



# Diagnosing HFpEF : The Elephant in the room

Hawani Sasmaya Prameswari

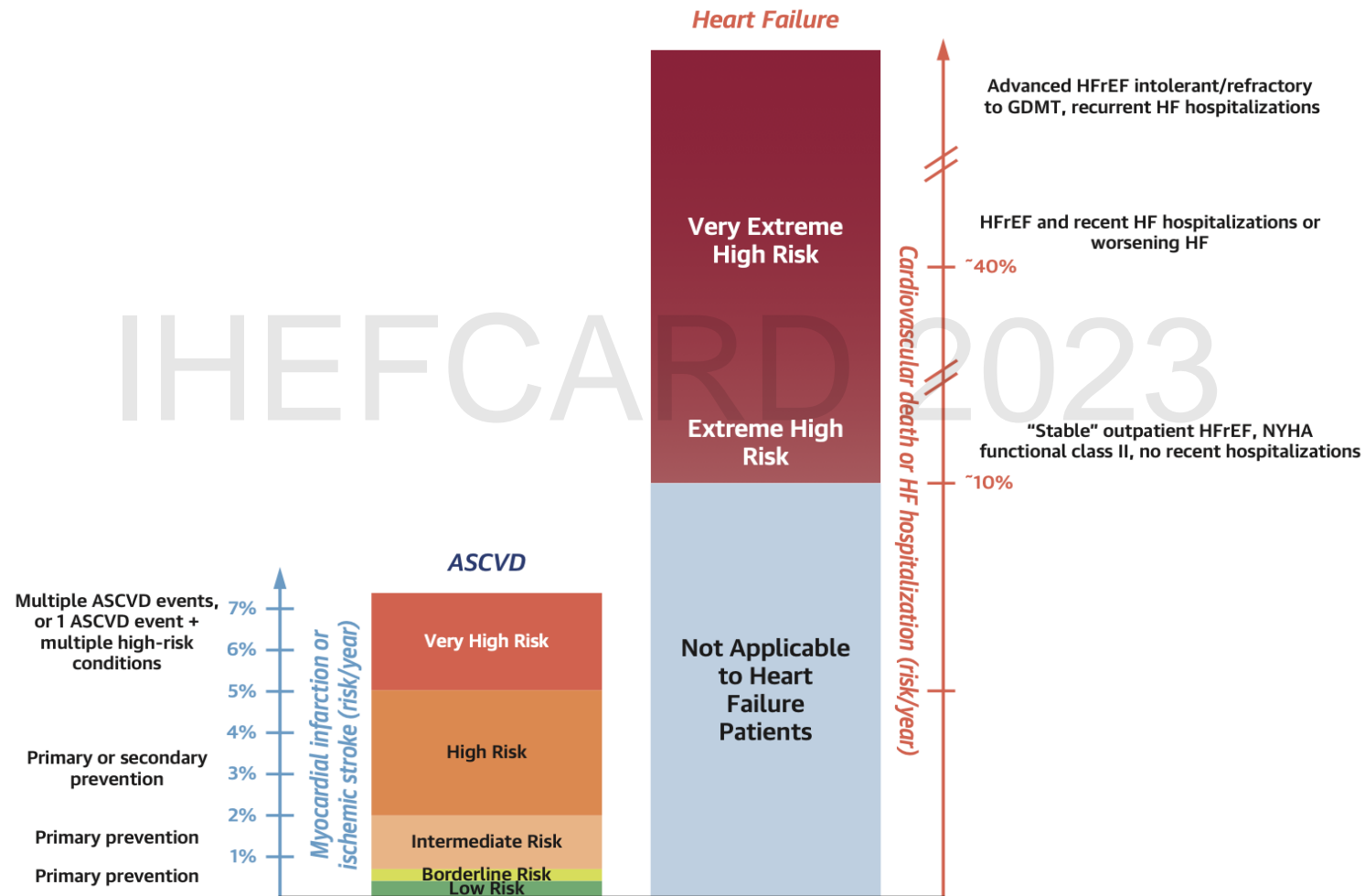
Indonesian Heart Failure and Cardiometabolic Working Group  
Indonesian Heart Association  
2023

# Disclosure

- This lecture has received financial support from PT. ZPT Indonesia
- I have the following financial relationship to disclose :  
Speaker honoraria from : Boehringer Ingelheim, Servier, Astra Zeneca, Otsuka, Novartis, Pfizer, Darya Varia, Menarini, Merc

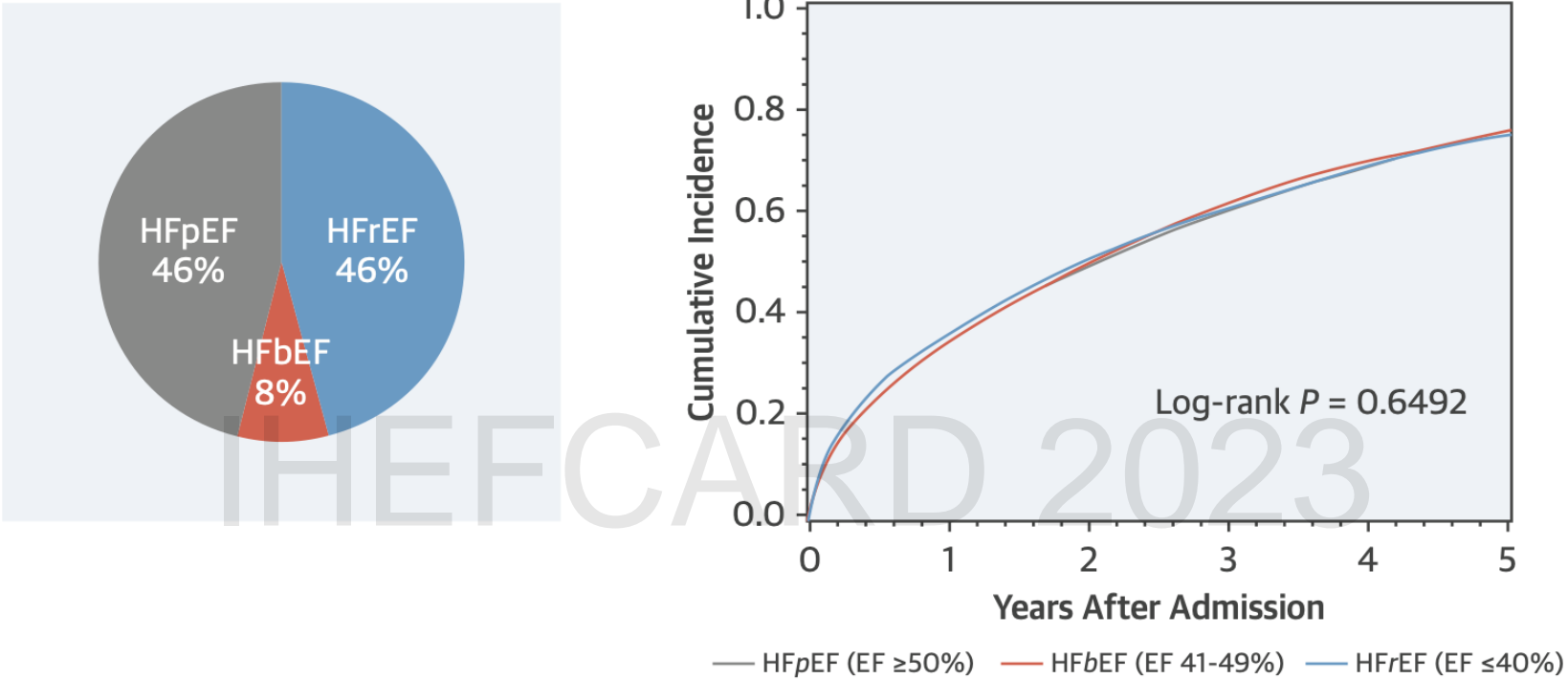
IHEFCARD 2023

# Mind-altering HF risk reality



Heart Failure

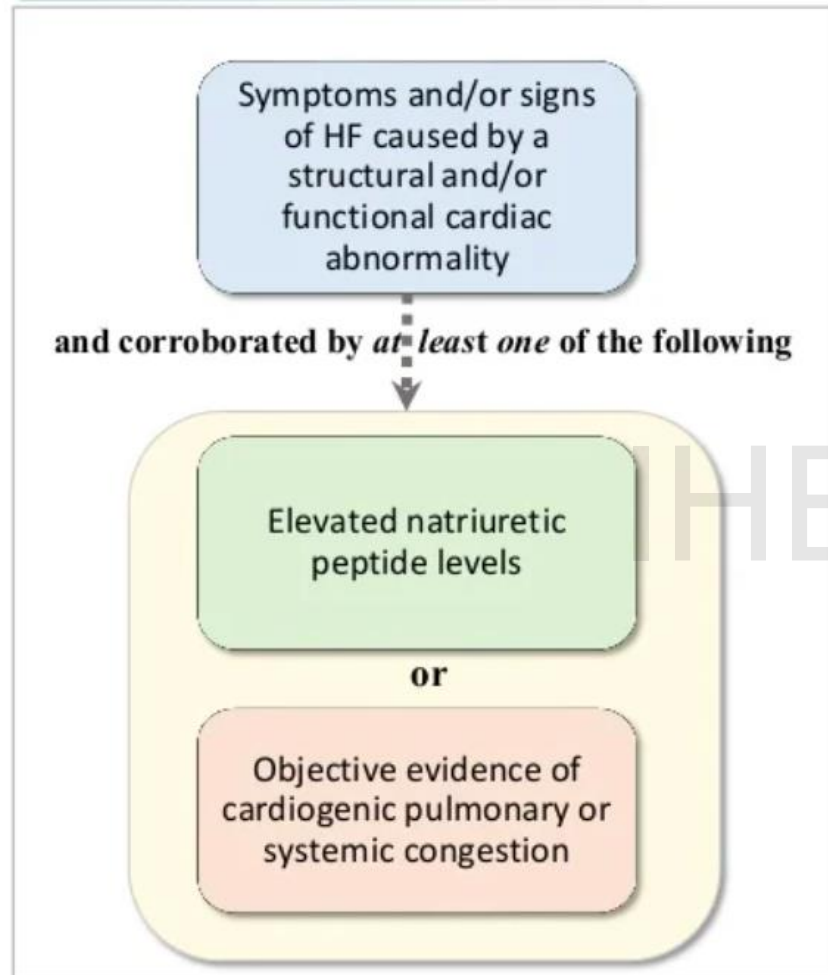
5-Year Mortality



Outcomes - 5-Year Event Rates (%)					
	Mortality	Readmission	CV Readmission	HF Readmission	Mortality/Readmission
HFrEF	75.3	82.2	63.9	48.5	96.4
HFbEF	75.7	85.7	63.3	45.2	97.2
HFpEF	75.7	84.0	58.9	40.5	97.3

Shah, K.S. et al. J Am Coll Cardiol. 2017;70(20):2476-86.

# Universal Definition of HF



HF is a clinical syndrome with current or prior

- **Symptoms and or signs caused by a structural and/or functional cardiac abnormality** (as determined by EF<50%, abnormal cardiac chamber enlargement, E/E' >15, moderate/severe ventricular hypertrophy or moderate/severe valvular obstructive or regurgitant lesion)
- **and corroborated by *at least one* of the following:**
  - elevated natriuretic peptide levels
  - objective evidence of cardiogenic pulmonary or systemic congestion by diagnostic modalities such as imaging (e.g. by CXR or elevated filling pressures by echocardiography) or hemodynamic measurement (e.g. right heart catheterization, PA catheter) at rest or with provocation (e.g. exercise)

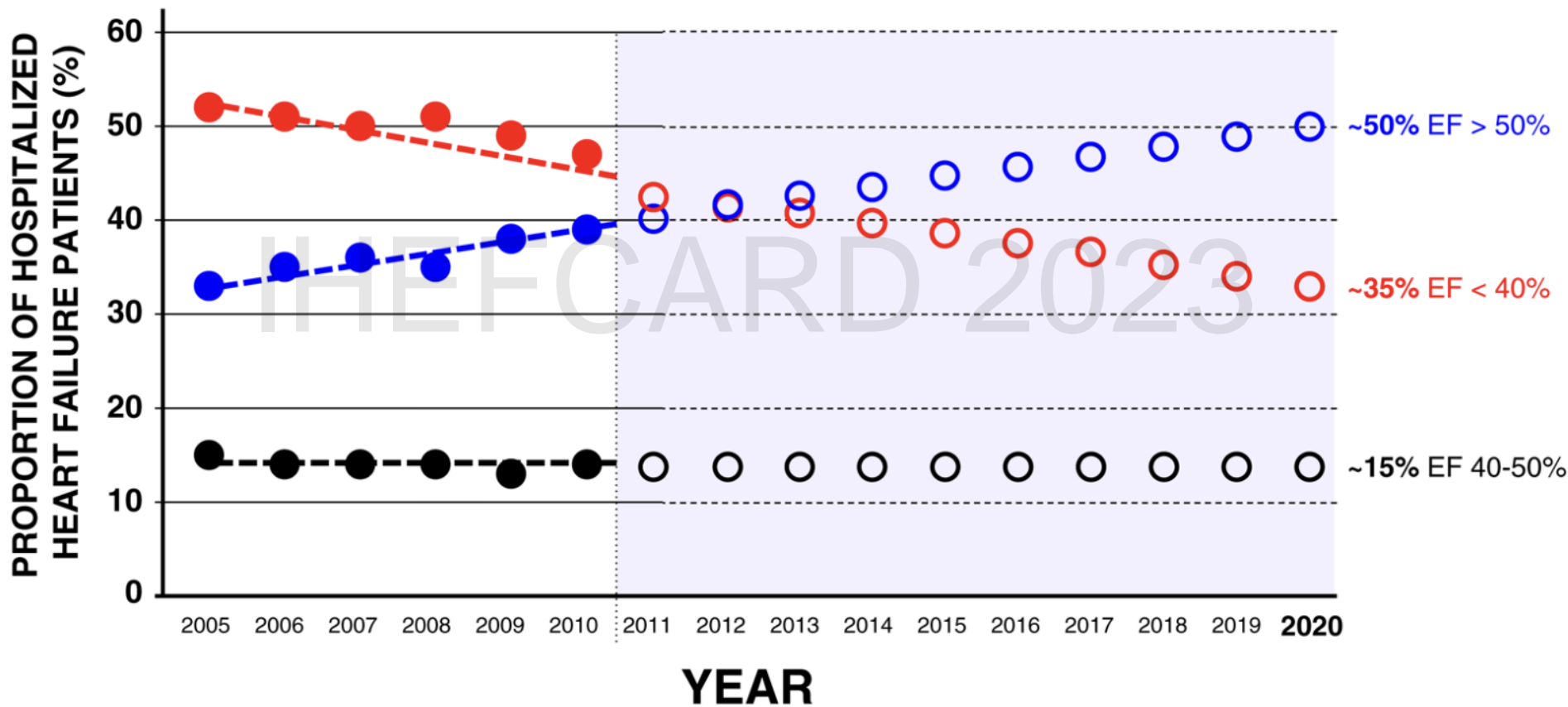
Cardiac dysfunction lead to congestion

Bozkurt, et al. Universal Definition and Classification of Heart Failure, Journal of Cardiac Failure, 2021, ISSN 1071-9164, <https://doi.org/10.1016/j.cardfail.2021.01.022>.





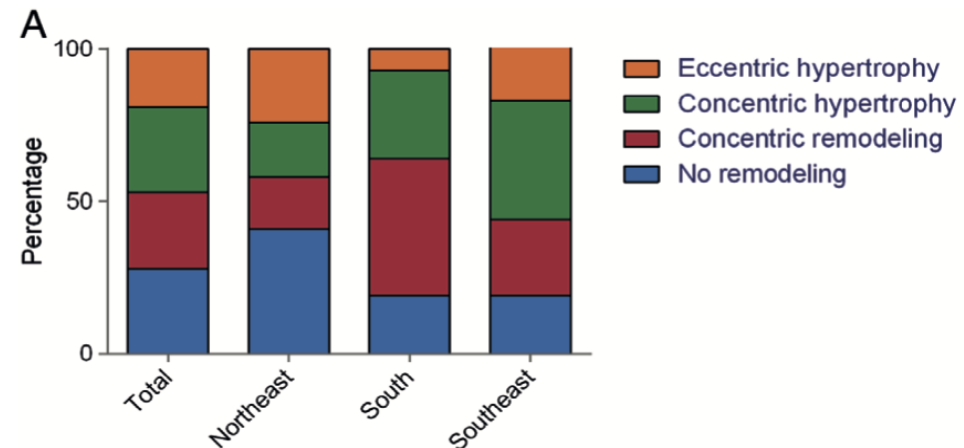
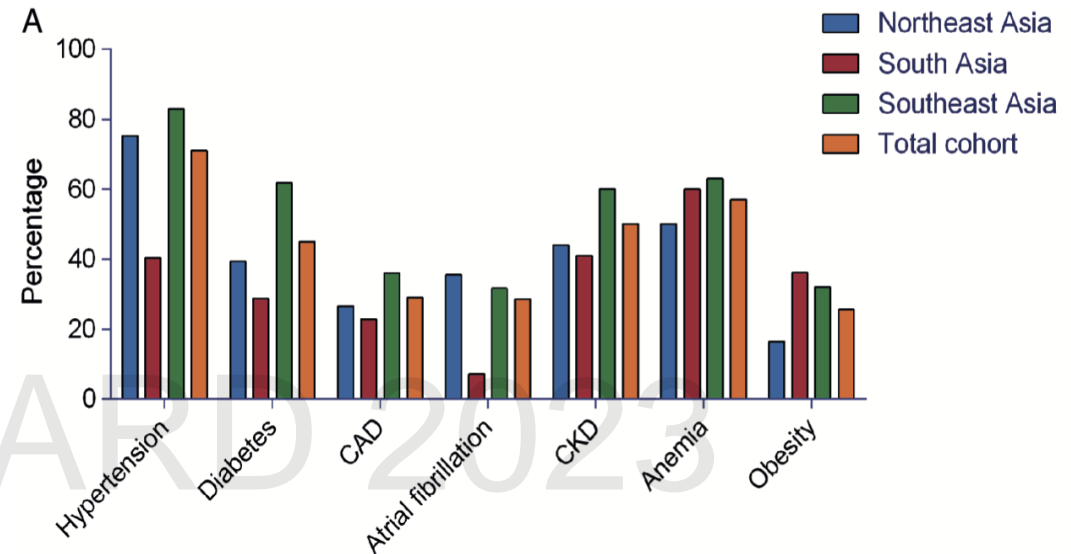
# The Changing Landscape of Heart Failure



Oktay AA, et al. Curr Heart Fail Rep.2013

# HFpEF Fact in Asian Population – South East Asia

- Younger age with mean age 54 y.o
- >> mortality number (4.8 vs 3%) vs US
- LOS was longer (6 vs 4.2 days) vs US
- Multiple comorbidities, esp T2DM and hypertension





# HFpEF diagnosis is challenging but **worth it**

Treatable → good prognostic 

- HFpEF heterogeneous
- Signs and symptoms are nonspecific
- No single test that definitively establishes the diagnosis esp. EF is preserved
- Patient often have significant comorbidities
- BNP or NT pro BNP levels are often unreliable

## NT pro BNP is not the Goddess in HF diagnosis

### *Factors that decrease BNP or NT-proBNP*

- Obesity

### *Factors that increase BNP or NT-proBNP*

#### Heart muscle disease

- Hypertrophic heart muscle diseases
- Infiltrative mycardiopathies, such as amyloidosis
- Acute cardiomyopathies, such as apical ballooning syndrome
- Inflammatory, including myocarditis and chemotherapy
- Coronary artery disease

#### Valvular heart disease

- Aortic stenosis and regurgitation
- Mitral stenosis and regurgitation

#### Arrhythmia

- Atrial fibrillation and flutter

#### Cardiotoxic drugs

- Anthracyclines and related compounds

#### Renal dysfunction

#### Anemia

#### Critical illness

- Bacterial sepsis
- Burns
- Adult respiratory distress syndrome

#### Stroke

#### Pulmonary heart disease

- Sleep apnea
- Pulmonary embolism
- Pulmonary hypertension
- Congenital heart disease

# Step by step in diagnosing HFpEF

## (1) Symptoms & Signs Of Heart Failure

- Typical symptoms: breathlessness, orthopnoea, paroxysmal nocturnal dyspnoea, exercise intolerance, fatigue, swelling
- Typical signs: raised jugular venous pressure, hepatojugular reflux, third heart sound, oedema, pulmonary crepitations

## (2) Preserved LV Ejection Fraction

- Currently taken as LV ejection fraction  $\geq 50\%$
- Without LV dilatation

## (3) LV Diastolic Dysfunction

- Structural: LV hypertrophy, left atrial dilatation
  - Doppler: raised E/e' ratio, abnormal mitral inflow, prolonged pulmonary venous A reversal duration
  - Biomarkers: raised NT-proBNP, BNP
  - Rhythm: atrial fibrillation
  - Invasive hemodynamics: increased LV end-diastolic pressure, prolonged tau, increased LV stiffness
- Inc LV filling pressure

Guidelines

Study inclusion criteria

Scoring system

## ESC and ACC guideline recommendations for diagnosis of HFpEF

### ESC 2021

- Symptoms and/or signs of HF
- LVEF  $\geq$  50%

AND

- Objective evidence of cardiac structural and/or functional abnormalities

### ACC 2022

- LVEF  $\geq$  50%

AND

- Evidence of spontaneous or provokable increased LV filling pressures (elevated natriuretic peptide/hemodynamic measurements)

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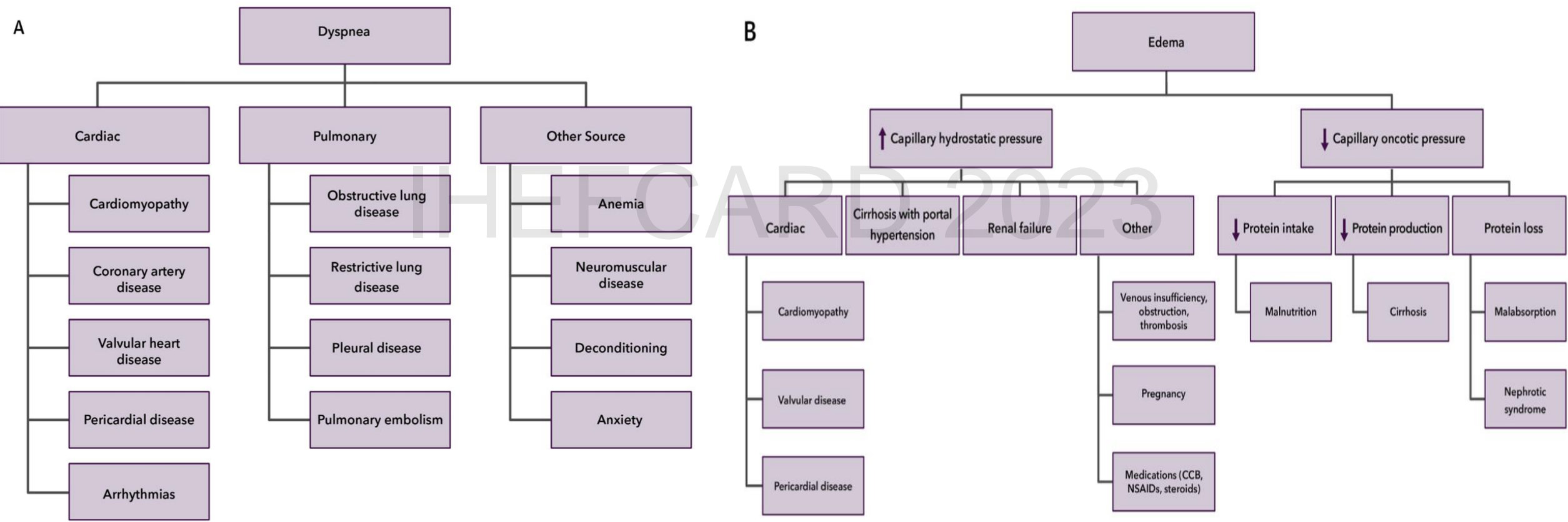
# ESC Guidelines 2021

Parameter <sup>a</sup>	Threshold	Comments
<b>LV mass index</b> <b>Relative wall thickness</b>	<b>≥95 g/m<sup>2</sup> (Female), ≥115 g/m<sup>2</sup> (Male)</b> <b>&gt;0.42</b>	Although the presence of concentric LV remodelling or hypertrophy is supportive, the absence of LV hypertrophy does not exclude the diagnosis of HFpEF
<b>LA volume index<sup>a</sup></b>	<b>&gt;34 mL/m<sup>2</sup> (SR)</b>	In the absence of AF or valve disease, LA enlargement reflects chronically elevated LV filling pressure (in the presence of AF, the threshold is >40 mL/m <sup>2</sup> )
<b>E/e' ratio at rest<sup>a</sup></b>	<b>&gt;9</b>	Sensitivity 78%, specificity 59% for the presence of HFpEF by invasive exercise testing, although reported accuracy has varied. A higher cut-off of 13 had lower sensitivity (46%) but higher specificity (86%). <sup>71,259,274</sup>
<b>NT-proBNP</b> <b>BNP</b>	<b>&gt;125 (SR) or</b> <b>&gt;365 (AF) pg/mL</b> <b>&gt;35 (SR) or</b> <b>&gt;105 (AF) pg/mL</b>	Up to 20% of patients with invasively proven HFpEF have NPs below diagnostic thresholds, particularly in the presence of obesity
<b>PA systolic pressure</b> <b>TR velocity at rest<sup>a</sup></b>	<b>&gt;35 mmHg</b> <b>&gt;2.8 m/s</b>	Sensitivity 54%, specificity 85% for the presence of HFpEF by invasive exercise testing <sup>259,261</sup>

# Inclusion criteria based on HFpEF study – EMPEROR PRESERVED

- CHF with preserved EF defined as LVEF > 40% ✓
- Elevated NT pro BNP > 300 pg/mL (SR) or NT pro BNP > 900 pg/mL (AF) ✓
- At least one :
  - Structural heart disease (left atrial enlargement and or LVH) ✓
  - Documented HHF within 12 mo
- On oral diuretics ✓

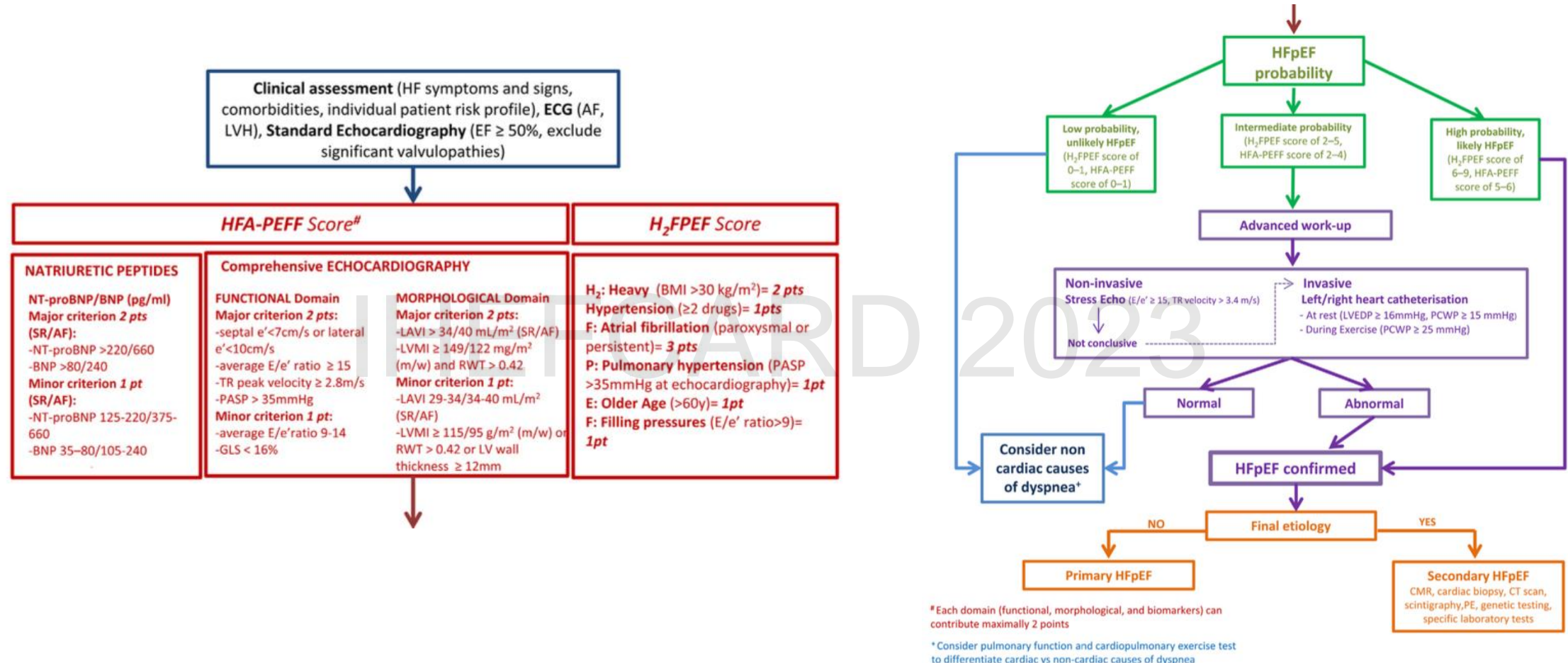
# However other conditions can cause these symptoms







# Scoring system (HFAPPEFF & H2FPEF)

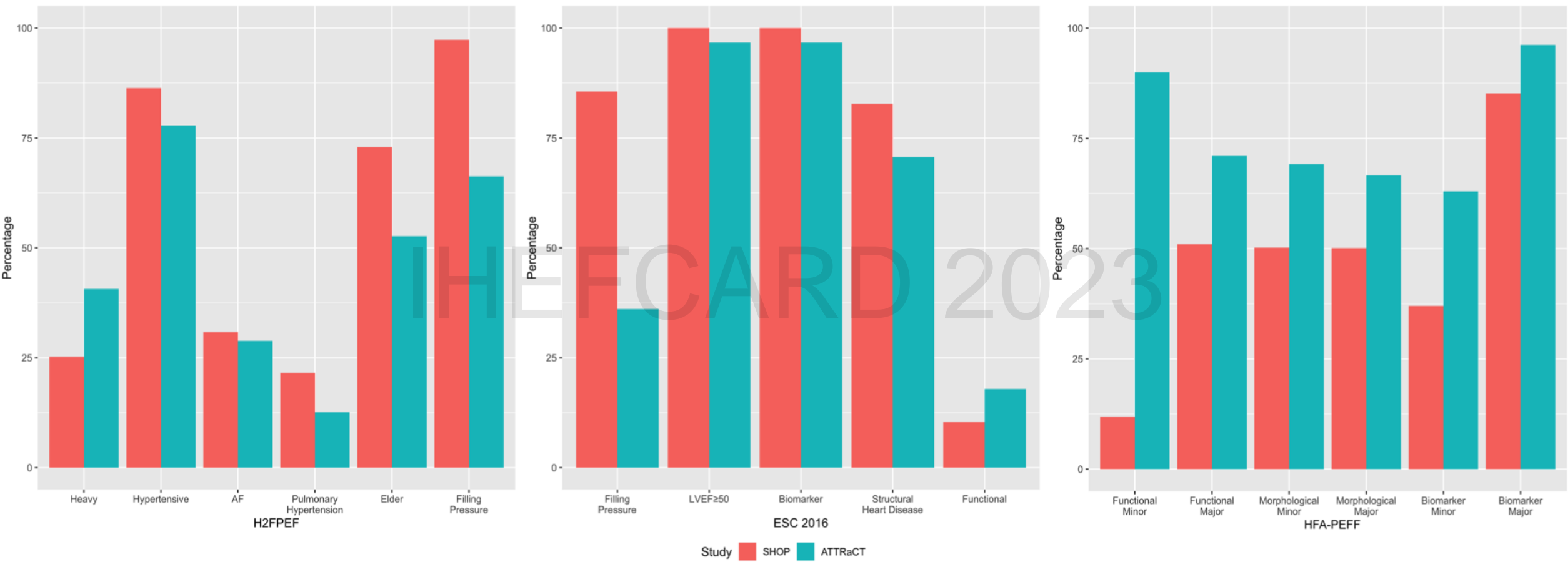


Help to facilitate discrimination of HFpEF from noncardiac causes of dyspnea and can assist in determination of the need for further diagnostic testing in the evaluation of patients with unexplained exertional dyspnea

# Scoring system (HFAPEFF & H2FPEF)

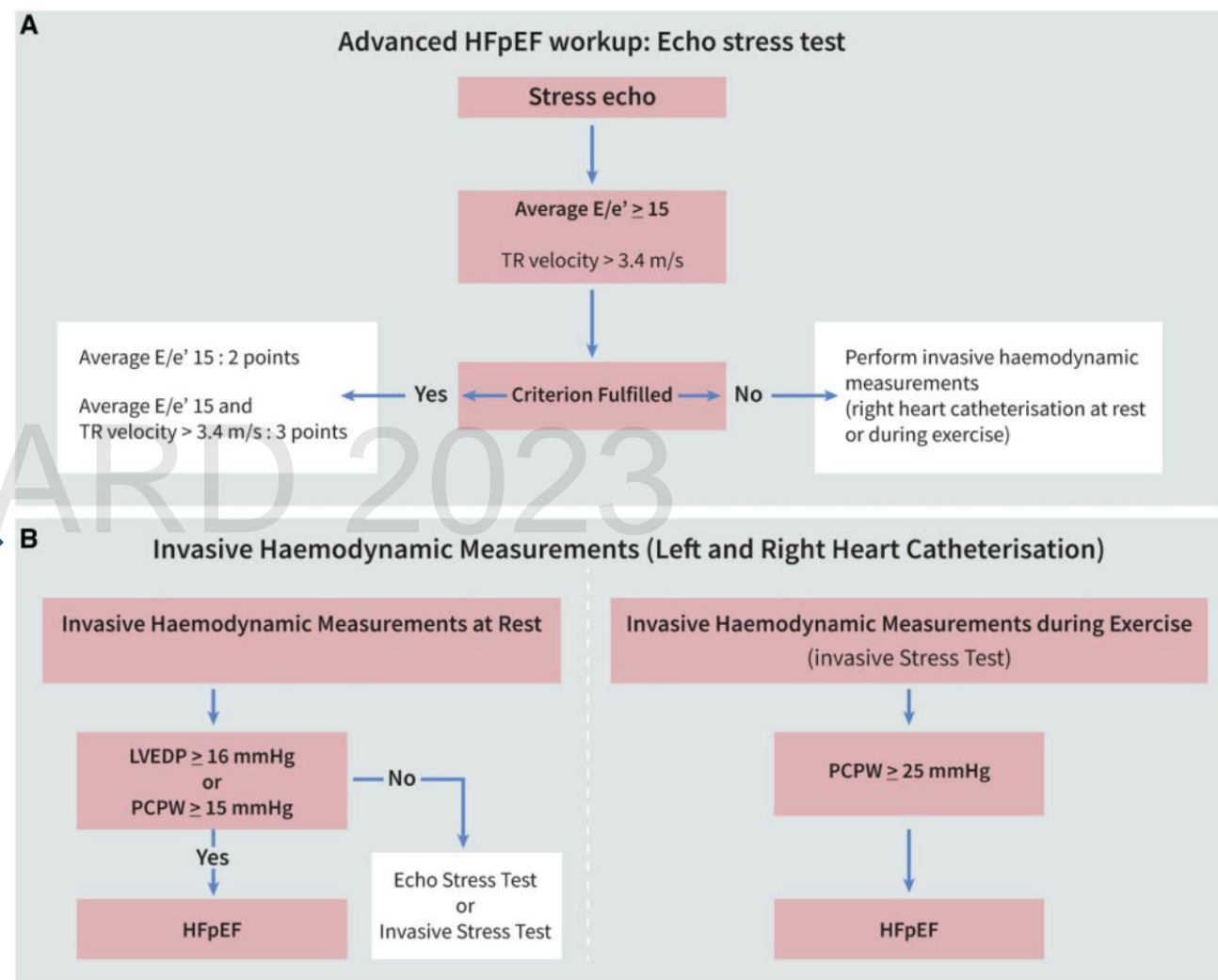
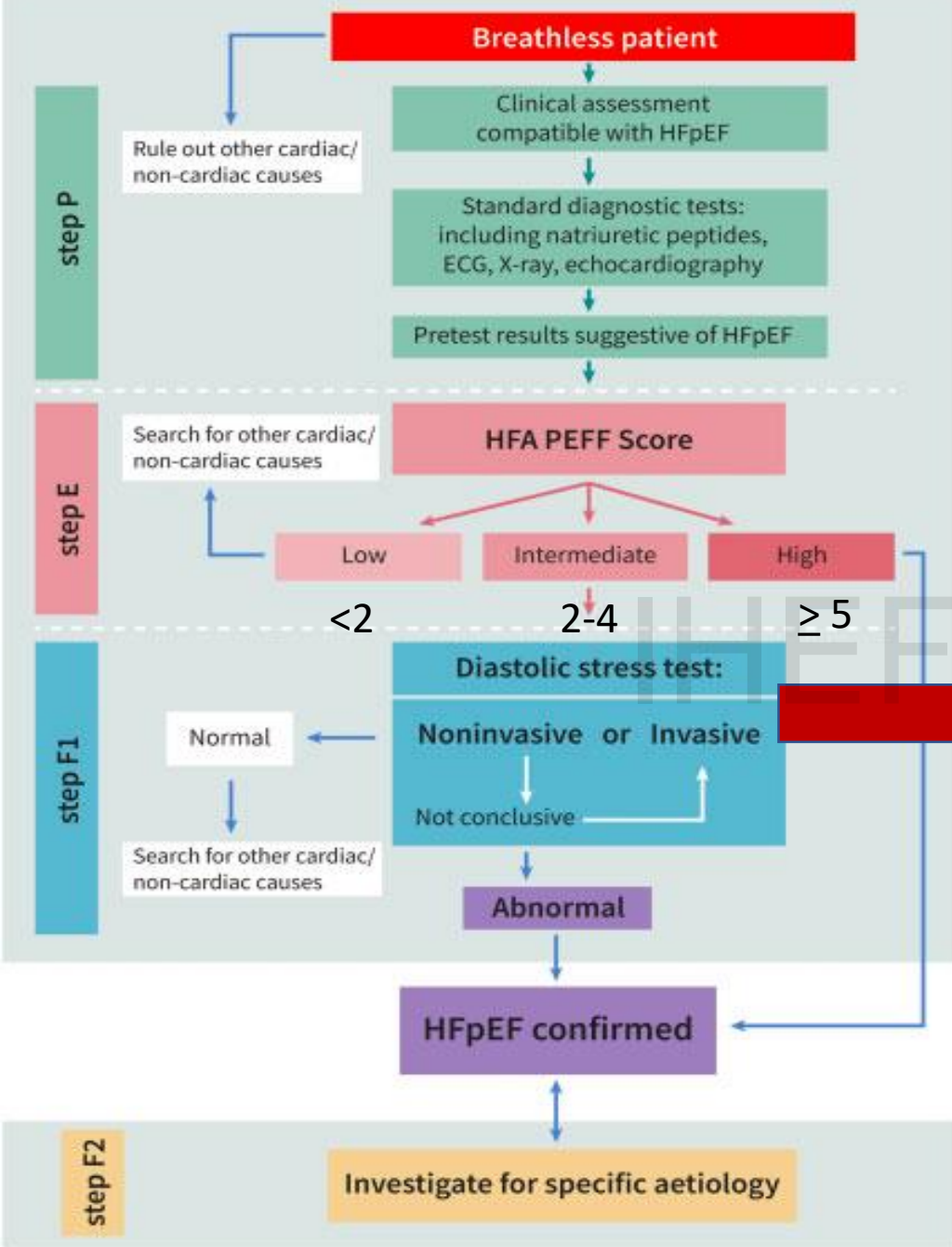
- Limitation of HFpEF scoring system → discrepancy
- Many patients with intermediate probability who need further test
- In Asian population HFpEF vs others : almost a decade younger, lower prevalence of obesity and AF, have smaller heart size with less LA enlargement
- Both scoring system have lower diagnostic performance in Asian compared to western populations
- However, HFAPEFF score has the best discrimination of HFpEF from control (AUC 0.776; 95% CI 0.739-0.776) in Asian population

# Singapore Heart failure Outcomes and Phenotypes (SHOP) study Asian neTwork for Translational Research and Cardiovascular Trials (ATTRaCT) study



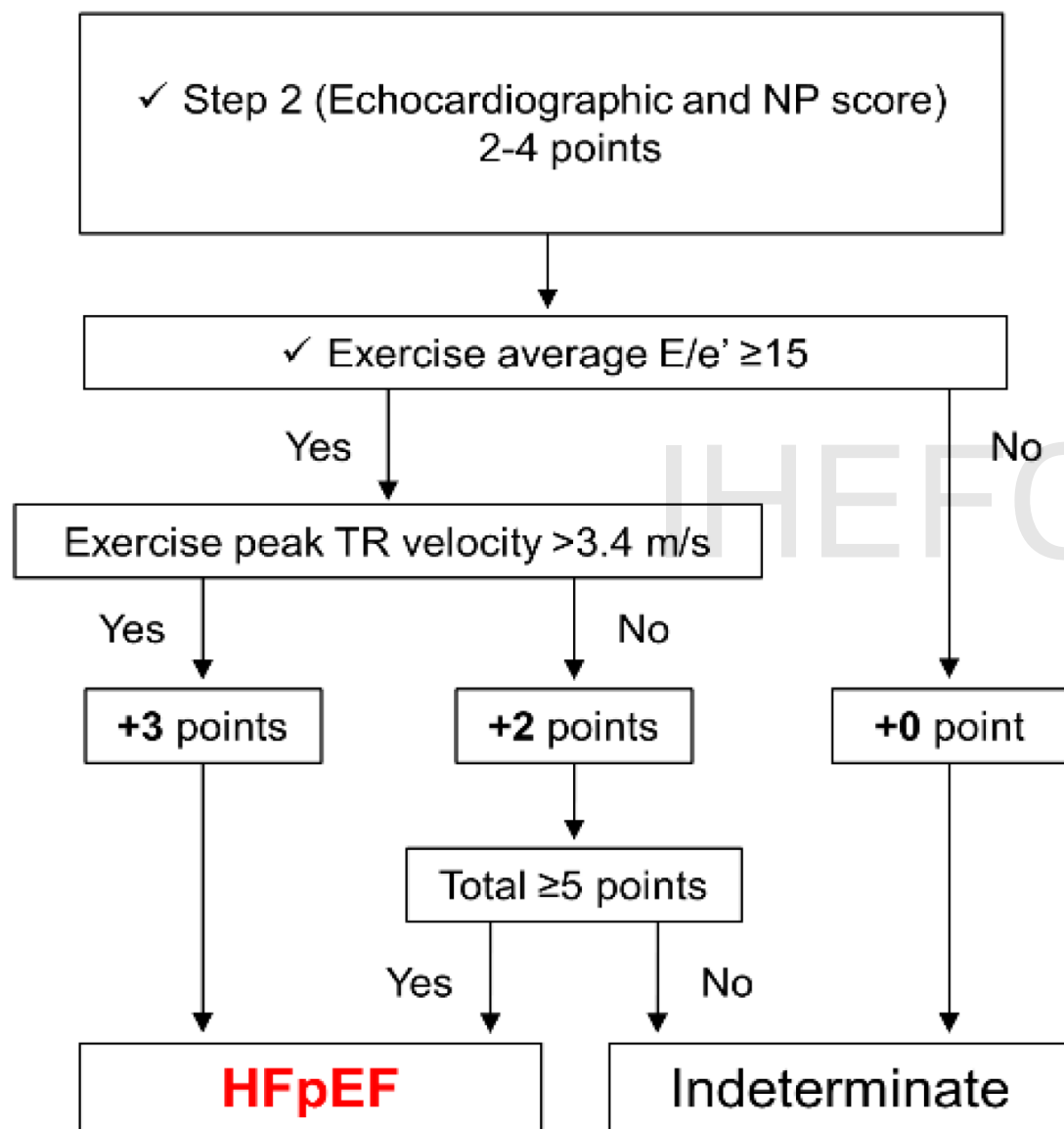
Both studies showed that scores were good at identifying patients with HFpEF but poor at ruling out HFpEF

Tromp J, et al.Eur Heart J.2020





## HFA-PEFF Algorithm



- Supine bicycle is recommended with workload starts at 25 W and increases in increments of 25 W every 3 min.
- E/e', TR jet should be recorded at baseline, during exercise and in the recovery after termination of exercise

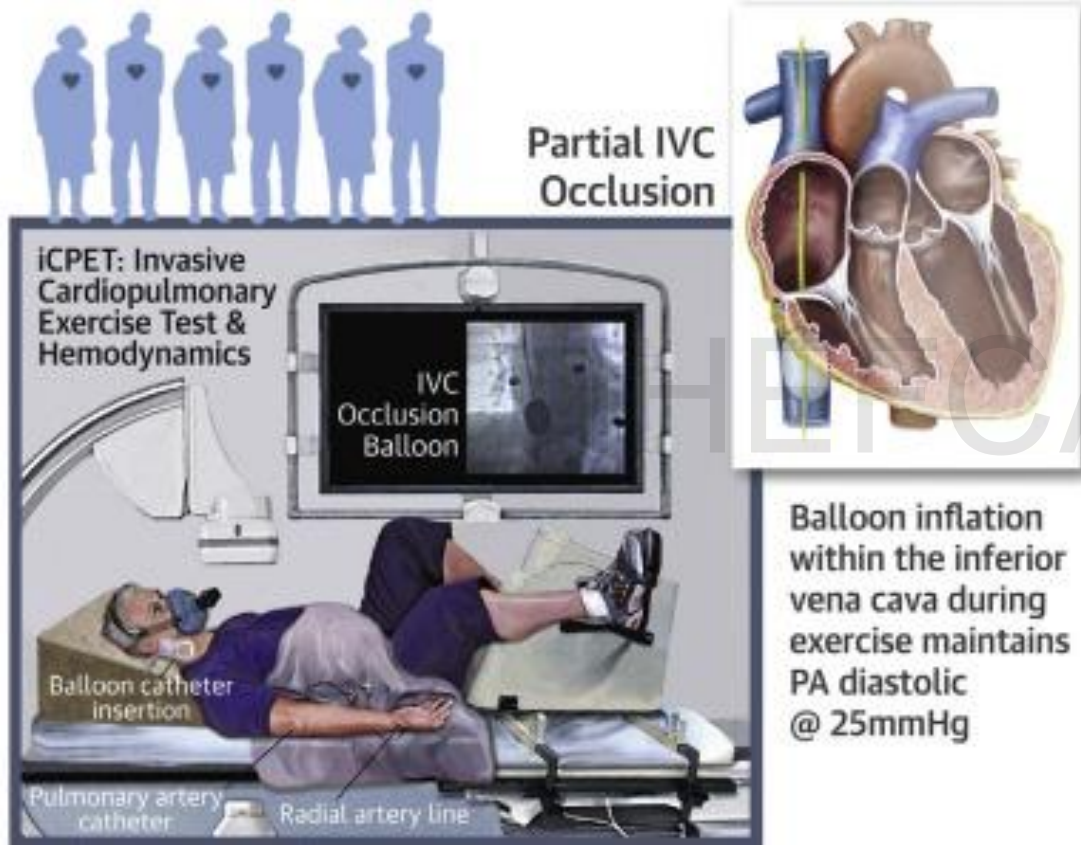


# Timing to do invasive hemodynamic measurements in HFpEF

Preference to perform invasive hemodynamic testing in HFpEF :

- Limitation of  $e'$  : significant mitral annular calcification (>5 mm), post surgical mitral rings or repair, prosthetic mitral valves, or ventricular paced rhythm or LBBB
- TR velocity may be diminished in very severe tricuspid insufficiency
- At higher workloads, the feasibility of obtaining diagnostic quality images is limited.
- Poor quality of echo imaging
- Echo findings showed PH
- Equivocal result

# Exercise Stress Test



- Real world, physiologic conditions, however many artefacts due to exercise, special equipment
- Increased by steps of 20-25 watts or up to the maximal exercise capacity.
- Stages should be held for >2 minutes
- Pressure should be averaged from at least 3 cardiac cycles
- Hemodynamic measurements during the recovery should be taken directly after discontinuation of the workload

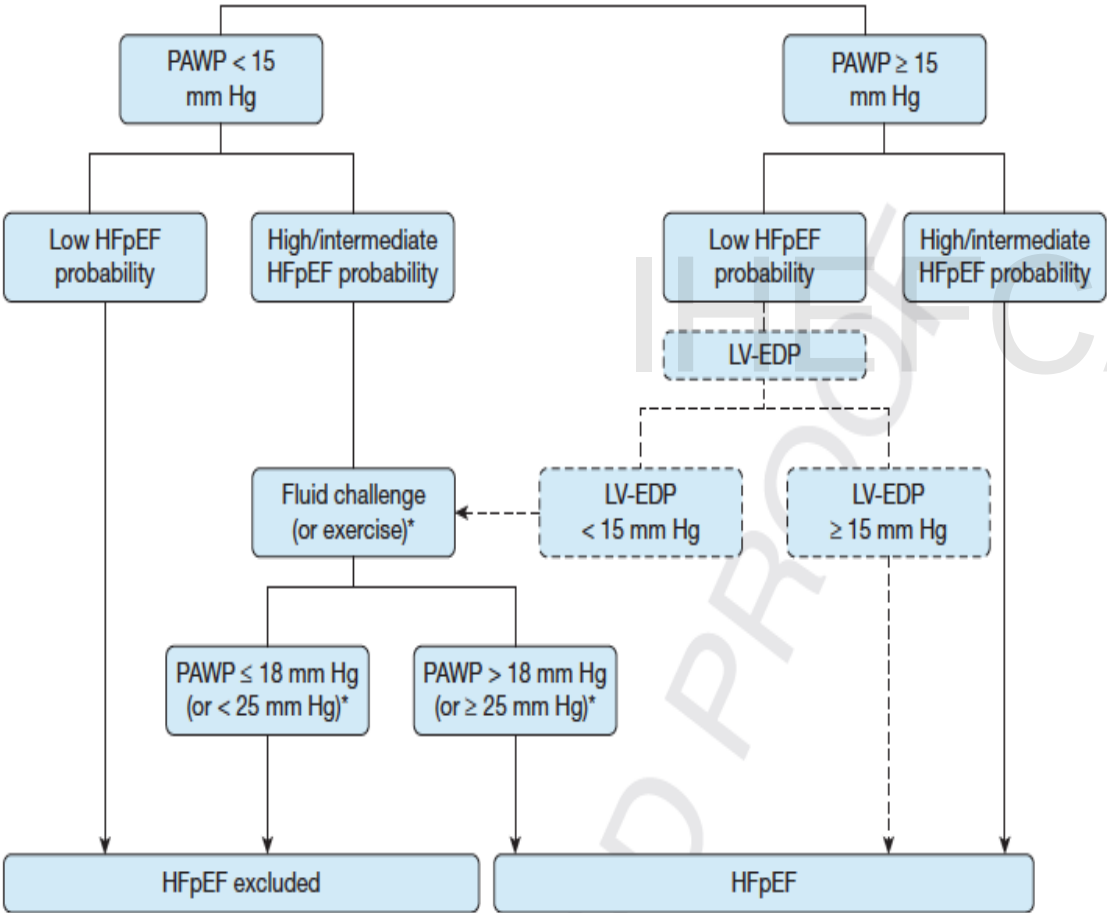
# Fluid Challenge Test

Clinical relevance of fluid challenge in patients evaluated for pulmonary hypertension

Running head: Fluid challenge in pulmonary hypertension

Michele D’Alto, MD, PhD<sup>\*</sup>; Emanuele Romeo, MD, PhD<sup>\*</sup>; Paola Argiento, MD, PhD<sup>\*</sup>;  
 Yoshiki Motoji, MD, PhD<sup>†</sup>; Anna Correra, MD<sup>\*</sup>; Giovanni Maria Di Marco, MD<sup>\*</sup>;  
 Agostino Mattera Iacono, MD<sup>\*</sup>; Rosaria Barracano, MD<sup>\*</sup>; Antonello D’Andrea MD, PhD<sup>\*</sup>;  
 Gaetano Rea, MD<sup>‡</sup>; Berardo Sarubbi, MD, PhD<sup>\*</sup>; Maria Giovanna Russo, MD<sup>\*</sup>;  
 Robert Naeije, MD, PhD<sup>†</sup>.

Proposed pulmonary artery wedge pressure-directed diagnosis of occult heart failure



## Fluid 500 cc NS in 10 minutes

- Less complex
- No specialized equipment required
- Less real world
- Less physiologic

# Learn from case : HFpEF ?

- Female 64 y.o
- DOE, bipedal edema
- CVRF : HTN, menopause
- Physical exam :  
Overweight, min bipedal edema
- ECG : SR LVH
- Echo : concentric LVH, dilated LA, preserved LVEF 60% global normokinetic, diastolic dysfunction ( $E/e' 15$ ), N RV function
- Lab : NT pro BNP 460 pg/mL

- Male 65 y.o
- DOE (+), orthopnea (-), bipedal edema
- CVRF : HTN, dyslipidemia
- PMH : **COPD, CKD st.3, OA**
- Physical exam :  
Obesity, HJR ?, min bipedal edema
- ECG : **AF nvr**, PRWP
- Echo : Suboptimal echo view, concentric LVH, Preserved LVEF 57% global normokinetic, Diastolic dysfunction, N RV function
- Lab : **NT pro BNP 320 pg/mL, Cr 2.27** (eGFR 31 ml/m/1.73 m<sup>2</sup>)

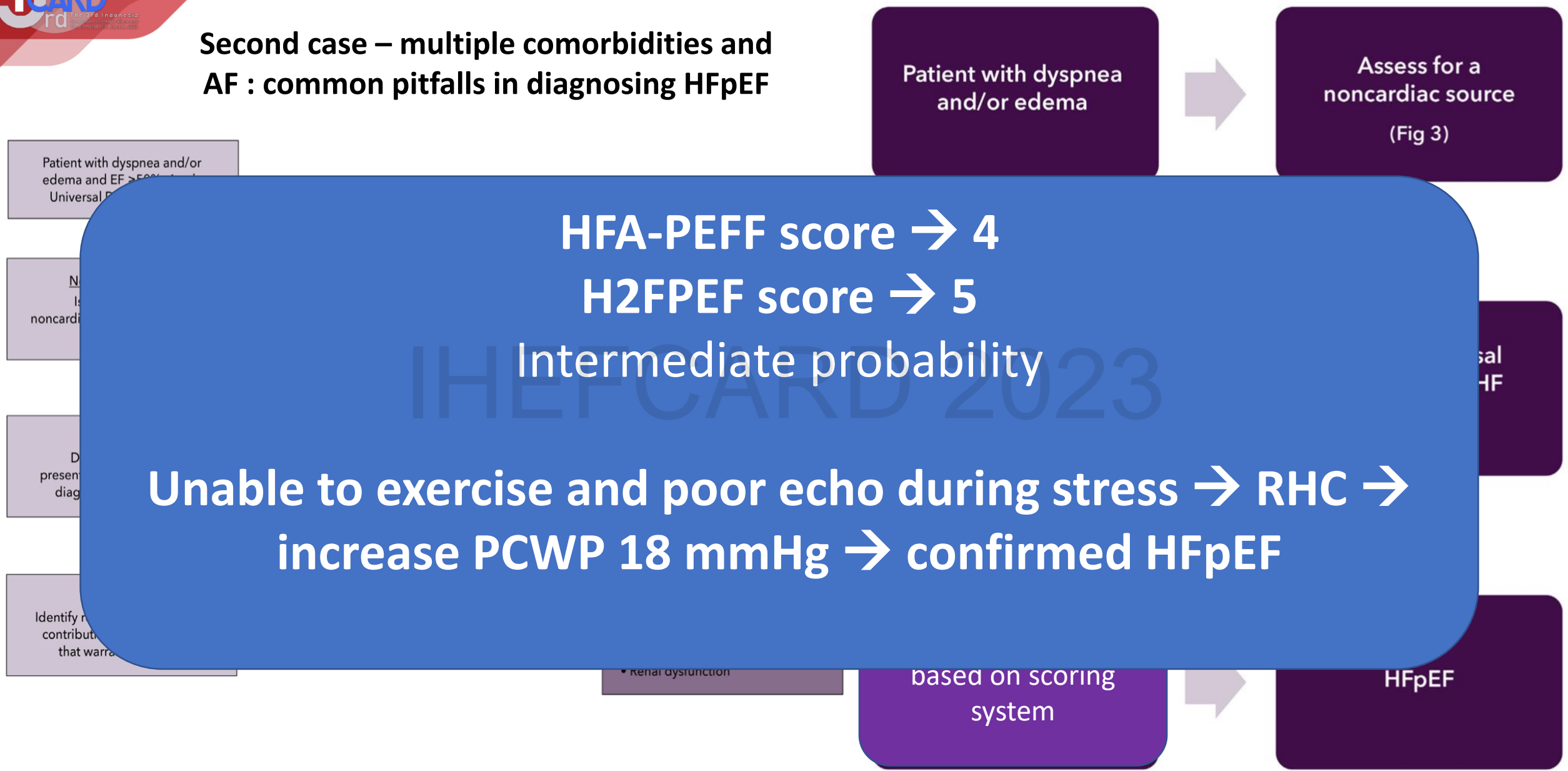
# ESC Guidelines 2021

## First Case – straight forward case

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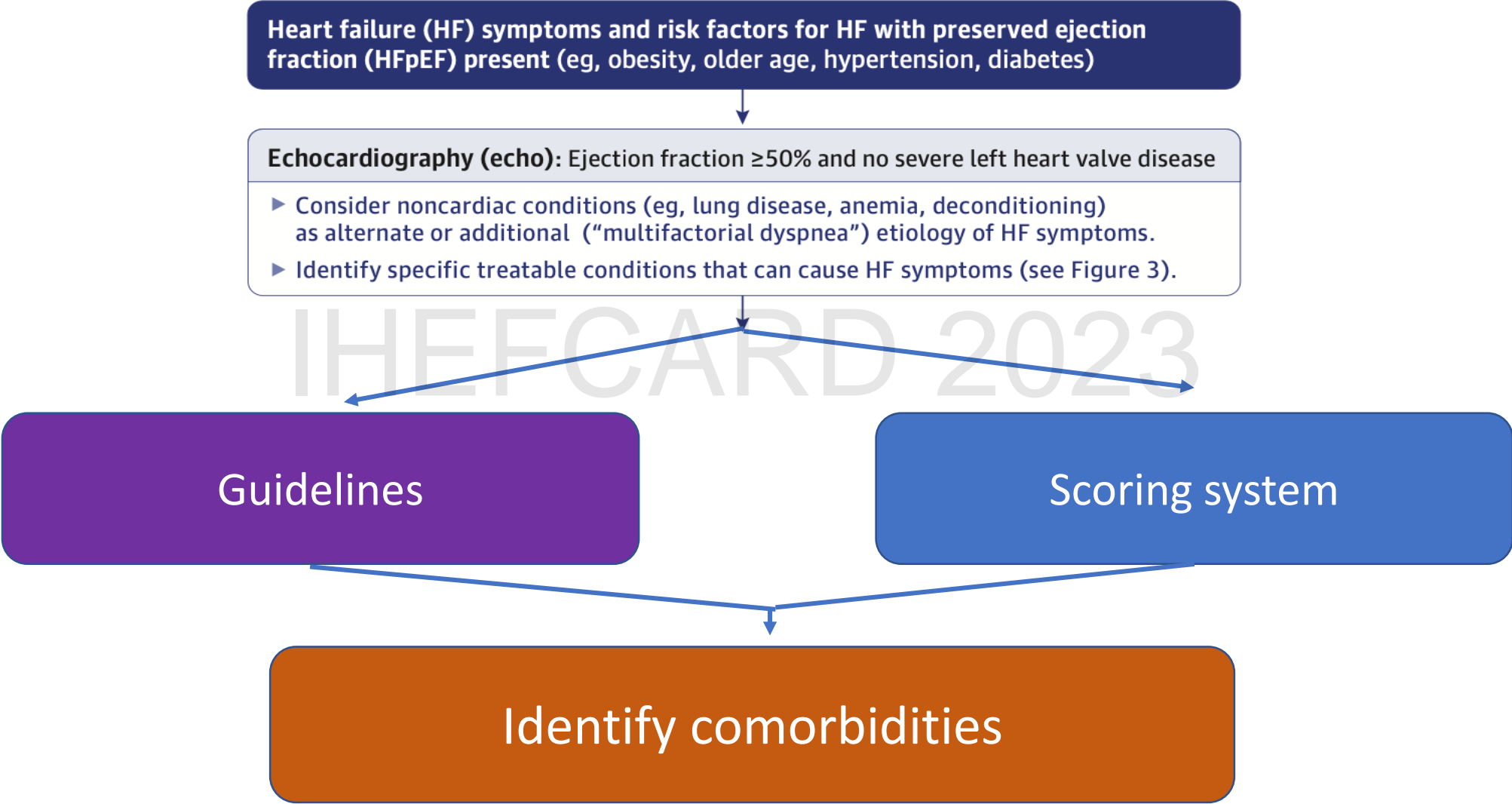
**Second case – multiple comorbidities and AF : common pitfalls in diagnosing HFpEF**

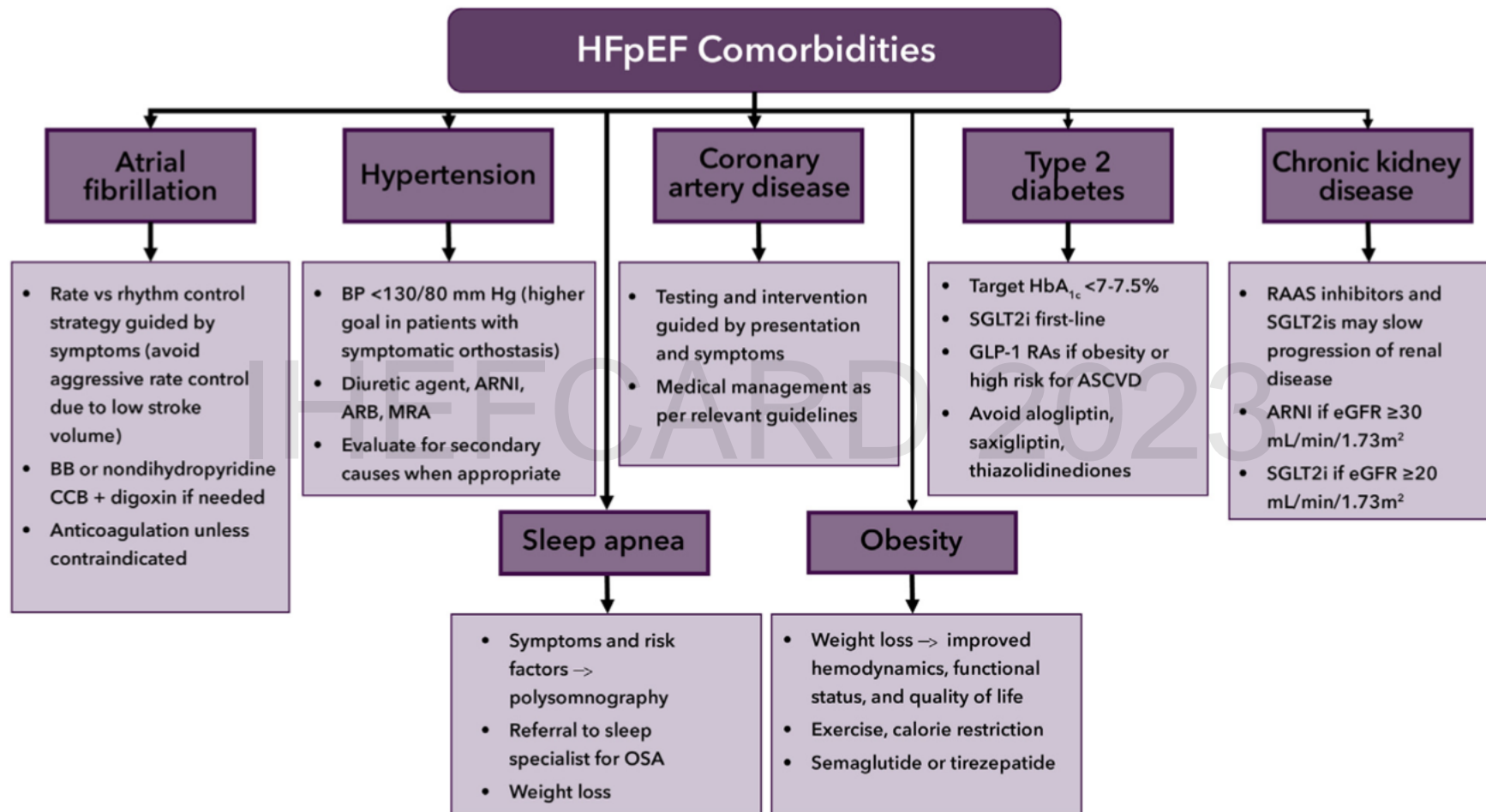


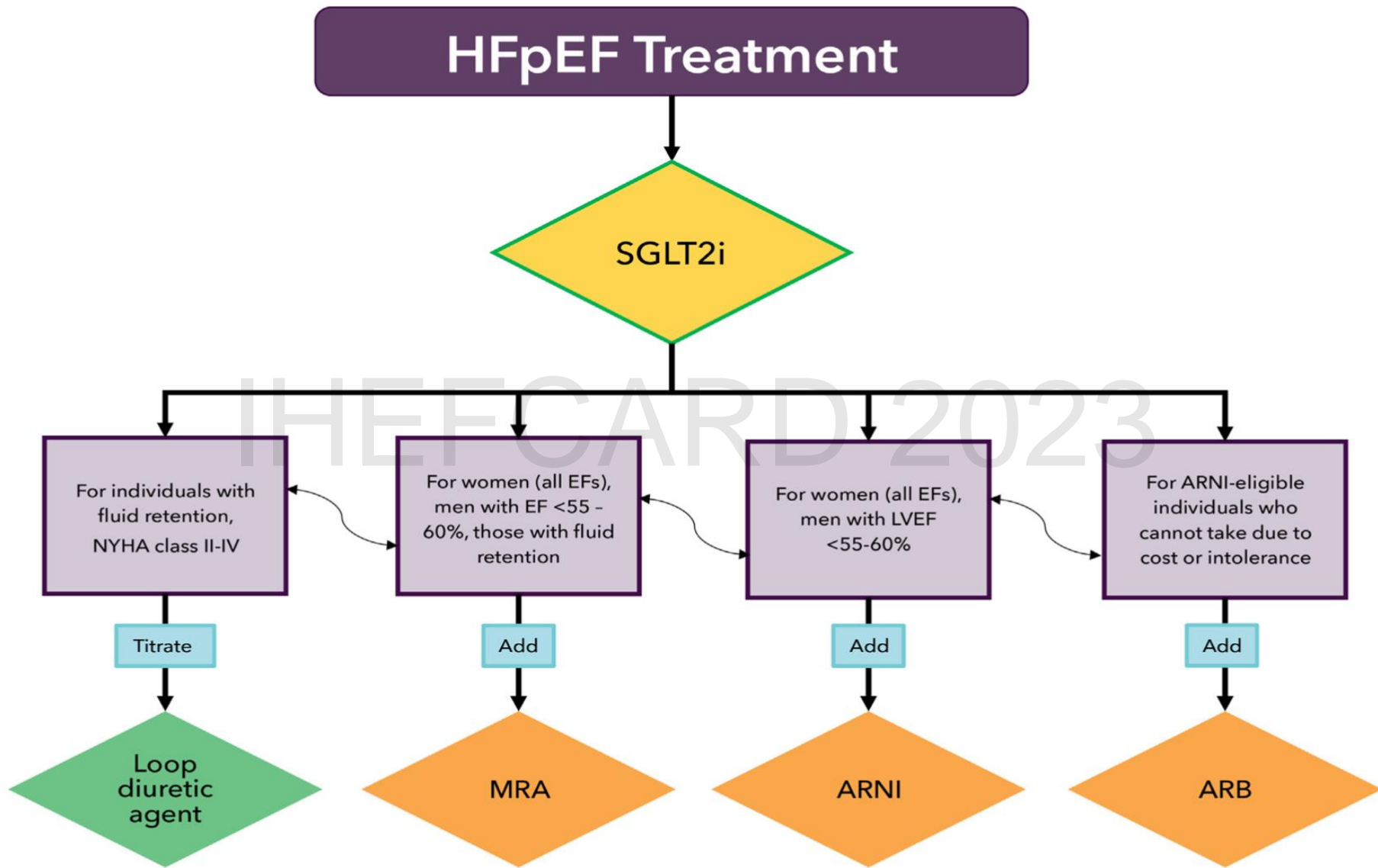




# Take Home Message(s)







Kittleson MM, et al. J Am Coll Cardiol.2023



"We're working on some exciting aspects of chaos theory."

## Breakthrough Year : one-meds-fits-all approach ?



**EMPEROR-Preserved Trial**

**Empagliflozin Outcome Trial in Patients with Chronic Heart Failure with Preserved Ejection Fraction**

Stefan D. Anker, MD PhD & Javed Butler, MD on behalf of the EMPEROR-Preserved Executive Committee, Trial Committees, Investigators & Coordinators

Dept. of Cardiology & BCRT (CVK), Charité Berlin, Germany  
University of Mississippi Medical Center, Jackson, Mississippi, USA

ESC CONGRESS 2021  
THE DIGITAL EXPERIENCE

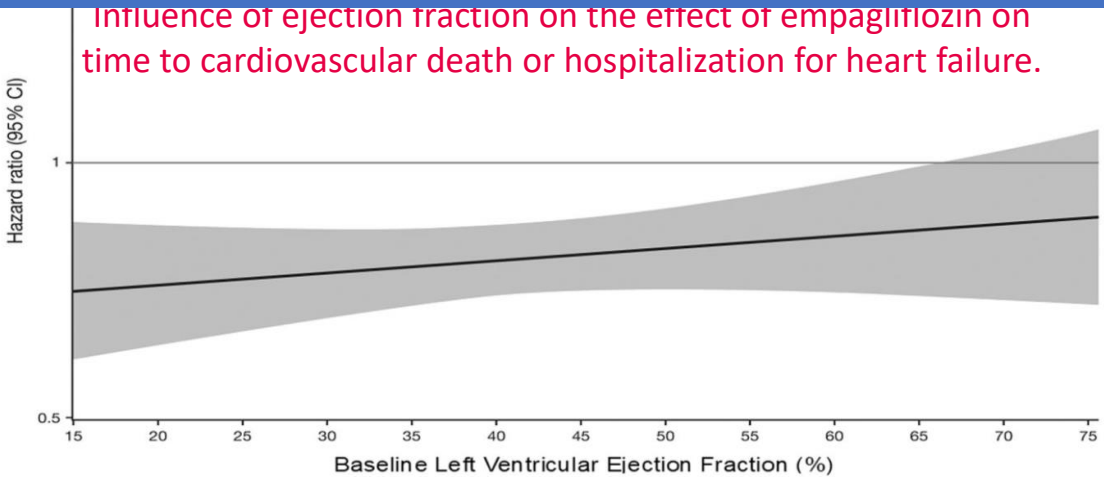
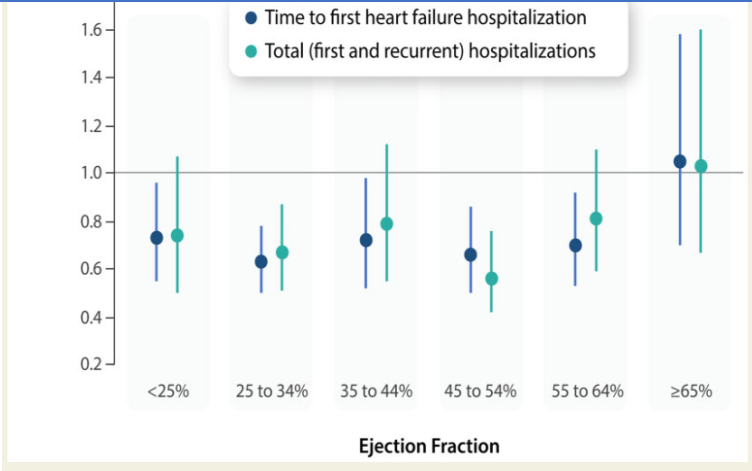
**EMPEROR-Preserved**

Effect of empagliflozin on CV death and HF hospitalisations in patients with HFpEF, with and without diabetes



	Left ventricular ejection fraction											
	<25%		25–34%		35–44%		45–54%		55–64%		≥65	
	Placebo	Empa	Placebo	Empa	Placebo	Empa	Placebo	Empa	Placebo	Empa	Placebo	Empa
	(n = 523)	(n = 476)	(n = 1115)	(n = 1115)	(n = 613)	(n = 659)	(n = 1149)	(n = 1111)	(n = 1021)	(n = 1071)	(n = 437)	(n = 428)
Heart failure hospitalization or cardiovascular death	0.77 (0.60–0.98)		0.72 (0.59–0.87)		0.82 (0.63–1.05)		0.74 (0.61–0.91)		0.78 (0.62–0.97)		0.98 (0.68–1.40)	
First heart failure hospitalization	0.73 (0.55–0.96)		0.63 (0.50–0.78)		0.72 (0.52–0.98)		0.66 (0.50–0.86)		0.70 (0.53–0.92)		1.05 (0.70–1.58)	
Total heart failure hospitalizations	0.74 (0.50–1.07)		0.67 (0.51–0.87)		0.79 (0.55–1.12)		0.56 (0.42–0.76)		0.81 (0.59–1.10)		1.03 (0.67–1.60)	
KCCQ clinical summary score at 52 weeks	3.01 (0.68–5.33)		0.92 (−0.63 to 2.46)		1.82 (−0.16 to 3.81)		1.59 (0.16–3.01)		1.95 (0.48–3.41)		0.26 (−2.01 to 2.53)	

## Do we still need EF for HF treatment ?







Thank you