

Heart Failure with Preserved Ejection Fraction and Pulmonary Edema, What Do the Guidelines Say?

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Disclosures

- **Research Grants**
 - *NHLBI*
 - *Amgen*
 - *Novartis*
 - *Pfizer*
 - *Alnylam*
- **Consultant**
 - *Novartis*
 - *Amgen*
 - *Merck*



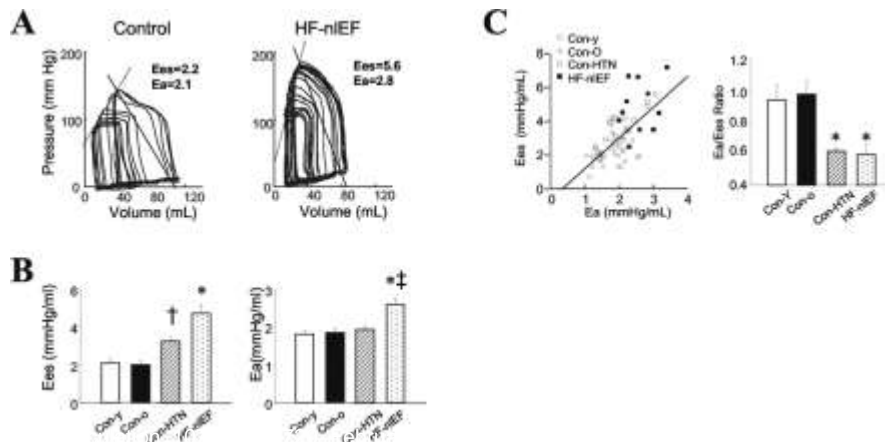


My patient has acute HFpEF with pulmonary edema – Why?, What should I do?

- Hypertension urgency
- Ischemia/CAD
- Don't forget the RV
- Arrhythmia/tachycardia
- Mechanical causes
 - Valvular disease
- Metabolic derangements
- Anemia
- Other stuff....



Ventricular-arterial Stiffening in HFpEF





Vasodilators in HFpEF: Reduce SBP

Vasodilators

i.v. vasodilators should be considered for symptomatic relief in AHF with SBP >90 mmHg (and without symptomatic hypotension).

Symptoms and blood pressure should be monitored frequently during administration of i.v. vasodilators.

IIa

B

In patients with hypertensive AHF, i.v. vasodilators should be considered as initial therapy to improve symptoms and reduce congestion.

IIa

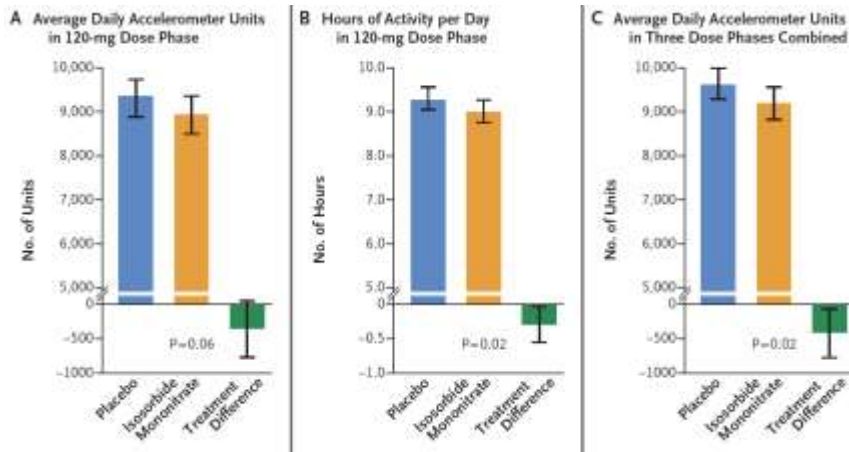
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Vasodilator	Dosing	Main side effects	Other
Nitroglycerine	Start with 10-20 µg/min, increase up to 200 µg/min	Hypotension, headache	Tolerance on continuous use
Isosorbide dinitrate	Start with 1 mg/h, increase up to 10 mg/h	Hypotension, headache	Tolerance on continuous use
Nitroprusside	Start with 0.3 µg/kg/min and increase up to 5 µg/kg/min	Hypotension, isocyanate toxicity	Light sensitive
Nesiritide*	Bolus 2 µg/kg + infusion 0.01 µg/kg/min	Hypotension	

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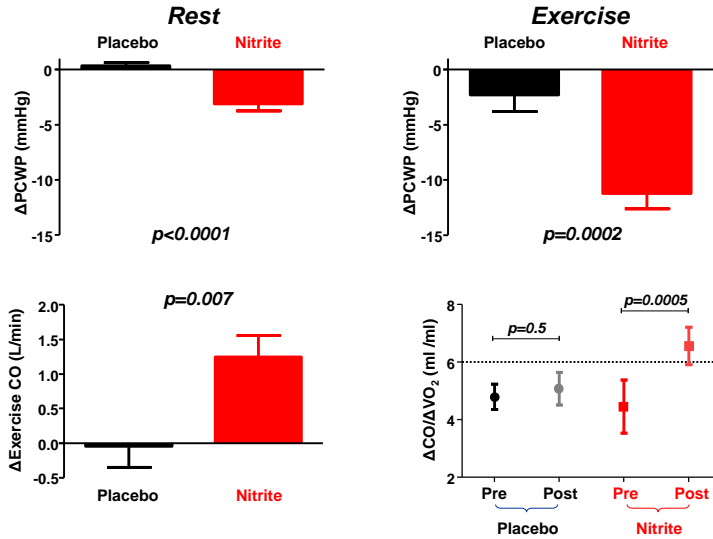
Oral nitrates long-term not effective possibly harmful...



Redfield et al. *N Eng J Med* 2015



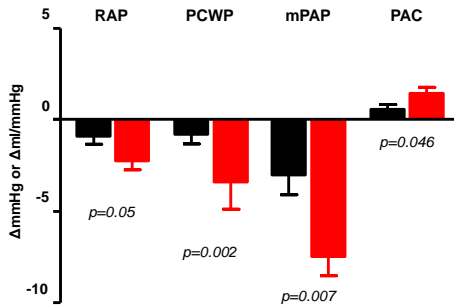
Acute Hemodynamic effects of IV NO₂⁻ in HFpEF



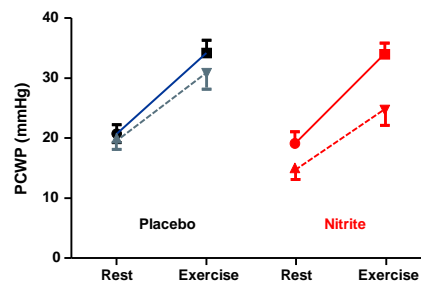
Borlaug et al. *J Am Coll Cardiol* 2015

Acute effects with Inhaled Nitrite (NO₂⁻)

Effects of inhaled NO₂ at Rest



↑ Benefit with Exercise

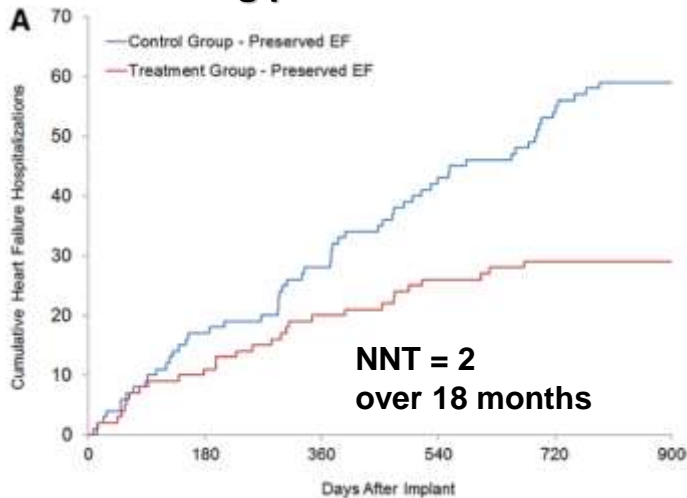


Borlaug et al. *Circ Res* 2016





Lower Filling pressures with diuretics



Adamson *Circ Heart Fail* 2014



Ischemia and HFpEF: Chicken or Egg?

- Ischemia and subsequent reperfusion lead to impaired followed by improved LV relaxation/filling/stiffness
- Subendocardial and subepicardial longitudinal myocardial fibers are particularly sensitive to ischemia with increasing LVEDP
- HFpEF is associated with systemic endothelial dysfunction/ platelet activation/ thrombogenicity ischemia

Bach AHJ 1996; Nagueh JACC 1997; Lee AHJ 2005





Ischemia & HFpEF: Chicken or Egg?

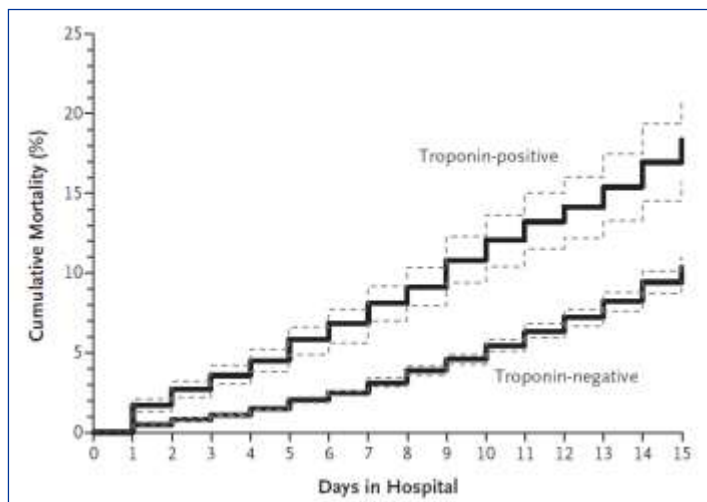
Ischemia (or HFpEF) can result in:

- ↕ Acute/transient reduction in regional function
- ↕ Acute/transient mitral regurgitation
- ↕ Increase filling pressures
- ↕ Increased diastolic stiffness
- ↕ Promoting myocyte hypertrophy and fibrosis in response to NE, dopamine and endothelin, Ang II release
- ↕ HFpEF (ischemia)

Velazquez, et al. Circ 2004



Troponin and AHF - ADHERE





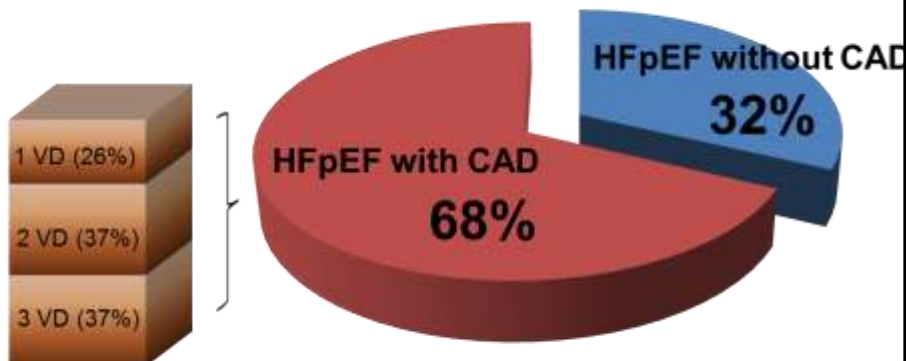
Acute HF and CAD: HFpEF vs HFrEF

- **STRONG Heart Study: LVEF known (N=3184)**
 - ~ 20% LVEF 40 – 54%; CAD 32%
 - ~ 52% LVEF > 54%; CAD 20%
- **ADHERE Registry (N=105,388)**
 - N=52187 thru Jan 2004 with known LVEF
 - 50.4% LVEF > 40%
 - Lower In Hosp Mortality – 2.8% vs 3.9%
 - Lower MI Hx - 24% vs 36%
 - Lower CAD Hx – 50% vs 59%
- **OPTIMIZE HF Registry: LVEF known (N=41267)**
 - ~ 51% LVEF > 40%; CAD 38%
 - ~ 24% LVEF > 50%; CAD 32%

Devereux et al AJC 2000; Yancy et al. JACC 2006; Fonorow et al JACC 2007



CAD is common in HFpEF

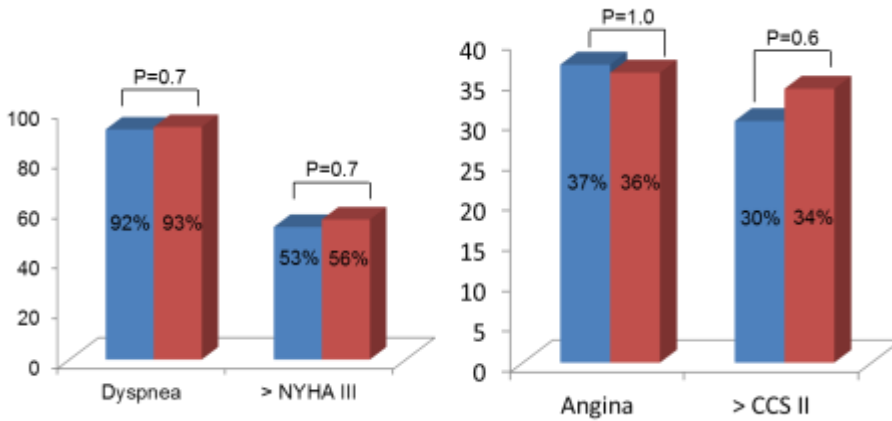


Hwang et al. J Am Coll Cardiol 2014





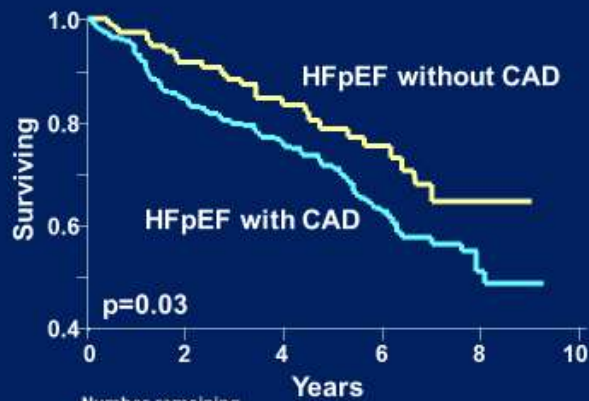
CAD in HFpEF: Symptoms not helpful



Hwang et al. *J Am Coll Cardiol* 2014



Impact of CAD on Outcome in HFpEF



	0	2	4	6	8	10
CAD (-)	121	90	60	34	14	
CAD (+)	255	193	129	83	23	

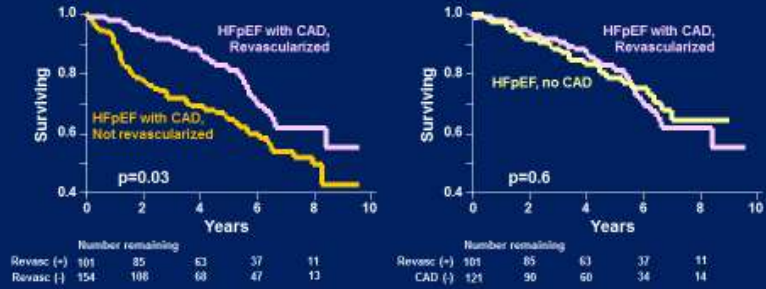
Hwang... Borlaug *J Am Coll Cardiol* 2014

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Does Revascularization improve survival?

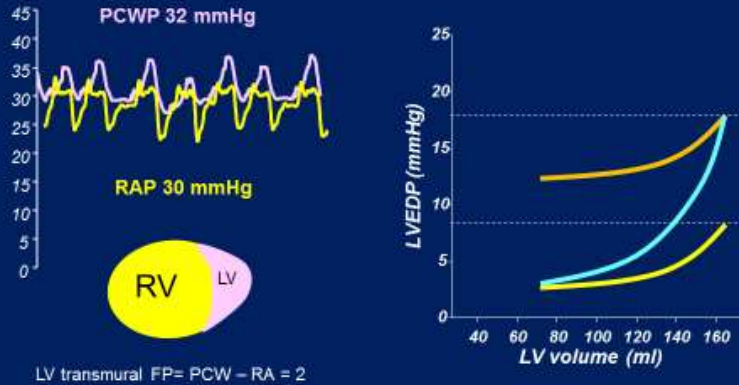


Hwang... Borlaug *J Am Coll Cardiol* 2014

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Not all ↑LVFP reflect LV pathologies



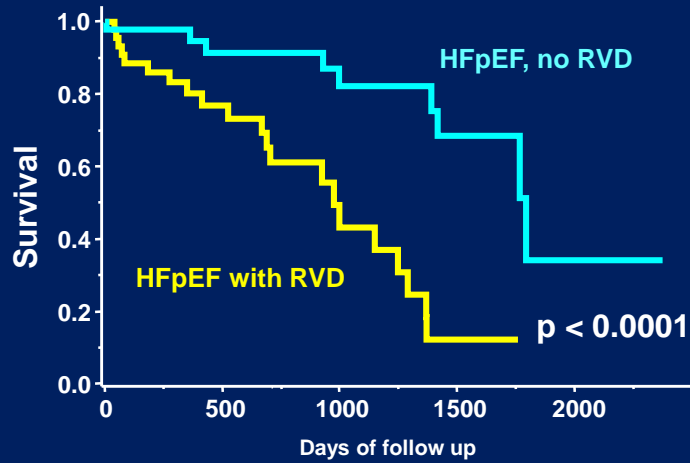
Guazzi & Borlaug *Circulation* 2013

Borlaug *Circ Heart Fail* 2014

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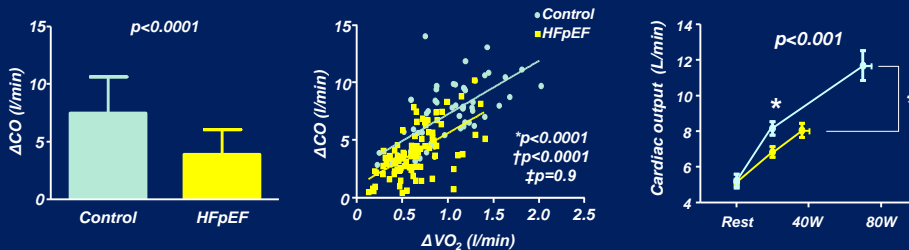


RVD predicts ↑mortality in HFpEF, independent of PA pressures



Melenovsky, Borlaug *Eur Heart J* 2014

CO reserve is depressed in HFpEF



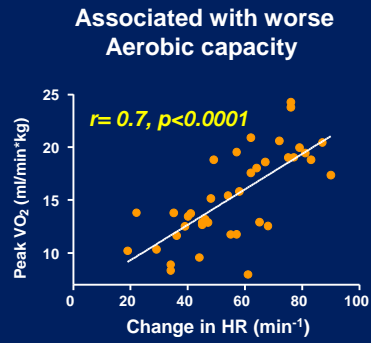
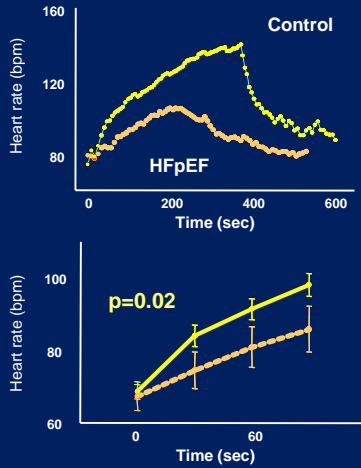
Borlaug et al. *Eur Heart J* 2016

Abudiab...Borlaug *Eur J Heart Fail* 2013



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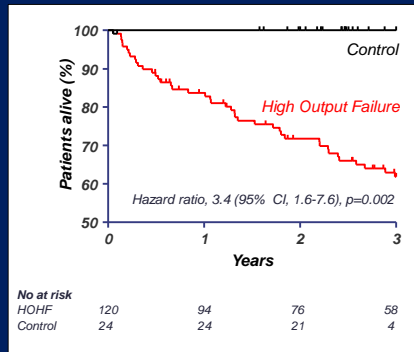
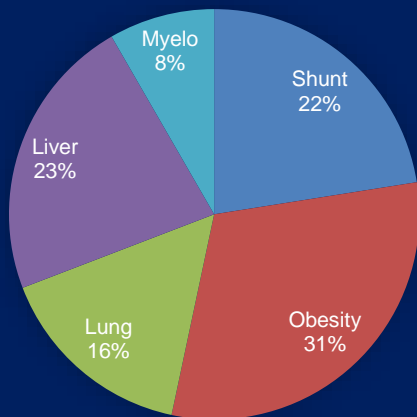
Pathophysiologic Observation: Chronotropic Incompetence is common in HFpEF



Borlaug *J Am Coll Cardiol* 2010

Borlaug *Circulation* 2006

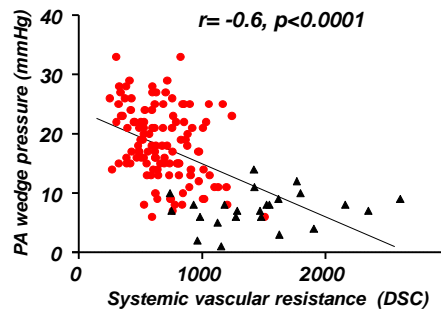
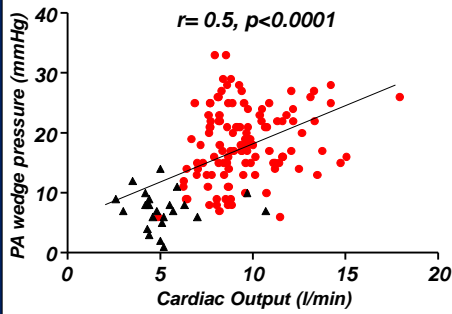
High Output Heart Failure is not Benign



Reddy et al. *J Am Coll Cardiol* 2016

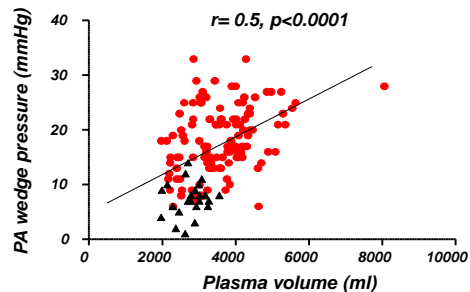
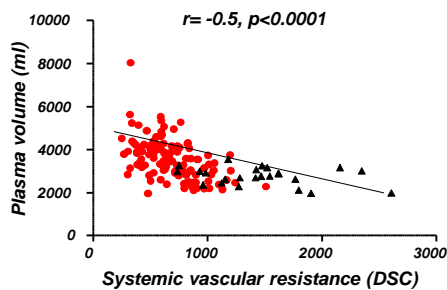


HOHF caused by excessive vasodilation



Reddy et al. *J Am Coll Cardiol* 2016

↑ Vasodilation drives PV Expansion



Reddy et al. *J Am Coll Cardiol* 2016



HFpEF with Excessive Vasodilation associated with Highest Mortality



Reddy et al. *J Am Coll Cardiol* 2016



Summary

- Acute HFpEF with pulmonary congestion is a highly heterogeneous syndrome
- Reduce high BP should be initial strategy, consider decongestion early
- Search for reversible causes and there may be several
 - Ischemia/CAD
 - Other contributing conditions
- Don't forget the RV may be playing a role
- Avoid worsening hemodynamics
- Get more data (invasive hemodynamics) if pulmonary edema persists, worsens despite initial approach

