How to spot HFpEF in patients with heart valve disease?

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Why this topic?

- ❑ Heart Valve Clinic – exercise echocardiography routinely
- ❑ Exercise echocardiography: in patients with discordance between symptoms and valve disease severity

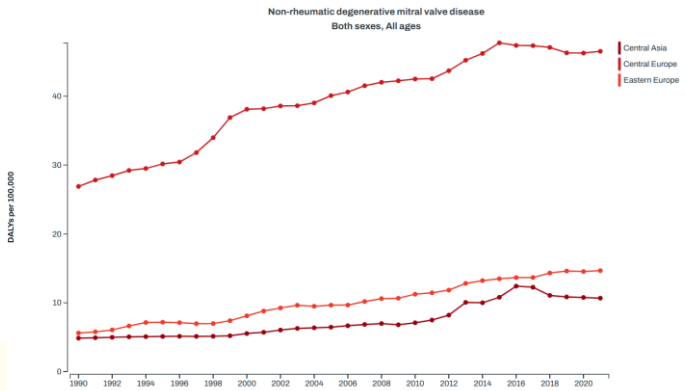
> Exercise echocardiography helps to identify the cause of dyspnoea, unveil symptoms in apparently asymptomatic patients, identifies dynamic changes of VHD severity, and can contribute to refinement of the indication for an intervention, especially for AS and mitral regurgitation (MR).[52]
>
> ESC Guidelines 2025

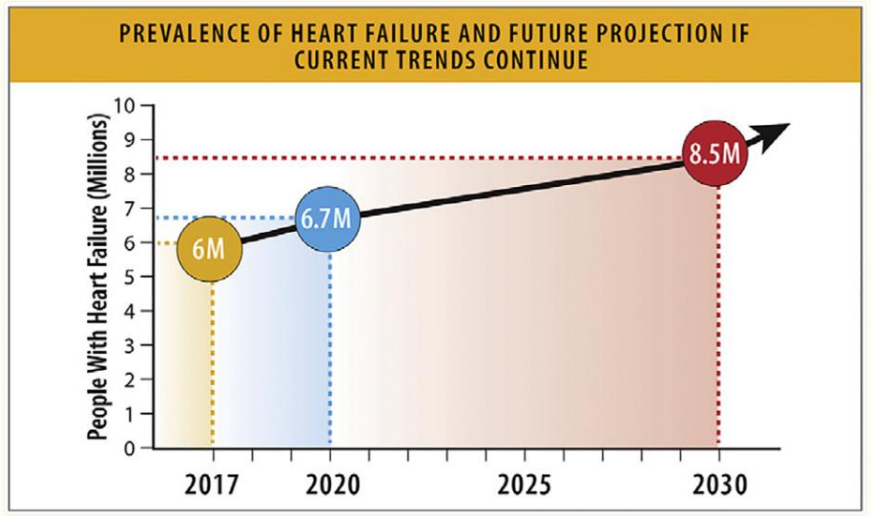
- ❑ More and more patients with moderate AS or MR , preserved LVEF that were really symptomatic (self reported symptoms, congestion signs, objective signs of heart failure during exercise testing)
- ❑ Can unrecognized HFpEF be responsible for this?

The prevalence and incidence of HF and non rheumatic HVD is increasing world wide

Prevalence of Aortic Valve Disease

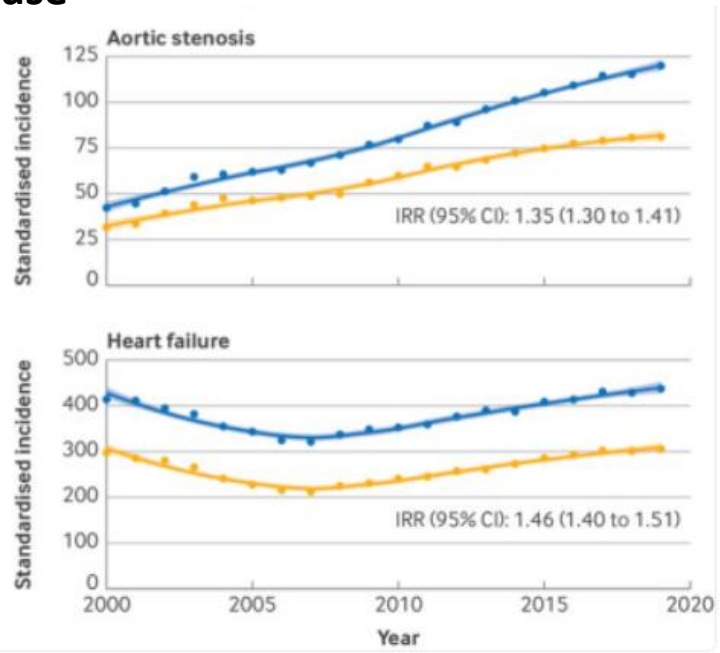
Prevalence of Degenerative MV Disease





Bosak et al. J Card Fail 2023

50% of HF is HFrEF
50% is HFpEF

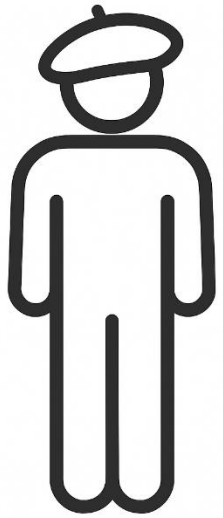


Data from UK, Conrad et al. BMJ 2024

More and more patients with moderate AS or MR and HFpEF will be seen in the future!

Clinical Case…

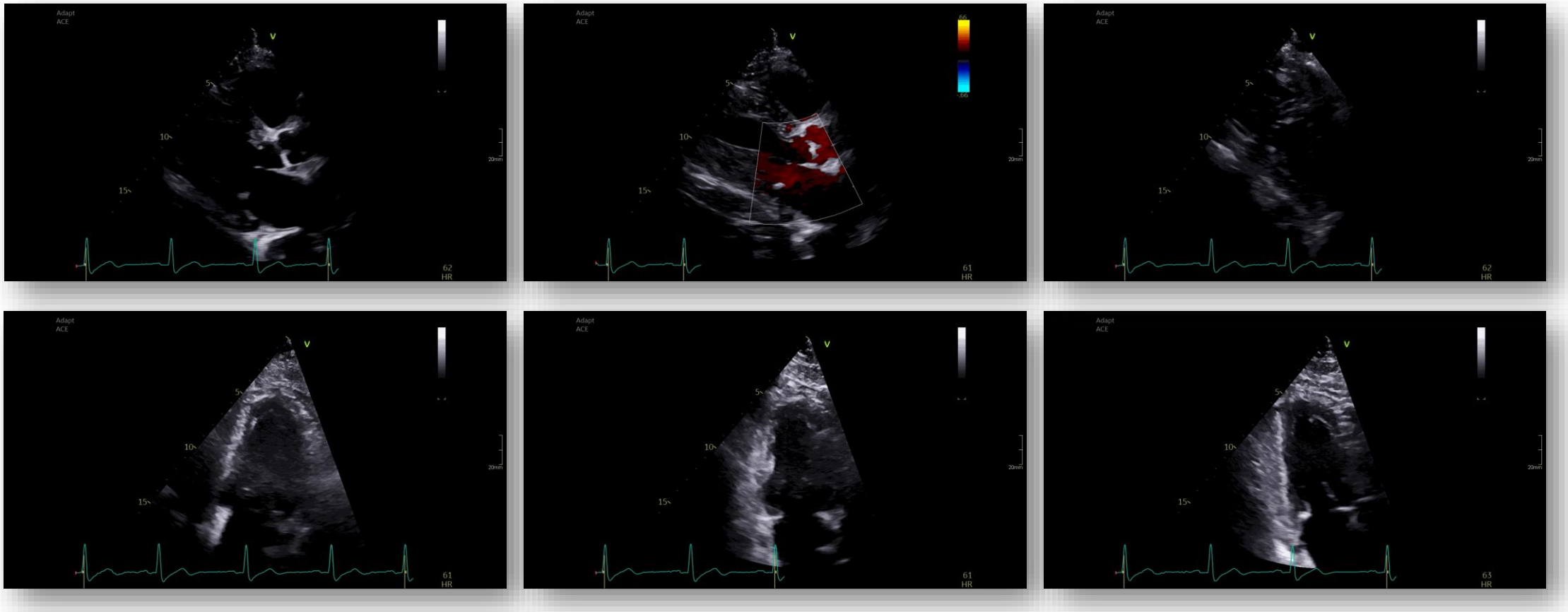
- ✓ Mr. M, 82 years old sedentary male
- ✓ 1, 78 m and 100 kg, BMI = 31.6, BSA =2.1 m^2
- ✓ Exercise induced dyspnoea
- ✓ CABG 10 years ago, LIMA + LAD, RIMA + RCA, coronary angiography 2 years ago ok
- ✓ Treated HTN and dyslipidemia
- ✓ Stable CKD
- ✓ Moderate AS, preserved LVEF



Mr M.

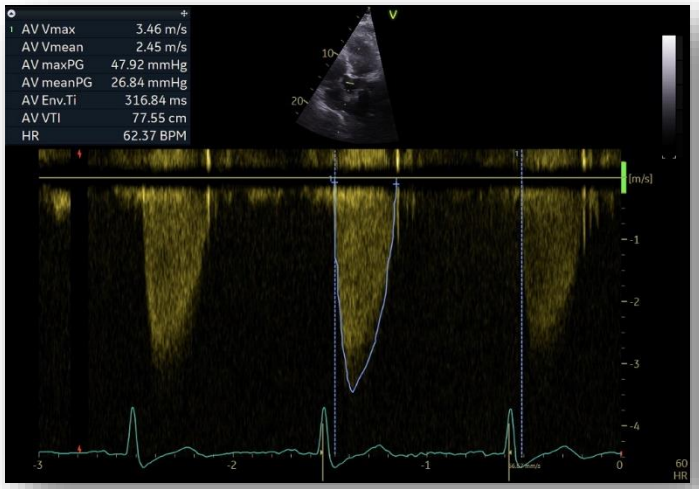
- ✓ No signs of congestion
- ✓ ECG in SR, no changes
- ✓ 12 g/dl Hb
- ✓ Normal K and Na
- ✓ 1.7 mg/dl creatinine, stable
- ✓ LDL 50 mg/dl
- ✓ TSH normal
- ✓ Tn levels normal
- ✓ No info on NT pro BNP

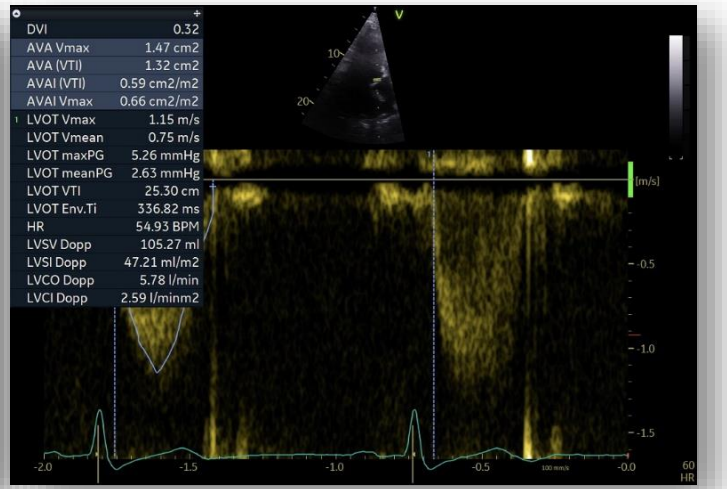
TTE of Mr. M

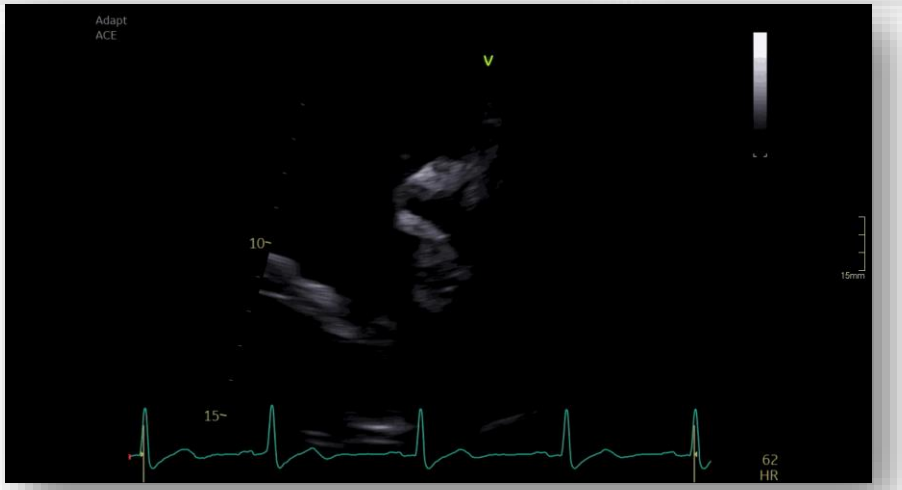


LVH, preserved LVEF, no MR, mild inferior wall hypokinesis, a calcified AV but no AR

TTE of Mr. M

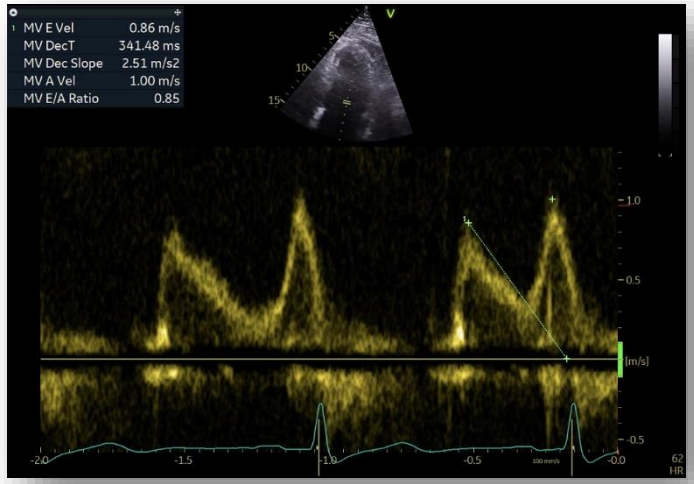


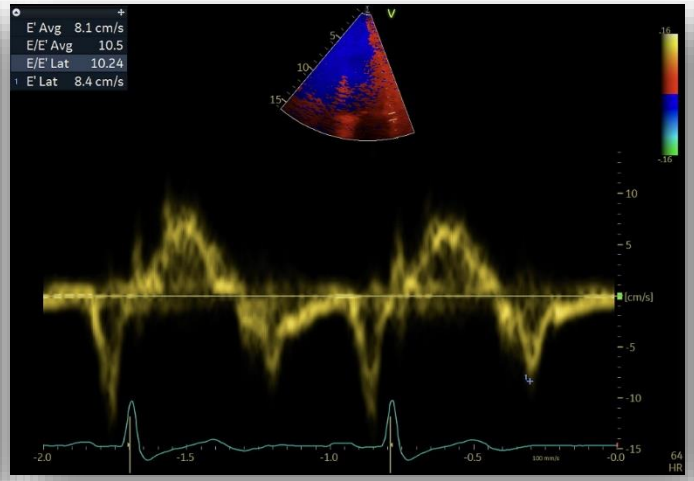


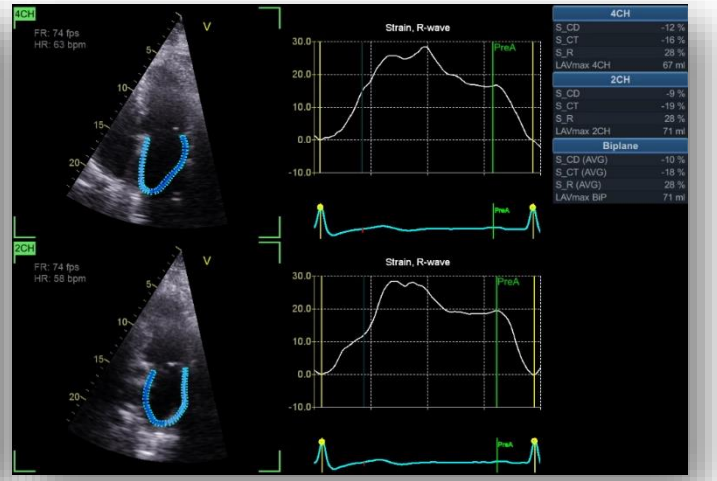


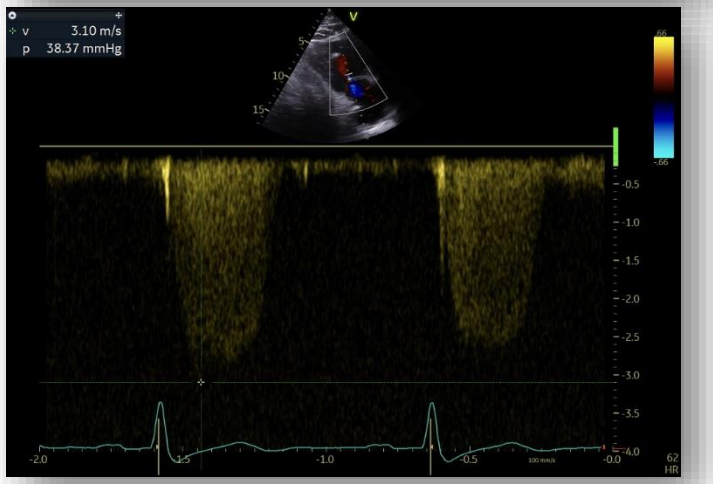
Moderate calcific AS (V max 3.5, AVA= 1.3 cm^2)
Valves looks ‘good’ in 2D (no severe calcification by echo)

TTE of Mr. M – diastolic function at rest









E/A = 0.85

Lat e’ = 8 cm/S

E/e’ = 10.5 (grey zone)

LAVi =33 ml/m²

TR V max 3.1 m/s

Does he have diastolic dysfunction?

Does the TTE explain his symptoms?

Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography and for Heart Failure With Preserved Ejection Fraction Diagnosis: An Update From the American Society of Echocardiography

Nagueh et al. JASE 2025

Mr. M

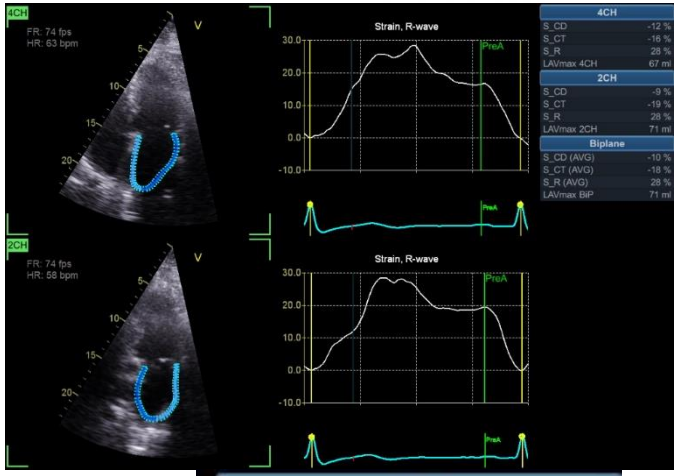
LV Diastolic Function Grading & LAP Estimation

Except in
MAC, MR, MS¶
Atrial Fibrillation
LVAD
Non-cardiac PH
HTX
Pericardial constriction

1. Reduced e' velocity: septal ≤6 or lateral ≤ 7 or average ≤ 6.5 cm/s *
2. Increased E/e': septal ≥ 15 or lateral ≥ 13 or average ≥ 14
3. Increased TR velocity ≥ 2.8 m/s or PASP ≥ 35 mm Hg

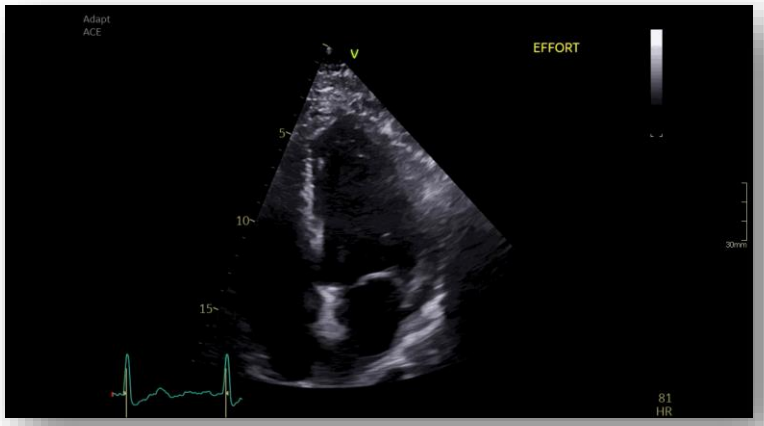
- All normal → Normal LAP → Normal DF
- Reduced e' only → E/A≤ 0.8 → Normal LAP → Grade 1
- Reduced e' only → E/A > 0.8 → Pulmonary Vein S/D ≤0.67 or LARS ≤ 18% or LAVi > 34 mL/m² (Alternatively IVRT ≤ 70 ms; If none available or reliable use Supplemental methods†)
- Increased TR/PASP only or Increased E/e' only or Any 2 abnormal variables → Pulmonary Vein S/D ≤0.67 or LARS ≤ 18% or LAVi > 34 mL/m² (Alternatively IVRT ≤ 70 ms; If none available or reliable use Supplemental methods†)
- Pulmonary Vein S/D ≤0.67 or LARS ≤ 18% or LAVi > 34 mL/m² (Alternatively IVRT ≤ 70 ms; If none available or reliable use Supplemental methods†) → None → Normal LAP
- Pulmonary Vein S/D ≤0.67 or LARS ≤ 18% or LAVi > 34 mL/m² (Alternatively IVRT ≤ 70 ms; If none available or reliable use Supplemental methods†) → ≥1 present → Increased LAP
- 3 of the above → Increased LAP
- Increased LAP → E/A < 2 → Grade 2 (Mild/Mod ↑ LAP)
- Increased LAP → E/A ≥ 2 → Grade 3 (Marked ↑ LAP)
- Normal DF → If symptomatic → Diastolic Exercise Echo
- Grade 1 → If symptomatic → Diastolic Exercise Echo

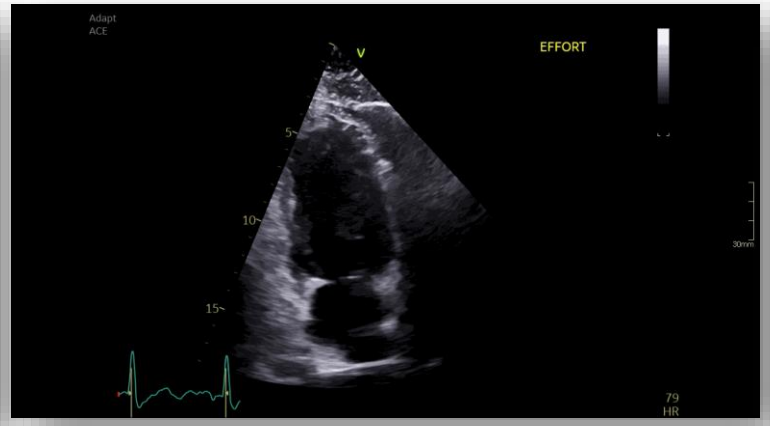
Figure 3 Algorithm for estimation of mean LAP for patients in sinus rhythm and who do not have severe primary MR, any degree of mitral stenosis (MS), or moderate or severe MAC. The algorithm should also not be applied to patients in atrial fibrillation, heart transplant (HTX) recipients, noncardiac PH, pericardial constriction or LV assist device (LVAD). *For annular e′ velocity, age-adjusted lower limits of normal values shown in Table 6 can be applied in place of the values shown in this figure. ¶The algorithm should also not be applied to patients with mitral valve repair, mitral valve replacement, or mitral-transcatheter edge-to-edge repair. *DF*, Diastolic function; *T*, PR end-diastolic velocity ≥ 2m/s, PA diastolic pressure ≥ 16 mm Hg, mitral inflow L-wave velocity ≥ 50 cm/s, Ar-A duration > 30 ms, and/or a decrease in mitral E/A ratio of ≥50% with Valsalva maneuver.

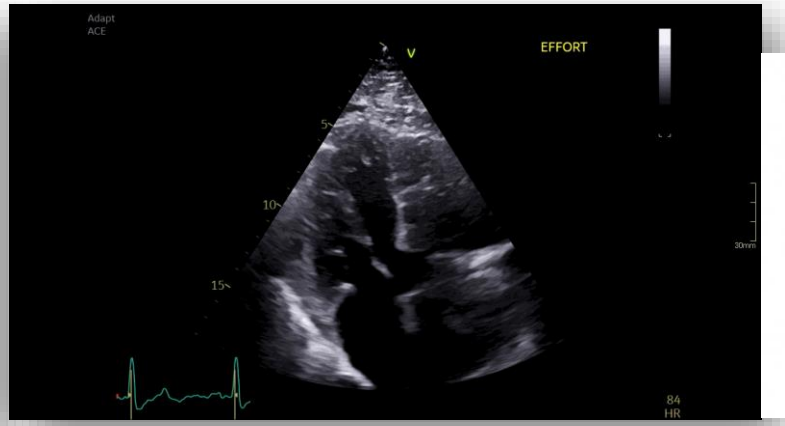


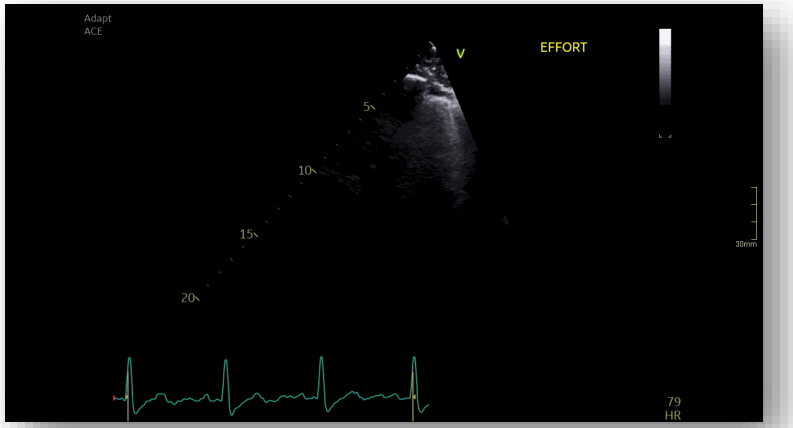
4CH	
S_CD	-12 %
S_CT	-16 %
S_R	28 %
LAVmax 4CH	67 ml
2CH	
S_CD	-9 %
S_CT	-19 %
S_R	28 %
LAVmax 2CH	71 ml
Biplane	
S_CD (AVG)	-10 %
S_CT (AVG)	-18 %
S_R (AVG)	28 %
LAVmax BiP	71 ml

Mr. M undergoes An Exercise Stress Echocardiography





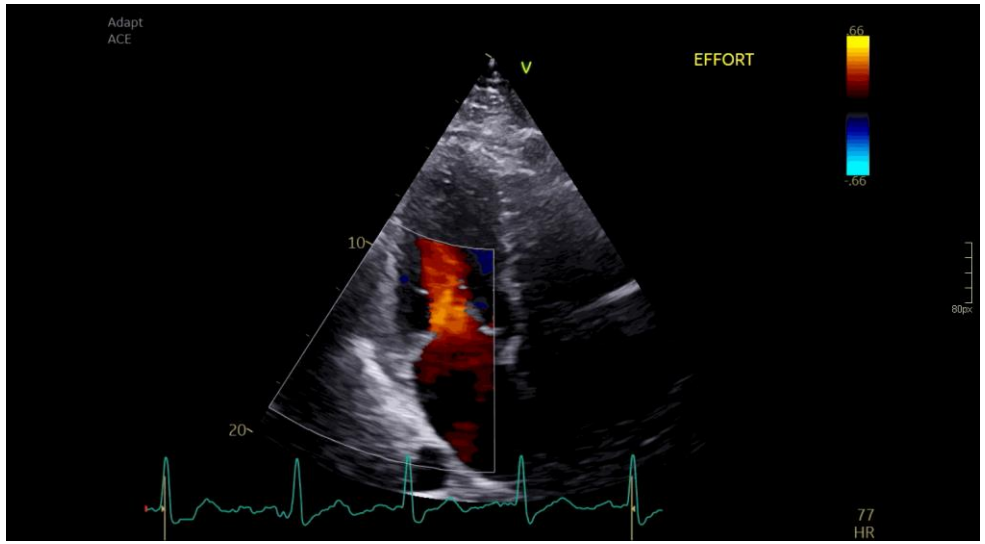


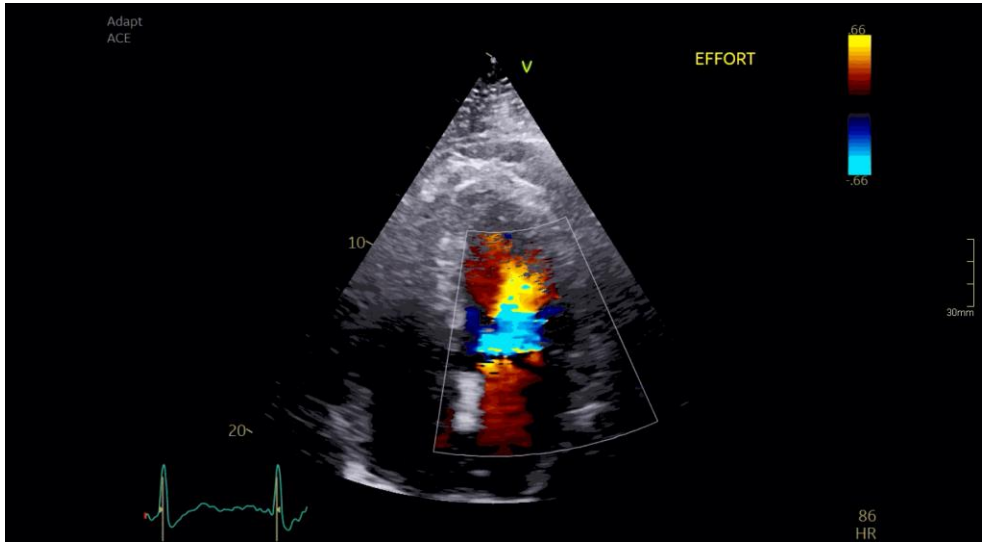


Exercise lung US

- 50 watts
- 80 bpm in RS
- No wall motion abnormality
- No drop in LVEF
- He is already a bit dyspnoeic

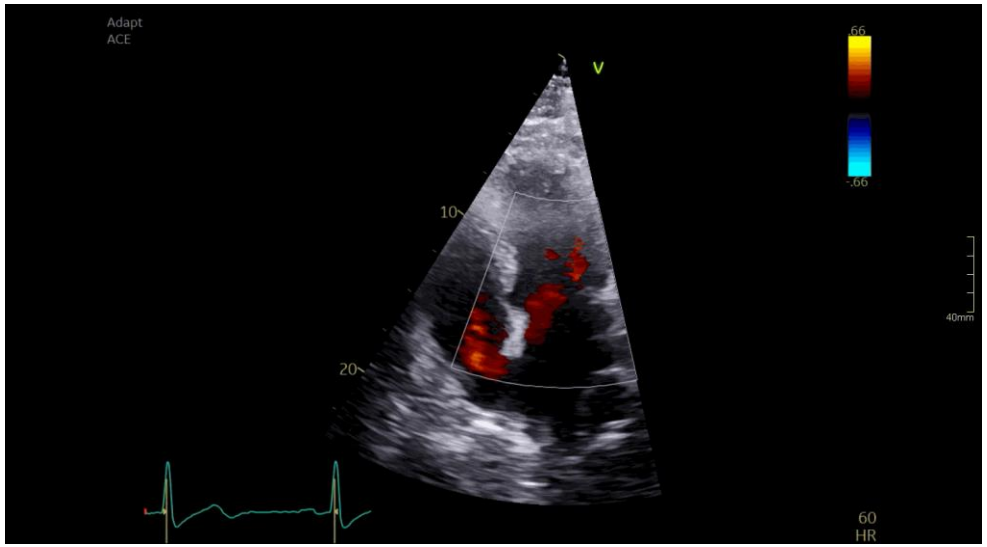
Mr. M undergoes An Exercise Stress Echocardiography





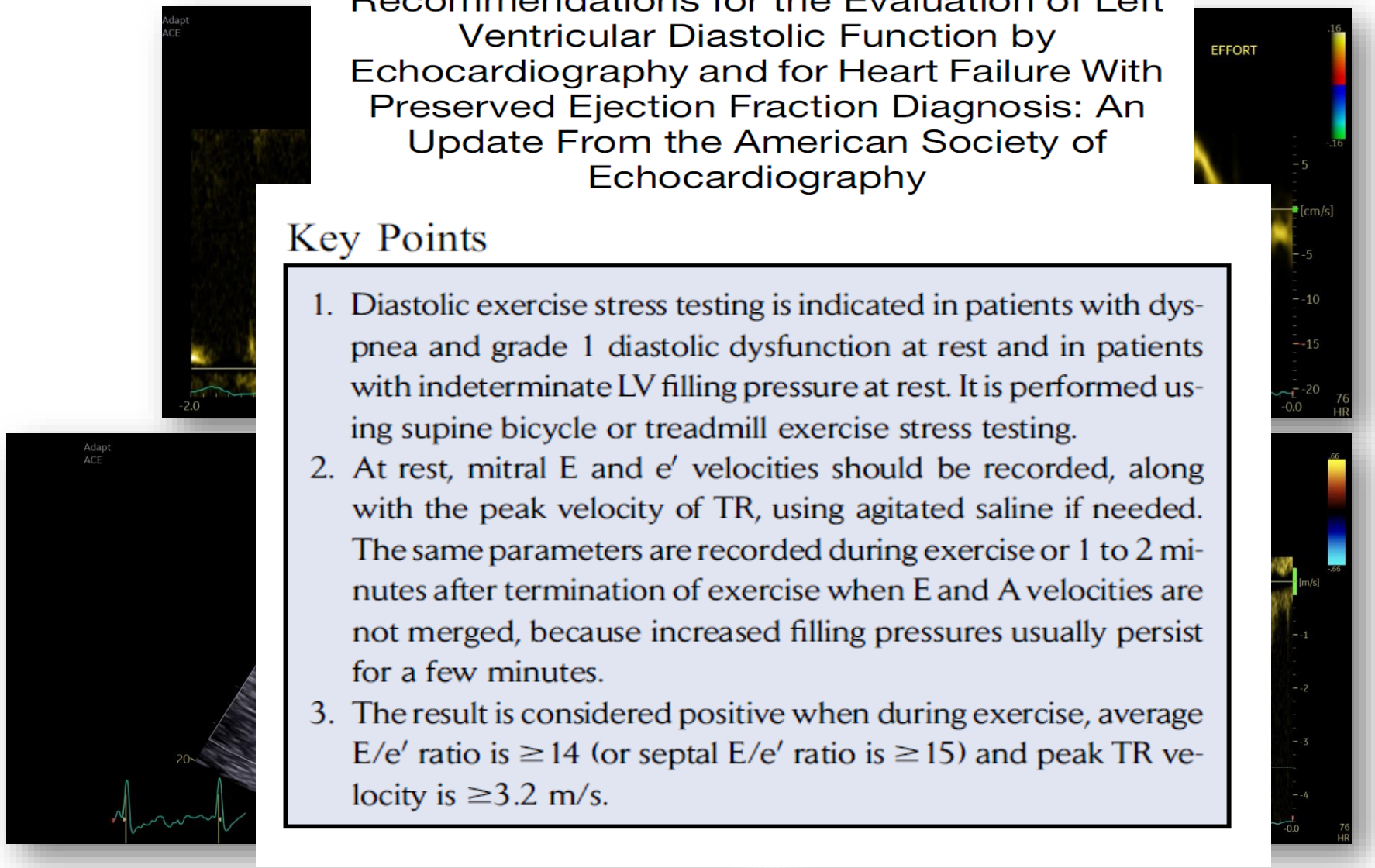
Exercise

- Mild MR appears
- LA seems to dilate a bit?



Rest

Mr. M undergoes An Exercise Stress Echocardiography



Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography and for Heart Failure With Preserved Ejection Fraction Diagnosis: An Update From the American Society of Echocardiography

Key Points

1. Diastolic exercise stress testing is indicated in patients with dyspnea and grade 1 diastolic dysfunction at rest and in patients with indeterminate LV filling pressure at rest. It is performed using supine bicycle or treadmill exercise stress testing.
2. At rest, mitral E and e′ velocities should be recorded, along with the peak velocity of TR, using agitated saline if needed. The same parameters are recorded during exercise or 1 to 2 minutes after termination of exercise when E and A velocities are not merged, because increased filling pressures usually persist for a few minutes.
3. The result is considered positive when during exercise, average E/e′ ratio is ≥14 (or septal E/e′ ratio is ≥15) and peak TR velocity is ≥3.2 m/s.

Nagueh et al. JASE 2025

Average e’ = 6.3 cm/s
Average E = 1 m/s
Exercise E/e’ = 15.8
TTG = 49 mmHg at 50 watts
PAPs = 59 mmHg at 50 watts

Mr. M undergoes An Exercise Stress Echocardiography

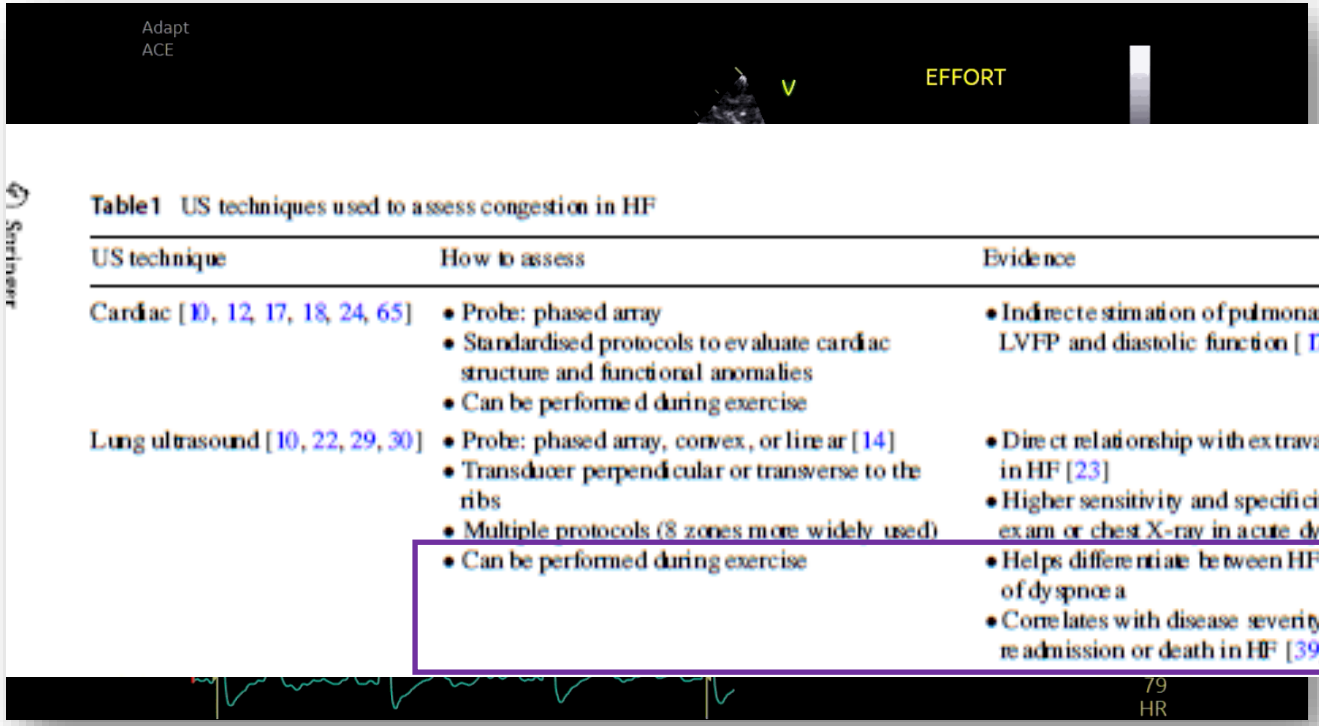


Table 1 US techniques used to assess congestion in HF

US technique	How to assess	Evidence	Limitations
Cardiac [10, 12, 17, 18, 24, 65]	• Probe: phased array • Standardised protocols to evaluate cardiac structure and functional anomalies • Can be performed during exercise	• Indirect estimation of pulmonary pressures, LVFP and diastolic function [17, 18]	• Poor acoustic windows (e.g., obese patients, lung disease, *et cetera*) • Pressures are indirectly estimated (limited accuracy compared to RHC) [12]
Lung ultrasound [10, 22, 29, 30]	• Probe: phased array, convex, or linear [14] • Transducer perpendicular or transverse to the ribs • Multiple protocols (8 zones more widely used) • Can be performed during exercise	• Direct relationship with extravascular lung water in HF [23] • Higher sensitivity and specificity than physical exam or chest X-ray in acute dyspnoea [28] • Helps differentiate between HF and other causes of dyspnoea • Correlates with disease severity and risk of readmission or death in HF [39]	• B-lines distribution is influenced by patient position and pleural effusions • B-lines may also be present in non-cardiogenic pulmonary oedema and interstitial lung disease [30] • Obesity is associated with a low number of B-lines

B lines +
Objective HF symptoms (interstitial lung oedema)

Diastolic dysfunction very likely to explain his symptoms in the presence of only moderate AS, no inducible ischemia, no significant dynamic MR

Di Fiore et al. Internal and Emergency Medicine 2025

Low threshold to suspect HFpEF in moderate VHD + symptoms

Use of H2FPEF and HFA-PEFF scores

- Used to determine the likelihood that HFpEF is the underlying etiology in a patient complaing of dyspnea

A

H_2FPEF

H_2	**H**eavy (BMI >30 kg/m²) On ≥2 anti**H**ypertensives	2 1
F	Atrial **F**ibrilllation	3
P	**P**ulmonary hypertension (PASP >35 mm Hg on Doppler echocardiography	1
E	**E**lder (age >60 years)	1
F	**F**illing pressure (E/e' >9 on Doppler echocardiography)	1

≥6 points: highly diagnostic of HFpEF

B

HFA-PEFF Score

P **Pretest assessment**

- Symptoms and/or signs of heart failure
- Comorbidities/risk factors
- Standard echocardiography

E **Echo and natriuretic peptide score**

- Comprehensive echocardiography
- Natriuretic peptides

F1 **Functional testing in case of uncertainty**

- Diastolic stress test (exercise echocardiography)
- Invasive hemodynamic measurements

F2 **Final etiology**

- Special imaging (CMR, CT, PET, scintigraphy)
- Biopsies
- Genetic testing

Functional
Septal e' <7 cm/s or
Lateral e' <10 cm/s or
Average E/e' ≥15 or
TR velocity >2.8 m/s
Average E/e' 9-14 or
GLS <16%

Morphological
LAVI >34 mL/m² or
LVMI ≥149/122 g/m² (M/F) and
RWT >0.42
LAVI 29.34 or
LVMI >115/95 g/m² (M/F) or
RWT >0.42 or
LV wall thickness ≥12 mm

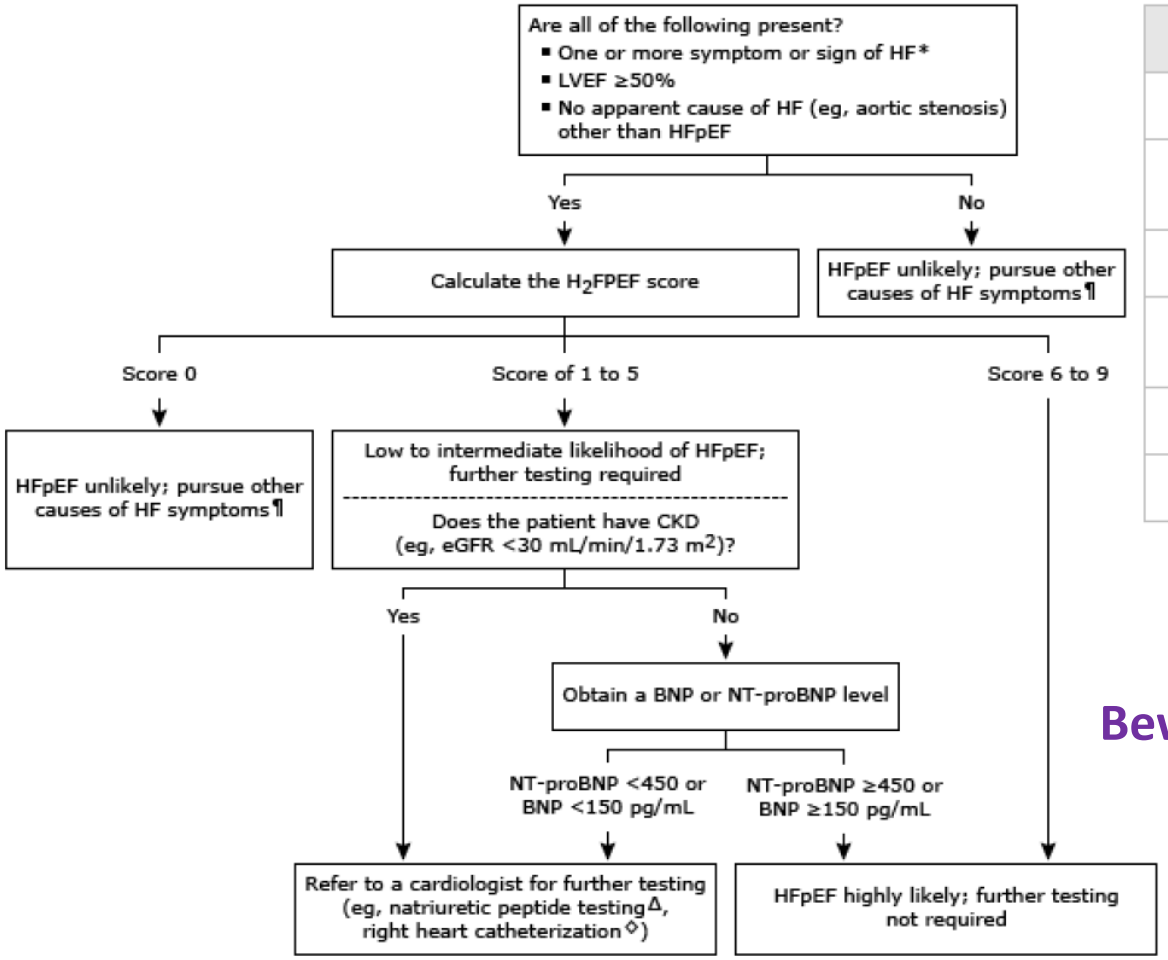
Biomarker (Sinus rhythm)
NT-proBNP >220 pg/mL or
BNP >80 pg/mL
NT-proBNP 125-220 pg/mL or
BNP 35-80 pg/mL

Biomarker (Atrial Fibrillation)
NT-proBNP >660 pg/mL or
BNP >240 pg/mL
NT-proBNP 365-660 pg/mL or
BNP 105-240 pg/mL

≥5 points: HFpEF
Major criteria (2 pts): bolded
Minor criteria (1 pt): non-bolded

Kittleson et al. JACC 2023

HFpEF detection algorithm

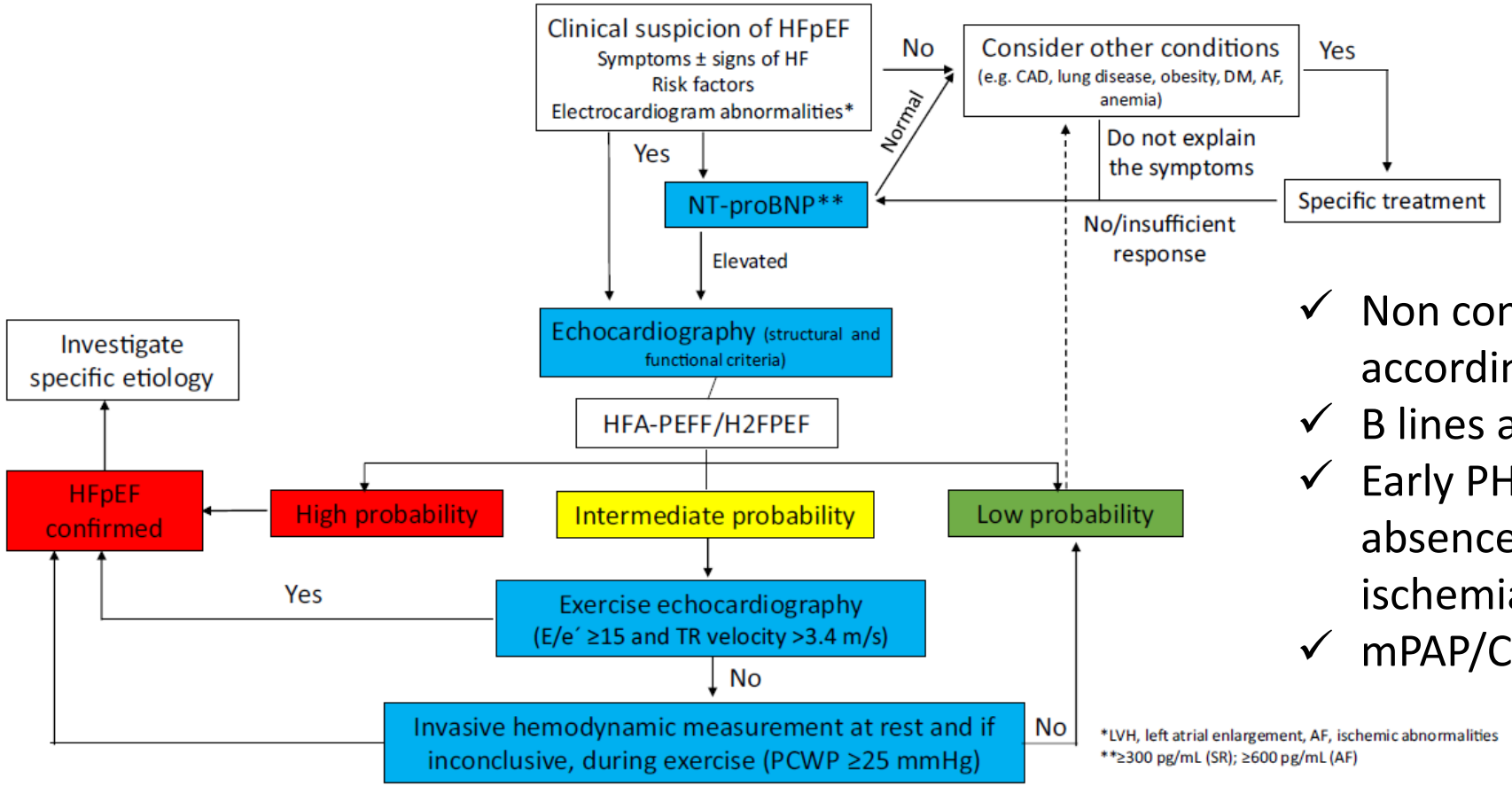


Calculation of the H_2FPEF score	
BMI ≥30 kg/m^2	2 points
Hypertensive or treated with ≥2 antihypertensive medications	1 point
Paroxysmal or persistent atrial fibrillation	3 points
Pulmonary artery systolic pressure >35 mmHg by echocardiography	1 point§
Age >60 years	1 point
E/e' >9 by echocardiography	1 point§

Beware of Obesity and Low BNP levels!

From UpToDate, https://www.uptodate.com/contents/search?search=H2FPEF

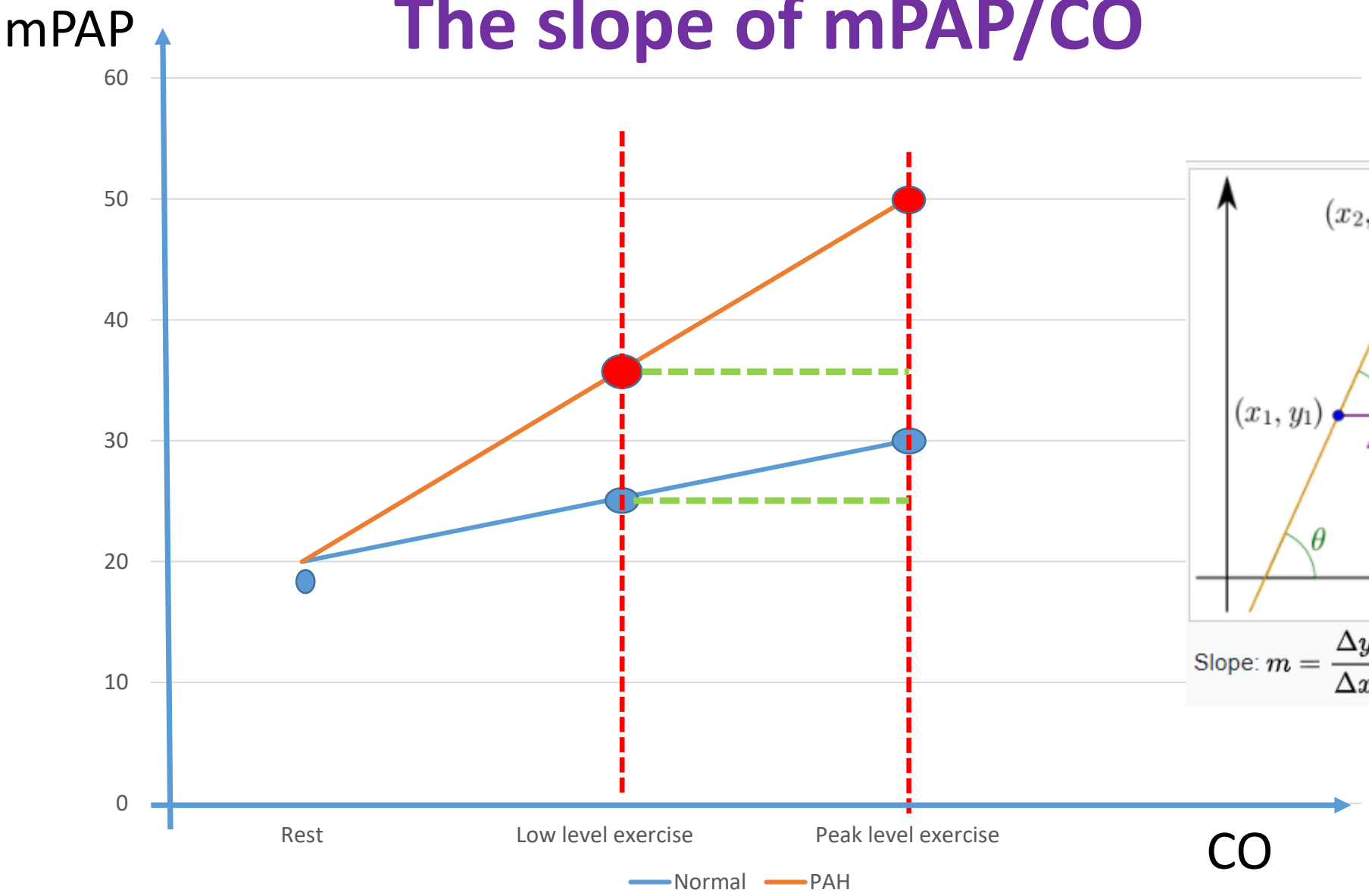
Exercise echocardiography in dyspnoea of undetermined cause

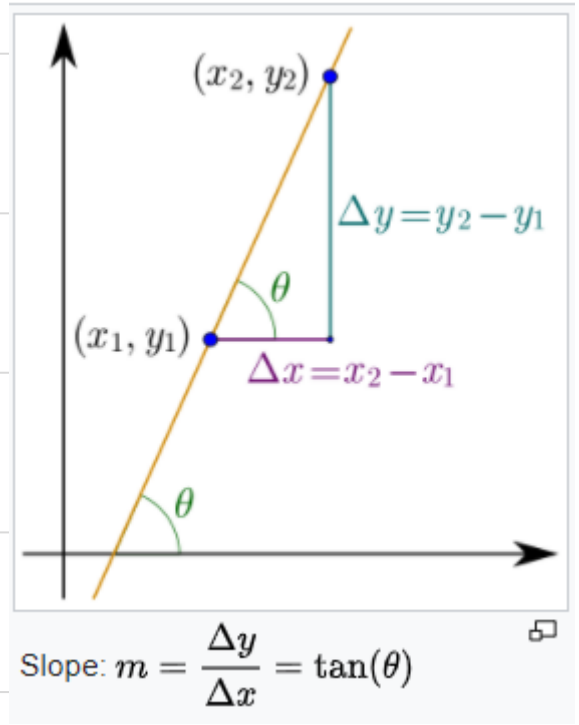


- ✓ Non conclusive exercise echo according to E/e’
- ✓ B lines assessment during ex helps
- ✓ Early PHT during exercise in the absence of dynamic MR/LV ischemia/dysfunction
- ✓ mPAP/CO slope helps

Think of an exercise echocardiography in definitely moderate AS and symptomatic patients!

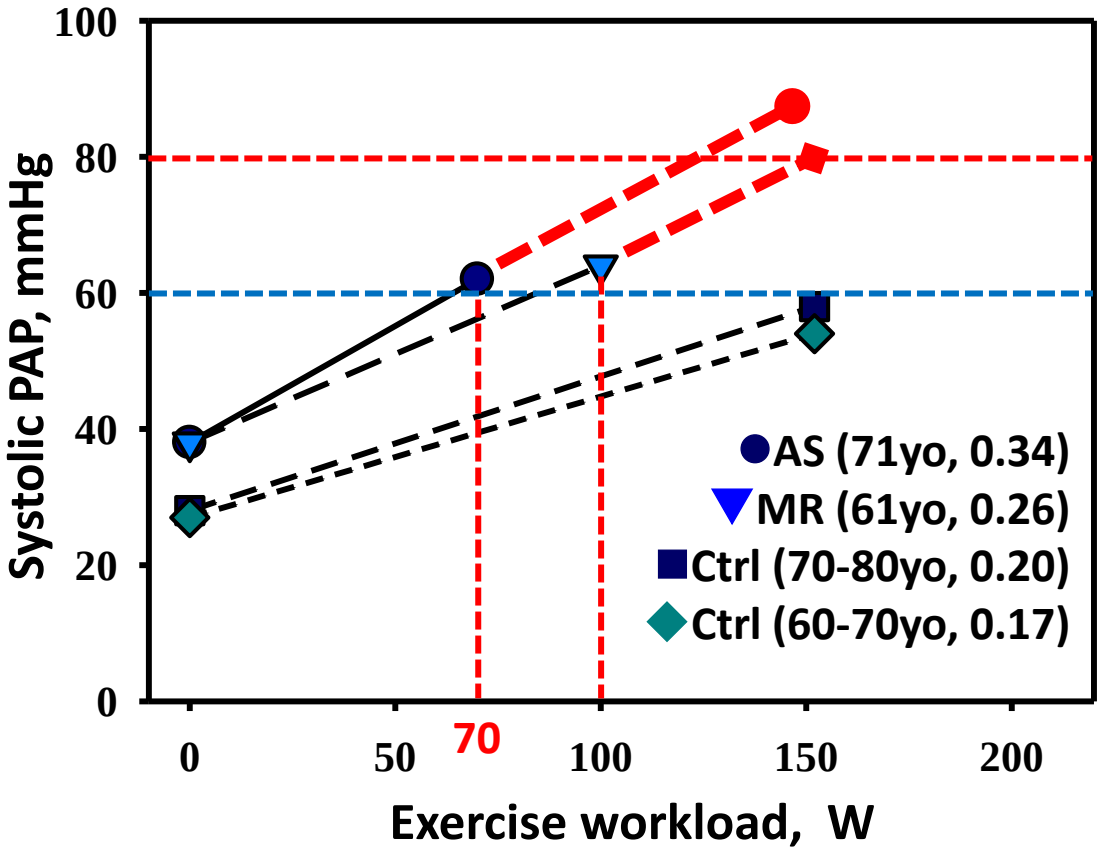
The slope of mPAP/CO





mPAP/CO slope = ΔmPAP/Δ CO *Naeije et al. Am J of Resp and Crit Care, 2013*

Ex-induced Changes in sPAP in Healthy



- Different maximal reached workload
- Different changes in sPAP slope
- Different kinetics
- Different physiological mechanisms

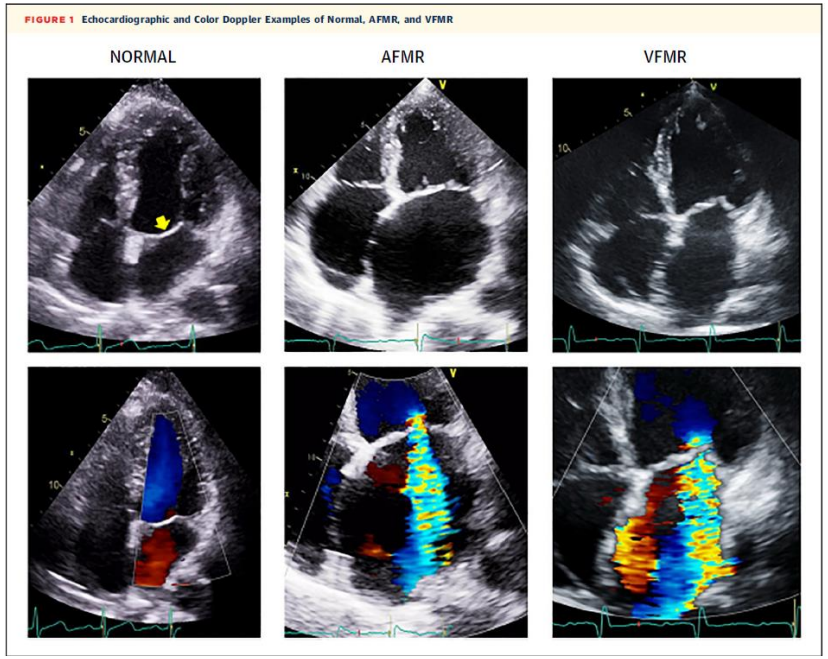
Courtesy prof Prof J Magne

HFpEF and moderate PMR

- ✓ Symptoms + moderate PMR (after confirmation by TOE or CMR when TOE inconclusive)
- ✓ H2FPEF and HFA-PEEF score to asses the likelihood of HFpEF
- ✓ **RF especially important to assess in MR + HFpEF** (small LV cavity, higher RF for RV < 60 mL)
- ✓ **Exercise echocardiography can be used to explain the cause of dyspnoea and hemodynamic burden of MR**:
  - ✓ Increase to severe MR during exercise
  - ✓ Diastolic function during exercise:
    - ✓ E/e' values less well validated
    - ✓ Rapid PHT at low level exercise with no changes in MR severity
    - ✓ Steep mPAP/CO slope > 3 mmHg/L/min with no changes in MR
- ✓ **Invasive hemodynamic assessment in symptomatic patients with truly moderate MR and suspicion of HFpEF?**

A-SMR and HFpEF

2 types of functional MR



Zoghbi el al. JACC Imaging 2022

- A-SMR as a distinctive form of SMR in Afib patients
- Afib frequent in HFpEF
- HFpEF patients with history of Afib may have A - SMR

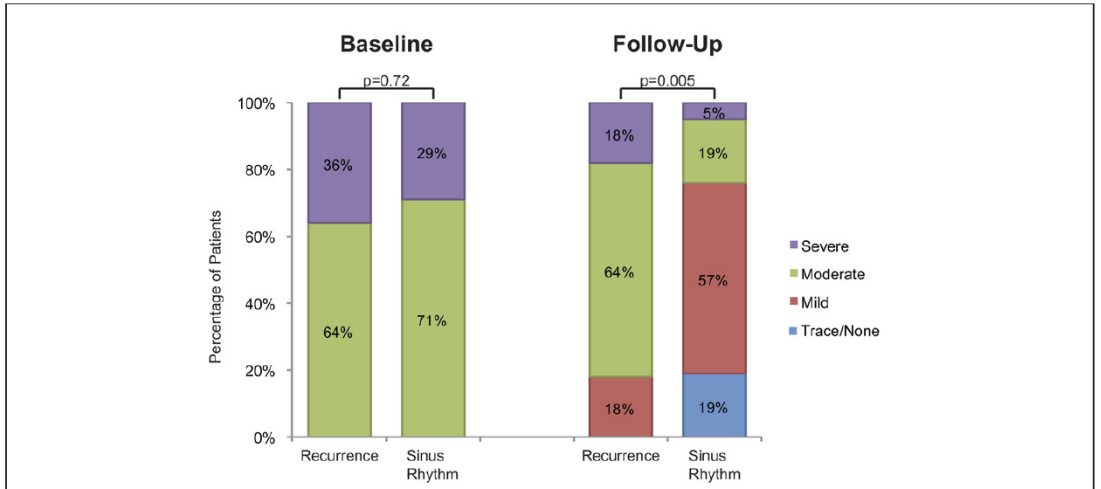


Figure 3 MR Severity at Baseline and Follow-Up

Patients are categorized by the rhythm at the time of follow-up as recurrence of atrial fibrillation or sinus rhythm. All patients had moderate or severe mitral regurgitation (MR) at initial echocardiogram. In patients in sinus rhythm at follow-up, only 24% still had moderate or severe MR.

	Rhythm at Follow-Up Echocardiogram (Recurrence n = 11, Sinus n = 21)*	Initial	Follow-Up	p Value (Initial vs. Follow-Up)
LA dimension, cm	Recurrence	4.72 ± 0.62	4.58 ± 0.64	0.15
	Sinus	4.31 ± 0.54†	4.16 ± 0.53	0.09
LAA, cm^2	Recurrence	25.5 ± 8.0	21.9 ± 4.0	0.04
	Sinus	20.7 ± 3.6†	18.5 ± 3.0	0.01
LA volume, cm^3	Recurrence	88.1 ± 50.4	66.4 ± 18.4	0.07
	Sinus	62.3 ± 17.8†	52.4 ± 12.7	0.02
LA volume index, cm^3/m^2	Recurrence	41.3 ± 22.0	31.2 ± 8.0	0.06
	Sinus	28.2 ± 7.6†	23.9 ± 6.0	0.02
Mitral annulus dimension, cm	Recurrence	3.59 ± 0.27	3.48 ± 0.34	0.29
	Sinus	3.41 ± 0.29	3.24 ± 0.31	0.02

Gertz et al. JACC 2011

What are the key echo findings in A-SMR?

This is the kind of patient in whom you should think of H2PEEF scores and of HFpEF!

1. LV “as normal as possible”
2. Leaflets move normally (Carpentier I)
3. Leaflets coapt edge to edge (annular dilatation)
4. MV annulus is dilated because LA is dilated and leaflet-to-area ratio of the MA is abnormal
5. Jet origin at the A2-P2 level and directed centrally

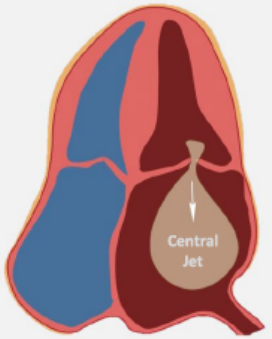
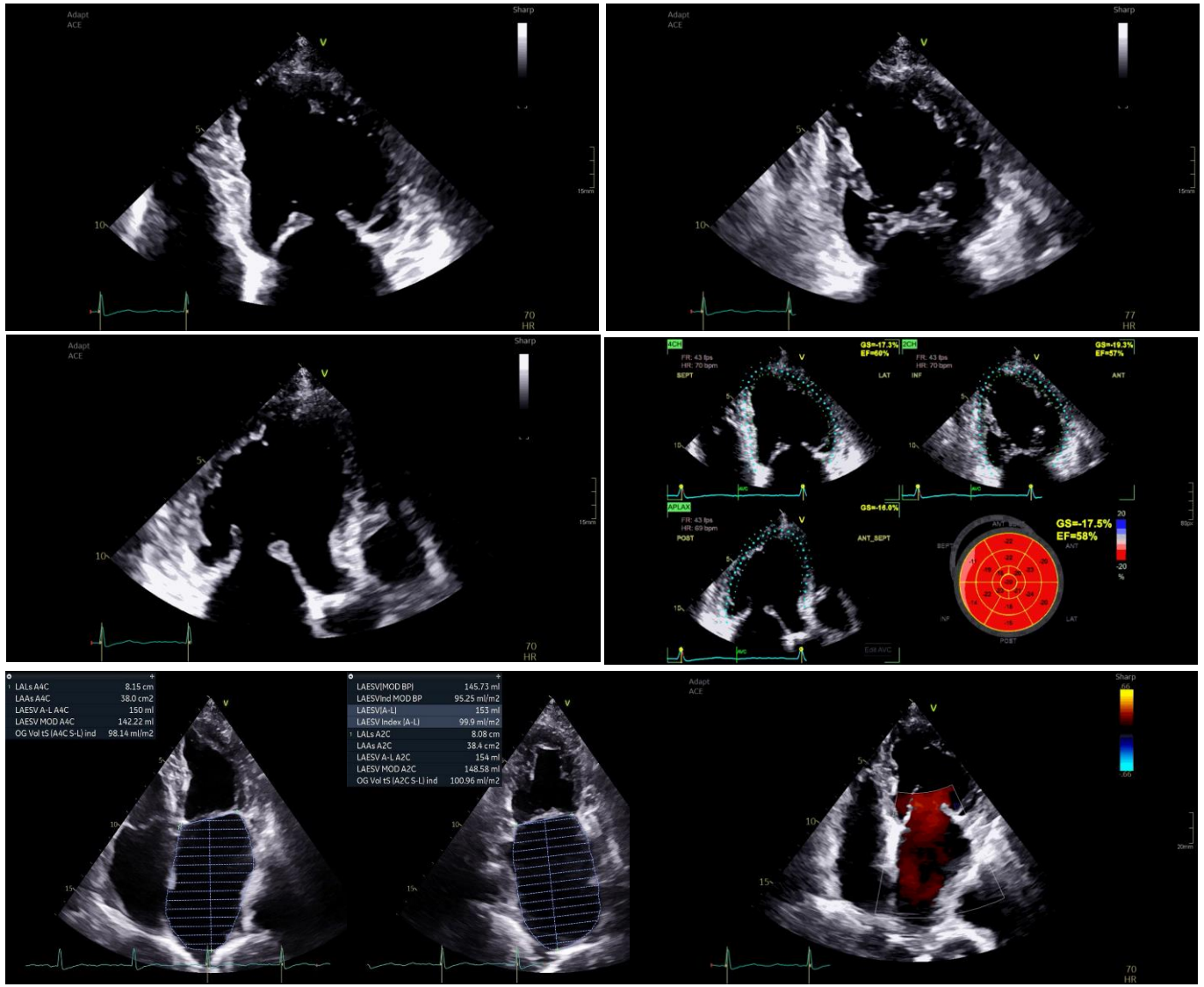
ATRIAL FUNCTIONAL MR	Left Ventricle
	LV volume ≤ 85 mL/m² male; ≤ 78 mL/m² female LV-EF ≥ 50% GLS may be impaired
	Left Atrium and Mitral Annulus
	LA ≥ 34 mL/m² Annulus > 35 mm (systole in PLAX) Annular flattening Systolic annular diameter to diastolic anterior leaflet > 1.3
	Mitral Leaflets
	Loss of systolic leaflet concavity towards the LV Leaflet coaptation at annular level Leaflet thickening

Image from Dhont et al. Curr Cardiol Reports 2025



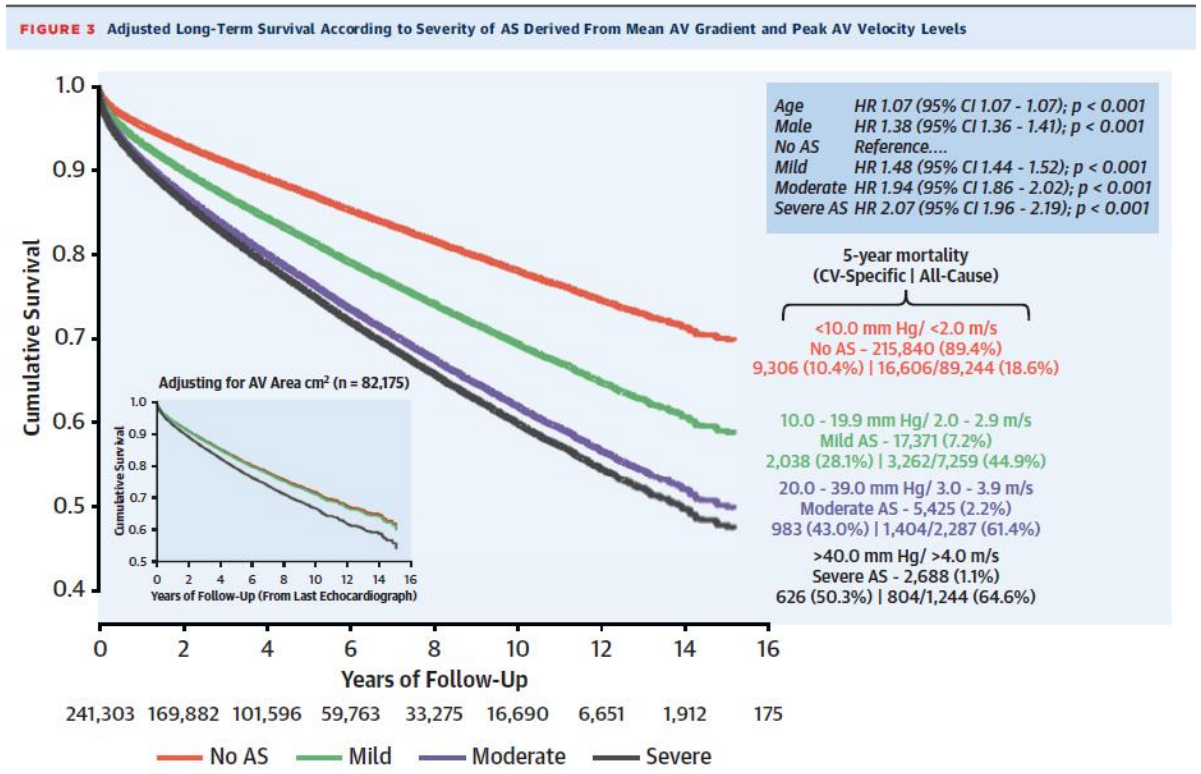
Treatment strategies for HFpEF and moderate VHD?

1. Aggressive treatment of cormorbidities (obesity, Afib, HTN etc)

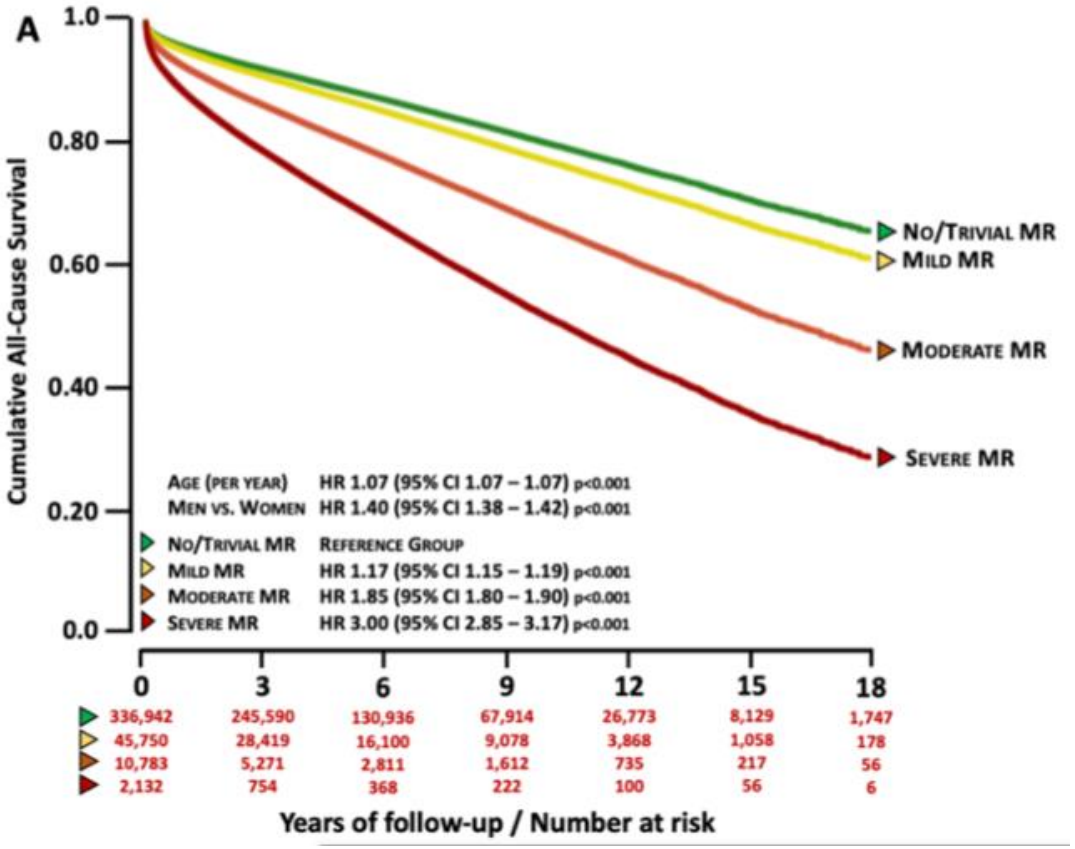
2. GDMT for HFpEF (SGLT2 inhibitors and MRAs + diuretics in congestive patients)

3. Should moderate AS/MR be treated if HFpEF (proven by Heart Catheterization) to be determined by further studies

Mortality in moderate AS and MR



Strange et al. JACC 2019



Playford et al. HEART 2025

Unrecognized and untreated HFpEF may account for higher mortality trends in moderate AS and MR?

Take home messages

1. Think of HFpEF in patients with moderate AS or MR that are truly symptomatic

2. Use clinical scores to assess the likelihood of HFpEF in such patients especially when they are old, obese, have Afib or are treated for hypertension

3. Use exercise echocardiography as a tool to understand the cause of dyspnoea (rules out LV ischemia, dynamic MR, may prove diastolic dysfunction, may prove lung congestion during exercise)

4. Aggressively treat comorbidities (Afib, obesity, HTN), give SGLt2 inhibitors and MRAs

5. Unrecognized and untreated HFpEF may account for higher mortality trends in moderate AS and MR?

6. Future studies will prove if treating moderate valve disease is beneficial /not