Is normal ejection fraction equivalent to normal systolic function?

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2\textsuperscript{nd} criterion (out of 3) for the diagnosis of HFNEF:

"Normal or mildly abnormal systolic LV function"
Topics

- How?
- Why?
- Implications?
LV structure and function

Radial

Longitudinal

Torsion

PLAX

A4C

A2C
Decreased longitudinal at rest

Systolic velocity (cm/s)


Increased radial at rest

Systolic velocity cm/s

![Bar chart comparing systolic velocity in controls and diabetics for longitudinal and radial directions.](chart.png)

- **Longitudinal**
  - Controls: ~5 cm/s (p < 0.01)
  - Diabetics: ~6 cm/s (p < 0.05)

- **Radial**
  - Controls: ~5 cm/s (p < 0.05)
  - Diabetics: ~6 cm/s (p < 0.001)


Preserving EF

Vinereanu et al. JACC 2009 (abstr).

$S_{TDE}$ (cm/s)

- Group 1 (no risk factors)
- Group 2 (1 risk factor)
- Group 3 (2 risk factors)
- Group 4 (3 risk factors)
- Group 5 (> 3 risk factors)

EF (%)

- Longitudinal
- Radial
- Global

$N = 246$
1. LV longitudinal, but neither radial function nor EF, is related to arterial stiffness.
2. Peak velocity of radial shortening of the left ventricle coincides with arrival of reflected waves.

3. Generation of longitudinal shortening persists against reflections.
Longitudinal/radial at stress

**Longitudinal systolic velocity**

![Bar chart showing comparison of peak stress $S_{TDE}$ (cm/s) and FR (cm/s) between control and different conditions.

- **Peak stress $S_{TDE}$ (cm/s):**
  - **Control:**
    - Longitudinal: ~11 cm/s
    - Radial: ~8 cm/s
  - **Rest:**
    - Longitudinal: ~6 cm/s
    - Radial: ~5 cm/s
  - **p < 0.0001**
  - **p ns**

- **FR (cm/s):**
  - Longitudinal: ~9 cm/s
  - Radial: ~5 cm/s
  - **p < 0.05**
  - **p < 0.01**

*Vinereanu et al. JACC 2009 (abstr).*
Torsion at rest/stress

Tan et al. JACC 2009.
But biphasic pattern

Park et al.  
JASE 2008.

Phan et al.  
EJE 2009.
Why increased in early stages?

1. Reduction of rotational deformation delay, because apical rotation occurs later in systole, close to the peak basal rotation (due probably to fibrosis of the conduction system);

2. Compensatory increase of the mid-wall and epicardial torque, unopposed by the affected subendocardial longitudinal fibers.

Tan et al. JACC 2009.
Phan et al. EJE 2009.
## Summary

<table>
<thead>
<tr>
<th>Systolic function in HFNEF</th>
<th>Rest</th>
<th>Stress</th>
</tr>
</thead>
<tbody>
<tr>
<td>Longitudinal function</td>
<td>↓</td>
<td>↓ ↓</td>
</tr>
<tr>
<td>Radial function</td>
<td>N/↑</td>
<td>↓</td>
</tr>
<tr>
<td>Torsion</td>
<td>↑ (early stages)</td>
<td>↓</td>
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<tr>
<td></td>
<td>↓ (advanced stages)</td>
<td>↓ ↓</td>
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</tbody>
</table>
Mechanisms of HFNEF?

Injury

- Neurohormonal activation
- Myocardial fibrosis
- Myocardial ischaemia
- Endothelial dysfunction

↓ myocardial (subendocardial) energetics

↓ Longitudinal systolic function
↑ Radial & torsion (compensatory)

↓ All systolic parameters with ↓ recoil
↓ Early/late diastolic filling

↑ End-diastolic pressure (E/E')

Breathlessness & ↑ BNP

Exercise/stress
Myocardial energetics

Phan et al.
JACC 2009.
Implications?

- Definition of HFNEF
- Diagnosis
- Prognosis
- Treatment
Definition of HFNEF

Systolic velocity of long-axis function

Diastolic heart failure?

Normal

HFNEF

Systolic heart failure

Diastolic velocity of long-axis function
Preserved ejection fraction = regional (long-axis) systolic dysfunction
Measuring only global function or radial Fr Sh is misleading
**Diagnosis**

“Assessment of longitudinal (subendocardial) **systolic** function = probably the most sensitive measure of ventricular function.”

_Yip et al. Heart 2009._

**Criteria to rule out heart failure**

- LVEF > 50%
- LVEDI < 76 ml/m²
- LAVI < 29 ml/m²
- No atrial fibrillation
- No LVH
- No valvular/pericardial disease
- E/E’ < 8
- **Longitudinal S > 6.5 cm/s**

_Paulus et al. Eur Heart J 2007._
Longitudinal S = best accuracy for the diagnosis of HF (increased BNP)

**Receiver operating characteristics**

- Longitudinal systolic velocity: 0.94
- Radial systolic velocity: 0.85
- Global ejection fraction: 0.74

Prognosis (1)

Best predictor of mortality in the general population

= combined systolic & diastolic index

\[ E_{as} = \frac{E'}{A' + S'}; \quad HR = 1.71 \]

Kaplan-Meier survival curves by tertiles of the eas index

**N = 1036**

*Kaplan-Meier survival curves by tertiles of the eas index*

Prognosis (2)

Best predictor of mortality in HFNEF = stress-corrected midwall fractional shortening (sc-mFS)

Borlaug et al. JACC 2009.
Treatment

New targets: longitudinal function instead of EF

New assessment of “conventional” therapies:
- SRAA antagonists: ACEI, ARB
- Vasodilatatory BB: Nebivolol, Carvedilol

New strategies:
- Aldosterone antagonists: Spironolactone, Eplerenone
- Renin inhibitors: Aliskiren
- Endothelin receptor A antag.: Sitaxsentan
- AGE-products breakers: Alagebrium
- Metabolic agents: Ranolazine, Perhexiline
Longitudinal strain & spironolactone

Conclusions

1. Resting LV systolic function is impaired in patients with HFNEF:
   • decrease of longitudinal function
   • compensatory increase of radial function
   • biphasic pattern of torsion

2. Functional reserve (longitudinal, radial, and torsion) is impaired

3. Mechanisms are related to inefficient ventriculo-arterial coupling

Diagnosis of HF as a continuum
• Assessment of long-axis function most sensitive
• Exercise/stress might be necessary

Treatment
• New targets
• New assessment of conventional therapies
• New strategies

Prognosis
• Systolic function most powerful