



*Heart failure preserved EF  
(HFpEF)*

*vs*

*High CO failure in renal failure*

Under-diagnosis, Under-treatment



# *Heart failure with preserved ejection fraction*

## ***HFpEF***

EF  $\geq$  50% with sign and symptoms of heart failure

About 5% in aged  $\geq$  *60 years*

*more than half of* all heart failure (HF) hospital admissions.

The 5-year *survival rate* for all patients with heart failure, regardless of EF, *is less than 50%*.

**Survival** has improved over time for patients with HFrEF, it has *not changed* for patients with *HFpEF*.



## ***Risk factors and comorbidities***

*-Advanced age*

*-Female sex*

*-Obesity*

*-Systemic arterial hypertension*

*-Diabetes mellitus*

***-Renal dysfunction***

*-Anaemia and Iron deficiency*

*-Sleep disorders*

*-Chronic obstructive pulmonary disease*



- Heart failure with preserved ejection fraction ‘*masqueraders*’ such as heart valve disease, arrhythmias, and pericardial constriction need to *be excluded*.

Patient with a normal LVEF and *HF-like symptoms* caused by significant coronary artery disease (CAD) is also not considered to have HFpEF



## ***Pathophysiological processes***

*Increased systemic vascular resistance*

*Increased conduit arterial stiffness*

*Abnormal ventricular arterial coupling*

***Reduced LV long-axis systolic function***

*Slowed early diastolic relaxation*

***Reduced LV compliance with increased end diastolic stiffness***

***Reduced LA reservoir and contractile function***

*Impaired right ventricular (RV) function and chronotropic incompetence.*



# *Pathophysiological processes*

*Reduced reserve of stroke volume :*

heart rate (*chronotropic incompetence*)

cardiac output (CO)

*High LV filling pressures* (at rest and or on exercise)

Fluid retention and an expanded plasma volume.



# Sign and symptoms

\***DOE** ( FC II or III) **highly sensitive** and moderately specific (about 50%)

\***Orthopnoea** is quite **specific** but relatively insensitive.

\*Reduced exercise capacity and **fatigue**, out of proportion to cardiac abnormalities at rest.

\***Edema**

\***Congestion**



# *ECG*

- *LVH*
- *LA enlargement*
- *AF rhythm*





# *Natriuretic peptides*

*NT-proBNP* <125 pg/mL or BNP <35 pg/mL

high negative predictive values (NPV= 95–99%) for *excluding any heart failure*.

-The main trigger for release of NPs is high LV end-diastolic wall stress, which is inversely proportional to wall thickness.



-the excellent NPV of NPs is true particularly for HFrEF with a dilated LV, but not necessarily for HFpEF where LVH tends to normalize wall stress.

*-up to 20%* of patients with invasively proven HFpEF have NPs below these diagnostic thresholds



BNP is *higher* in PFpEF compared to normal people

BNP is *lower* in HFpEF compared to HFrEF(due to less wall stress)

BNP is *lower* in obesity

BNP is *higher* in women, older age, CKD and pulmonary diseases.



## ***HFpEF- like syndromes***

*Ischemia*

*Toxic(Alcohol,Cocaine)*

*Radiation,Inflamations*

*Infections*

*Hormonal(thyroid)*

### ***Loading conditions***

*Valvular*




*Pericardial*

*High output state(Anemia,AV fistula,Sepsis,Pregnancy,Hyperthyroidism)*

***Volume overload(Renal failure and fluid load)***



# How to diagnose heart failure with preserved ejection fraction: the HFA–PEFF diagnostic algorithm: a consensus recommendation from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC)

**Burkert Pieske<sup>1,2,3,4\*</sup>, Carsten Tschöpe<sup>1,2,5</sup>, Rudolf A. de Boer <sup>6</sup>, Alan G. Fraser<sup>7</sup>, Stefan D. Anker<sup>1,2,5,8</sup>, Erwan Donal<sup>9</sup>, Frank Edelmann<sup>1,2</sup>, Michael Fu<sup>10</sup>, Marco Guazzi<sup>11,12</sup>, Carolyn S.P. Lam<sup>13,14</sup>, Patrizio Lancellotti<sup>15</sup>, Vojtech Melenovsky<sup>16</sup>, Daniel A. Morris<sup>1</sup>, Eike Nagel <sup>17,18</sup>, Elisabeth Pieske-Kraigher<sup>1</sup>, Piotr Ponikowski<sup>19</sup>, Scott D. Solomon<sup>20</sup>, Ramachandran S. Vasan<sup>21</sup>, Frans H. Rutten <sup>22</sup>, Adriaan A. Voors<sup>6</sup>, Frank Ruschitzka<sup>23</sup>, Walter J. Paulus<sup>24</sup>, Petar Seferovic<sup>25</sup> and Gerasimos Filippatos<sup>26,27</sup>**



A

**Clinical Evidence of Heart Failure**

- Clinical presentation of HF (including HF symptoms and signs)
- Framingham criteria, or
- Boston criteria

**Supportive Lab Evaluation**

- $\uparrow$  Plasma BNP, NT-proBNP
- Chest x-ray or Chest CT scan showing edema
- Abnormal cardiopulmonary ETT or 6MHW

B

LVEF "preserved"  $>$ (50%), LV EDV Normal  $<$ 97 mL/m<sup>2</sup>

C

**Antecedent/Comorbid Disease:**

Hypertension, diabetes, advanced age, atrial fibrillation, CKD

**Exclusion:**

Noncardiac cause of symptoms/signs

D

**Additional Noninvasive Supportive Evidence**



*Despite a preserved LVEF, patients with HFpEF have **impaired LV**  
**long-axis systolic function***

*measured using Tissue echo from mitral annular velocity, **e'** or LV  
global longitudinal strain (**GLS**).*



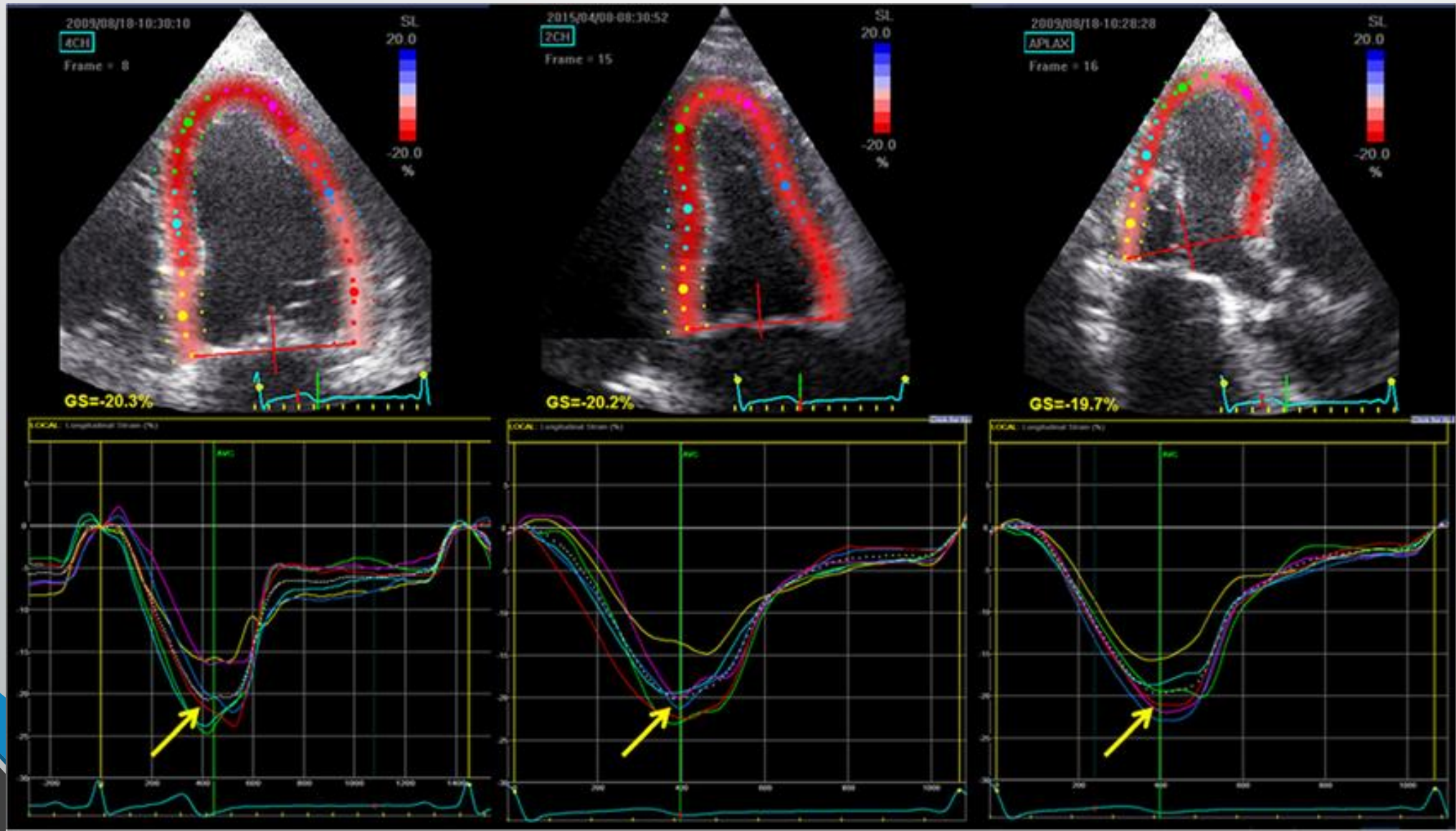
*$E/e'$ : less age dependent relative to  $e'$*

*Less dependent to volume relative to  $E$*





# Global longitudinal strain (GLS)

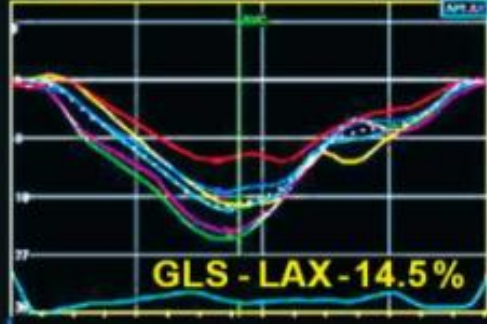
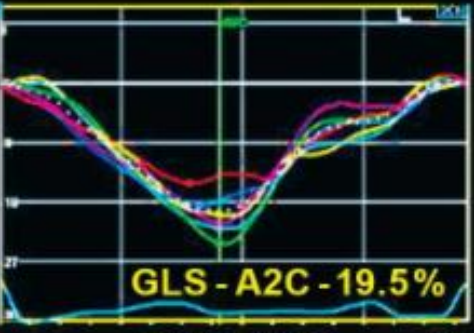
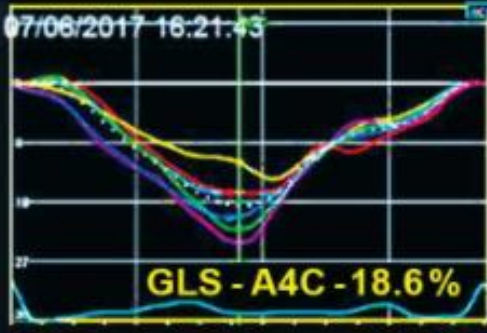
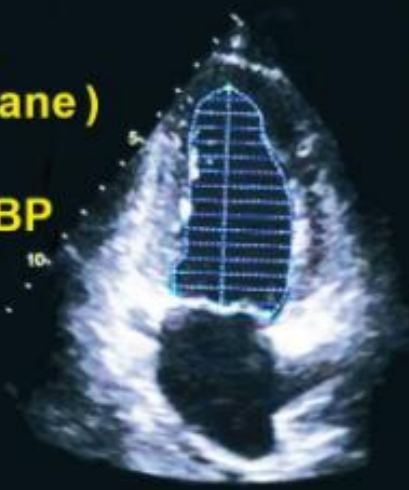


(a)

EF ( Biplane )  
58%

LV EDV BP  
112 ml

LV ESV BP  
47 ml

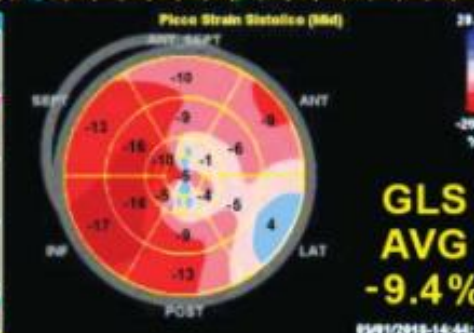
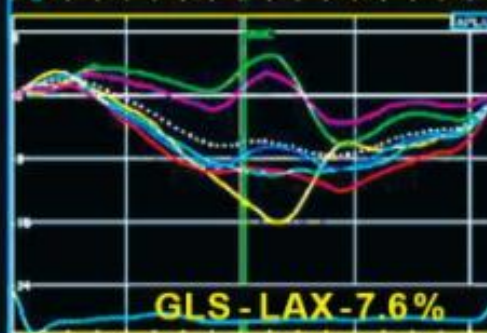
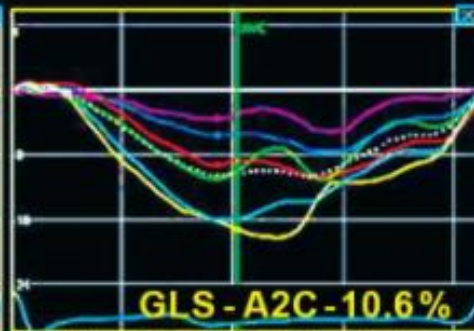
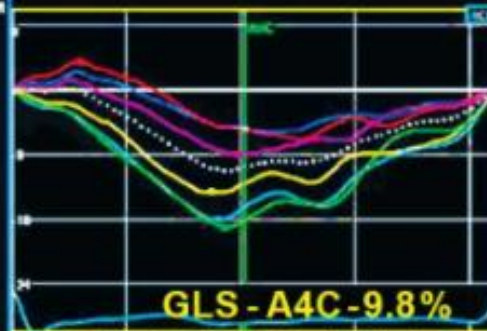
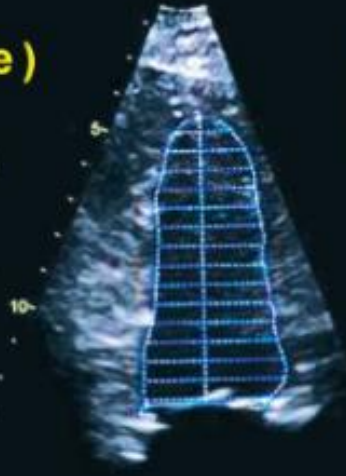


(b)

EF ( Biplane )  
51%

LV EDV BP  
113 ml

LV ESV BP  
56 ml





	Functional	Morphological	Biomarker (SR)	Biomarker (AF)
Major	septal $e' < 7$ cm/s or lateral $e' < 10$ cm/s or Average $E/e' \geq 15$ or TR velocity $> 2.8$ m/s (PASP $> 35$ mmHg)	LAVI $> 34$ ml/m <sup>2</sup> or LVMI $\geq 149/122$ g/m <sup>2</sup> (m/w) and RWT $> 0,42$ #	NT-proBNP $> 220$ pg/ml or BNP $> 80$ pg/ml	NT-proBNP $> 660$ pg/ml or BNP $> 240$ pg/ml
Minor	Average $E/e' 9-14$ or GLS $< 16\%$	LAVI 29-34 ml/m <sup>2</sup> or LVMI $> 115/95$ g/m <sup>2</sup> (m/w) or RWT $> 0,42$ or LV wall thickness $\geq 12$ mm	NT-proBNP 125-220 pg/ml or BNP 35-80 pg/ml	NT-proBNP 365-660 pg/ml or BNP 105-240 pg/ml

Major Criteria: 2 points

Minor Criteria: 1 point

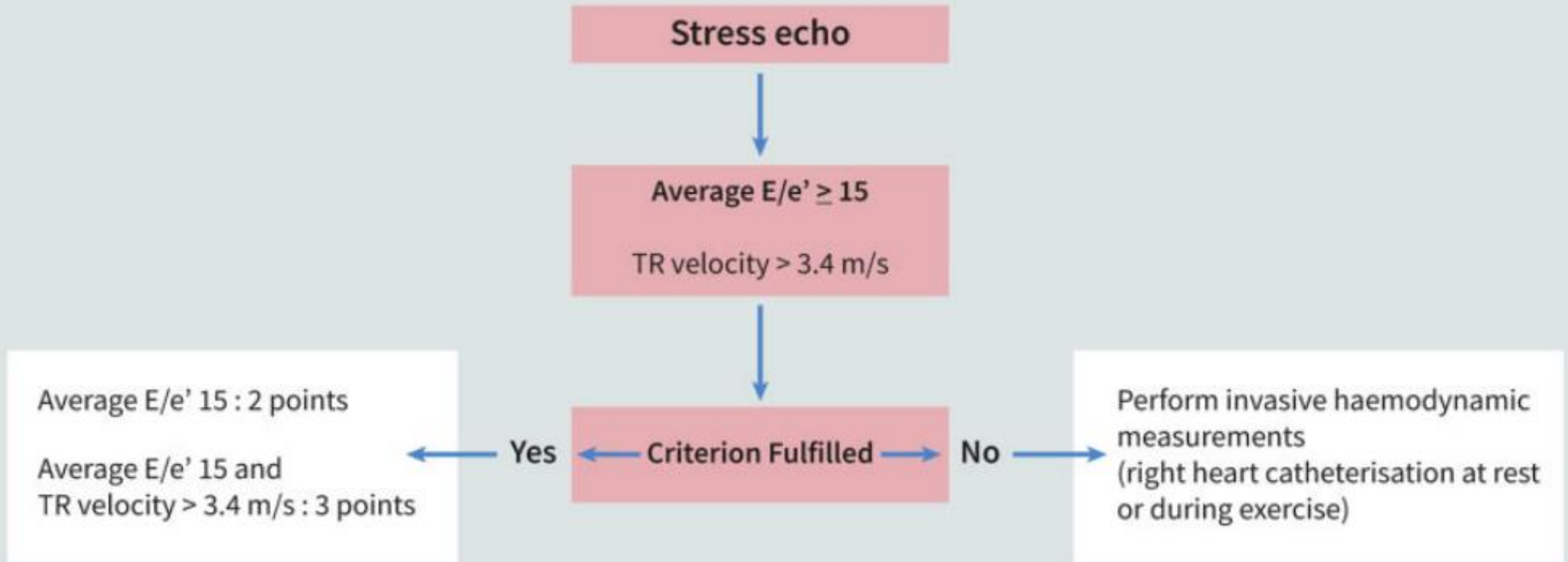
$\geq 5$  points: HFpEF

2-4 points: Diastolic Stress Test or Invasive Haemodynamic Measurements



A

## Advanced HFpEF workup: Echo stress test



## *invasive haemodynamic stress test*

The score remains  $<5$  points

Exercise echocardiography cannot be performed

Any case of doubt

A therapeutic decision depends on the results



B

## Invasive Haemodynamic Measurements (Left and Right Heart Catheterisation)

Invasive Haemodynamic Measurements at Rest

LVEDP  $\geq$  16 mmHg  
or  
PCPW  $\geq$  15 mmHg

Yes

HFpEF

No

Echo Stress Test  
or  
Invasive Stress Test

Invasive Haemodynamic Measurements during Exercise  
(invasive Stress Test)

PCPW  $\geq$  25 mmHg

HFpEF



All causes of the clinical syndrome of heart failure with a normal ejection fraction are not under the term 'HFpEF'

*Non-myocardial aetiologies* that may mimic HFpEF, such as:

constrictive pericarditis, primary VHD ***or high output failure***

*should not be considered part of the HFpEF syndrome.*





*High CO failure*





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# High-Output Heart Failure

## A 15-Year Experience

Yogesh N.V. Reddy, MD, Vojtech Melenovsky, MD, PhD, Margaret M. Redfield, MD,  
Rick A. Nishimura, MD, Barry A. Borlaug, MD



*High output HF is an important cause of clinical HF*

*Most frequently caused by :*

*-Obesity (31%)*

*-Arteriovenous shunts (23%). Mostly upper arm (Brachiocephalic > radial cephalic AV fistula ) and in patient with volume flow > 2L/min and  $Q/CO > 0.3$*

*-liver disease (23%)*

*-Lung disease (%) and Myeloproliferative dis*

*(Severe anemia, thyrotoxicosis and reversible causes was excluded)*



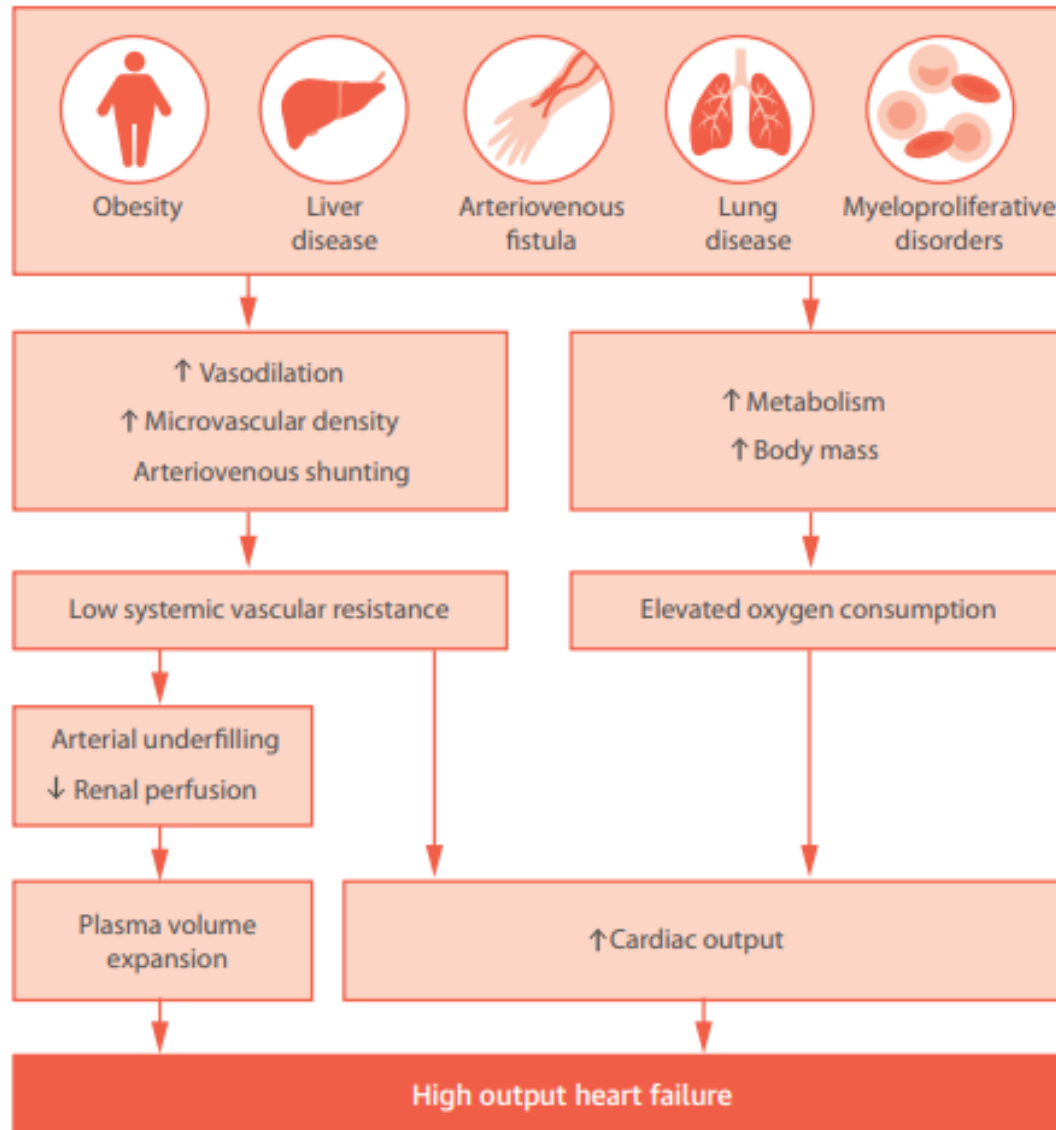
- *Patients with high-output HF displayed **increased 3-year mortality** compared with controls*

*(38% vs. 0%; hazard ratio [HR]: 3.4; 95% confidence interval [CI]: 1.6 to 7.6; p = 0.002)*

***Excessive vasodilation was associated with the poorest prognosis***



## CENTRAL ILLUSTRATION Pathophysiology of High-Output Heart Failure



Reddy, Y.N.V. et al. *J Am Coll Cardiol.* 2016;68(5):473-82.



# *Physical exam*

- Bounding (water hammer ) pulses
- Wide pulse pressure
- Pistol-shot sounds on femoral artery
- Edema and congestion



# ***NONINVASIVE IDENTIFICATION OF HIGH-OUTPUT HF***

***Cardiac index*** : ( by echocardiography ) : 3.54 l/min/m<sup>2</sup> or greater (CO >8L)  
( 62% sensitivity and 96% specificity )

***RVSP (PH)*** : 42 mm Hg

*92% sensitivity; 100% specificity*

***Increased filling pressure (E/e')***: 16± 6 (PCWP)

***Rised NT-pro BNP***

***Reduced PVR (Mean BP- mean RA pr/ CO) x 80*** : 400-800 dyne/s.cm<sup>5</sup>



- Because of **elevated E/e' ratio and normal EF**, many of these patients might have been **erroneously** diagnosed as having **HF with preserved EF (HFpEF)** if there had been no direct assessment of cardiac output.
- This observation emphasizes the importance of considering high output HF in the differential diagnosis.



- *the presence of an increased echocardiographic **Doppler-derived cardiac index**  $>3.5$  l/min/m<sup>2</sup> (CO  $> 8$  L) should prompt clinicians to consider further evaluation to clarify the diagnosis.*





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