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جمعية القلب السعودية
Saudi Heart Association

THE PROPER APPROACH TO DIAGNOSING HEART FAILURE WITH PRESERVED EJECTION FRACTION

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Disclosures

- Data Safety Monitoring Board
  - SOPRANO (J&J), EVALUATE-HF (Novartis)
- Steering Committee
  - GALACTIC-HF (Amgen), DELIVER-HF (AstraZeneca)
- Adjudication Committee
  - ARCHITECT BNP (Abbott)
- Grants
  - AHA
  - NIH

Heart Failure with Preserved EF

- Increasing in prevalence
- Disease of the elderly in a population that is aging
- Morbidity and mortality are high and comparable to HFrEF
- Diagnosis can be challenging

Owan, NEJM 2006; Borlaug, JACC 2009; Lee, Circulation 2009

Which patient has HFpEF?

All four patients present with exertional dyspnea, LVEF > 50%, no valvular abnormalities, no CAD.

A. 55 WM with BMI 38, HTN, 1+ edema
B. 70 BF with BMI 35, HTN, DM, arthritis and LVH
C. 86 WF with afib, anemia, LAE
D. 70 BM with CKD, “COPD”, RVSP 50

Definition of HFpEF

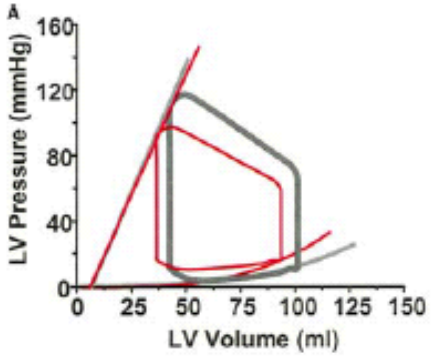
2013 AHA ACC HF Guidelines, EF >50%

"…also referred to as diastolic HF. Several different criteria have been used to further define HFpEF. The diagnosis of HFpEF is challenging because it is largely one of excluding other potential noncardiac causes of symptoms suggestive of HF. To date, efficacious therapies have not been identified."

HFPEF

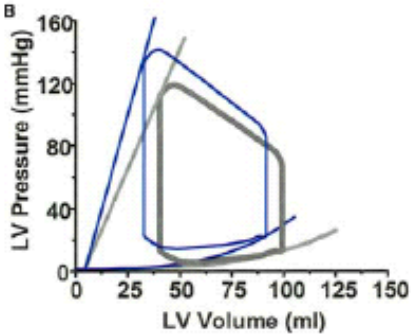
A Hemodynamically Heterogeneous Disease

Non-HTN HFPEF (HCM)

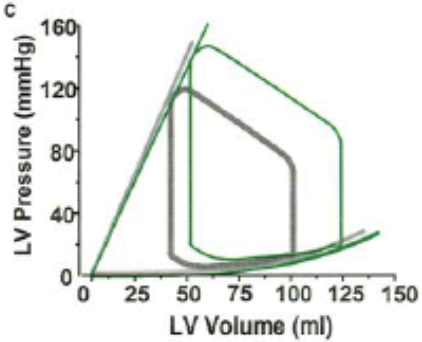


Maurer M, et al. J Card Failure 2005;11:177

HTN HFPEF (↑Ees)

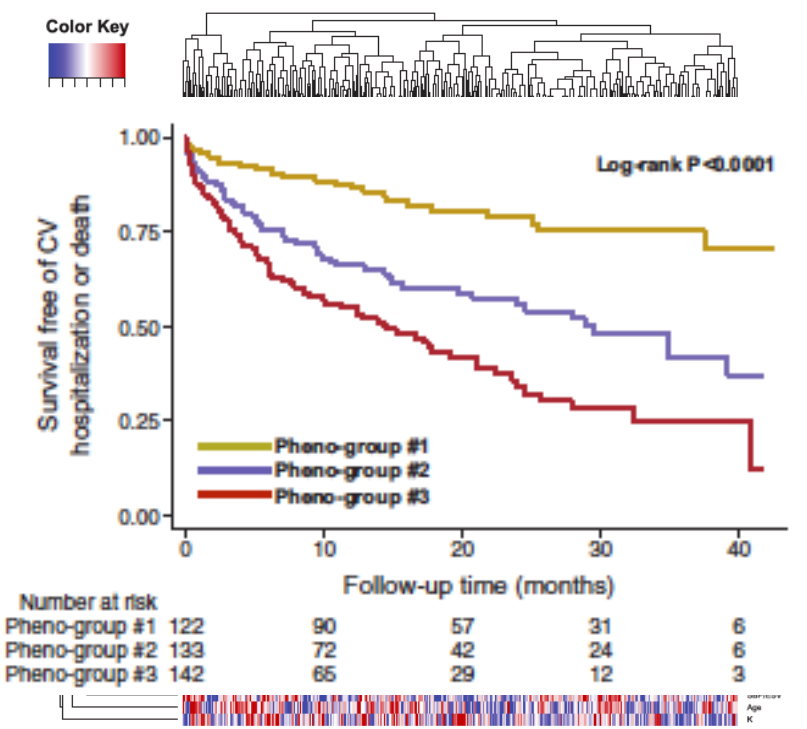


HTN HFPEF (↑EDV)



Heterogeneity in HFpEF

Phenomapping



Younger, low BNP

DM, obesity, OSA

Older, high BNP, MAGGIC, CKD

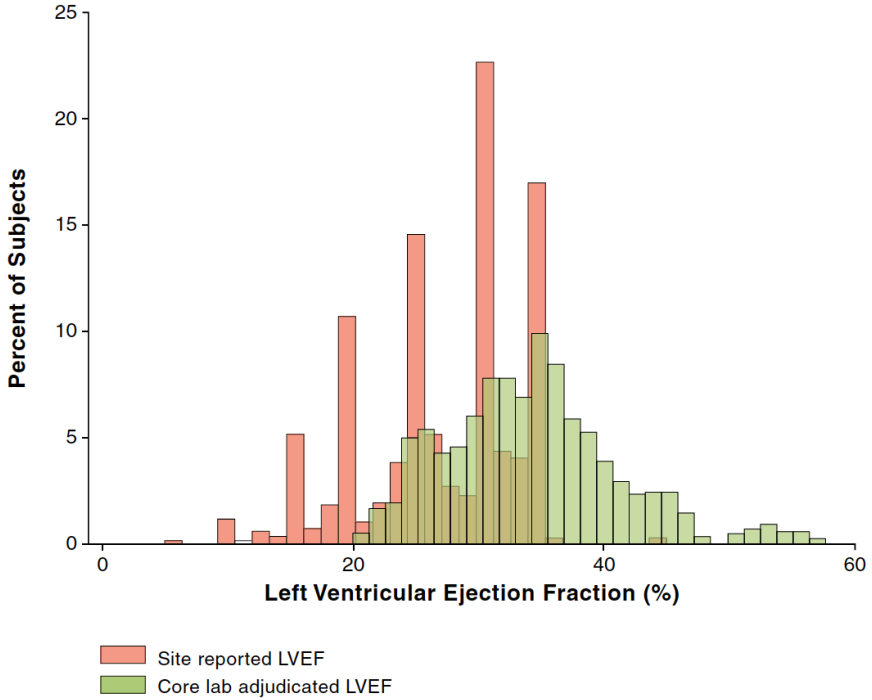
Shah S, et al. Circulation 2014

Diagnostic approach

- Signs of HF => Volume overload
  - *LVEF Normal?*
  - Excluded other causes?
- Symptoms of HF => Dyspnea (w/o Volume overload)
  - LVEF Normal?
  - Resting or provokable elevation in PCW? Or surrogate?

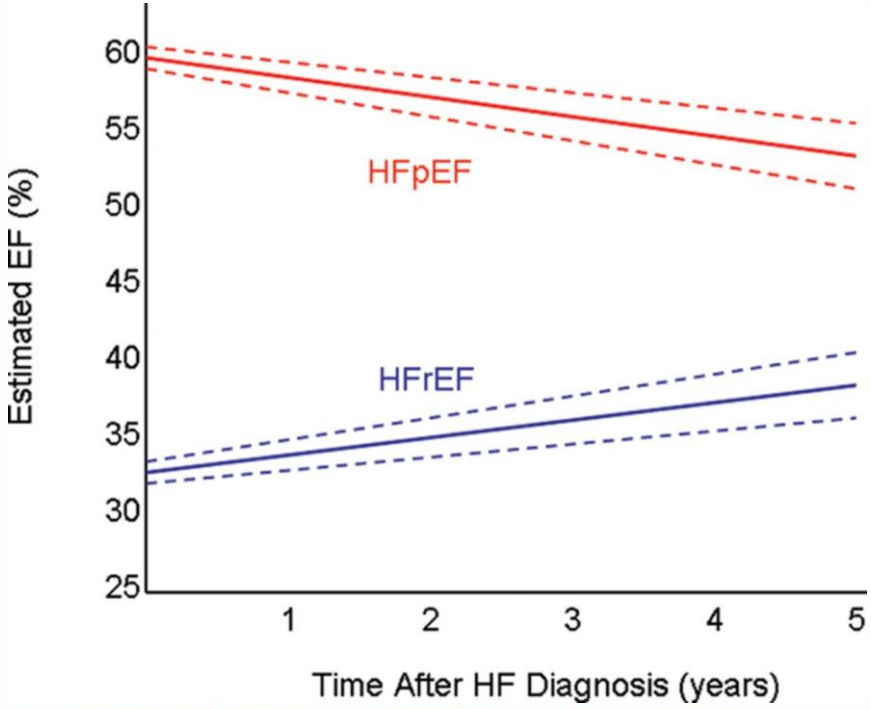
Misclassification of EF

Comparison to a Core Lab



Shah AM, et al. JACC CV Img 2012

LVEF Changes Over Time



At some point over 5 yrs,

- 39% of HFpEF, had EF <50%
- 39% of HFrEF, had EF >50%

- *Dunlay SM et al. Circ Heart Fail 2012;5:720-726*

Heart Failure with Mid-Range EF

HFrEF	HFmrEF	HFpEF
Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
LVEF <40%	LVEF 40–49%	LVEF ≥50%
–	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).

Classification	EF (%)	Description
I. Heart failure with reduced ejection fraction (HF*r*EF)	≤40	Also referred to as systolic HF. Randomized controlled trials have mainly enrolled patients with HF*r*EF, and it is only in these patients that efficacious therapies have been demonstrated to date.
II. Heart failure with preserved ejection fraction (HF*p*EF)	≥50	Also referred to as diastolic HF. Several different criteria have been used to further define HF*p*EF. The diagnosis of HF*p*EF is challenging because it is largely one of excluding other potential noncardiac causes of symptoms suggestive of HF. To date, efficacious therapies have not been identified.
a. HF*p*EF, borderline	41 to 49	These patients fall into a borderline or intermediate group. Their characteristics, treatment patterns, and outcomes appear similar to those of patients with HF*p*EF.

Diagnostic approach

- Signs of HF => Volume overload
  - LVEF Normal?
  - *Excluded other causes?*
- Symptoms of HF => Dyspnea (w/o Volume overload)
  - LVEF Normal?
  - Resting or provokable elevation in PCW? Or surrogate?

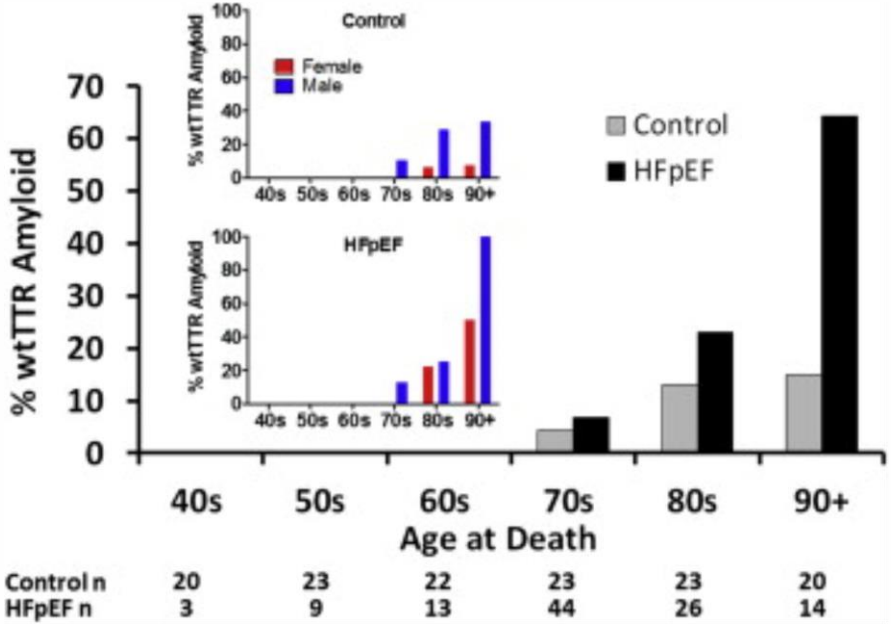
Signs and Symptoms of HFpEF
Not specific

- Constriction
- Restriction
- Mitral valve disease
- CAD
- Chronotropic incompetence

- Pulmonary
- Thoracic
- PAH
- Deconditioning
- Anemia
- Neuromuscular
- “Volume overload”

Amyloid in HFPEF

may be more common than you think…



- OR 3.8
- 5% w/ wTTR amyloid
- 12% w/ mild wTTR deposition but severe fibrosis

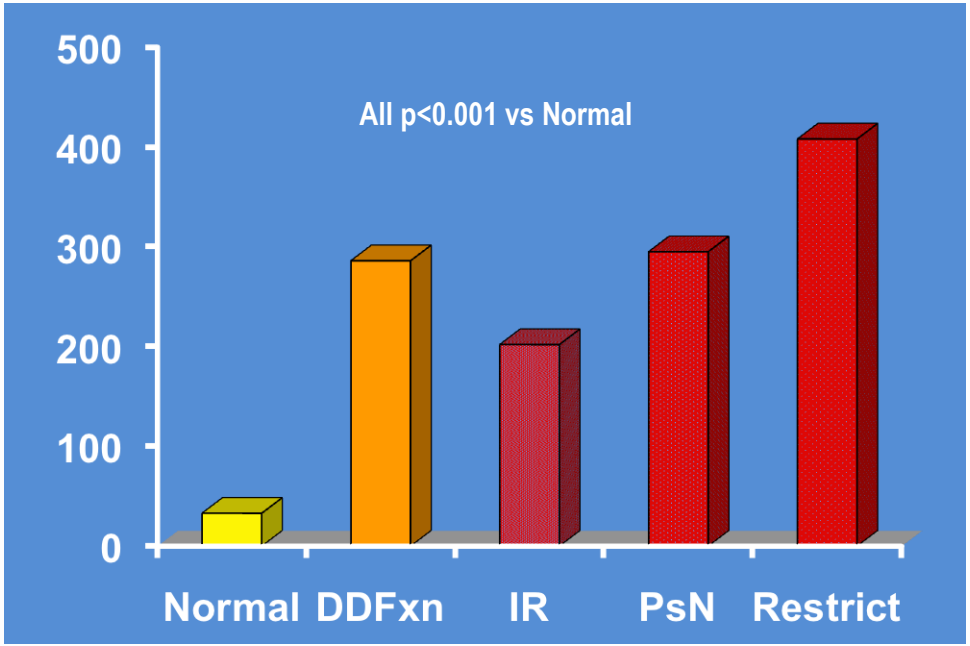
Mohammed SF, et al. JACC-HF. 2014;2(2):113-122

Diagnostic approach

- Signs of HF => Volume overload
  - LVEF Normal?
  - Excluded other causes?
- Symptoms of HF => Dyspnea (w/o Volume overload)
  - LVEF Normal?
  - *Resting or provokable elevation in PCW? Or surrogate?*

Diagnosing HFpEF

How about Natriuretic Peptides?



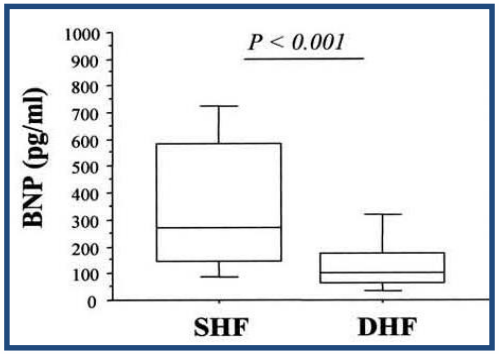
AUC 0.92
95% CI 0.87 - 0.95
p=0.001

BNP	62 pg/mL
Sens	85%
Spec	83%
Accuracy	84%

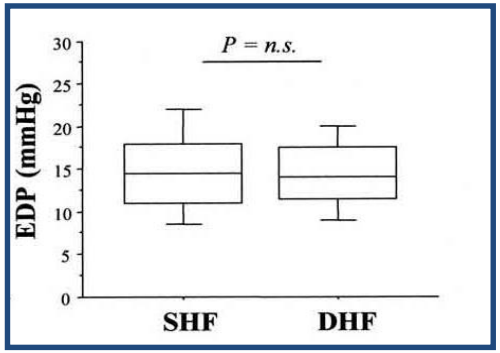
Lubien E, et al. Circulation 2002

NP in HFpEF

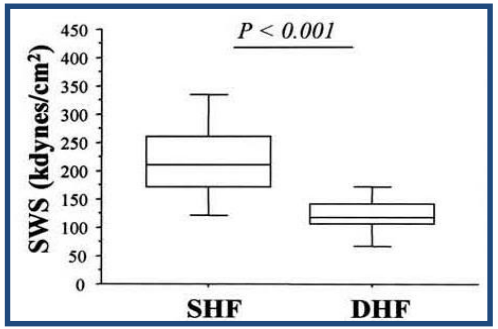
BNP



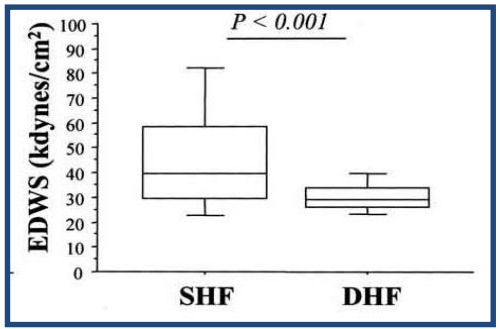
End Diastolic Pressure



Systolic Wall Stress



End Diastolic Wall Stress



Other putative mechanisms

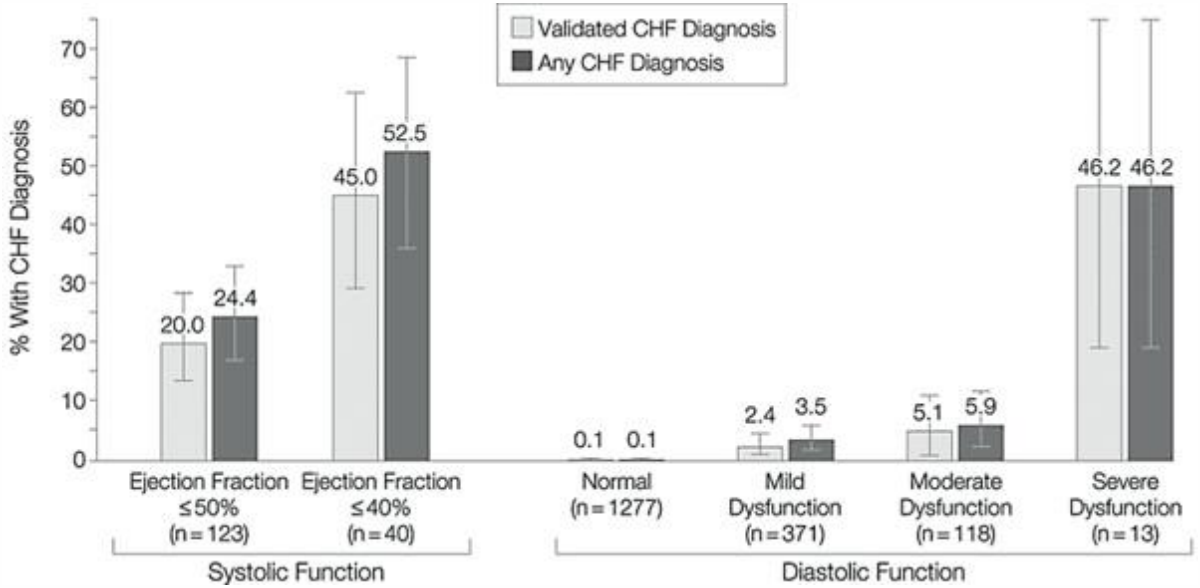
- Adipocyte clearance
- Reduced production
- Hyperinsulinemia
- Decreased lipolysis

Iwanaga Y et al. JACC. 2006

Limitations of Doppler for Assessing Diastolic Function

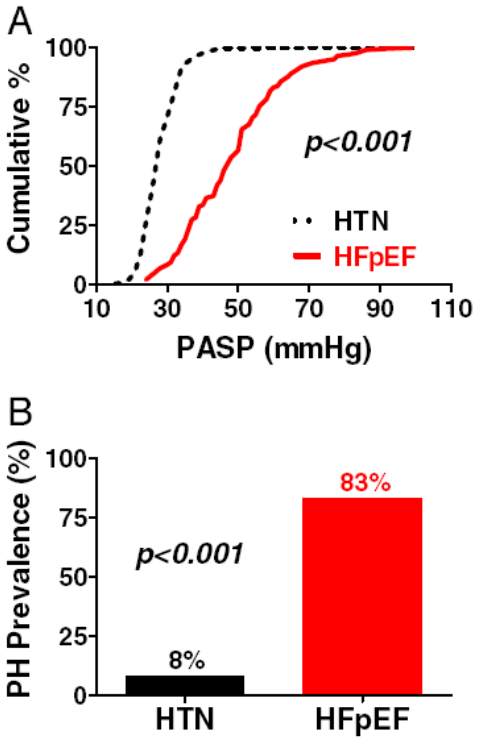
- Integrates several phases of diastole (active vs passive components)
- Operator dependent
- No single measure sufficient
- All measures are load dependent
- Not sufficient or necessary to make diagnosis of heart failure

Diastolic Dysfunction May Not Be Specific for HFPEF



Redfield MM, et al. JAMA 2003;289:194

Pulmonary Hypertension in HFPEF



244 HFpEF pts
719 HTN without HF

Women 57 – 68%
Age 67 – 79 yrs
BMI 28 – 30 kg/m2

PH defined by PASP > 35 mmHg
PCW estimated from E/E'

Lam CS, et al. JACC 2009

HFPEF in TOPCAT

Heterogeneity of Structure and Function

- Mean LVEF 59.3±7.9%
- Concentric LV remodeling (34%) and hypertrophy (43%)
- **Left atrial enlargement (53%)**
- Diastolic dysfunction was present in 66% of gradable participants
  - greater LVH and a higher prevalence LAE
- **Doppler evidence of PH (36%)**
- But at least 1 measure of structural heart disease was present in 93%

Shah AM, et al. Circulation HF 2014

HFpEF

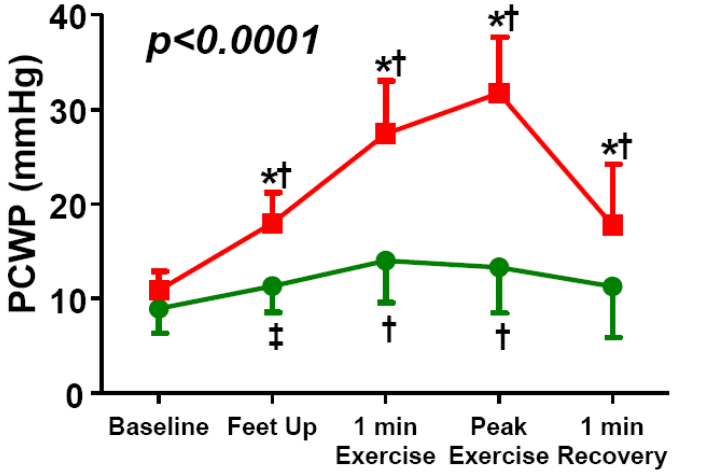
Diagnosis from Exercise Hemodynamics

55 pts referred for dyspnea

Normal BNP
No CAD
EF > 50%

Normal resting hemodynamics
Mean PA < 25 mmHg
Mean PCW <15 mmHg

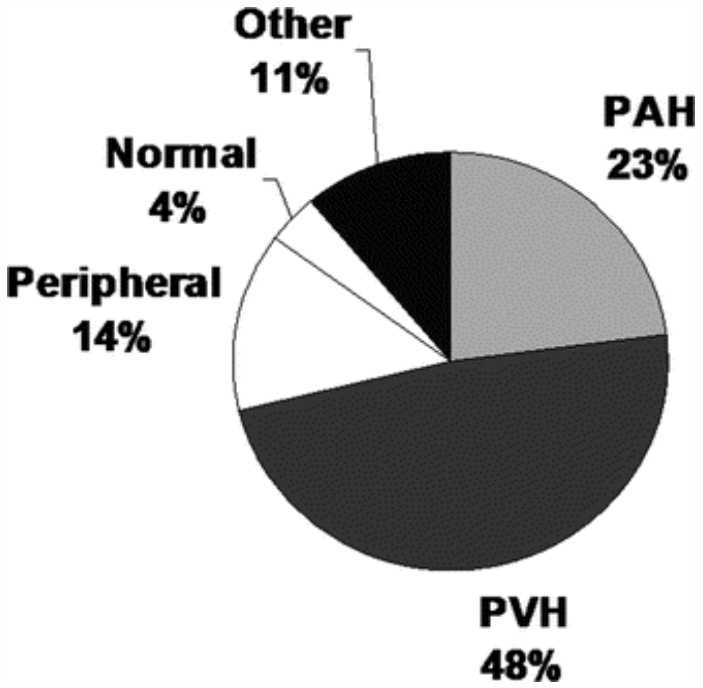
HFPEF
Exercise PCW > 25 mmHg
Exercise mPA > 30 mmHg



Borlaug BA, et al. Circ HF 2010

Cryptic dyspnea

Diagnoses by Exercise RHC



- 406 pts over 3 yrs
- CPET, radial and PA lines, RVG
- 305 referred for exertional intolerance
- PVH defined as exercise PCW >20 mmHg

Tolle JJ, Circ 2008

TOPCAT Criteria

Definition of Heart Failure (LVEF ≥ 45%)

SYMPTOMS (≥1 at screening)	SIGNS (>1 in the last 12 mos)
• Paroxysmal nocturnal dyspnea • Orthopnea • Dyspnea on mild or moderate exertion	• Any rales post cough • Jugular venous pressure (JVP) ≥ 10 cm H_2O • Lower extremity edema • Chest X-ray demonstrating pleural effusion, pulmonary congestion, or cardiomegaly

At least one hospitalization in last 12 months for which HF was a *major* component

OR

Elevated BNP>100 pg/mL or N-terminal pro-BNP>360 pg/mL within the last 30 days

ESC HF Guidelines 2016

HFrEF	HFmrEF	HFpEF
Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
LVEF <40%	LVEF 40–49%	LVEF ≥50%
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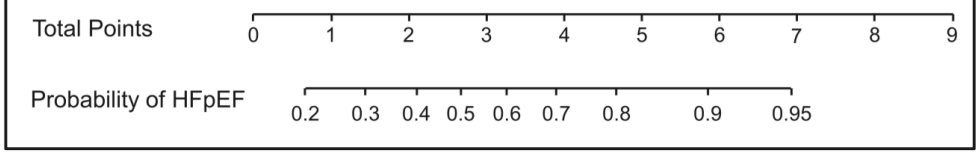
The H2FPEF score

	Clinical Variable	Values	Points
H_2	**H**eavy	Body mass index > 30 kg/m^2	2
	Hypertensive	2 or more antihypertensive medicines	1
F	Atrial **F**ibrillation	Paroxysmal or Persistent	3
P	**P**ulmonary Hypertension	Doppler Echocardiographic estimated Pulmonary Artery Systolic Pressure > 35 mmHg	1
E	**E**lder	Age > 60 years	1
F	**F**illing Pressure	Doppler Echocardiographic E/e' > 9	1
H_2FPEF score			Sum (0-9)



Odds of HFpEF doubled every 1-unit (OR 1.98; 95%CI, 1.73–2.30).

AUC 0.841 (95%CI, 0.802–0.881).

NT-proBNP levels did not add discriminatory power.

Reddy YNV, Borlaug BA
Circulation 2018

Which patient has HFPEF?

All four patients present with exertional dyspnea, LVEF > 50%, no valvular abnormalities, no CAD.

A. 55 WM with BMI 38, HTN, 1+ edema
B. 70 BF with BMI 35, HTN, DM, arthritis and LVH
C. 86 WF with afib, anemia, LAE
D. 70 BM with CKD, “COPD”, RVSP 50