Learning Objectives for Diastology
After this talk, you will be able to

• Understand physiology and hemodynamics of diastole
• Know correlation between Echo diastolic parameters and underlying hemodynamics
• Classify and grade diastolic function
• Estimate filling pressure reliably in most patients at rest and with exercise
• Understand pitfalls of Echo diastolic function assessment
Myocardial relaxation is one of the earliest manifestations of mechanical dysfunction of the human LV. The time constant tau (T) is higher in the elderly and patients with HCM, CAD, and cardiomyopathies.
Echo evaluation of diastolic function
Trans-mitral inflow velocity

Diastolic Function Grading
Mitral Inflow (U curve)

<table>
<thead>
<tr>
<th>LAP</th>
<th>Normal</th>
<th>Abnormal relaxation</th>
<th>Pseudo-normalization</th>
<th>Restrictive</th>
</tr>
</thead>
<tbody>
<tr>
<td>NL (&lt;15)</td>
<td>Normal</td>
<td>↑ ↑</td>
<td>↑ ↑ ↑</td>
<td></td>
</tr>
<tr>
<td>TAU</td>
<td>NL (&lt;45)</td>
<td>↑</td>
<td>↑</td>
<td>↑ ↑</td>
</tr>
</tbody>
</table>

Grade
1 2 3

Concept from Appleton and Hatle, 1985
Mitral Inflow and Pulmonary Vein Flow
Diastolic Function Assessment

Grade 1  Grade 2  Grade 3

LV Relaxation by Cath and Echo
\( \tau \) (tau) vs e’ (mitral annulus velocity)

\( y = -6.80x + 85.68 \)
\( r = 0.70 \)
\( P < 0.001 \)

Assessment of LV Relaxation by Echo

*e’* velocity reflects LV relaxation

Myocardial Relaxation is the Key for Diastole

Myocardial Relaxation (*e’*)

*e’* = 12 cm/s
*e’* = 7 cm/s
*e’* = 4 cm/s
### Evaluation of Diastolic Function
**Mitral Inflow and Annulus Velocity**

<table>
<thead>
<tr>
<th>Normal</th>
<th>Ab Relax</th>
<th>Pseudo</th>
<th>Restrictive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>Grade 2</td>
<td>Grade 3</td>
<td></td>
</tr>
</tbody>
</table>

- **Mitral flow**
- **Mitral annulus velocity**

**Preload dependent**

**Preload independent**

---

**As LV filling pressure ↑**

- **Mitral E ↑**
- **Annulus E ↓**
- **E/E’ ↑**

\[
y = 1.9 + 1.24x \\
r = 0.87 \\
n = 60
\]

- **PCWP (mm Hg)**

Nagueh et al: JACC, 1997
Ommen et al: Circ, 2000
Estimation of LV Filling Pressures
E/e’ (Medial MV annulus)

E/E' <8  E/E' 8-15  E/E' >15

LV filling pressure

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What are normal values for e’ and E/e’ ?
Echocardiographic reference ranges for normal cardiac Doppler data: results from the NORRE Study

Luis Caballero et al. EHJ 2015

Original Research
Serial Doppler Echocardiography and Tissue Doppler Imaging in the Detection of Elevated Directly Measured Left Atrial Pressure in Ambulant Subjects With Chronic Heart Failure

Ritzema et al JACC Imaging 2011
LA Volume Index vs Diastolic Dysfunction

Indexed LA volume

Diastolic function grade

Normal  I  II  III

n=147 pt

r=0.78

Hypertensive Heart Disease vs HFpEF
Importance of PASP and E/e’

Sensitivity

1-Specificity

PASP*

E/e’ ratio†

Left atrial volume index†

Relative wall thickness†

Left ventricular mass index†

Line of no information

p<0.01

*vs line of no information;

†vs PASP

Lam C et al, JACC, 2009
Four Major Diagnostic Parameters

Normal Values

1. E' velocity ≥ 7 (med), 10 (lat) cm/s
2. E/e' ≤ 14 (Av), 15 (Med)
3. TR velocity ≤ 2.8 m/sec
4. LAVI ≤ 34 mL/m²

New Criteria for Diastolic Function Assessment

In pts with normal LVEF ≥ 50%

1 – Septal e’ velocity ≥ 7 cm/s or lateral e’ velocity ≥ 10 cm/s
2 – Average E/e’ ≤ 14 , 15 (Med)
3 – TR velocity ≤ 2.8 m/s
4 – LA volume index ≤ 34 mL/m²

≥ 3 Normal
≥ 3 Abnormal
2 and 2

Normal diastolic function
Diastolic dysfunction

Criteria for diagnosis of LV diastolic dysfunction in patients with normal LVEF in JASE 2016
Normal Diastolic Function

Medial e' 12 cm/s

Lateral e' 16 cm/s

True Normal Diastolic Function
71 year old woman with LAVI = 39 mL/m²

Lateral e’ = 10 cm/sec
Medial e’ = 9 cm/sec

E/e’ = 9
E/e’ = 10

E/e’ NL < 14
e’ NL > 7
LAVI Enlarged
TR NL < 2.8

Lateral e’ = 10 cm/sec

LVOT TVI = 26 cm
Reasons for LA enlargement

• Diastolic dysfunction
• Increased filling pressure
• Increased volume
• Athlete’s heart
• Measurement error

Normal or Grade 1 Diastolic Dysfunction?
LAVI 28 mL/m²

E/e' = 6 cm/sec
E/e' = 8

E = 50
A = 100
E/A = 0.5

E/e’ NL < 14
e’ ABNL < 7
LAVI Normal
TR NL < 2.8
New Criteria for Diastolic Function Assessment

In pts with normal LVEF ≥ 50%

1 – Septal e’ velocity ≥7 cm/s or lateral e’ velocity ≥10 cm/s
2 – Average E/e’ ≤14 , 15 (Med)
3 – TR velocity ≤2.8 m/s
4 – LA volume index ≤34 mL/m²

≥ 3 Normal

Normal diastolic function

2 and 2

Indeterminate

≥ 3 Abnormal

Diastolic dysfunction

Normal Diastolic Filling Pressure

Increased Diastolic Filling Pressure

Diastolic Function?

E = 120 cm/s

e’ = 4 cm/sec

E/e’ = 30

TR = 4 m/sec

e’ ABNL < 7
E/e’ ABNL > 14
LAVI ??
TR NL > 2.8
New Criteria for Diastolic Function Assessment

In pts with normal LVEF ≥ 50%

1 – Septal e′ velocity ≥7 cm/s or lateral e′ velocity ≥10 cm/s
2 – Average E/e′ ≤14, 15 (Med)
3 – TR velocity ≤2.8 m/s
4 – LA volume index ≤34 mL/m²

≥ 3 Normal

Normal diastolic function

2 and 2

Indeterminate

≥ 3 Abnormal

Diastolic dysfunction

Normal Diastolic Filling Pressure

Increased Diastolic Filling Pressure

Diastolic Function Assessment
Take Home Point #1

• LV myocardial relaxation is reduced in all stages of diastolic dysfunction
• Mitral annulus e′ velocity reflects myocardial relaxation
• Normal e′ = Normal diastolic function
• Algorithm #1 separates normal filling from elevated filling pressure
• Initial assessment of diastolic function is based on
  • E′, E/e′, TR velocity, and LAVI
Diastolic Function?

- e' = 4 cm/sec
- E/e' = 30
- TR = 4 m/sec
- E= 120 cm/s
- A= 20 cm/s
- E/A = 6
- e' ABNL < 7
- E/e' ABNL > 14
- LAVI ??
- TR NL > 2.8

In patients with depressed LVEF or normal EF with diastolic dysfunction:

- Mitral inflow
  - E/A ≤ 0.8 + E ≤ 50 cm/s
  - E/A ≤ 0.8 + E > 50 cm/s or E/A > 0.8 < 2
  - E/A ≥ 2
- Grade I diastolic dysfunction
  - Average E/e' > 14
  - TR velocity > 2.8 m/s
  - LA volume index > 34 mL/m²
- Grade II diastolic dysfunction
  - ≥ 2 of 3 negative
  - ≥ 2 of 3 or ≥ 3 of 3 positive
  - 2 positive
- Grade III diastolic dysfunction
  - ≥ 2 of 3 negative
  - ≥ 2 of 3 or ≥ 3 of 3 positive
  - 2 positive

Normal LAP
- Cannot determine LAP and diastolic dysfunction grade

In patients with depressed LVEF or normal EF with diastolic dysfunction:

If symptomatic consider CAD or proceed to diastolic stress test

When only 2 criteria are available

LAP

1 positive and 1 negative

2 positive
67 yo man with ischemic CM and HF
Gr. 1 dysfunction with normal filling pressure

Grade 1 Dysfunction

- E/A ≤ 0.8
- E < 50 cm/sec

E = 45 cm/sec  A = 90 cm/sec
E/A = 0.5

Grade 1 Dysfunction

- E/A ≤ 0.8
- E < 50 cm/sec

- E/e’ NL < 14
- e’ ABNL < 7
- LAVI ABNL
- TR NL < 2.8

Medial e’ = 4 cm/s
E/e’ = 11
Grade 1 Diastolic Dysfunction

- E = 45 cm/sec  A = 90 cm/sec
- E/A = 0.5
- Medial e' = 4 cm/s
- E/e' = 11

- E' = 50  A = 100  E/A = 0.5
- e' = 6 cm/sec
- E/e' = 8

67 year old man with ischemic CM and HF

- E = 45 cm/s  E/A = 0.5
- E/e' = 12
- Medial e' = 4 cm/s

2 months before

- E = 120 cm/sec  E/A = 0.9
- E/e' = 30
- TR Vel = 3 m/sec
67 yo man with ischemic CM and HF
Gr. 2 dysfunction with increased filling pressure

E = 120 cm/sec E/A = 0.9
E/e' = 30

TR Vel = 3 m/sec

Ischemic Cardiomyopathy Echo Predictor
STICH Trial (N=1511)

Best survival with E/A 0.6-0.8

Lin et al. 2014 AHA
Grade 3 Dysfunction
L wave

- $e' = 4 \text{ cm/sec}$
- $E/e' = 30$
- $E = 120 \text{ cm/s}$
- $A = 20 \text{ cm/s}$
- $E/A = 6$
- $TR = 4 \text{ m/sec}$

- $e' \text{ ABNL < 7}$
- $E/e' \text{ ABNL > 14}$
- LAVI ??
- TR NL > 2.8

Mid-diastolic mitral flow (L)
Delayed relaxation

Distribution of 2D and Doppler Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Elevated filling pressure (n=165)</th>
<th>Normal filling pressure (n=155)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral E/A ratio ≤0.8 + E ≤50 cm/s</td>
<td>0</td>
<td>23</td>
</tr>
<tr>
<td>Mitral E/A ratio ≥2</td>
<td>53</td>
<td>5</td>
</tr>
<tr>
<td>None of the cutoff values met for the 3 variables in patients with diastolic dysfunction</td>
<td>15</td>
<td>70</td>
</tr>
</tbody>
</table>

- **Normal Filling Pressure**
  - 3 normal parameters
  - LAVI >34 mL/m²
  - E/A ≤ 0.8 + E ≤ 50 cm/s

- **Increased Filling Pressure**
  - E/A ≥2
  - E/e' > 14 + LAVI >34 mL/m²
  - 3 abnormal
  - 2 abnormal


23 YO with HCM

- Grade 1
- Grade 2
- Grade 3
- Possibly normal

E = 70 cm/s  A = 30 cm/s  E/A = 2.3
Can he have a normal diastolic function?

23 yo man with HCM
LAVI  29 mL/m²
TR = 2 m/sec  IVRT = 120 msec

23 yo with HCM
Medial e' = 8 cm/sec  Lateral e' = 10 cm/sec
E = 70 cm/s  E/e' = 9  E/e' = 7

Valsalva in 23 yo HCM
Normal filling pressure

IVRT 100 msec

E/A = 2.3
E/A = 2.0

Mitral A duration is shorter than PV AR
Increased LVEDP
**Doppler Determination of LVEDP**

- EDP (mm Hg)
- PVa-Ad (ms)
- $r = 0.68$
- $P < 0.001$

**Diastolic Function Assessment**

**Take Home Message #2**

- Grade 1 diastolic dysfunction is the best pattern for the patients with Heart Failure
- Evidence for diastolic dysfunction needs an objective evidence
  - Hypertension
  - Hypertrophic CM
  - Old age

The best evidence is reduced relaxation
- Reduced e’
- L wave
- Prolonged IVRT

LVEDP can be increased with normal mean LV diastolic pressure

Rossvoll and Hatle: JACC, 1993
**Difficult Situations**

- Assess diastolic function or filling pressure in
  - 2 normal and 2 abnormal
  - HCM
  - LBBB
  - MAC
  - Atrial Fibrillation

- Additional supportive parameters
  - Pulmonary vein
  - Valsalva
  - IVRT and timing intervals
  - Strain

---

67 year old woman with HPT and SOB
LAVI = 54 and TR= 2.8 m/s

1. E’ +/-
2. E/e’ NL
3. TR ≤ 2.8
4. LAVI ++

E= 90 A= 40 E/A=2.3
Lat e’ =8
E/e’ = 12
Med e’ = 7
E/e’ =13
Indeterminate?

- $E' \pm$
- $E/e' < 15$
- $LA > 34$
- $TR > 2.8 \text{ m/sec}$

TR = 2.83 m/s

Pulmonary Vein Velocity
PVs decreases as filling pressure increases

- Normal
- Impaired relaxation
  - ↓ compliance LAP
  - ↑↑ compliance LAP

PVs PVd

PVa
Conclusions—In 100 symptomatic patients with HCM, Doppler echo estimates of LV filling pressure correlate modestly with direct measurement of LAP. Given the complex nature of diastolic dysfunction in HCM, precise characterization of LV filling pressure in an individual patient cannot be determined with the use of these noninvasive parameters. (Circulation. 2007;116:2702-2708.)
**Medial E/e’ Ratio Versus Mean LAP**

- **All studies**: $y = 0.45x + 11.5$, $r = 0.44$, $P < 0.001$
- **Simultaneous studies**: $y = 0.28x + 13.8$, $r = 0.28$, $P = 0.07$

**Mean LAP vs Medial E-e’ ratio**

- **Hypertrophic CM**

Diastolic Function Evaluation in HCM

- E’ velocity is reduced in almost all patients
- E/e’ predicts clinical outcome
- Use following parameters (ASE 2016 Guideline)
  - E/e’ >15
  - LAVI >34 mL/m²
  - TR velocity > 2.8 m/sec
  - PV Ar-A duration ≥ 30 msec
- The majority rules

72 yo woman with HCM

E=80  A=95  E/A = 0.85
Med e’ = 2  E/e’ = 40
Lat e’ = 5  E/e’=15
72 yo woman with apical HCM Grade 2 dysfunction with LAVI 37 mL/m²

Mitral annulus e’ velocity

- ASE/EACVI recommends average value
- E’ from one location is acceptable
- We need a caution in using e’
  - Primary pulmonary hypertension
  - Pacemaker
  - LBBB
  - Wall motion abnormality
  - Mitral annulus calcification
  - Hypertrophic CM
67 yo woman with LBBB

E = 60  A = 80  E/A = 0.7

Medial e' = 3 cm/s  E/e' = 23

Lat e' = 9 cm/s  E/e' = 8

67 yo with LBBB

TR = 2.4 m/sec
Mitral annulus calcification and TAVR

Lat e’ = 4 cm/s

Med e’ = 3 cm/s

E = 100 cm/sec

TR = 2.4 m/sec

Pulmonary Vein
**Mitral annulus e’ velocity vs MAC**

**Mean age 73 years**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1 n=79 no MAC</th>
<th>Group 2 n=38 mild MAC</th>
<th>Group 3 n=38 mod-severe MAC</th>
<th>P for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agatston Score</td>
<td>0</td>
<td>1-119</td>
<td>&gt;119</td>
<td></td>
</tr>
<tr>
<td>Septal e’</td>
<td>5.96±1.82</td>
<td>5.15±1.56</td>
<td>5.05±1.93</td>
<td>0.01</td>
</tr>
<tr>
<td>Lateral e’</td>
<td>7.37±2.44</td>
<td>6.89±2.71</td>
<td>6.28±1.81</td>
<td>0.01</td>
</tr>
<tr>
<td>Average e’</td>
<td>6.63±2</td>
<td>6.02±1.79</td>
<td>5.67±1.69</td>
<td>0.01</td>
</tr>
<tr>
<td>E/avg e’ ratio</td>
<td>13±4.93</td>
<td>15±8.95</td>
<td>18±8.26</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

LV diastolic parameters are altered in the presence of MAC. This could be due to direct effects of MAC or might reflect truly reduced diastolic function. Interpretation of diastolic parameters in patients with MAC should be performed with caution.

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**Doppler Echocardiography for the Estimation of LV Filling Pressure in Patients With Mitral Annular Calcification**

Muaz M. Abudiab, MD, Lakshmi H. Chebrolu, MD, Robert C. Schutt, MD, Sherif F. Naguch, MD, William A. Zoghbi, MD

**Representative Images of Patients With Mitral Annular Calcification**

Mild  
Moderate  
Severe

Abudiab et al: Am Coll Cardiol Img, 2017
Correlation of Selected Doppler Variables With Left Ventricular Filling Pressure

- Mitral E/A
  - LVFP (mm Hg)
  - \( r=0.66, P<0.001 \)

- IVRT
  - LVFP (mm Hg)
  - \( r=-0.50, P<0.001 \)

- \( E/e' \) (avg)
  - LVFP (mm Hg)
  - \( r=0.42, P=0.003 \)

Proposed Clinical Algorithm for Estimation of Left Ventricular Filling Pressure in Subjects With Mitral Annular Calcification

Initial Cohort (n=50):
- Sensitivity: 81%
- Specificity: 100%
- PPV: 100%
- NPV: 67%

Total Cohort (n=71):
- Sensitivity: 85%
- Specificity: 95%
- PPV: 97%
- NPV: 78%

Initial: 8/9 (89%) 10/10 (100%)
Total 12/13 (92%) 23/24 (96%)

Mitral E/A
- <0.8
  - Normal LVFP
    - Initial: 8/9 (89%)
    - Total 12/13 (92%)
  - 0.8-1.8
  - >1.8

IVRT
- ≥80 ms
  - Normal LVFP
    - 4/9 (44%)
    - 9/14 (64%)
  - <80 ms

High LVFP
- 16/16 (100%)
  - 23/24 (96%)

Abudiab et al: Am Coll Cardiol Img, 2017
Diastolic Function in A. Fib

- DT < 160 msec (with reduced EF)
- DT < 130 msec poor survival (Hurley, Oh)
- Other measurements
  - $E$ acceleration > 1900 cm/sec$^2$
  - IVRT ≤ 65 msec
  - $E/e'$ ≥ 11
  - IVRT/ T E-e'
  - TR velocity

Mitral Annulus Velocity in the Evaluation of Left Ventricular Diastolic Function in Atrial Fibrillation

Dae-Won Sohn, MD, Jong-Min Song, MD, Joo-Hee Zo, MD, In-Ho Chai, MD, Hyo-Soo Kim, MD, Hong-Gu Chun, MA, and Hee-Chan Kim, PhD, Seoul, Korea

JASE 1999
Atrial Fibrillation
Variation in E velocities: NL Pressure

DT = 100 msec
DT = 210 msec

Atrial Fibrillation
Variation in E velocities and E/e’ <11

E/e’ = 9
66 yo woman with dyspnea and EF 20%

- E'-A = 105 cm/sec
- Lat e' = 5 cm/sec, E/e' = 21
- Medial e' = 7 cm/sec, E/e' = 15

66 yo woman with HF and severe MR

- LVEF 20%
- TR = 2.9 m/s
- IVRT = 75 msec
My Recommendations

- For patients with reduced EF (<35%) or with preserved EF with known diastolic dysfunction, evaluate diastolic function based on E/A ratio.
- For all other patients, based on the 4 parameters:
  - Normal: $\geq 3$ normal (for patient’s age)
  - Abnormal: $\geq 3$ abnormal (grade 2 or 3 based on E/A)
  - Indeterminate: Need help from PV, IVRT, Valsalva, Time interval, Exercise, Strain Imaging
My recommendation based on e’ velocity
LV relaxation is the key for normal diastole

• True Normal
  • Medial e’ >10 cm/sec or Lateral e’ > 15 cm/sec

• Age-related Normal
  • Medial e’ 7-10 cm/s or Lateral e’ 10-15 with normal TR

• Abnormal
  • Medial e’ < 7 cm/s or lateral e’<10 cm/s
  • Grade 1, 2, and 3 based on E/e’, TR, and LAVI

Thank you!
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