



# Simposio Sindromi Cliniche con Disfunzione Diastolica

**Ines Monte**

Dip. Cardio-  
Toraco-Vascolare  
e Trapianti  
d'Organo

A.O.U. Policlinico  
Vittorio  
Emanuele  
Catania

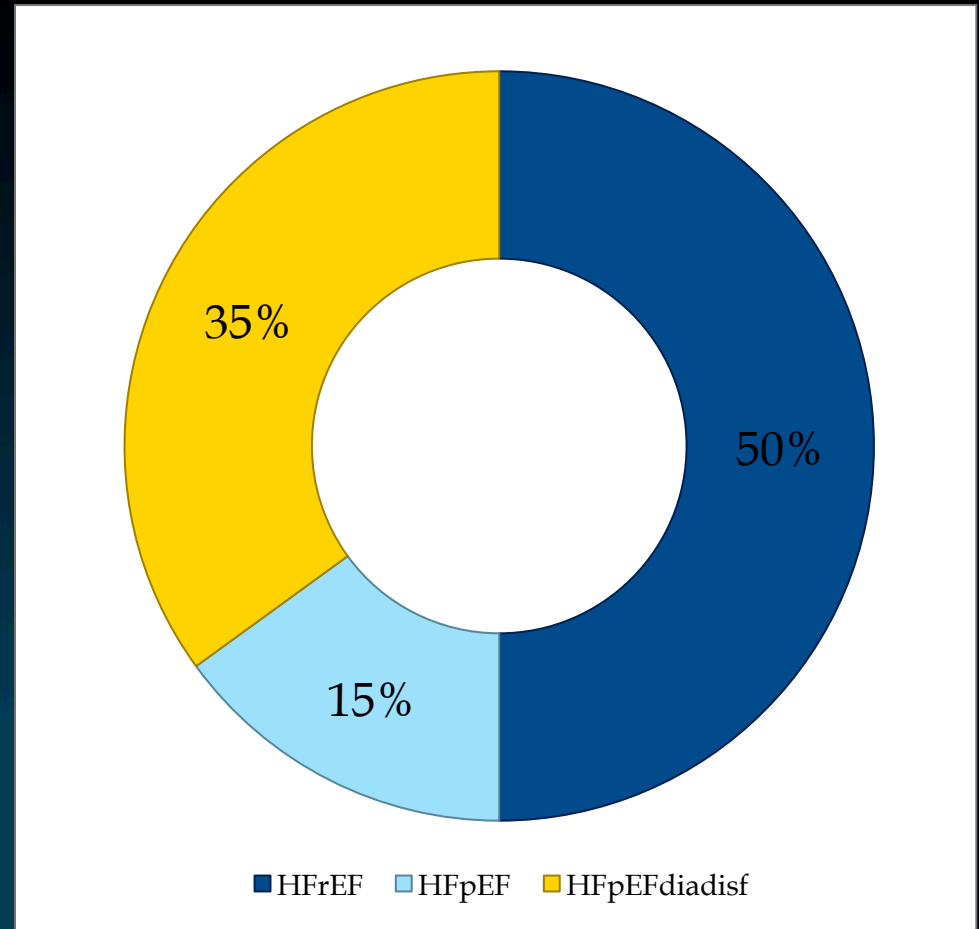


- **Scompensso cardiaco a EF ridotta (HF-rEF):**

- si caratterizza per una compromissione della funzione sistolica cardiaca espressa da una riduzione della frazione di eiezione del ventricolo sinistro

- **Scompensso cardiaco a funzione preservata (HF-pEF)**

- conserva una buona funzione sistolica, ma rappresenta un gruppo eterogeneo in cui la disfunzione diastolica è l'alterazione più comune nel 70% di questi pazienti

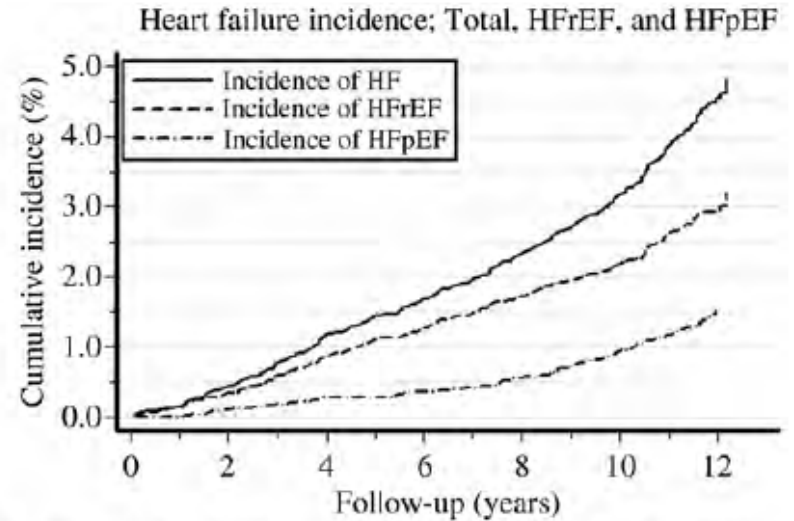


- ... The prevalence of diastolic heart failure varied from 13 to 74% of all heart failure cases
- ... Natural history of diastolic heart failure was considered to be more benign than systolic heart failure with a lower mortality and morbidity rate

• *Echeverria 1983, Dougherty 1984, Soufer 1985, Cohn 1990, Wheeldon 1994, Vasan 1995*

- ...Epidemiological and clinical studies reported prevalences of HFpEF between 40% and 71% in heart failure patients (average 54%)

- *Owan 2006, Abhayaratna 2006, Mosterd 2007, Biagi 2007, Tsutsui 2010*



Total HF	8569	8313	7966	7638	7312	6633	1273
HFrEF	8569	8322	7991	7669	7351	6693	1287
HFpEF	8569	8336	8031	7721	7412	6747	1306

- ...Moreover, the prognosis of patients suffering from diastolic HF is as ominous as the prognosis of patients suffering of systolic heart failure

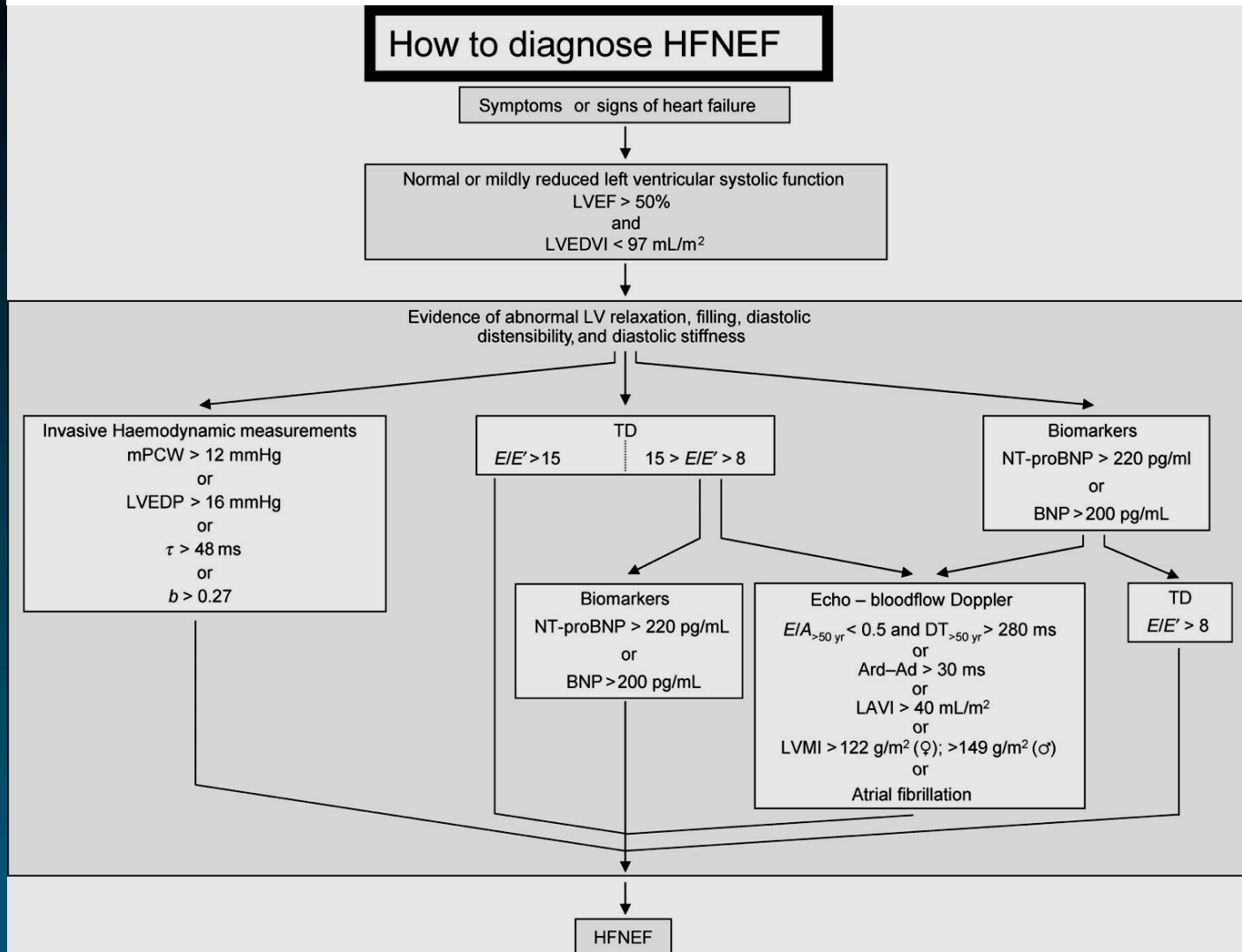
- *Cleland 2003, Owan 2005, Yancy 2006, Liao 2006, Bhatia 2006, Aurigemma 2006*



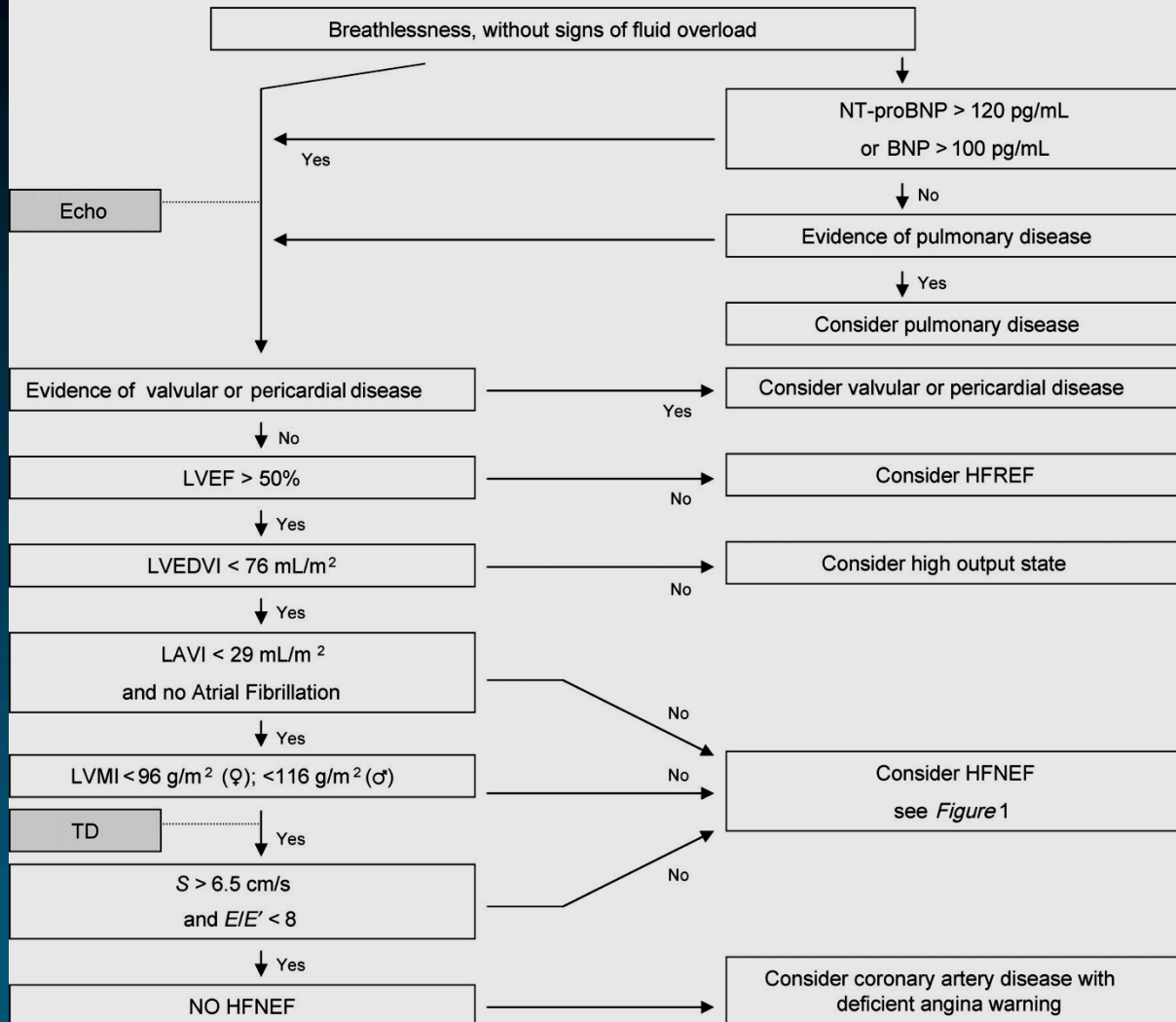
Study (study period)	Setting	HFPEF no.	LVEF criteria	Inclusion criteria	Key exclusion criteria	Approximate follow-up duration (years)	Average annual mortality rate (%)
<b>Population-based studies</b>							
Adabag et al. <sup>29</sup> (1995–2000)	22 hospitals, USA	787	≥45%	Index HF hospitalization		5	10
Owan et al. <sup>2</sup> (1987–2001)	Mayo Clinic Hospital, USA	2167	≥50%	Index HF hospitalization + echo in ≤30 days		10	13
Bhatta et al. <sup>15</sup> (1999–2001)	103 hospitals, Canada	880	>50%	Index HF hospitalization		1	22.2
Perez de Isla et al. <sup>23</sup> (2002–2003)	Single-centre hospital, Spain	679	≥50%	≥70 years, index HF hospitalization, clinical and radiographic diagnosis of HF		1.5	25.4
<b>Randomized clinical trials</b>							
I-PRESERVE <sup>9</sup> (2002–2005)	25 Countries, Europe, USA, South Africa, and Australia	4128	≥45%	≥60 years, NYHA ≥II, HF hospitalization ≤6 mths	SBP <100 or >160 mmHg, DBP >95 mmHg, Hb <11g/dL	4	5.2
DIG-PEP <sup>8</sup> (1991–1993)	USA (186 centres), Canada (116 centres)	988	>45%	Clinical diagnosis of HF, sinus rhythm at baseline	Cor pulmonale	3	7.6
CHARM-Preserved <sup>10</sup> (1999–2000)	618 centres in 26 countries	3023	>40%	≥18 years, NYHA II–IV ≥4 weeks, previous hospitalization for cardiac reason	Persistent systolic or diastolic hypertension	3	5
PEP-CHF <sup>7</sup> (2000–2003)	53 centres in 8 countries	846	>40%	≥70 years, clinical and echo diagnosis of HF, treated with diuretics, HF hospitalization ≤6 months	Significant valve disease, stroke history	2.2	5.9
TIME-CHF <sup>19</sup> (2004)	15 hospitals, Switzerland and Germany	123	>45%	≥60 years, NYHA ≥II, hospitalization ≤1 year, NT-proBNP level 2x ULN		1.5	14
<b>National Heart Failure Registries</b>							
Heart Failure Survey in Israel (HFSIS) <sup>16</sup> (2003)	25 hospitals, Israel	1364	≥40%	Clinical diagnosis of HF, confirmed by echo and radiography		1	22
Japanese Cardiac Registry of Heart Failure in Cardiology (JCARE-CARD) <sup>14</sup> (2009)	164 hospitals, Japan	429	≥50%	HF as primary cause of hospitalization		2.4	11.6



# Diagnostic flowchart on 'How to diagnose HFNEF' in a patient suspected of HFNEF.



# How to exclude HFNEF



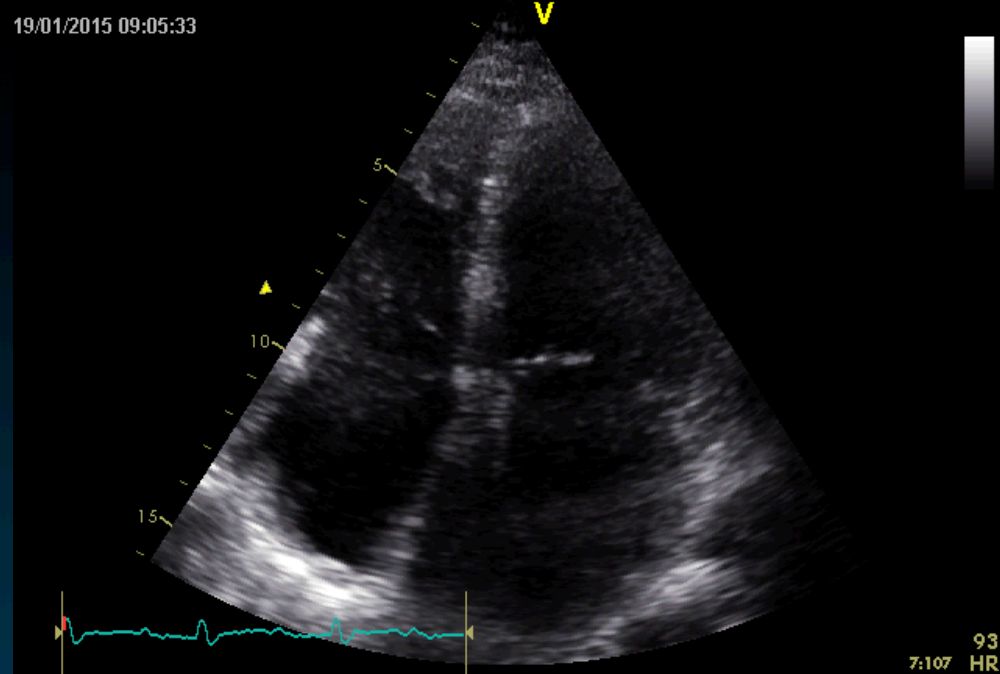
▣ B.N. (f. 59 a)

▣ Dispnea CF 3

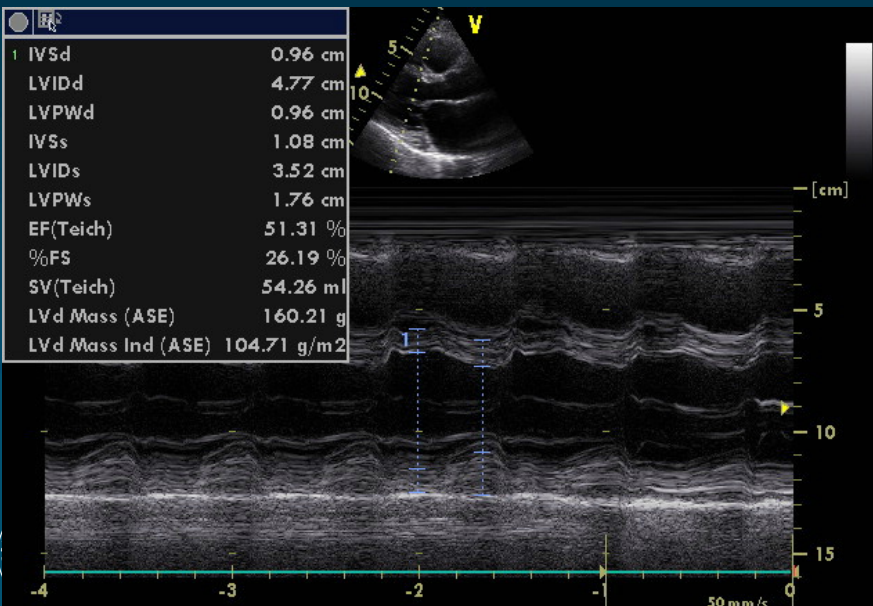
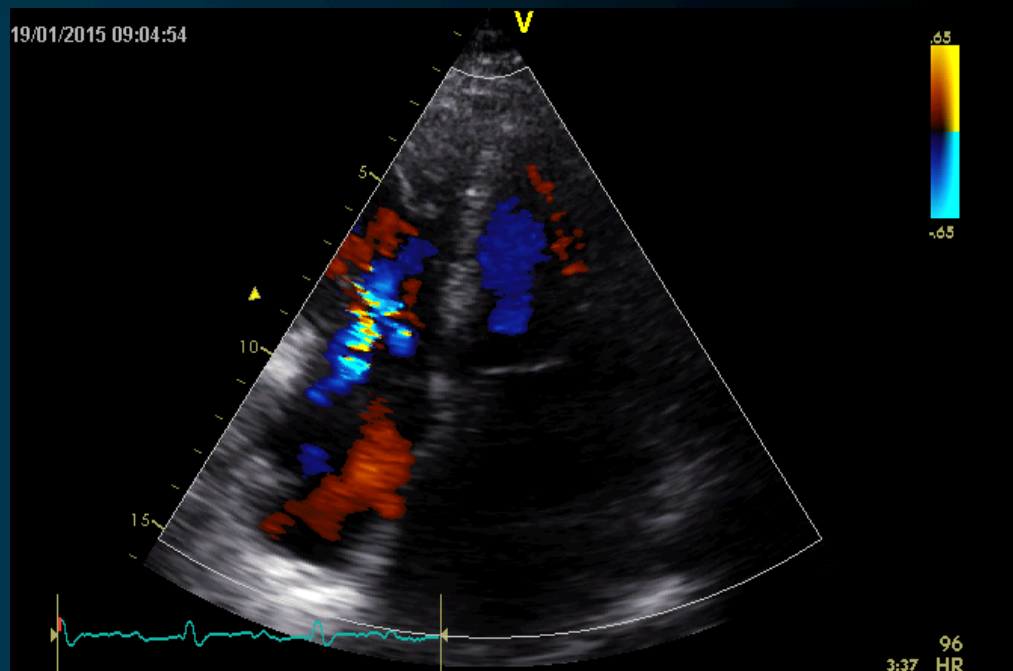
▣ IDDM

▣ LVEF 2D 53%

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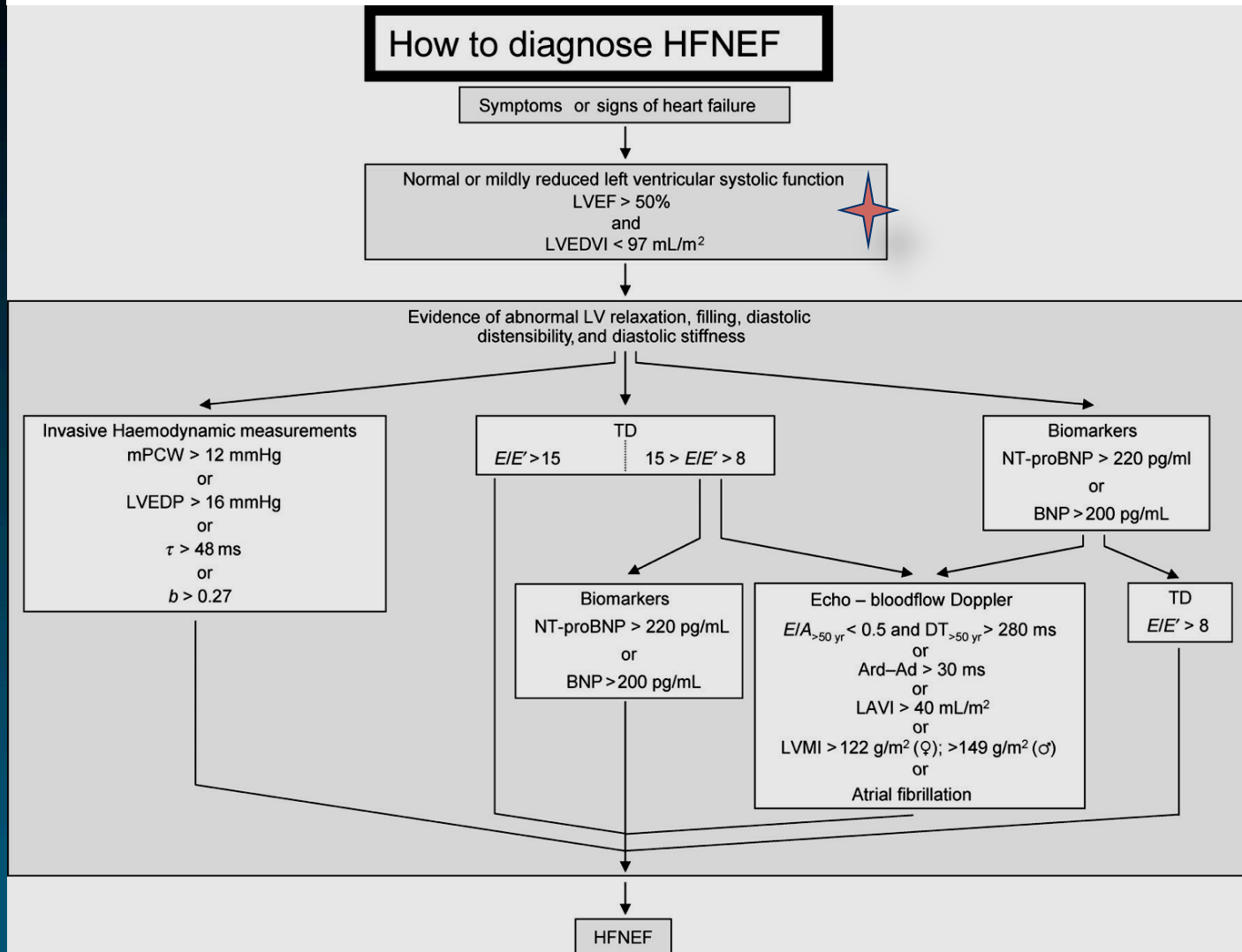


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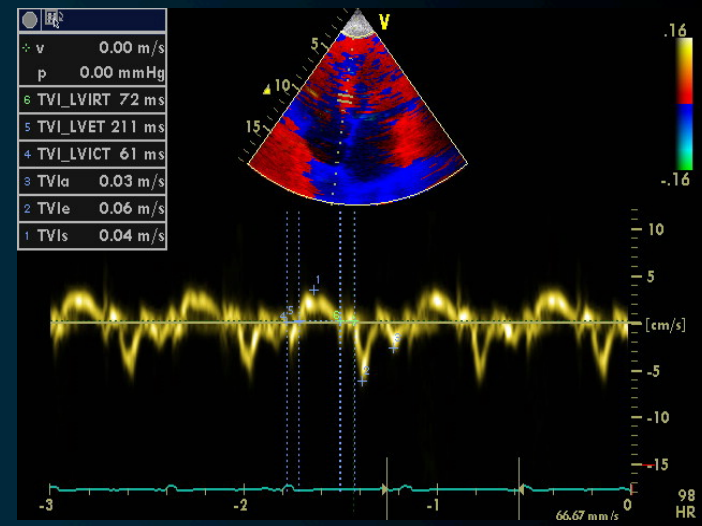
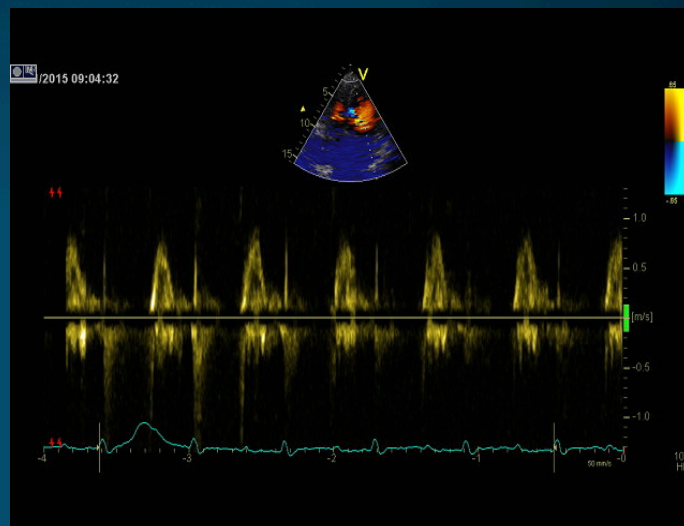
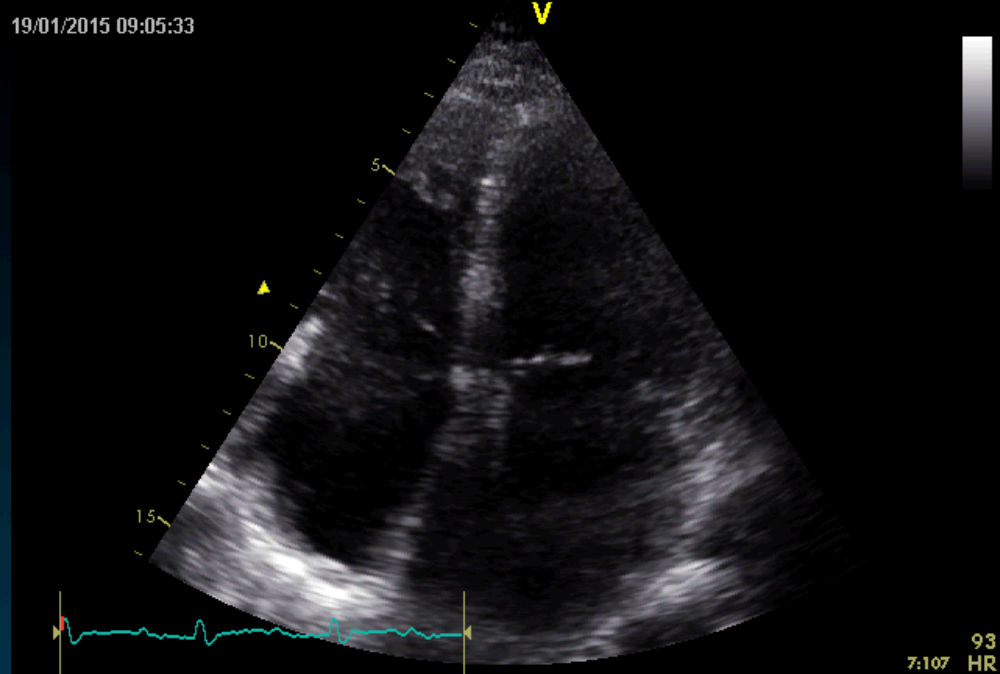


# Diagnostic flowchart on 'How to diagnose HFNEF' in a patient suspected of HFNEF.

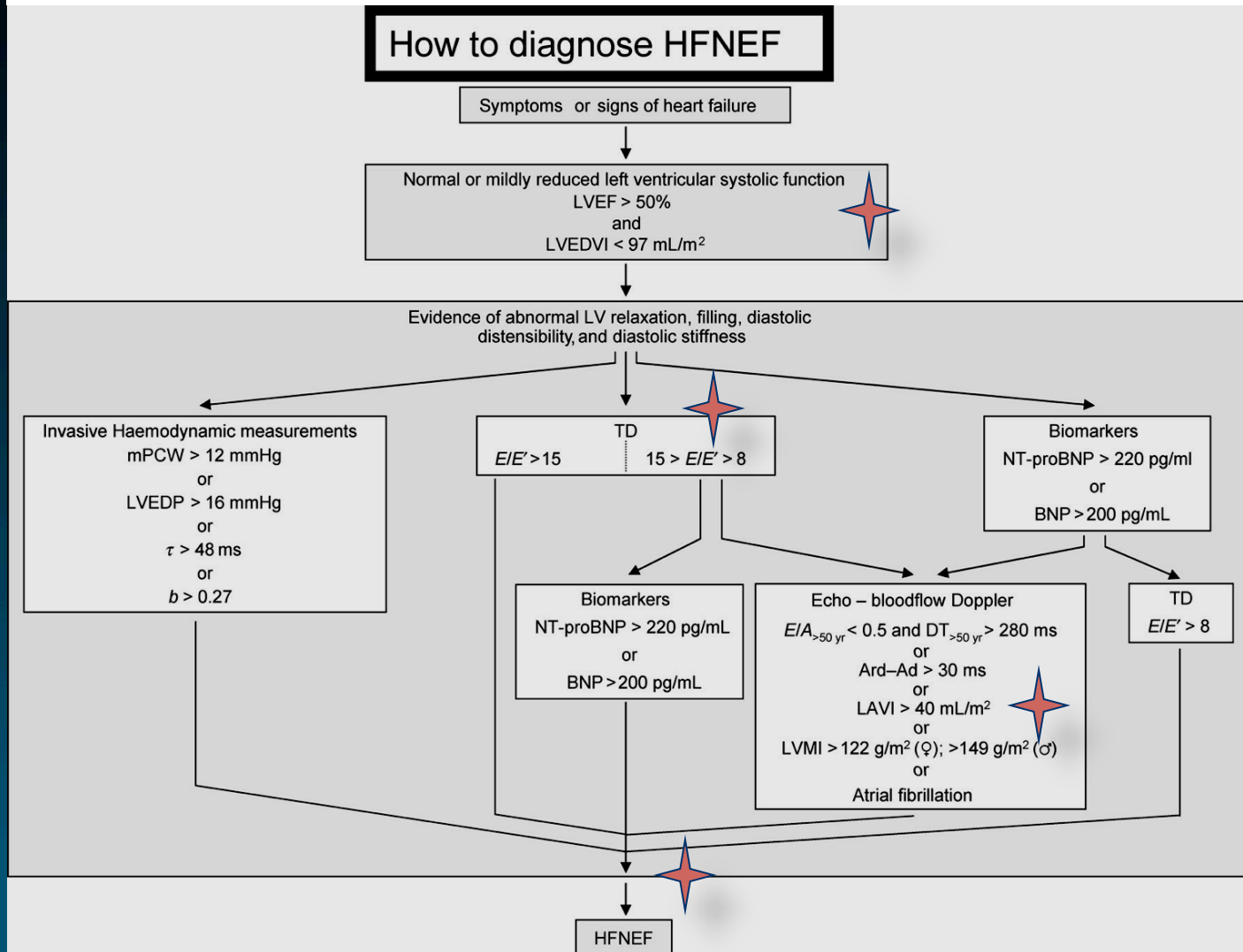


- ▣ B.N. (m. 59 a)
- ▣ Dispnea CF 3
- ▣ IDDM

- ▣ LVEF 53%
- ▣ LVDVI 61 ml/mq
- ▣ LAVI 71 ml/mq
- ▣ E/A 0.8
- ▣ E/E' 11

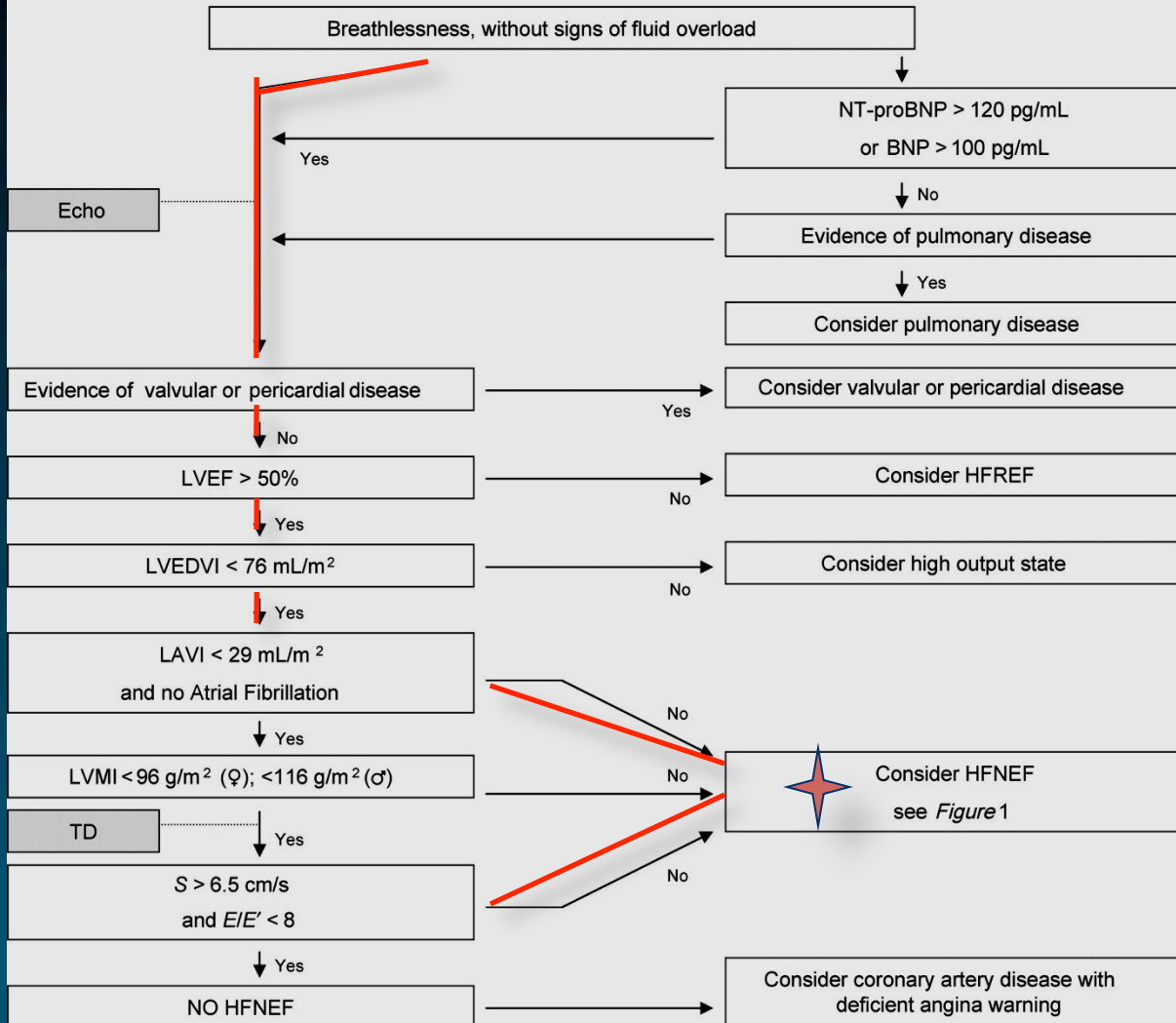


# Diagnostic flowchart on 'How to diagnose HFNEF' in a patient suspected of HFNEF.



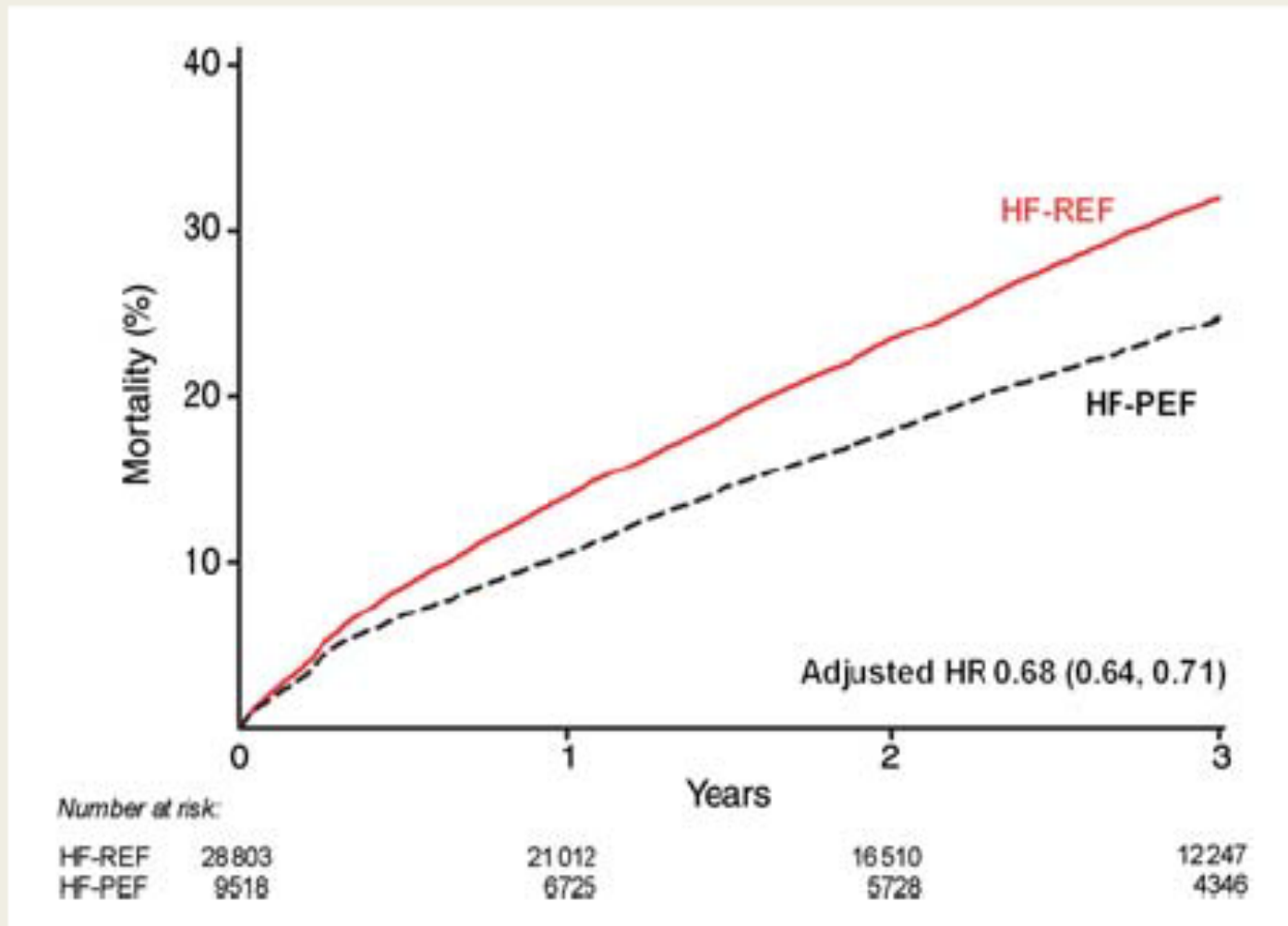


# How to exclude HFNEF



## The survival of patients with heart failure with preserved or reduced left ventricular ejection fraction: an individual patient data meta-analysis

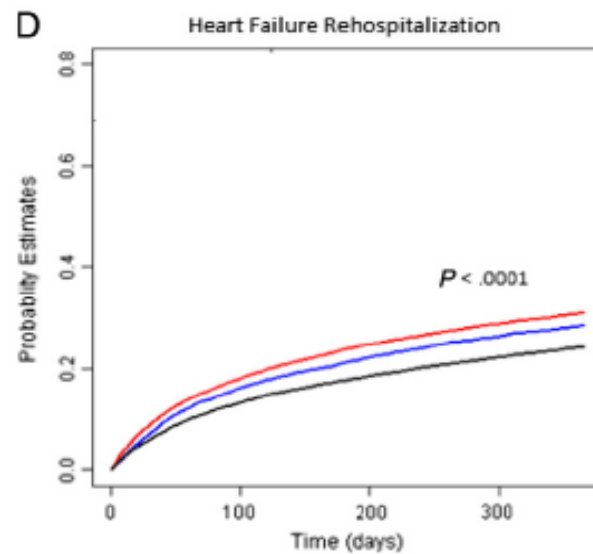
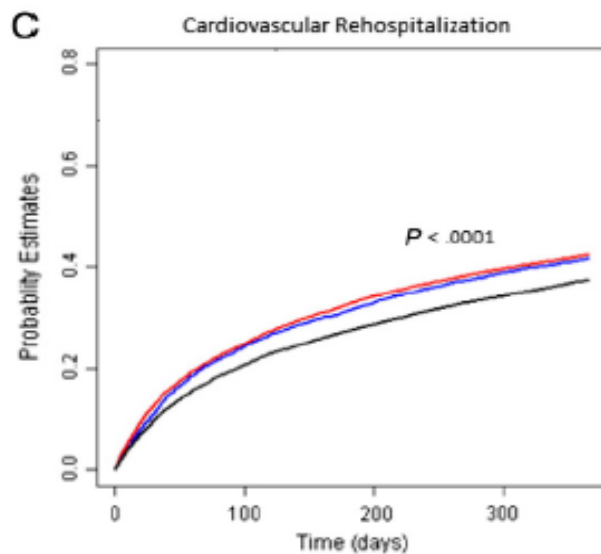
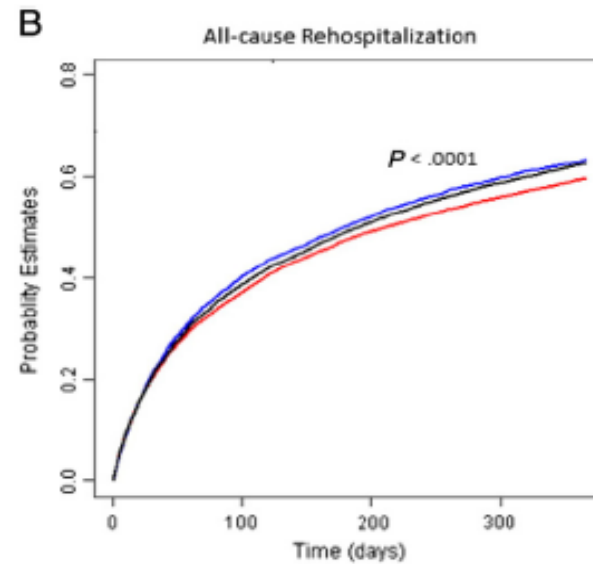
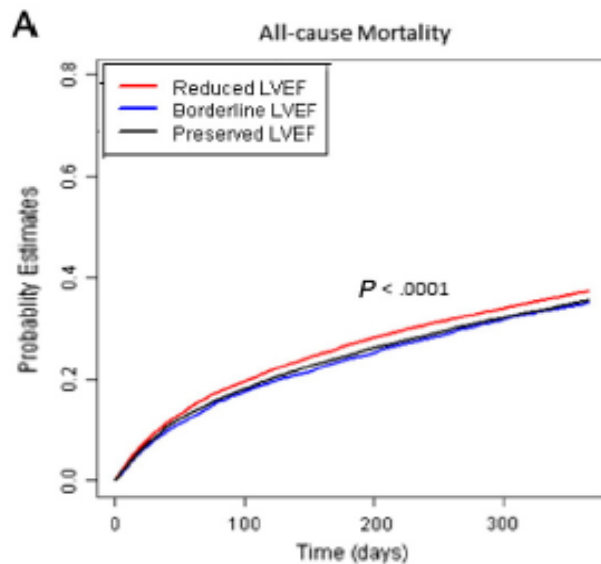
Meta-analysis Global Group in Chronic Heart Failure (MAGGIC)



# Outcomes in patients with heart failure with preserved, borderline, and reduced ejection fraction in the Medicare population



Richard K. Cheng, MD, MS,<sup>a</sup> Marguerite Cox, MS,<sup>b</sup> Megan L. Neely, PhD,<sup>b</sup> Paul A. Heidenreich, MD, MS,<sup>c</sup> Deepak L. Bhatt, MD, MPH,<sup>d</sup> Zubin J. Eapen, MD, MHS,<sup>b</sup> Adrian F. Hernandez, MD, MHS,<sup>b</sup> Javed Butler, MD, MPH,<sup>e</sup> Clyde W. Yancy, MD, MS,<sup>f</sup> and Gregg C. Fonarow, MD<sup>g</sup> *Richmond, VA and Durham, NC*  
[Am Heart J 2014;168:721-730.e3.]

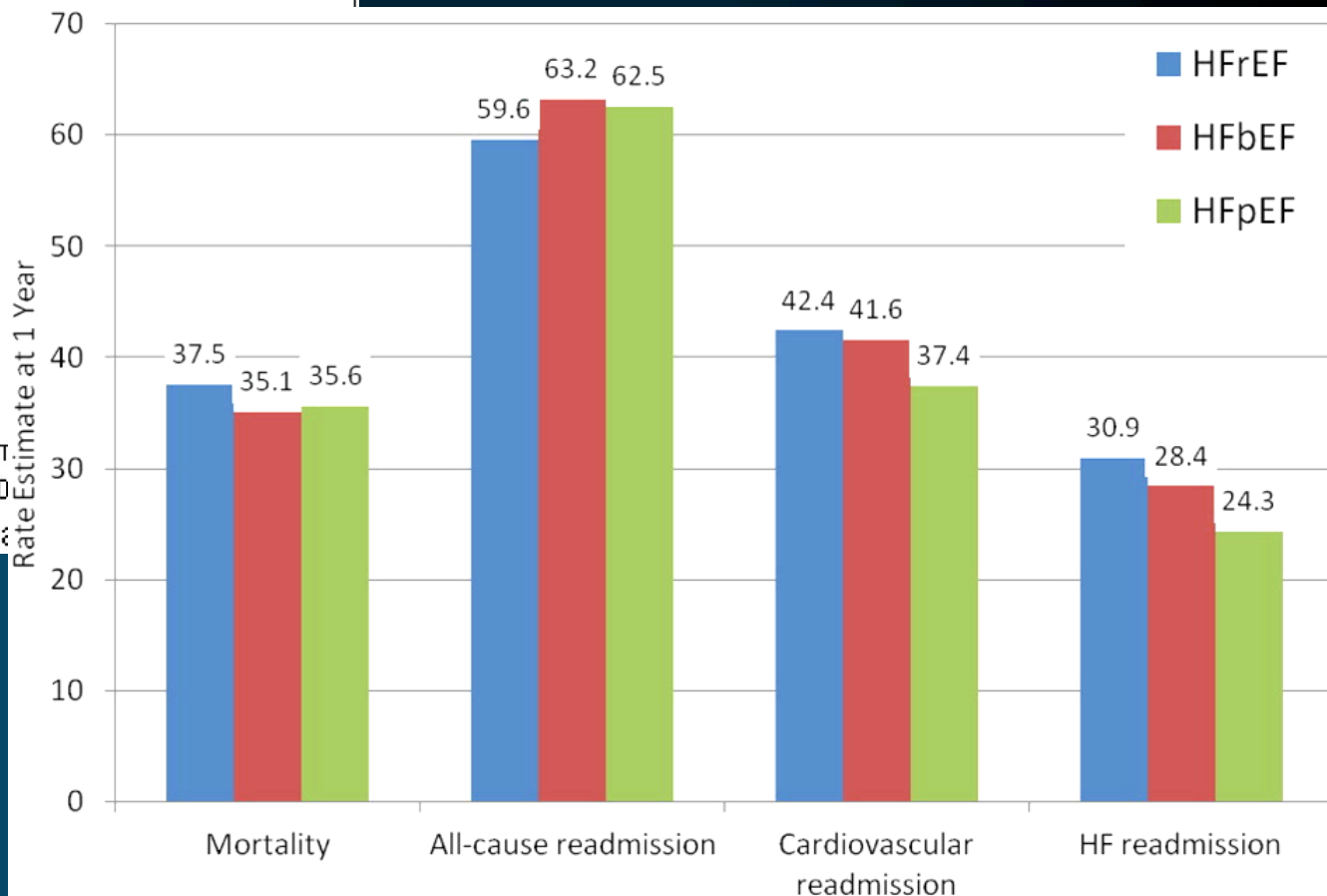
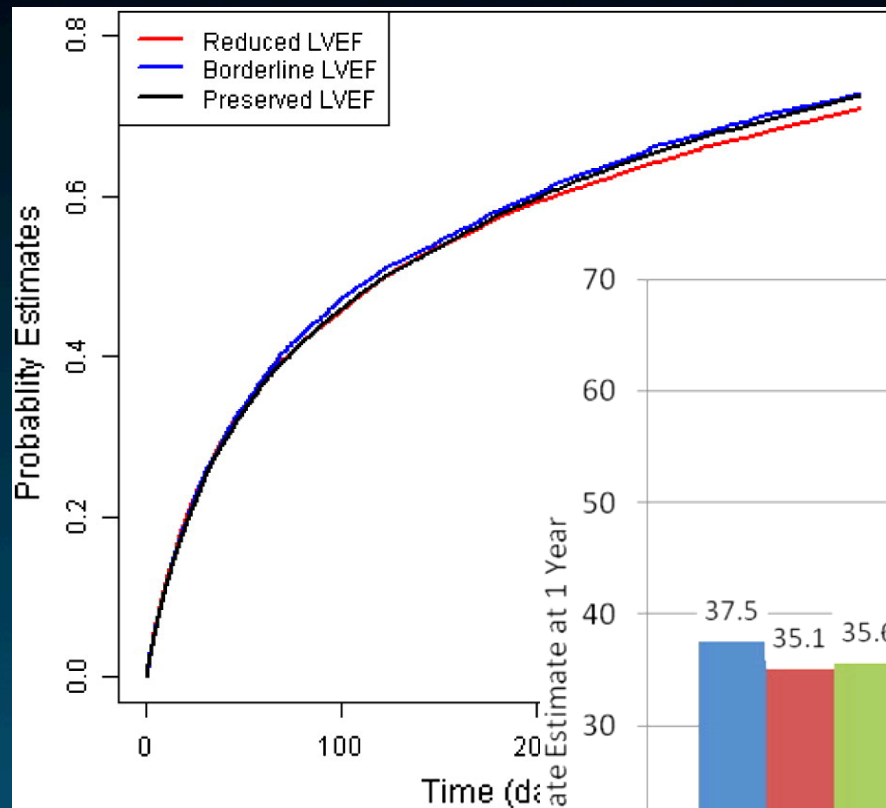




# Outcomes in patients with heart failure with preserved, borderline, and reduced ejection fraction in the Medicare population

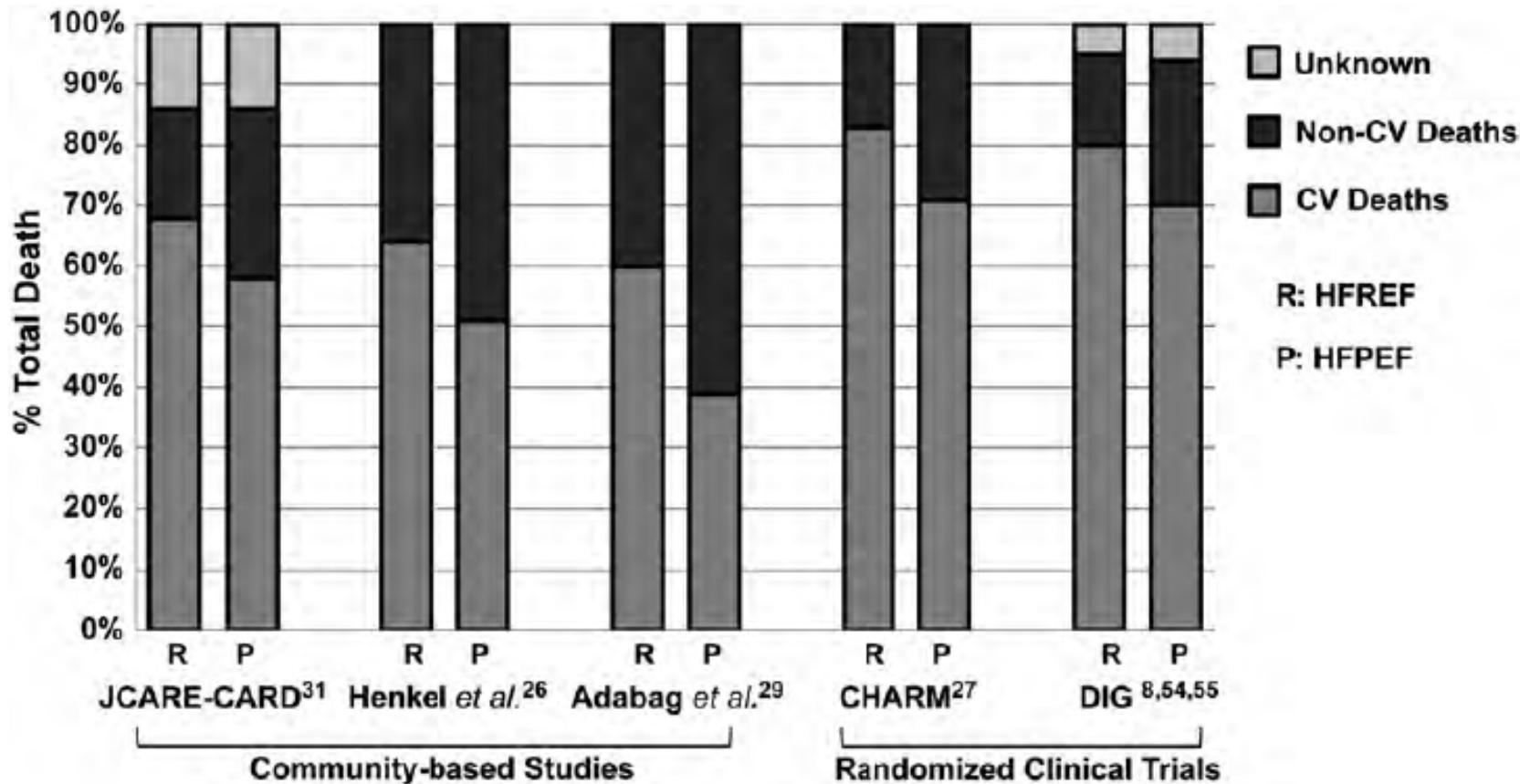


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 [Am Heart J 2014;168:721-730.e3.]



# How do patients with heart failure with preserved ejection fraction die?

Michelle M.Y. Chan<sup>1,2</sup> and Carolyn S.P. Lam<sup>1,3\*</sup>

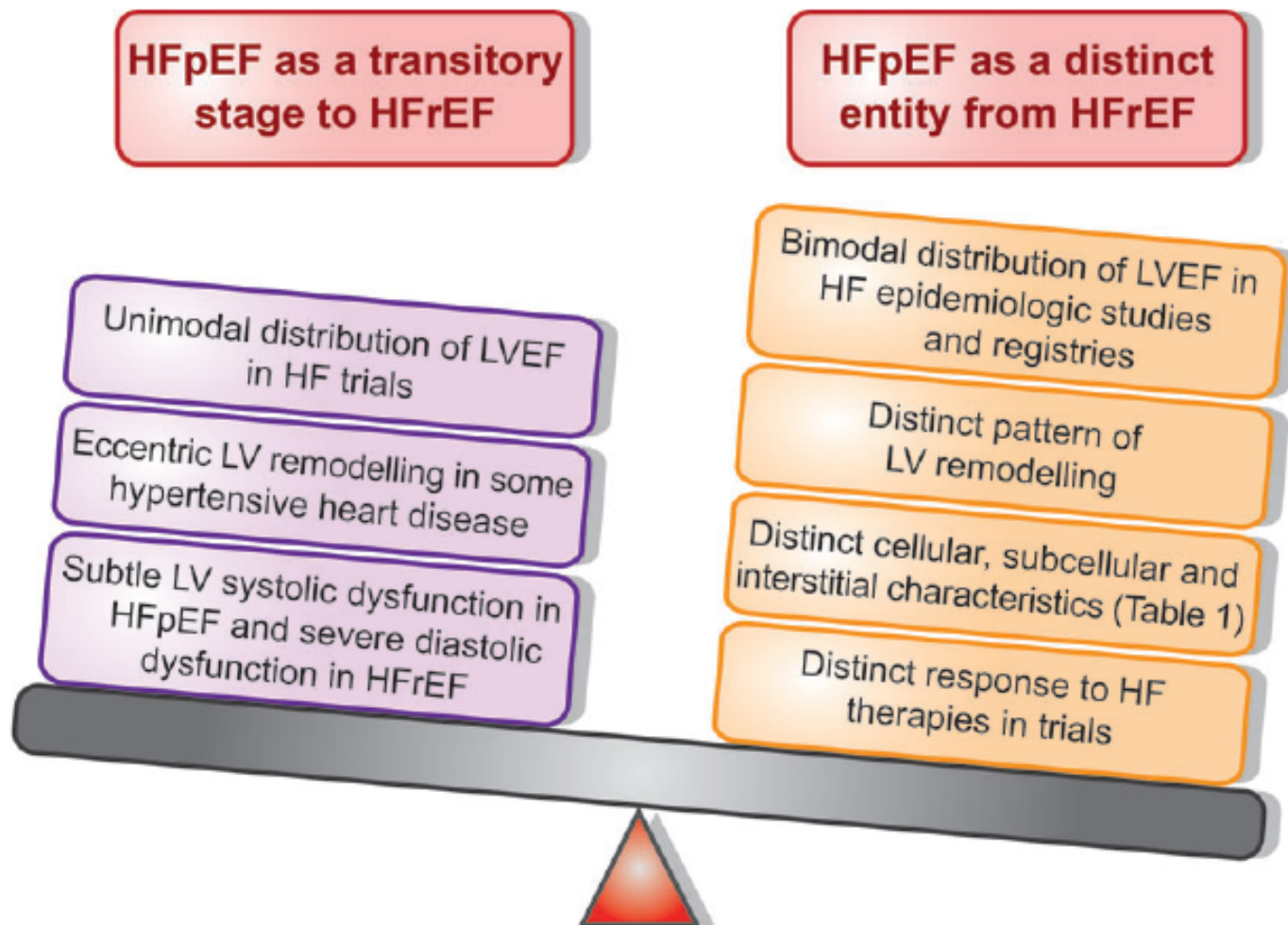


- Total deaths-cardiovascular related: 60% HFREF vs. 50% HFPEF, whether considering data from RCTs or 80% vs. 70% from no-RCT studies.
- Conversely, non-cardiovascular deaths constitute a larger proportion of deaths in HFPEF than in HFREF (30% vs. 15% from RCTs; 50% vs. 30% in community-based studies)

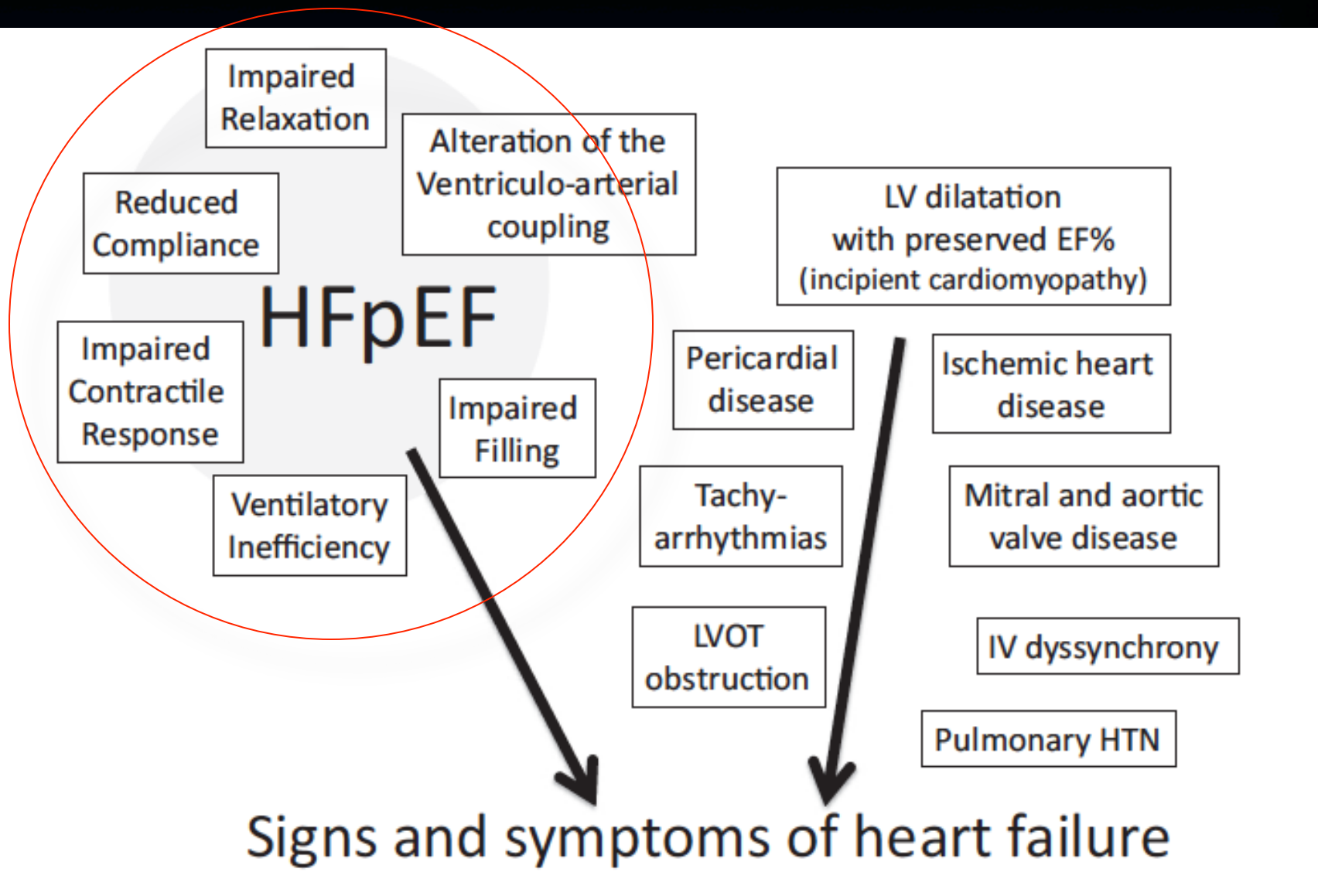
Controversies in cardiovascular medicine

## Heart failure with preserved ejection fraction: a clinical dilemma

Michel Komajda<sup>1\*</sup> and Carolyn S.P. Lam<sup>2</sup>





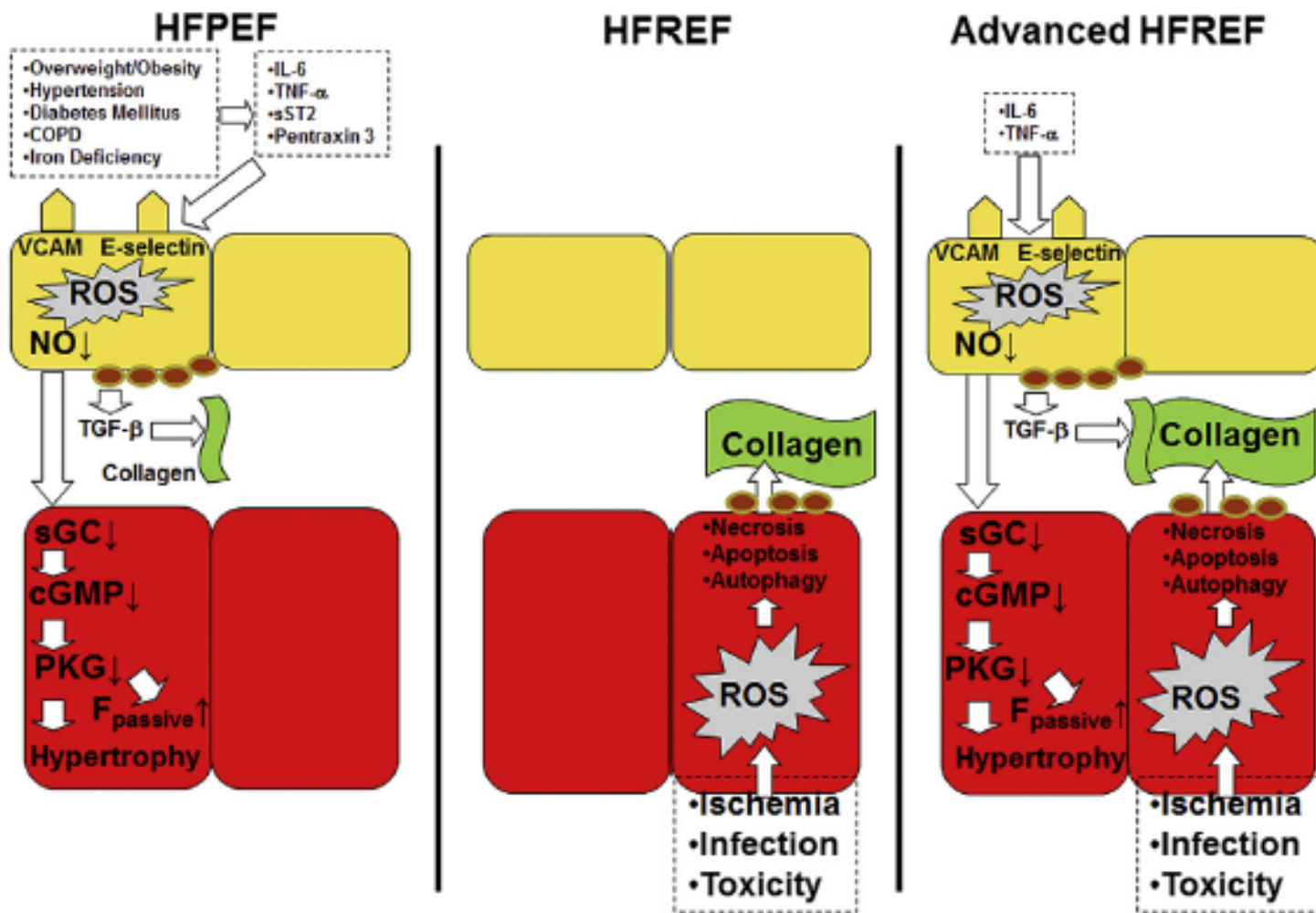


## A Novel Paradigm for Heart Failure With Preserved Ejection Fraction

Comorbidities Drive Myocardial Dysfunction and Remodeling Through Coronary Microvascular Endothelial Inflammation

Walter J. Paulus, MD, PhD,\* Carsten Tschöpe, MD, PhD†

### Myocardial Remodeling in HFPEF, HFREF and Advanced HFREF



Impaired Relaxation

Energy depletion  
Dysregulation of  $Ca^{++}$   
Impaired NO synthesis  
Abnormal neuro-adrenergic tone

Elevated Filling Pressures

Sodium and water retention

Alteration of the Ventriculo-arterial coupling

Stiffening of the major arteries  
Paradoxical  $\uparrow$  SVR

Reduced Compliance

$\uparrow$  Cardiomyocyte Stiffness  
(Titin posttx changes)  
 $\uparrow$  Cardiomyocyte Hypertrophy  
 $\uparrow$  Fibrosis

**Diastolic Dysfunction**

Impaired contractile Response

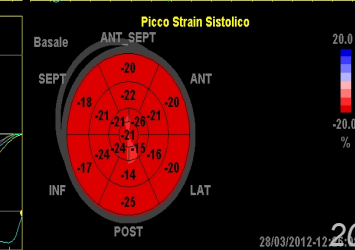
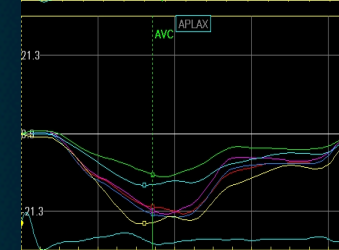
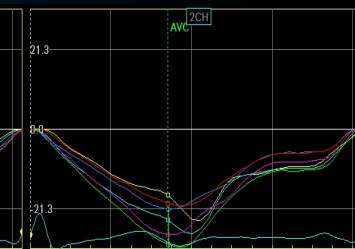
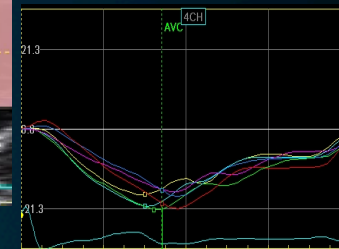
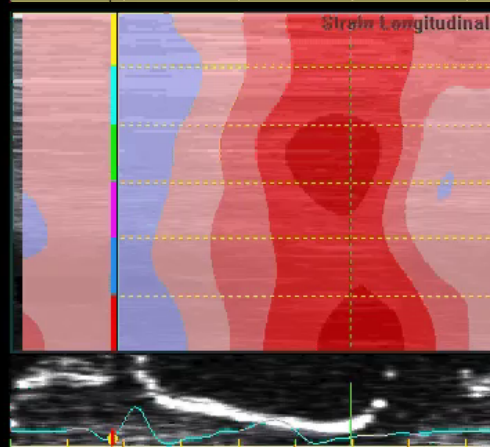
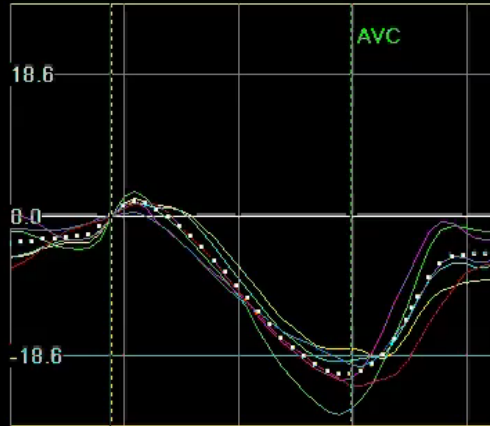
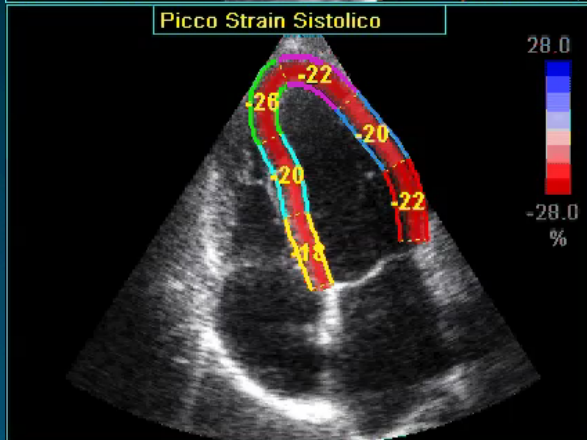
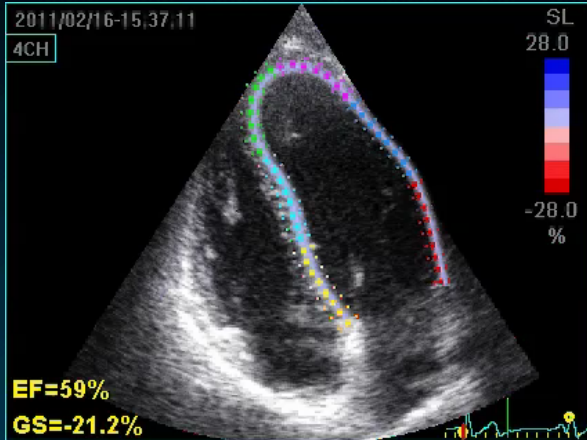
Energy depletion  
Dysregulation of  $Ca^{++}$   
 $\beta$ -adrenergic receptor desensitization

Ventilatory Inefficiency

V/Q mismatch  
Abnormal chemical sensors

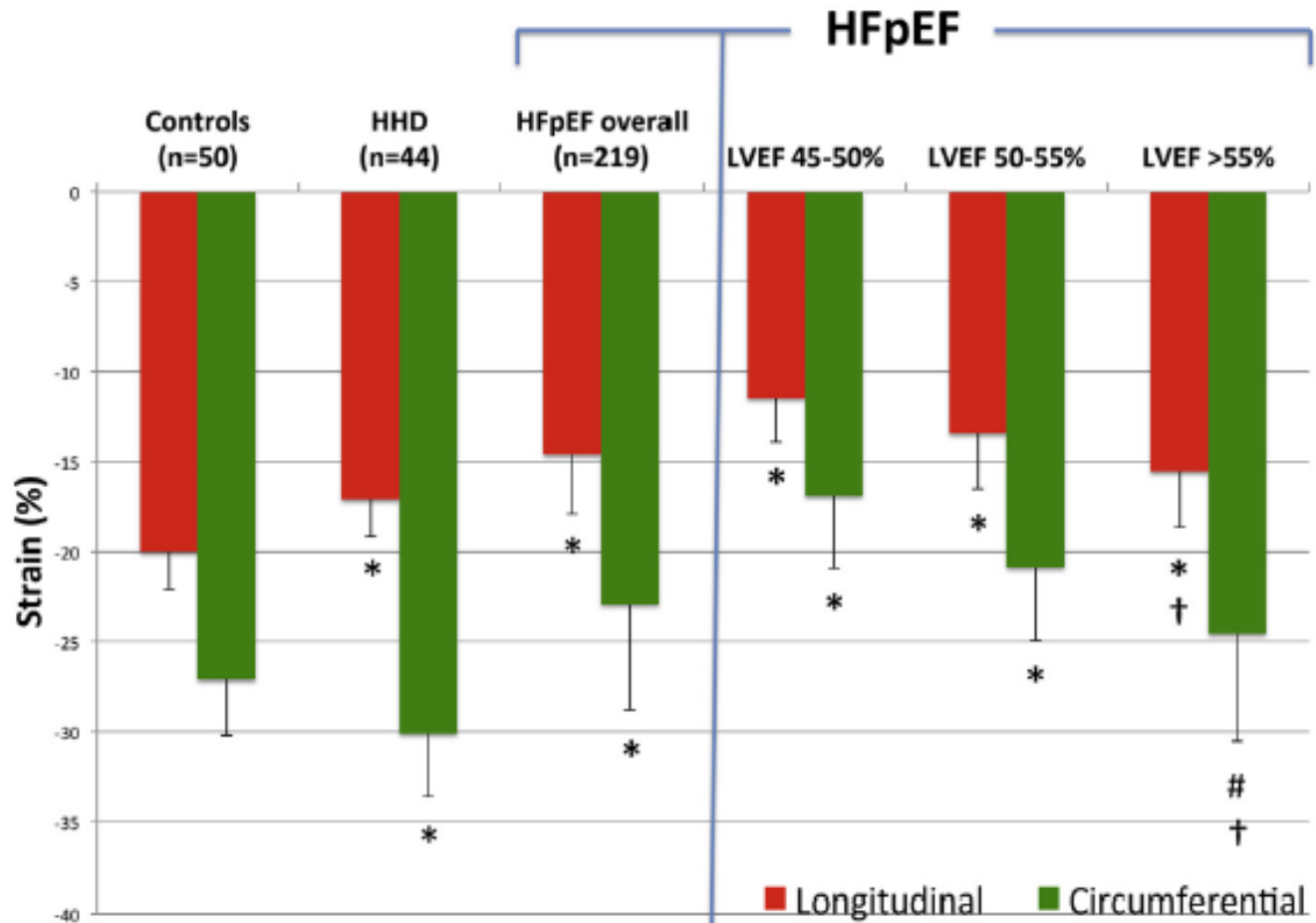
**HFpEF**

# GLS



## Impaired Systolic Function by Strain Imaging in Heart Failure With Preserved Ejection Fraction

Elisabeth Kraigher-Krainer, MD,\* Amil M. Shah, MD, MPH,\* Deepak K. Gupta, MD,\* Angela Santos, MD,\* Brian Claggett, PhD,\* Burkert Pieske, MD,† Michael R. Zile, MD,‡ Adriaan A. Voors, MD,§ Marty P. Lefkowitz, MD,|| Milton Packer, MD,¶ John J. V. McMurray, MD,# Scott D. Solomon, MD,\* for the PARAMOUNT Investigators

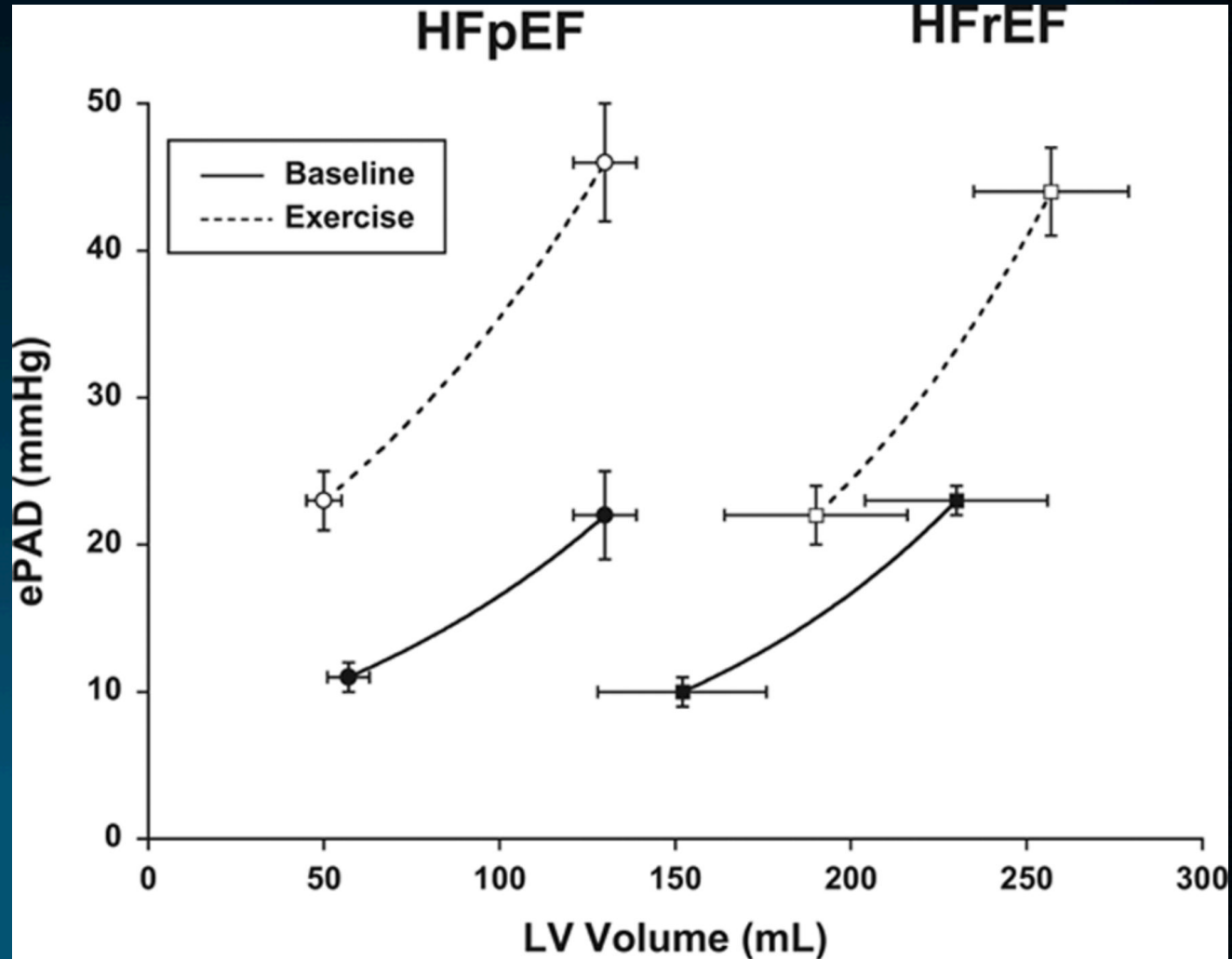


Average Longitudinal and Circumferential Systolic Strain



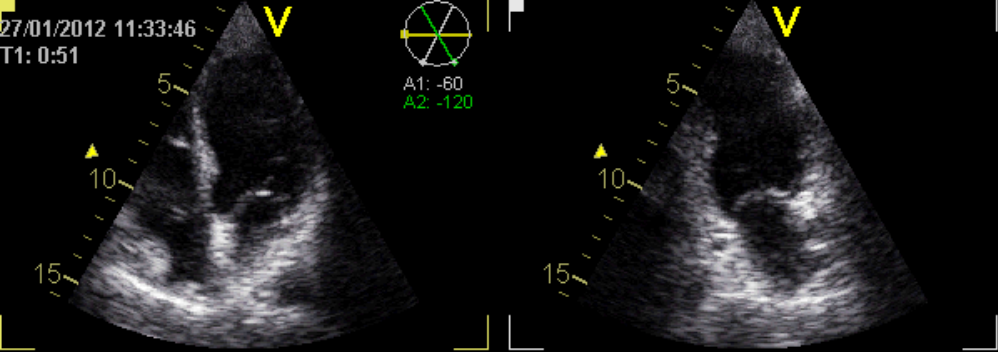
# Effects of Exercise on Left Ventricular Systolic and Diastolic Properties in Patients With Heart Failure and a Preserved Ejection Fraction Versus Heart Failure and a Reduced Ejection Fraction

Michael R. Zile, MD; Barbro Kjellstrom, BMA, PhD; Tom Bennett, PhD; Yong Cho, PhD; Catalin F. Baicu, PhD; Mark F. Aaron, MD; William T. Abraham, MD; Robert C. Bourge, MD; Fred J. Kueffer, MS  
(*Circ Heart Fail.* 2013;6:508-516.)

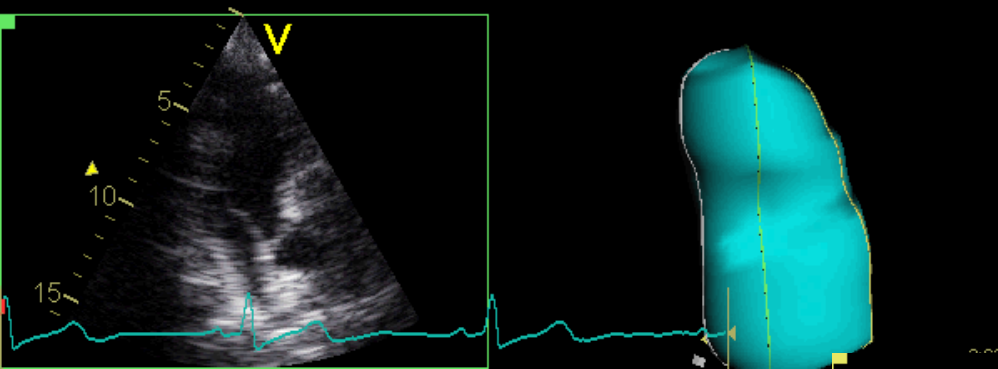


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A2: -120

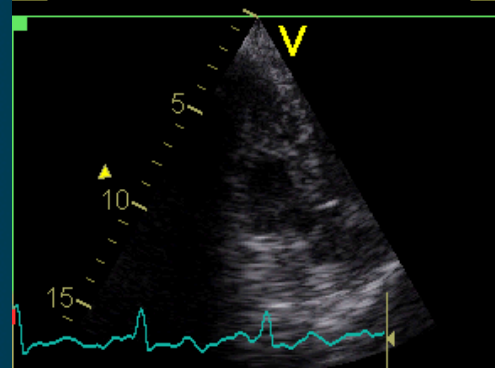


# Riserva contrattile - EF



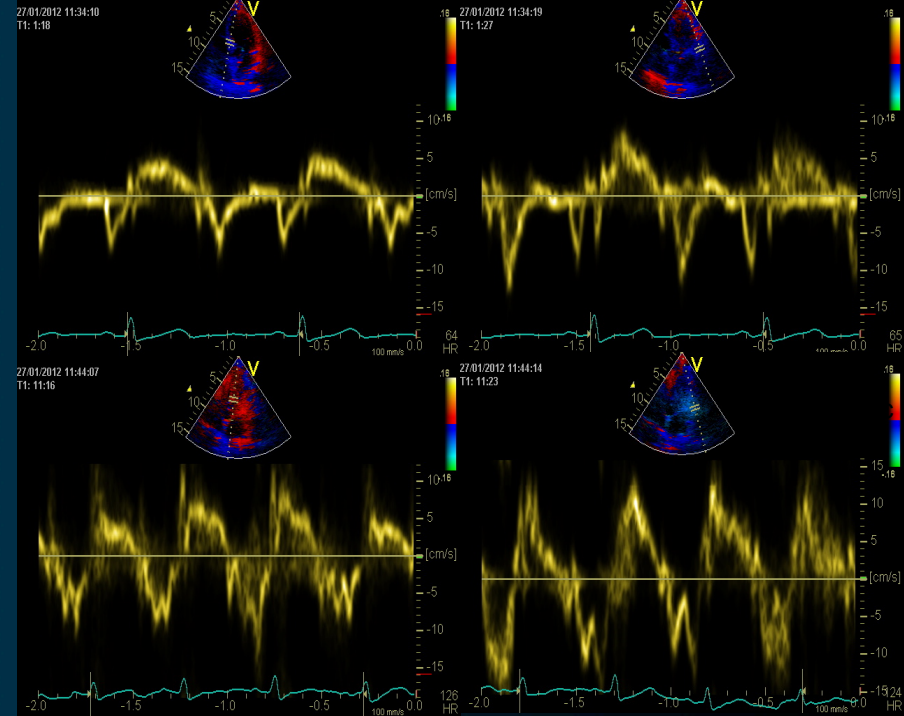
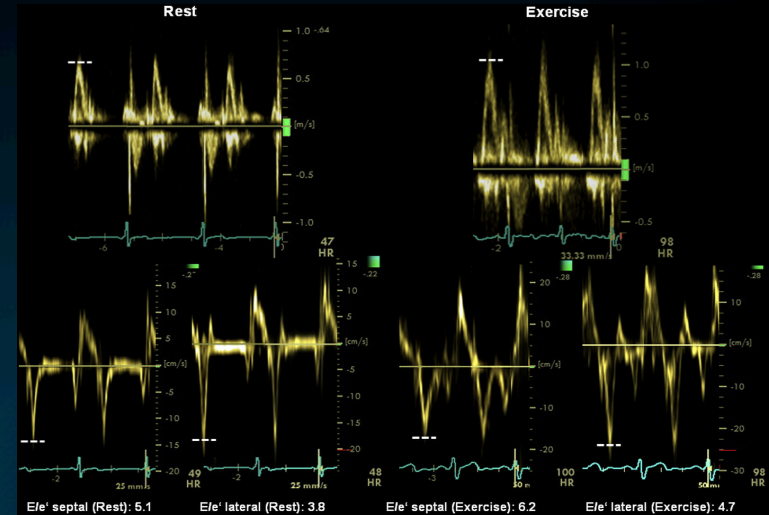
27/01/2012 11:43:50  
T1: 10:57

A1: -60  
A2: -120



# Riserva sistolica e diastolica

- In normali aumento E, E' durante sforzo
  - E/E' costante
- Disfunzione diastolica latente
  - E/E' sforzo > E/E' riposo
  - E/E' > 15



Indice di riserva Sistolica longitudinale =  $\Delta S' \times [1 - (1/S'_{\text{basale}})]$

Indice di riserva Diastolica longitudinale =  $\Delta E' \times [1 - (1/E'_{\text{basale}})]$

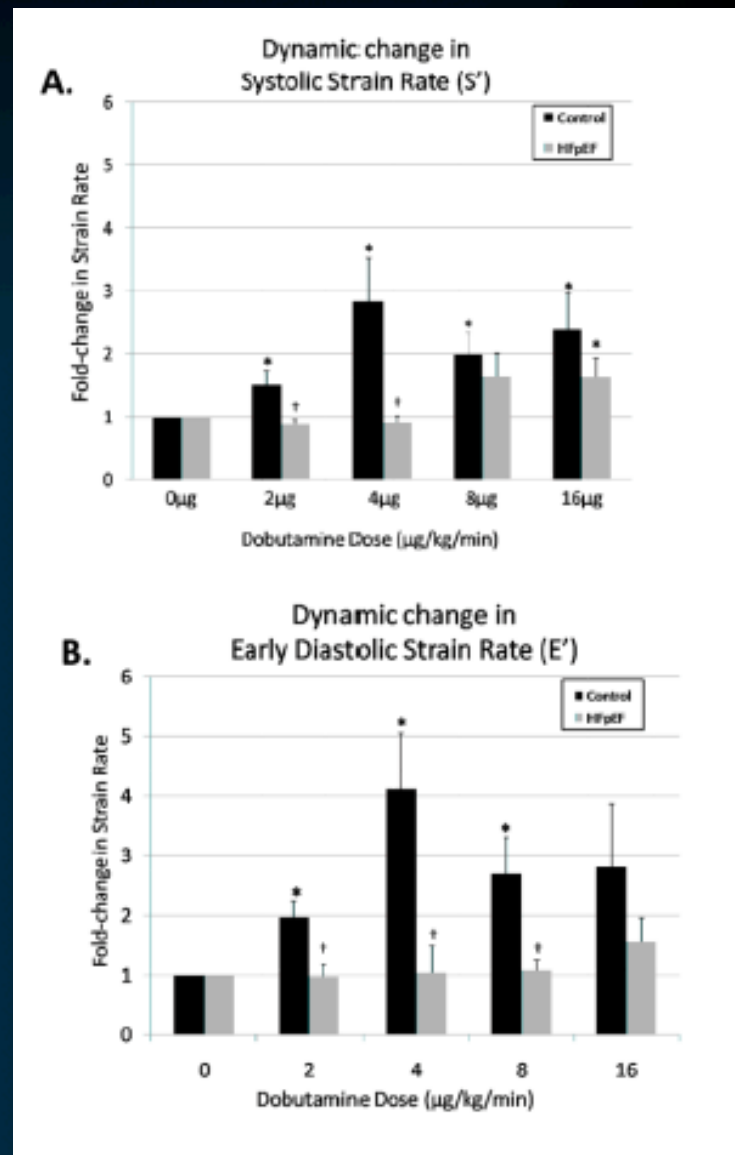
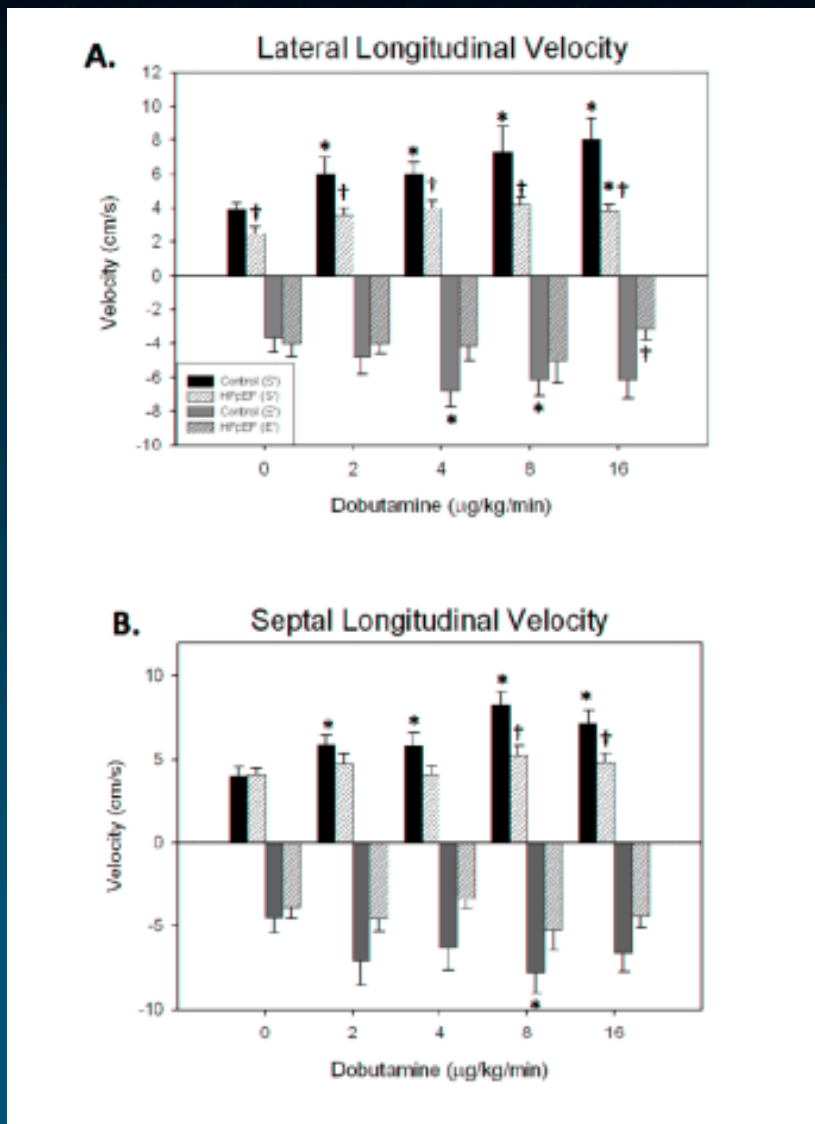
Variazione percentuale onda S' =  $\Delta S' / S'_{\text{basale}} \times 100$

Variazione percentuale onda E' =  $\Delta E' / E'_{\text{basale}} \times 100$

## Decreased Cardiac Functional Reserve in Heart Failure with Preserved Systolic Function

Holly S. Norman, PhD<sup>1</sup>, James Oujiri, MD<sup>2</sup>, Shane J. LaRue, MD<sup>2</sup>, Carrie B. Chapman, MD<sup>2</sup>, Kenneth B. Margulies, MD<sup>3</sup>, and Nancy K. Sweitzer, MD, PhD<sup>2</sup>

$\Delta$  EF HFpEF =  $0.4 \pm 1.9\%$  vs. control =  $19.0 \pm 1.4\%$ ;  $p < 0.001$   
 Velocities HFpEF vs. control  $p < 0.05$







Left ventricular long-axis performance during exercise is an important prognosticator in patients with heart failure and preserved ejection fraction



Jing Wang<sup>a,1</sup>, Fang Fang<sup>a,1</sup>, Gabriel Wai-Kwok Yip<sup>b,1</sup>, John E. Sanderson<sup>a,1</sup>, Wei Feng<sup>a,1</sup>, Jun-Min Xie<sup>a,1</sup>, Xiu-Xia Luo<sup>a,1</sup>, Alex Pui-Wai Lee<sup>a,1</sup>, Yat-Yin Lam<sup>a,\*,1</sup>

**Table 2**  
Echocardiographic parameters of HFPEF patients.

	Event (n = 43)	No event (n = 37)	p value
LVSI_rest (ml/m <sup>2</sup> )	42.2 ± 8.7	45.9 ± 11.2	NS
LVSI_exercise (ml/m <sup>2</sup> )	43.6 ± 10.9	48.3 ± 9.7	NS
LVCI_rest (l/min/m <sup>2</sup> )	2.9 ± 1.0	3.2 ± 0.8	NS
LVCI_exercise (l/min/m <sup>2</sup> )	5.3 ± 0.9	5.5 ± 1.3	NS
Sm_rest (cm/s)	4.8 ± 1.4	5.0 ± 1.0	NS
Sm_exercise (cm/s)	5.7 ± 1.6	6.6 ± 1.8	0.018
Em_rest (cm/s)	4.2 ± 1.2	4.5 ± 1.1	NS
Em_exercise (cm/s)	8.5 ± 2.3	9.5 ± 2.1	0.045
E/e' ratio_rest	14.4 ± 6.6	13.3 ± 5.5	NS
E/e' ratio_exercise	12.5 ± 5.3	9.2 ± 3.2	0.004
MAPSE_rest (mm)	10.4 ± 1.9	11.0 ± 1.2	NS
MAPSE_exercise (mm)	12.9 ± 3.1	13.7 ± 2.7	NS
GCS_rest (%)	21.1 ± 4.9	22.3 ± 3.5	NS
GCS_exercise (%)	21.6 ± 4.6	22.8 ± 4.0	NS
GRS_rest (%)	26.3 ± 5.9	28.3 ± 4.9	NS
GRS_exercise (%)	30.6 ± 9.7	33.4 ± 8.9	NS
GLS_rest (%)	17.5 ± 3.7	18.8 ± 2.9	NS
GLS_exercise (%)	18.2 ± 3.9	21.4 ± 3.9	0.001
Twist_rest (°)	20.3 ± 8.9	20.7 ± 8.9	NS
Twist_exercise (°)	22.0 ± 7.3	24.0 ± 7.5	NS
SBP_rest (mm Hg)	135 ± 21	139 ± 17	NS
SBP_exercise (mm Hg)	195 ± 23	196 ± 23	NS
DBP_rest (mm Hg)	73 ± 11	77 ± 11	NS
DBP_exercise (mm Hg)	88 ± 12	87 ± 15	NS
Heart rate_rest (bpm)	67 ± 12	72 ± 13	NS
Heart rate_exercise (bpm)	118 ± 15	130 ± 19	0.002



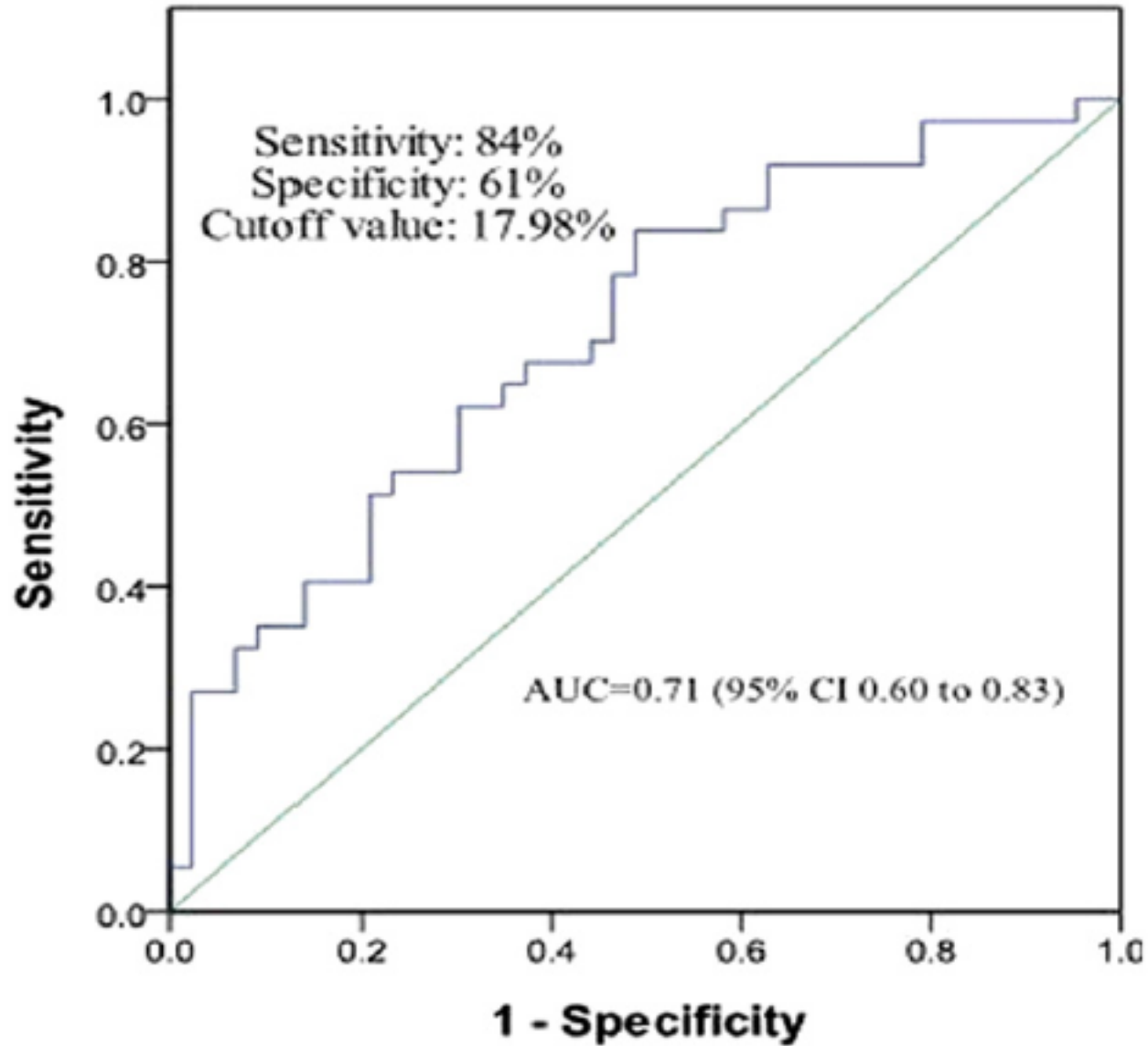




# ROC Curve

Left ventricular long-axis performance during exercise is an important prognosticator in patients with heart failure and preserved ejection fraction

Jing Wang <sup>a,1</sup>, Fang Fang <sup>a,1</sup>, Gabriel Wai-Kwok Yip <sup>b,1</sup>, John E. Sanderson <sup>a,1</sup>, Wei Feng <sup>a,1</sup>, Jun-Min Xie <sup>a,1</sup>, Xiu-Xia Luo <sup>a,1</sup>, Alex Pui-Wai Lee <sup>a,1</sup>, Yat-Yin Lam <sup>a,\*,1</sup>

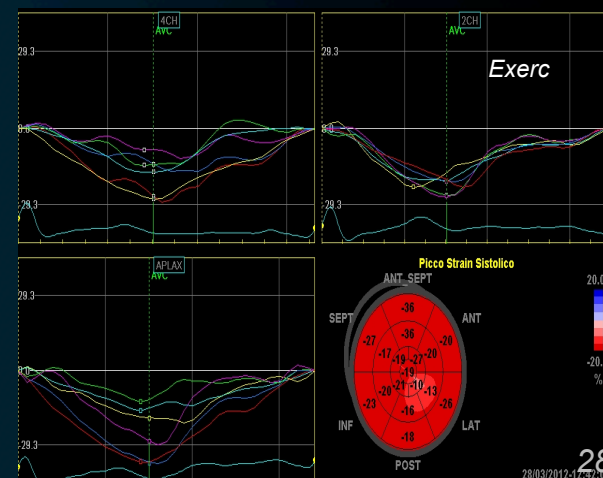
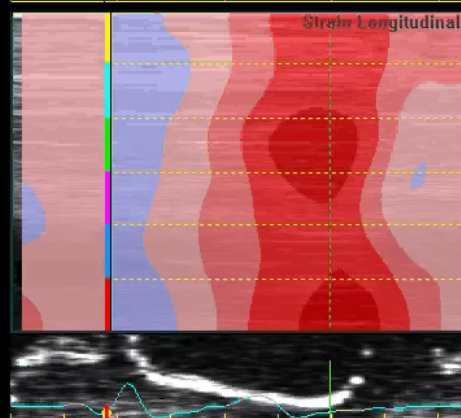
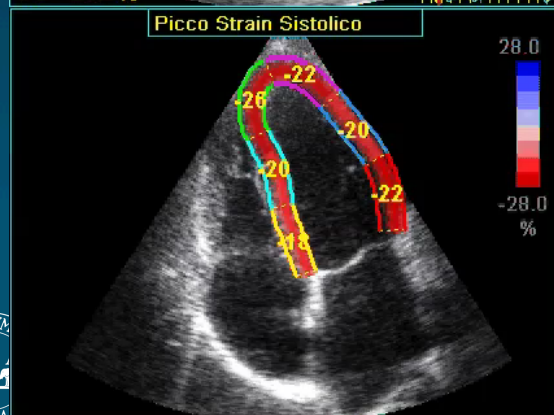
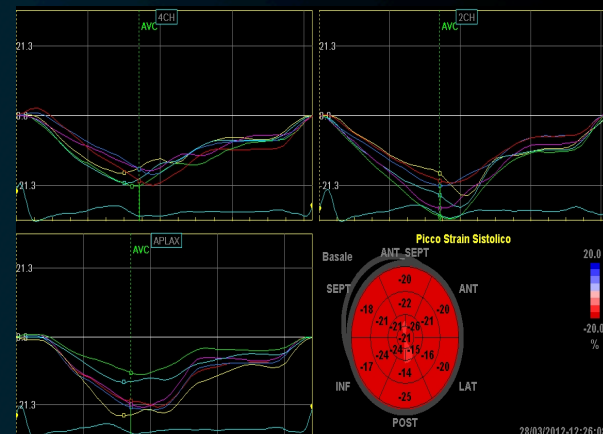
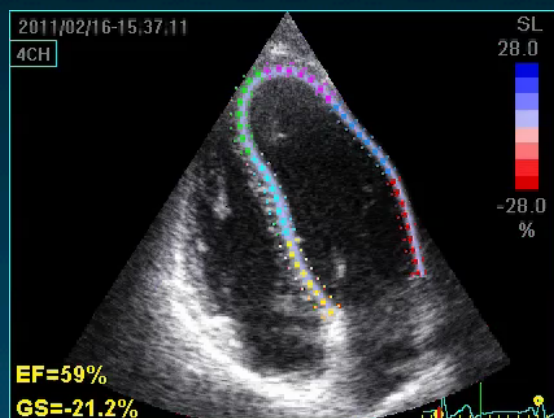


# Riserva contrattile - GLS

Rest

- Migliore valore prognostico della riserva contrattile da Global Longitudinal Strain (GLS)
- Aumento GLS  $<1.9\%$  peggiore prognosi

— Lancellotti, J Am Soc Echocard 2008







GRAZIE PER L'ATTENZIONE!

