When is HFNEF clinically relevant?

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Definition of HFNEF

• The diagnosis of HFNEF requires the following conditions to be satisfied:

1. signs or symptoms of heart failure
2. normal or mildly abnormal systolic LV function
3. objective evidence of diastolic LV dysfunction
Case 1: Orpha, 80 years

- Diabetes type II,
- 2003 CABG; 2007 thyroïdectomy, 2007 stent in native & venous bypass
- Febr 2010: increasingly short of breath for the last two weeks. No fever.
- Referred by the pneumologist
- Dyspnea III, cough, wheezing, some minor rales over the bases
- No signs of fluid retention.
Orpha, 80 years
Orpha, 80 years

EF 0.65
135 gr/m²
E/e’ = 81/4.85 = 17
TR = 2.5 m/s
PAP = 25+5 = 30 mm Hg
Signals unchanged when compared to echo in November 2009
Orpha, 80 years

- NT-pro-BNP = 881 pg/ml
- Blood gas analysis
  - pO2 = 67 mm Hg
  - pCO2 = 32 mm Hg
  - pH = 7.51
- CRP = 10.5 mg%
- Hematocrite 33% and Hb 11.5 mg%
- Leukocytes 7900/mm³
Diagnosis?

• Diastolic heart failure?

• Atypical pulmonary infection?
  – Interstitial pneumonia
Orpha: evolution

• Diuretics: furosemide 2x20 mg iv
  – no improvement
  – thirsty+++ 

• Start moxifloxacine (quinolones)
  – Progressive improvement over 4 days

• DIAGNOSIS: interstitial pneumonia in the presence of a moderate and chronic diastolic heart failure

• Follow up: persistent NYHA II plus
How to diagnose HFNEF

1. Symptoms or signs of heart failure

2. Normal or mildly reduced left ventricular systolic function
   - LVEF > 50%
   - LVEDVI < 97 mL/m²

3. Evidence of abnormal LV relaxation, filling, diastolic distensibility, and diastolic stiffness

- Invasive Haemodynamic measurements
  - mPCW > 12 mmHg
  - LVEDP > 16 mmHg
  - τ > 48 ms
  - b > 0.27

- TD
  - E/E’ > 15
  - 15 > E/E’ > 8

- TD
  - TD

- Biomarkers
  - NT-proBNP > 220 pg/ml
  - BNP > 200 pg/mL

- Echo – bloodflow Doppler
  - E/A_{30-p}< 0.5 and DT_{30-p} > 280 ms
  - Ard–Ad > 30 ms
  - LAVI > 40 mL/m²
  - LVMI > 122 g/m² (♂); >149 g/m² (♂)
  - Atrial fibrillation

4. HFNEF
Case 2: Paul, 75 years old

- Obese, hypertensive and diabetic
- Hospitalised 4 weeks ago with a HYPERTENSIVE pulmonary oedema, responding to sublingual then intravenous vasodilators
- He presents at the policlinic and feels presently fairly well
  - Short of breath on exercise NYHA II
Classification of AHFS

Figure 3 Clinical classification of acute heart failure. Modified from reference 205.
AHFS: CS1
Dyspnea & elevated BP

- Flash pulmonary edema
- No important fluid retention
- BP > 140 mm Hg
- Decreased renal function
The Pathogenesis of Acute Pulmonary Edema Associated with Hypertension

Ghandi...Little, NEJM, 2001;344:17.
Afterload induced diastolic dysfunction (rabbit)

Afterload induced diastolic dysfunction

Paul’s inflow signal

![Graph showing Paul’s inflow signal with various time points and measurements.]
HFNEF in outpatients with unexplained dyspnea

1. Increased ED stiffness
2. Dyssynchrony
3. Dynamic mitral regurgitation

Cardiovascular system in HFNEF

Heart failure with normal EF
Stiffening of both heart and vessels

Barry Massie, 2003 JACC
What is HFNEF?

1. Diastolic dysfunction:
   - Steep diastolic PV relation
   - Impaired load dependent myocardial relaxation
   - Impaired untwist
2. Matched increase systolic LV & arterial stiffening
3. Pulmonary hypertension (venous & art.)
4. Impaired contractility
   - Load corrected estimates of contractility
   - Impaired longitudinal function
   - Impaired torsion
5. Impaired left atrial function

- David Kass et al.
- Redfield, Lam, Borlaug
- Sanderson, Yu, Yip
Case 3: Ann, 63 years

- Suffered from metabolic syndrome and hypertension for many years. BMI 32
- Treated with telmisartan 80 mg and amlodipine 5 mg.
- She still works halftime as a secretary
- She complains about dyspnea when carrying files, when walking upstairs, or when cleaning the home (NYHA II-III)
Ann, 63 years

- Clinical nl. BP 135/85 mmHg
- Exercise testing.
  - 80 watts, BP 210/80 mmHg, HR 125 pm
  - Interrupted because of dyspnea
- Normal pulmonary testing
- Echo
  - LV mass 95 gr/m²; EF .62; LAV 60 ml
  - E/A 1.1 and E/e’ 0.10
  - PASP 33 mm Hg
- NT-pro-BNP = 110 pg/ml
Haemodynamics

• Rest hemodynamics
  – BP 137/94 mmHg; HR 72 pm
  – PCW = 11 mm Hg
  – PASP = 31 mmHg

Exercise hemodynamics
  – 50 watts; 182/90 mmHg; HR 104 pm
  – PCW = 28 mmHg
  – PASP = 59 mmHg
Exercise hemodynamics enhance diagnosis of early HFpEF
Borlaug et al. (Circulation Imaging)

- 55 patients with exertional dyspnea
  - EF > 0.50
  - No CHD
  - Normal BNP
  - Normal resting hemodynamics

- Stratification
  - Exercise PCW ≥ 25 mm Hg n=32 (age 63)
  - Exercise PCW ≤ 25 mm Hg n=23 (age 45)
A

\[ p < 0.0001 \]

PCWP (mmHg)

- Baseline
- Feet Up
- 1 min Exercise
- Peak
- 1 min Recovery

* \( p < 0.0001 \) for \( \Delta \text{PCWP} \) (vs NCD)

† \( p < 0.0001 \) vs base (within group)

‡ \( p < 0.01 \) vs base (within group)

NCD: Green
HFpEF: Red

B

LVEDP (mmHg)

- Rest
- Exercise

- Rest
- Exercise

\[ p < 0.0001 \]

C

PA Mean (mmHg)

- Rest
- Exercise
- Rest
- Exercise

\[ p < 0.0001 \]
Contraction-Relaxation Coupling and Impaired Left Ventricular Performance in Coronary Surgery Patients.
De Hert, Stefan; Gillebert, Thierry; Ten Broecke, Pieter; Mertens, Els; Rodrigus, Inez; Moulijn, Adriaan
Anesthesiology. 90(3):748-757, March 1999.
Take home messages

HFNEF

1. An increase in intrinsic myocardial stiffness and impaired relaxation
2. Increased systolic ventricular and arterial stiffening
3. Impaired systolic function and impaired torsion
4. Enhanced sensitivity to volume overload from increased LV remodelling and dilatation with volume-dependent elevation of filling pressures
5. In the earlier phases of the disease, these alterations are only present during exercise (leg lifting)

Gabriel Wai-Kwok Yip, Michael Frenneaux and John E Sanderson

Olmsted County study
The Pathophysiology of Heart Failure With Normal Ejection Fraction: exercise echocardiography reveals abnormalities of

• **longitudinal** motion
• **torsion** and untwist
• abnormalities of **atrial** function
Figure 1: Cumulative Frequency Distribution of PASP and Prevalence of PH by Subject Group

In patients with heart failure and preserved ejection fraction (HFrEF) (in red), the cumulative frequency distribution of pulmonary artery systolic pressure (PASP) was shifted toward higher pressures (A), whereas the prevalence of pulmonary hypertension (PH) was markedly increased (B) compared with subjects with hypertension (HTN) (in black) without heart failure in the community.

Figure 2: Association of PASP With Pulmonary Venous Hypertension

PASP increased with pulmonary capillary wedge pressure (PCWP) in patients with HFrEF, as well as in subjects with HTN without heart failure, but remained higher in HFrEF than HTN after adjusting for PCWP (p < 0.001). Raw data points and linear regression line for the association are shown for HFrEF (in red) and HTN (in black). Abbreviations as in Figure 1.