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

Sources of Passive Elasticity

<table>
<thead>
<tr>
<th>Source</th>
<th>Contribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collagen</td>
<td>++++</td>
</tr>
<tr>
<td>Titin</td>
<td>++++</td>
</tr>
<tr>
<td>Actin</td>
<td>++</td>
</tr>
<tr>
<td>Intermediate</td>
<td>+</td>
</tr>
<tr>
<td>Microtubules</td>
<td>-</td>
</tr>
</tbody>
</table>

Passive Tension in Cardiac Muscle: Contribution of Collagen, Titin, Microtubules, and Intermediate Filaments
Diastology 2018
Available Echocardiographic Methods

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

Mitral Inflow: E/A Velocity

SV at MV Leaflet Tips
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 $\Delta p$ and the more rapid the deceleration

$$\frac{dv}{dt} \approx - \frac{MVA}{(LA-LV \text{ Compliance})}$$
Physical Determinants of Deceleration

**Stiffer Ventricle = Shorter Decel Time**

\[ DT \propto 1/LV \text{ stiffness} \]

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

*Little et al. Circulation 1995;92:1933*
Transmitral Flow and Prognosis
Restrictive Cardiomyopathy

![Graph showing survival and DT](image)

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

Some Ventricles LOOK Like Amyloid

Are there new diagnostic methods for less obvious ones?
Relative ‘apical sparing’ of longitudinal strain using two-dimensional speckle-tracking echocardiography is both sensitive and specific for the diagnosis of cardiac amyloidosis.

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 transmitral pressure gradient, $\Delta p$, 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
- **Pulmonary venous profiles**
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- Future directions
Pulmonary Vein Doppler

Acquisition

Pulmonary Vein Doppler

Determinants of Waves

Atrial contractility ↑
LA pressure ↑
LV stiffness ↑
MV area ↓

LV relaxation ↑
MV area ↓
MR ↑
Cardiac output ↑

Atrial contractility ↑
LA pressure ↑
LV stiffness ↑
MV area ↓

LV contractility ↑
Descent of annulus ↑
MR ↓
Predicting LVEDP
From Mitral and PV A-wave Duration

Mitral valve

Pulmonary vein

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

\[ \Delta t (PV - MV A-duration) \text{ [msec]} \]

\[ \text{LVEDP [mmHg]} \]

\[ r = 0.68 \]

The Problem with All Flow-Based Indices of Diastolic Function
Preload Sensitivity

E/A ratio

Diastolic Function

Really good
Good
Bad
Really bad
Really, really bad
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
- Pseudonormal
- Restrictive

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

M-mode

Doppler
MV Flow

Constriction vs Restriction
Doppler Differentiation

Mitral Pulsed Doppler

Annular DTI

Garcia et al., JACC 1996; 27: 108-114
Assessment of LV Relaxation

*DTE E-wave Inversely Related to* $\tau$

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

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

Estimation of $P_{LA}$

*The “Magic” of E/e’*

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*

![Graph showing the relationship between $E/E'$ and Pulmonary Capillary Wedge Pressure (mmHg). The equation is $y = 0.019x + 6.11$ with $r = 0.01$ and SEE: 3.04 mmHg.]

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, RDGS; Ronan J. Curtin, MD; James D. Thomas, MD; W.H. Tang, MD

Circ 2009; 119: 62-70

EF = 24%
E = 135 cm/sec
Lateral e' = 2
E/Ea = 67
PCW = 14 mmHg

EF = 31%
E = 89 cm/sec
Lateral e' = 6.9
E/Ea = 14
PCW = 33 mmHg
Correlation Mitral E/E’ - PCWP


Correlation Mitral E/E’ – Direct LAP

HCM Patients

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

How to Get Diastolic Dysfunction

3) Lose Diastolic Suction

IVPG are Critical During Exercise
*Diastole Disproportionately Shortened*


Invasive Measurement of Intraventricular Pressures

*Completely impractical in clinical practice*
Color M-Mode Methodology
Measurement of Propagation Velocity

\[ V_p = 30 \text{ cm/sec} \]

Color M-mode Doppler

*Does Not Pseudonormalize*
CMM Calculation of IVPG

Euler equation


Intraventricular Pressure Gradient

Correlation Between Delta IVPG and VO$_2$ max

\[ \text{VO2}_\text{max} = 7.82 \times \Delta \text{IVPG} + 9.79 \]
\[ R = 0.79 \]
\[ P < 0.001 \]

- Heart Failure
- Normal Subjects


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
Timing and Magnitude of LV Mechanics

*Impact of Exercise*

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

**Torsion-Volume Loop**

![Torsion-Volume Loop图](image)

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

**LV Untwisting Predicts Suction Gradient**

![LV Untwisting Predicts Suction Gradient图](image)

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

• Pump
• Conduit
• Reservoir

Diseases with Atrial Dysfunction

• Atrial fibrillation/flutter
• Heart transplant
• Amyloidosis
• Mitral stenosis/regurgitation
• Atrial fibrosis

Guidelines Approach to Grading Diastolic Dysfunction, ca. 2009

Septal e’ ≥ 8
Lateral e’ ≥ 10
LA < 34 ml/m²
Normal function

Septal e’ ≥ 8
Lateral e’ ≥ 10
LA ≥ 34 ml/m²
Normal function, Athlete’s heart, or constriction

E/A < 0.8
DT > 200 ms
Av. E/e ≤ 8
Ar-A < 0 ms
Val ΔE/A < 0.5
Grade I

E/A 0.8-1.5
DT 160-200ms
Av. E/e 9-12
Ar-A ≥ 30 ms
Val ΔE/A ≥ 0.5
Grade II

E/A ≥ 2
DT < 160 ms
Av. E/e ≥ 13
Ar-A ≥ 30 ms
Val ΔE/A ≥ 0.5
Grade III

Big Problem
There are 8 combinations of these parameters, but only 3 fit the algorithm!

Nagueh et al. JASE 2009; 22: 108-33
A Room with Eight Ways Out

But 5 of them are locked!

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 ΔE/A with Valsalva), “concordance” (3+/5 indices in agreement) occurred in only 64% of cases.

Let’s take another swing at the guidelines!
**Grading Diastolic Dysfunction**

*With LVEF <50% or Other LV Disease*

1. **Mitrail Inflow**
   - E/A ≤ 0.8 + E ≤ 50 cm/s or E/A > 0.8 + <2
   - 3 criteria to be evaluated:
     1. Average E/e' > 14
     2. TR velocity > 2.8 m/s
     3. LA volume index > 34 mll/m²

2. **When only 2 criteria are available**
   - 2 negative
     - No LAP
     - If Symptomatic: Consider CAD, or proceed to diastolic stress test
   - 1 positive and 1 negative
     - Cannot determine LAP and Diastolic Dysfunction
   - 2 positive
     - 1 LAP
     - Grade I Diastolic Dysfunction

3. **E/A ≥ 2**
   - 2 of 3 or 3 of 3
     - Positive
     - 1 LAP
     - Grade II Diastolic Dysfunction

4. **E/A ≤ 0.8**
   - 1 LAP
   - Grade III Diastolic Dysfunction

(*) 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

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Nagueh et al. JASE 2016; 29: 277-314
How applicable are the new guidelines???

Stay tuned for Jae Oh’s analysis…

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
Diastole is Not a Single Entity
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