Physiology of Diastole: What Are We Trying to Measure?

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Echo Hawaii, January 17, 2022

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Relevant Disclosures

none

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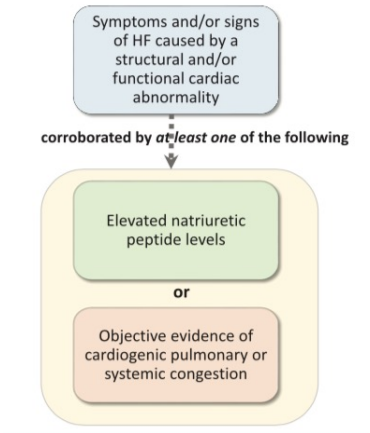
Universal Definition of Heart Failure



As determined by:
- EF <50%
- abnormal cardiac chamber enlargement
- E/E' >15
- moderate/severe ventricular hypertrophy
- moderate/severe valvular obstructive or regurgitant lesion

Bozkurt et al. European Journal of Heart Failure (2021) **23**, 352–380

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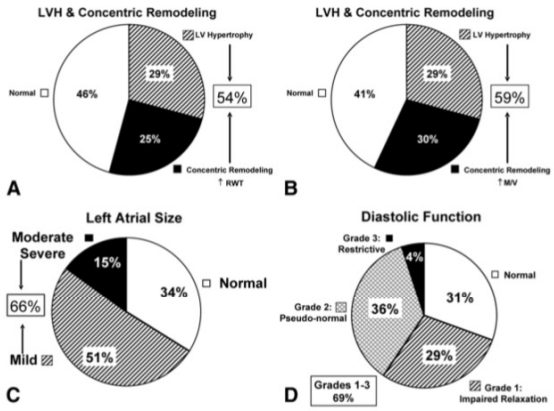
HFpEF is associated with structural abnormalities



Zile et al. Circulation. 2011;124:2491-2501

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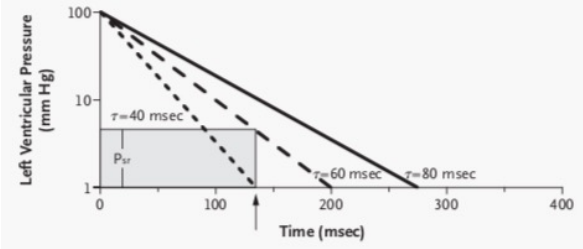
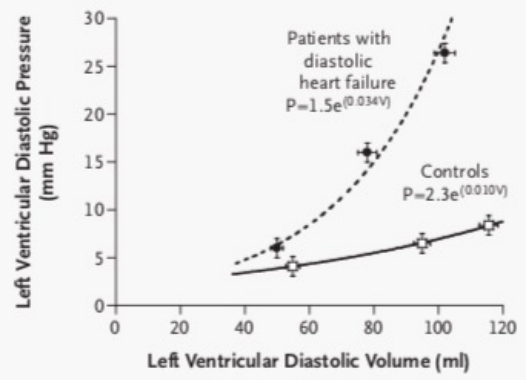
HFpEF results in prolonged diastole and increased LV stiffness





Zile et al. N Engl J Med 2004;350:1953-9.

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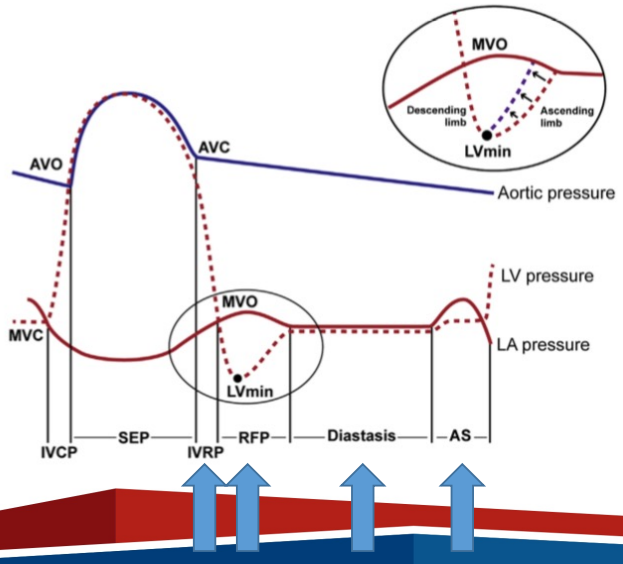
Breaking down Diastole



LV Diastole has 4 periods:

1. **Isovolemic relaxation (IVRP)**
2. **Rapid Filling Period (RFP)**
3. **Diastasis**
4. **Atrial systole**

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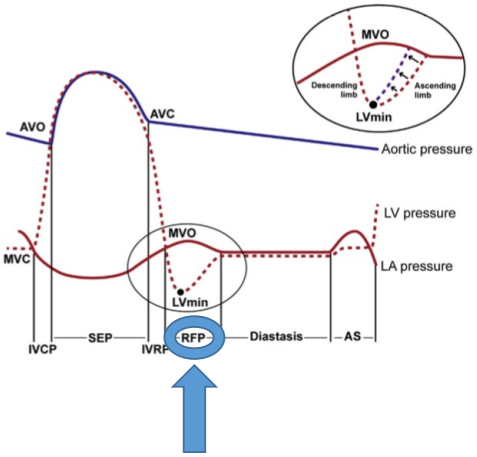
Rapid Filling Period

- **Begins with mitral valve opening**
- **Mediated by:**
  - (1) active relaxation
  - (2) elastic recoil
  - (3) ventricular lengthening
- **Has 2 parts:**
  - (1)a descending limb (suction)
  - (2) an ascending limb (compliance)



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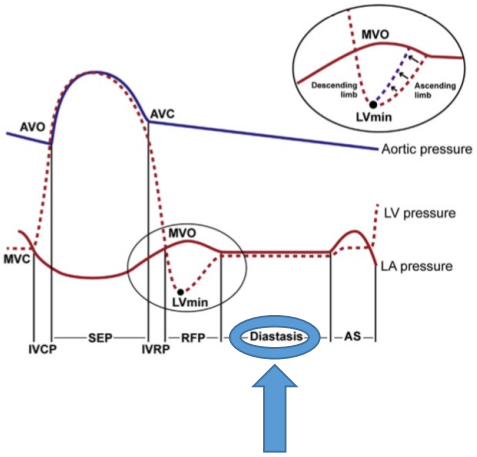
Diastasis

- **The Period from end of RFP until onset of atrial systole**
- **LA and LV pressures are near equilibrium**
- **Shorts as heart rate increases**



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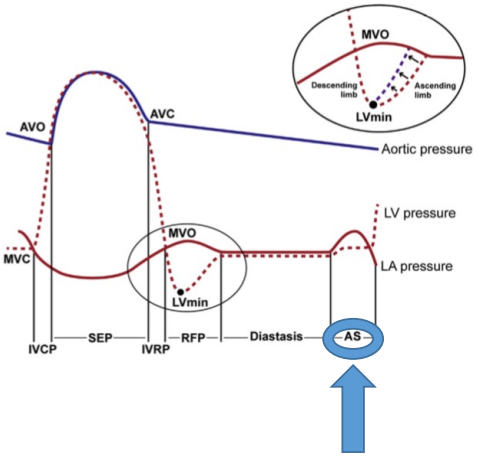
Atrial Systole

- **Accounts for contribution to LV preload beyond rapid filling**
- **In young normal patients 20% of LVEDV contributed to by atrial contraction**
- **Captured by Dopper A wave**



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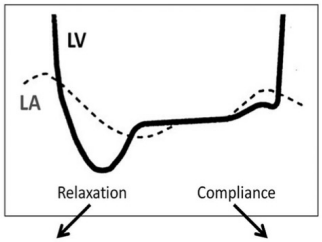
Echo Variables in Patients with HFpEF



- Reduced / delayed untwisting
- Reduced e longitudinal velocity
- Reduced e longitudinal deformation
- Slow flow propagation velocity
- Prolonged isovolumic relaxation time *
- Reduced mitral E inflow velocity *
- Prolonged mitral E deceleration time *
- Pronounced L wave
- Reduced -dp/dt of mitral regurgitant velocity

- Low velocity & time integral of mitral A inflow
- Short duration of mitral A wave
- Truncated filling during atrial contraction
- (End-) diastolic mitral regurgitation
- Reduced myocardial deformation (strain and strain rate) during atrial contraction
- Increased duration and velocity of pulmonary venous retrograde flow during atrial contraction

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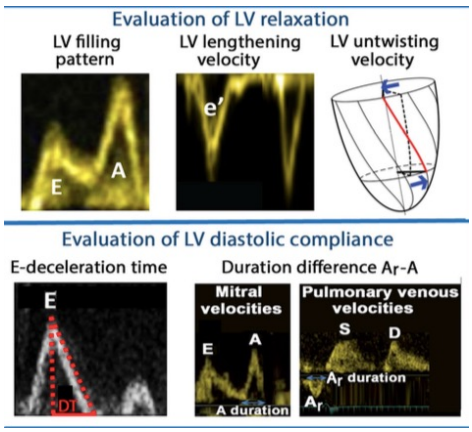
Echo Provides a Noninvasive Assessment of LV relaxation and Compliance



Smiseth et al. Journal of Echocardiography (2018) 16:55–64

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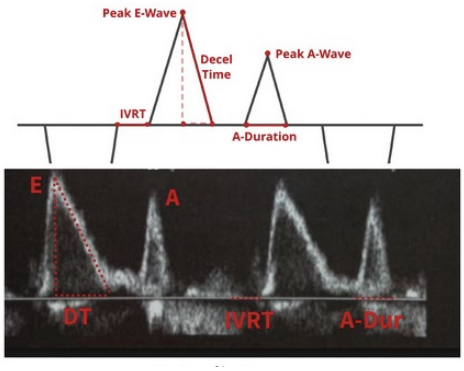
Transmitral Dopper Assessment – E and A

Variable	Utility and physiologic background
Mitral E velocity	E-wave velocity reflects the LA-LV pressure gradient during early diastole and is affected by alterations in the rate of LV relaxation and LAP.
Mitral A velocity	A-wave velocity reflects the LA-LV pressure gradient during late diastole, which is affected by LV compliance and LA contractile function.
Mitral E/A ratio	Mitral inflow E/A ratio and DT are used to identify the filling patterns: normal, impaired relaxation, PN, and restrictive filling.
Mitral E-velocity DT	DT is influenced by LV relaxation, LV diastolic pressures following mitral valve opening, and LV stiffness.
Mitral "L" velocity	Markedly delayed LV relaxation in the setting of elevated LV filling pressures allows for ongoing LV filling in mid diastole and thus L velocity. Patients usually have bradycardia.
IVRT	IVRT is ≤ 70 msec in normal subjects and is prolonged in patients with impaired LV relaxation but normal LV filling pressures. When LAP increases, IVRT



ASE/EACVI Diastolic Guidelines. JASE 2016;29:277-314.

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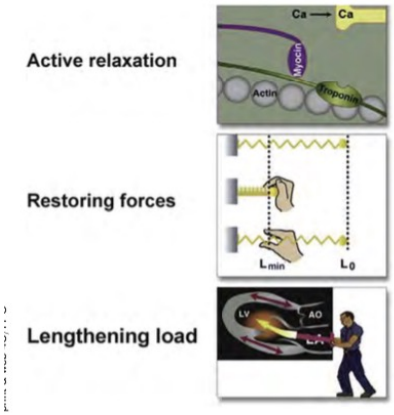
Determinants of Tissue Doppler (e')



Opdahl et al. Circulation 2009;119: 2578-86.

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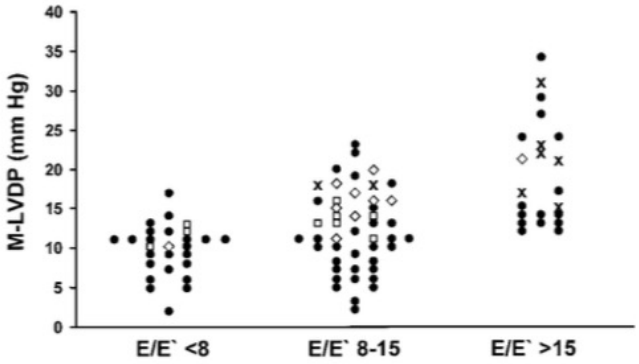
Estimation of Filling Pressures (E/e')



Ommen et al. *Circulation*. 2000;102:1788-1794

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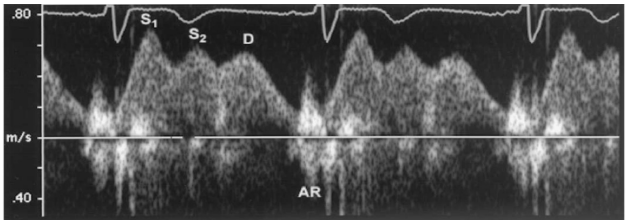
Pulmonary Vein Flow



PV S1 – systolic forward flow in early systole related to atrial relaxation

PVS2 – occurs in late systole produced by increase in pulmonary venous pressure

	Ventricular Function	Atrial Function
First systolic wave		Atrial relaxation
Second systolic wave	LV contraction	Reservoir function
	RV contraction	Atrial compliance
Early diastolic wave	Ventricular relaxation	Conduit function
	Ventricular chamber stiffness	
Atrial reversal wave	Ventricular chamber stiffness	Booster pump function
		Atrial compliance

LV = left ventricular; PVF = pulmonary venous flow; RV = right ventricular.

Tabata et al. JACC 2003

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LV Diastolic Filling Pressures
Pulsed wave Pulmonary Vein Flow

Peak A wave velocity Reversal

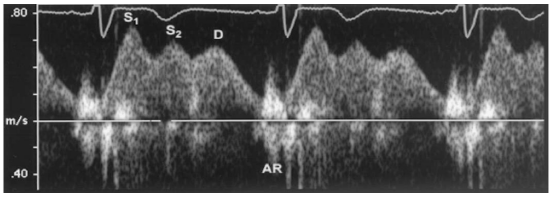
>35 cm/s is increased LVEDP

Pulmonary – Mitral Venous A-wave Duration

>30 msec longer is increased LVEDP

% systolic fraction (%) forward flow

<40% is increased mean LAP



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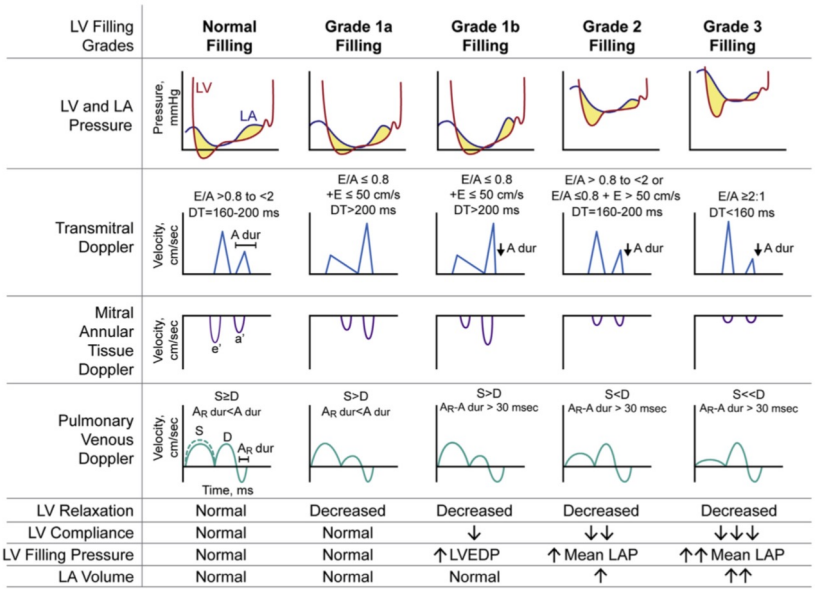
LV Filling Grades
Normal Filling
Grade 1a Filling
Grade 1b Filling
Grade 2 Filling
Grade 3 Filling
LV and LA Pressure
Pressure, mmHg
LV
LA
Transmitral Doppler
E/A >0.8 to <2
DT=160-200 ms
E/A ≤ 0.8
+E ≤ 50 cm/s
DT>200 ms
E/A ≤ 0.8
+E ≤ 50 cm/s
DT>200 ms
E/A > 0.8 to <2 or
E/A ≤0.8 + E > 50 cm/s
DT=160-200 ms
E/A ≥2:1
DT<160 ms
Velocity, cm/sec
A dur
Mitral Annular Tissue Doppler
e'
a'
Pulmonary Venous Doppler
S≥D
AR dur<A dur
S>D
AR dur<A dur
S>D
AR-A dur > 30 msec
S<D
AR-A dur > 30 msec
S<<D
AR-A dur > 30 msec
S
D
AR dur
Time, ms
LV Relaxation
Normal
Decreased
Decreased
Decreased
Decreased
LV Compliance
Normal
Normal
↓
↓↓
↓↓↓
LV Filling Pressure
Normal
Normal
↑LVEDP
↑Mean LAP
↑↑Mean LAP
LA Volume
Normal
Normal
Normal
↑
↑↑

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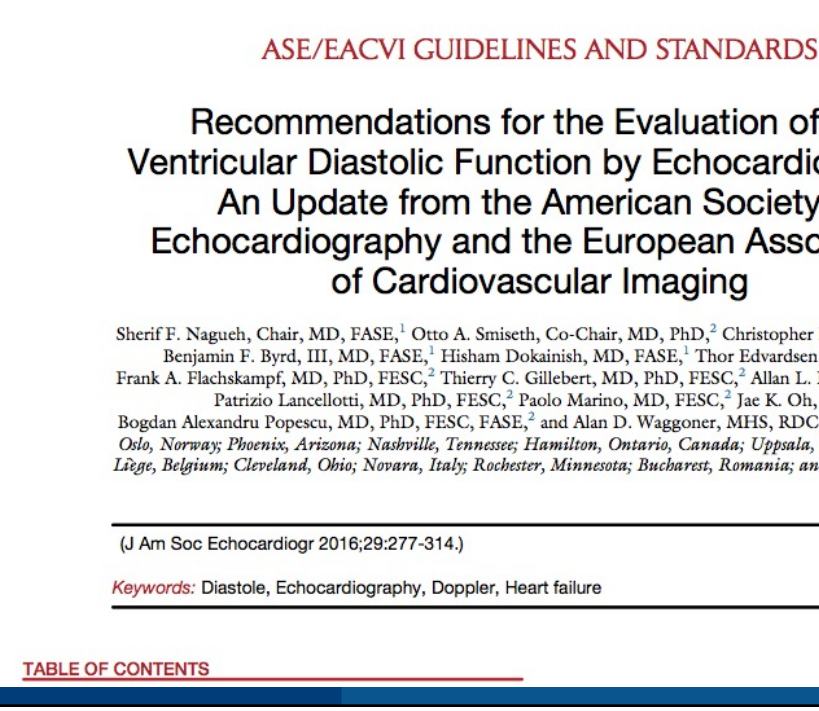
ASE/EACVI GUIDELINES AND STANDARDS
Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging
Sherif F. Nagueh, Chair, MD, FASE,[1] Otto A. Smiseth, Co-Chair, MD, PhD,[2] Christopher P. Appleton, MD,[1] Benjamin F. Byrd, III, MD, FASE,[1] Hisham Dokainish, MD, FASE,[1] Thor Edvardsen, MD, PhD,[2] Frank A. Flachskampf, MD, PhD, FESC,[2] Thierry C. Gillebert, MD, PhD, FESC,[2] Allan L. Klein, MD, FASE,[1] Patrizio Lancellotti, MD, PhD, FESC,[2] Paolo Marino, MD, FESC,[2] Jae K. Oh, MD,[1] Bogdan Alexandru Popescu, MD, PhD, FESC, FASE,[2] and Alan D. Waggoner, MHS, RDCS[1], Houston, Texas; Oslo, Norway; Phoenix, Arizona; Nashville, Tennessee; Hamilton, Ontario, Canada; Uppsala, Sweden; Ghent and Liège, Belgium; Cleveland, Ohio; Novara, Italy; Rochester, Minnesota; Bucharest, Romania; and St. Louis, Missouri
(J Am Soc Echocardiogr 2016;29:277-314.)
Keywords: Diastole, Echocardiography, Doppler, Heart failure
TABLE OF CONTENTS

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Normal systolic function; Four Key Variables to determine diastolic function:

Mitral annular e' velocity (septal e'< 7cm/sec, lateral e' < 10cm/sec)

Average E/e' ratio (> 14)

LA maximum volume index (> 34mL/m2)

Peak TR velocity (> 2.8m/sec)

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2016 ASE/EACVI Diastolic Guidelines: Reporting

1. **Conclusions on LV diastolic function should be routinely in reports when feasible**
2. **The report should comment on LV filling pressures and grade of LV diastolic dysfunction**
3. **If available, comparison with previous studies is encouraged to detect and comment on changes in diastolic function grade over time**

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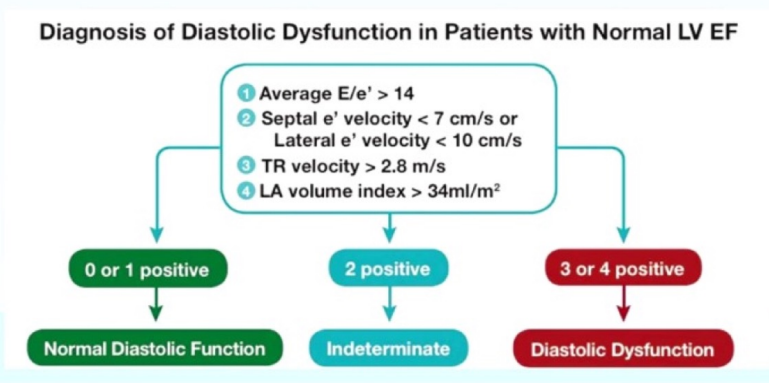
If the EF is normal



ASE/EACVI Diastolic Guidelines. JASE 2016;29:277-314.

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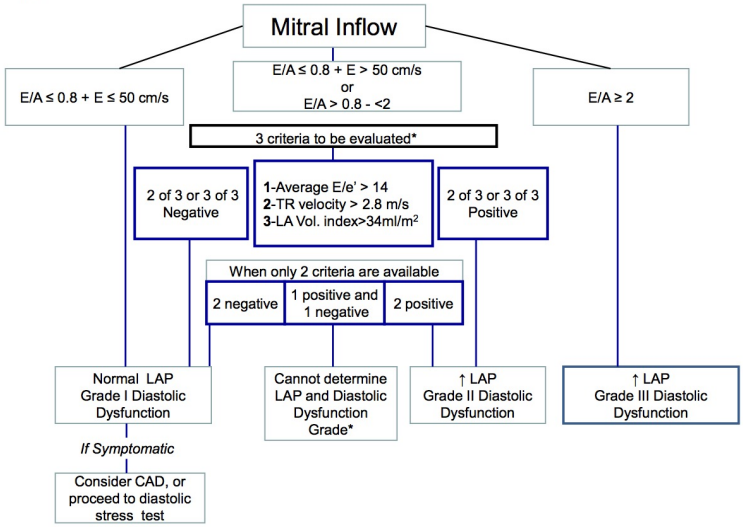
Estimation of Filling pressure



(* : 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)

ASE/EACVI Diastolic Guidelines. JASE 2016;29:277-314.

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Exceptions to Application of Diastolic Guidelines

Atrial fibrillation

Significant mitral valve disease – moderate MAC, mitral stenosis (any), or mitral regurgitation (>mod)

Mitral valve repair or prosthetic mitral valve

Left ventricular assist device (LVAD)

LBBB

Ventricular paced rhythm

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Atrial Fibrillation

1. Peak TR velocity > 2.8 m/sec is suggestive of elevated LAP.
2. In patients with depressed LVEFs, mitral DT (≤160 msec) has reasonable accuracy for the prediction of increased LV diastolic pressures and adverse clinical outcomes.
3. In patients with incomplete TR jet other Doppler measurements can be applied, including peak acceleration rate of mitral E velocity ≥ 1,900 cm/sec^2, IVRT ≤ 65 msec, DT of pulmonary venous diastolic velocity ≤ 220 msec, E/Vp ratio ≥ 1.4, and E/e′ ratio ≥ 11.
4. The variability of mitral inflow velocity with the RR cycle length is of value in patients with AF, as patients with increased filling pressures have less beat to beat variation.

ASE/EACVI Diastolic Guidelines. JASE 2016;29:277-314.

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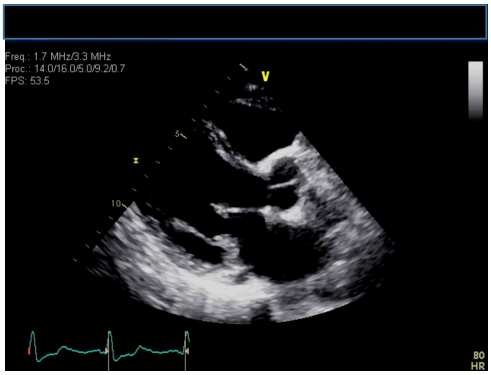
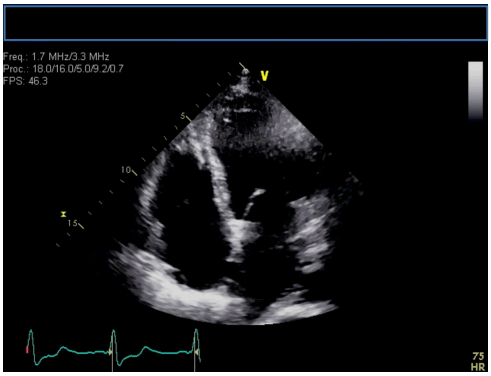
64 yo lady with history of anthracycline cardiomyopathy





EF =38% (Biplane Simpson's)
LAVi = 66.2 ml/m^2

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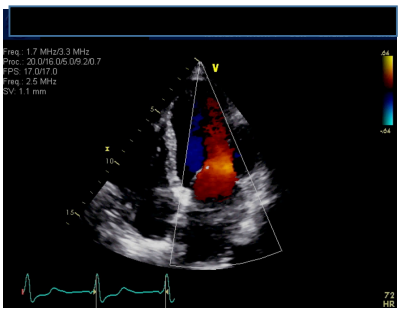

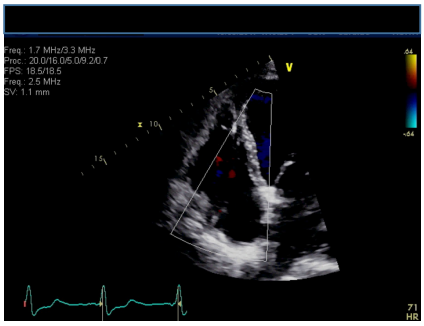

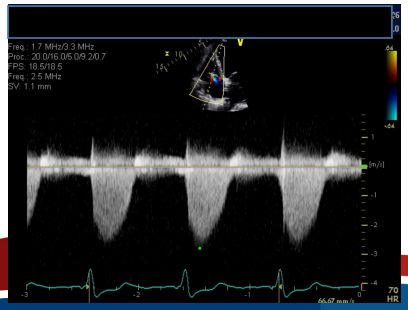

TR velocity = 2.9 m/s

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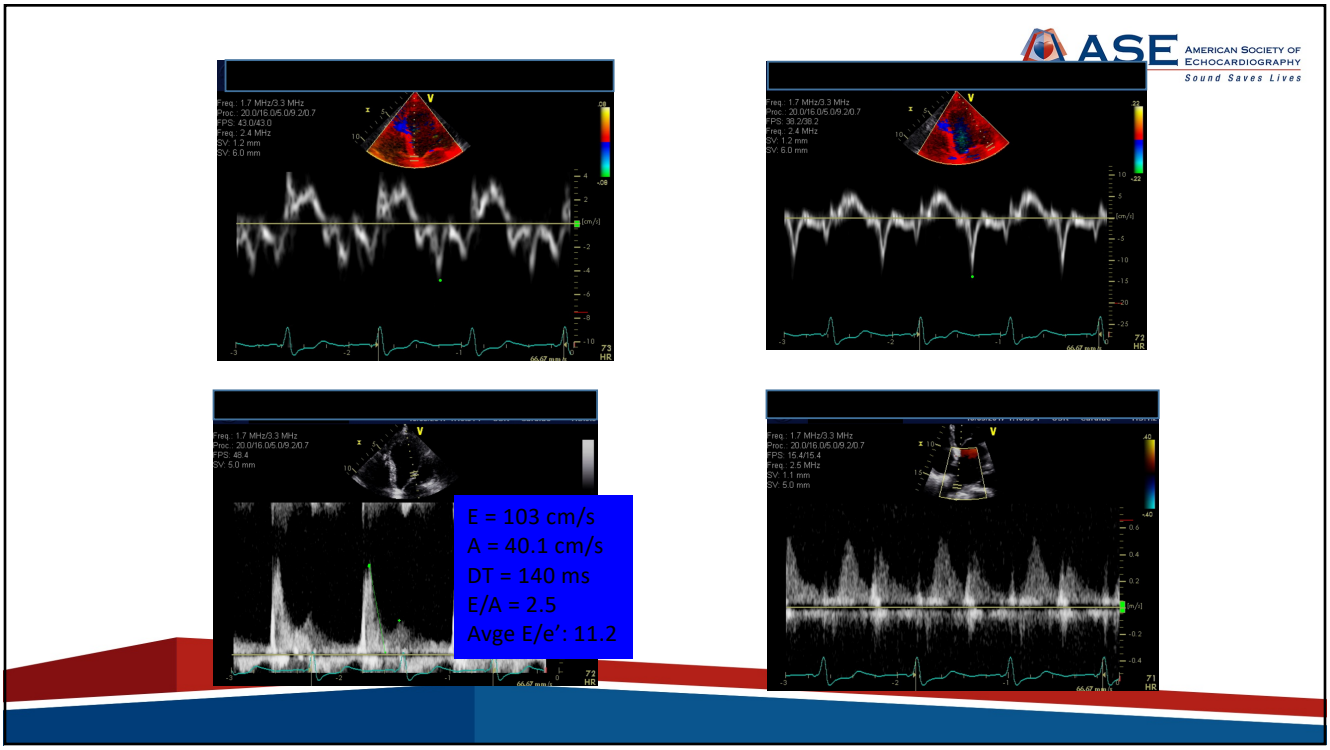
E = 103 cm/s
A = 40.1 cm/s
DT = 140 ms
E/A = 2.5
Avge E/e': 11.2

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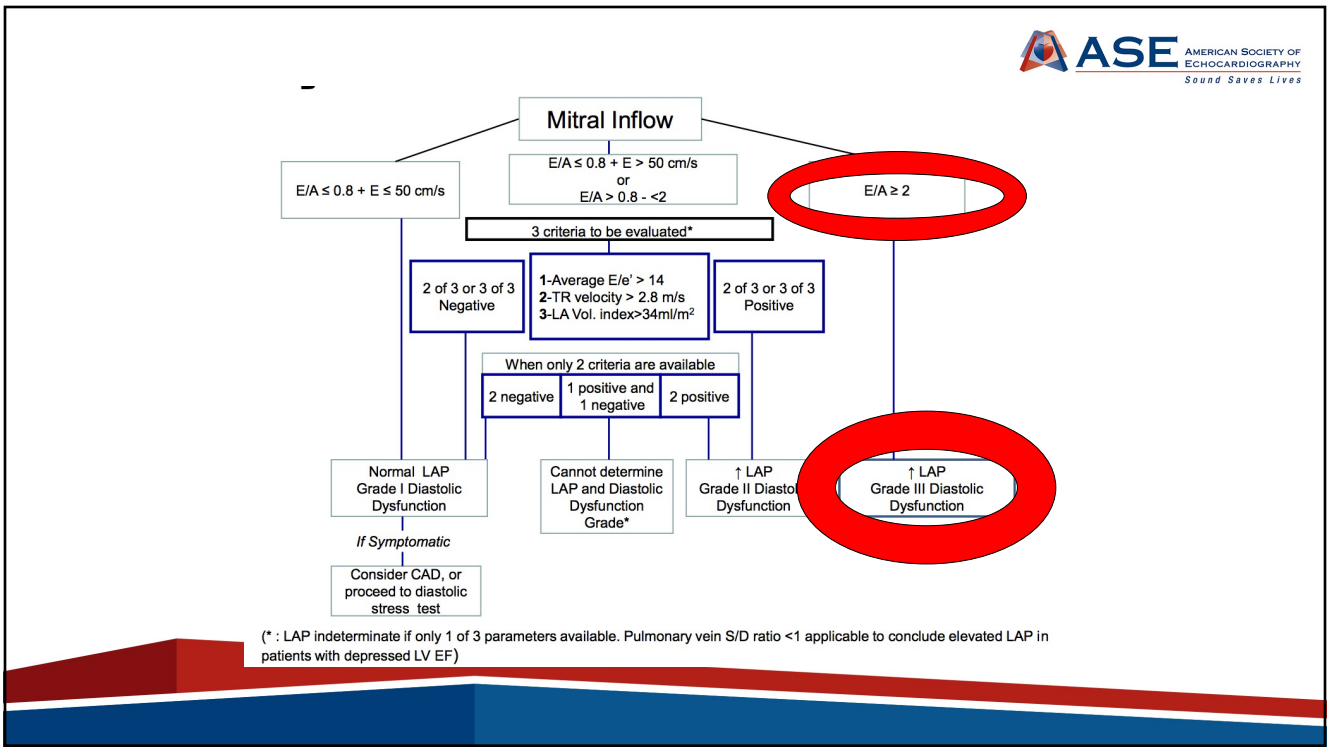
Mitral Inflow
E/A ≤ 0.8 + E ≤ 50 cm/s
E/A ≤ 0.8 + E > 50 cm/s
or
E/A > 0.8 - <2
E/A ≥ 2
3 criteria to be evaluated*
2 of 3 or 3 of 3 Negative
1-Average E/e' > 14
2-TR velocity > 2.8 m/s
3-LA Vol. index>34ml/m²
2 of 3 or 3 of 3 Positive
When only 2 criteria are available
2 negative
1 positive and 1 negative
2 positive
Normal LAP Grade I Diastolic Dysfunction
Cannot determine LAP and Diastolic Dysfunction Grade*
↑ LAP Grade II Diastol Dysfunction
↑ LAP Grade III Diastolic Dysfunction
If Symptomatic
Consider CAD, or proceed to diastolic stress test
(* : 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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62 year old woman

1 year history of worsened dyspnea on exertion

Presents to clinic NYHA IV

Physical exam:

BP 100/60 HR 70

- S1, S2 diminished +S3 JVP at angle of jaw
- Bibasilar crackles
- +2 peripheral edema

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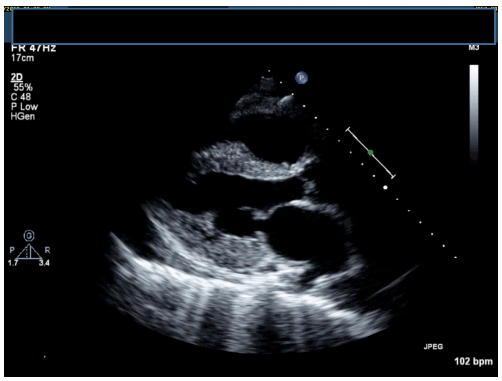

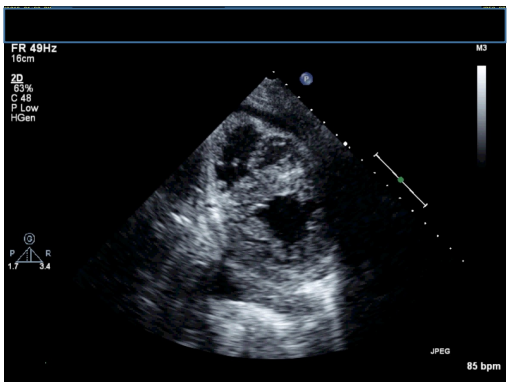

Septum measures 15 mm, Posterior wall 16 mm

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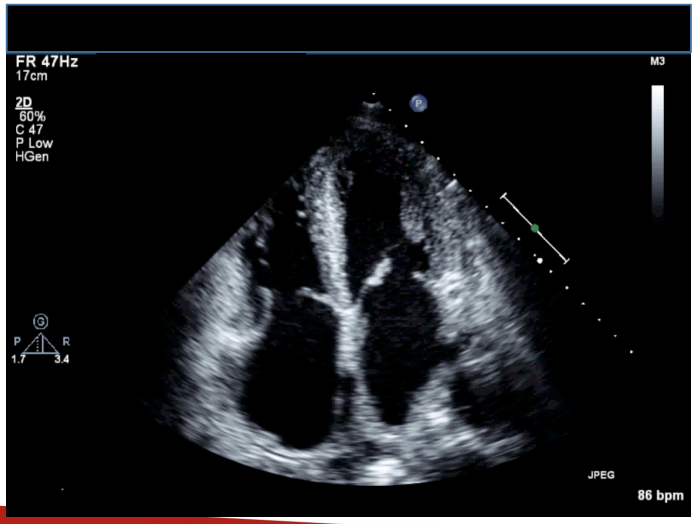

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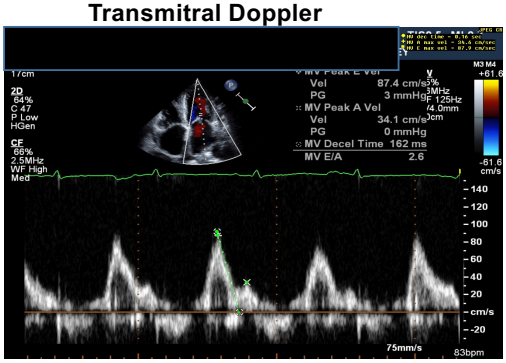
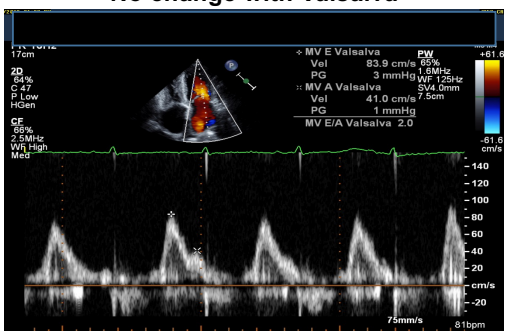
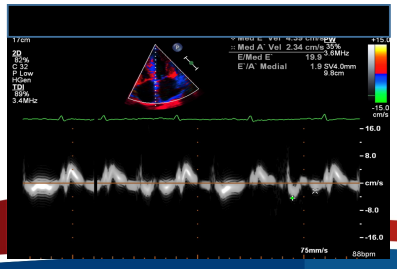
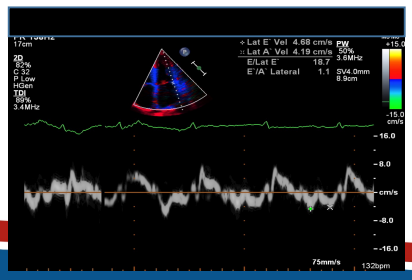
Transmitral Doppler



No change with Valsalva







Medial e' = 4.4
Lateral e'= 4.7

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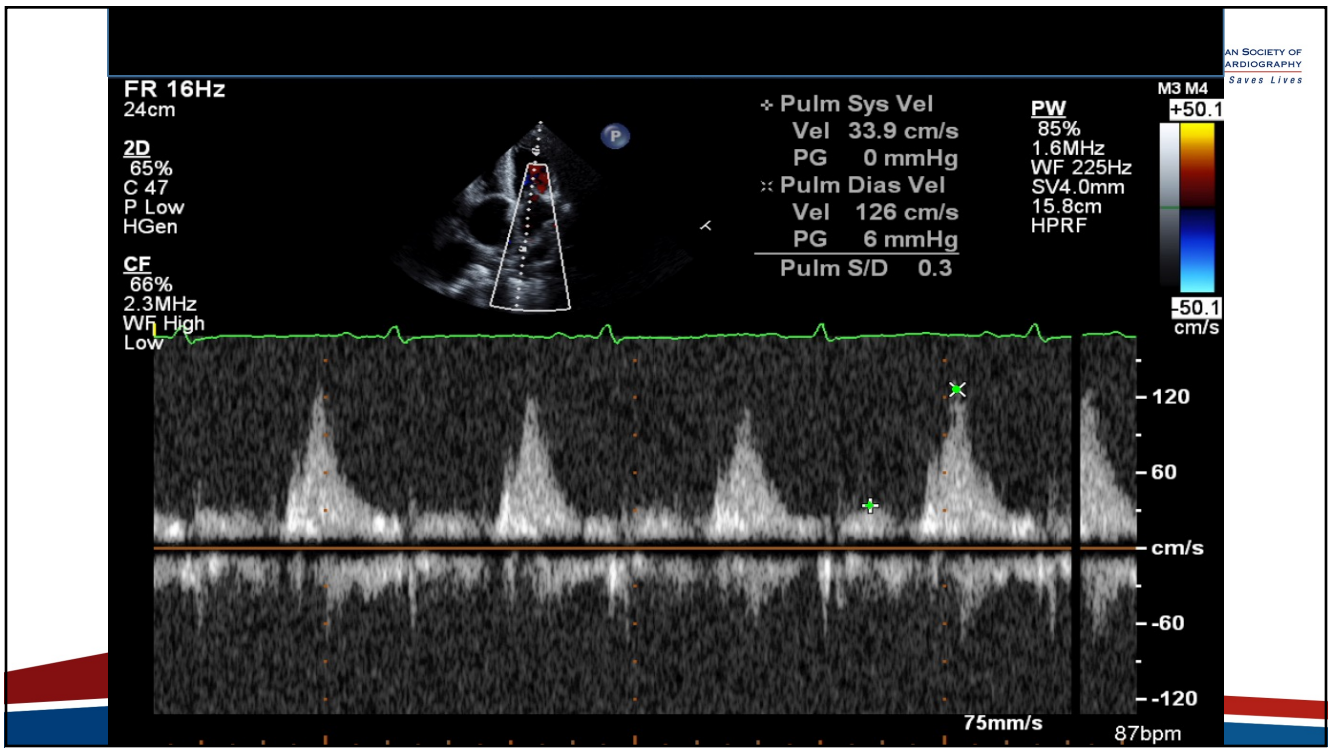
FR 16Hz
24cm
2D
65%
C 47
P Low
HGen
CF
66%
2.3MHz
WF High
Low
Pulm Sys Vel
Vel 33.9 cm/s
PG 0 mmHg
Pulm Dias Vel
Vel 126 cm/s
PG 6 mmHg
Pulm S/D 0.3
PW
85%
1.6MHz
WF 225Hz
SV4.0mm
15.8cm
HPRF
M3 M4
+50.1
-50.1
cm/s
120
60
cm/s
-60
-120
75mm/s
87bpm

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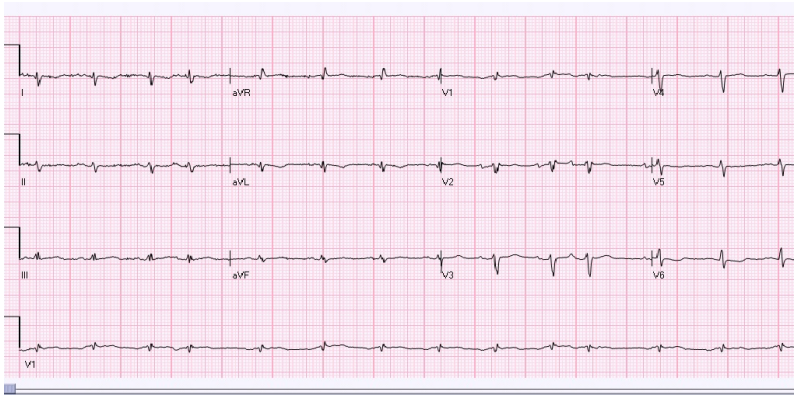
I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
V1

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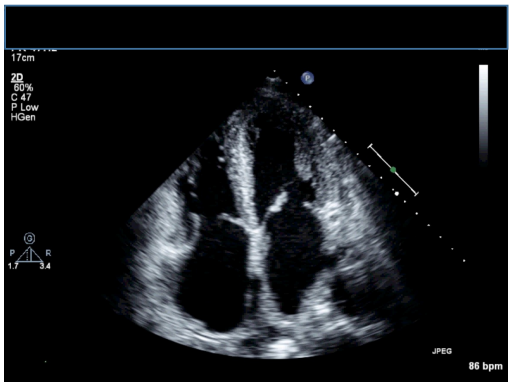
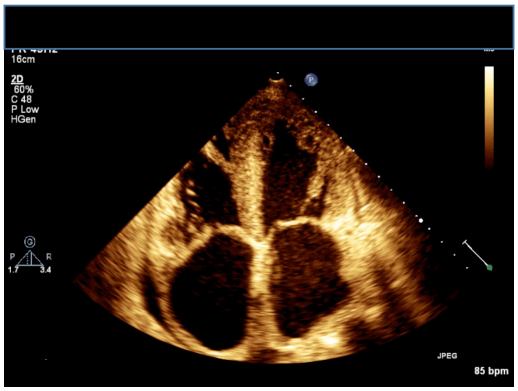
On Initial Presentation



One Month Later



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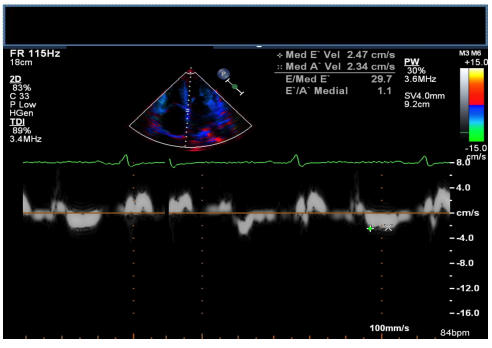
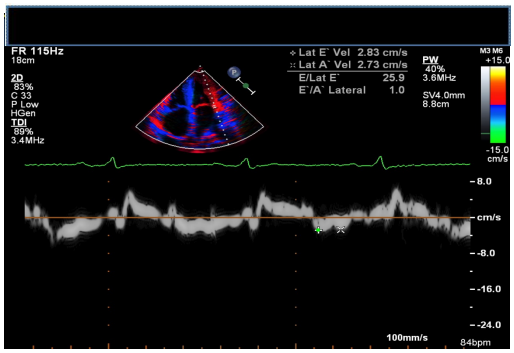


Medial e' = 2.5
(previously 4.4)



Lateral e' = 2.8
(previously 4.7)

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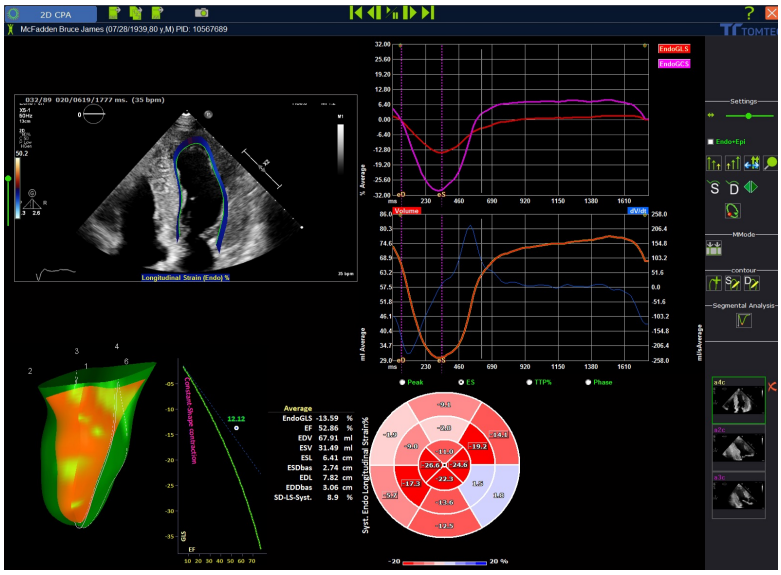

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LV filling pressures in Special Populations

Disease	Echocardiographic measurements and cutoff values
AF[43,94-99]	Peak acceleration rate of mitral E velocity (≥1,900 cm/sec^2) IVRT (≤65 msec) DT of pulmonary venous diastolic velocity (≤220 msec) E/Vp ratio (≥1.4) Septal E/e′ ratio (≥11)
Sinus tachycardia[41,44]	Mitral inflow pattern with predominant early LV filling in patients with EFs <50% IVRT ≤70 msec is specific (79%) Pulmonary vein systolic filling fraction ≤40% is specific (88%)
Restrictive cardiomyopathy[13,107-109]	DT (<140 msec) Mitral E/A (>2.5) IVRT (<50 msec has high specificity) Average E/e′ (>14)
MR[110-112]	Ar-A (≥30 msec) IVRT (<60 msec has high specificity) IVRT/$T_{E-e'}$ (<5.6) may be applied for the prediction of LV filling pressures in patients with MR and normal EFs Average E/e′ (>14) may be considered only in patients with depressed EFs

ASE/EACVI Diastolic Guidelines. JASE 2016;29:277-314.

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Case

42 year old male with familial TTR cardiac amyloidosis dx 2010 (ASP10Glu mutation)

Transthoracic Echo

- LVEF 35%
- marked biventricular hypertrophy
- severe diastolic dysfunction
- Bi-atrial enlargement

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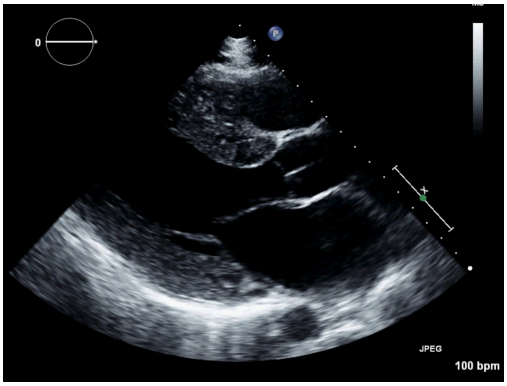
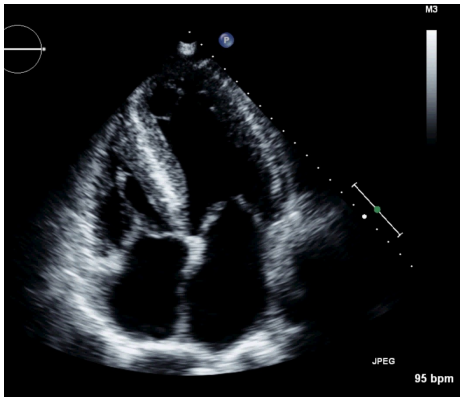
Case – LV systolic function





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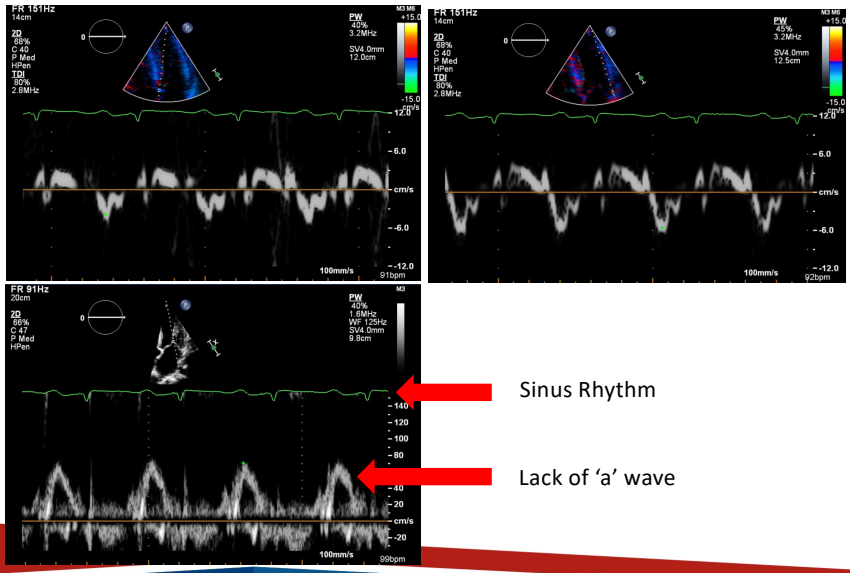
Case – atrial function/LV diastolic function



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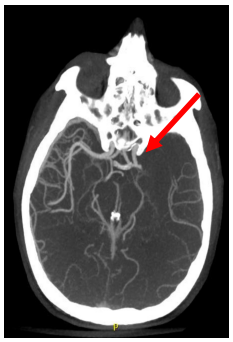
Case

Presented with acute ischemic stroke Jan 2019

- Altered level of consciousness
- Right sided weakness

→Left middle cerebral artery infarction



Underwent successful endovascular treatment with mechanical thrombectomy

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Case – stroke work up

12 lead ECG → sinus rhythm

2 weeks of continuous cardiac monitoring → occasional atrial ectopy

Imaging of head, neck and lower limb vasculature → no source of embolism

TTE – patent foramen ovale

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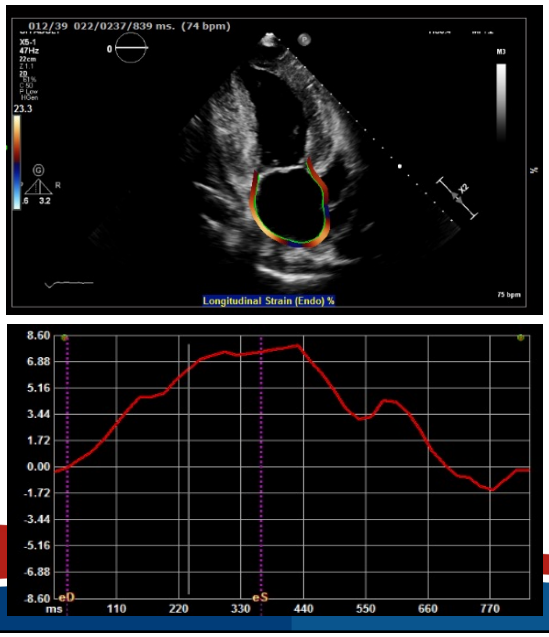
TTE – LA strain analysis



EndoGLS	7.70	%
EF	23.27	%
EDV	78.75	ml
ESV	102.63	ml
FAC	14.88	%

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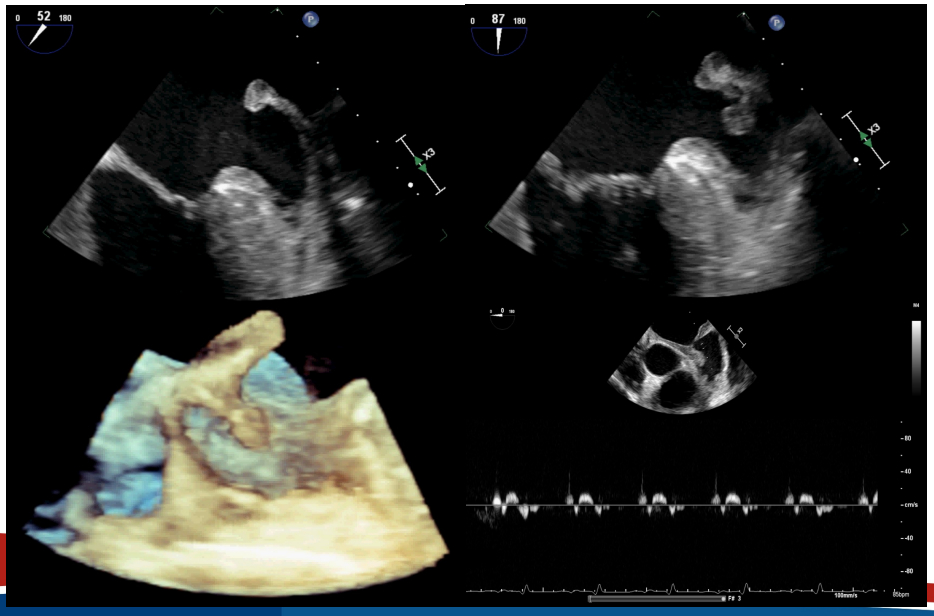
TEE



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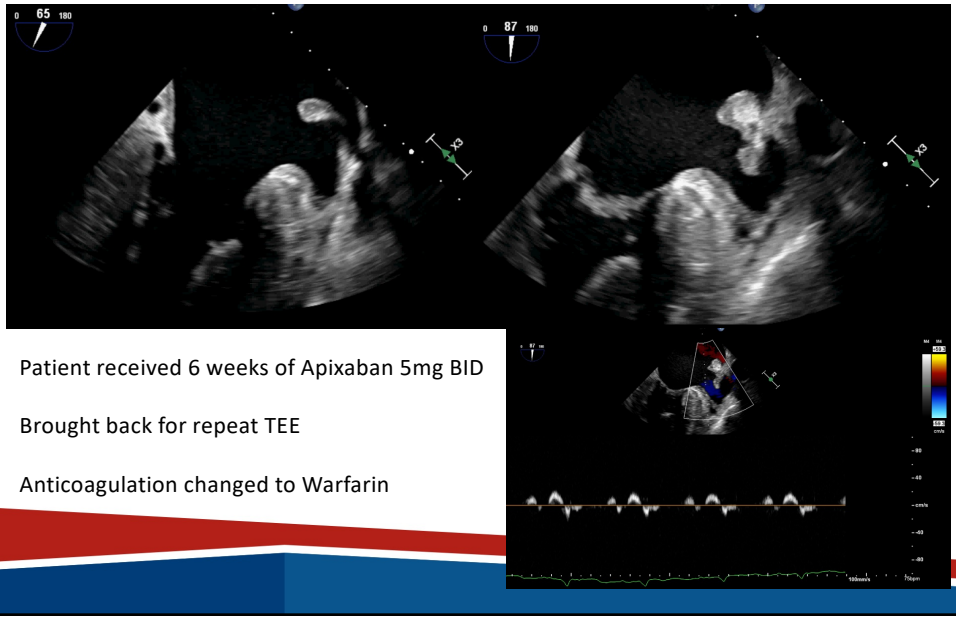
Repeat TEE



Patient received 6 weeks of Apixaban 5mg BID

Brought back for repeat TEE

Anticoagulation changed to Warfarin

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Conclusions

1. Diastolic function is assessed using a single algorithm for normal and reduced LV function
2. Key variables include: mitral annular e', E/e' ratio, LAVi, and TR
3. Diastolic function provides important prognostic information and insight into LV relaxation, compliance and filling pressures

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Thank-you!

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