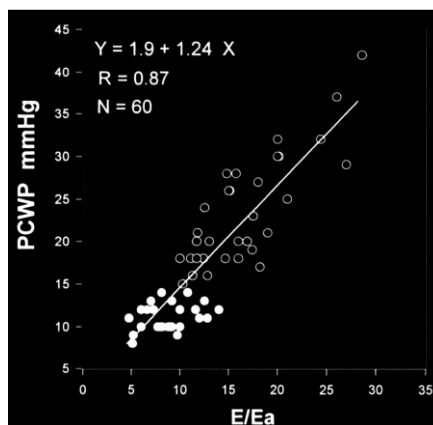
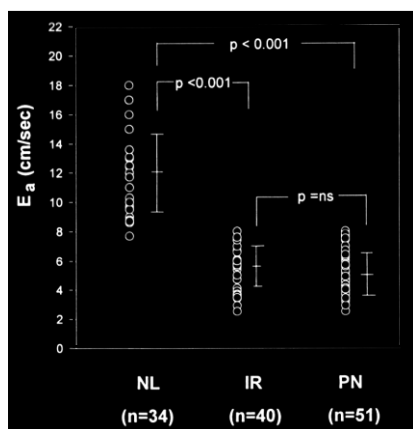
*If $E \propto LAP/\tau$
and $Ea \propto 1/\tau$,
then $LAP \propto E/Ea$*

Oki et al, Am J Cardiol 1997;79:928

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Internal Medicine

Estimation of P_{LA}

The "Magic" of E/e'



Nagueh et al. JACC 1997;30:1527-33.

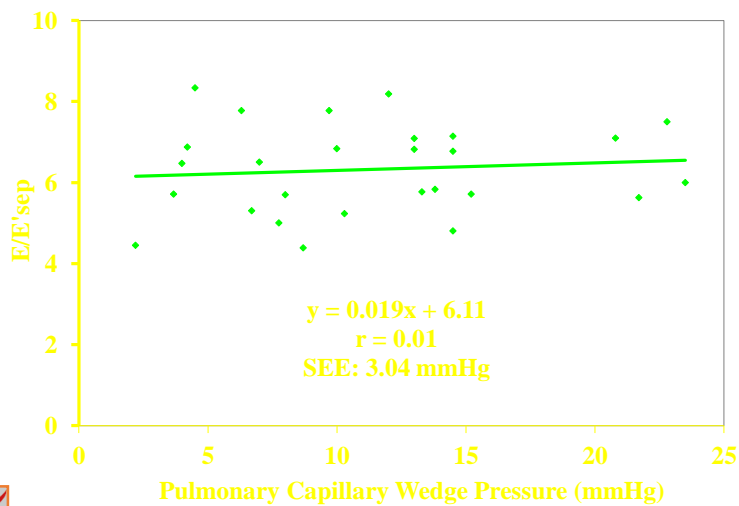
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Internal Medicine

Estimation of P_{LA}
The "Magic" of E/e'

Does this always work?

Not if the heart is normal

Estimation of Left Atrial Pressure
Subjects without Heart Disease



Firstenberg et al. *J Am Coll Cardiol* 2000; 36: 1664-9.

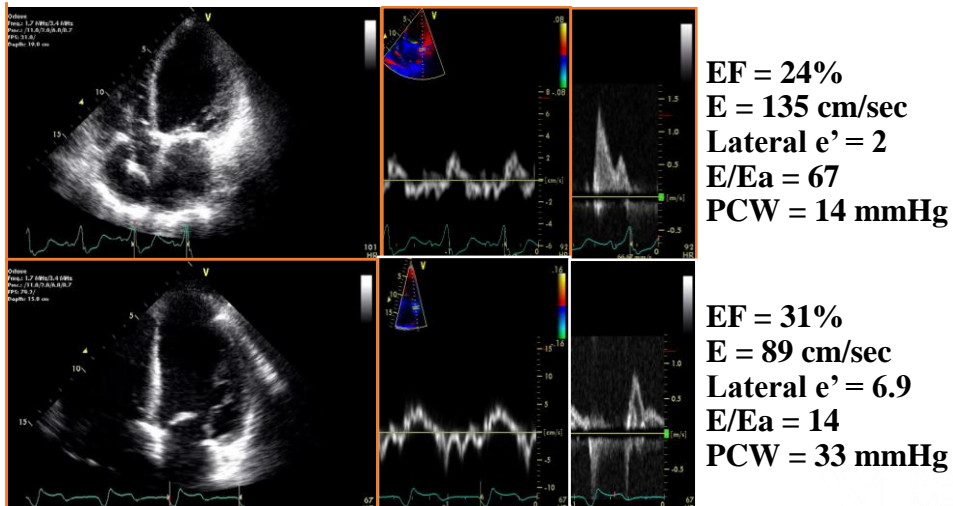
Estimation of P_{LA}
The "Magic" of E/e'

Does this always work?

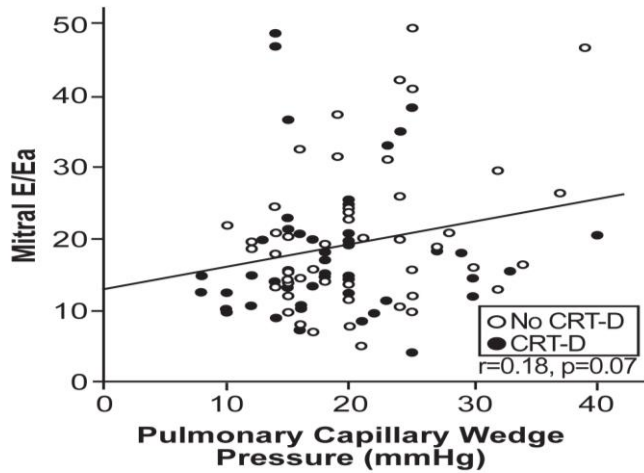
**Not if the heart is normal
And not if the heart is really, really sick**

Tissue Doppler Imaging in the Estimation of Intracardiac Filling Pressure in Decompensated Patients With Advanced Systolic Heart Failure

Wilfried Mullens, MD; Allen G. Borowski, RDCS; Ronan J. Curtin, MD;
James D. Thomas, MD; W.H. Tang, MD
Circ 2009; 119: 62-70

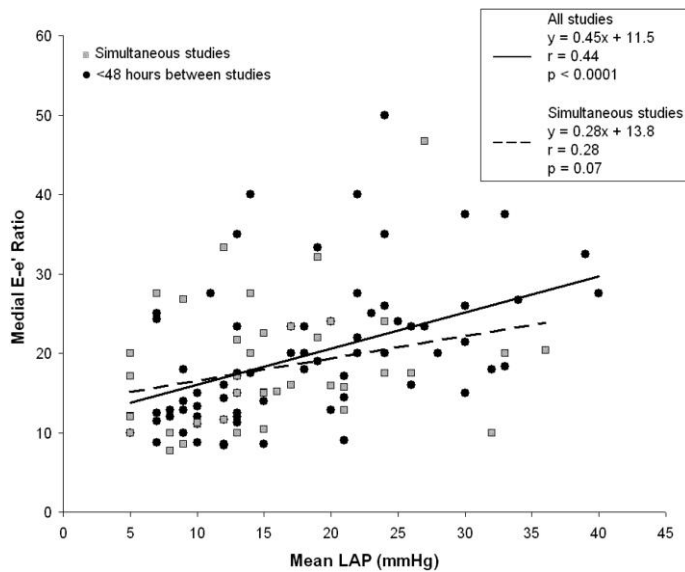


Correlation Mitral E/E' - PCWP



Mullens et al. *Circulation* 2009; 119: 62-70

Correlation Mitral E/E' – Direct LAP *HCM Patients*



Geske et al. *Circulation* 2007; 116: 2702-8

*Don't forget left atrial area!!
The HbA1c of end-diastolic pressure*

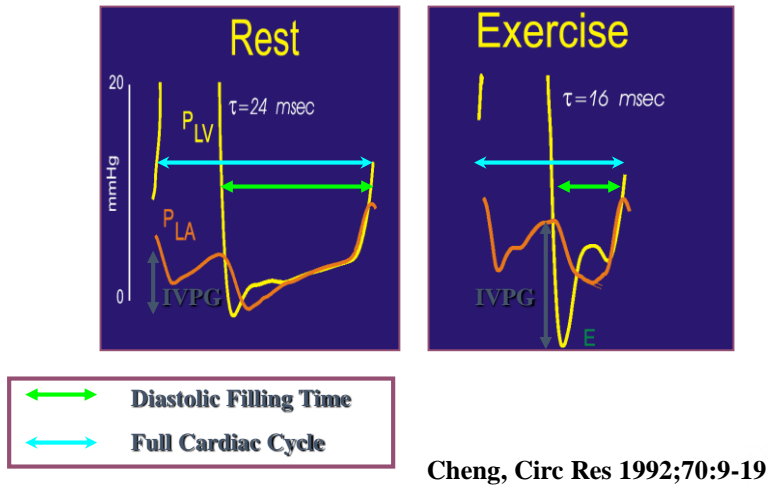
How to Get Diastolic Dysfunction
3) Lose Diastolic Suction



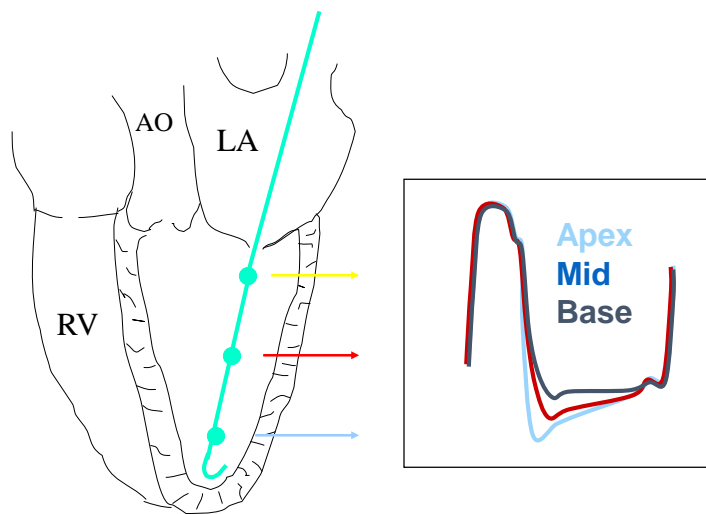
Courtois et al. Circulation 1990;81:1688-96

IVPG are Critical During Exercise

Diastole Disproportionately Shortened

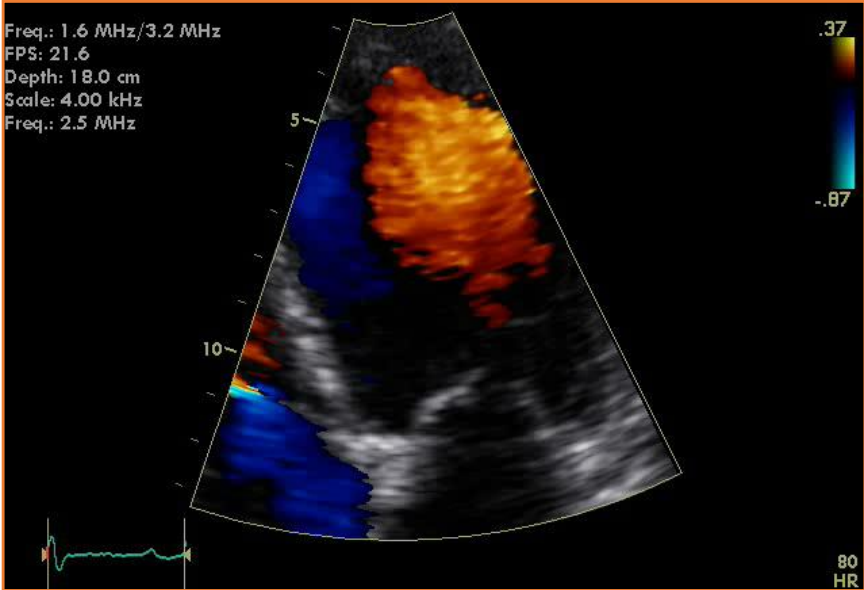


Invasive Measurement of Intraventricular Pressures

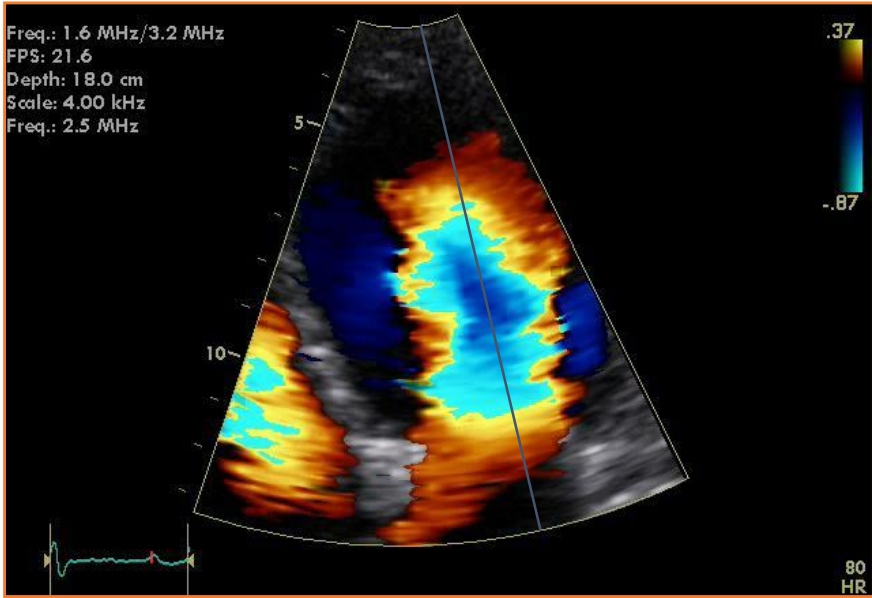


Completely impractical in clinical practice

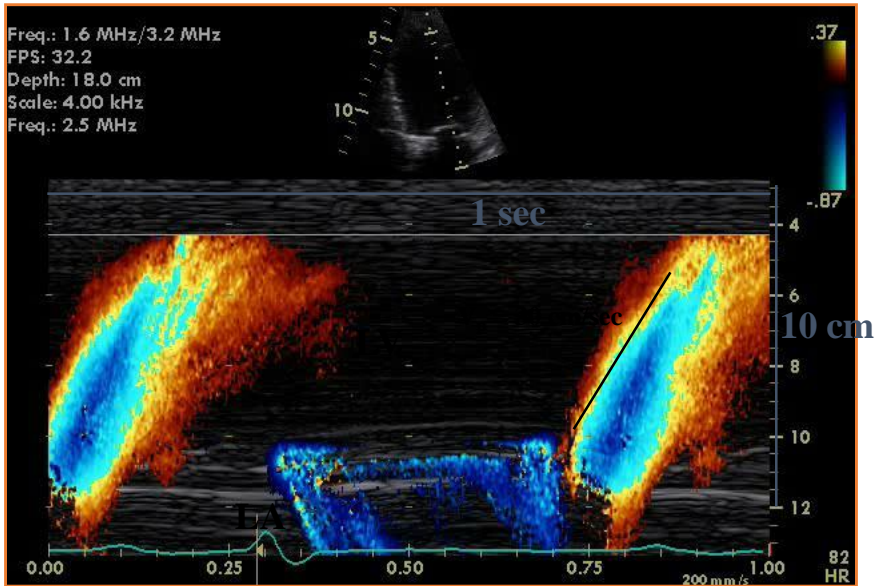
Color M-Mode Methodology



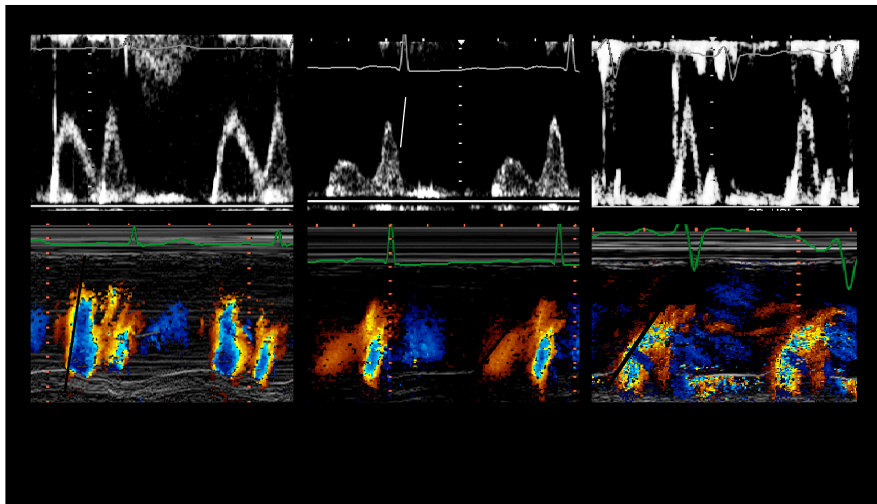
Color M-Mode Methodology



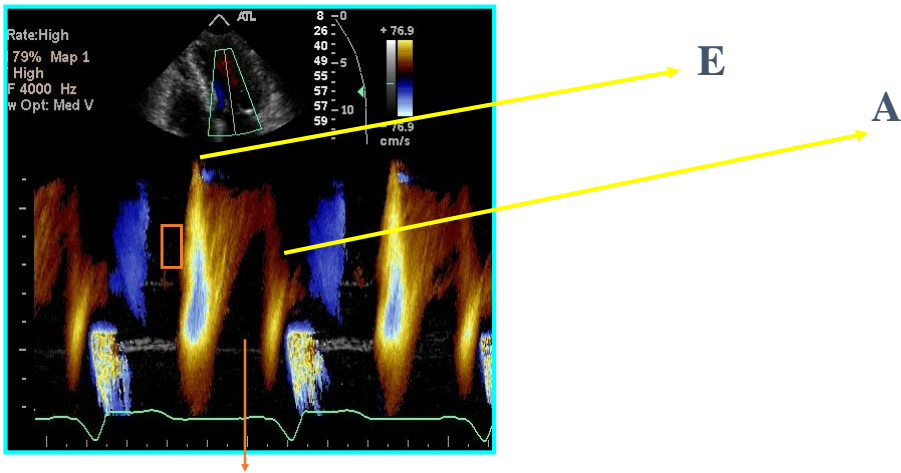
Measurement of Propagation Velocity



Color M-mode Doppler *Does Not Pseudonormalize*



CMM Calculation of IVPG

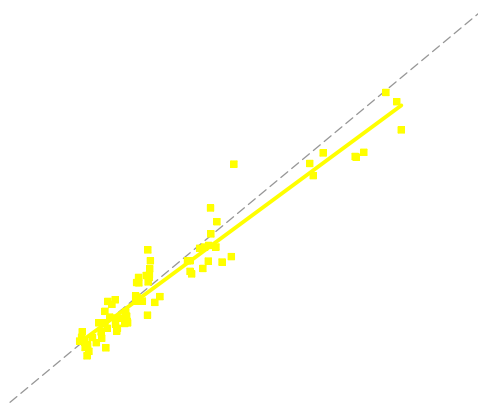


Euler equation

Greenberg et al. Am J Physiol 2001;280:H2507-15



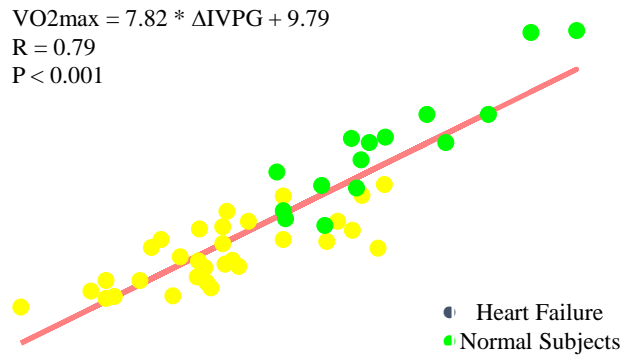
Intraventricular Pressure Gradient



Greenberg et al: Am J Physiol 2001; 280; H2507-H2515

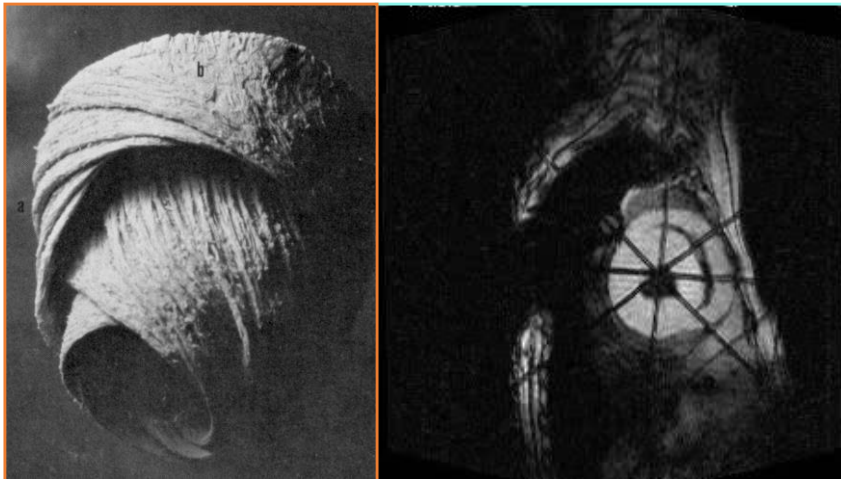


Correlation Between Delta IVPG and VO₂ max



Rovner et al. Am J Physiol 2005; 289: H2081-8

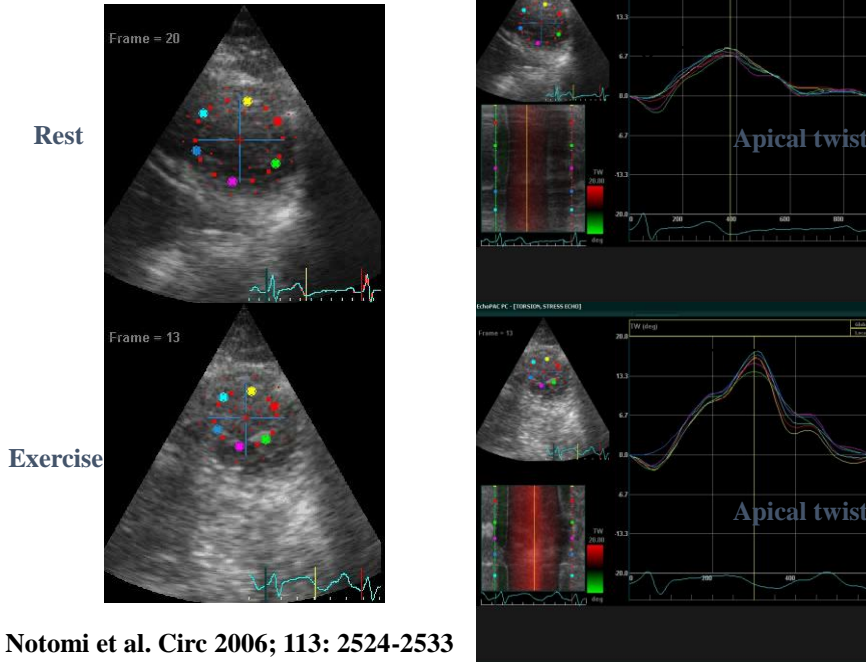
Left Ventricular Torsion



- The spiral architecture of the LV produces base-apex torsion
- This stores energy in systole that is released in diastole (suction)
- Though important in LV mechanics, torsion has been difficult to measure

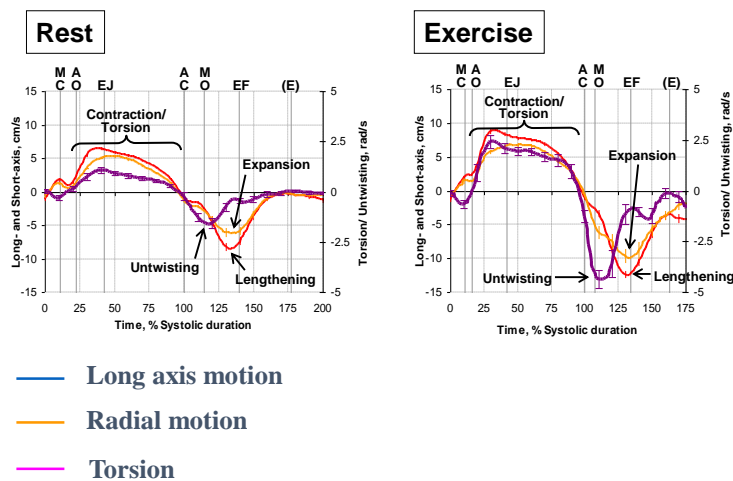
MRI courtesy of Ed Shapiro, Johns Hopkins University

Torsion During Exercise



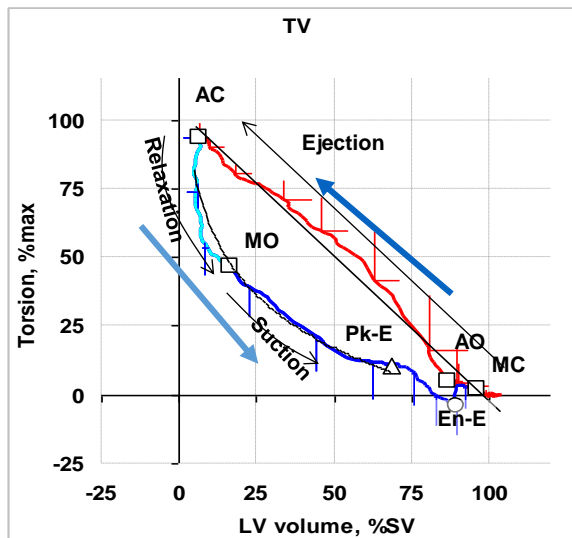
Notomi et al. Circ 2006; 113: 2524-2533

Timing and Magnitude of LV Mechanics *Impact of Exercise*



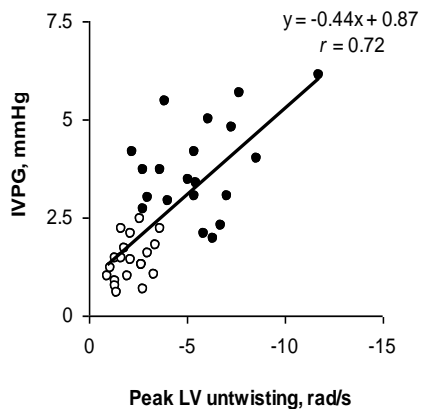
Notomi et al. Circ 2006; 113: 2524-2533

Torsion-Volume Loop



Notomi et al. Circ 2006; 113: 2524-2533

LV Untwisting Predicts Suction Gradient



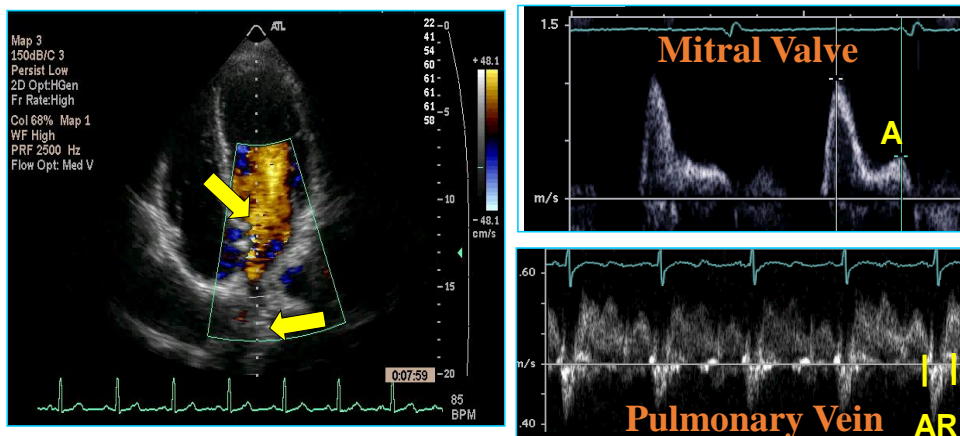
Notomi et al. Circ 2006; 113: 2524-2533

Putting It All Together

- During systole, a significant amount of elastic energy is stored in the myocyte and the interstitium as torsion
- The earliest mechanical manifestation of diastole is an abrupt untwisting that is largely completed before the mitral valve opens
- This untwisting helps to establish a base-to-apex intraventricular pressure gradient in early diastole that assists in the low pressure filling of the heart
- Modulation of this mechanism allows the heart to augment its function many-fold during exercise

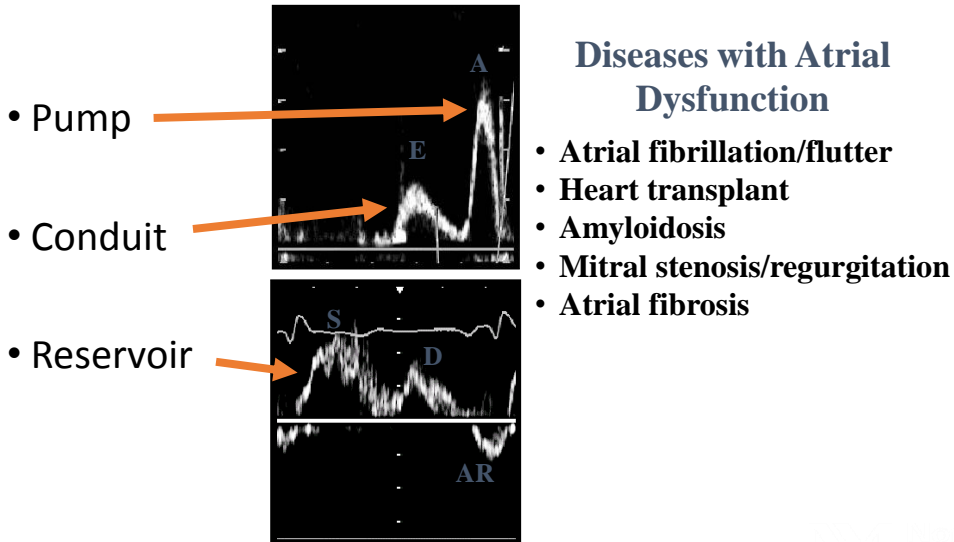
How to Get Diastolic Dysfunction

4) Atrial Dysfunction

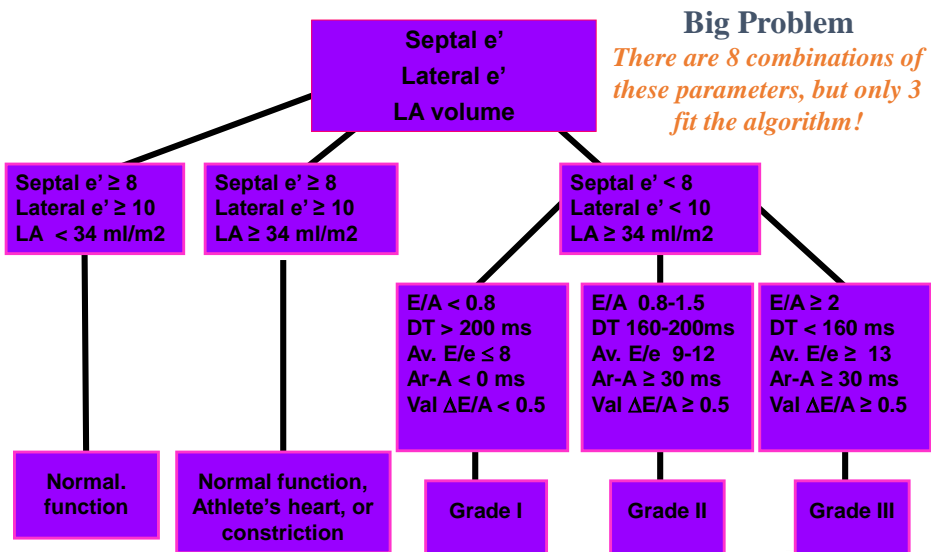


Assessment complicated by having two outlets and no isovolumic period

Three Components of Atrial Function



Guidelines Approach to Grading Diastolic Dysfunction, ca. 2009



Nagueh et al. JASE 2009; 22: 108-33

A Room with Eight Ways Out



How Well Do These Work in Practice?

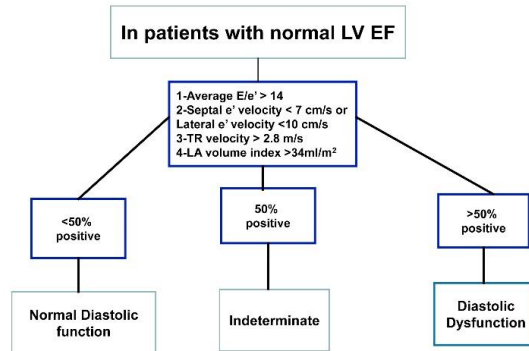
- 401 consecutive patients, age 59 ± 16 years (60%M)
- Using only the 3 primary classifiers (LAVi, septal and lateral e'), diastolic function could be assigned in only 34% of cases
- For the 5 secondary indices (E/A ratio, E deceleration time, E/E', PV AR reversal duration, and $\Delta E/A$ with Valsalva), "concordance" (3+/5 indices in agreement) occurred in only 64% of cases.

Let's take another swing at the guidelines!

ASE/EACVI GUIDELINES AND STANDARDS

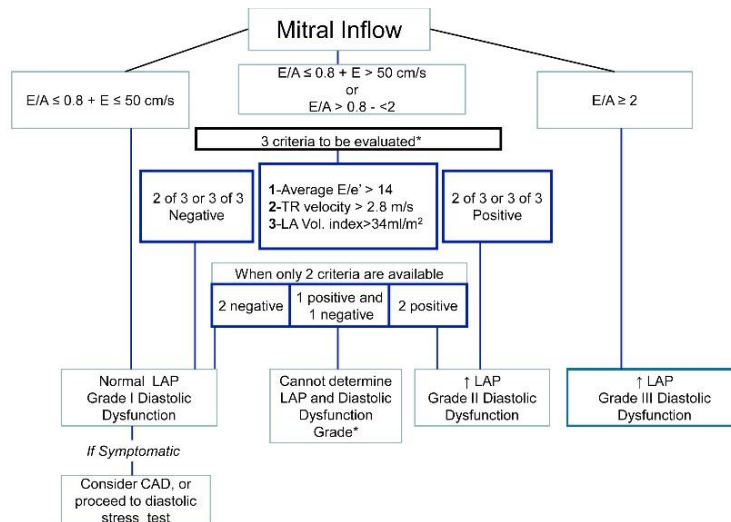
Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography:
An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging

A



Nagueh et al. JASE 2016; 29: 277-314

Grading Diastolic Dysfunction
With LVEF < 50% or Other LV Disease



(* : LAP indeterminate if only 1 of 3 parameters available. Pulmonary vein S/D ratio < 1 applicable to conclude elevated LAP in patients with depressed LV EF)

How applicable are the new guidelines???

Stay tuned for Jae Oh's analysis...

2020 Washington
State Medicine

Keys to Handling Discrepant Indices

- Discount technically limited indices
 - Don't overinterpret garbage
- Look at the atrium
 - Normal atrial size virtually precludes severe DD
 - Large atrium must be explained but DD isn't only cause (consider AF, MR, and MS)
 - Atrial systolic failure must be recognized
- Despite our "linear" grading scheme, diastole is far more complex
 - Consider early and late diastole separately

2020 Washington
State Medicine

Diastole is Not a Single Entity

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These rarely occur in isolation but considering them separately helps to understand diastole