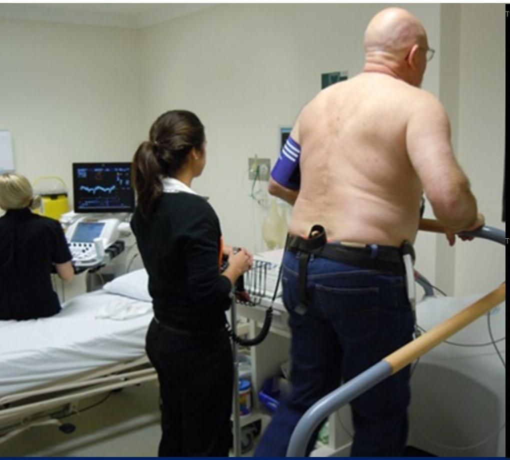
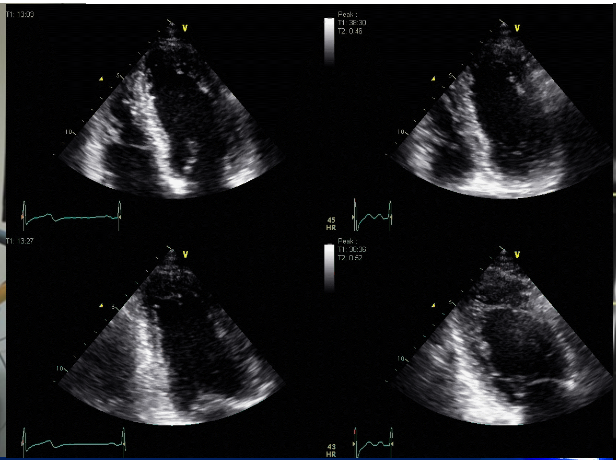
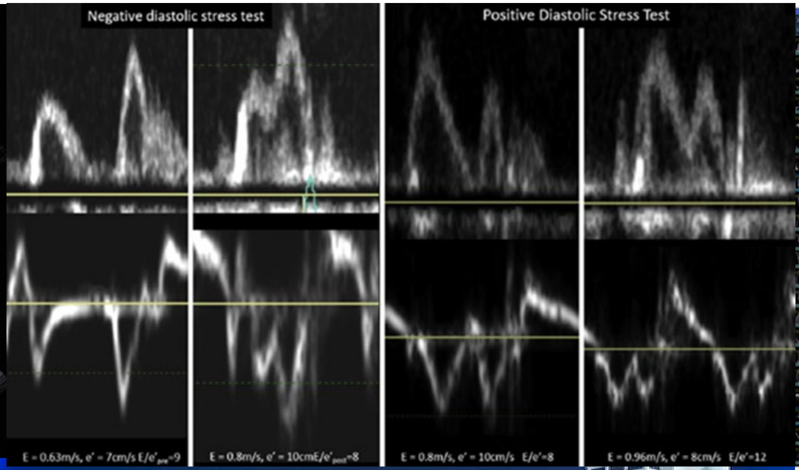
Diastolic stress echocardiography

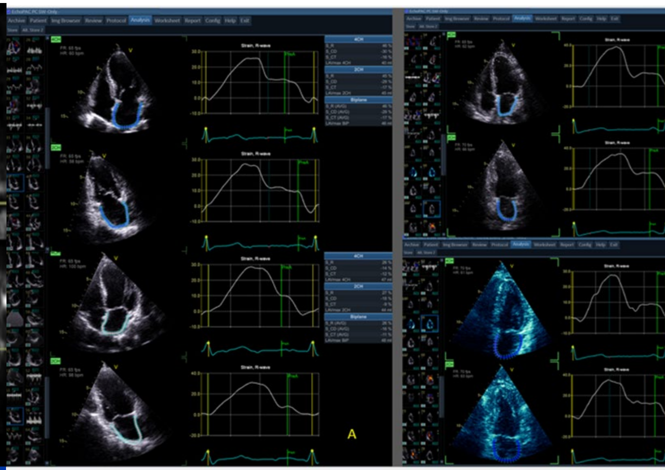
Dr Ben Fitzgerald, Cardiologist

TPCH & The Wesley Hospital, Brisbane







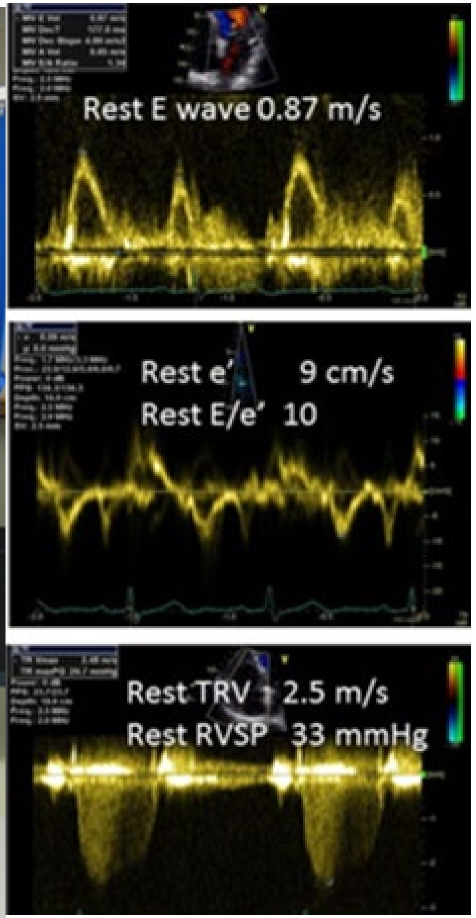


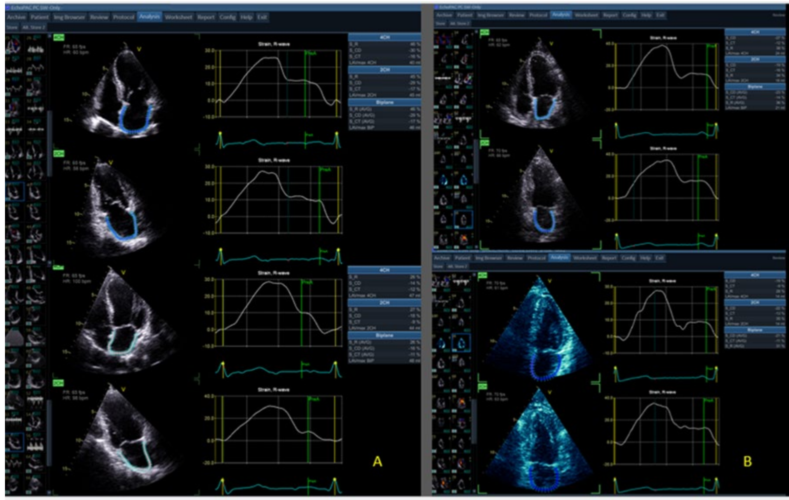
ECHO AUSTRALIA

17-19 March 2025

Diastolic stress echocardiography

No disclosures





Advara HeartCare

ECHO AUSTRALIA

Diastolic stress test

- What is the Diastolic Stress Test?
- What is the basis?
- What do the Guidelines say?
- What is the research?
- Why would I do it?
- How do I do it?

Diastolic stress test

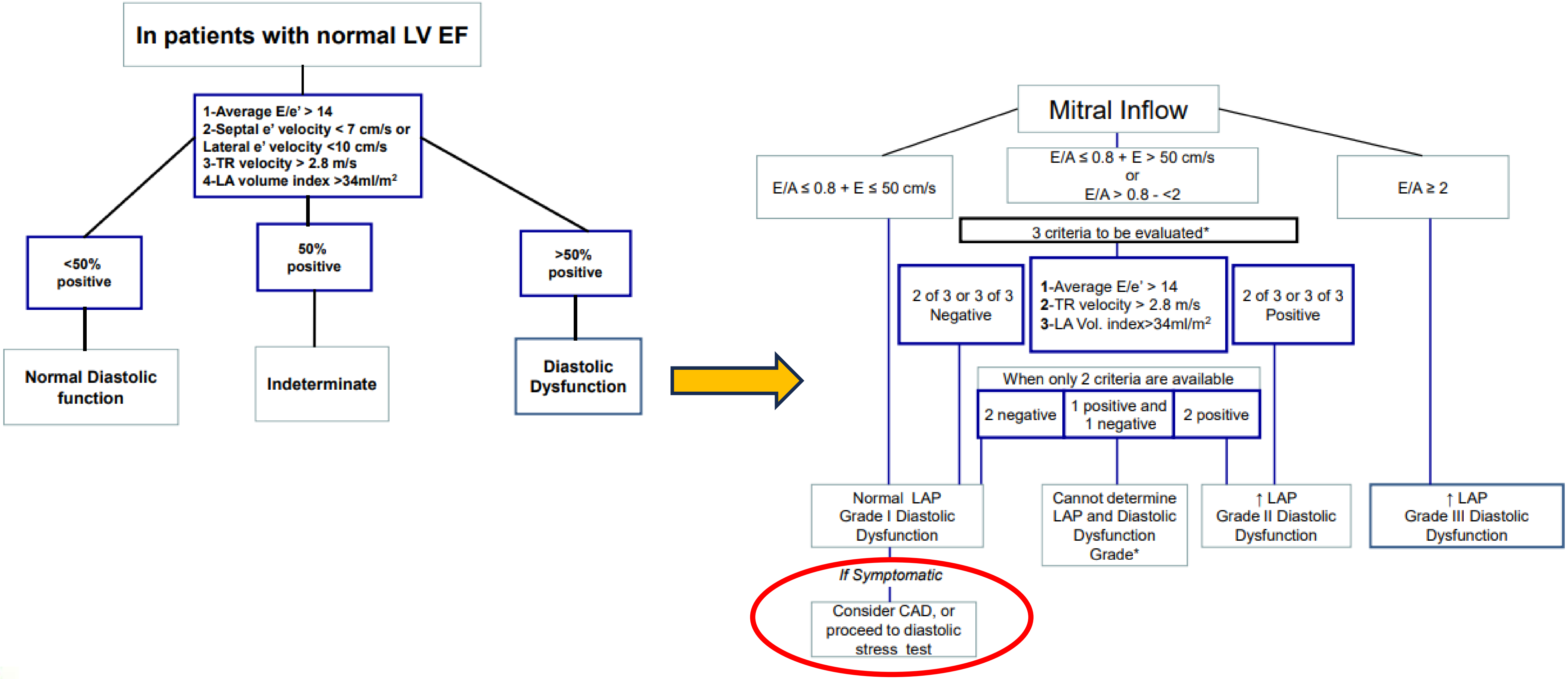
ASE/EACVI GUIDELINES AND STANDARDS

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.)

Diastolic assessment



Diastolic stress test

Recommended in 2016 ASE 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

VI. DIASTOLIC STRESS TEST

Exercise echocardiography[156] is usually performed to detect reduced LV systolic and/or diastolic reserve capacity in the setting of coronary disease or diastolic dysfunction, as patients with diastolic dysfunction may have a similar hemodynamic profile (in terms of cardiac output and filling pressure) at rest as healthy individuals who have normal diastolic function. When normal subjects exercise,

Diastolic stress test

ESC European Society of Cardiology
European Heart Journal - Cardiovascular Imaging (2022) **23**, e34–e61
doi:10.1093/ehjci/jeab154

Multimodality imaging in patients with heart failure and preserved ejection fraction: an expert consensus document of the European Association of Cardiovascular Imaging

Otto A. Smiseth (Chair)[1,2,3]*, Daniel A. Morris[4], Nuno Cardim[5], Maja Cikes[6], Victoria Delgado[7], Erwan Donal[8,9], Frank A. Flachskampf[10], Maurizio Galderisi[11,†], Bernhard L. Gerber[12], Alessia Gimelli[13], Allan L. Klein[14], Juhani Knuuti[15], Patrizio Lancellotti[16,17], Julia Mascherbauer[18], Davor Milicic[6], Petar Seferovic[19,20], Scott Solomon[21], Thor Edvardsen[1,2,3], and Bogdan A. Popescu (Co-Chair)[22,*]

Diastolic stress test by echocardiography

Recent studies have shown that in some patients with HFpEF increased LV filling pressure occurs only during exercise and that echocardiographic parameters at rest have relatively low sensitivity to diagnose HFpEF in these patients.[73–78] Measurements of the *E/e′* ratio and peak TR velocity during exercise are feasible and have been invasively validated for the estimation of elevated LV filling pressure during exercise.[25,74,75,77,79] In this respect, recent studies have shown that adding diastolic stress testing (i.e. analysis of the *E/e′* ratio and TR velocity during exercise) to the standard resting echocardiography increases diagnostic sensitivity in patients suspected of HFpEF who have normal estimated LV filling pressure at rest.[73–75,77,80] Therefore, a diastolic stress test can be added to the echocardiographic diagnostic approach in the setting of suspected HFpEF and normal resting LV filling pressure (*Figure 16*, *Table 4*). Importantly, GLS should be measured and when <16–18% in absolute value, suspicion of HFpEF is strengthened, and diastolic stress testing should be considered.

Diastolic stress test

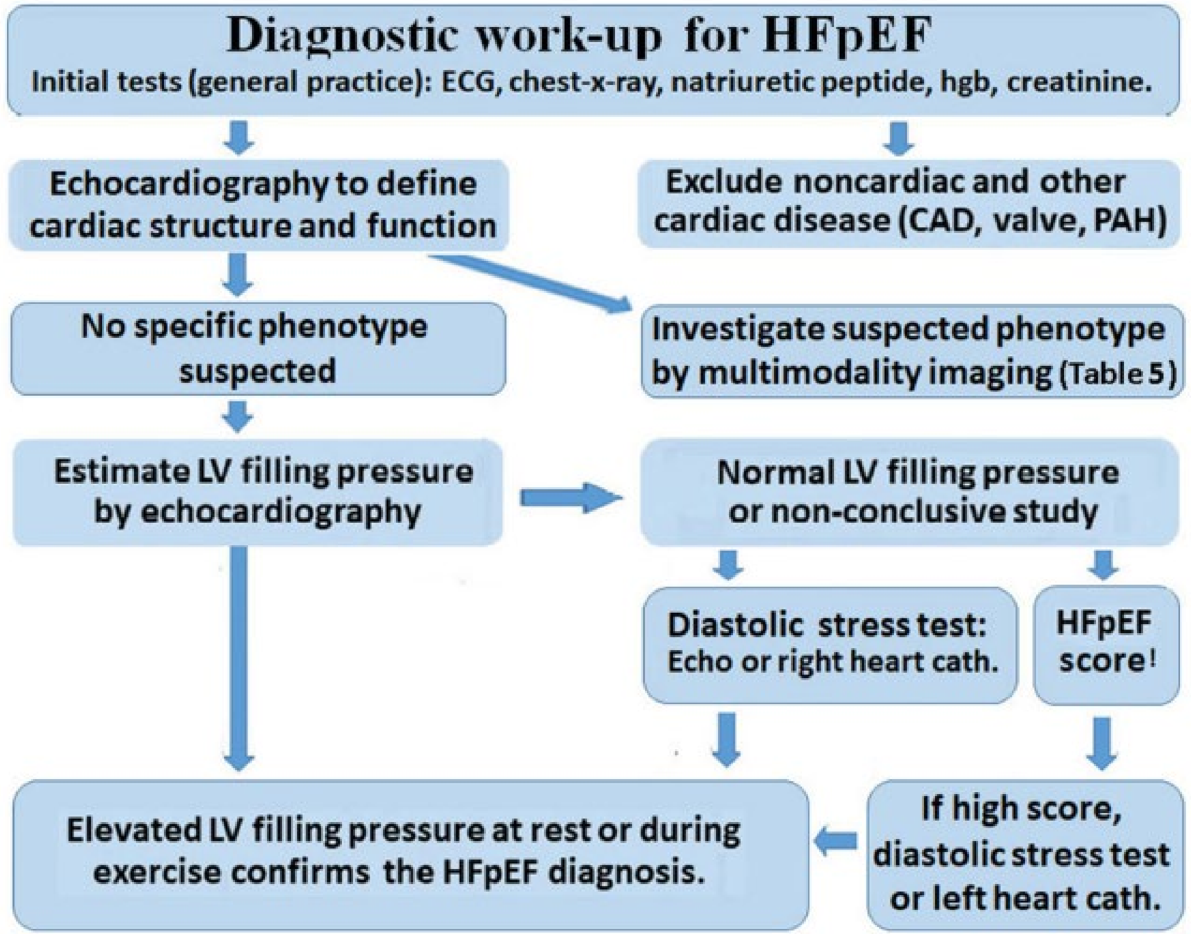


Figure 3 Diagnostic work-up for HFpEF.! According to Pieske *et al.*[2]

Diastolic stress test

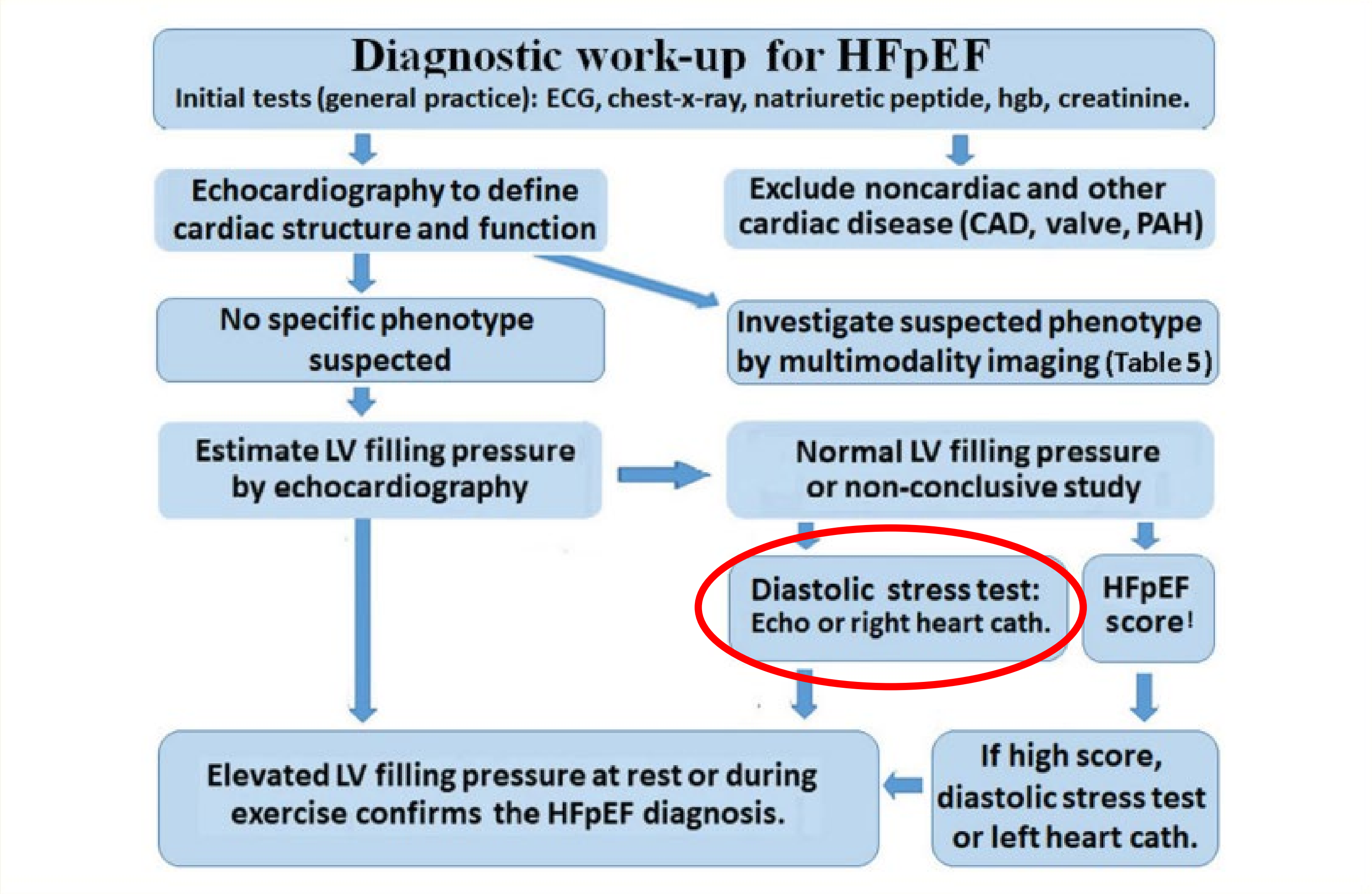
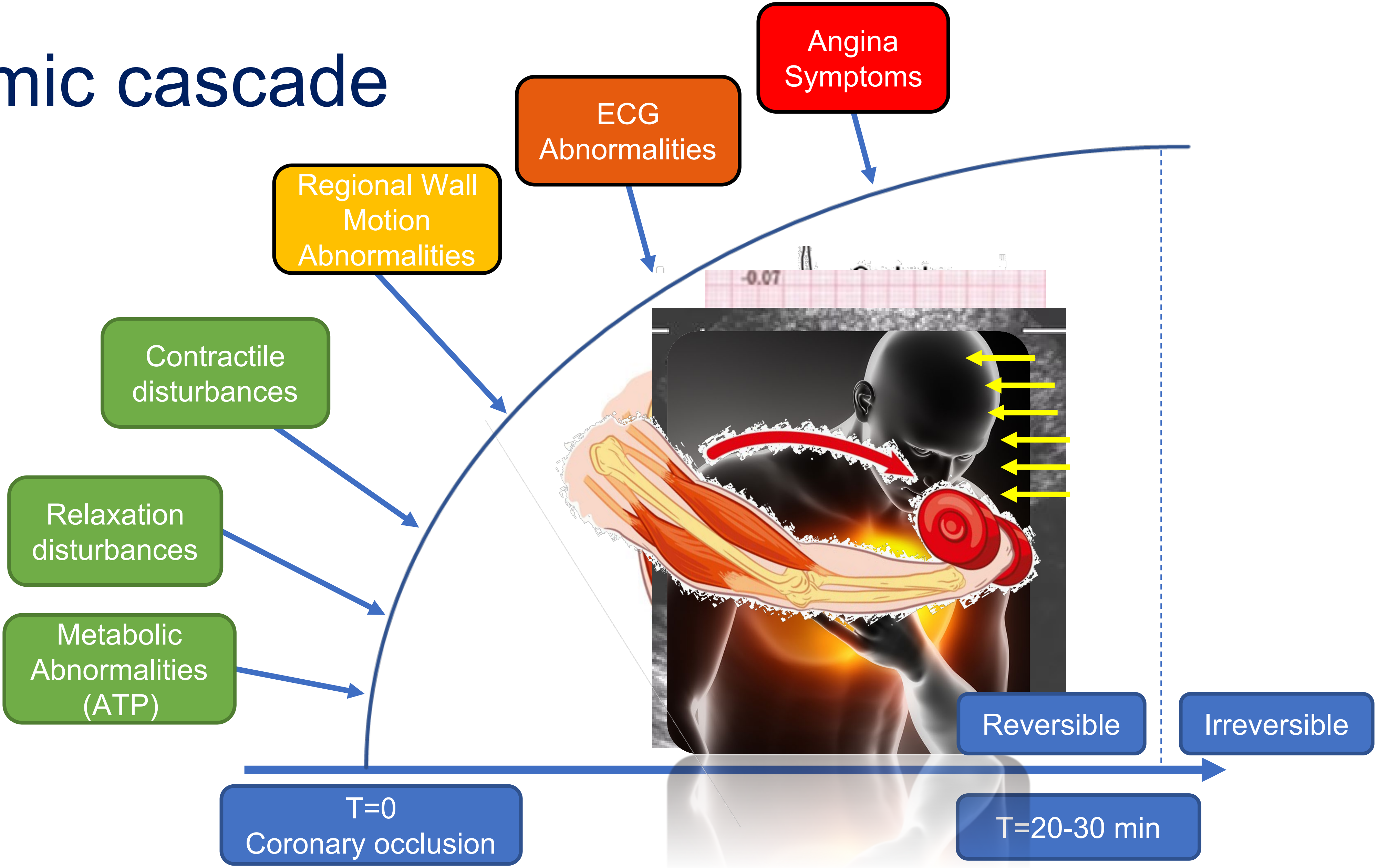
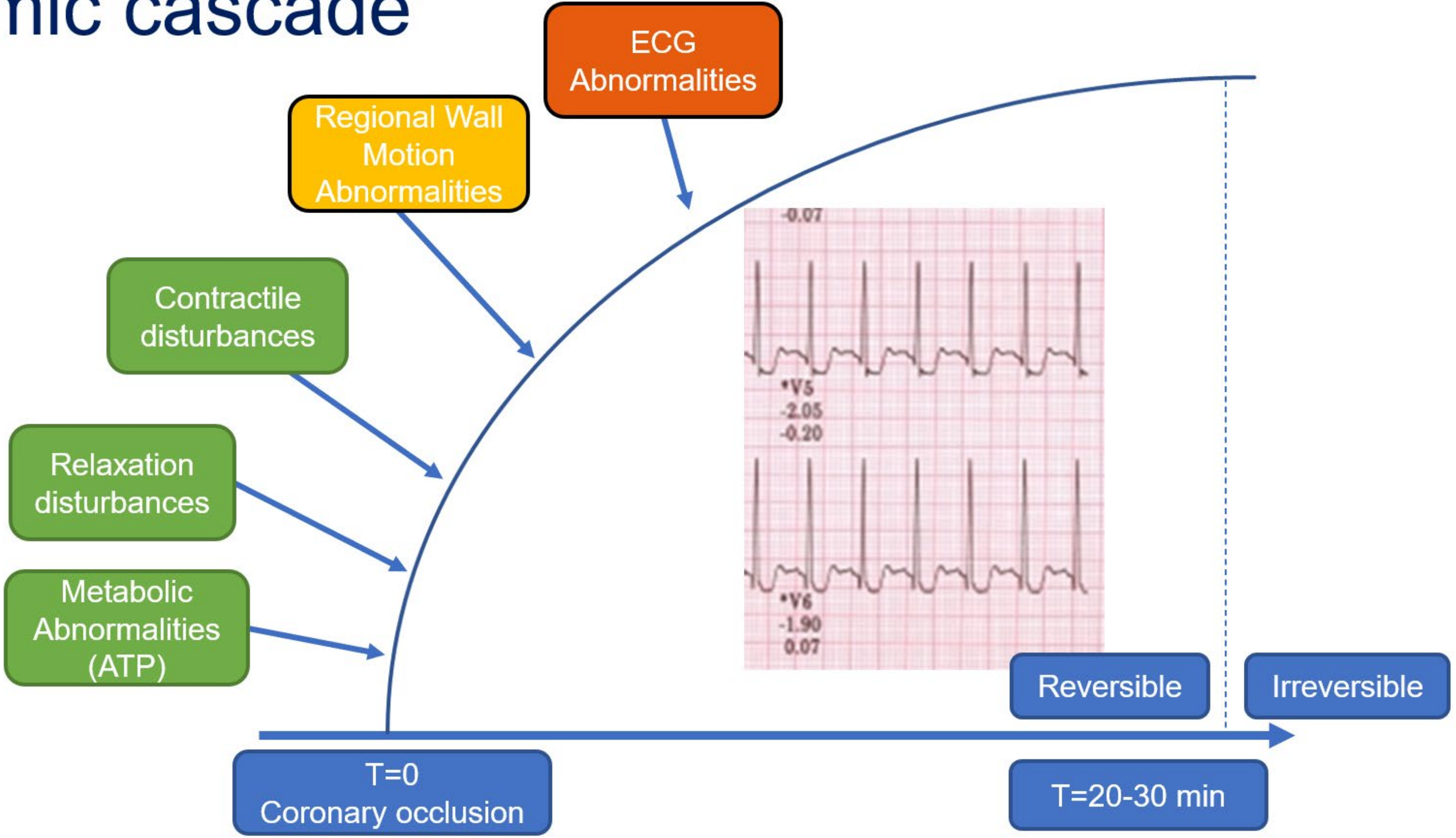


Figure 3 Diagnostic work-up for HFpEF.! According to Pieske *et al.*[2]

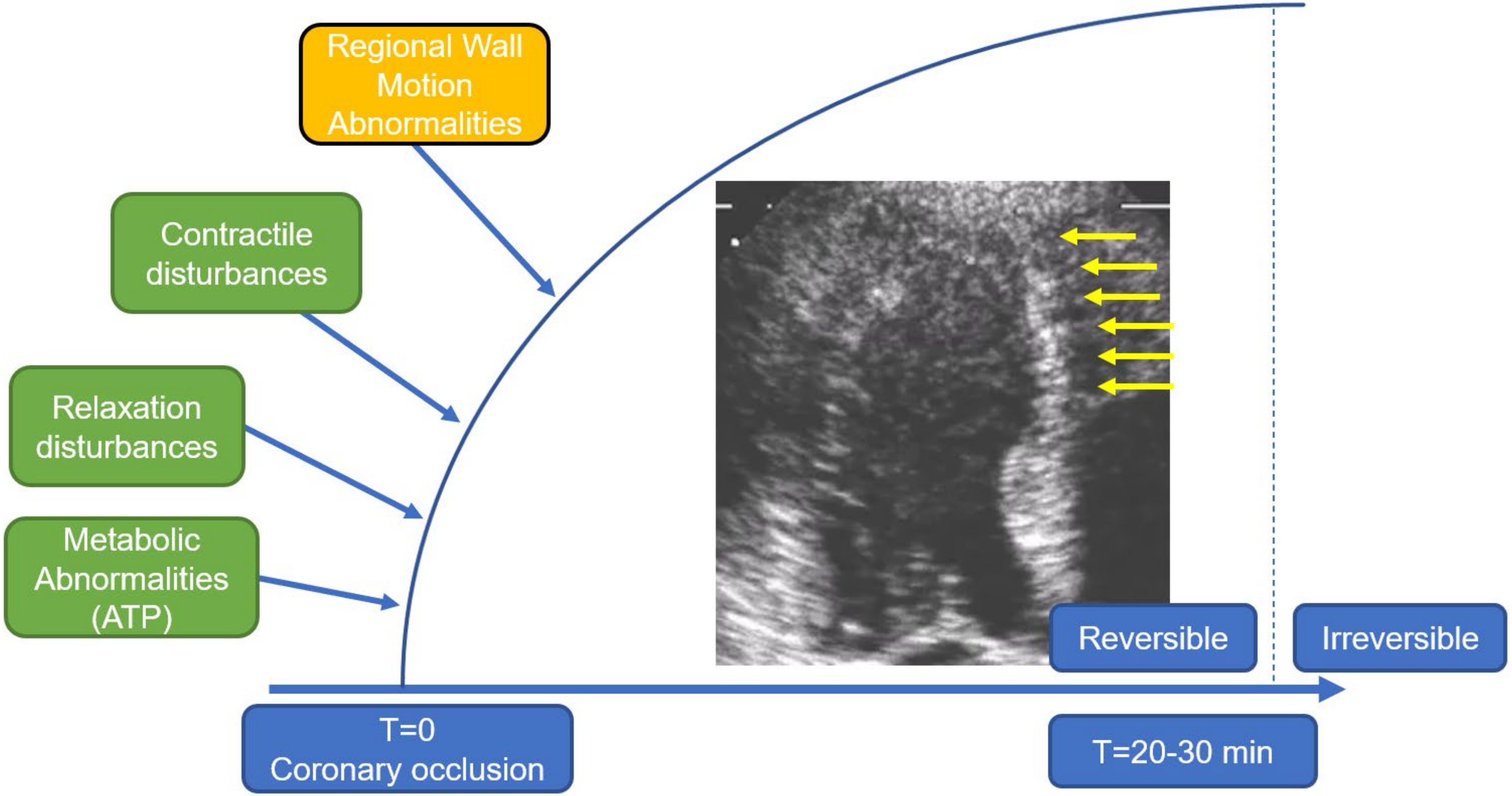
Ischaemic cascade



Ischaemic cascade

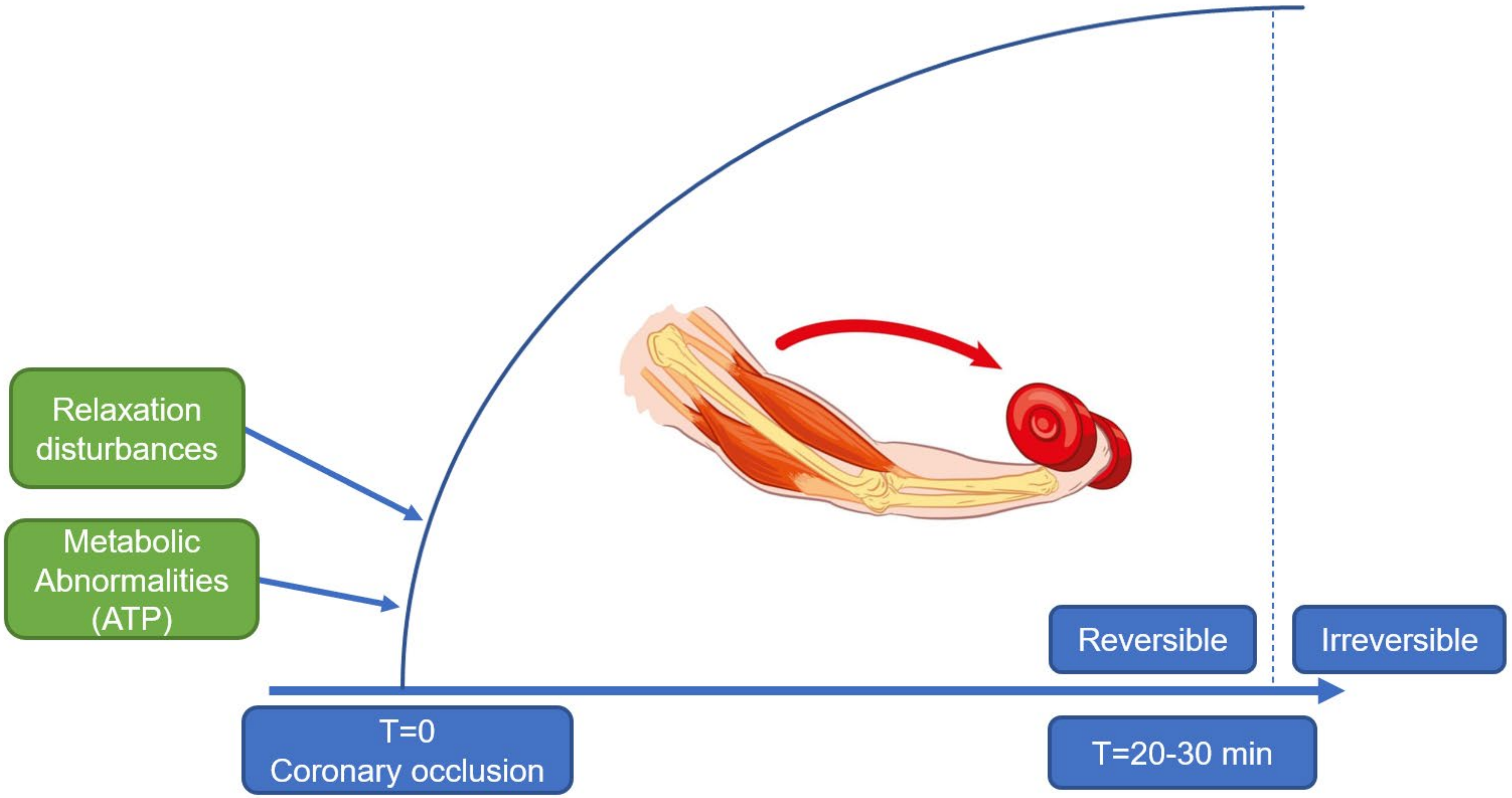


Ischaemic cascade



Ischaemic cascade

Diastolic
dysfunction



Diastolic stress test

- Shortness of breath is key symptom in heart failure
- Many patients only develop symptoms on exertion

SHORTNESS OF BREATH

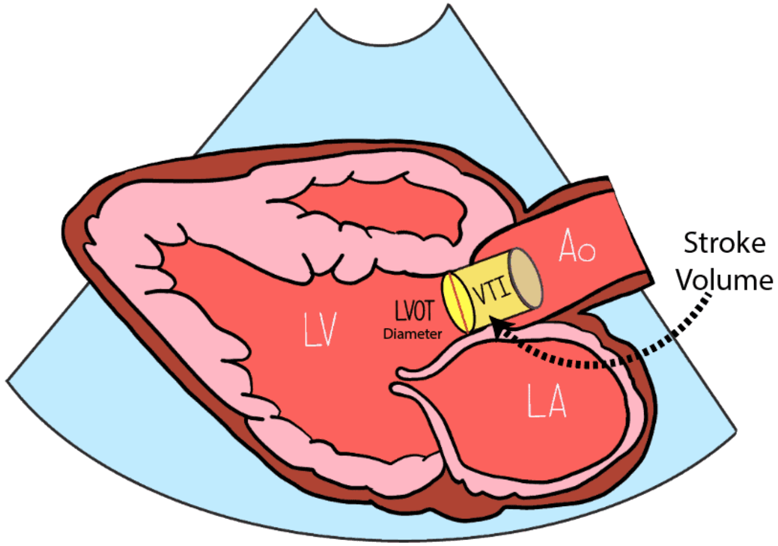
- Approximately 50% of patients with heart failure have preserved ejection fraction
- LV filling pressures may be normal at rest, but significantly increase with exertion
- In patients with HFpEF, 40-50% have normal filling pressures at rest

Diastolic stress test

Normally, SV and CO increase without significant change in filling pressures, due to augmentation of myocardial relaxation and early increased diastolic suction

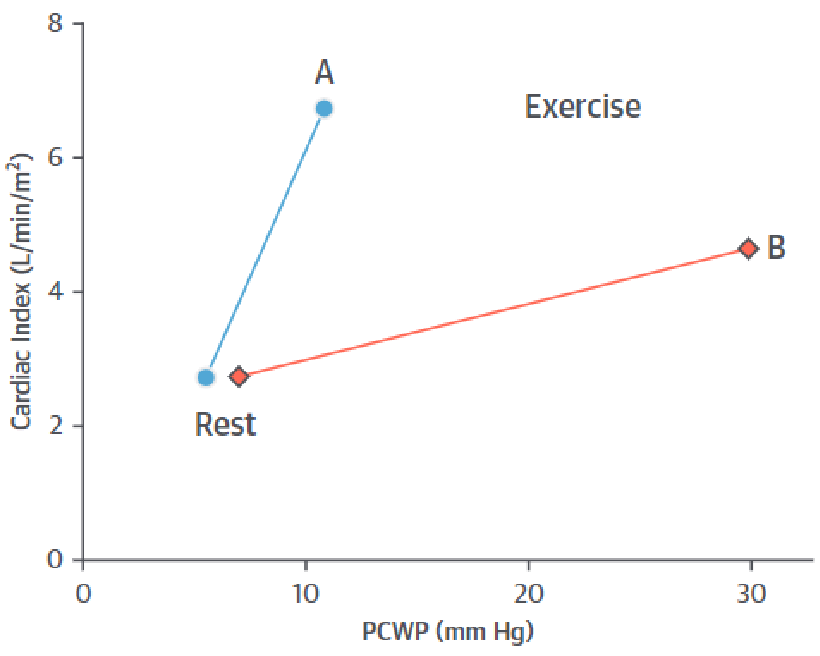
One of the earliest manifestations of dysfunction is reduced LV relaxation

Patients may only be able to increase CO by increasing LV filling pressures



Diastolic stress test

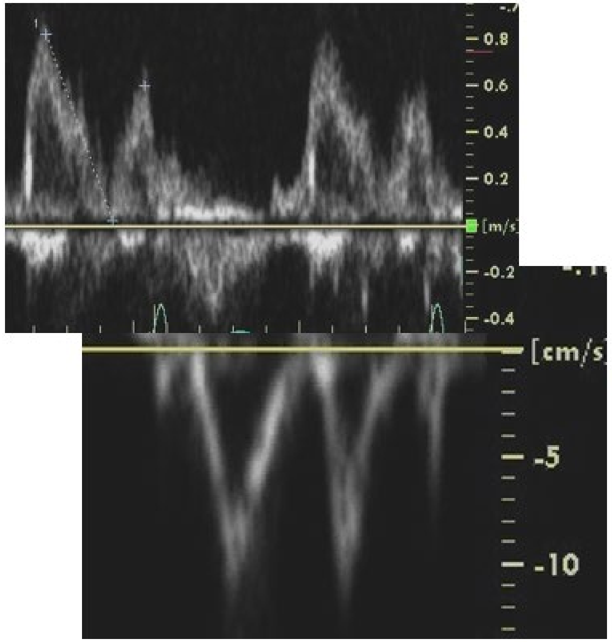
FIGURE 1 **Hemodynamic Response to Exercise**



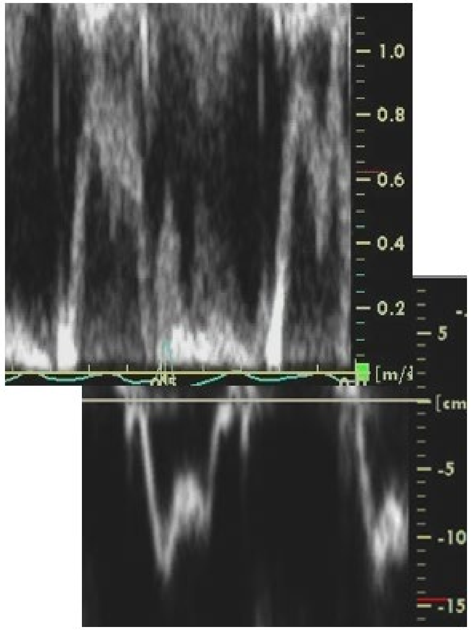
Changes of cardiac output and pulmonary capillary wedge pressure pressures (PCWP) during exercise. Patients A and B have almost identical left ventricular filling pressures and cardiac index at rest. In Patient A, there is a significant increase in cardiac index with a small change in left ventricular filling pressure (normal response), whereas in Patient B, there is a significant increase in left ventricular filling pressure but smaller increase in cardiac index during exercise.

Diastolic stress test

Exercise normally results in a proportional increase in the mitral inflow E velocity and the mitral annular e' velocity, so that E/e' does not change



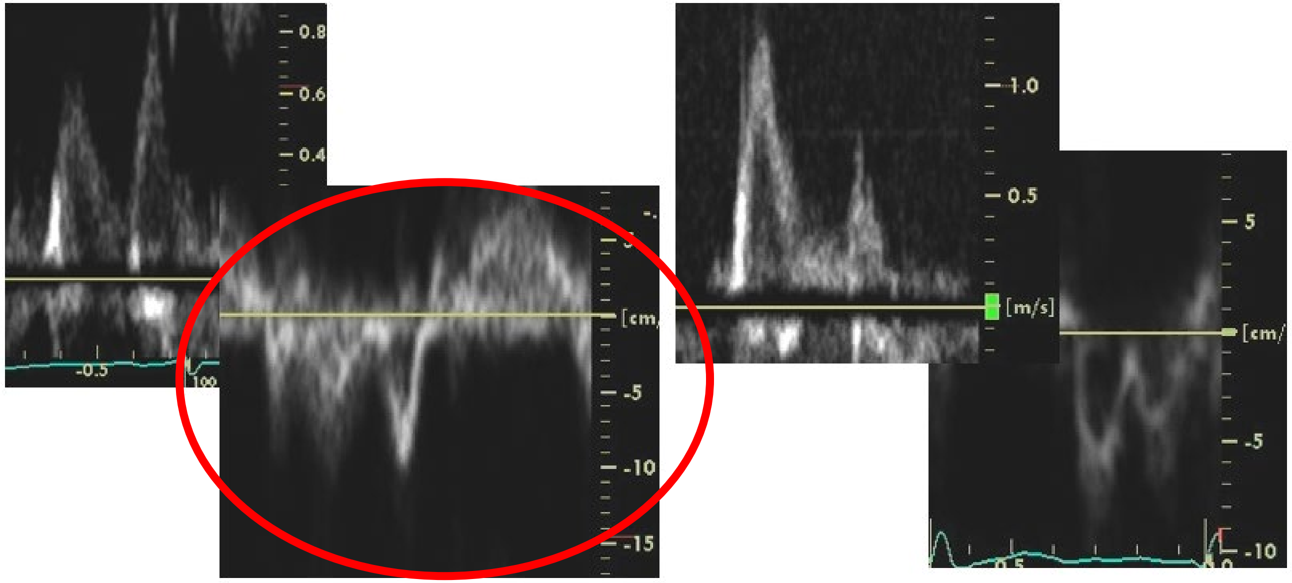
Rest E 80cm/s e' 10cm/s E/e' 8



Peak E 95cm/s e' 13cm/s E/e' 7

Diastolic stress test

- Diastolic dysfunction results in decreased LV relaxation
- Augmentation of myocardial relaxation is best reflected by the e’ velocity, which is limited in diastolic dysfunction

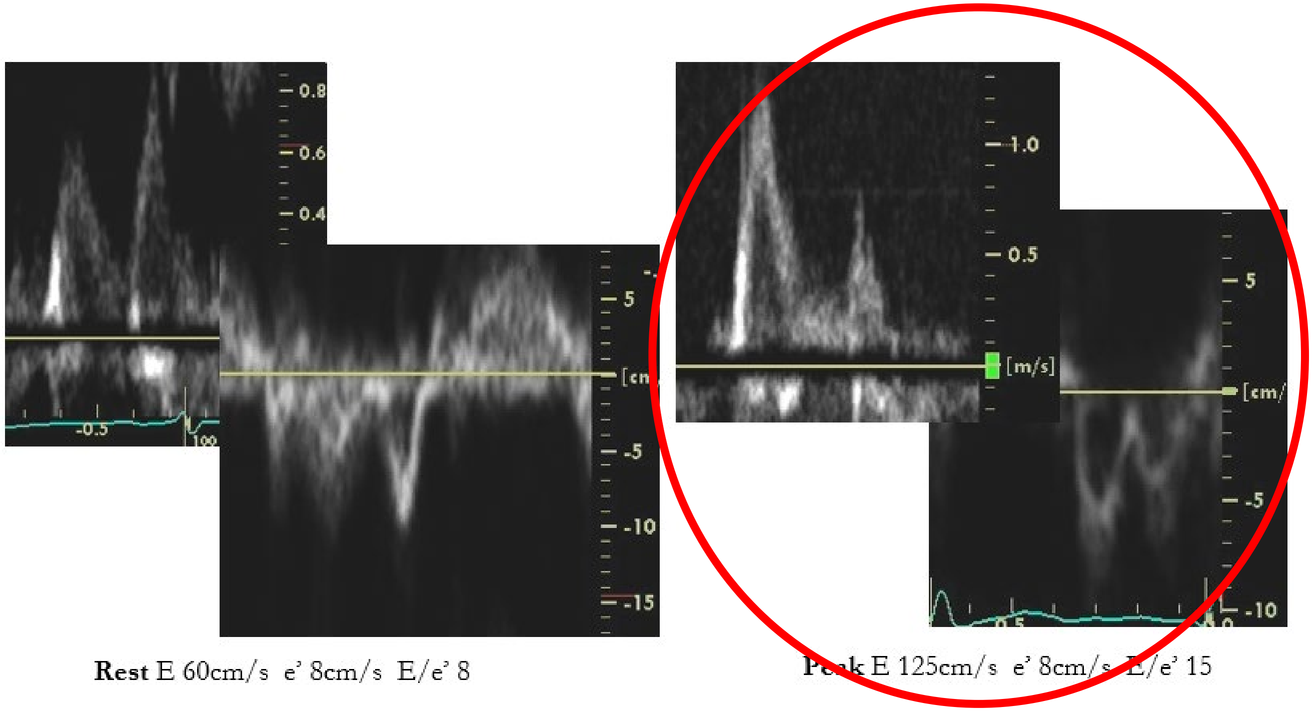


Rest E 60cm/s e’ 8cm/s E/e’ 8

Peak E 125cm/s e’ 8cm/s E/e’ 15

Diastolic stress test

- Diastolic dysfunction results in decreased LV relaxation
- Augmentation of myocardial relaxation is best reflected by the e’ velocity, which is limited in diastolic dysfunction
- There is more limitation to the e’ velocity compared to the E velocity
-This results in an increase in the E/e’ with exercise

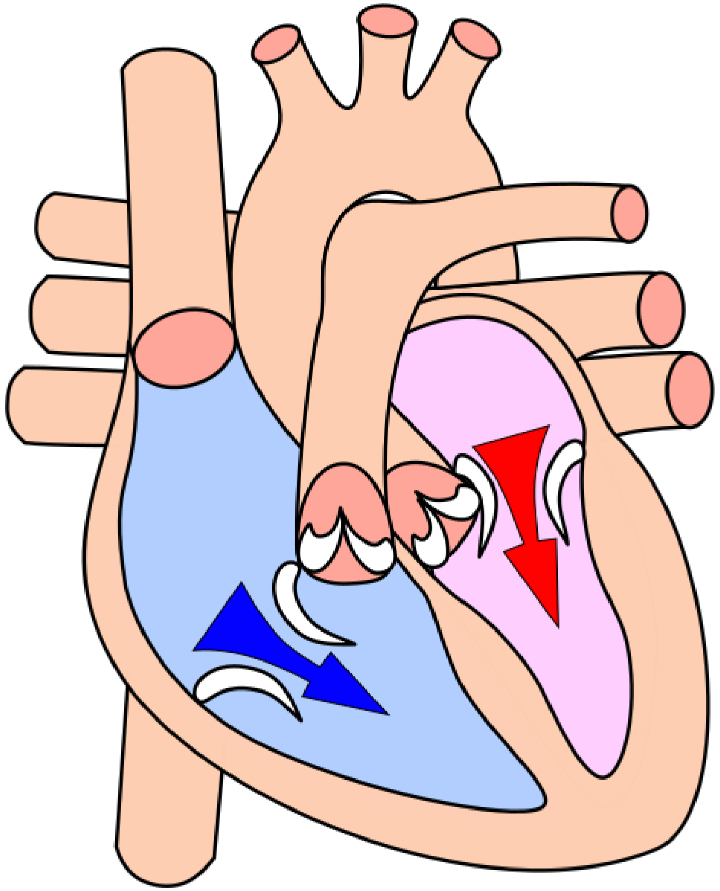


Rest E 60cm/s e’ 8cm/s E/e’ 8

Peak E 125cm/s e’ 8cm/s E/e’ 15

Diastolic stress test

Additionally, exercise produces an increase in HR, resulting in decreased duration of diastole, with a subsequent decrease in diastolic filling time

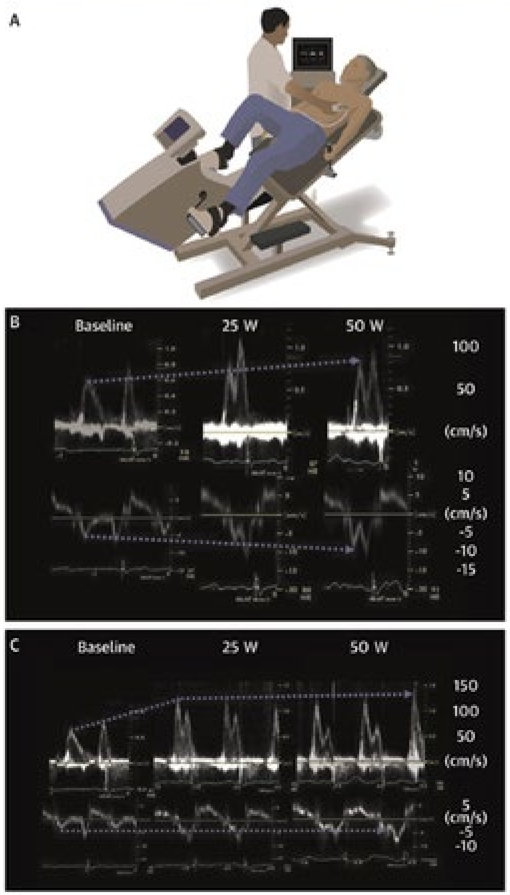


Diastolic stress test

Post exercise:

- E/e’ > 10 sensitive predictor of advanced diastolic dysfunction
- E/e’ > 15 is more a specific predictor for advanced diastolic dysfunction

CENTRAL ILLUSTRATION: Noninvasive Diastolic Stress Test



Ha, J.-W. et al. J Am Coll Cardiol Img. 2020;13(1):272-82.

Diastolic stress test

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.)

ESC European Society of Cardiology
European Heart Journal - Cardiovascular Imaging (2022) **23**, e34–e61
doi:10.1093/ehjci/jeab154

Multimodality imaging in patients with heart failure and preserved ejection fraction: an expert consensus document of the European Association of Cardiovascular Imaging

Otto A. Smiseth (Chair)[1,2,3]*, Daniel A. Morris[4], Nuno Cardim[5], Maja Cikes[6], Victoria Delgado[7], Erwan Donal[8,9], Frank A. Flachskampf[10], Maurizio Galderisi[11,†], Bernhard L. Gerber[12], Alessia Gimelli[13], Allan L. Klein[14], Juhani Knuuti[15], Patrizio Lancellotti[16,17], Julia Mascherbauer[18], Davor Milicic[6], Petar Seferovic[19,20], Scott Solomon[21], Thor Edvardsen[1,2,3], and Bogdan A. Popescu (Co-Chair)[22,*]

Diastolic stress test

- Recommended in 2016 ASE 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

VI. DIASTOLIC STRESS TEST

Exercise echocardiography[156] is usually performed to detect reduced LV systolic and/or diastolic reserve capacity in the setting of coronary disease or diastolic dysfunction, as patients with diastolic dysfunction may have a similar hemodynamic profile (in terms of cardiac output and filling pressure) at rest as healthy individuals who have normal diastolic function. When normal subjects exercise,

Diastolic stress test

- Recommended in 2016 ASE Guidelines
- For patients where resting echocardiography does not explain patient's symptoms
- Not recommended for patients with definite diastolic dysfunction at rest
- They recommend doing on the supine bicycle (but concede that it can be done on the treadmill)

Diastolic stress test

- Recommended in 2016 ASE Guidelines
- For patients where resting echocardiography does not explain patient’s symptoms
- Not recommended for patients with definite diastolic dysfunction at rest
- They recommend doing on the supine bicycle (but concede that it can be done on the treadmill)
- They consider the test as being **abnormal** if averaged E/e’ > 14 or septal E/e’ > 15
- PLUS TR velocity > 2.8m/s
- AND septal e’ velocity < 7cm/s (or lateral e’ velocity < 10cm/s)

Diastolic stress test

- Recommended in 2016 ASE Guidelines
- For patients where resting echocardiography does not explain patient's symptoms
- Not recommended for patients with definite diastolic dysfunction at rest
- They recommend doing on the supine bicycle (but concede that it can be done on the treadmill)
- They consider the test as being **abnormal** if averaged E/e' > 14 or septal E/e' > 15
- PLUS TR velocity > 2.8m/s
- AND septal e' velocity < 7cm/s (or lateral e' velocity < 10cm/s)
- **Normal test**: E/e' < 10 AND peak TR velocity < 2.8m/s

Diastolic stress test

BUT

- Based on three (3) studies which used a variety of different measuring points and totalled 109 patients, and one (1) additional study of 522 patients, where an abnormal DST was determined if the septal E/e' increased to more than 10
- Two (2) studies were performed on supine bicycle and two (2) on treadmills
- Two (2) looked at change to E/e', two (2) assessed more comprehensively
- One (1) with 12 patients compared stress diastology to right heart catheter pulmonary pressures

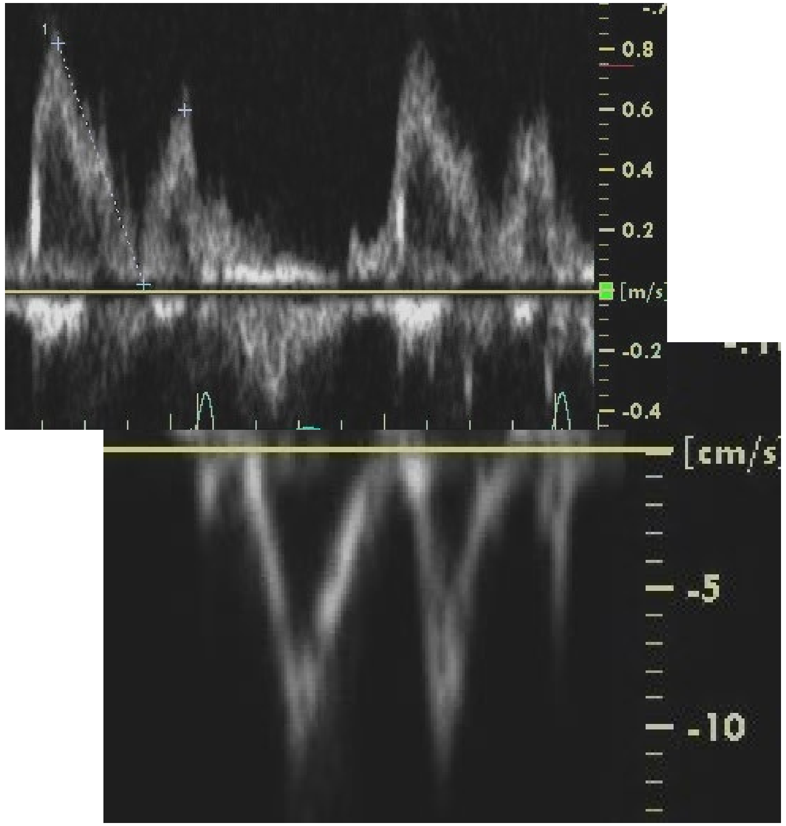
Diastolic stress test

BUT

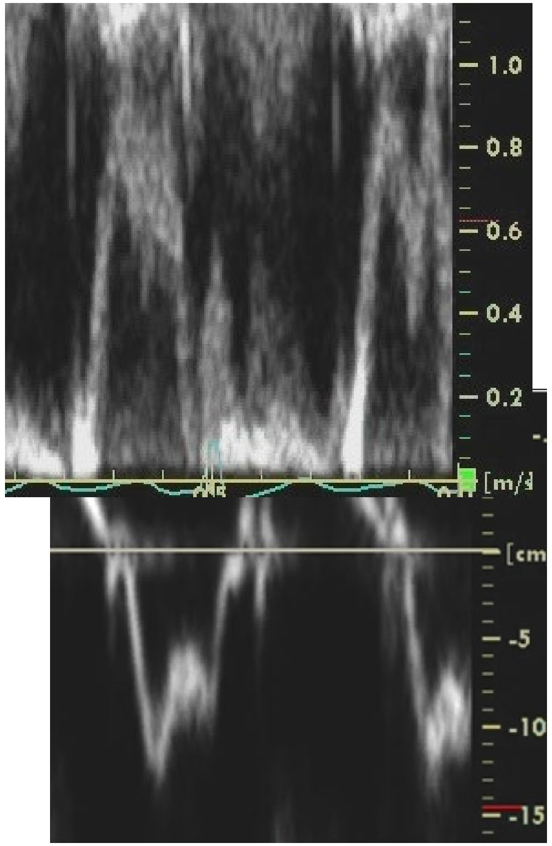
- Based on three (3) studies which used a variety of different measuring points and totalled 109 patients, and one (1) additional study of 522 patients, where an abnormal DST was determined if the septal E/e' increased to more than 10
- Two (2) studies were performed on supine bicycle and two (2) on treadmills
- Two (2) looked at change to E/e', two (2) assessed more comprehensively
- One (1) with 12 patients compared stress diastology to right heart catheter pulmonary pressures
- Guidelines diastolic stress test: “expert opinion”

Stress diastology

Normal response is for the E/e' ratio essentially not change



Rest E 80cm/s e' 10cm/s E/e' 8

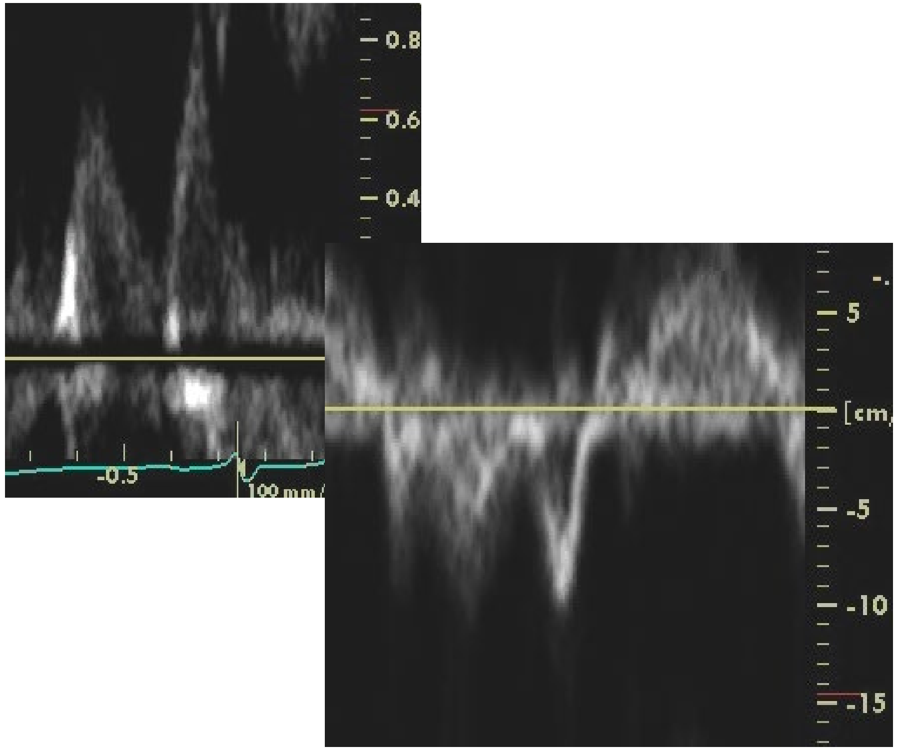


Peak E 95cm/s e' 13cm/s E/e' 7

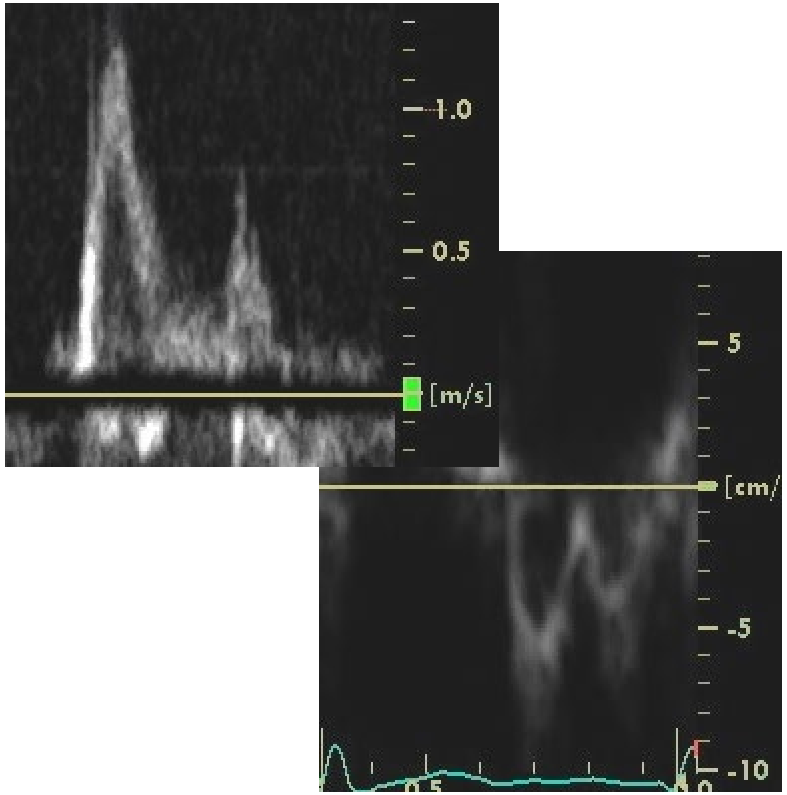
J Am Coll Cardiol. 2006;47(9):1891-900

Stress diastology

The abnormal response if for the E/e’ to significantly increase

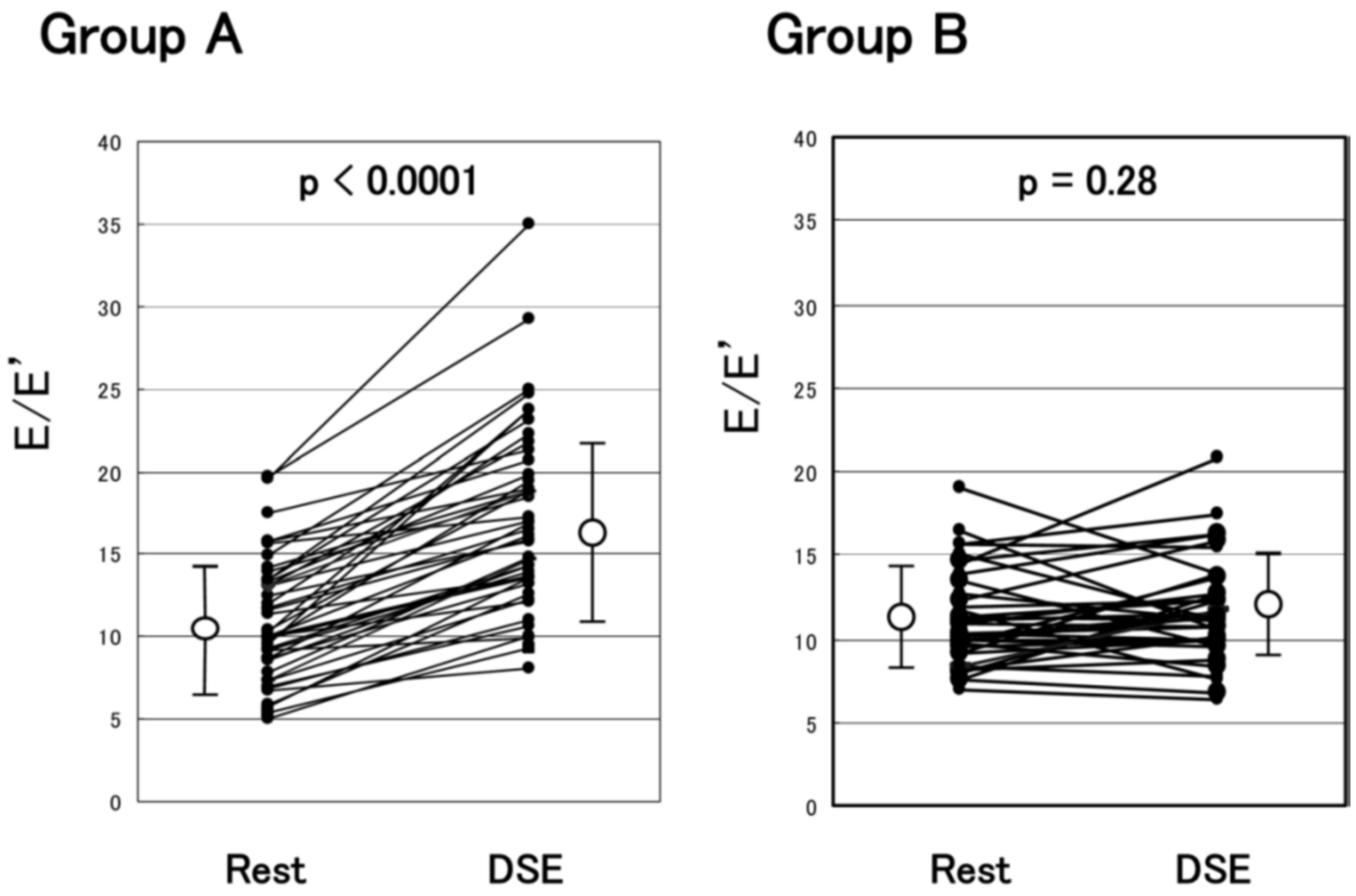


Rest E 60cm/s e’ 8cm/s E/e’ 8



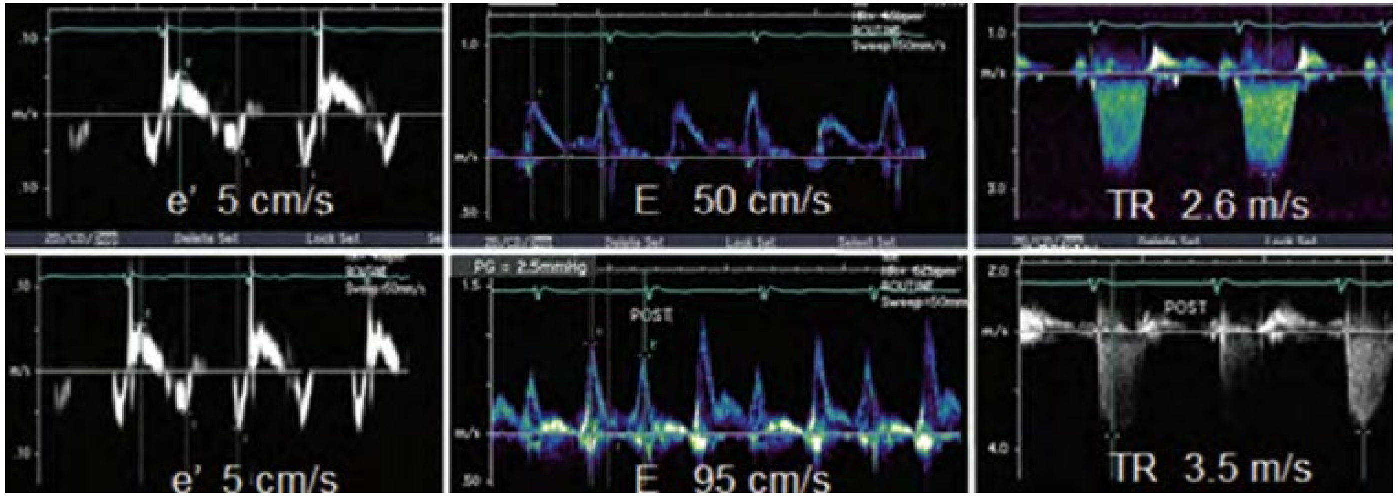
Peak E 125cm/s e’ 8cm/s E/e’ 15

Stress diastology



Diastolic stress test

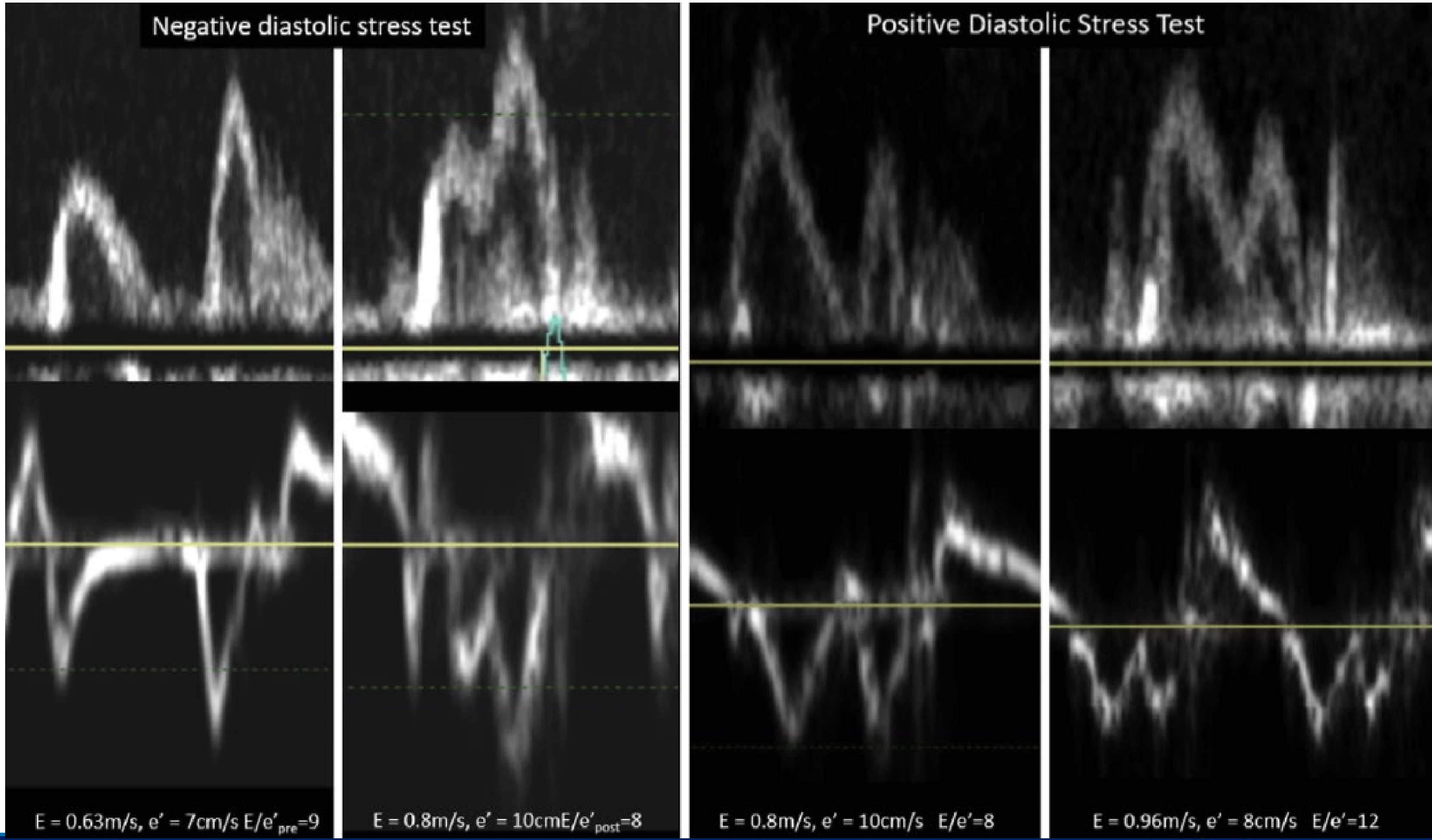
- Guidelines recommend exercise related diastolic dysfunction with E/e’ > 14 and 15
- Research defining an abnormal DST as a septal E/e’ >10



Stress diastology

- Subsequent research suggests that it also may predict HF outcomes

- 2201 consecutive stress echocardiograms
- Septal E/e’ was determined to be the best marker
- Increased E/e’ to ≥ 12 was determined to be the prognostic cut point for statistical significance



Fitzgerald, Presneill, Scalia I, Hawkins, Celemajer, Scalia W, Scalia GM
JASE 2019;32(10):1298-1306

Stress diastology

This research suggests that it also may be a marker of increased HF outcomes (n=2201)

		Adjusted**		
		HR	95% CI	P
Echo group				
	Negative	1.0		
	Ischaemic	28	17-44	<0.0005
	Pos diastolic	4.2	1.6-11.0	0.001
	High baseline	1.3	0.7-2.4	0.49
Age*		1.3	1.1-1.4	<0.0005
Female		1.1	0.8-1.7	0.53

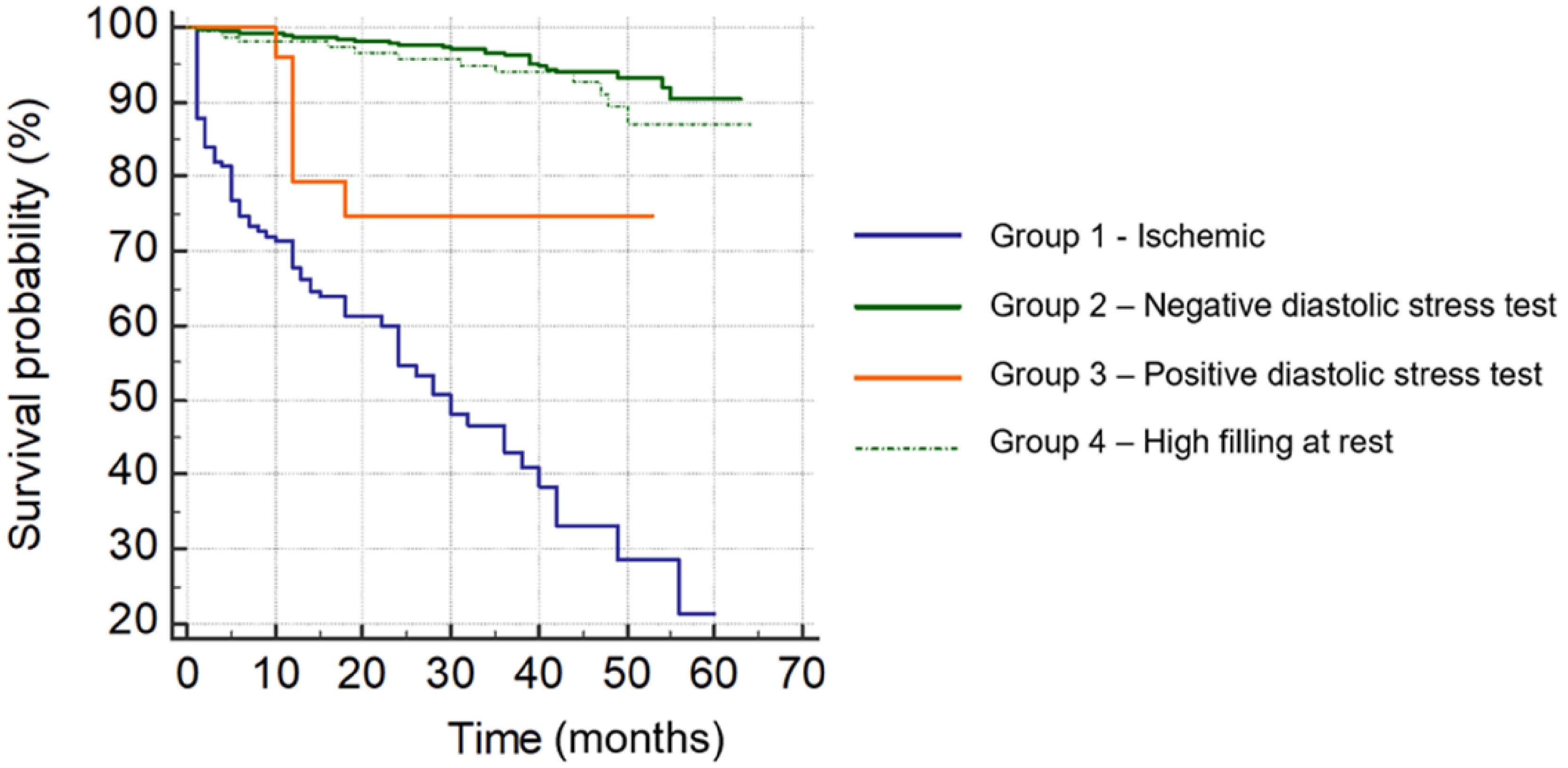
* Age centered at 60y, effect is for a 5 year increment

** Effect estimated adjusted for all other variables in the table

Fitzgerald, Presneill, Scalia I, Hawkins, Celemajer, Scalia W, Scalia GM
JASE 2019;32(10):1298-1306

Stress diastology

Kaplan Meier curves estimating heart failure events after diastolic stress testing



Fitzgerald, Presneill, Scalia I, Hawkins, Celemajer, Scalia W, Scalia GM
JASE 2019;32(10):1298-1306

Diastolic stress test

CLINICAL INVESTIGATIONS

DIASTOLIC EXERCISE ECHOCARDIOGRAPHY AND OUTCOME

Prognostic Significance of Elevated Left Ventricular Filling Pressures with Exercise: Insights from a Cohort of 14,338 Patients

Christina L. Luong, MD, MHSc, Vidhu Anand, MBBS, Ratnasari Padang, MD, PhD, Jae K. Oh, MD, Adelaide M. Arruda-Olson, MD, PhD, Jared G. Bird, MD, Cristina Pislaru, MD, Jeremy J. Thaden, MD, Sorin V. Pislaru, MD, PhD, Patricia A. Pellikka, MD, Robert B. McCully, MD, and Garvan C. Kane, MD, PhD, *Rochester, Minnesota, and Vancouver, British Columbia, Canada*

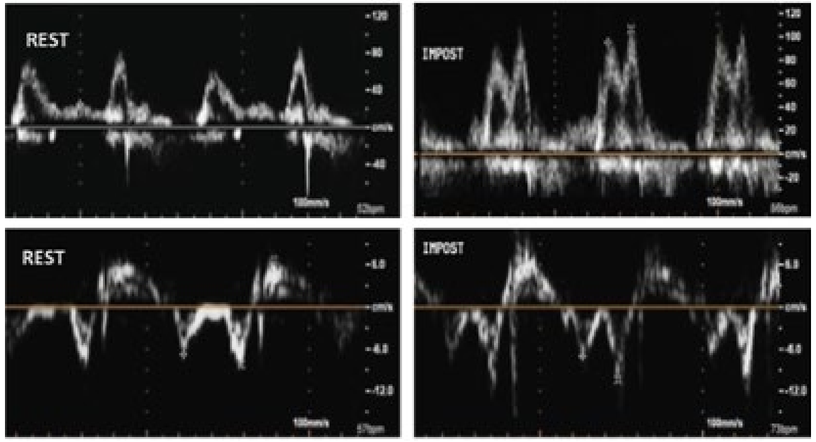
Background: Exercise echocardiography can assess for cardiovascular causes of dyspnea other than coronary artery disease. However, the prevalence and prognostic significance of elevated left ventricular (LV) filling pressures with exercise is understudied.

Methods: We evaluated 14,338 patients referred for maximal symptom-limited treadmill echocardiography. In addition to assessment of LV regional wall motion abnormalities (RWMAs), we measured patients' early diastolic mitral inflow (E), septal mitral annulus relaxation (e'), and peak tricuspid regurgitation velocity before and immediately after exercise.

Results: Over a mean follow-up of 3.3 ± 3.4 years, patients with E/e' ≥15 with exercise (*n* = 1,323; 9.2%) had lower exercise capacity (7.3 ± 2.1 vs 9.1 ± 2.4 metabolic equivalents, *P* < .0001) and were more likely to have resting or inducible RWMAs (38% vs 18%, *P* < .0001). Approximately 6% (*n* = 837) had elevated LV filling pressures without RWMAs. Patients with a poststress E/e' ≥15 had a 2.71-fold increased mortality rate (2.28-3.21, *P* < .0001) compared with those with poststress E/e' ≤ 8. Those with an E/e' of 9 to 14, while at lower risk than the E/e' ≥15 cohort (hazard ratio [HR] = 0.58 [0.48-0.69]; *P* < .0001), had higher risk than if E/e' ≤8 (HR = 1.56 [1.37-1.78], *P* < .0001). On multivariable analysis, adjusting for age, sex, exercise capacity, LV ejection fraction, and presence of pulmonary hypertension with stress, patients with E/e' ≥15 had a 1.39-fold (95% CI, 1.18-1.65, *P* < .0001) increased risk of all-cause mortality compared with patients without elevated LV filling pressures. Compared with patients with E/e' ≤ 15 after exercise, patients with E/e' ≤15 at rest but elevated after exercise had a higher risk of cardiovascular death (HR = 8.99 [4.7-17.3], *P* < .0001).

Conclusion: Patients with elevated LV filling pressures are at increased risk of death, irrespective of myocardial ischemia or LV systolic dysfunction. These findings support the routine incorporation of LV filling pressure assessment, both before and immediately following stress, into the evaluation of patients referred for exercise echocardiography. (J Am Soc Echocardiogr 2024;37:382-93.)

Diastolic stress test

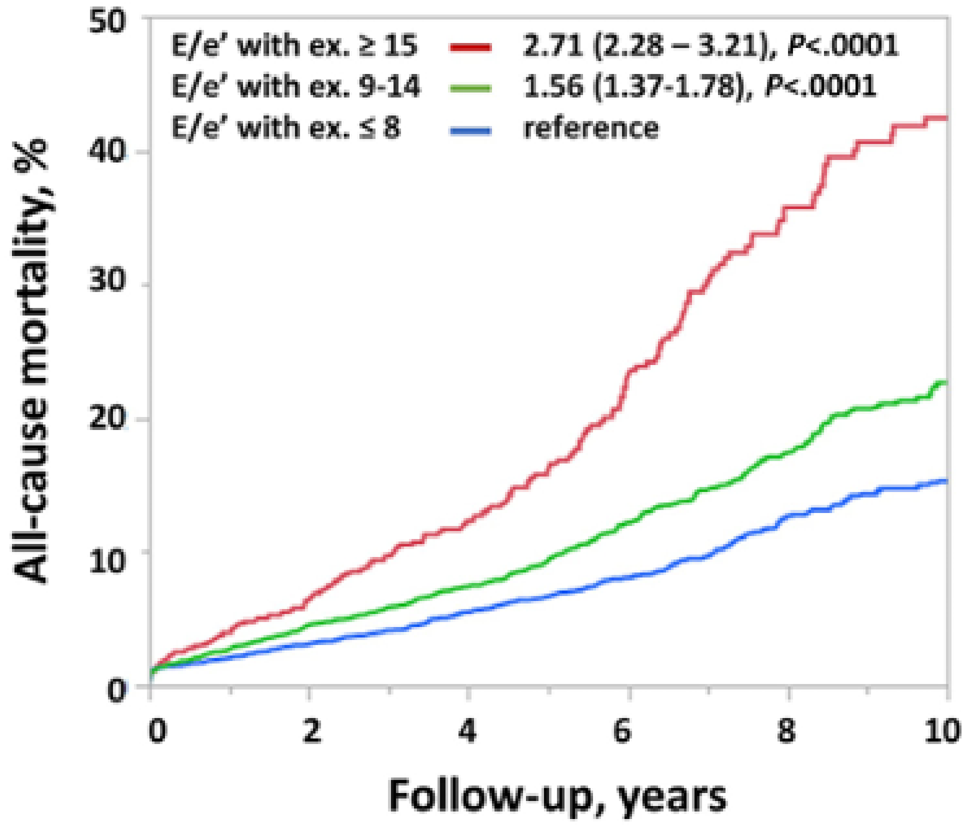


- 14 338 Patients
- Defined
  - LV filling pressures by septal E/e’
  - Normal Doppler response to stress as a 15-25% increase in mitral E velocity and a 20-30% increase in the septal e’ velocity
  - Abnormal response was a marked increase in E velocity and little or no increase in e’ velocity

JASE 2024; 37: 382-393

Diastolic stress test

- Findings:
  - Increase in E/e’ resulted in an increase in mortality
  - The higher the E/e’ post exercise, the worse the survival

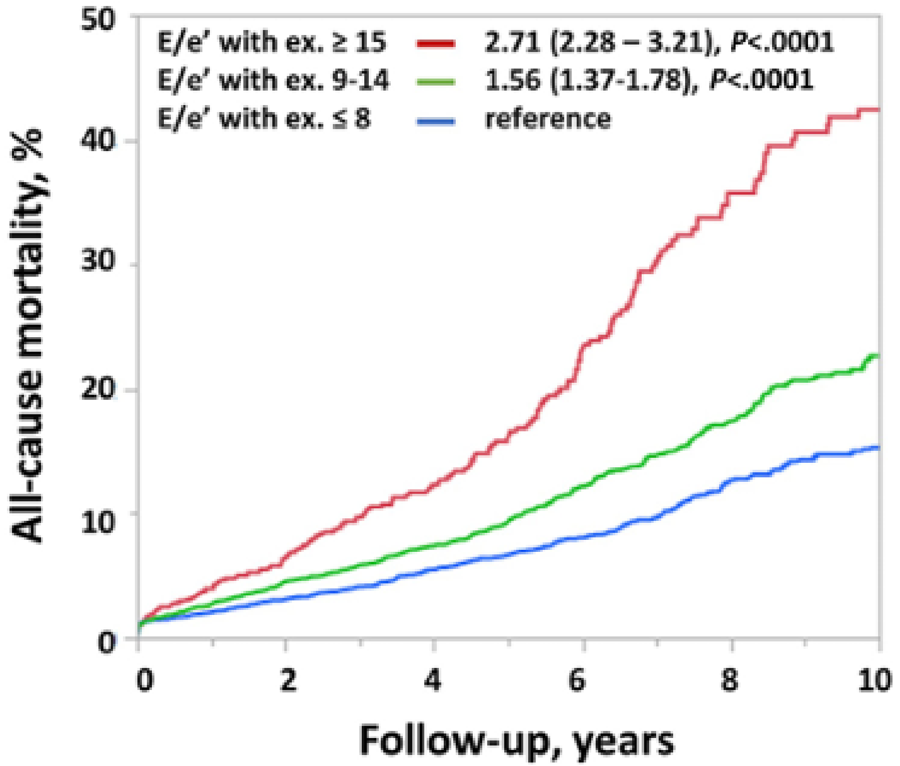


Number at risk:

E/e’ ≥ 15	1323	674	424	238	131	91
E/e’ 9-14	7174	3785	247	1575	888	618
E/e’ ≤ 8	5841	3298	2336	1554	830	576

Diastolic stress test

- A post stress E/e’ ≥ 15 resulted in the highest mortality
- An E/e’ ≥ 10 still produced statistically significant increase in mortality

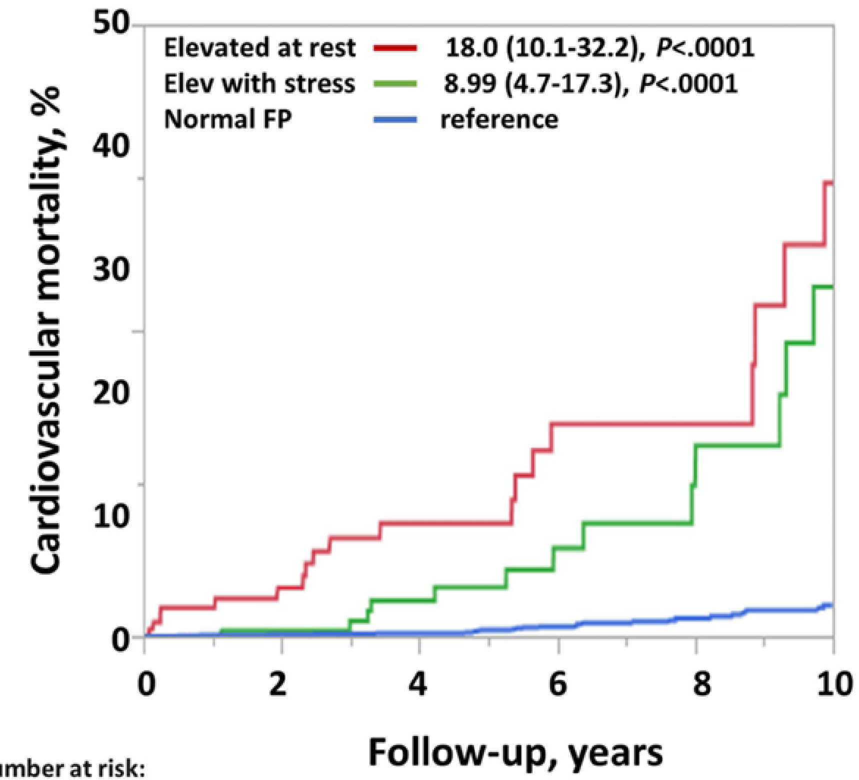


Number at risk:

E/e’ ≥ 15	1323	674	424	238	131	91
E/e’ 9-14	7174	3785	247	1575	888	618
E/e’ ≤ 8	5841	3298	2336	1554	830	576

Diastolic stress test

- A post stress E/e’ ≥ 15 resulted in the highest mortality
- An E/e’ ≥ 10 still produced statistically significant increase in mortality
- But the highest mortality occurred with an elevated E/e’ at rest



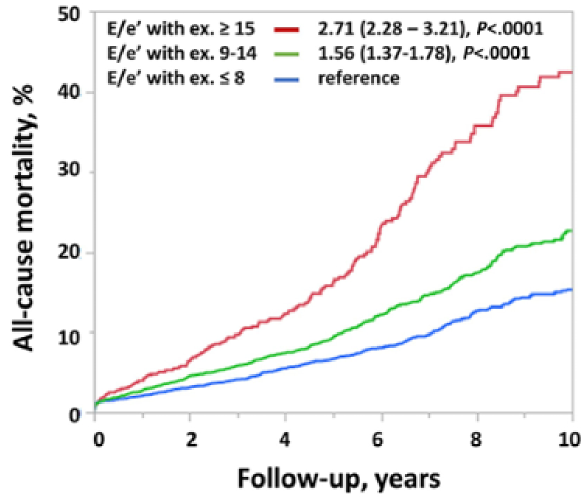
Number at risk:

Elev. at rest	515	279	178	105	56	43
Elev. with Ex	808	399	247	134	76	48
Normal FP	13015	7083	4823	3129	1717	1194

Diastolic stress test

- Authors’ comment:
  - Elevated post exercise E/e’ ≥ 15 is an independent predictor of mortality

    but a post exercise E/e’ ≥ 10 is also!



Number at risk:

E/e’ ≥ 15	1323	674	424	238	131	91
E/e’ 9-14	7174	3785	247	1575	888	618
E/e’ ≤ 8	5841	3298	2336	1554	830	576

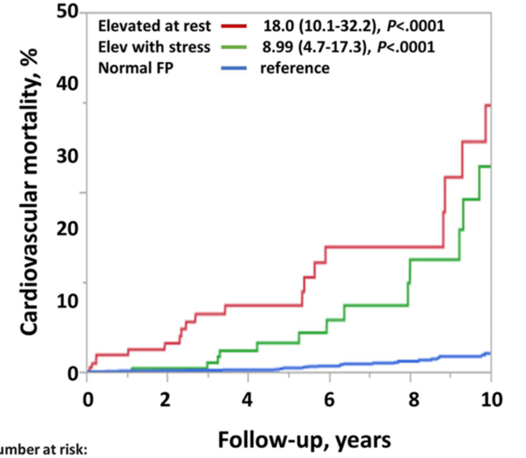
Advara HeartCare

JASE 2024; 37: 382-393

ECHO AUSTRALIA

Diastolic stress test

- Guidelines recommend exercise related diastolic dysfunction with E/e’ > 14 and 15
- Research defining an abnormal DST as a septal E/e’ ≥ 10
- 2019 paper showed increased heart failure outcomes after a post exercise septal E/e’ ≥ 12

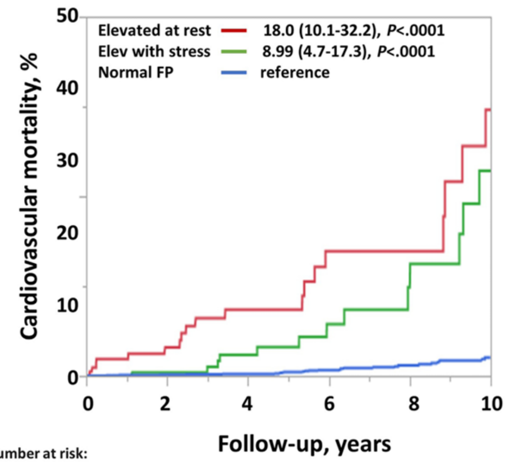


Number at risk:

Elev. at rest	515	279	178	105	56	43
Elev. with Ex	808	399	247	134	76	48
Normal FP	13015	7083	4823	3129	1717	1194

Diastolic stress test

- Research has showed exercise related diastolic dysfunction with E/e’ > 14 and 15
- Research defining an abnormal DST as a septal E/e’ >10
- 2019 paper showed increased heart failure outcomes after a post exercise septal E/e’ ≥ 12
- 2024 paper showed steadily worsening mortality with progressive increase from a post exercise septal E/e’ ≥ 10 and greatest more than 15



Number at risk:

Elev. at rest	515	279	178	105	56	43
Elev. with Ex	808	399	247	134	76	48
Normal FP	13015	7083	4823	3129	1717	1194

Diastolic stress test

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

es not explain patient's

sym

for t

They recommend doing on the supine bicycle

done on the treadmill)

VI. DIASTOLIC STRESS TEST

Exercise echocardiography[156] is usually performed to detect reduced LV systolic and/or diastolic reserve capacity in the setting of coronary disease or diastolic dysfunction, as patients with diastolic dysfunction may have a similar hemodynamic profile (in terms of cardiac output and filling pressure) at rest as healthy individuals who have normal diastolic function. When normal subjects exercise,

- **They consider the test as being abnormal if averaged E/e' > 14 or septal E/e' > 15** PLUS TR velocity > 2.8m/s AND septal e' velocity < 7cm/s (or lateral < 10cm/s)

Normal test: E/e' < 10 AND peak TR velocity < 2.8m/s

JASE 2016; 29:277-314

Diastolic stress test

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

es not explain patient's

sym

for t

They recommend doing on the supine bicycle

done on the treadmill)

VI. DIASTOLIC STRESS TEST

Exercise echocardiography[156] is usually performed to detect reduced LV systolic and/or diastolic reserve capacity in the setting of coronary disease or diastolic dysfunction, as patients with diastolic dysfunction may have a similar hemodynamic profile (in terms of cardiac output and filling pressure) at rest as healthy individuals who have normal diastolic function. When normal subjects exercise,

- They consider the test as being abnormal if averaged E/e' > 14 or septal E/e' > 15 PLUS **TR velocity > 2.8m/s** AND septal e' velocity < 7cm/s (or lateral < 10cm/s)

Normal test: E/e' < 10 AND peak TR velocity < 2.8m/s

2.8m/s = 32mmHg

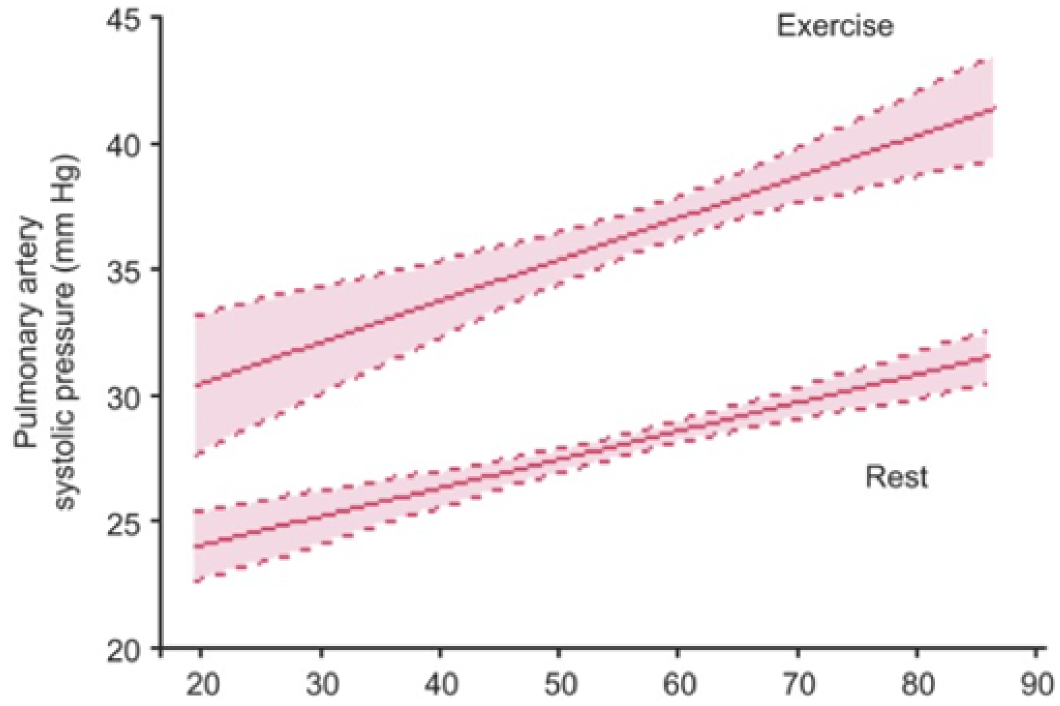
PASP with exercise

	20-30 yrs	30-40 yrs	40-50 yrs	50-60 yrs	60-70 yrs	70-80 yrs
PASP at rest (mmHg)	27±4 (22-34)	29±3 (22-32)	28±3 (23-35)	26±4 (19-35)	27±4 (21-33)	28±6 (20-38)
EF at rest	65%	63%	68%	68%	66%	69%
PASP at peak (mmHg)	45±7 (33-55)	51±6 (36-56)	52±9 (41-65)	53±4 (45-60)	54±12 (37-70)	58±7 (46-65)
EF at peak(%)	76%	72%	76%	75%	69%	71%
% of PASP≥60mmHg	0	0	26% (n=4)	0.08% (n=1)	36% (n=4)	50% (n=5)

Mahjoub et al, European Congress of Cardiology, 2009

Normal pulmonary pressure response to stress

Kane et al. Echo Res Pract. 2016 Jun; 3: 53–61.



Age (years)	**<40** (*n*=38)	**40–49** (*n*=93)	**50–59** (*n*=127)	**60–69** (*n*=127)	**>70** (*n*=84)
Pulmonary artery systolic pressure (mmHg*, **)	33±7 (31–35)	36±8 (34–37)	36±9 (34–38)	37±10 (35–39)	41±12 (38–43)
	50	53	54	54	56

**Upper normal defined as the 5% limit derived from semi-parametric logistic regression of normative data factoring in age.

RVSP with exercise

- n=1100
- TR velocity increased from 2.6±0.6m/s to 3.2±0.4m/s
- RVSP increased from 30mmHg to 45mmHg, with an upper limit of normal of 55mmHg or 3.7m/s
- ePLAR increased from 0.27m/s to 0.36m/s
- Normal cardiac output increase with exertion

Diastolic stress test

CLINICAL INVESTIGATIONS
DIASTOLIC EXERCISE ECHOCARDIOGRAPHY AND OUTCOME

Prognostic Significance of Elevated Left Ventricular Filling Pressures with Exercise: Insights from a Cohort of 14,338 Patients

Christina L. Luong, MD, MHSc, Vidhu Anand, MBBS, Ratnasari Padang, MD, PhD, Jae K. Oh, MD, Adelaide M. Arruda-Olson, MD, PhD, Jared G. Bird, MD, Cristina Pislaru, MD, Jeremy J. Thaden, MD, Sorin V. Pislaru, MD, PhD, Patricia A. Pellikka, MD, Robert B. McCully, MD, and Garvan C. Kane, MD, PhD, *Rochester, Minnesota, and Vancouver, British Columbia, Canada*

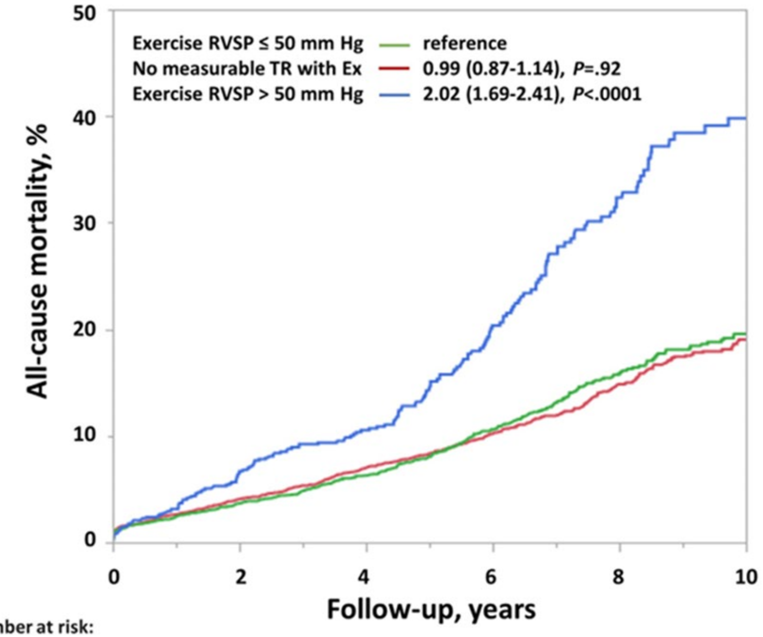
Background: Exercise echocardiography can assess for cardiovascular causes of dyspnea other than coronary artery disease. However, the prevalence and prognostic significance of elevated left ventricular (LV) filling pressures with exercise is understudied.

Methods: We evaluated 14,338 patients referred for maximal symptom-limited treadmill echocardiography. In addition to assessment of LV regional wall motion abnormalities (RWMAs), we measured patients' early diastolic mitral inflow (E), septal mitral annulus relaxation (e'), and peak tricuspid regurgitation velocity before and immediately after exercise.

Results: Over a mean follow-up of 3.3 ± 3.4 years, patients with E/e' ≥15 with exercise (*n* = 1,323; 9.2%) had lower exercise capacity (7.3 ± 2.1 vs 9.1 ± 2.4 metabolic equivalents, *P* < .0001) and were more likely to have resting or inducible RWMAs (38% vs 18%, *P* < .0001). Approximately 6% (*n* = 837) had elevated LV filling pressures without RWMAs. Patients with a poststress E/e' ≥15 had a 2.71-fold increased mortality rate (2.28-3.21, *P* < .0001) compared with those with poststress E/e' ≤ 8. Those with an E/e' of 9 to 14, while at lower risk than the E/e' ≥15 cohort (hazard ratio [HR] = 0.58 [0.48-0.69]; *P* < .0001), had higher risk than if E/e' ≤8 (HR = 1.56 [1.37-1.78], *P* < .0001). On multivariable analysis, adjusting for age, sex, exercise capacity, LV ejection fraction, and presence of pulmonary hypertension with stress, patients with E/e' ≥15 had a 1.39-fold (95% CI, 1.18-1.65, *P* < .0001) increased risk of all-cause mortality compared with patients without elevated LV filling pressures. Compared with patients with E/e' ≤ 15 after exercise, patients with E/e' ≤15 at rest but elevated after exercise had a higher risk of cardiovascular death (HR = 8.99 [4.7-17.3], *P* < .0001).

Conclusion: Patients with elevated LV filling pressures are at increased risk of death, irrespective of myocardial ischemia or LV systolic dysfunction. These findings support the routine incorporation of LV filling pressure assessment, both before and immediately following stress, into the evaluation of patients referred for exercise echocardiography. (J Am Soc Echocardiogr 2024;37:382-93.)

- RVSP assessment



Number at risk:

Ex RVSP ≤ 50	5215	2917	1966	1195	613	410
No TR	7853	4095	2767	1880	1087	779
Ex RVSP > 50	1270	745	514	291	148	84

Advara HeartCare

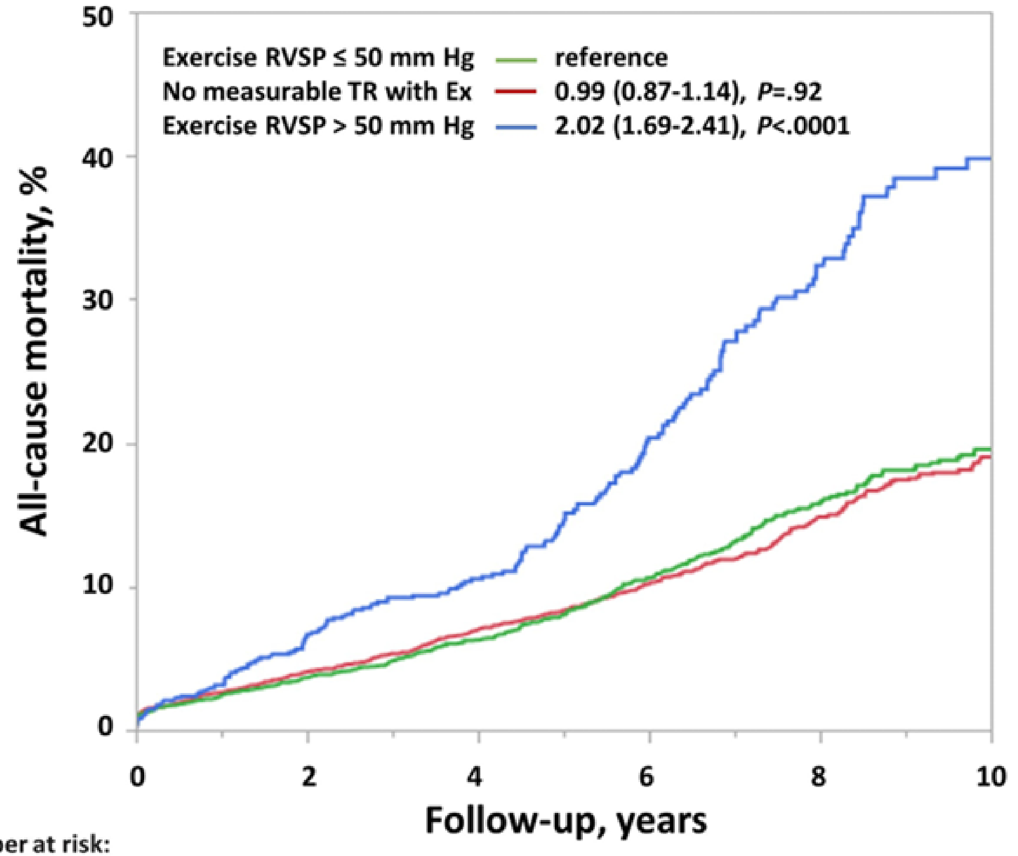
ECHO AUSTRALIA

RVSP with exercise

- 2024   n=14 338

- RVSP > 50mmHg (3.5m/s) associated with increased mortality

- RVSP < 50mmHg NOT associated with increased mortality



Number at risk:

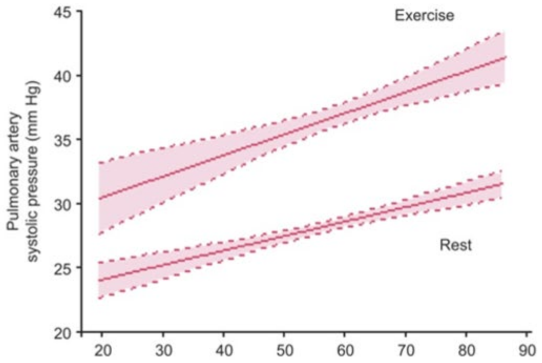
Ex RVSP ≤ 50	5215	2917	1966	1195	613	410
No TR	7853	4095	2767	1880	1087	779
Ex RVSP > 50	1270	745	514	291	148	84

RVSP with exercise

	20-30 yrs	30-40 yrs	40-50 yrs	50-60 yrs	60-70 yrs	70-80 yrs
PASP at rest (mmHg)	27±4 (22-34)	29±3 (22-32)	28±3 (23-35)	26±4 (19-35)	27±4 (21-33)	28±6 (20-38)
EF at rest	65%	63%	68%	68%	66%	69%
PASP at peak (mmHg)	45±7 (33-55)	51±6 (36-56)	52±9 (41-65)	53±4 (45-60)	54±12 (37-70)	58±7 (46-65)
EF at peak(%)	76%	72%	76%	75%	69%	71%
% of PASP≥60mmHg	0	0	26% (n=4)	0.08% (n=1)	36% (n=4)	50% (n=5)

Normal pulmonary pressure response to stress

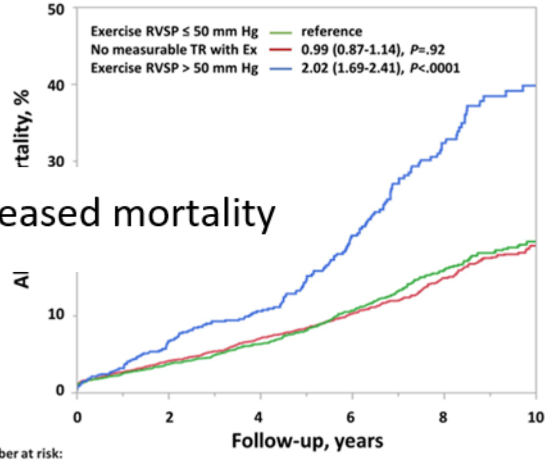
Kane et al. Echo Res Pract. 2016 Jun; 3: 53–61.



Age (years)	<40 (n=38)	40–49 (n=93)	50–59 (n=127)	60–69 (n=127)	>70 (n=84)
Pulmonary artery systolic pressure (mmHg*, **)	33±7 (31–35)	36±8 (34–37)	36±9 (34–38)	37±10 (35–39)	41±12 (38–43)
	50	53	54	54	56

**Upper normal defined as the 5% limit derived from semi-parametric logistic regression of normative data factoring in age.

- TR velocity increased from 2.6±0.6m/s to 3.2±0.4m/s
- RVSP increased from 30mmHg to 45mmHg, with an upper limit of normal of 55mmHg or 3.7m/s
- RVSP > 50mmHg (3.5m/s) associated with increased mortality



Number at risk:

Ex RVSP ≤ 50	5215	2917	1966	1195	613	410
No TR	7853	4095	2767	1880	1087	779
Ex RVSP > 50	1270	745	514	291	148	84

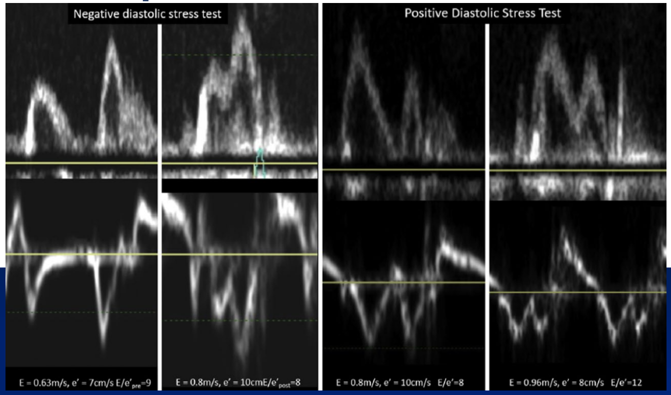
? Diastolic stress test requiring a peak exercise TR velocity of > 2.8 m/s, and for a normal test to have a peak TR velocity of < 2.8m/s

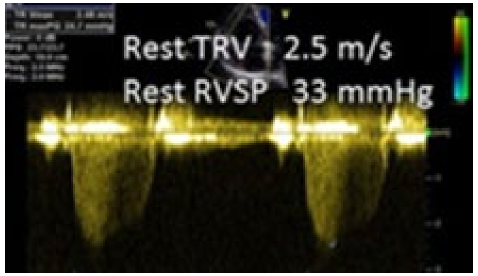
Diastolic stress test

- 2016 ASE Guidelines
- For patients where resting echocardiography does not explain patient's
- **Abnormal** DST
- Averaged E/e' > 1
- PLUS TR velocity
- AND septal e' velocity < 7cm/s (or lateral < 10cm/s)
- **Normal** test:
- E/e' < 10 AND peak TR velocity < 2.8m/s

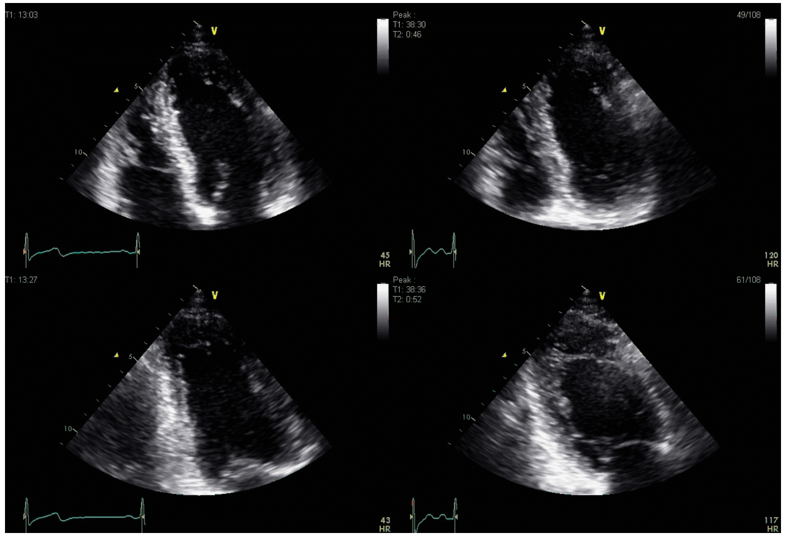
RVSP > 50mmHg (3.5m/s) associated with increased mortality

- BUT
- Research has mainly looked at E/e'
- /e' values have
- o be significant
- nal post exercise
- Only recordable in about 60% of patients

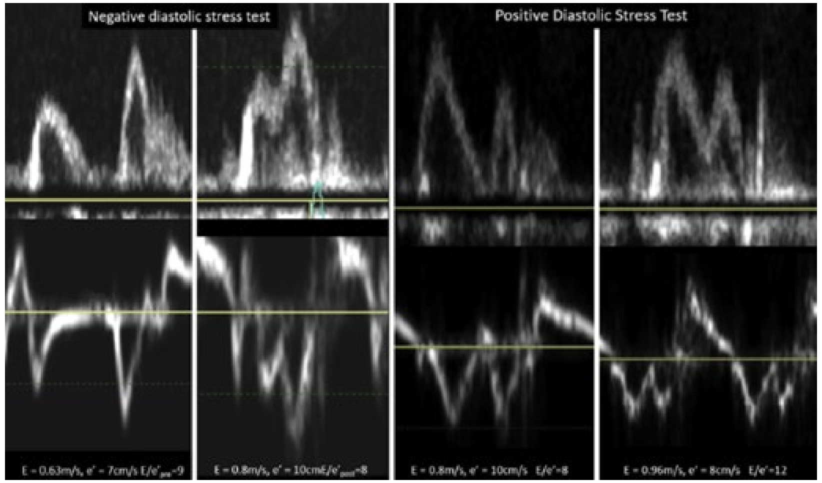


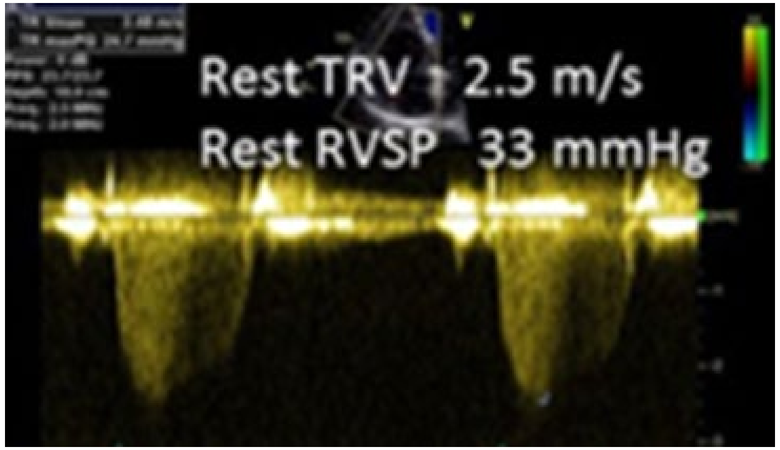


Diastolic stress test



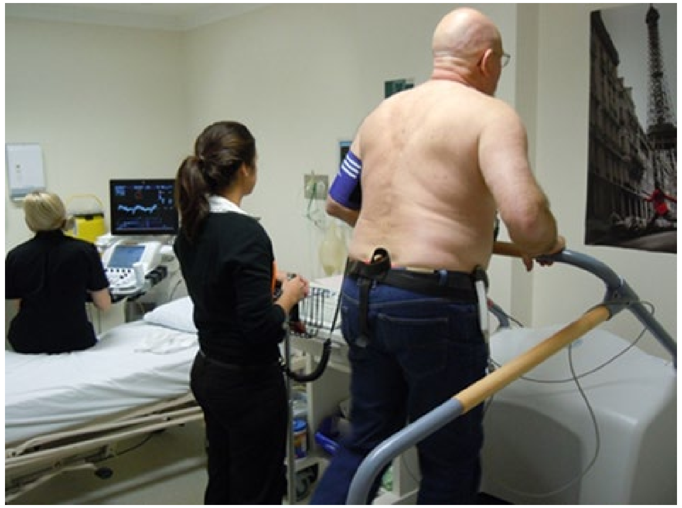
What to do?





Exercise capacity

- Diastolic dysfunction produces ↑ SOB, especially with exertion
- Therefore, patients with diastolic dysfunction should have reduced exercise capacity



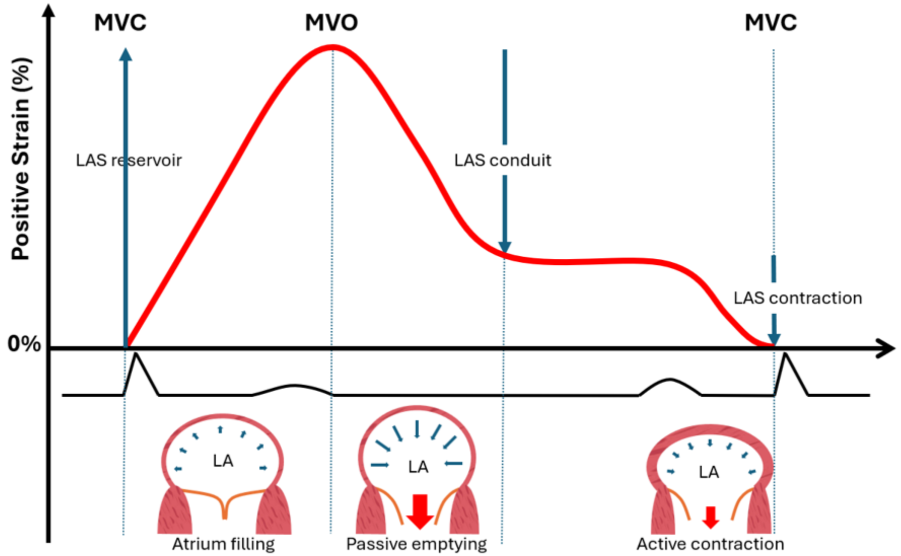
Exercise capacity

- 2019 DST paper
  - Mean exercise capacity in Normal DST (n=2001) was 10.9 METs ± 3.3
  - Mean exercise capacity in the Abnormal DST (n=200) was 8.9 METs ± 2.7 p=0.01
  - Upper 95th percentile for exercise for patients with diastolic dysfunction was < 9.5 METs

Fitzgerald, Presneill, Scalia I, Hawkins, Celemajer, Scalia W, Scalia GM
JASE 2019;32(10):1298-1306

Left atrial strain

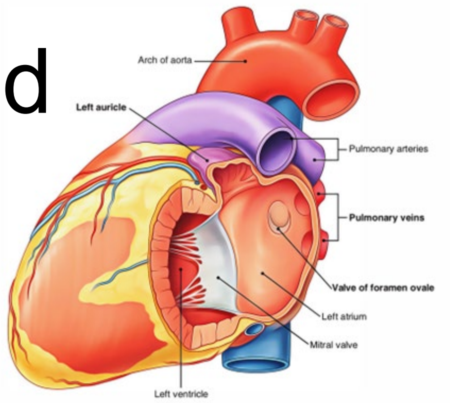
- Left atrial strain is a speckle tracking technique that quantifies magnitude and rate of LA myocardial deformation
- The 3 most commonly used parameters currently measure
  - Reservoir
  - Conduit
  - Contractile LA function



ECG – electrocardiogram; LA – left atrium; LAS – left atrial strain; MVC – mitral valve closure; MVO – mitral valve opening

Left atrial strain

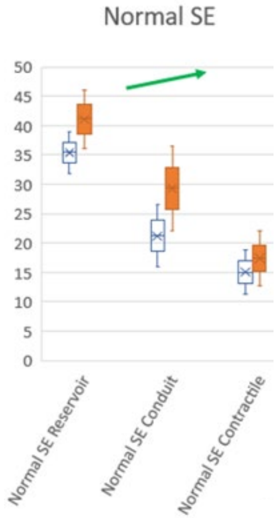
- Left atrium receives returning venous blood, acting as a reservoir
- The small pressure gradient between the LA and LV then permits the passive transfer of blood (acting as a conduit)



- In late ventricular systole, the LA actively pumps, adding to LV SV (contractile pump)
- Finally, LA suction assists in LA early systolic filling

Left atrial strain

- Assessment of LAS before and after treadmill exercise is feasible, quick and reproducible
- In patients with non-ischaemic stress echocardiograms with normal filling pressures, LAS parameters increase post exercise

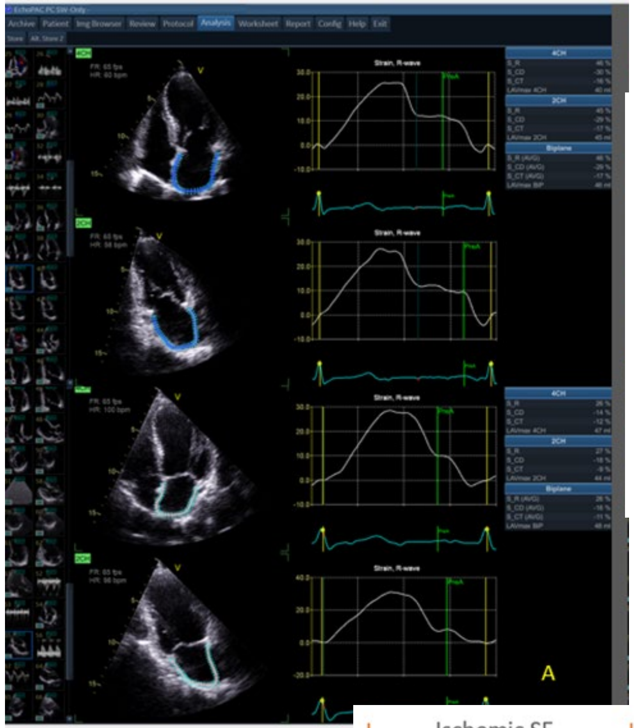


	Pre-exercise	Post-exercise
A4 Chamber Reservoir	37	42
A4C Conduit	-20	-25
A4C Contractile	-18	-20
A2 Chamber Reservoir	32	45
A2C Conduit	-22	-25
A2C Contractile	-15	-20
Biplane Reservoir	34	43
Biplane Conduit	-21	-25
Biplane Contractile	-16	-21

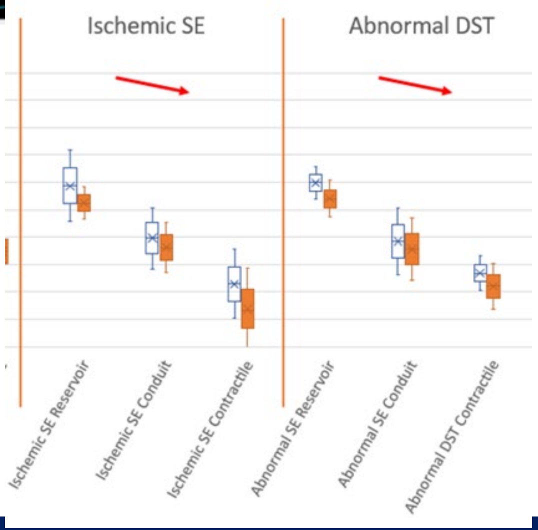
Left atrial strain

- LAS did not increase in patients with an **ischaemic SE**

Ischaemic

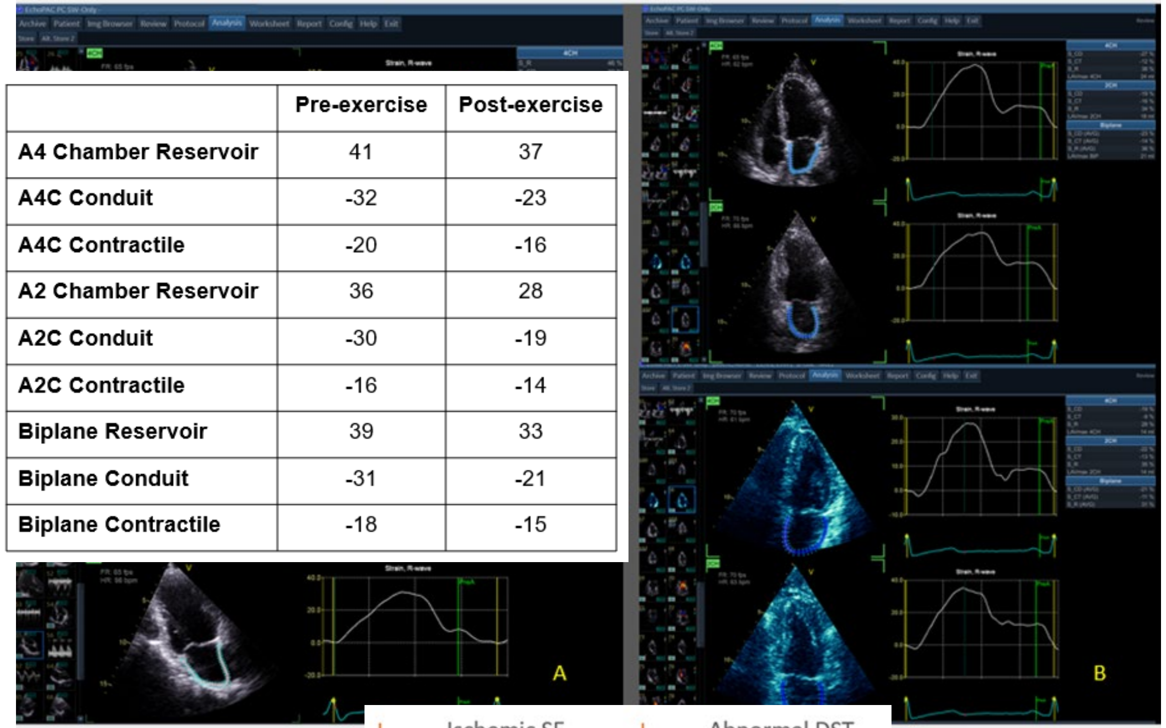


	Pre-exercise	Post-exercise
A4 Chamber Reservoir	38	37
A4C Conduit	-23	-20
A4C Contractile	-26	-13
A2 Chamber Reservoir	39	34
A2C Conduit	-21	-16
A2C Contractile	-20	-9
Biplane Reservoir	39	36
Biplane Conduit	-22	-18
Biplane Contractile	-18	-11

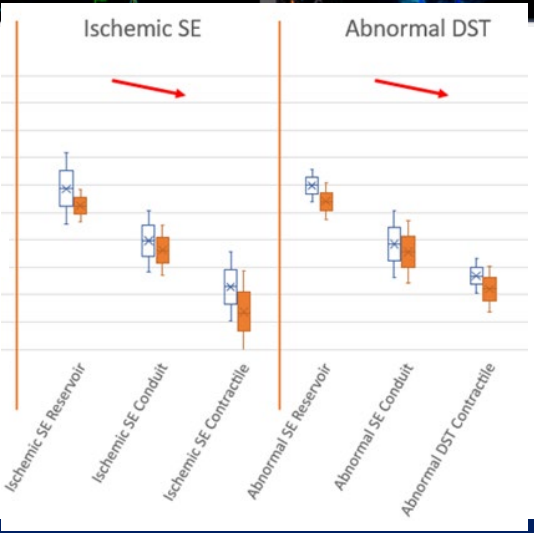


Left atrial strain

- LAS did not increase in patients with an **ischaemic SE**
- LAS did not increase in patients with an **Abnormal DST** (non-ischaemic SE with elevation in filling pressures)



	Pre-exercise	Post-exercise
A4 Chamber Reservoir	41	37
A4C Conduit	-32	-23
A4C Contractile	-20	-16
A2 Chamber Reservoir	36	28
A2C Conduit	-30	-19
A2C Contractile	-16	-14
Biplane Reservoir	39	33
Biplane Conduit	-31	-21
Biplane Contractile	-18	-15

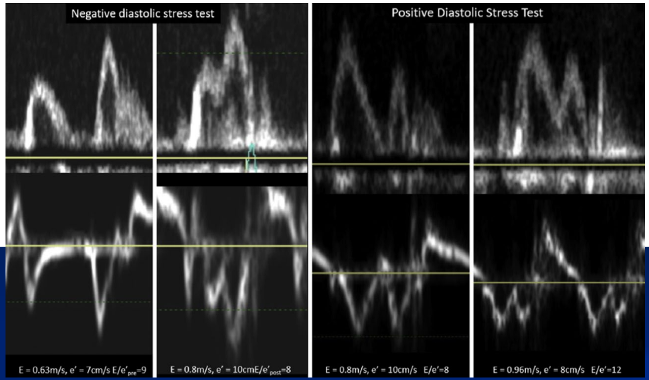


Left atrial strain

- These data suggest that LAS may have a role in the DST (as well as myocardial ischaemia)

Diastolic stress test

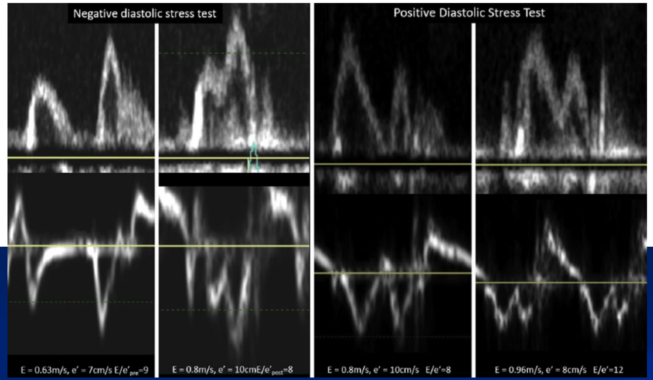
- 2016 ASE Guidelines
- For patients where resting echocardiography does not explain patient's symptoms
- **Abnormal** DST:
- Averaged E/e' > 14 or septal E/e' > 15
- PLUS TR velocity > 2.8m/s
- AND septal e' velocity < 7cm/s (or lateral < 10cm/s)
- **Normal** test:
- E/e' < 10 AND peak TR velocity < 2.8m/s



Diastolic stress test

- 2016 ASE Guidelines
- For patients where resting echocardiography does not explain patient’s symptoms
- **Abnormal** DST:
- Averaged E/e’ > 14 or septal E/e’ > 15
- PLUS TR velocity > 2.8m/s
- AND septal e’ velocity < 7cm/s (or lateral < 10cm/s)
- **Normal** test:
- E/e’ < 10 AND peak TR velocity < 2.8m/s

- How I perform the DST:
- For patients where resting echocardiography does not explain patient’s symptoms
- **Abnormal** if post exercise septal E/e’ increases to ->12 10
- **And** exercise capacity is reduced
- **Normal** test if the post exercise septal E/e’ < 10



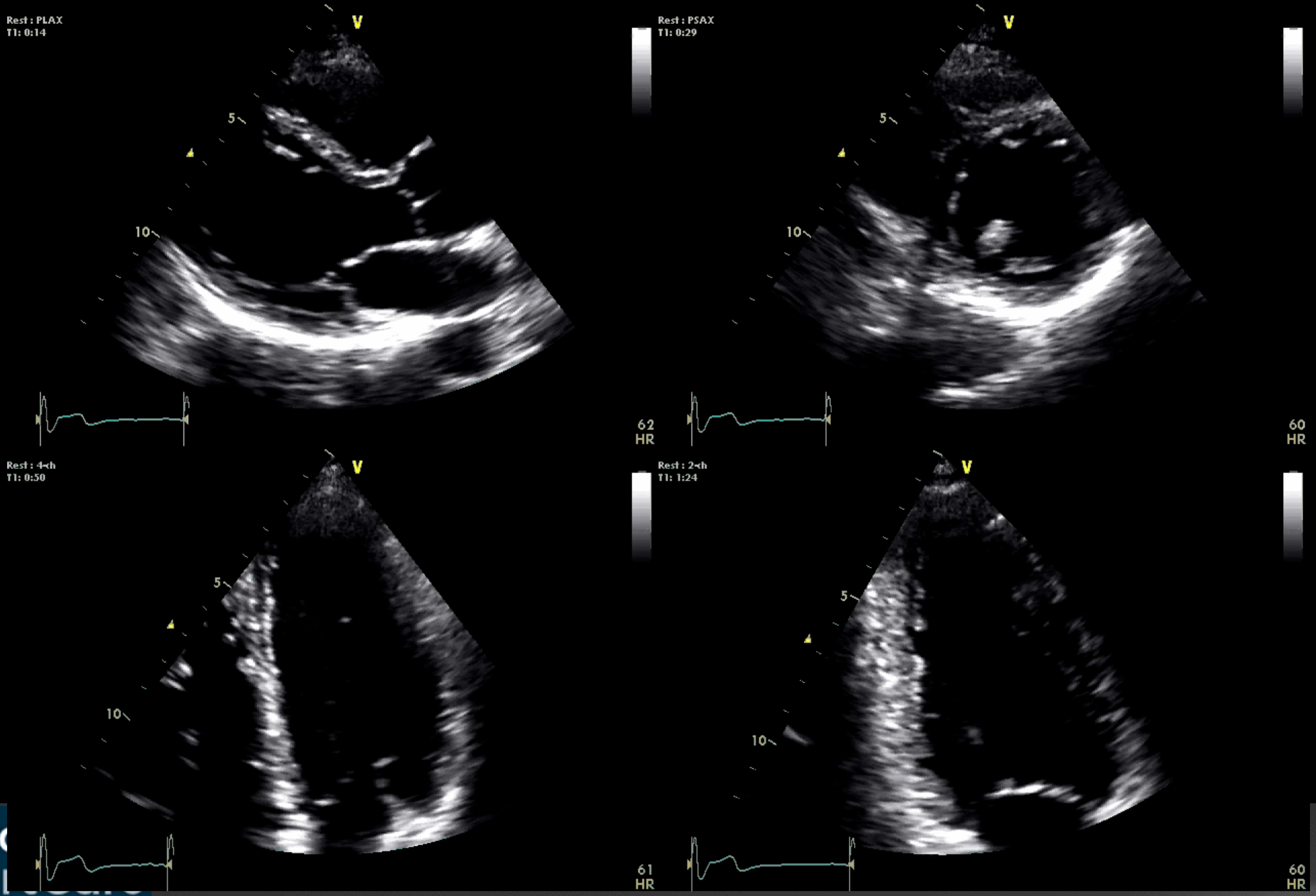
Advara HeartCare

ECHO AUSTRALIA

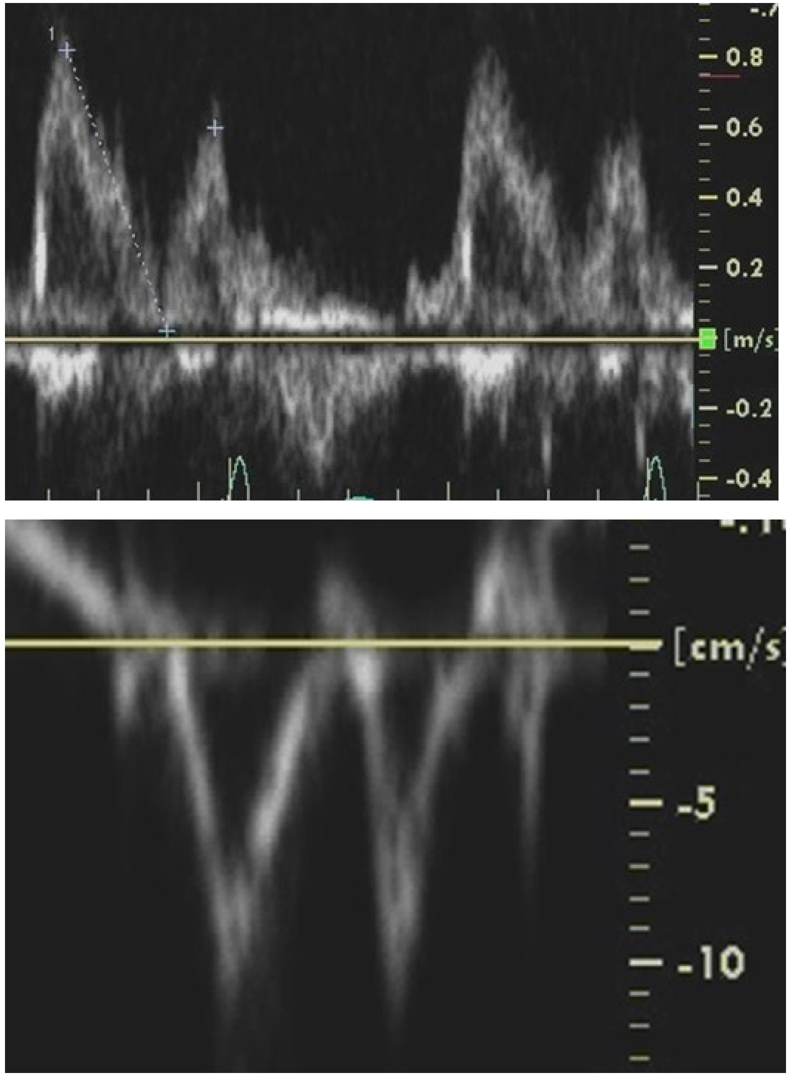
Diastolic stress test

- How I perform the DST:
- For patients where resting echocardiography does not explain patient’s symptoms
- **Abnormal** if post exercise septal E/e’ increases to -≥12 10
- **Normal** test if the post exercise septal E/e’ < 10
- **And** exercise capacity is reduced
- Utilise LAS to confirm the diagnosis

Resting quads

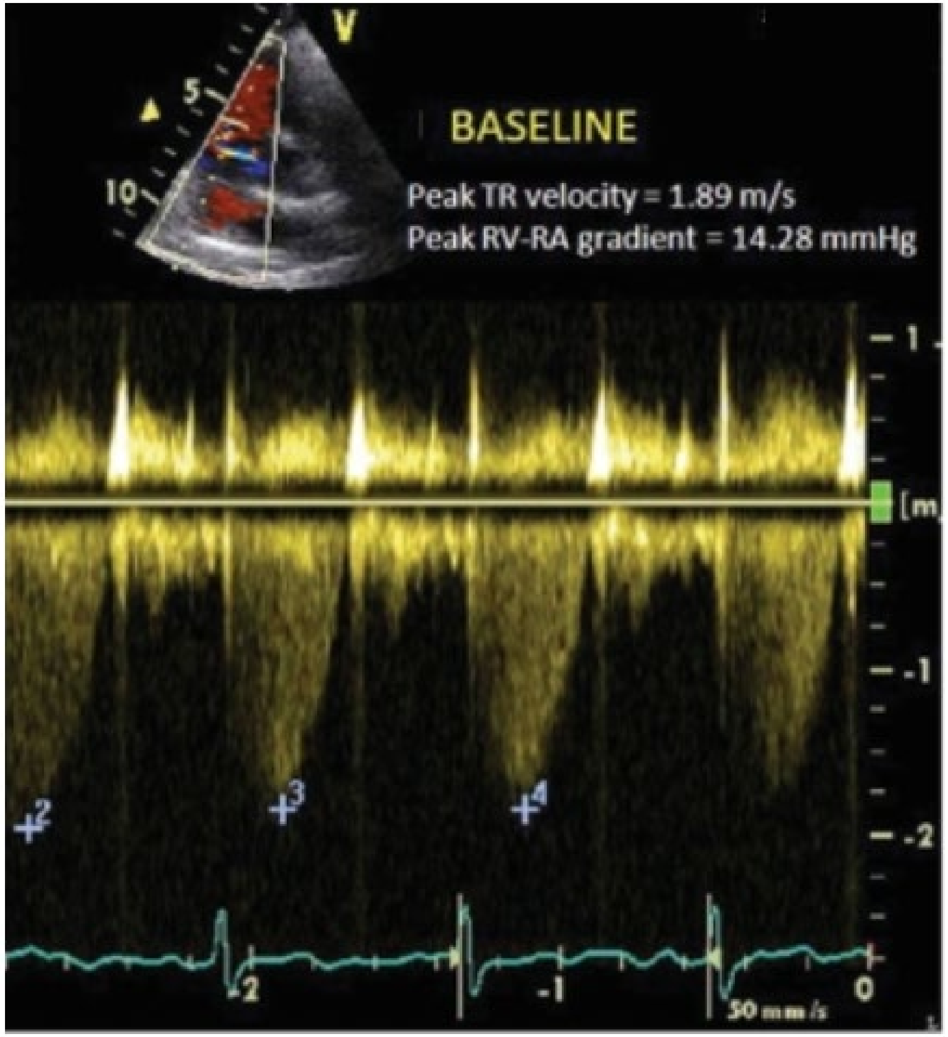


Diastolic stress test

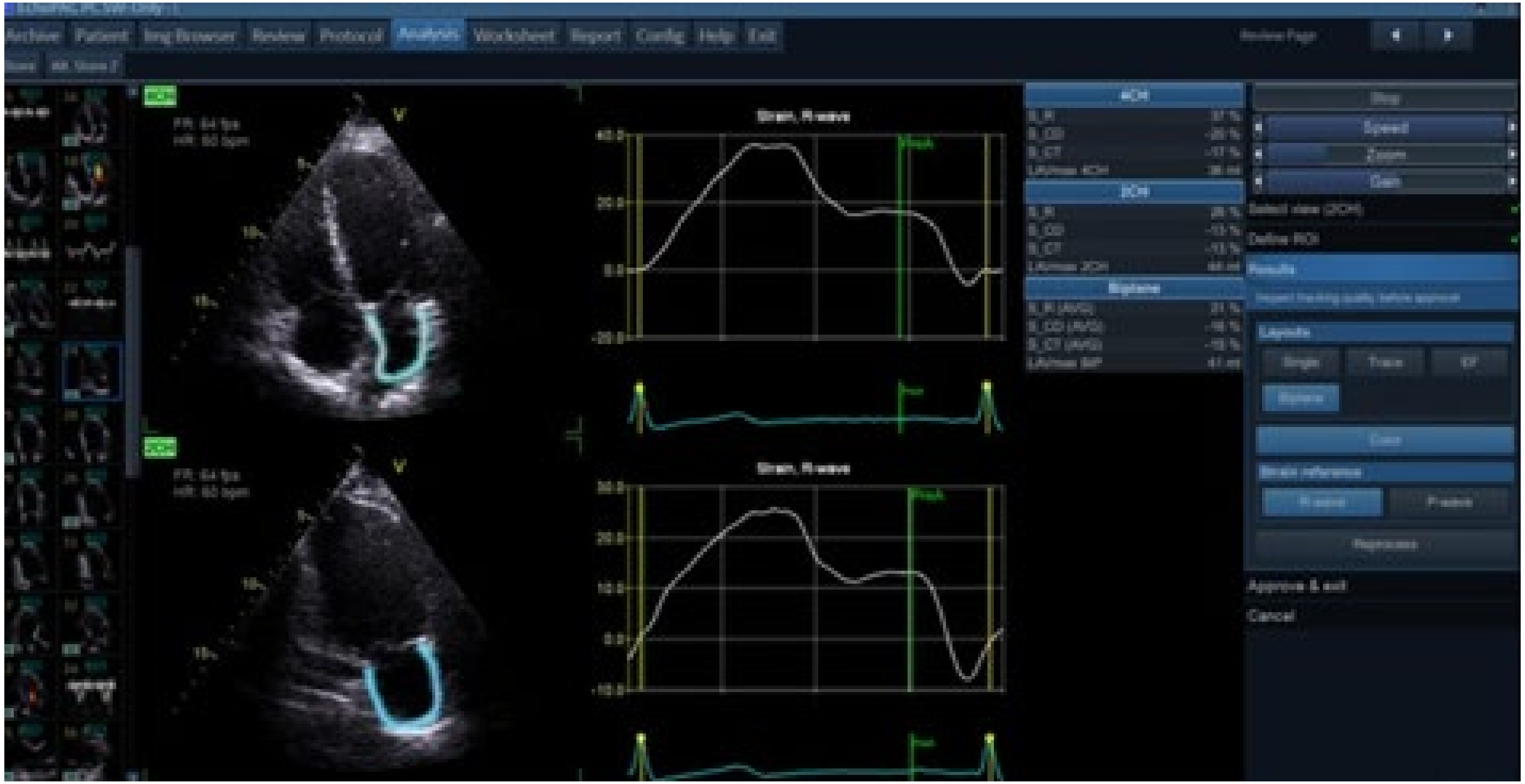


E/e’ = 7

Diastolic stress test

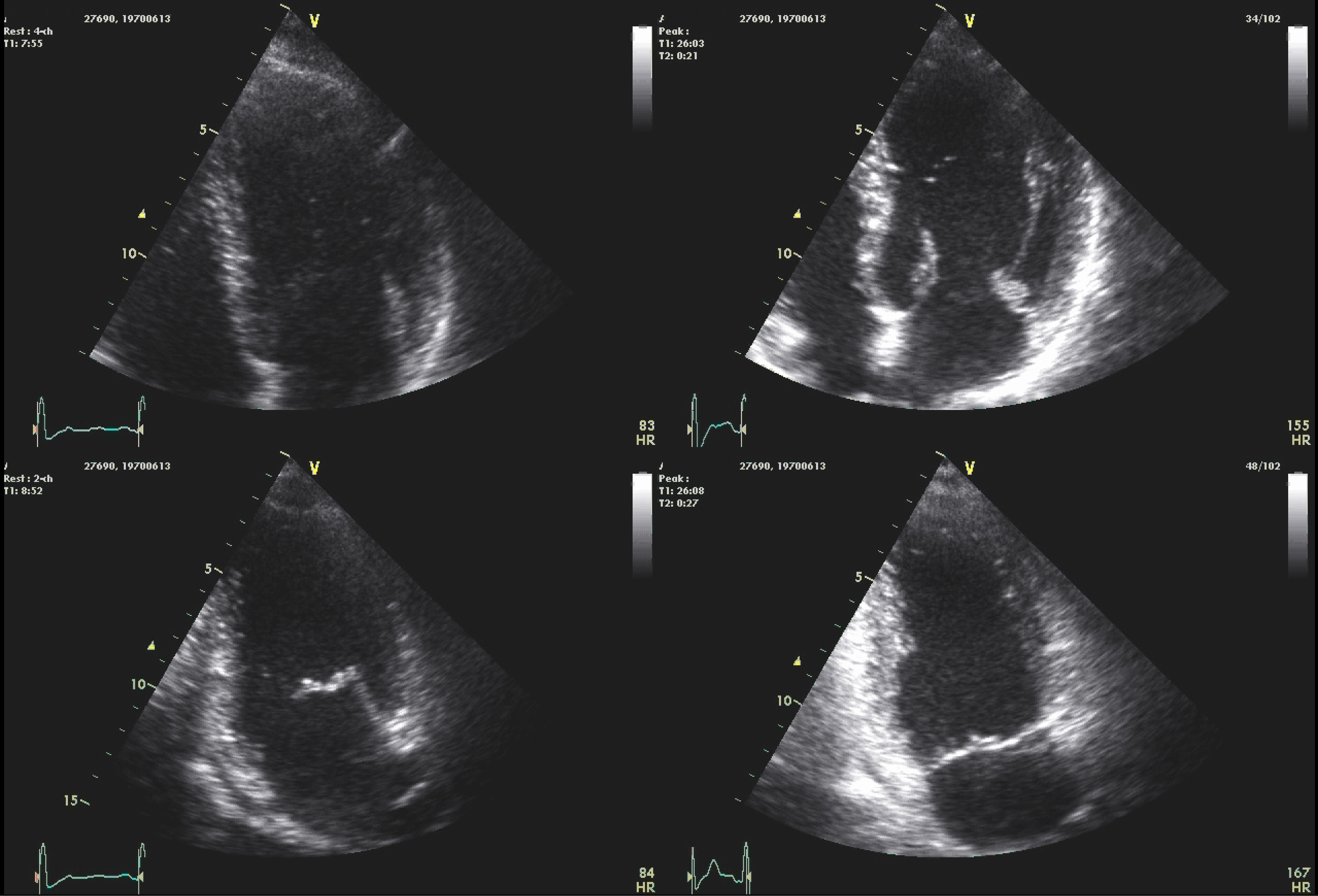


Diastolic stress test



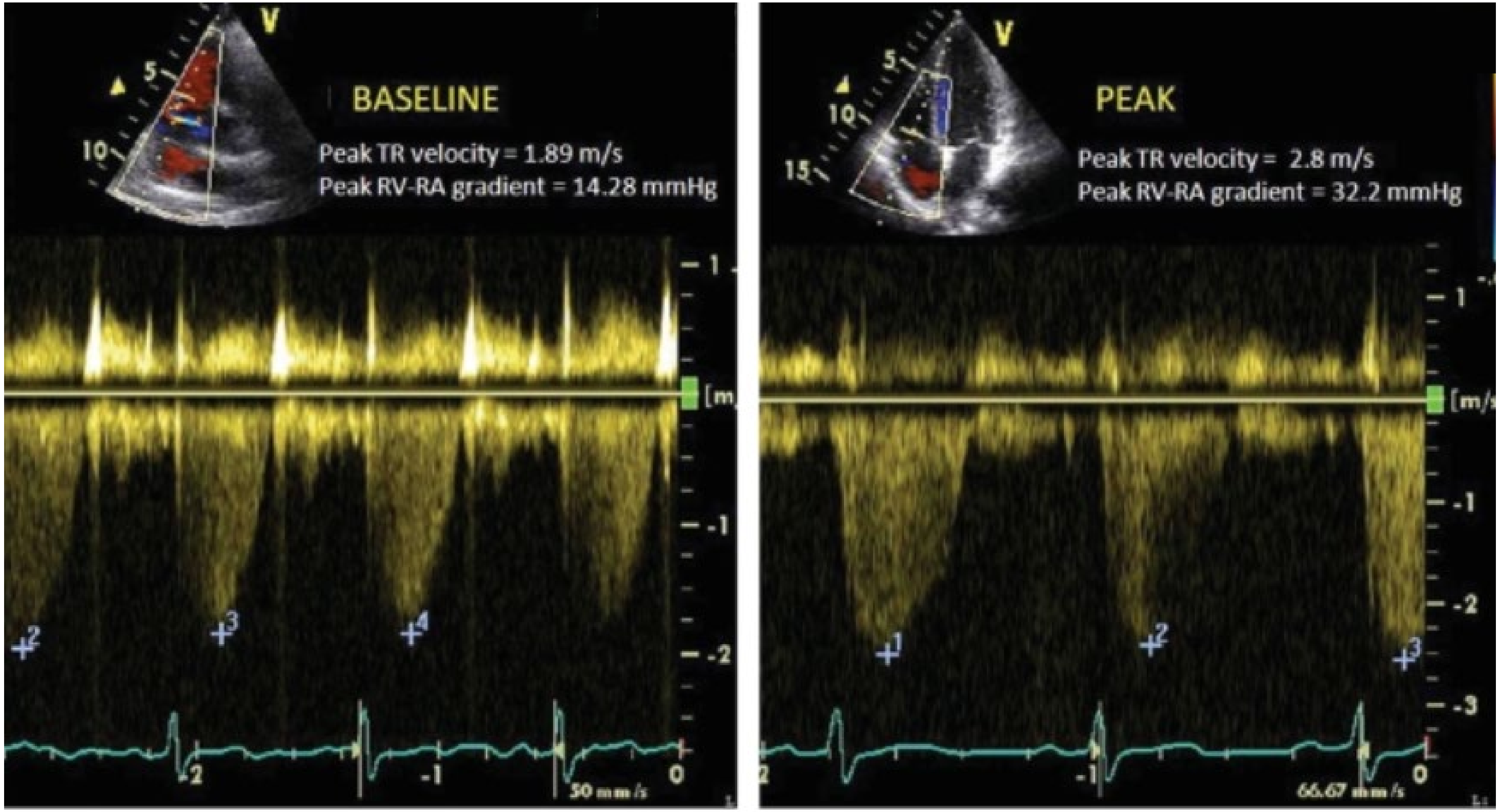
Diastolic stress test

Diastolic stress test

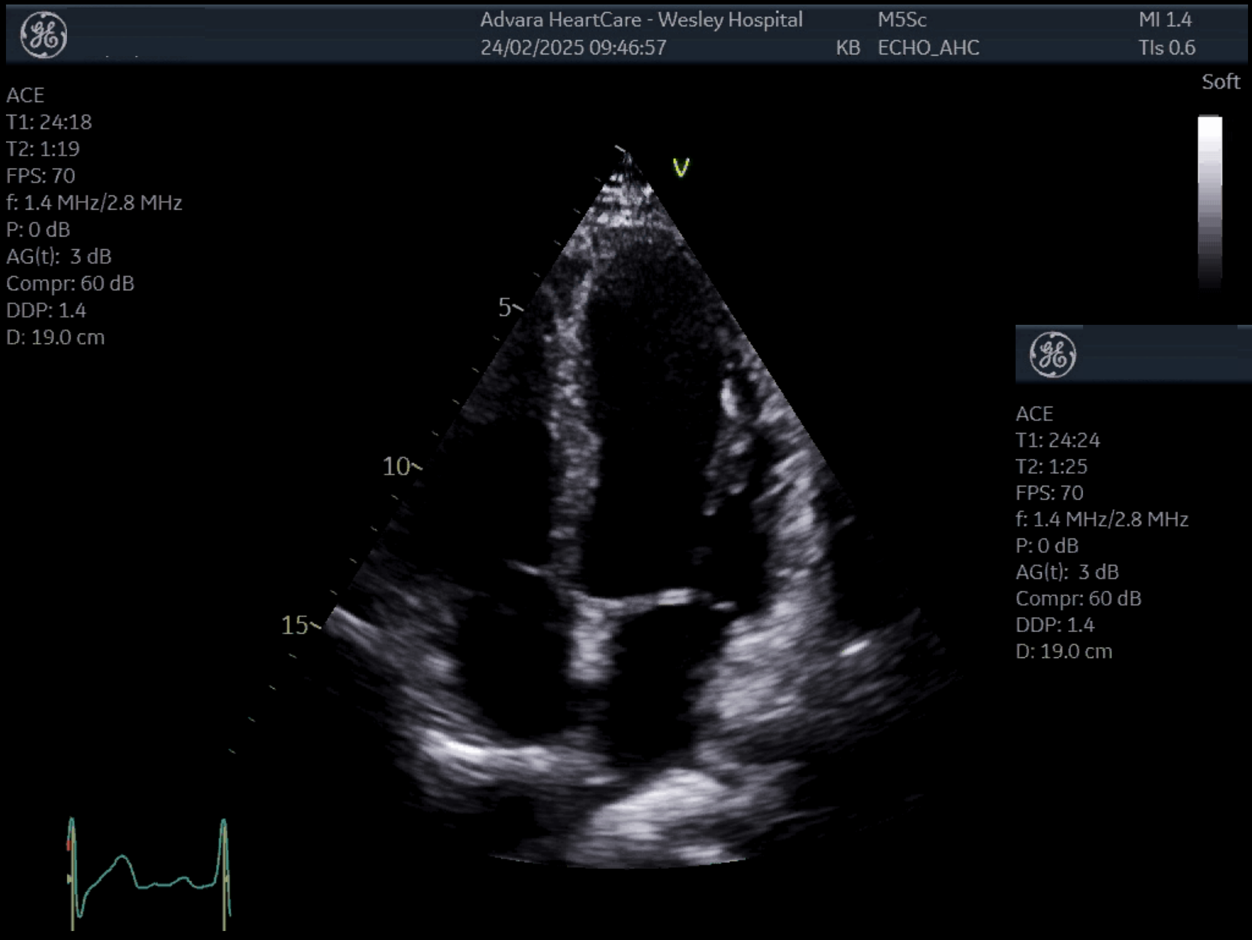


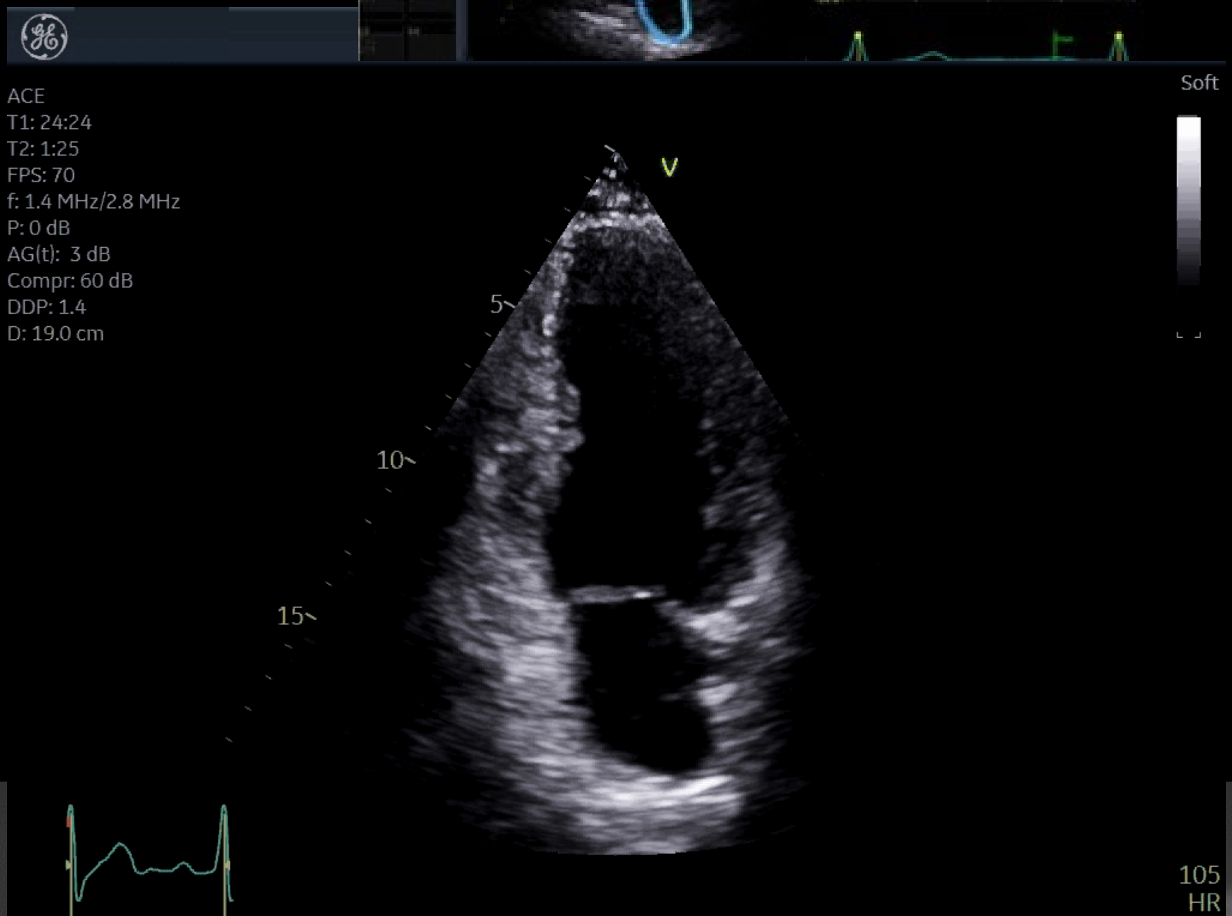
Complete in less than 90 seconds

Diastolic stress test

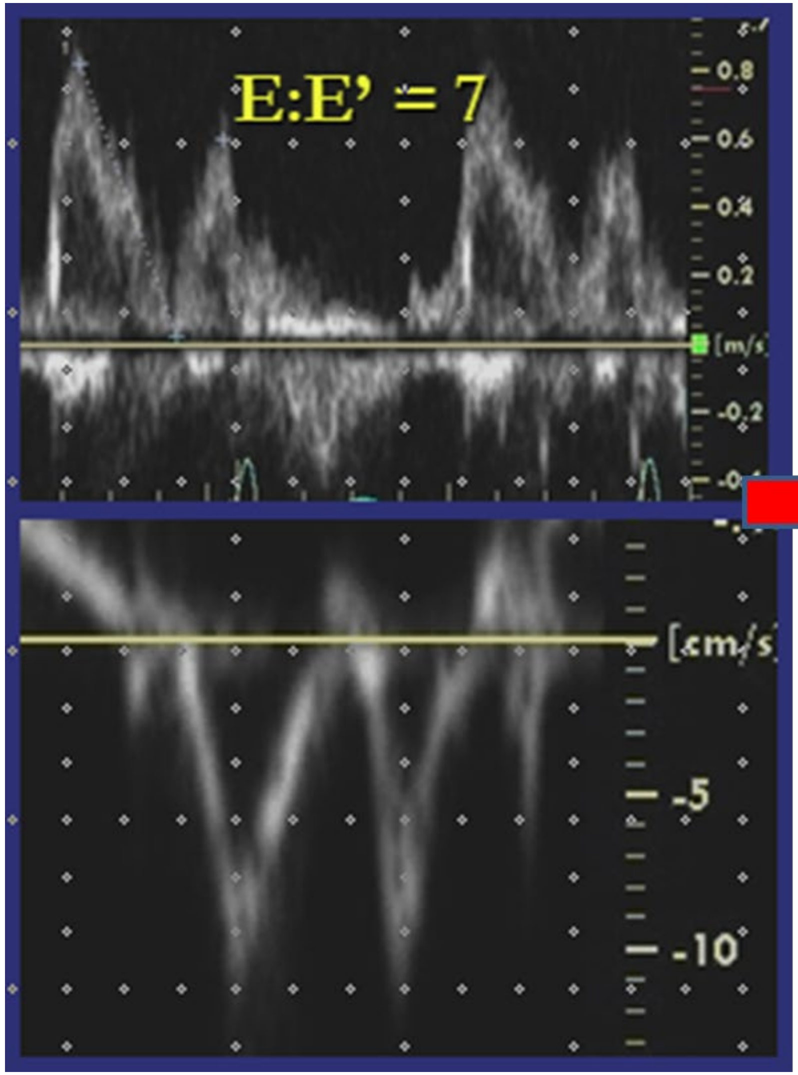


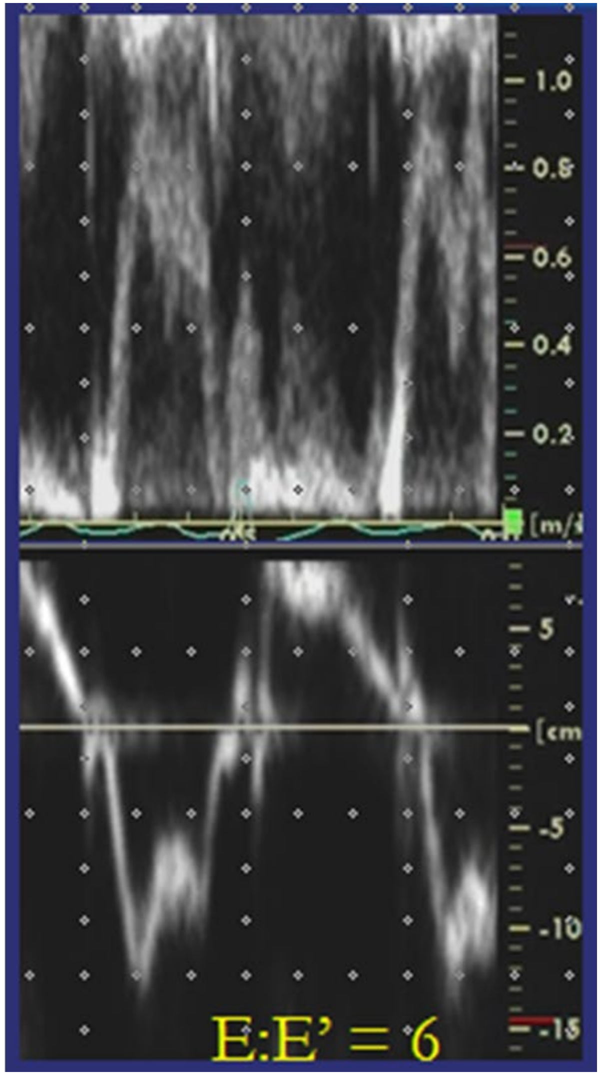
Diastolic stress test



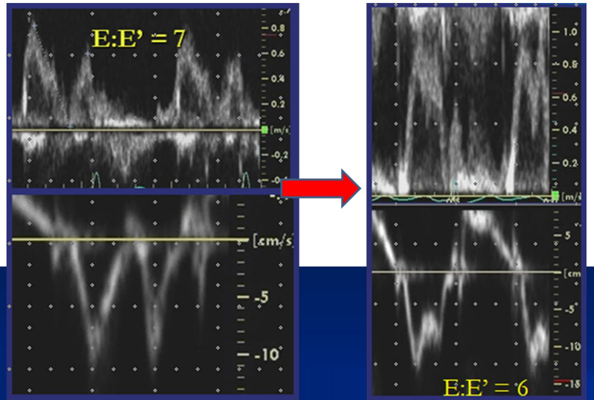
Diastolic stress test





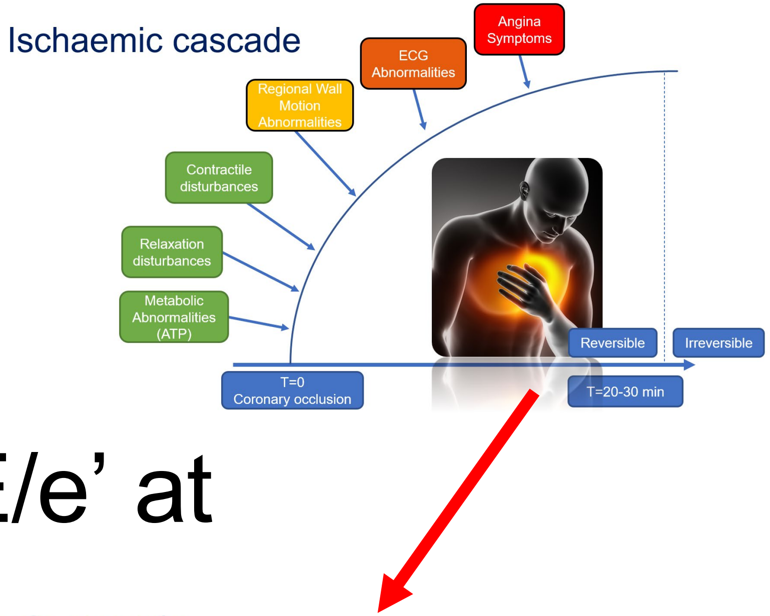
Diastolic stress test

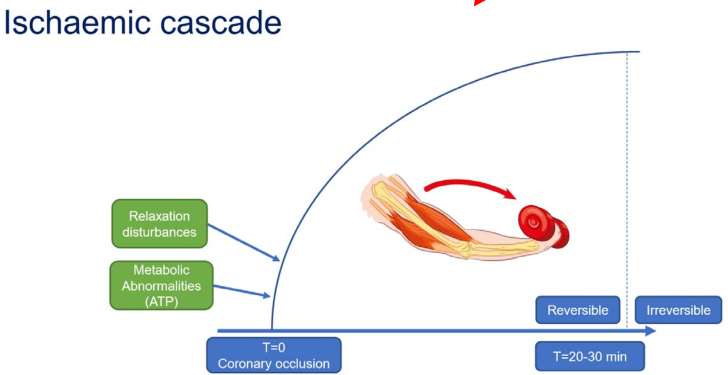
- You have time to do the mitral inflow Doppler and Doppler tissue imaging
- Early DST research performed the diastolic parameters between 5-10 minutes post exercise!



Diastolic stress test

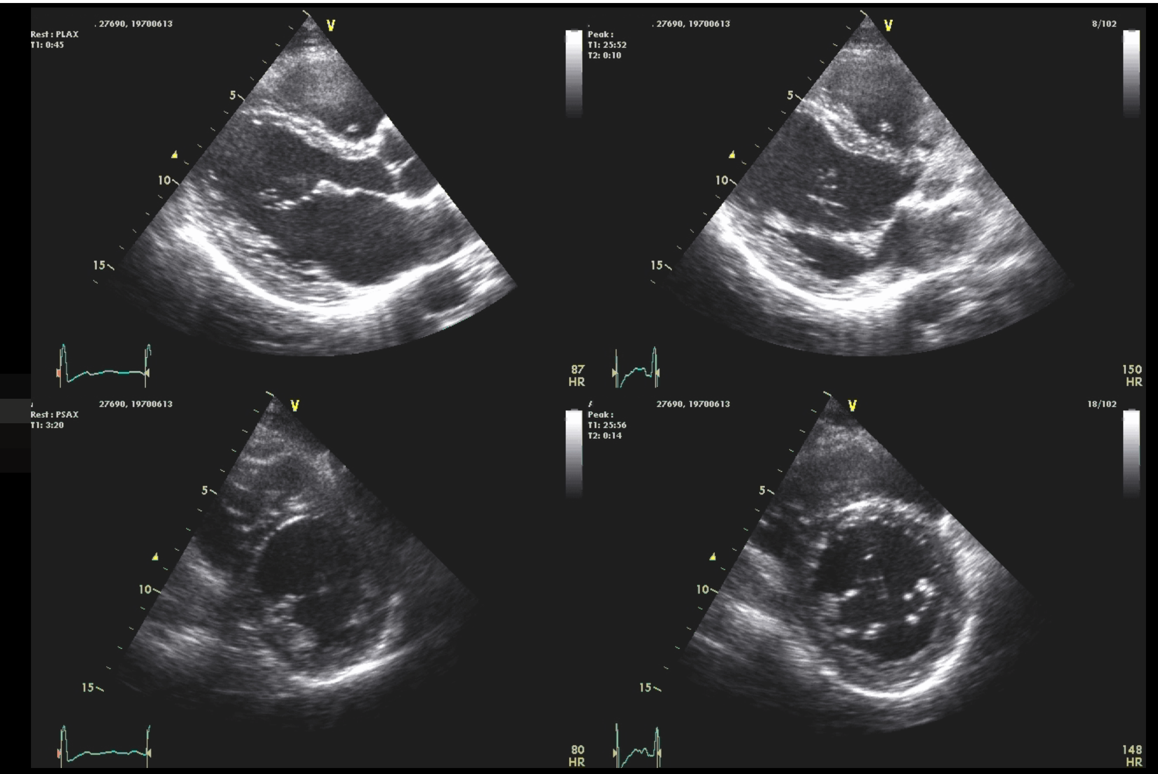
- You have time to do the mitral inflow Doppler and Doppler tissue imaging
- Early DST research performed the diastolic parameters between 5-10 minutes post exercise!
- Current research has performed E/e’ at 2-3 minutes post exertion

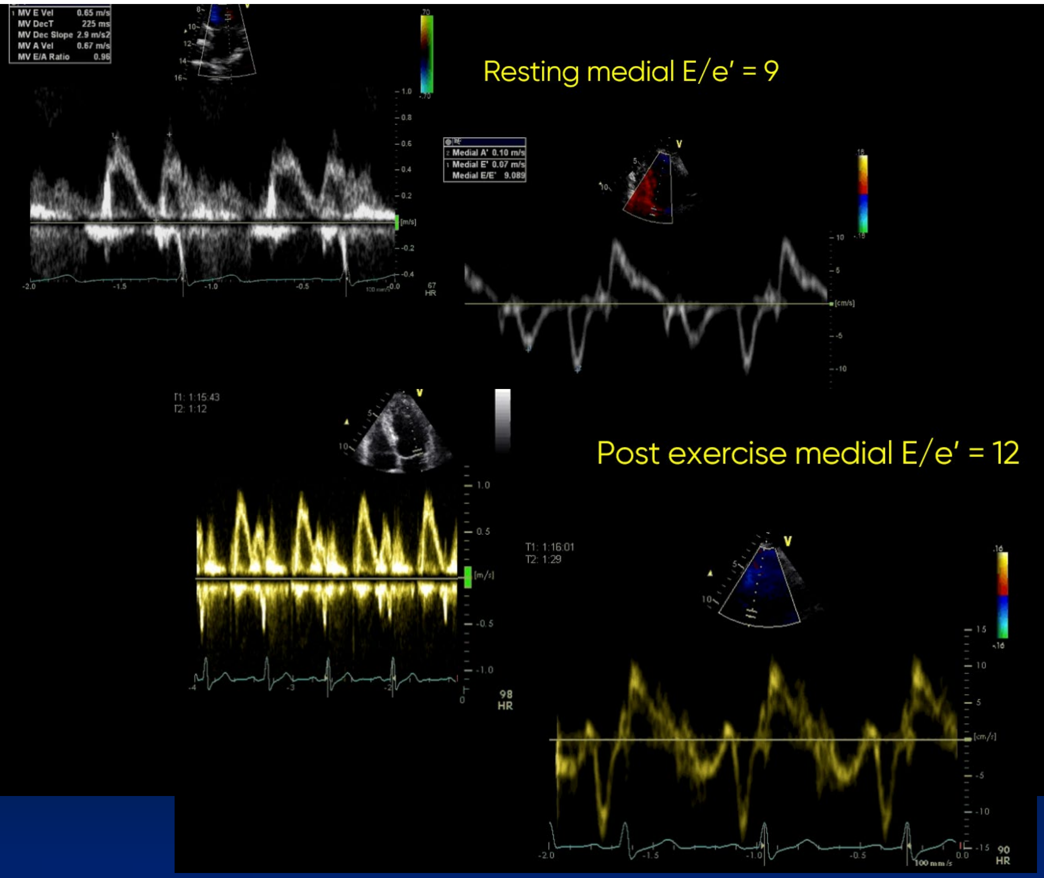




Diastolic Stress Testing

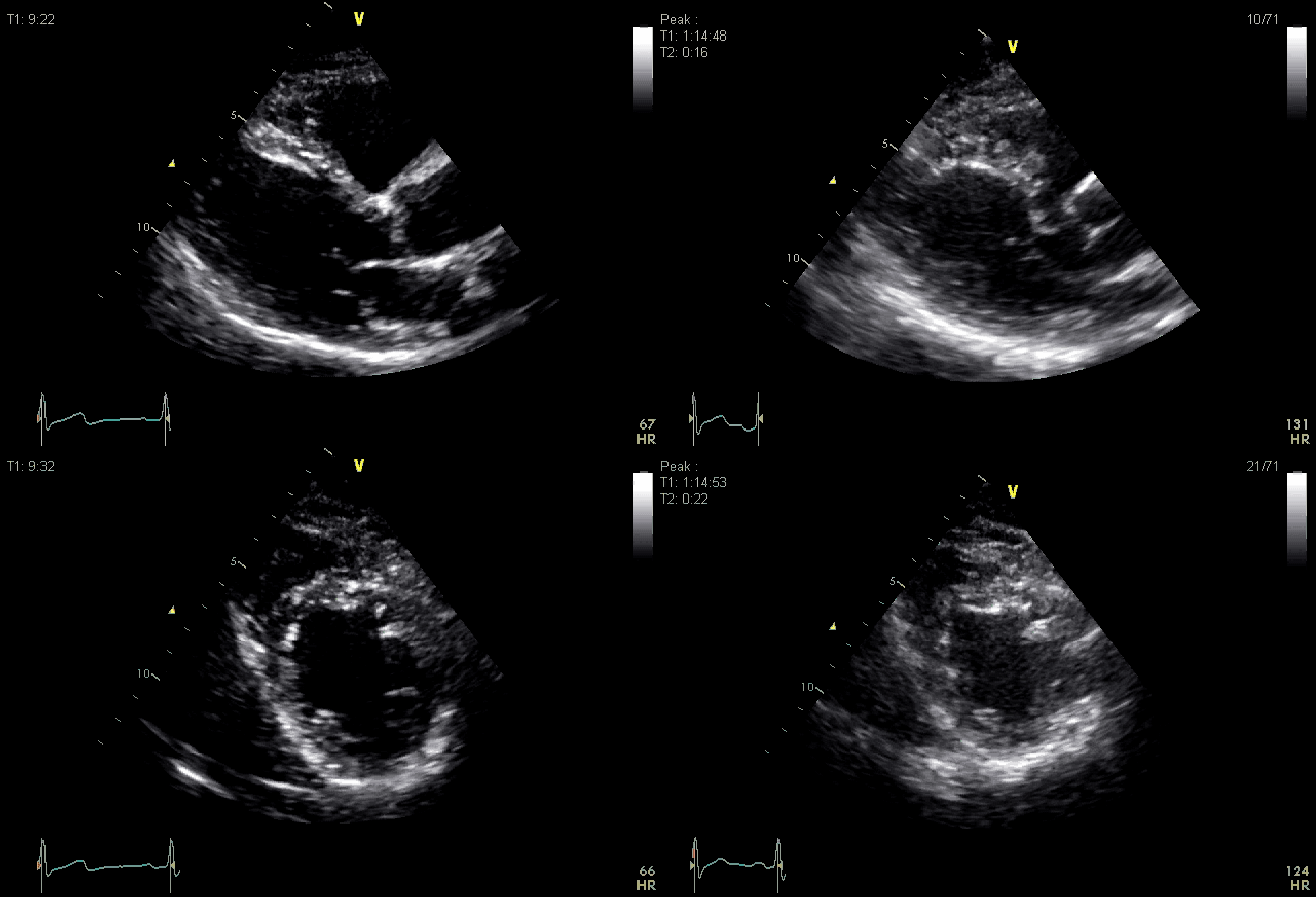
- Measure the E and the e' at the same phase of respiration (and the LAS clips)

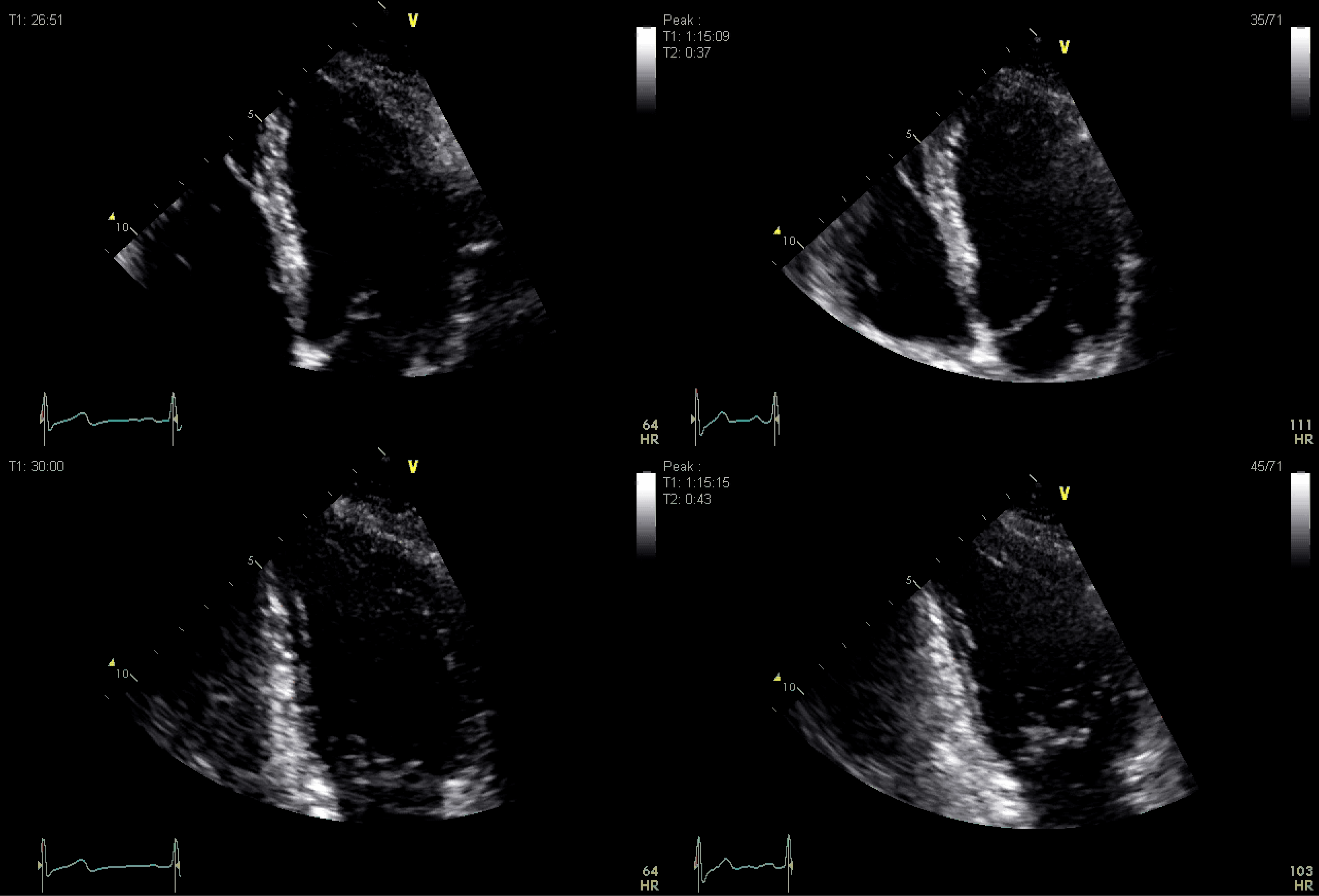




Case

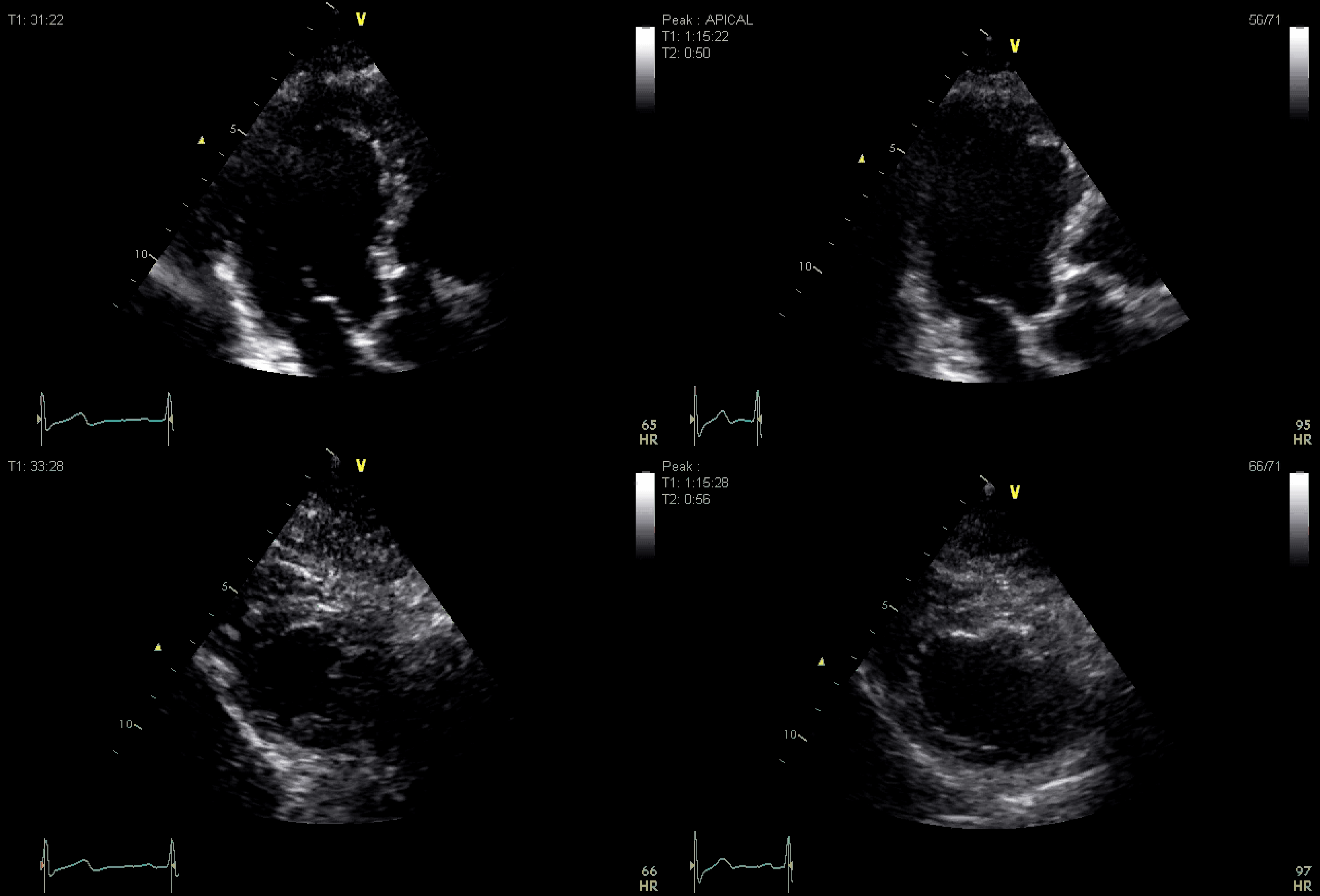
- 68F
- Progressive SOBOE over 6 months
- Progressively limiting activities


T1: 9:22
Peak :
T1: 1:14:48
T2: 0:16
10/71
67
HR
131
HR
T1: 9:32
Peak :
T1: 1:14:53
T2: 0:22
21/71
66
HR
124
HR



Advara HeartCare

ECHO AUSTRALIA

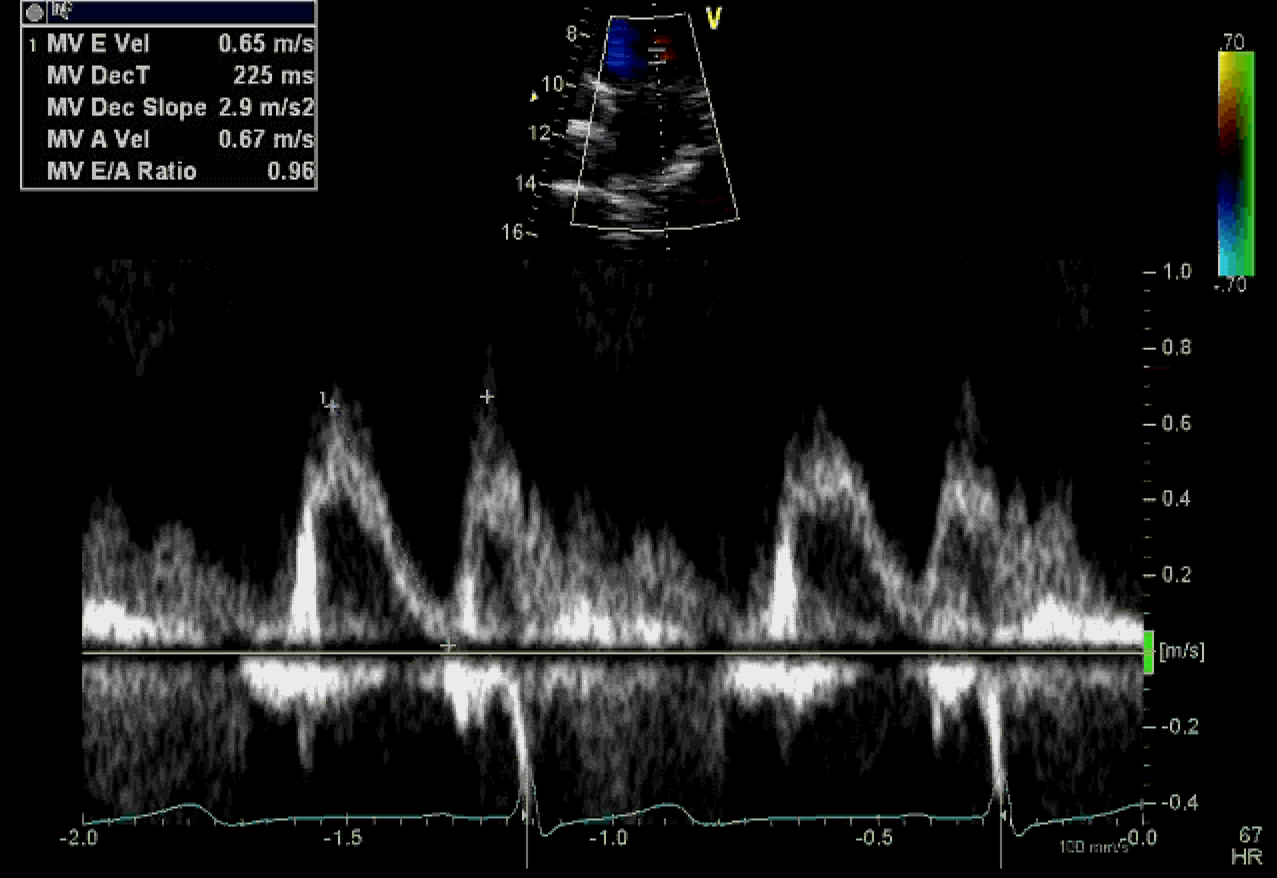


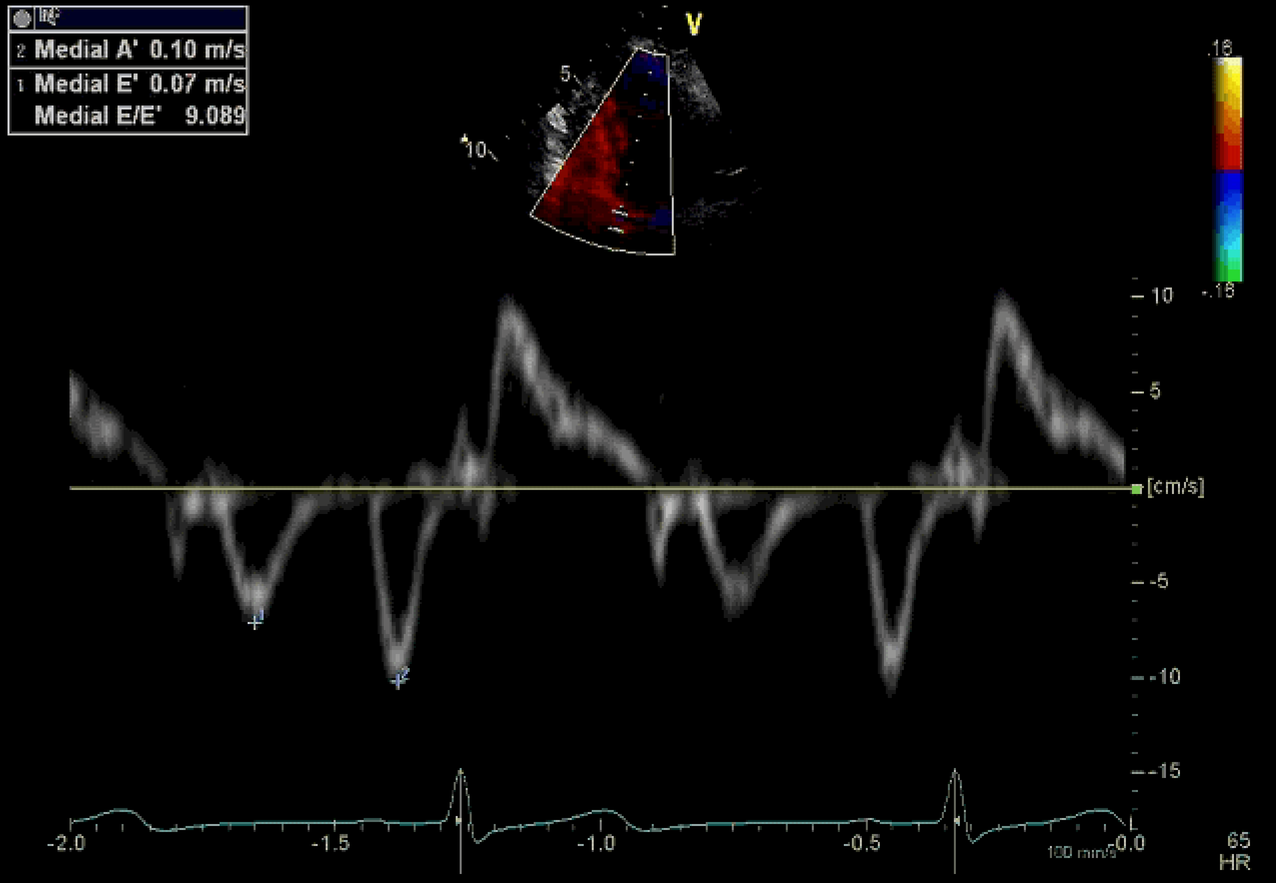
Advara HeartCare

Complete in less than 90 seconds

ECHO AUSTRALIA

Resting septal E/e’ = 9

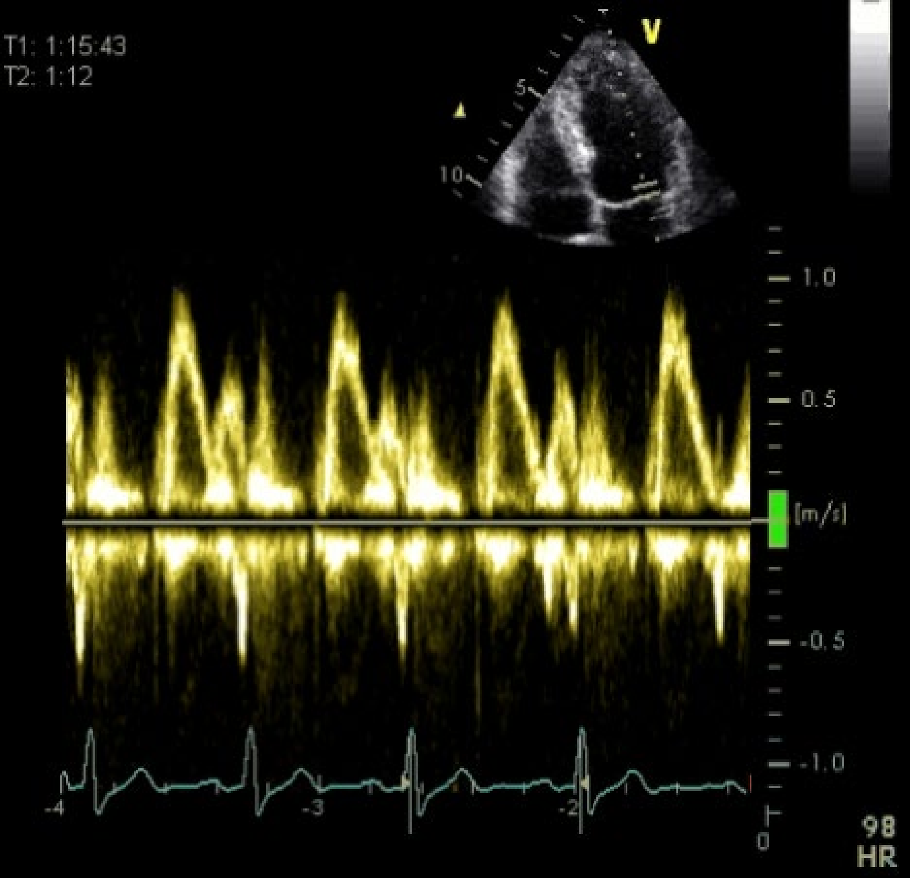


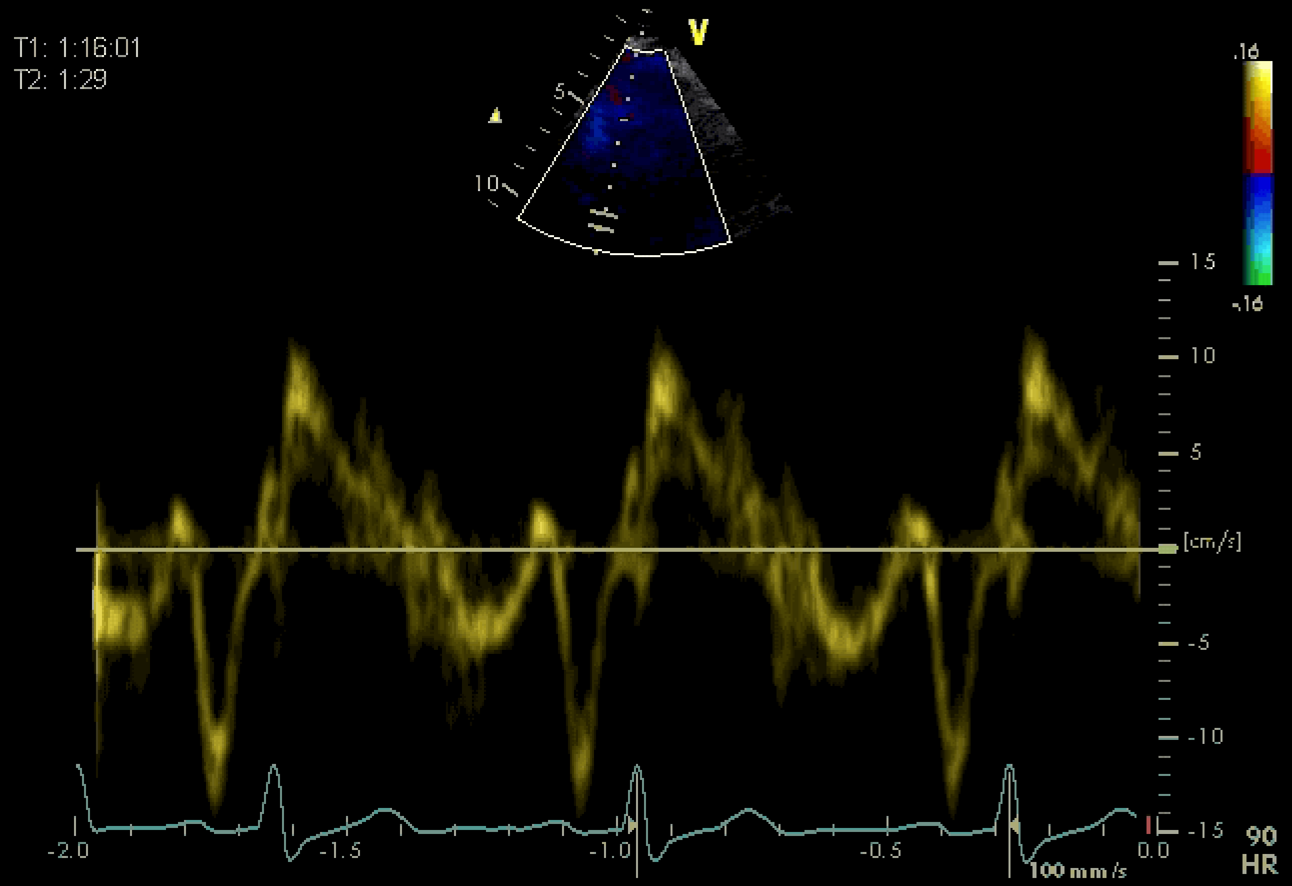


Advara HeartCare

ECHO AUSTRALIA

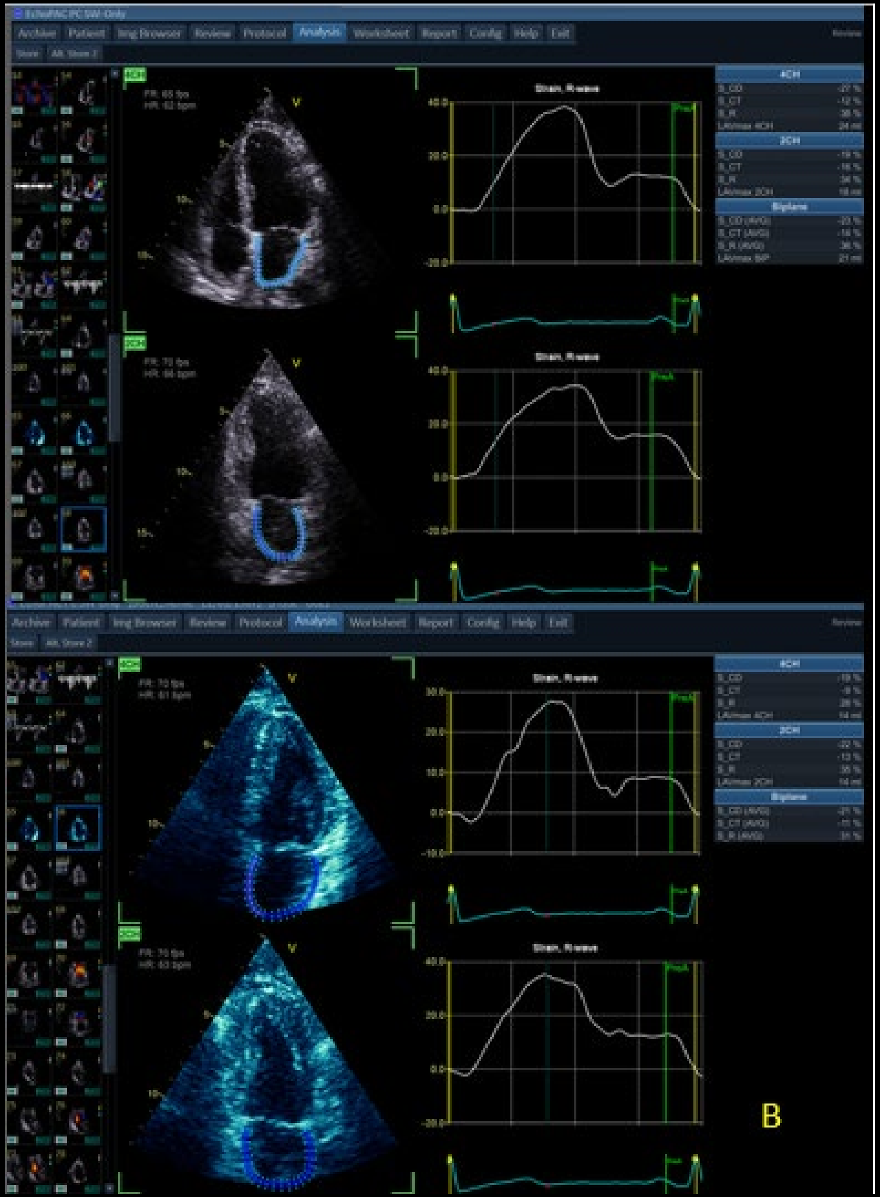
Post exercise septal E/e’ = 12





Advara HeartCare

ECHO AUSTRALIA



	Pre-exercise	Post-exercise
A4 Chamber Reservoir	41	36
A4C Conduit	-29	-23
A4C Contractile	-18	-16
A2 Chamber Reservoir	42	35
A2C Conduit	-28	-24
A2C Contractile	-15	-15
Biplane Reservoir	42	36
Biplane Conduit	-28	-24
Biplane Contractile	-17	-16

Case

- Non-ischaemic stress images
- Poor exercise capacity (achieved 5.9 METs)
- Septal E/e' increased 9 to 12 with exertion
- Abnormal LAS response
- **Abnormal diastolic stress test**
- Commenced on Forxiga
- 6 months later back playing golf and feeling much improved

Diastolic stress test

- Future directions:
  - New 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

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.)

ESC European Society of Cardiology
European Heart Journal - Cardiovascular Imaging (2022) **23**, e34–e61
doi:10.1093/ehjci/jeab154

Multimodality imaging in patients with heart failure and preserved ejection fraction: an expert consensus document of the European Association of Cardiovascular Imaging

Otto A. Smiseth (Chair)[1,2,3]*, Daniel A. Morris[4], Nuno Cardim[5], Maja Cikes[6], Victoria Delgado[7], Erwan Donal[8,9], Frank A. Flachskampf[10], Maurizio Galderisi[11,†], Bernhard L. Gerber[12], Alessia Gimelli[13], Allan L. Klein[14], Juhani Knuuti[15], Patrizio Lancellotti[16,17], Julia Mascherbauer[18], Davor Milicic[6], Petar Seferovic[19,20], Scott Solomon[21], Thor Edvardsen[1,2,3], and Bogdan A. Popescu (Co-Chair)[22,*]

Diastolic stress test

- Future directions:
  - New guidelines
  - LA strain….
  - Utilising exercise capacity

MET Levels

Listed alphabetically by category of intensity

Light activities (<3 METs)*	METs
Canoeing leisurely	2.5
Croquet	2.5
Dancing, ballroom, slow	2.9
Fishing, standing	2.5
Golf with a cart	2.5
Housework, light	2.5
Playing catch	2.5
Playing a piano	2.5
Sitting quietly	1.0
Stretching exercises, yoga	2.5
Walking, 2 mph	2.5

*Calories burned = up to 215/hour

Moderate activities (3-6 METs)*	METs
Aerobic dance, low impact	5.0
Archery	3.5
Badminton	4.5
Baseball or softball	5.0
Basketball, shooting baskets	4.5
Bicycling, leisurely	3.5
Bowling	3.0
Calisthenics, light to moderate	3.5
Canoeing, 3 mph	3.0
Chopping wood	6.0
Dancing, aerobic or ballet	6.0
Dancing, modern, fast	4.8
Fencing	6.0
Fishing, walking and standing	3.5
Foot bag, hacky sack	4.0
Gardening, active	4.0
Golf, walking	4.4
Gymnastics	4.0
Hiking cross country	6.0
Horseback riding	4.0
Ice skating	5.5

Moderate activities (3-6 METs)*	METs
Jumping on mini tramp	4.5
Kayaking	5.0
Mowing lawn, walking	5.5
Raking the lawn	4.0
Shoveling snow	6.0
Skateboarding	5.0
Skiing downhill, moderate	6.0
Snorkeling	5.0
Snowmobiling	3.5
Surfing	6.0
Swimming, moderate pace	4.5
Table tennis	4.0
Tai chi	4.0
Tennis, doubles	5.0
Trampoline	3.5
Volleyball, noncompetitive	3.0
Walking, 15 min/mile	5.0
Walking, brisk up hills	6.0
Water skiing	6.0
Weight lifting, heavy workout	6.0
Wrestling	6.0

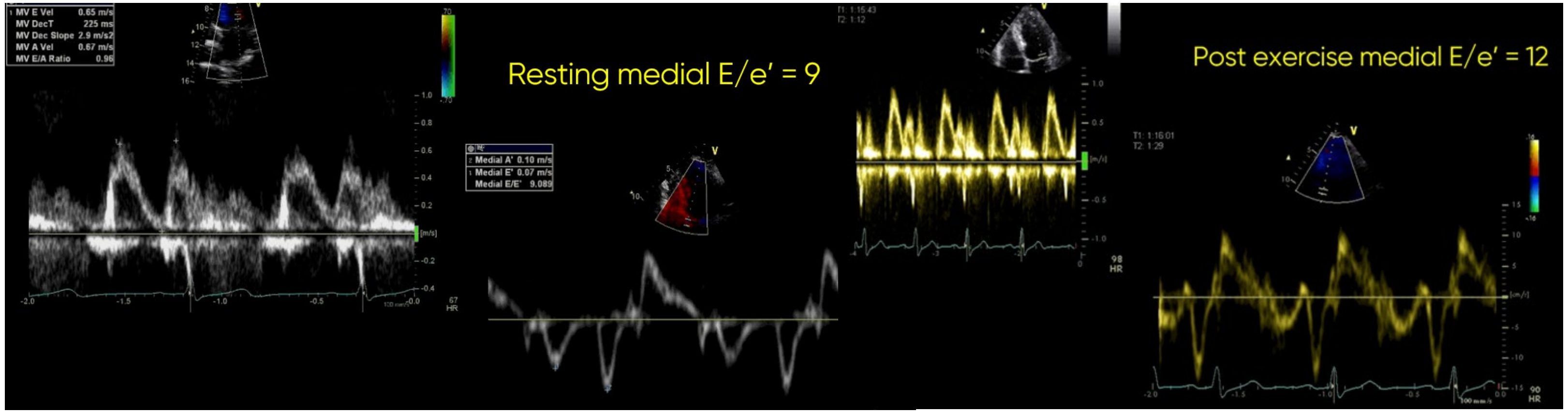
*Calories burned = 215–430/hour

Diastolic stress test

- For patients where resting echocardiography does not explain patient’s symptoms

- Measure the E and the e’ at the same phase of respiration

- You have time to get your measurements



Diastolic stress test

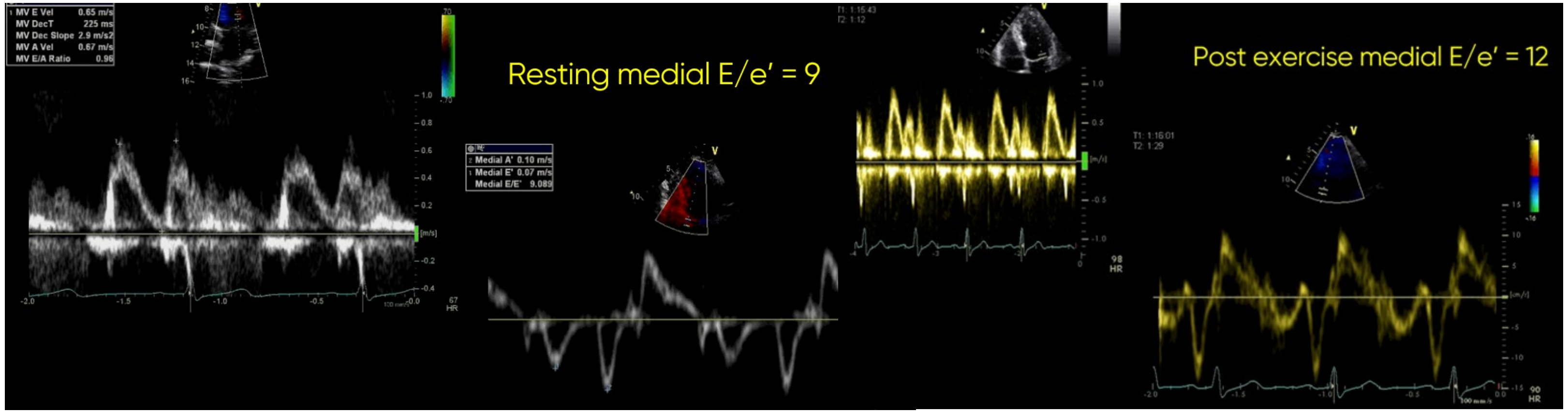
- What to do?
- Can follow the 2016 ASE Guidelines

  or

- **Abnormal** if post exercise septal E/e’ increases to ≥ 10 - 12

  in patients with reduced exercise capacity ± abnormal LAS

- **Normal** test if the post exercise septal E/e’ < 10 (? 9)

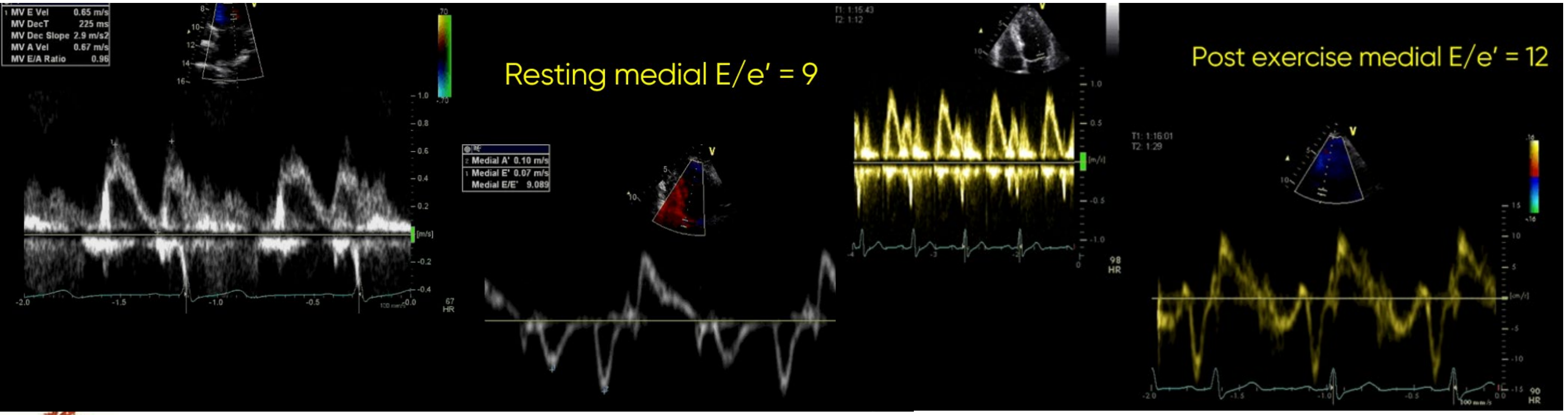


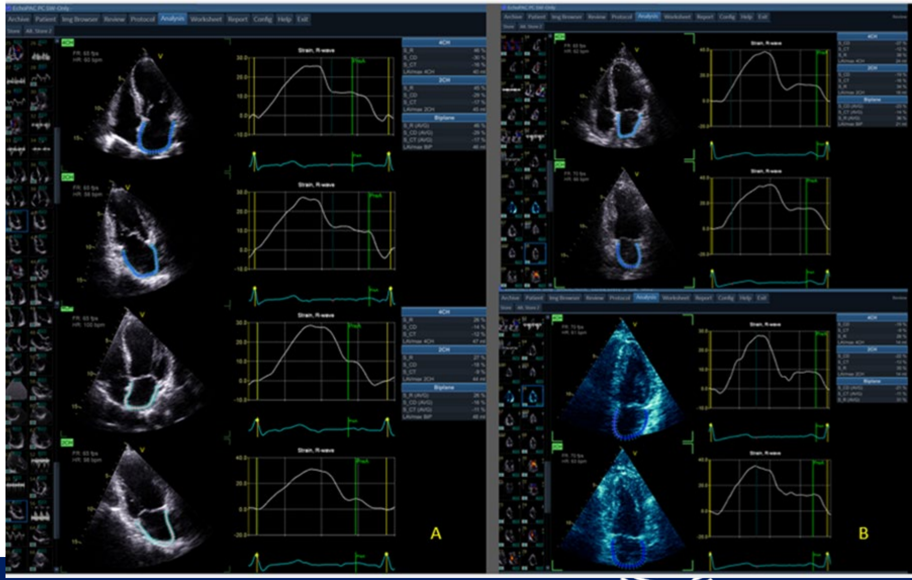
Diastolic stress test

- What to do?
- Can follow the 2016 ASE Guidelines

    or

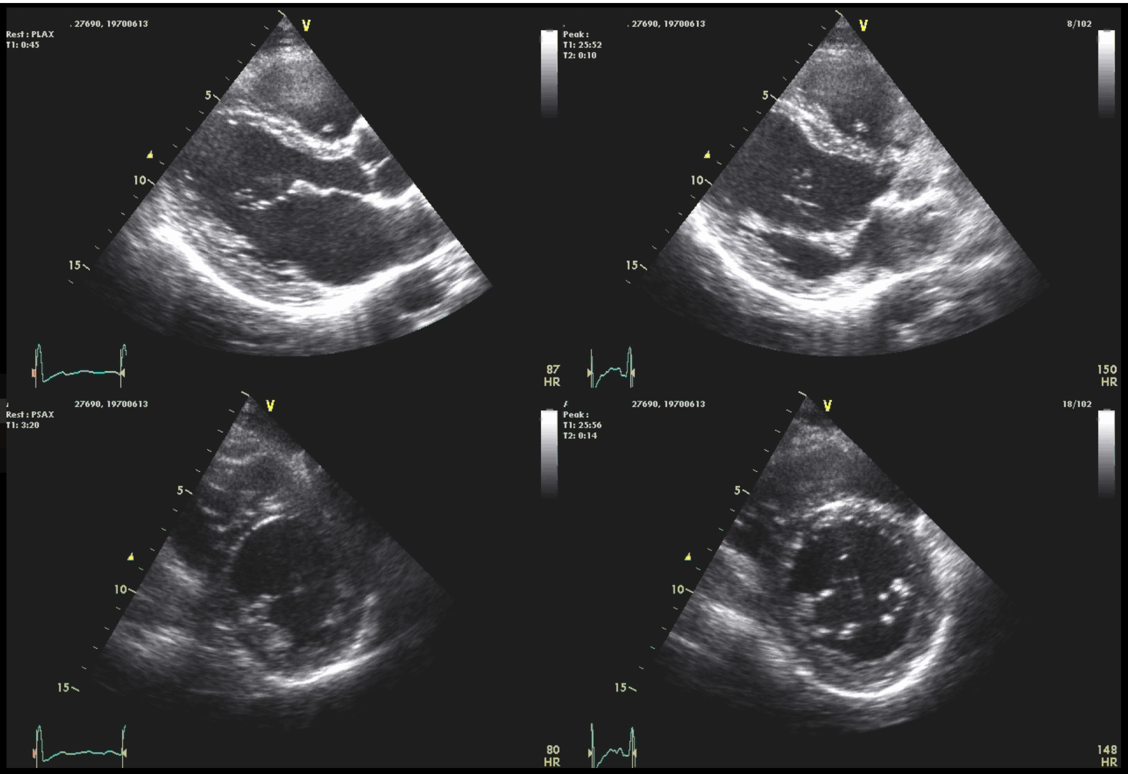
- **Abnormal** if post exercise septal E/e' increases to ≥ 10 - 12 with poor exercise capacity
- **Normal** test if the post exercise septal E/e' < 10 (? 8)
- Consider using LAS

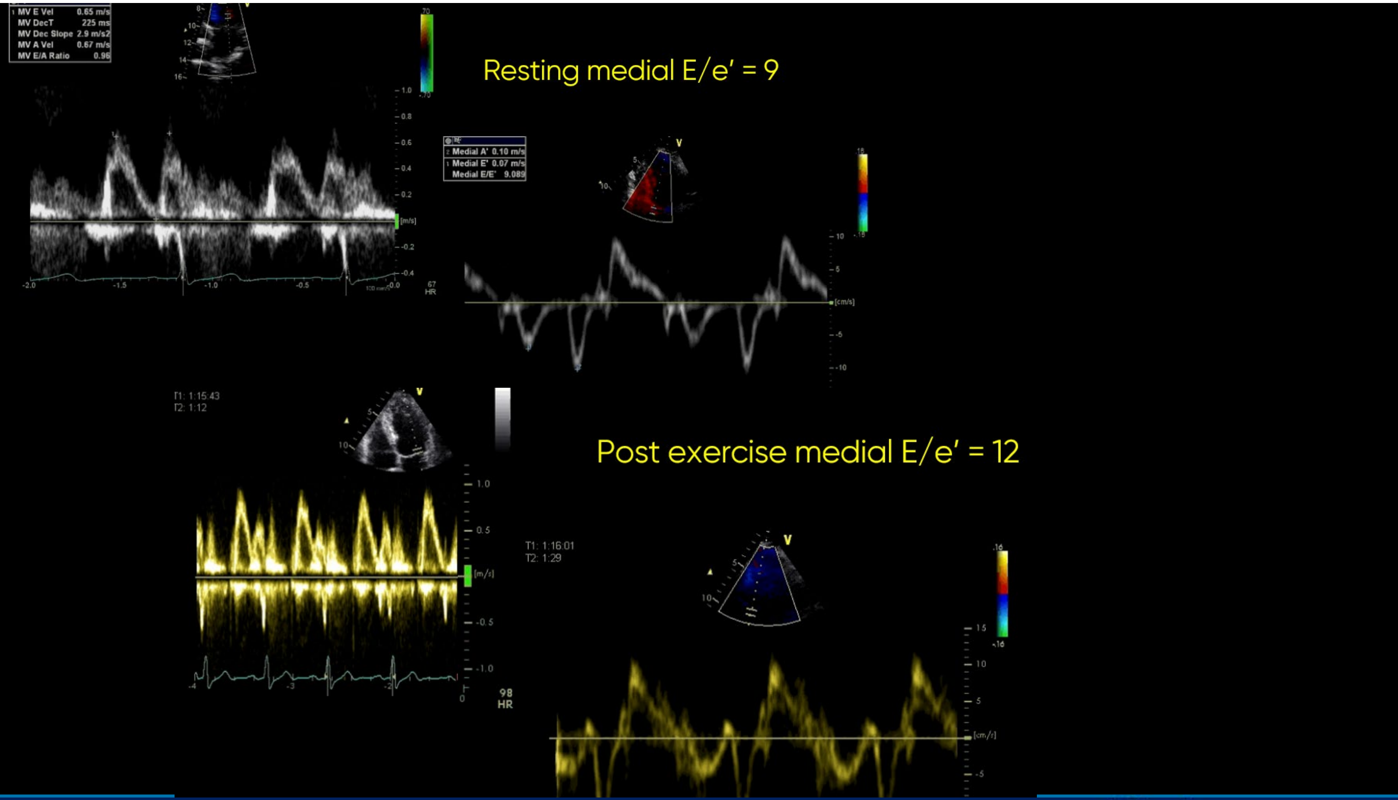


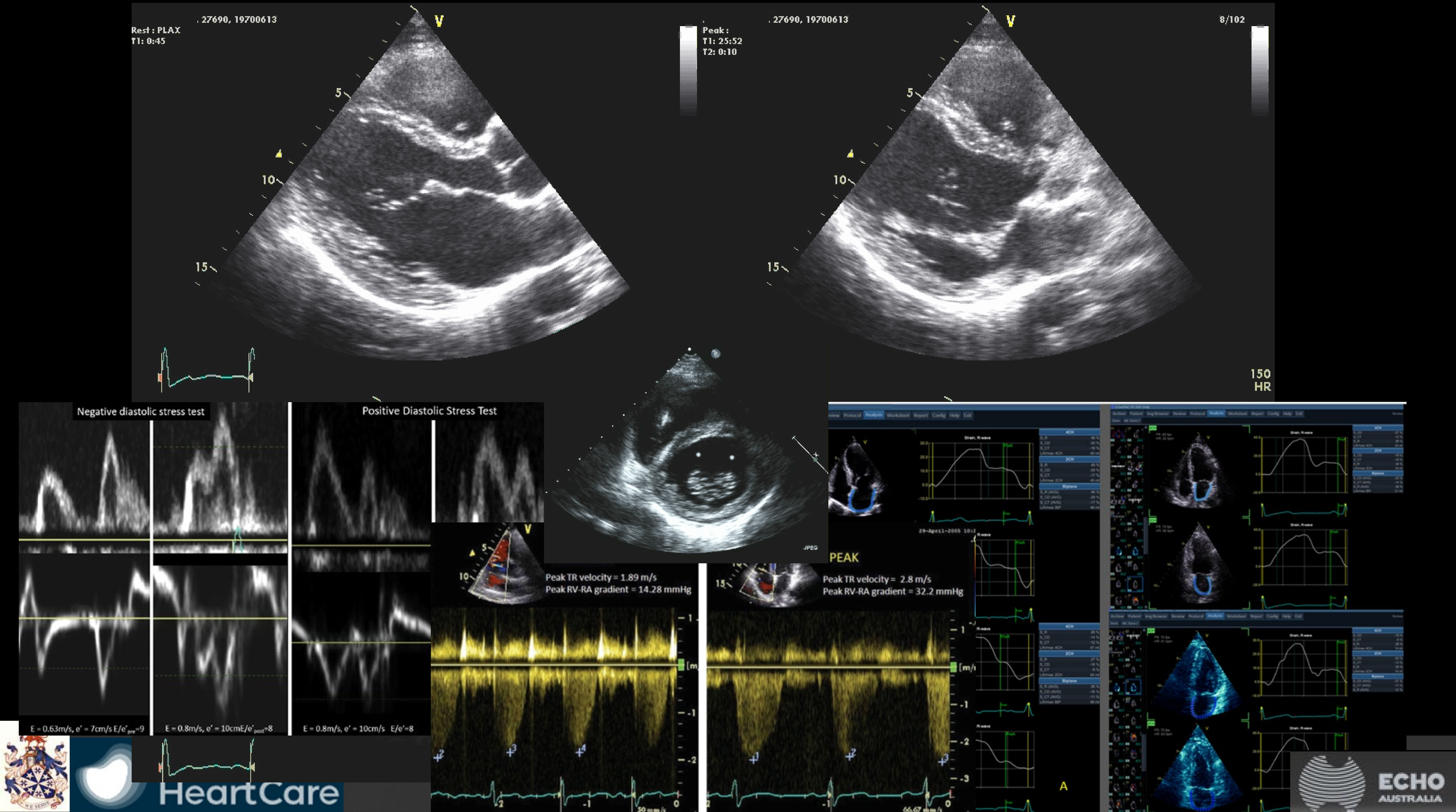


Diastolic stress echocardiography

- What diastolic stress echocardiography is and how to do it
  - The value and meaning of this form of testing
    - Very valuable part of cardiac assessment







Rest : PLAX
T1: 0:45
. 27690, 19700613
Peak :
T1: 25:52
T2: 0:10
. 27690, 19700613
8/102
150
HR
Negative diastolic stress test
Positive Diastolic Stress Test
E = 0.63m/s, e' = 7cm/s E/e'pre=9
E = 0.8m/s, e' = 10cmE/e'post=8
E = 0.8m/s, e' = 10cm/s E/e'=8
Peak TR velocity = 1.89 m/s
Peak RV-RA gradient = 14.28 mmHg
PEAK
Peak TR velocity = 2.8 m/s
Peak RV-RA gradient = 32.2 mmHg
HeartCare
ECHO
AUSTRALIA