

HFpEF Diagnosis: Clinical Tools and Workflow

06/07/2022 ACC HFpEF Heart House Roundtable

Jennifer E. Ho, MD
 Director of Research, Division of Cardiology
 Advanced Heart Failure | Beth Israel Deaconess Medical Center
 Associate Professor of Medicine, Harvard Medical School

Beth Israel Lahey Health 

 @JenHoCardiology

Beth Israel Deaconess
 Medical Center

 HARVARD MEDICAL SCHOOL
 TEACHING HOSPITAL

1

Overview

1. What are clinical and diagnostic tools – pros/cons of each
2. How do we put together a practical clinical approach for HFpEF diagnosis?
3. **Breakout Session:** Can we develop a clinical roadmap for HFpEF diagnosis?



Beth Israel Deaconess
 Medical Center

 HARVARD MEDICAL SCHOOL
 TEACHING HOSPITAL

Beth Israel Lahey Health 

2

2

Guideline and Trial Definitions of HFpEF

Beth Israel Deaconess
Medical Center

HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

	ACC/AHA	ESC	HFSA	TOPCAT	PARAGON	I-PRESERVE	RELAX	UDHF
Reference	Yancy C, Circ, 2013	Ponikowsky P, Eur Heart J, 2016	Lindenfeld J, JCF, 2010	Pitt B, N Engl J Med, 2014	Solomon SD, JACC HF, 2017	Massie B, N Engl J Med, 2008	Redfield MM, JAMA, 2013	Bozkurt B, JCF, 2021
Symptoms	✓	✓	✓	✓	✓	✓	✓	✓
Signs		±✓	✓	✓		Alt to HF admission*	✓	✓
Echo		LVH, LAE, or DD and not dilated	clVH, LAE (in absence of AF), DD		LAE or LVH	Alt to HF admission*	Alt to HF admission: LAE with diuretic	E/e' > 15, LVH, LAE, valve dz.
HF admission				✓		✓	✓	
CV admission			✓					
Exclude	Noncardiac causes		Nonmyocardial disease					
NT-proBNP		≥125		Alt to HF admission: >360	Different cut-offs depending on HF admission and AF history		≥400 or elevated filling pressures	Elevated
CPET						Alt to HF admission*	Peak V _{O₂} <=50% pred	
Other		Alt: rPCWP ≥15			Chronic diuretic age >50	Age ≥60	Alt to HF admission: previous invasive documented elevated filling pressures	Alt to BNP: objective evidence of congestion (CXR, echo, RHC, CPET)

Ho JE ... Lewis GD, Circulation, 2019
Bozkurt B et al, J Card Fail, 2021

Beth Israel Lahey Health

3

3

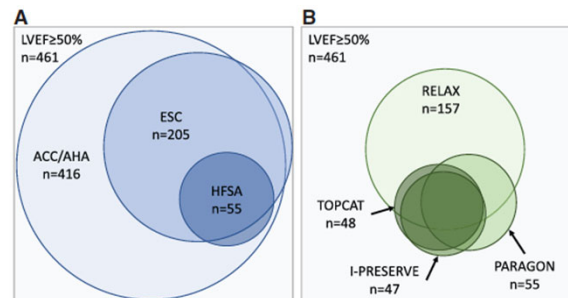
Heterogeneity across HFpEF Definitions

Beth Israel Deaconess
Medical Center

HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

MGH CPET sample:

- 461 patients with NYHA class II-III symptoms and LVEF > 50%
- ~53% met physiologic criteria for HFpEF



Ho JE ... Lewis GD, Circulation, 2019

Beth Israel Lahey Health

4

4

Natriuretic Peptides for HFpEF Diagnosis

Beth Israel Deaconess
Medical Center
HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

Current recommendations:

- **Class I:** Patients with dyspnea, NPs to support / exclude HF diagnosis
- **Cut-points:**

	Ambulatory	Hospitalized
BNP, pg/mL	≥35	≥100
NT-proBNP, pg/mL	≥125	≥300

- ≥125 pg/mL cut-point: sensitivity 77%, specificity 53% for HFpEF
- In general, NPs are lower in HFpEF vs HFrEF (less wall stress)
- NPs are 3-3.5 fold higher in atrial fibrillation vs NSR --> ESC algorithm uses different cutpoints

Heidenreich P et al, JACC, 2022
Bozkurt B et al, JCF, 2021
Iwanaga Y et al, JACC 2006
Pieske B et al, EHJ, 2019
Reddy YNV et al, Circ, 2018

Beth Israel Lahey Health

5

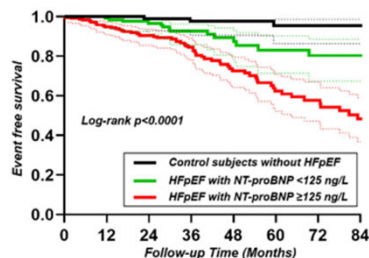
5

Natriuretic Peptides for HFpEF Diagnosis

Beth Israel Deaconess
Medical Center
HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

False negatives:

- Mayo CPET sample: ~35-40% had NT-proBNP <125



Verbrugge FH et al, EHJ, 2022
Khan AM et al, JCEM, 2011
Lam CS et al, JACC, 2011
Shah SJ, EHJ, 2022

Beth Israel Lahey Health

6

Pitfalls in NPs for HFpEF:

- 20-35% with HFpEF have low NPs
- **NP deficiency:** obesity, NPPB gene polymorphisms, insulin resistance, androgens, others

Questions:

- Role of NP in HFpEF diagnosis ('rule in' vs 'rule out' tests)?
- Specific thresholds based on BMI, sex, AF, NP deficiency states?

6

Echocardiography for HFpEF Diagnosis

Beth Israel Deaconess
Medical Center

HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

- HFpEF: LVEF $\geq$ 50%
- “Abnormality in cardiac structure and/or function”

	UDHF 2021	ACC/AHA 2022	ESC HFA-PEFF 2019
Cardiac structure	• Chamber enlargement • Mod/sev LVH	• LAVI$\geq$29 • LVMI$\geq$116 (M), $\geq$96 (F) • RWT$\geq$0.42 • LVWT$\geq$12	• LAVI: $\geq$34 (SR) / $\geq$40 (AF); 29-34 (SR), 34-40 (AF) • LVMI: $\geq$149 (M), $\geq$122 (F) & RWT$\geq$0.42; $\geq$115 (M), $\geq$95 (F), or RWT$\geq$0.42 or LVWT $\geq$12
Cardiac function	• E/e'$\geq$15	• E/e' $\geq$15 • Septal e'$\leq$7 • Lateral e'$\leq$10 • TR velocity $\geq$2.8 • PASP $\geq$35 • GLS $\leq$16%	• Mitral e' (age$\leq$75): sept $\leq$7, lat $\leq$10 • Mitral e' (age$\geq$75): sept $\leq$5, lat $\leq$7 • Mitral E/e' (avg): $\geq$ 15; 9-14 • TR velocity: $\geq$2.8, PASP $\geq$35 • GL strain: $\leq$16%

*grey font indicates minor criteria

Bozkurt B et al, JCF, 2021
Heidenreich P et al, JACC, 2022
Pieske B et al, EHJ, 2019

Beth Israel Lahey Health

7

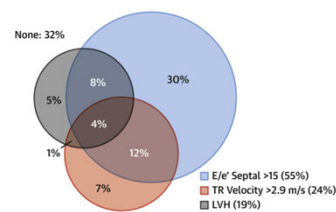
7

Echocardiography for HFpEF Diagnosis

Beth Israel Deaconess
Medical Center

HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

- PARAGON-HF: 32% with HFpEF had no echocardiographic abnormalities
- Test characteristics for each criterion are variable (26-70% sensitivity, 59-88% specificity)
- E/e' correlation with invasive LV filling pressures $r\sim$ 0.62 across 9 studies



Questions:

- Interpretation in context of aging and other comorbidities?
- Clinical applicability of advanced measures (GLS)?

Shah AM et al, JACC, 2019
Nauta JF et al, EJHF, 2018
Reddy YNV et al, Circ, 2018

Beth Israel Lahey Health

8

8

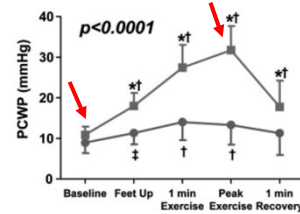
Provocative Testing in Diagnosis of HFpEF

Beth Israel Deaconess
Medical Center

HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

Exercise

- Exercise intolerance is the **hallmark** symptom of HFpEF
- Exercise can “**unmask**” abnormal cardiovascular reserve even in the absence of apparent volume overload



Other provocative maneuvers

- Passive leg raise
- Volume challenge

Kitzman D et al, JAMA, 2002
Borlaug BA et al, Circ Heart Fail, 2010
Fujimoto N et al, Circ, 2012
D'Alto M et al, Chest, 2021

Beth Israel Lahey Health

9

9

Exercise Echocardiography

Beth Israel Deaconess
Medical Center

HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

TABLE 1 Summary of the Studies Validating Noninvasive Diastolic Stress Testing

	Burgess et al., 2006 (18)	Talreja et al., 2007 (10)	Obokata et al., 2017 (11)	Hong et al., 2018 (7)
Study design	Prospective	Prospective	Prospective	Prospective
Population	Unselected patients	Exertional dyspnea	50 HFpEF, 24 noncardiac dyspnea	Asymptomatic previous PCI
Study patients, n	37	12	74	21
Mode of exercise	Supine bicycle	Supine bicycle	Supine bicycle	Supine bicycle
Parameter of LV filling pressure during exercise	Mean LVDP	PCWP	PCWP	ΔLV minimal pressure
Parameter of noninvasive LV filling pressure during exercise	E/e' medial	E/e' medial	E/e' medial	ΔE/e' medial
Sensitivity/specificity for identifying elevated LV filling pressure, %	73/96	89/100	—	—
Correlation coefficient	0.59	—	0.57	0.51

HFA-PEFF criteria for 'abnormal' diastolic stress test:

- Average E/e' increases to $\geq 15 \pm$ TR velocity > 3.4 m/s

Limitations:

- E/e' not measurable in 10% at submax, 20% at peak exercise
- TR detected in only half

Ha, J-W, et al, JACC CV Imaging, 2020
Obokata M et al, Circulation, 2017

Beth Israel Lahey Health

10

10

Invasive Hemodynamic Testing

Resting RHC:

- 'abnormal' mPCWP ≥ 15 mmHg

What is abnormal with exercise?

- supine PCWP ≥ 25 mmHg
- PCWP/CO slope > 2
- PCWP/workload > 25.5
- Associated with adverse CV outcomes

Other provocative maneuvers:

- Passive leg raise: PCWP ≥ 19 mmHg had specificity of 100% at HFpEF diagnosis

Questions

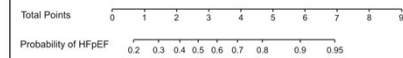
- Who should be considered for advanced testing?
- Non-invasive correlates or other approaches that may improve accessibility?

Borlaug BA et al, Circ Heart Fail, 2010
Eisman AS et al, Circ Heart Fail, 2018
Ho JE et al, Circulation, 2019
Dorfs S et al, Eur Heart J, 2014
van de Bovenkamp AA et al, Circ HF, 2022

11

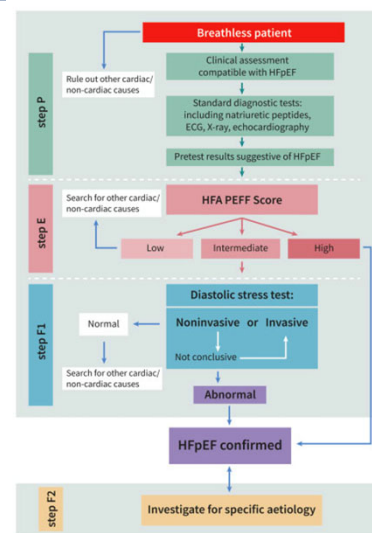
Diagnostic Algorithms

	Clinical Variable	Values	Points
H ₂	Heavy	Body mass index > 30 kg/m ²	2
	Hypertensive	2 or more antihypertensive medicines	1
F	Atrial Fibrillation	Paroxysmal or Persistent	3
P	Pulmonary Hypertension	Doppler Echocardiographic estimated Pulmonary Artery Systolic Pressure > 35 mmHg	1
E	Elder	Age > 60 years	1
F	Filling Pressure	Doppler Echocardiographic E/e' > 9	1
H ₂ FPEF score			Sum (0-9)
Total Points			
Probability of HFpEF			



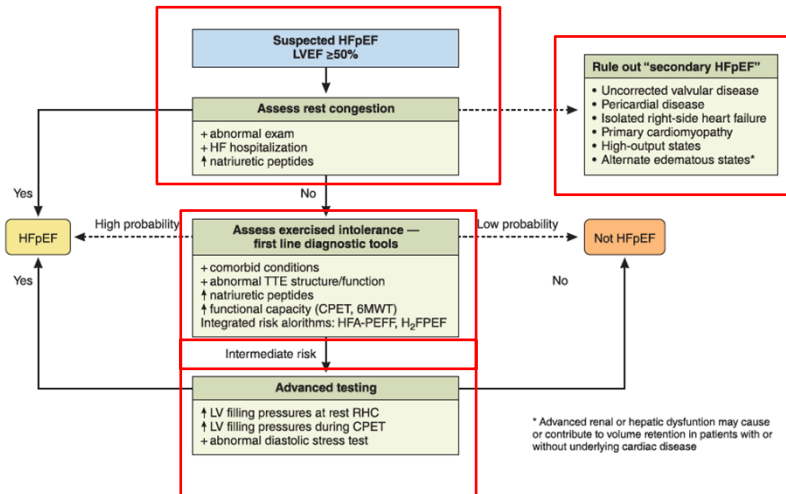
Reddy YNV et al, Circulation, 2018
Pieske B et al, Eur Heart J, 2019

12



A Practical Approach to HFpEF Diagnosis

Beth Israel Deaconess
Medical Center
HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL



Ho JE, Redfield MM, Lewis GD, Paulus WJ, Lam CSP, Circulation, 2020

Beth Israel Lahey Health

13

13

Thank you

Beth Israel Deaconess
Medical Center
HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

Beth Israel Lahey Health

14

14