Dyspnea in Women: What Does it Mean?

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Off-Label/Investigational Uses

None

Outline

- Review the evaluation and management of dyspnea in women through illustrative cases

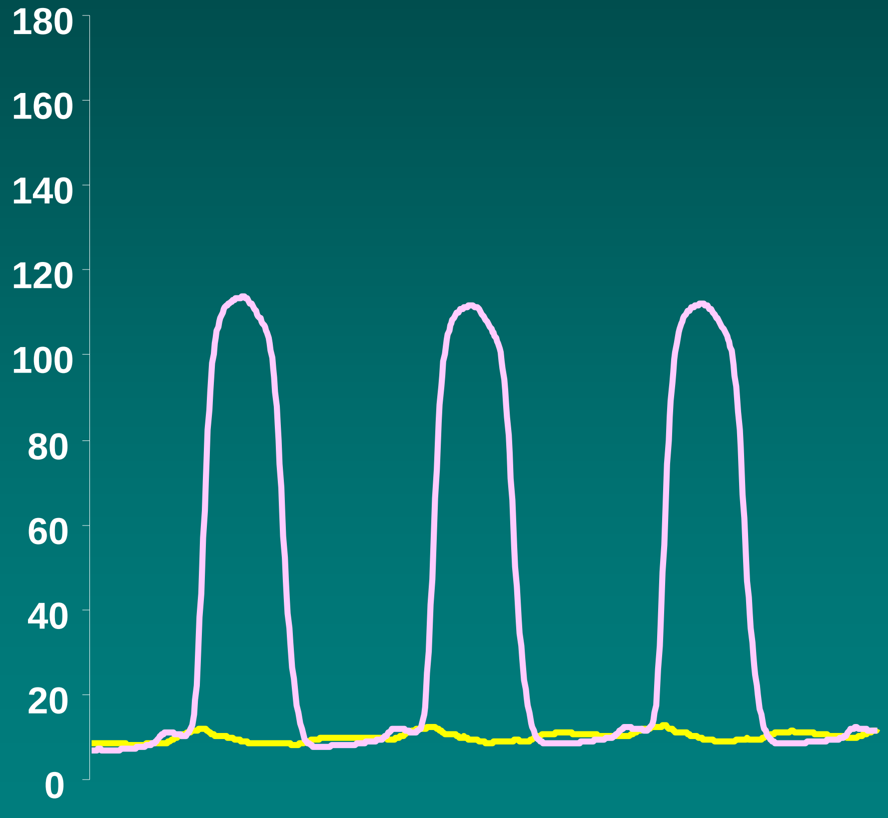
Case 1: 70 yo woman with DOE & Chest pain

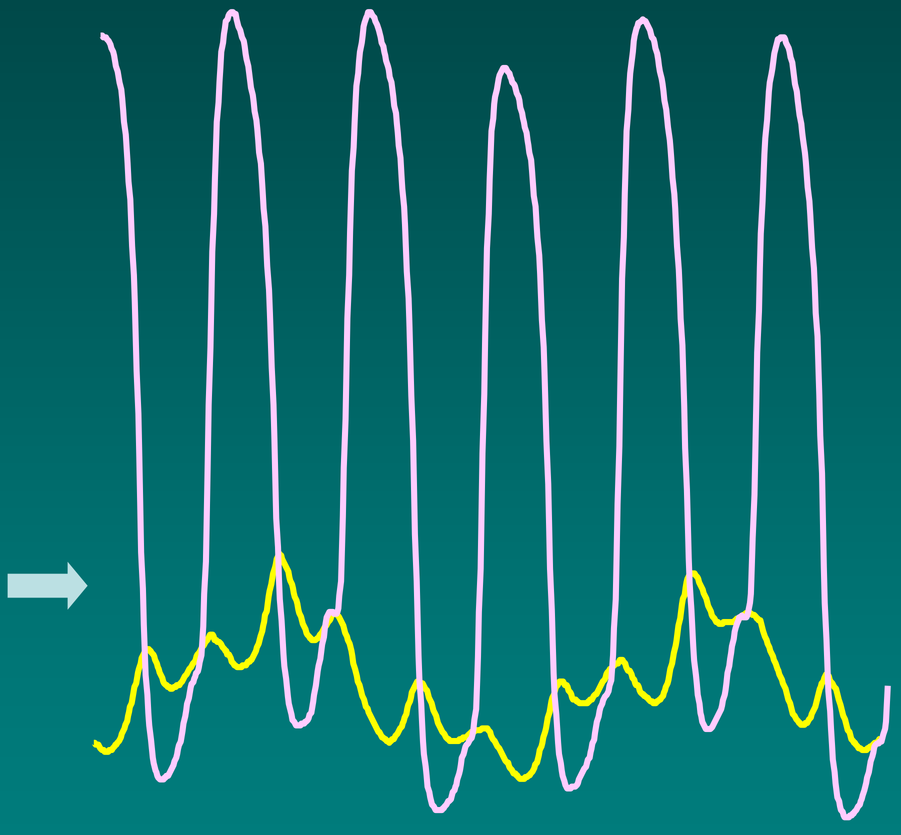
- EF = 60%, h/o HTN
- NYHA III symptoms of dyspnea/fatigue
- No clear episodes of marked volume overload
- Appears "Euvolemic", normal BNP
- Echo:
  - Mild LAE
  - E/A 1.1, E/e' 11, RVSP 32

ESC criteria says "no HFpEF"

Referred for Catheterization

40 Watts Exercise





PCWP=LVEDP=12 mmHg

PCWP & LVEDP>40 mmHg

Dx: HFpEF

Exercise Hemodynamics Enhance Diagnosis of Early Heart Failure With Preserved Ejection Fraction

Barry A. Borlaug, MD; Rick A. Nishimura, MD; Paul Sorajja, MD; Carolyn S.P. Lam, MBBS; Margaret M. Redfield, MD

Background—When advanced, heart failure with preserved ejection fraction (HFpEF) is readily apparent. However, diagnosis of earlier disease may be challenging because exertional dyspnea is not specific for heart failure, and biomarkers and hemodynamic indicators of volume overload may be absent at rest.

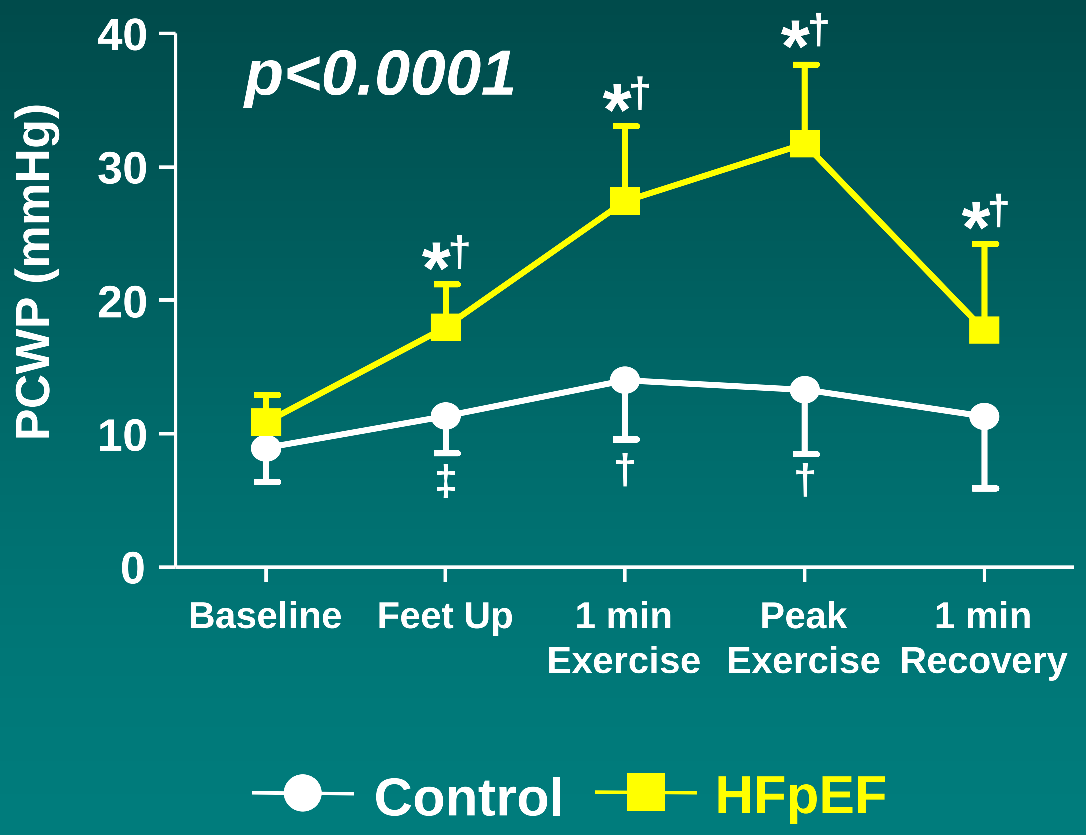
Methods and Results—Patients with exertional dyspnea and ejection fraction >50% were referred for hemodynamic catheterization. Those with no significant coronary disease, normal brain natriuretic peptide assay, and normal resting hemodynamics (mean pulmonary artery pressure <25 mm Hg and pulmonary capillary wedge pressure [PCWP] <15 mm Hg) (n=55) underwent exercise study. The exercise PCWP was used to classify patients as having HFpEF (PCWP ≥25 mm Hg) (n=32) or noncardiac dyspnea (PCWP <25 mm Hg) (n=23). At rest, patients with HFpEF had higher resting pulmonary artery pressure and PCWP, although all values fell within normal limits. Exercise-induced elevation in PCWP in HFpEF was confirmed by greater increases in left ventricular end-diastolic pressure and was associated with blunted increases in heart rate, systemic vasodilation, and cardiac output. Exercise-induced pulmonary hypertension was present in 88% of patients with HFpEF and was related principally to elevated PCWP, as pulmonary vascular resistances dropped similarly in both groups. Exercise PCWP and pulmonary artery systolic pressure were highly correlated. An exercise pulmonary artery systolic pressure ≥45 mm Hg identified HFpEF with 96% sensitivity and 95% specificity.

Conclusions—Euvolemic patients with exertional dyspnea, normal brain natriuretic peptide, and normal cardiac filling pressures at rest may have markedly abnormal hemodynamic responses during exercise, suggesting that chronic symptoms are related to heart failure. Earlier and more accurate diagnosis using exercise hemodynamics may allow better targeting of interventions to treat and prevent HFpEF progression. (***Circ Heart Fail*. 2010;3:588-595.**)

Key Words: heart failure ■ exercise ■ hemodynamics ■ diastole ■ diagnosis

58% of pts with normal exam, echo, BNP & resting hemos have HF by exercise

Intermittent ↑LVFP in early stage HFpEF



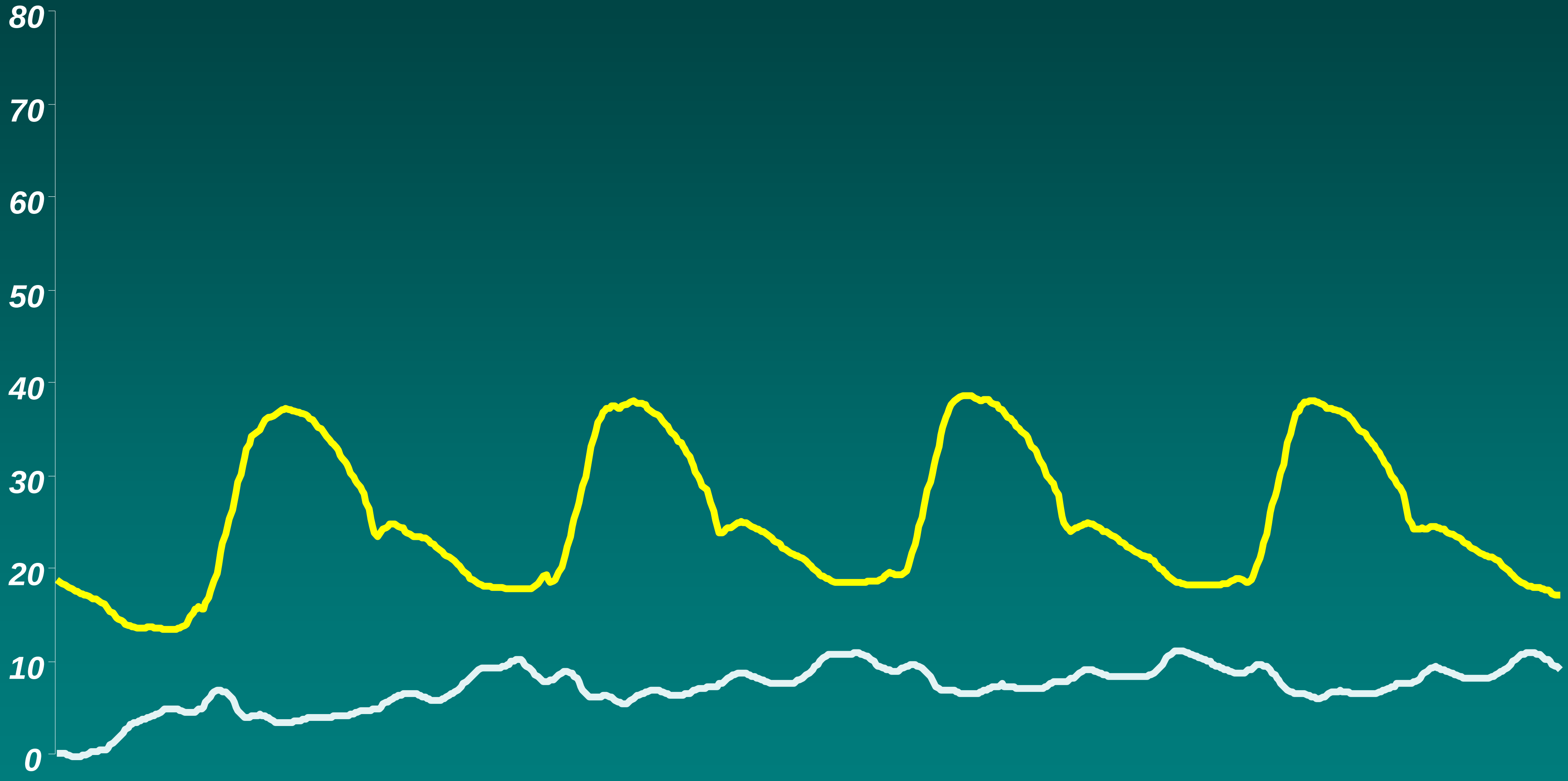
Borlaug *Circ Heart Fail* 2010

Clinical Evaluation Prior to Hemodynamic Assessment

	Non-Cardiac Dyspnea (n=25)	"Early" HFpEF (n=32)	p
Cardiomegaly (%)	4	25	0.02
Congestion (%)	0	0	-
LV EF (%)	61±5	62±7	0.5
LV Hypertrophy (%)	10	45	0.005
LA enlargement (%)	40	65	0.09
E/A	1.3±0.5	1.1±0.5	0.14
E/E'	9±4	10±3	0.16
E/E'>15 (%)	10	10	0.99
ESC HFpEF Dx (%)	32	41	0.6

Borlaug *Circ Heart Fail* 2010

Case 2: 76 yo woman with DOE, no chest pain

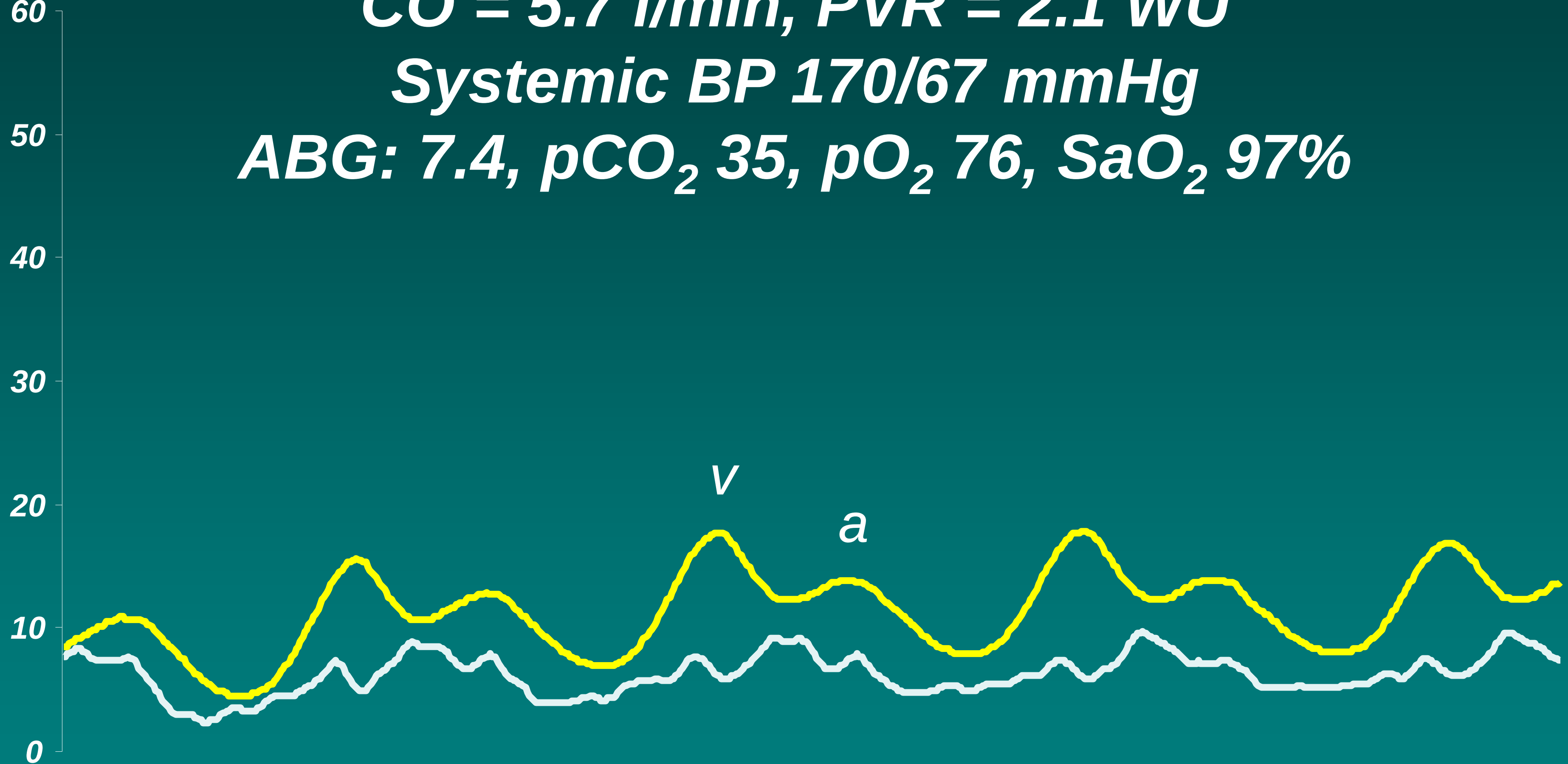


PCWP 12 mmHg

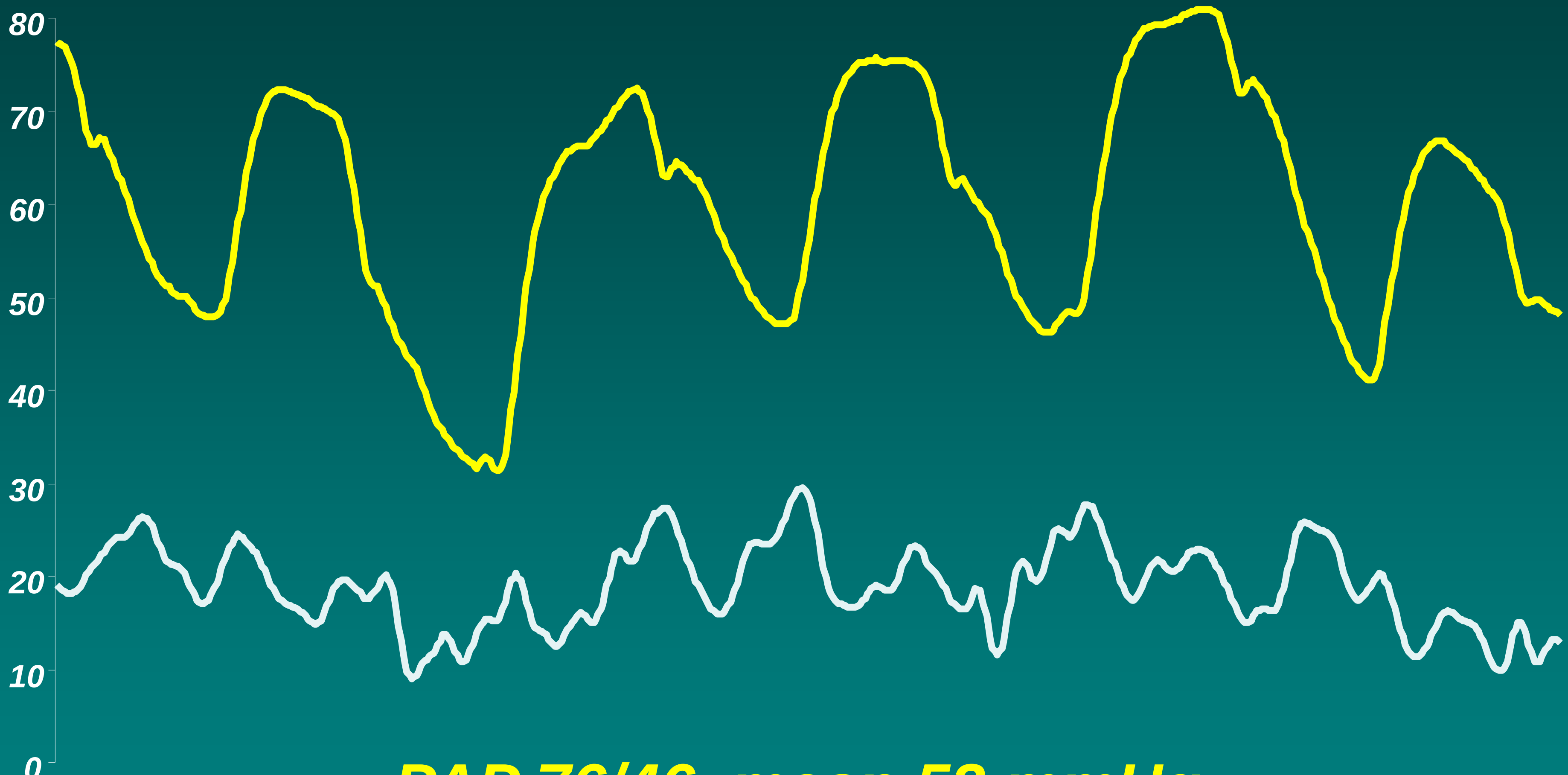
CO = 5.7 l/min, PVR = 2.1 WU

Systemic BP 170/67 mmHg

ABG: 7.4, pCO_2 35, pO_2 76, SaO_2 97%



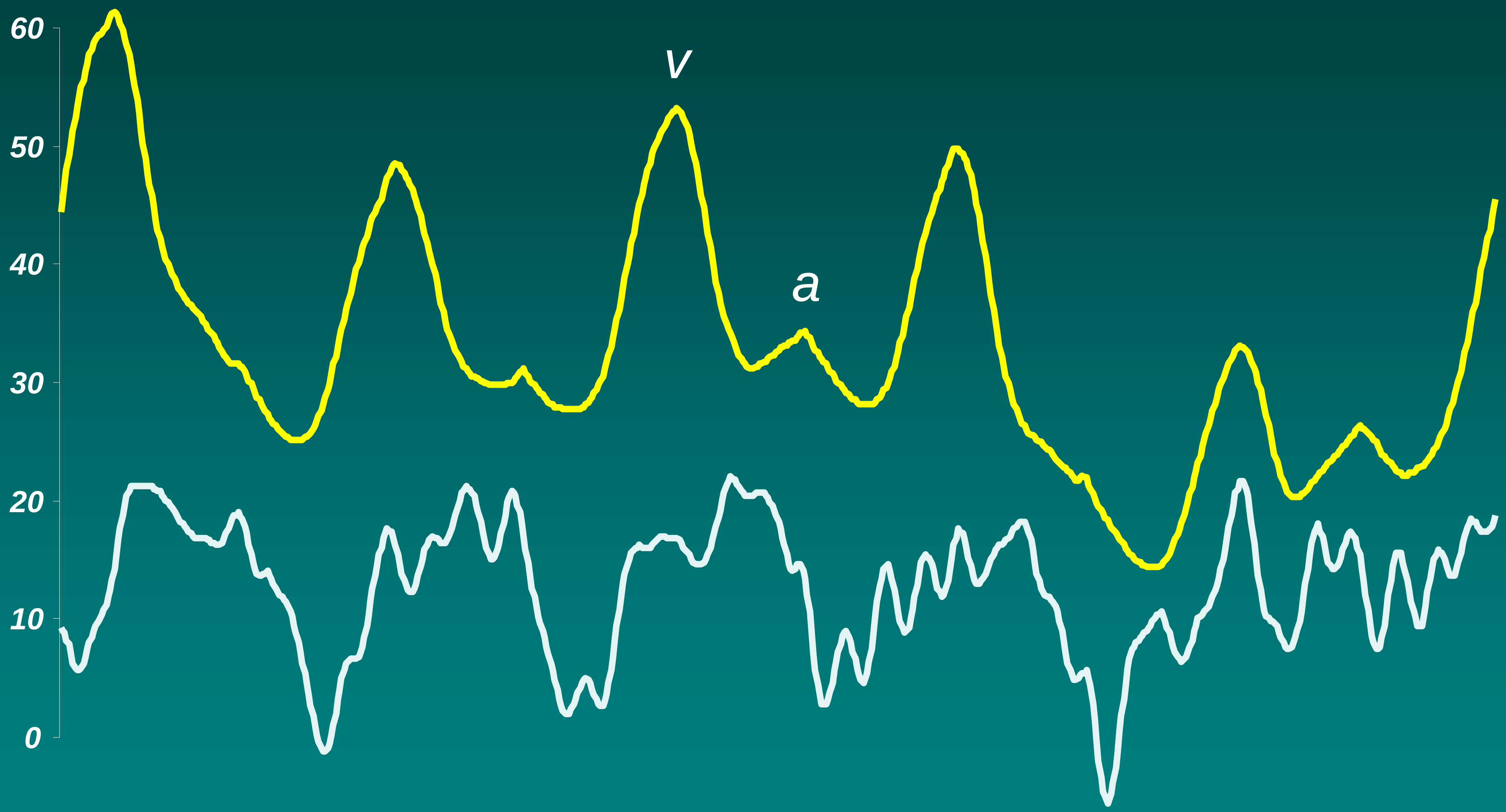
20 Watts Exercise



PAP 76/46, mean 52 mmHg

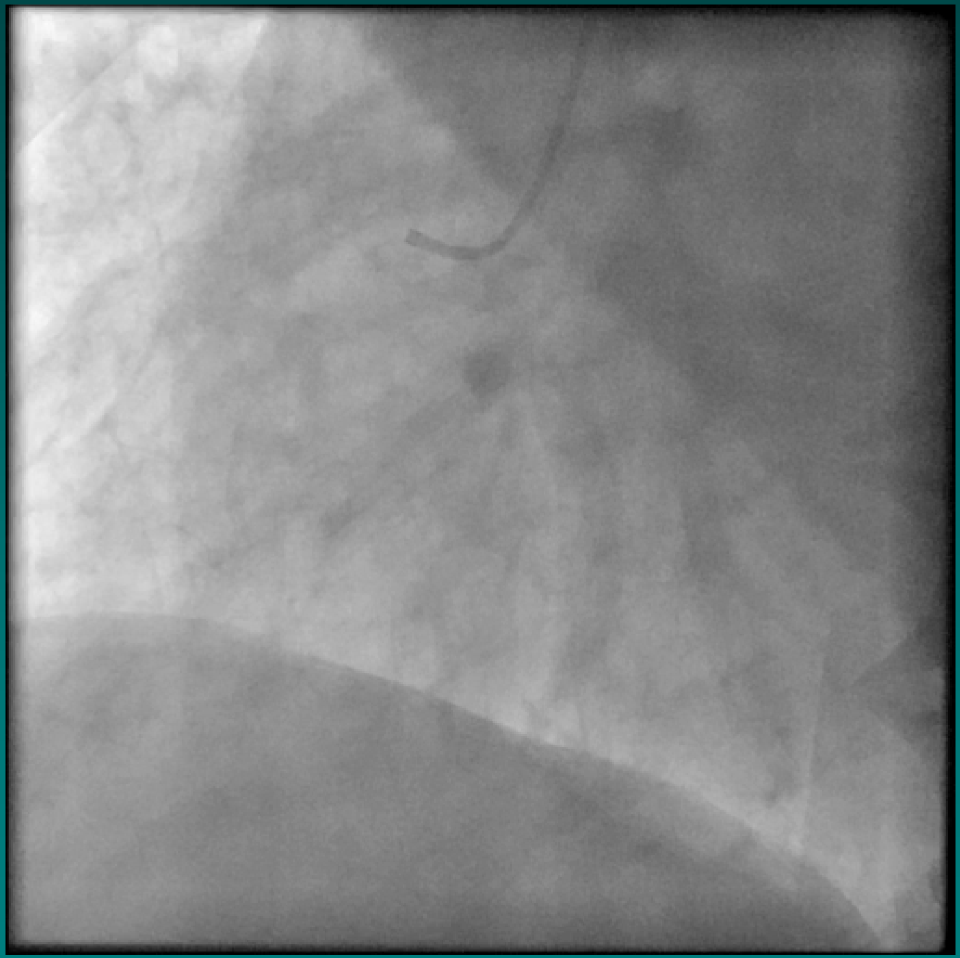
RAP 21 mmHg

PCWP 37 mmHg, CO = 7.8 l/min, PVR = 1.9 WU
BP 160/77; ABG: 7.4, pCO_2 38, pO_2 70, SaO_2 95%



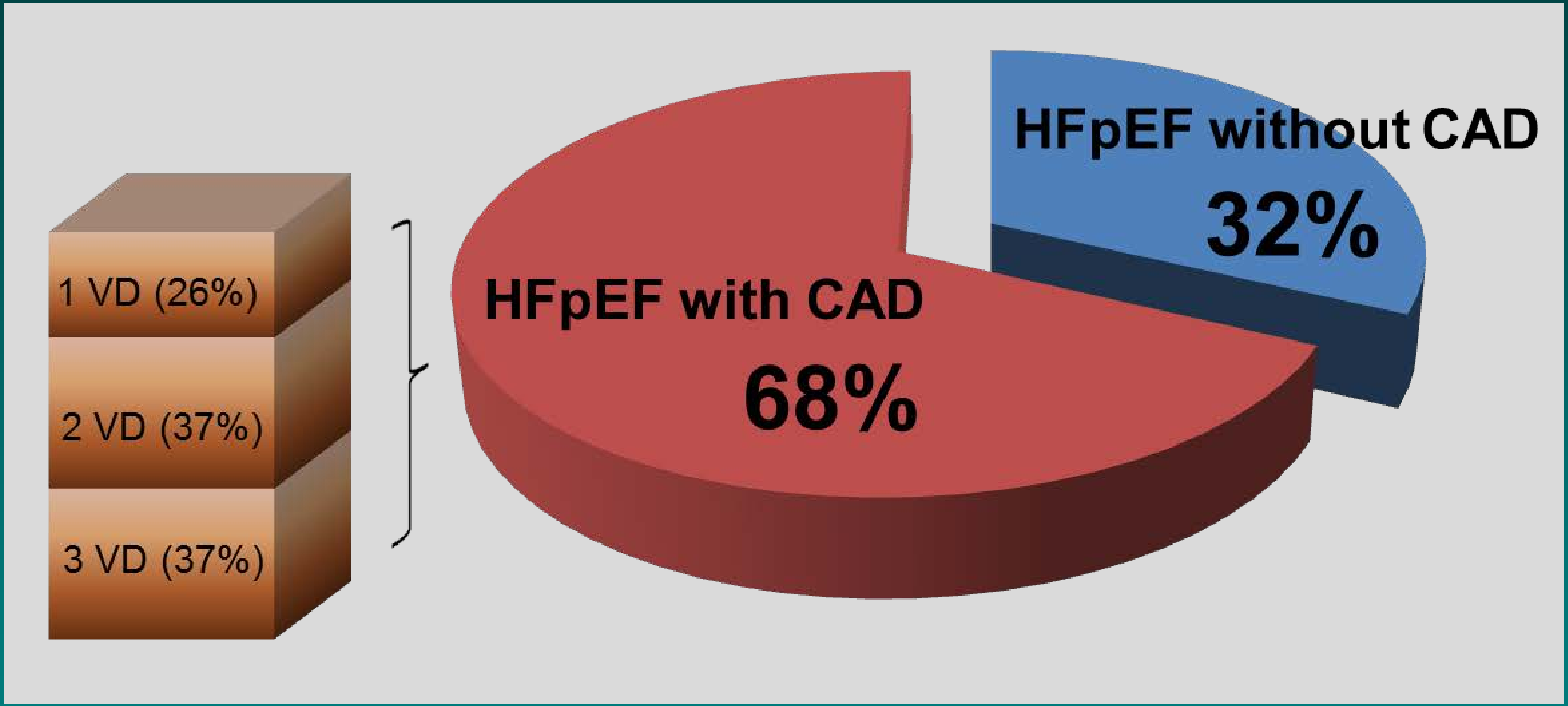
So, more HFpEF?

Back to the case…



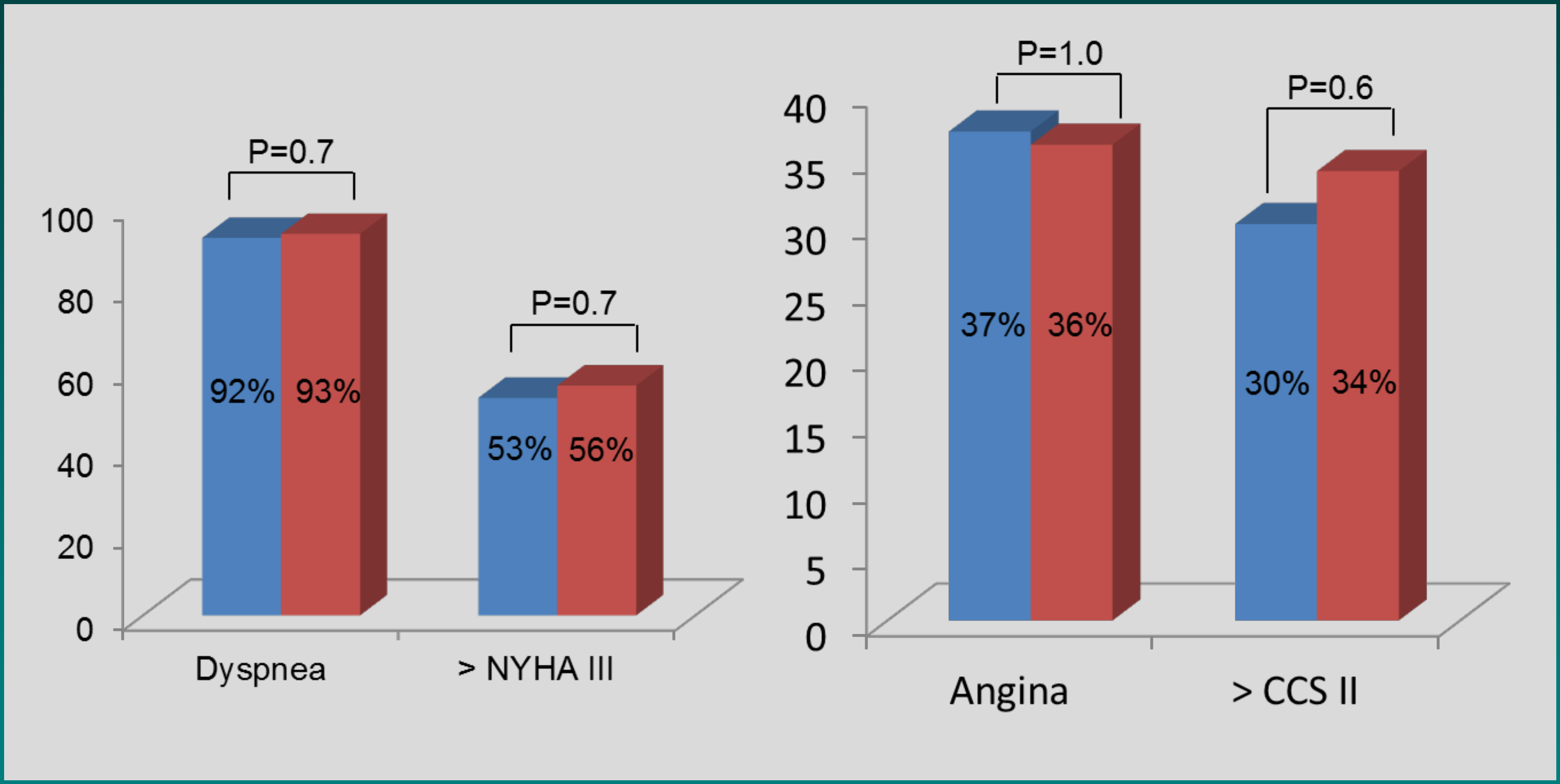
What do we know about CAD in HFpEF?

It is common…



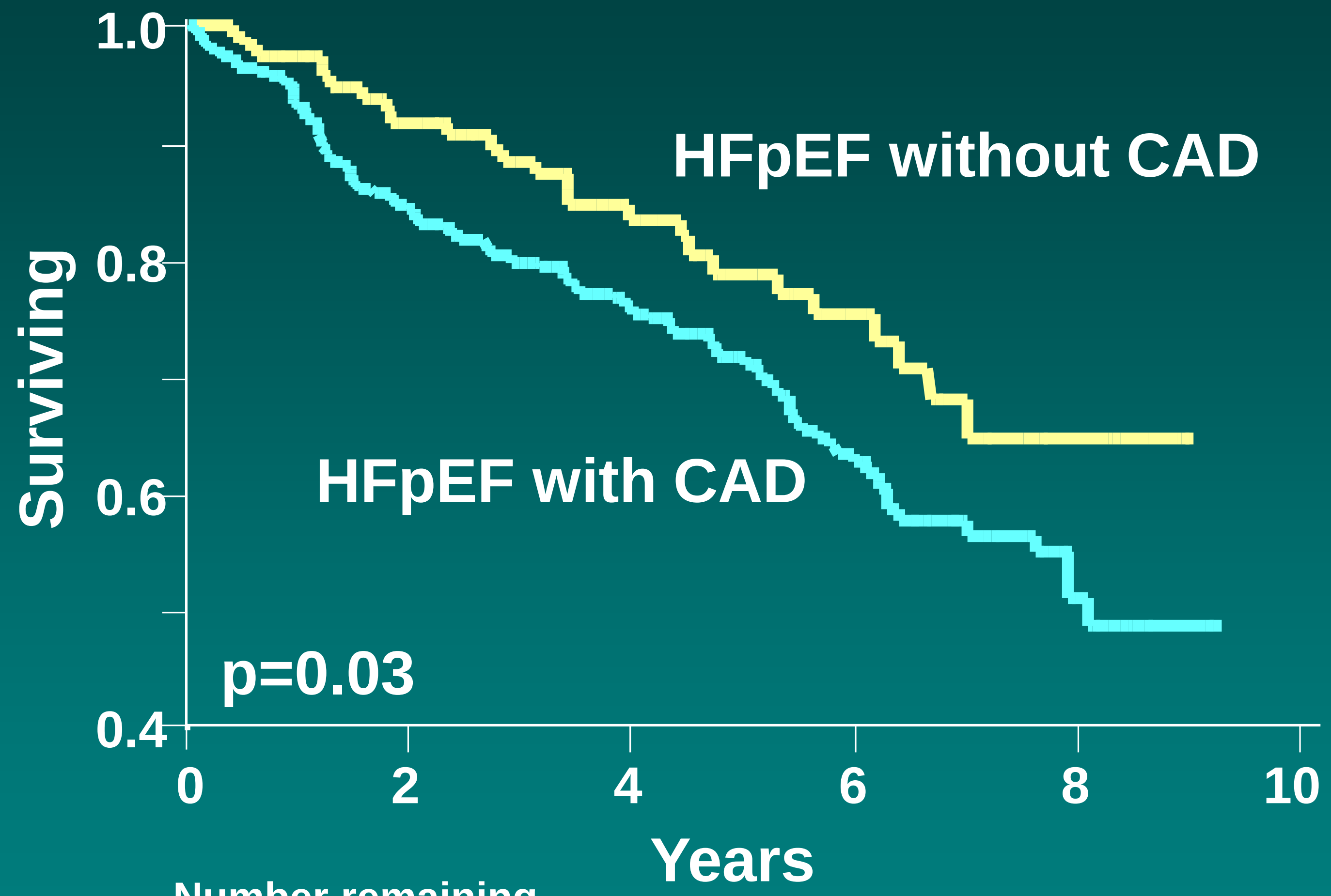
Hwang…Borlaug *J Am Coll Cardiol* 2014

Symptoms do not discriminate



Hwang…Borlaug *J Am Coll Cardiol* 2014

Impact of CAD on Outcome in HFpEF

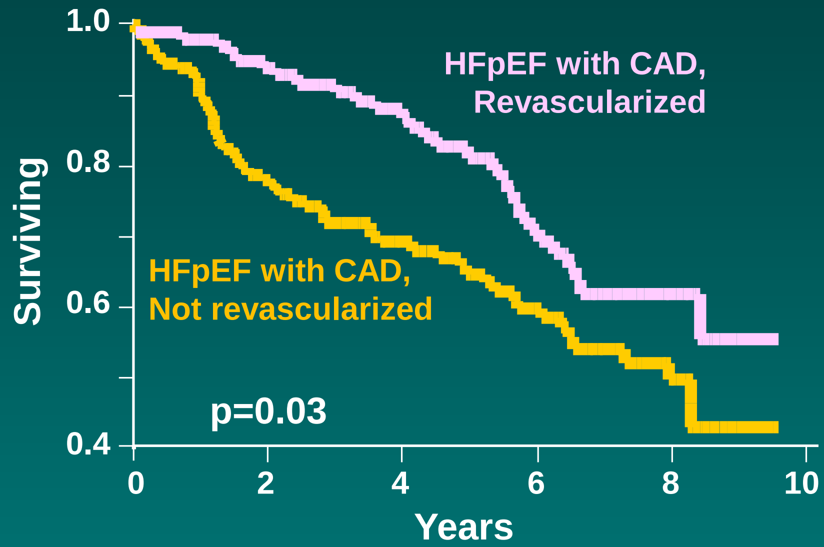


Number remaining

CAD (-)	121	90	60	34	14
CAD (+)	255	193	129	83	23

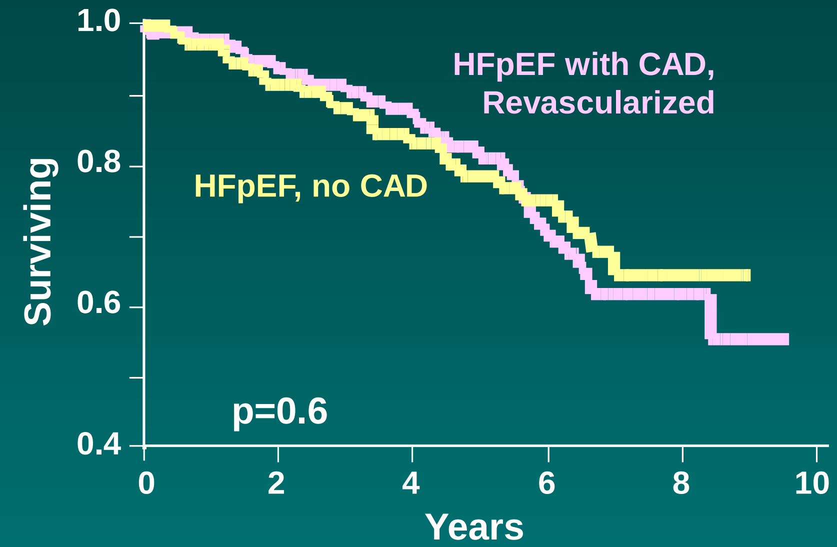
Hwang *J Am Coll Cardiol* 2014

Does Revascularization improve survival?



Number remaining

Revasc (+)	101	85	63	37	11
Revasc (-)	154	108	68	47	13



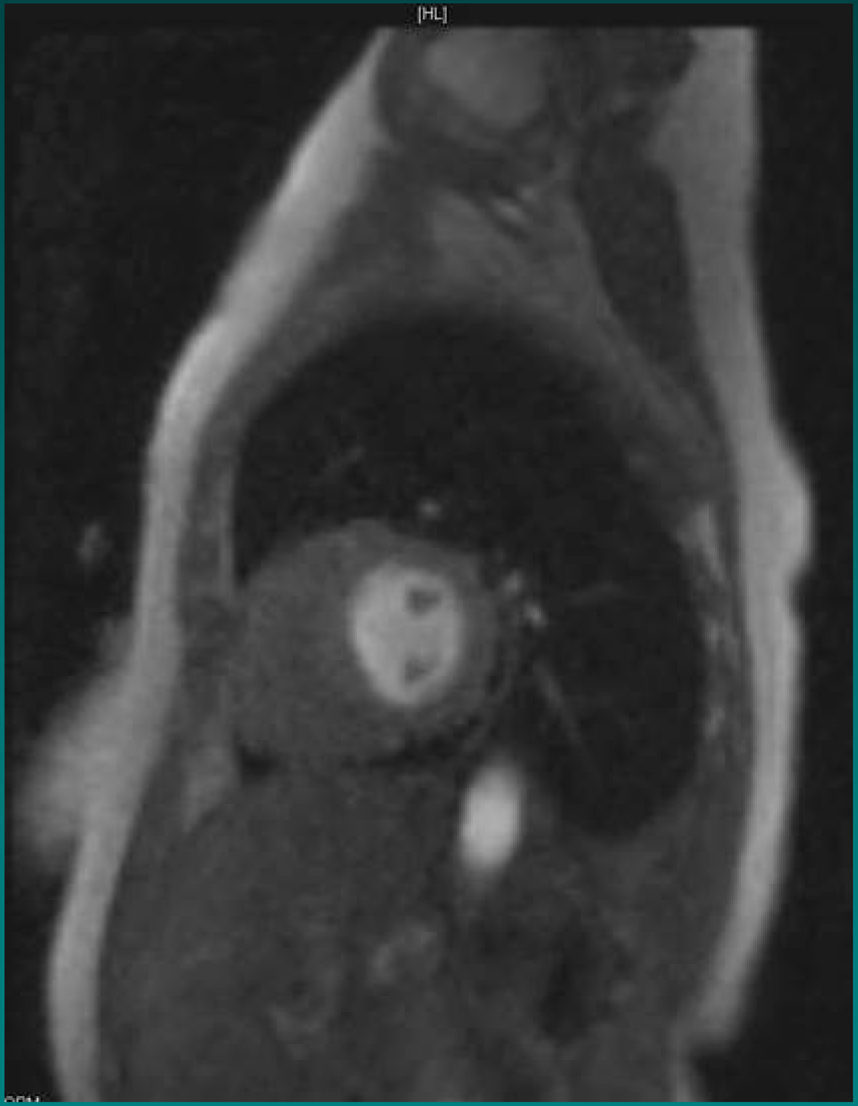
Number remaining

Revasc (+)	101	85	63	37	11
CAD (-)	121	90	60	34	14

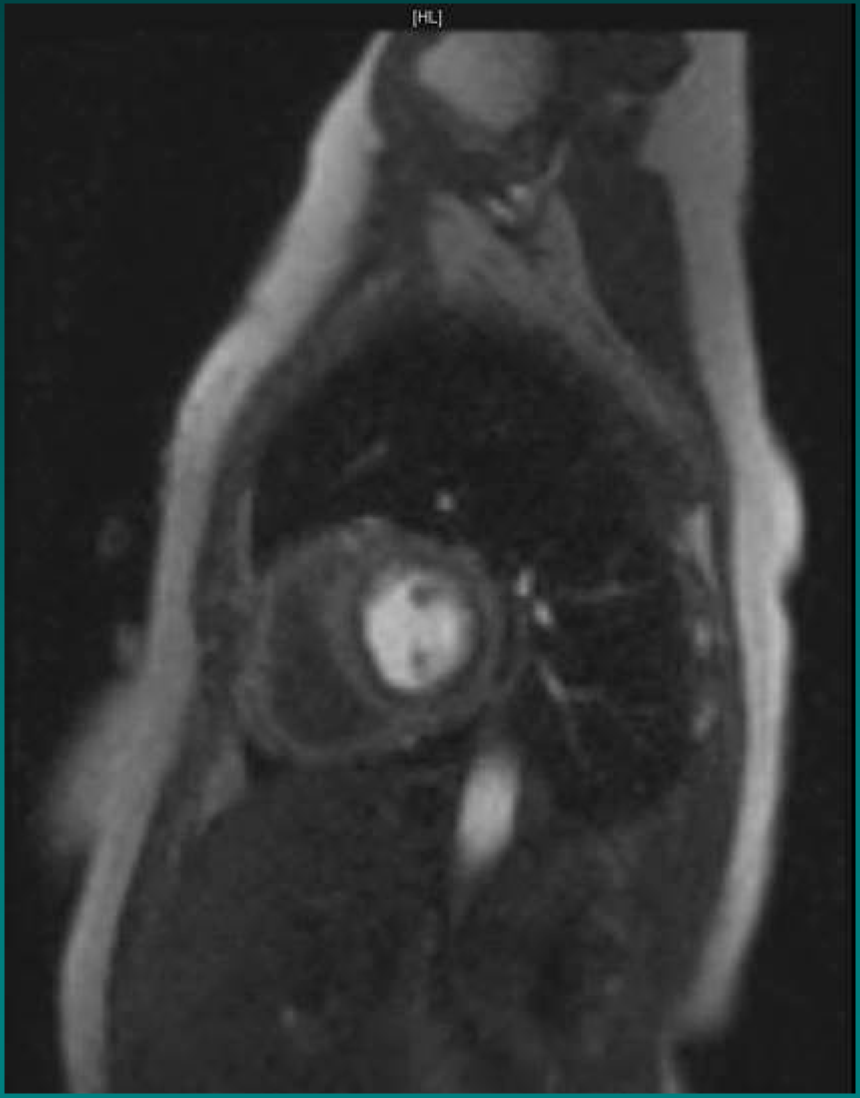
Hwang…Borlaug *J Am Coll Cardiol* 2014

Case 3: 66 yo woman with DOE & atypical CP

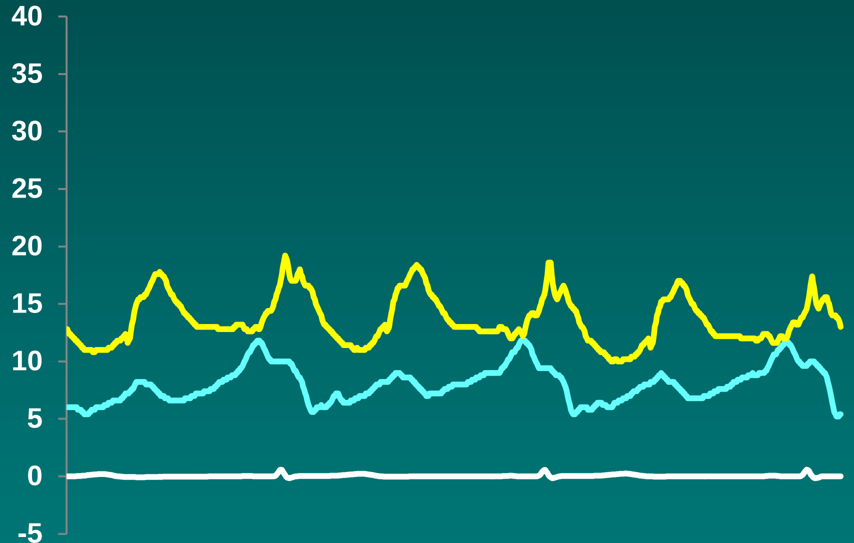
Rest

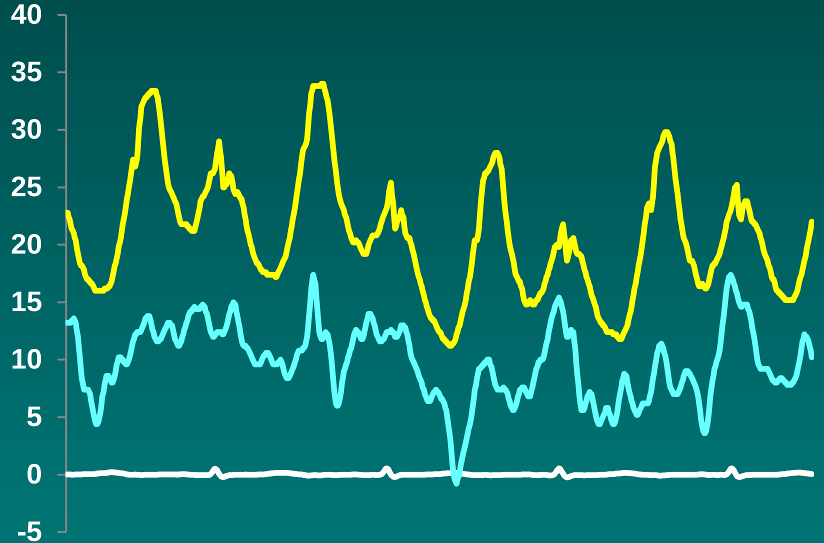


Stress



Angiogram: normal coronaries

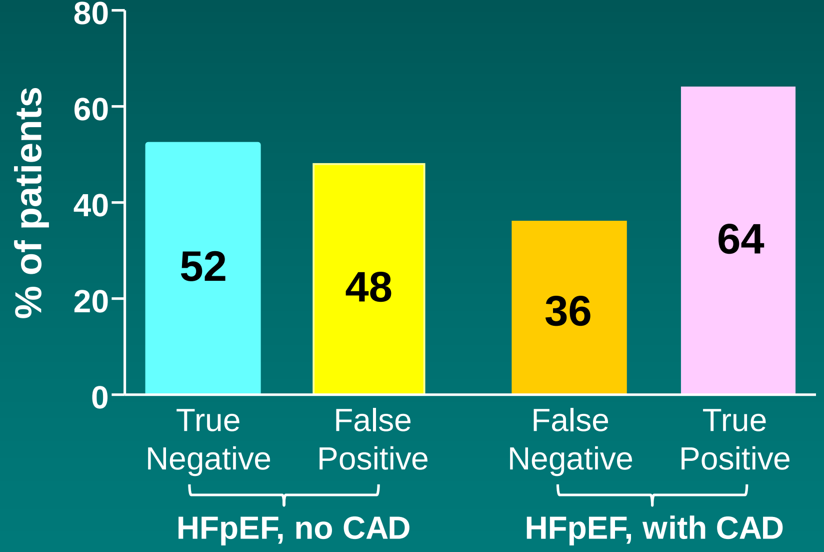




20 Watt exercise

What is the role of stress testing in HFpEF?

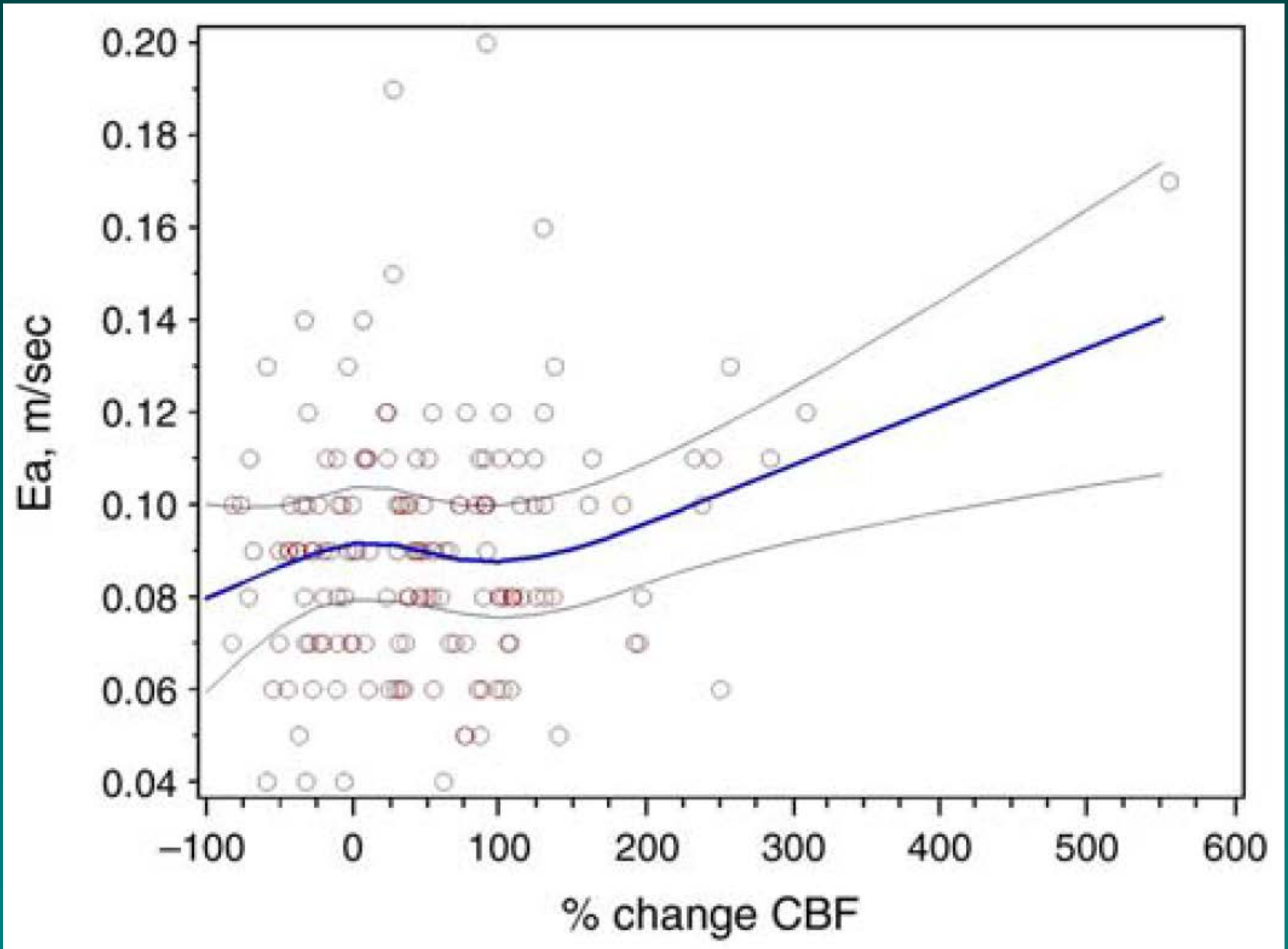
Patients with angina



Are these really false positives?

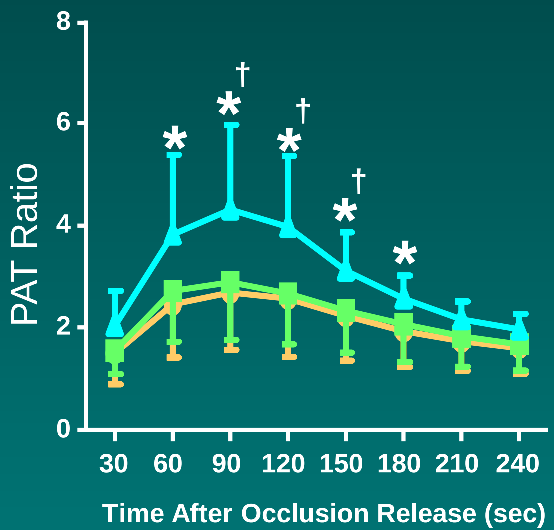
Hwang…Borlaug *J Am Coll Cardiol* 2014

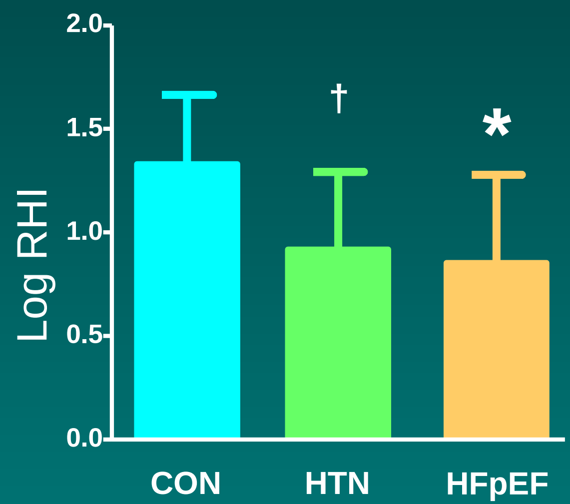
Coronary endothelial dysfunction
Can cause ischemia & Diastolic dysfunction

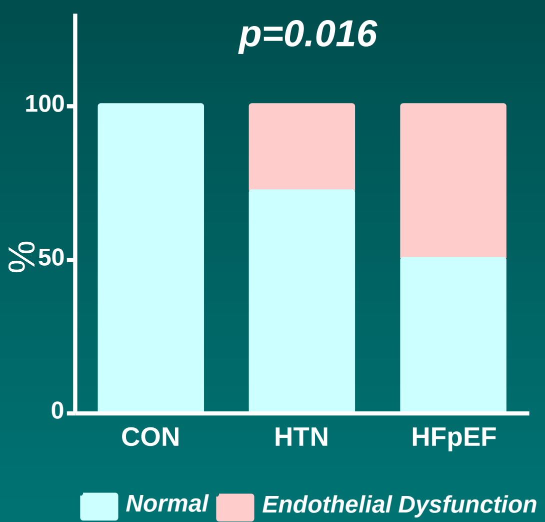


Elesber…Lerman *Am Heart J* 2007

Patients with HFpEF display endothelial dysfunction

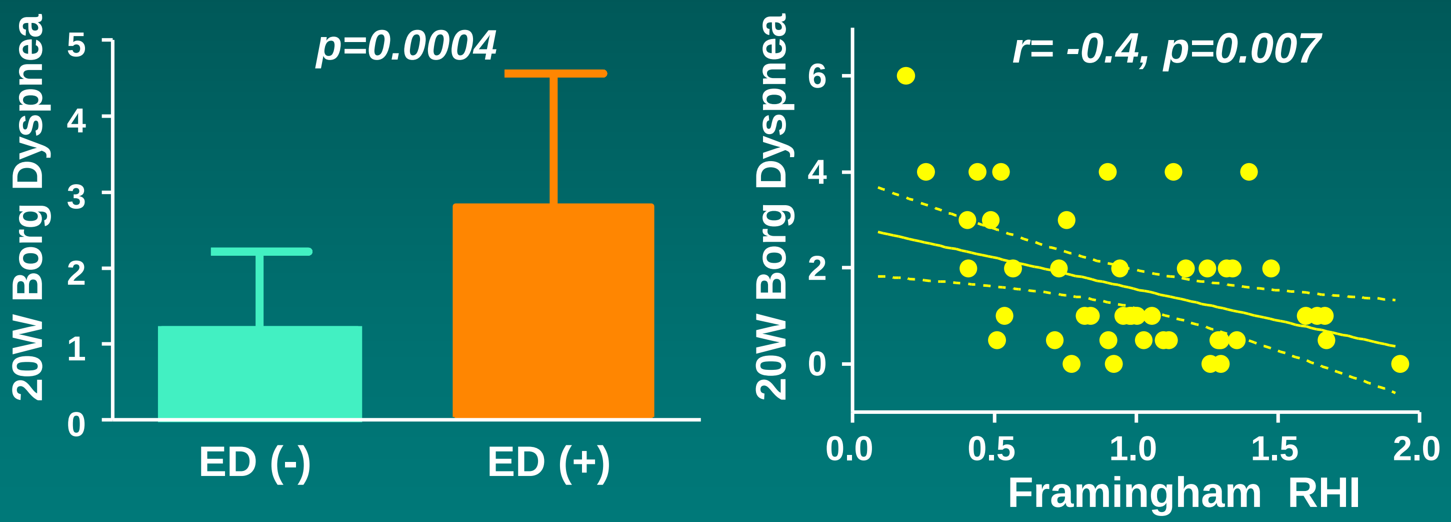






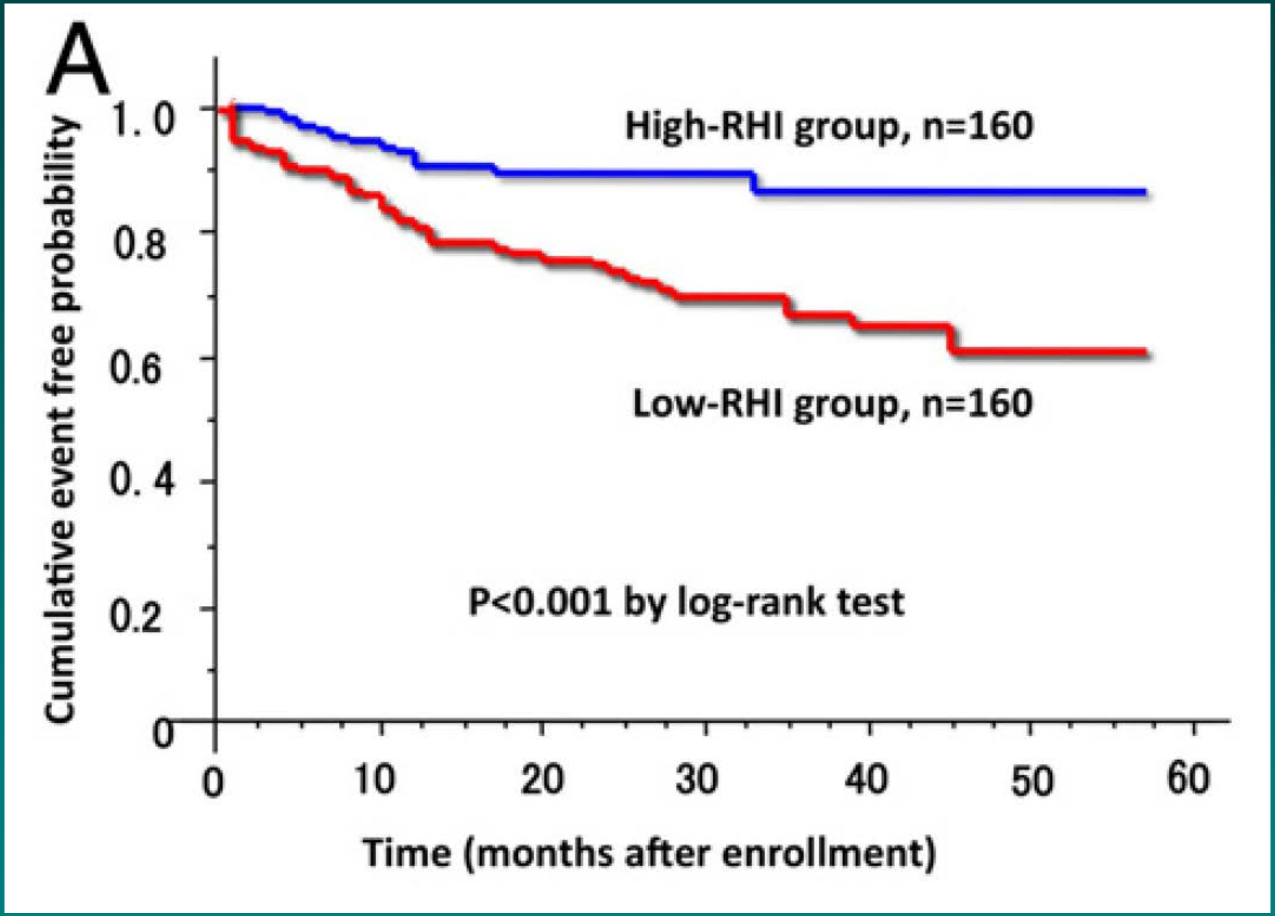
Borlaug *J Am Coll Cardiol* 2010

Endothelial Dysfunction associated with ↑DOE in HFpEF



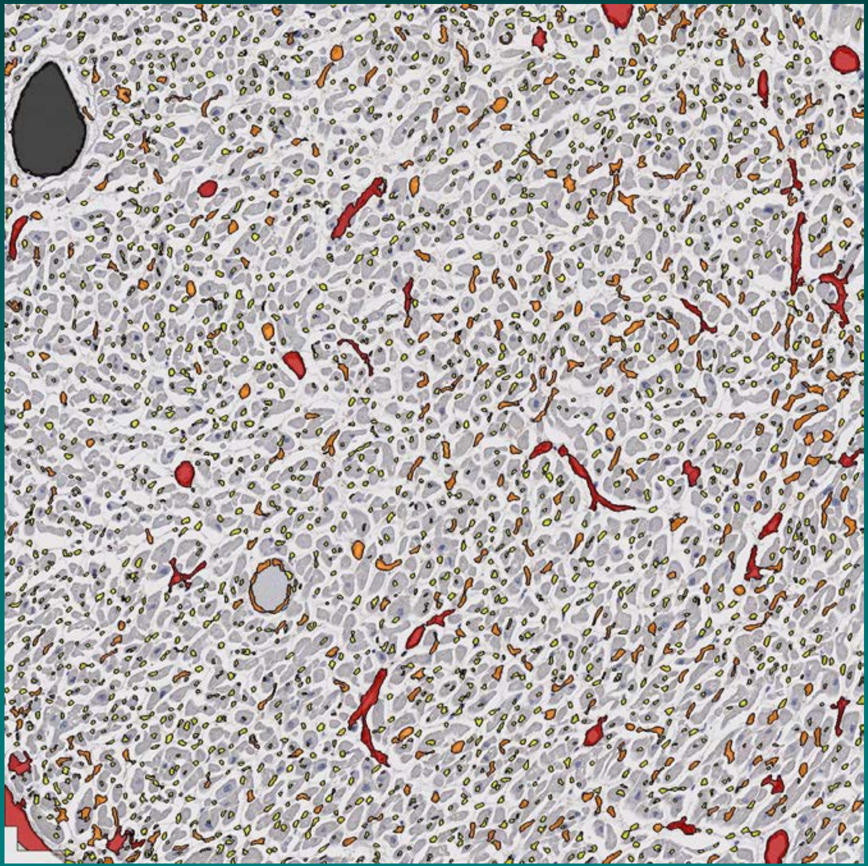
Borlaug *J Am Coll Cardiol* 2010

Endothelial Dysfunction Predicts ↑events in HFpEF

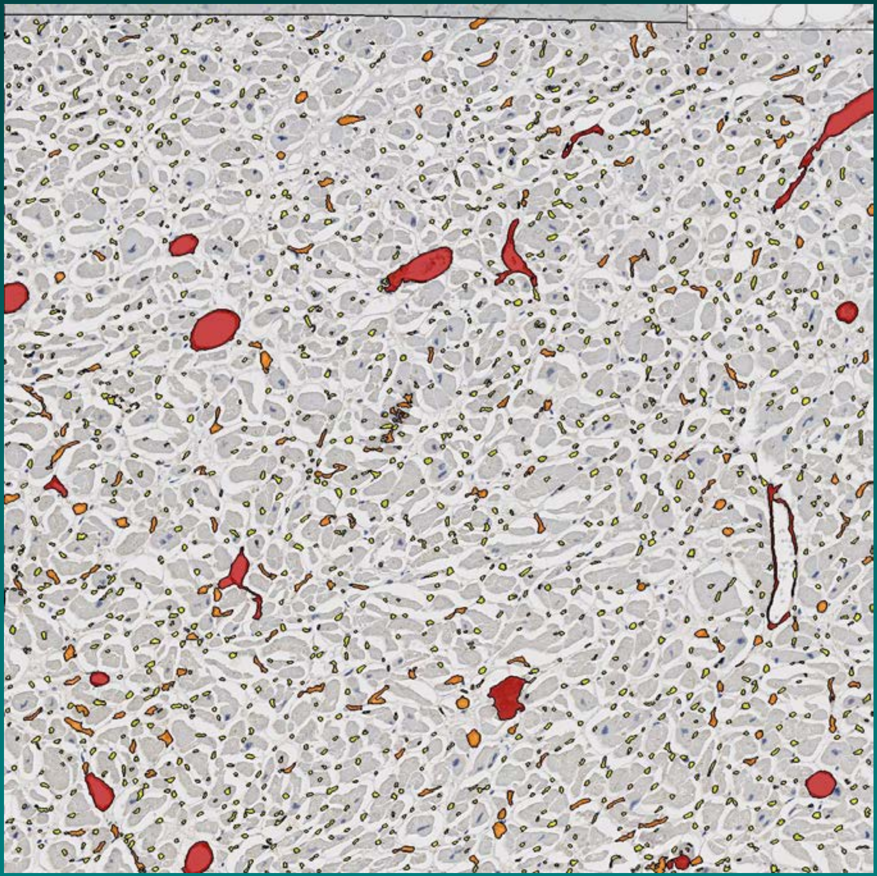


Ayikama *J Am Coll Cardiol* 2012

Microvascular structure may be affected in HFpEF, in addition to microvascular function



Control



HFpEF

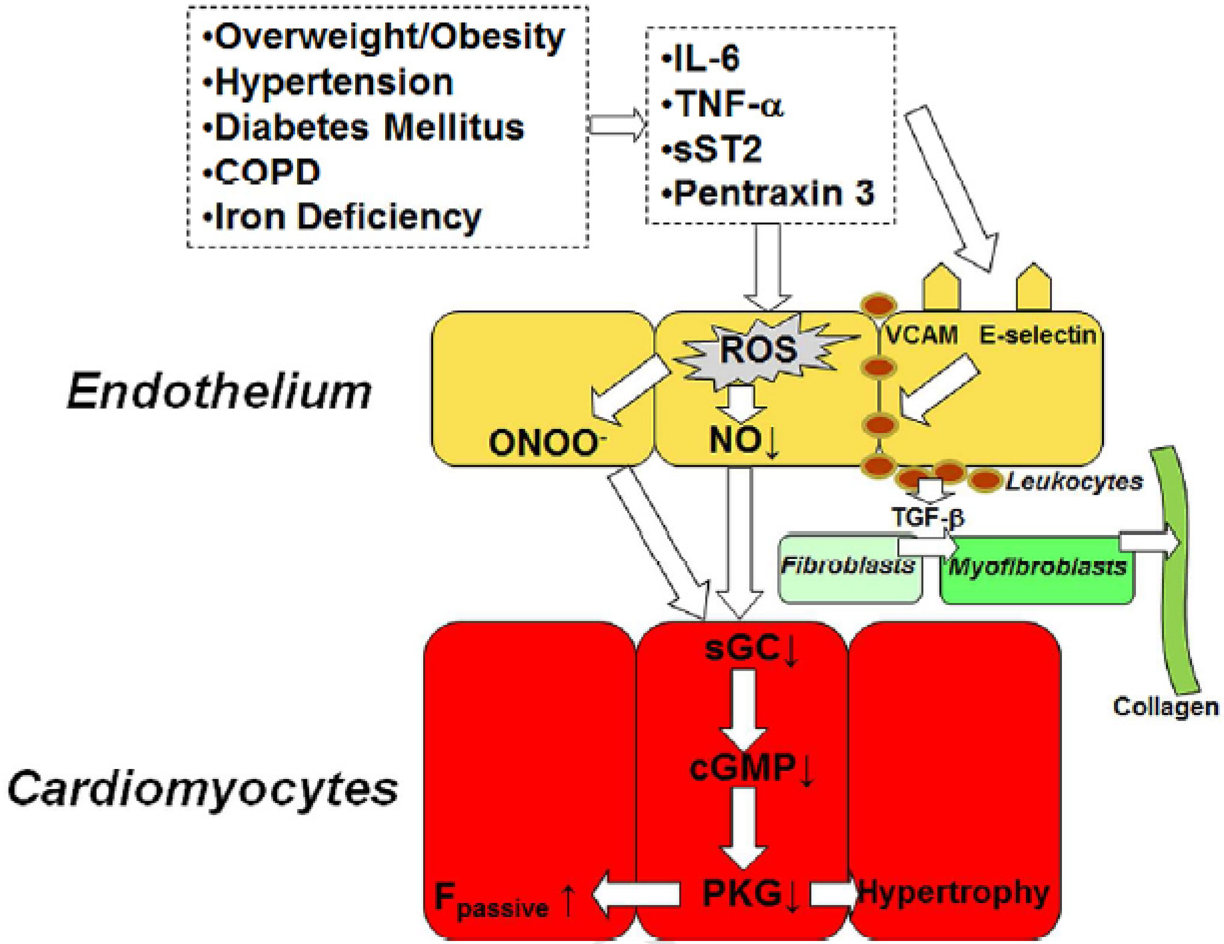
Mohammed…Redfield *Circulation 2015*

Conclusions

- Cardiac etiologies of dyspnea are common in women, often challenging to diagnose
  - HFpEF
  - Epicardial coronary disease
  - Microvascular/endothelial disease
- More research needed to define optimal treatment of HFpEF ± ischemic or valvular heart disease

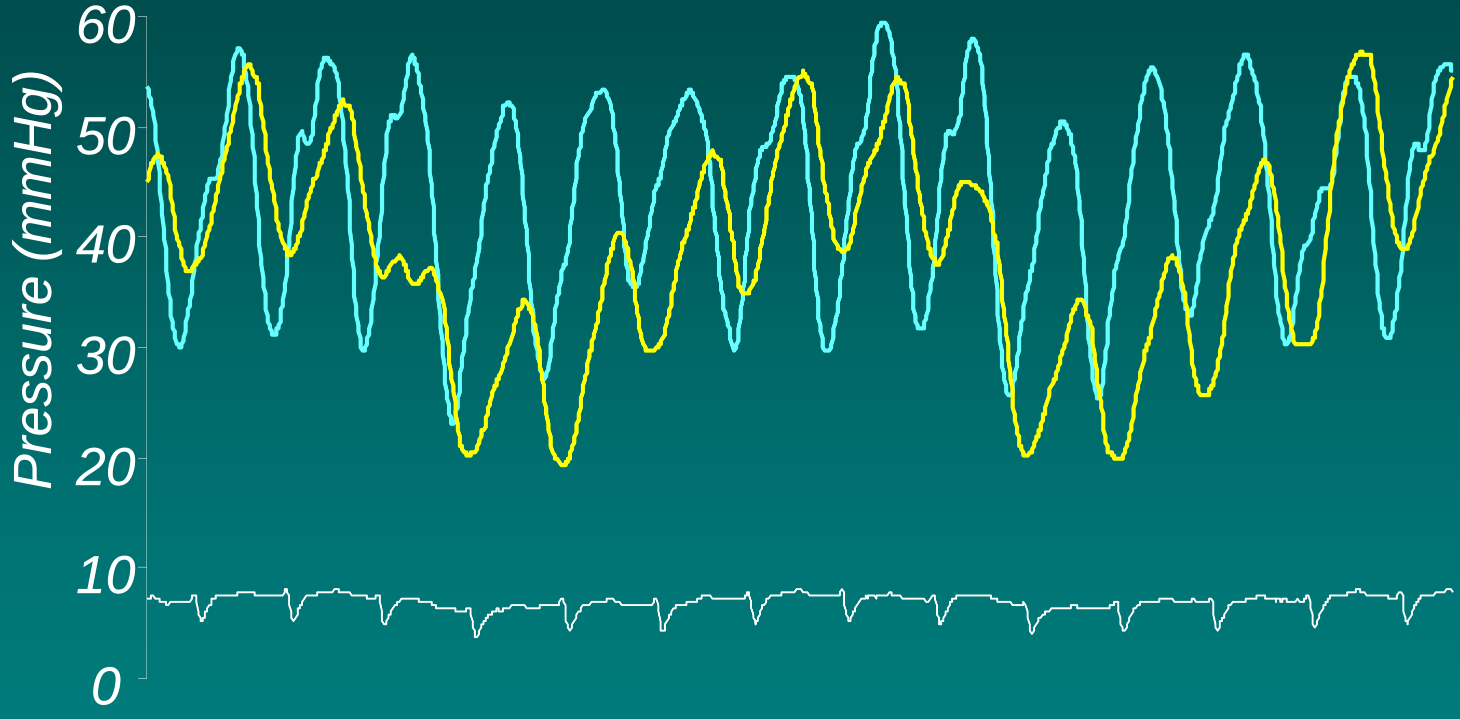
Myocardial Remodeling in HFPEF

Importance of Comorbidities

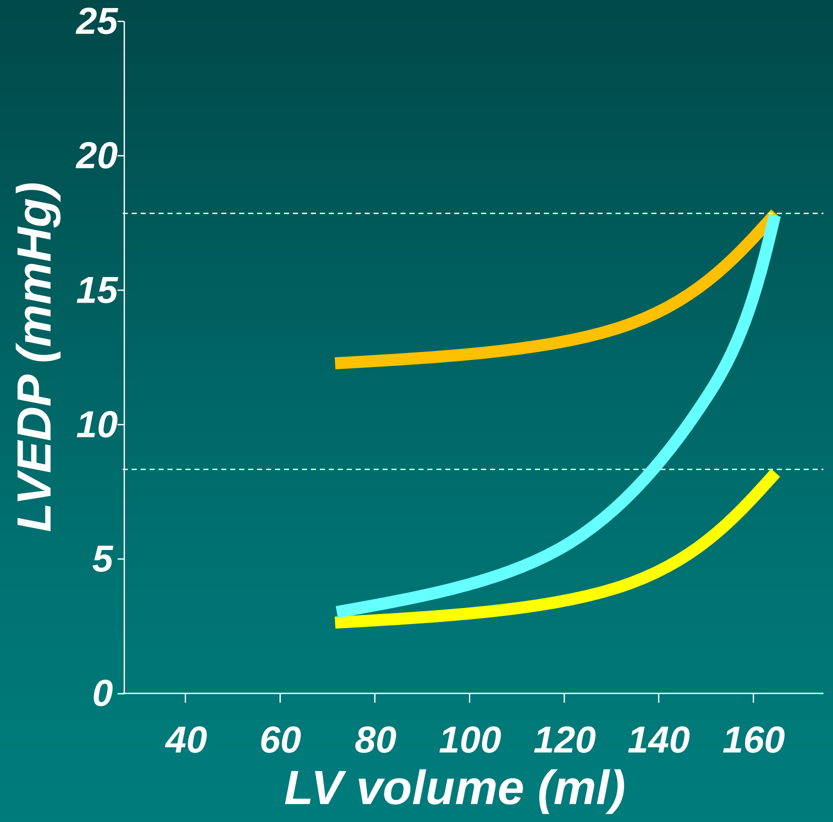


Paulus & Tschope *J Am Coll Cardiol* 2013

Case 4: 78 yo f with AF, DOE – 20 W Exercise



Not all ↑LVFP reflect LV pathologies



Borlaug Circ Heart Fail 2014

Original Article

The Hemodynamic Basis of Exercise Intolerance in Tricuspid Regurgitation

Mads J. Andersen, MD, PhD; Rick A. Nishimura, MD; Barry A. Borlaug, MD

Background—Patients with severe tricuspid regurgitation (TR) frequently present with exertional fatigue and dyspnea, but the hemodynamic basis for exercise limitation in people with TR remains unclear.

Methods and Results—Twelve subjects with normal left ventricular (LV) ejection fraction and grade ≥3 TR underwent high-fidelity invasive hemodynamic exercise testing with simultaneous expired gas analysis and were compared with 13 age- and sex-matched controls. At rest, TR subjects had lower pulmonary blood flow (3.6±0.4 versus 5.1±1.9 L/min; *P*=0.01), increased right atrial pressure (12±5 versus 4±1 mm Hg; *P*=0.0002), and higher pulmonary capillary wedge pressure (17±5 versus 9±3 mm Hg; *P*=0.0001). However, LV transmural pressure (pulmonary capillary wedge pressure−right atrial pressure), which reflects LV preload independent of right heart congestion and pericardial restraint, was similar in TR and controls (6±3 versus 4±2 mm Hg; *P*=0.3). With exercise, TR subjects displayed lower peak Vo_2 (10.3±2.8 versus 13.8±4.2 mL/min per kg; *P*=0.02), lower pulmonary blood flow (6.4±1.3 versus 10.3±3.3 L/min; *P*=0.001), and less increase in pulmonary blood flow relative to Vo_2 (+4.6±1.1vs +6.2±0.7; *P*=0.001). TR subjects displayed higher pulmonary capillary wedge pressure with exercise, but this was solely because of RA hypertension (27±9 versus 8±3 mm Hg; *P*<0.0001), because LV transmural pressure dropped with exercise in subjects with TR (−5±6 versus +3±3 mm Hg; *P*=0.0007), suggesting inadequate LV diastolic filling, despite high pulmonary capillary wedge pressure.

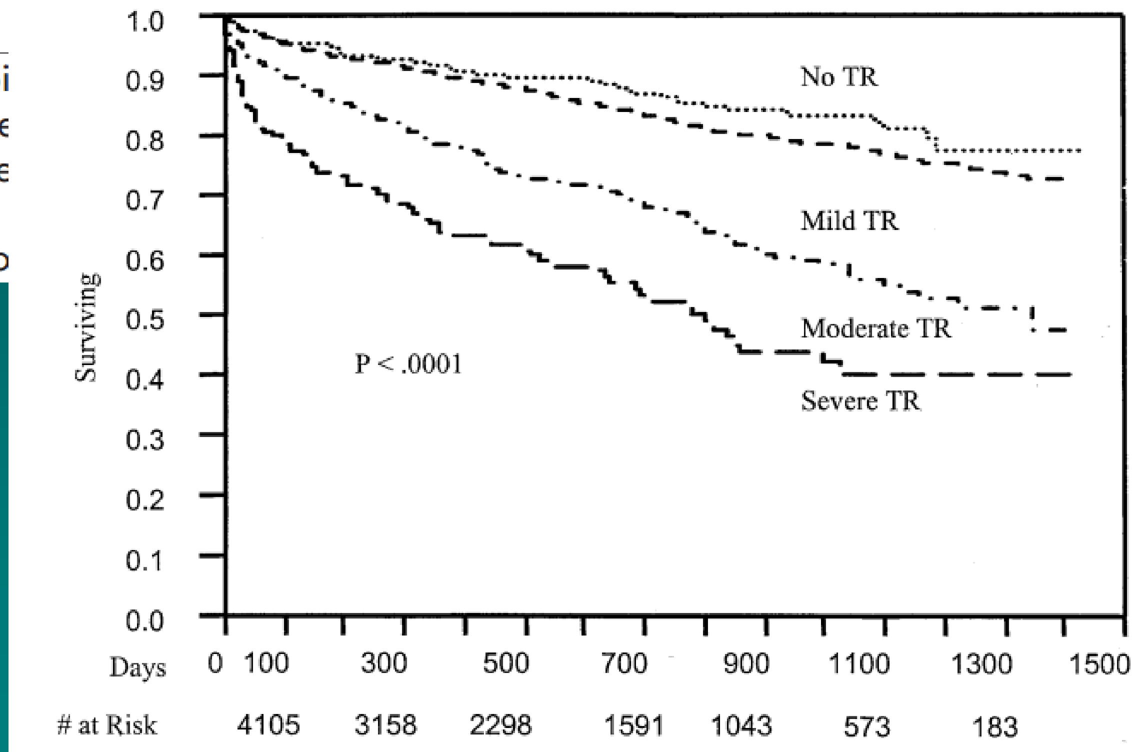
Conclusions—Impaired exercise capacity in people with severe TR is related to low cardiac output reserve relative to metabolic needs, coupled with elevated systemic and pulmonary venous pressures. Left heart pressures are elevated with exercise in subjects with TR, despite low LV preload, secondary to enhanced ventricular interaction. **(*Circ Heart Fail.* 2014;7:00-00.)**

Key Words: exercise ■ heart failure ■ hemodynamics

TR is very common in women, associated with increased mortality

TABLE IIb Prevalence of Valvular Regurgitation Stratified by Age and Severity in Women

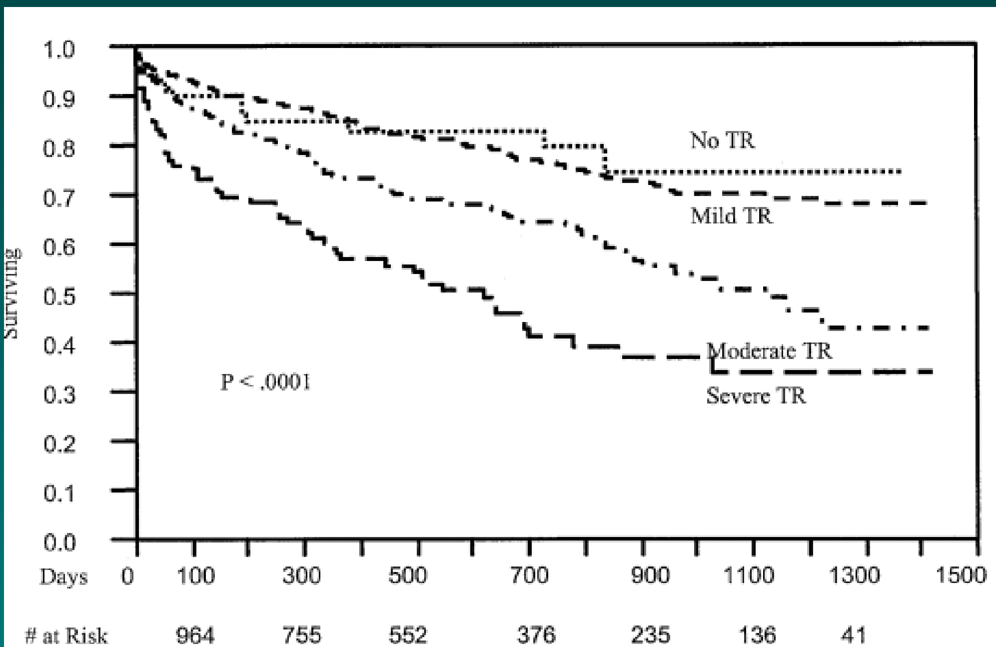
	Age (yr)
	70–83
	(n = 71)
Tricuspi	
None	14.1
Trace	56.4
Mild	23.9
≥Mo	5.6

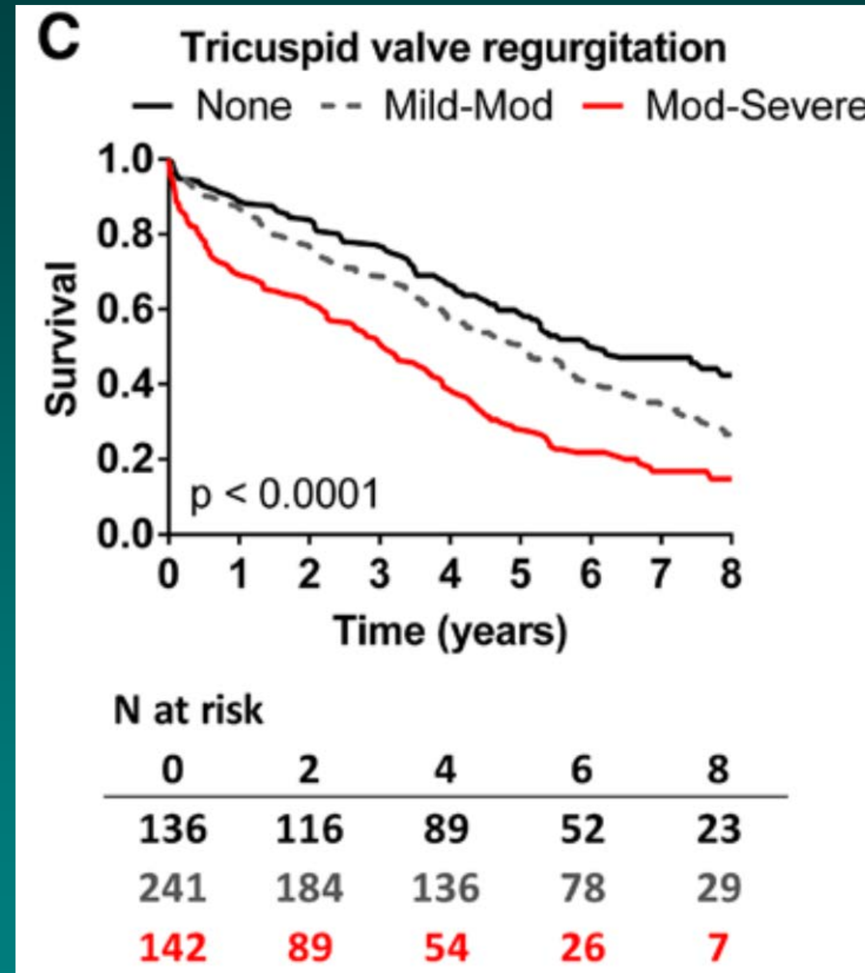


Singh Am J Cardiol 1999

Nath J Am Coll Cardiol 2004

Poor outcomes in HFrEF & HFpEF

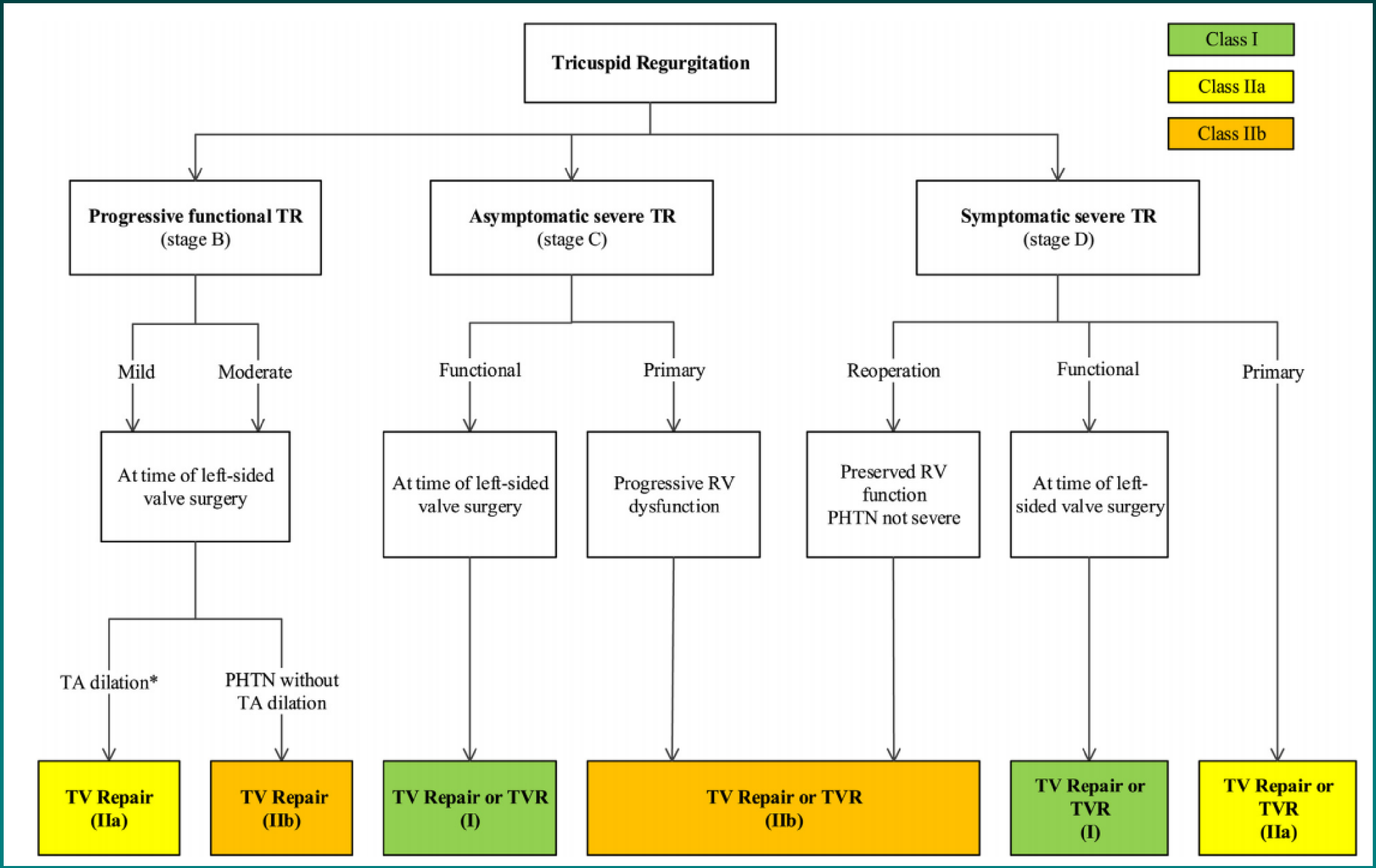




Nath J Am Coll Cardiol 2004

Mohammed Circulation 2014

Not clear what to do about it…



Nishimura et al. Circulation 2014