# Assessment of Atrial Function

## *What is the Answer?*

**Sanjiv J. Shah, MD, FASE**

*Stone Professor of Medicine*

*Director of Research, Bluhm Cardiovascular Institute*

*Director, Northwestern HFpEF Program*

*Division of Cardiology, Department of Medicine*

*Northwestern University Feinberg School of Medicine*

*sanjiv.shah@northwestern.edu • http://www.hfpef.org • Twitter: @HFpEF*

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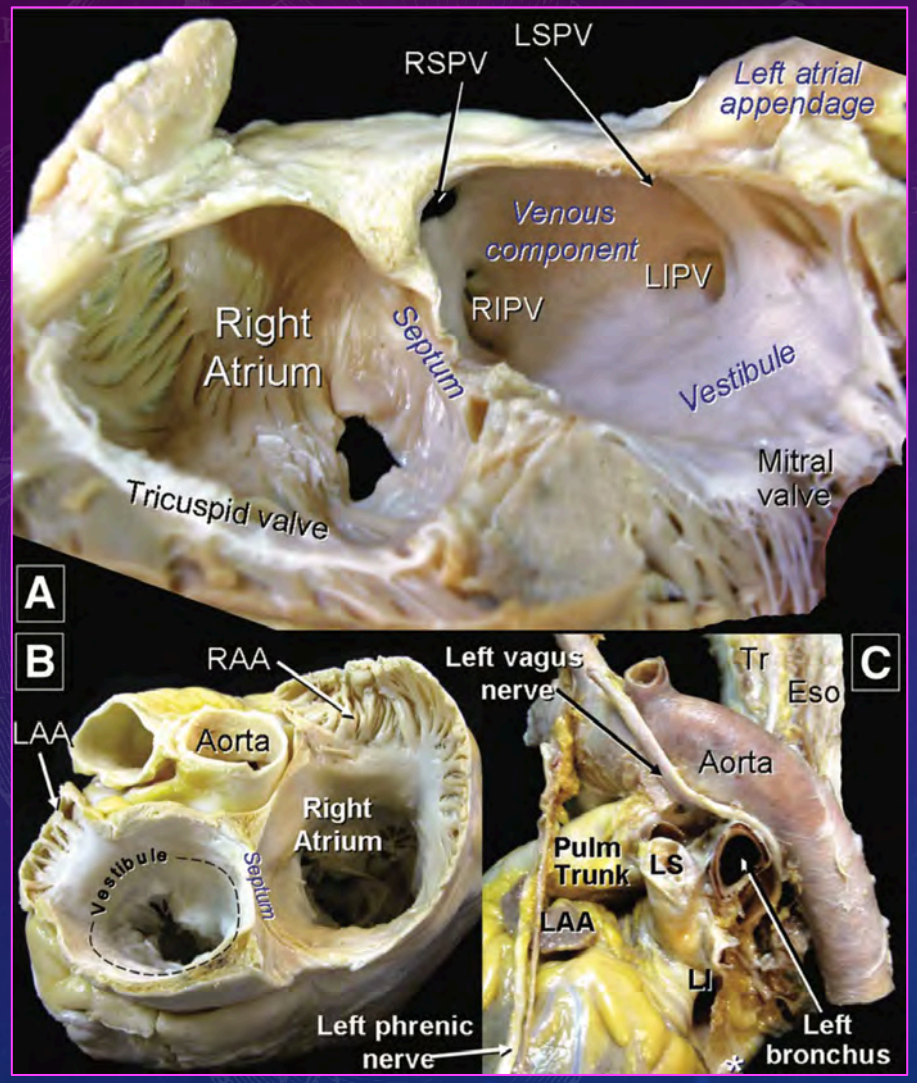
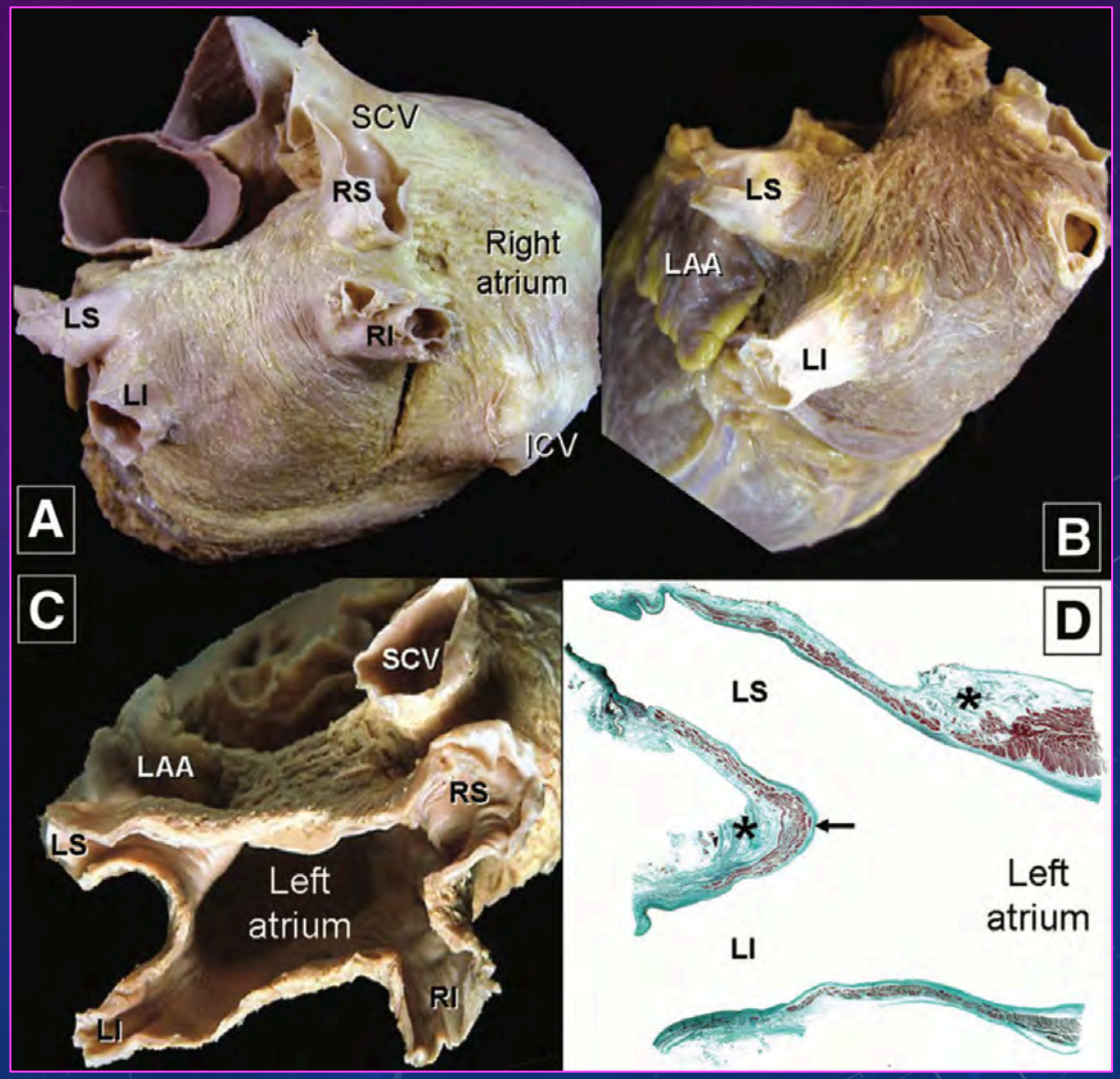
# Anatomy of the left atrium

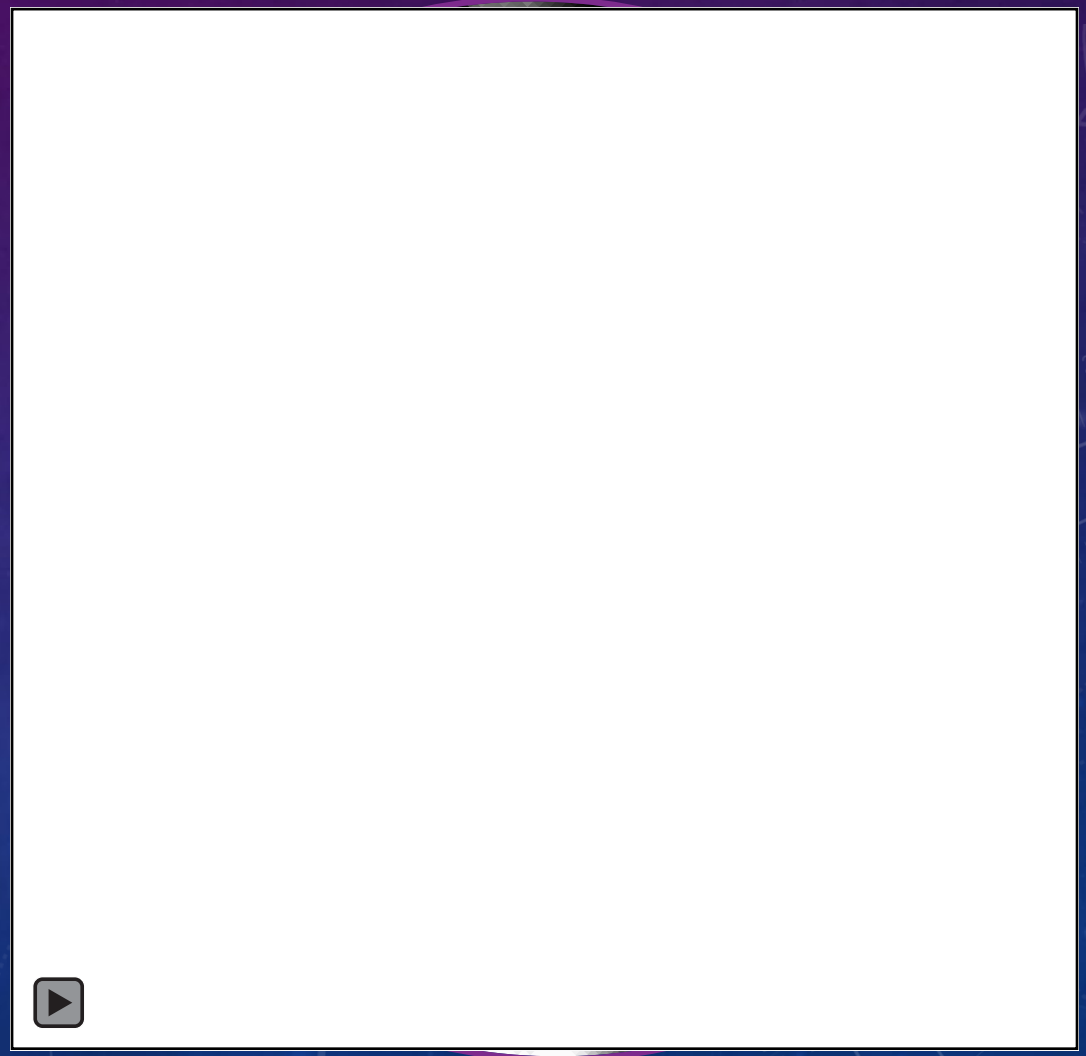



Ho SY, et al.
*Circ EP* 2011

# Basic roles of the left atrium

- ***Reservoir*** for pulmonary venous return during LV systole
- ***Conduit*** for pulmonary venous return during early LV diastole
- ***Booster pump*** to augment LV filling during late LV diastole



# Basic roles of the left atrium

- ***Reservoir*** for pulmonary venous return during LV systole

***LA filling***

- ***Conduit*** for pulmonary venous return during early LV diastole

***LA passive emptying***

- ***Booster pump*** to augment LV filling during late LV diastole

***LA contraction***

# Basic roles of the left atrium

- ***Reservoir*** for pulmonary venous return during LV systole
  - Dependent on LA compliance during LV systole
  - Influenced by LA contractility/relaxation, and descent of the LV base during LV systole
- ***Conduit*** for pulmonary venous return during early LV diastole
  - Closely related to LV relaxation and compliance Also influenced by LA compliance (reciprocal of LA reservoir function)
- ***Booster pump*** to augment LV filling during late LV diastole
  - Based on magnitude/timing of LA contractility
  - Influenced by pulm. venous return (LA preload), LVEDP (LA afterload), and LV systolic reserve

# Basic roles of the left atrium

- ***Reservoir*** for pulmonary venous return during LV systole
- ***Conduit*** for pulmonary venous return during early LV diastole
- ***Booster pump*** to augment LV filling during late LV diastole

***What decreases LA compliance?***

- LA fibrosis
- ↑LA cardiomyocyte stiffness
- Poor LA emptying (e.g., AF)
- ↑LA blood volume (CHF)
- Mitral regurgitation
- LV systolic dysfunction
- LA-RA interaction
- Extrinsic compression of the LA

# Additional roles of the left atrium

- **Rhythm:** Essential for coordinated emptying and filling at rest and during exercise. The worse the LV, the more adequate LA emptying will be essential
- **Endocrine:** The LA is a source of ANP, with minimal BNP production in health. However, in HTN and CHF, LA hypertrophies → starts making ↑↑BNP
- **Neural control:** The LA is richly innervated by sympathetic and parasympathetic nerve fibers that can get activated in states of LA disease/dysfunction

# LA: A major neuroendocrine organ?


Lakkireddy D et al.
*JACC* 2018

# Indices of LA function

Pulmonary venous flow

LA strain

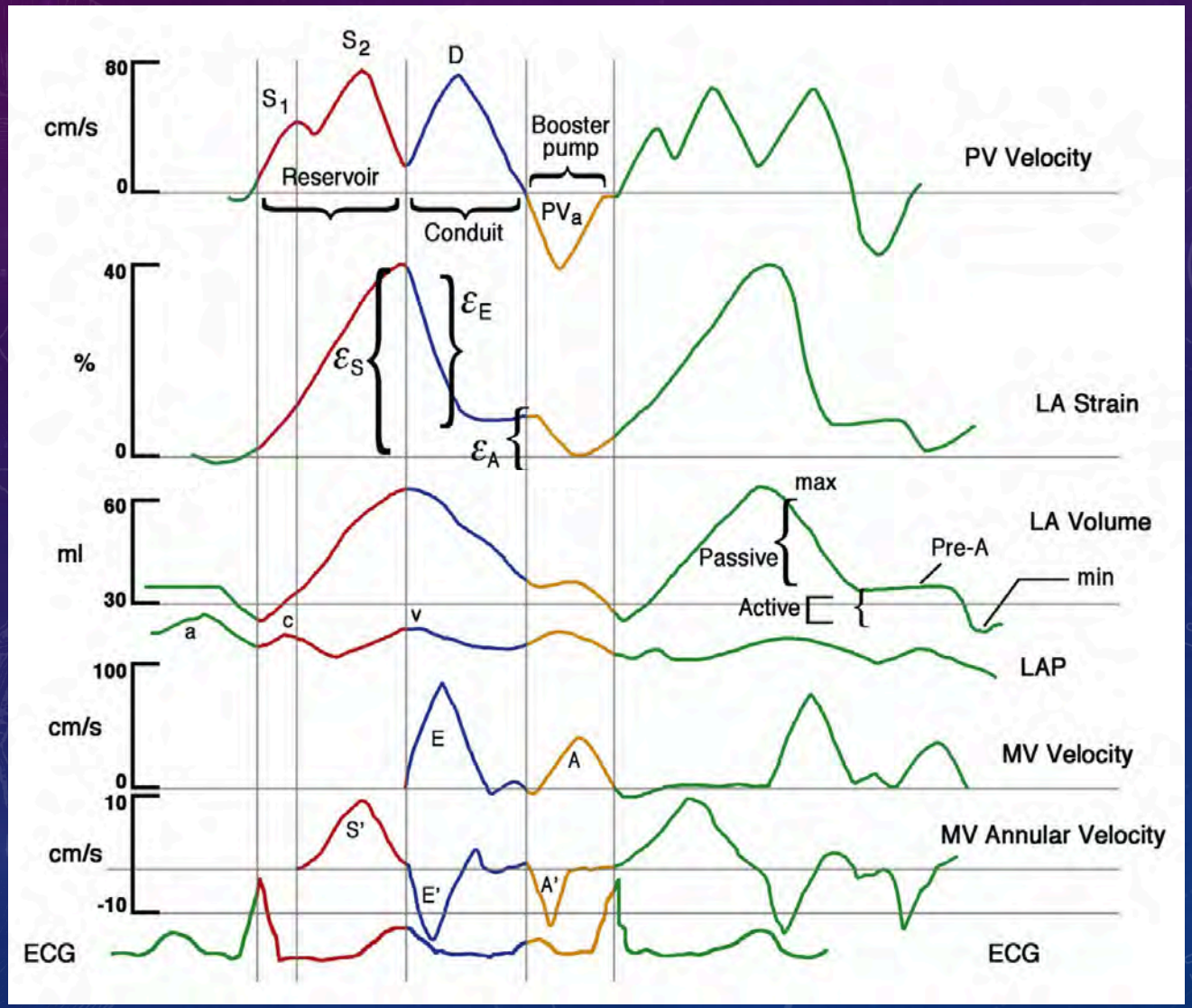
LA volume

LA pressure

Mitral inflow

Tissue Doppler

ECG

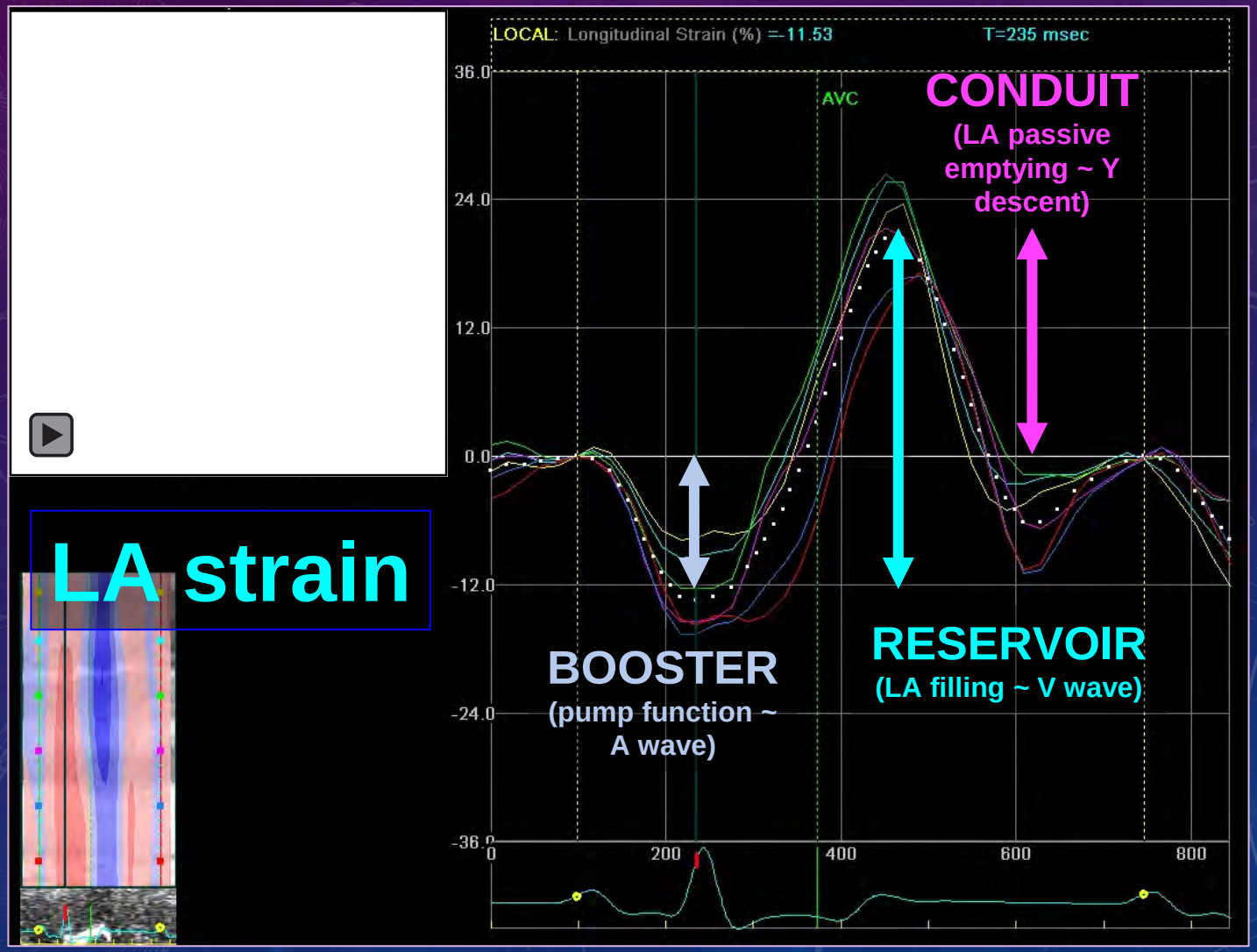



Hoit BD. *JACC* 2014

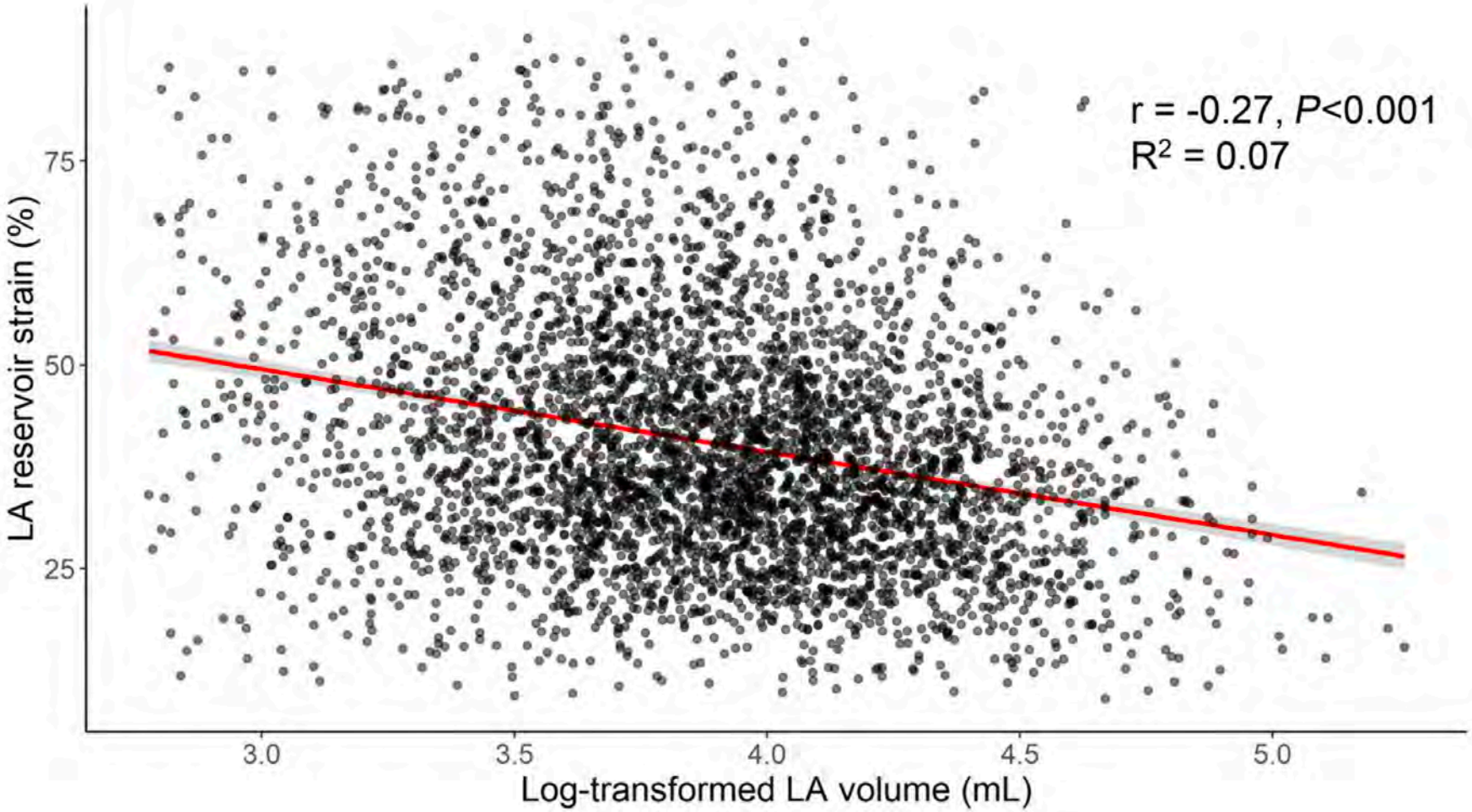
# Indices of LA function in disease

| Index of LA function | ↑LA pressure | ↓LA filling | ↓Passive LA emptying | ↓LA contractility |
|---|---|---|---|---|
| Pulmonary vein flow | ↓ S/D ratio | ↓ S wave | ↓ D wave | ↓ A reversal |
| Mitral inflow | ↑ E wave | — | ↑ E decel time | ↓ A wave |
| Tissue Doppler | ↑ E/e’ | ↓ s’ | ↓ e’ | ↓ a' |
| LA strain | ↓ Reservoir | ↓ Reservoir | ↓ Conduit | ↓ Booster |
| LA pressure (PCWP tracing) | ↑ PCWP | ↑ V wave | Blunted *y* descent | ↓ A wave |

# Overview of LA strain



# LA volume vs. LA strain: which is best?

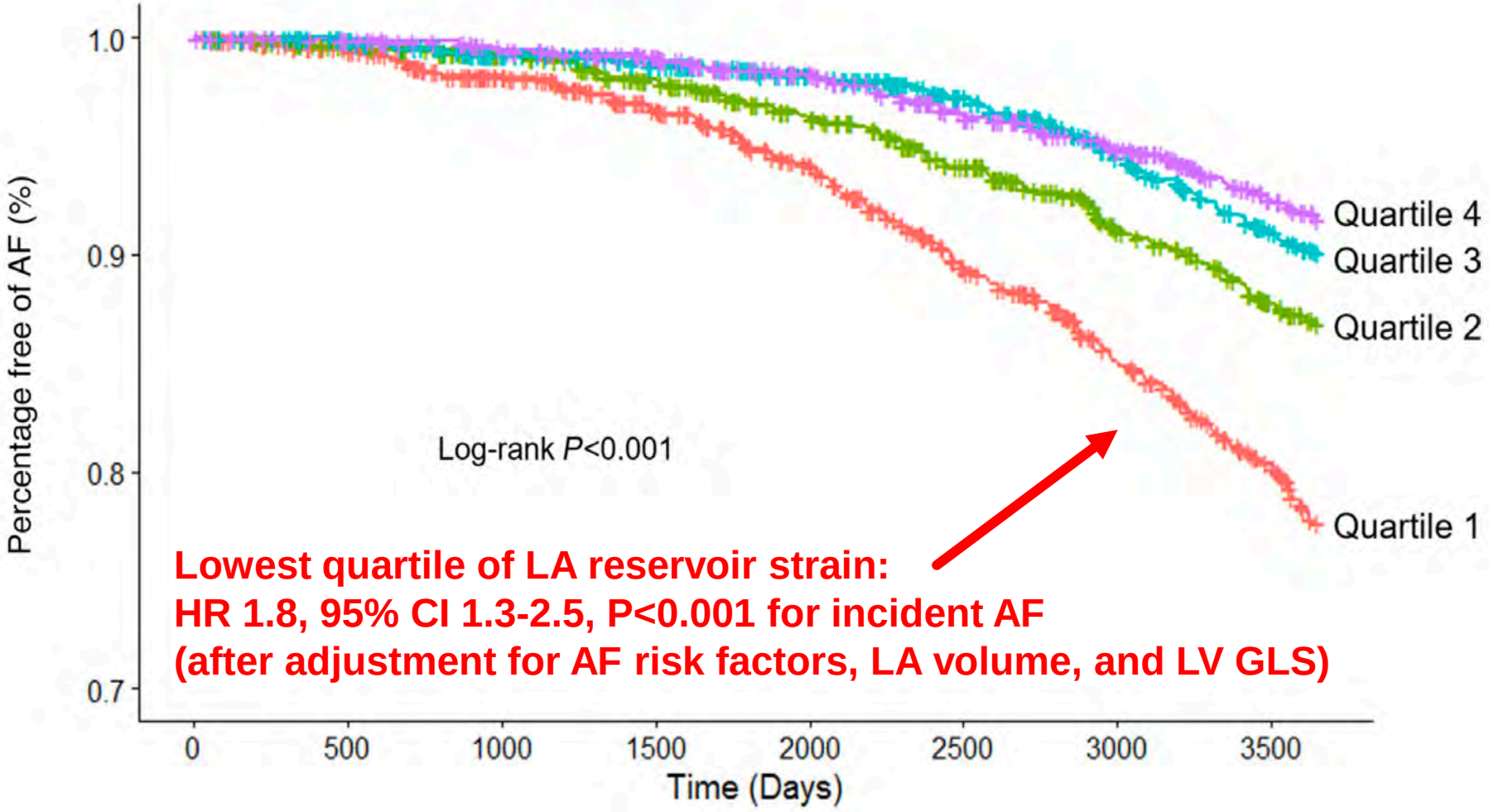



## Cardiovascular Health Study

- Population-based study, age > 65 years
- N=4341 with measurable LA strain at baseline
- Only modest correlation between LA volume and LA strain

Patel RB…Shah SJ. *JCI Insight* 2020

# LA volume vs. LA strain: which is best?



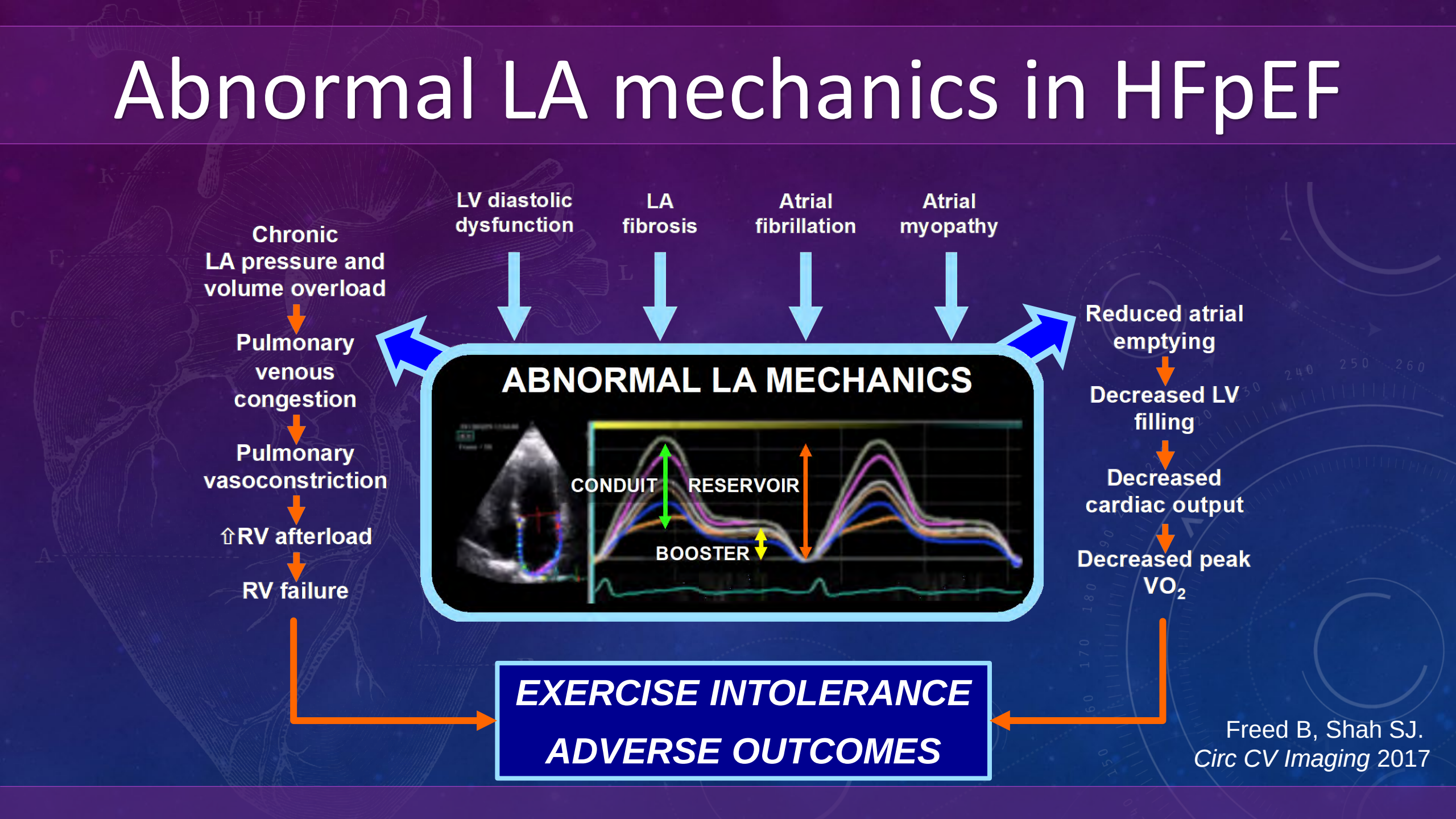

**Lowest quartile of LA reservoir strain:**
**HR 1.8, 95% CI 1.3-2.5, P<0.001 for incident AF**
**(after adjustment for AF risk factors, LA volume, and LV GLS)**

## Cardiovascular Health Study

- Population-based study, age > 65 years
- N=4341 with measurable LA strain at baseline
- Mean follow-up 10 years → 11.4% with incident AF

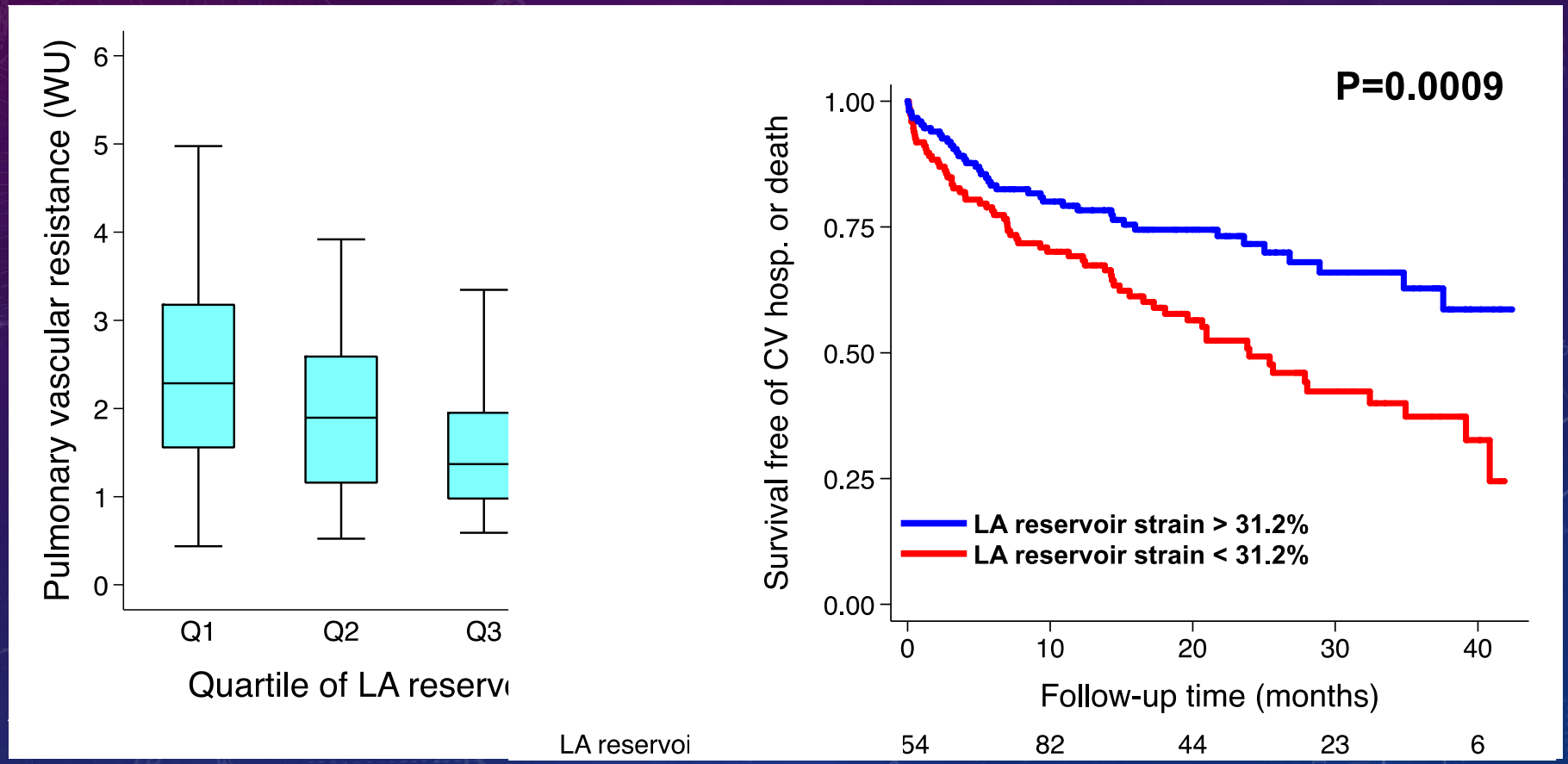
Patel RB…Shah SJ.
*JCI Insight* 2020

# Abnormal LA mechanics in HFpEF




Freed B, Shah SJ.
*Circ CV Imaging* 2017

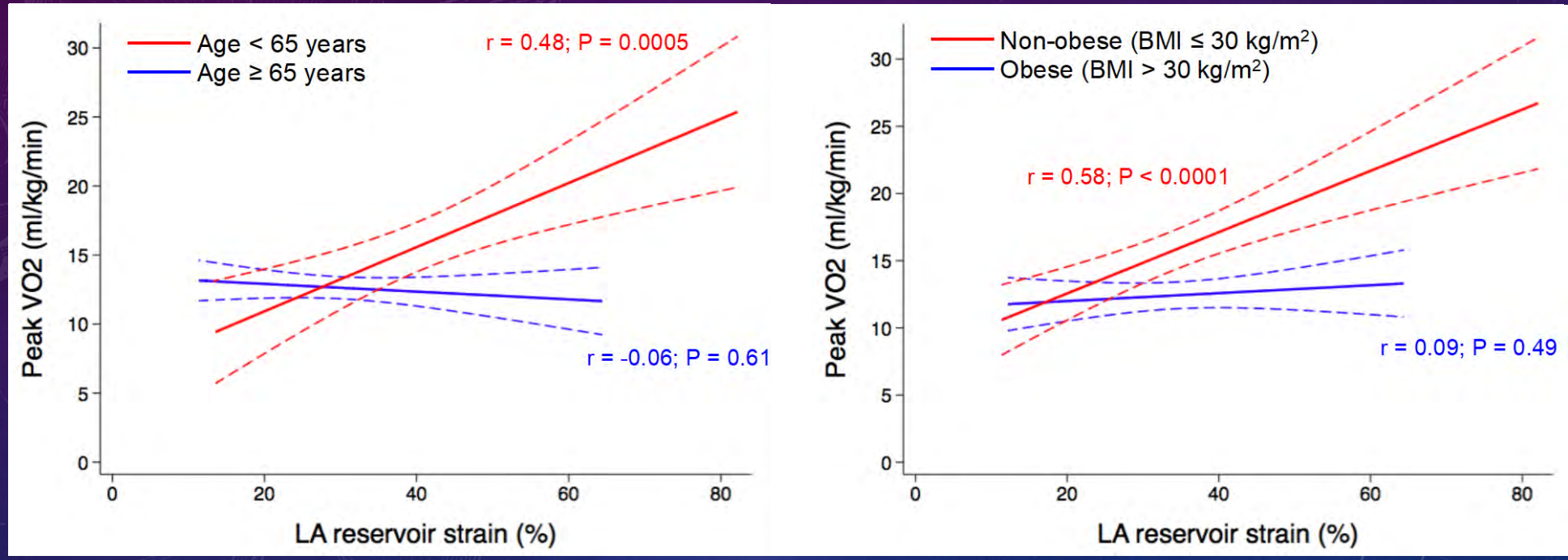
# Abnormal LA mechanics in HFpEF




Freed B…Shah SJ. *Circ CV Imaging* 2016

***LA strain is a better predictor of outcomes compared to LV or RV longitudinal strain***

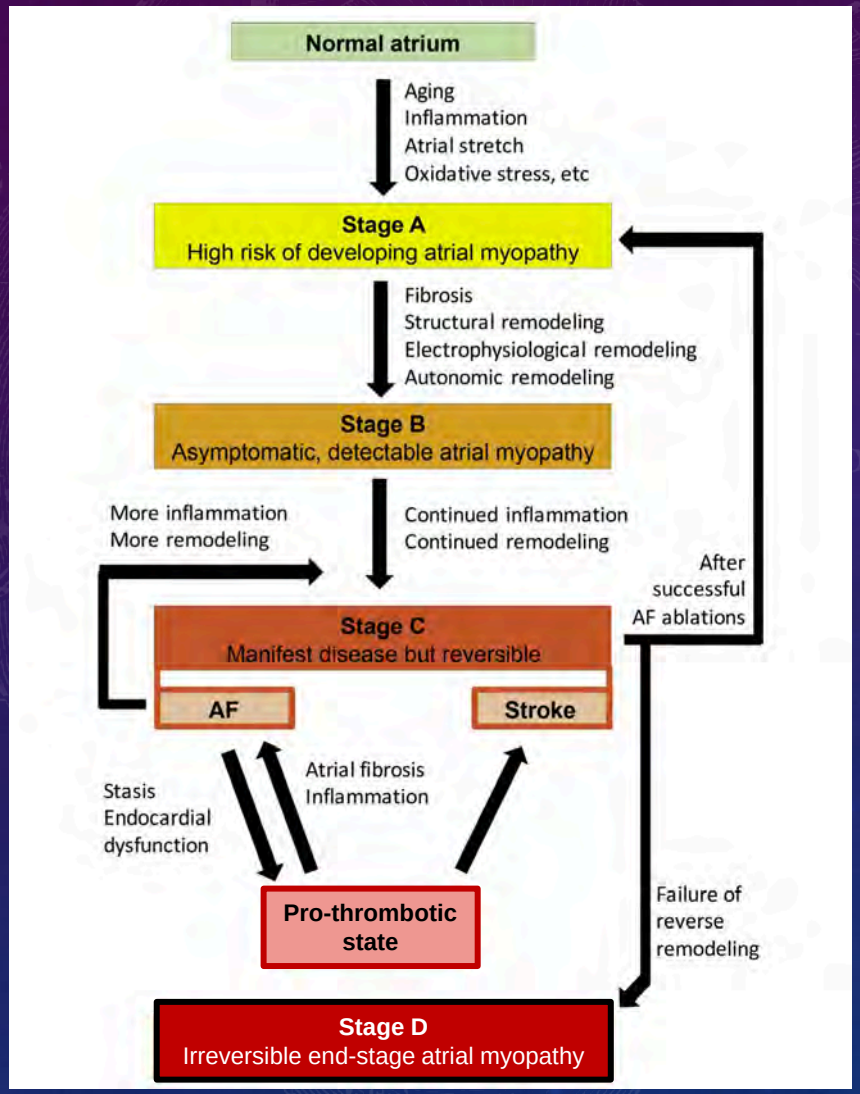
# Abnormal LA mechanics in HFpEF

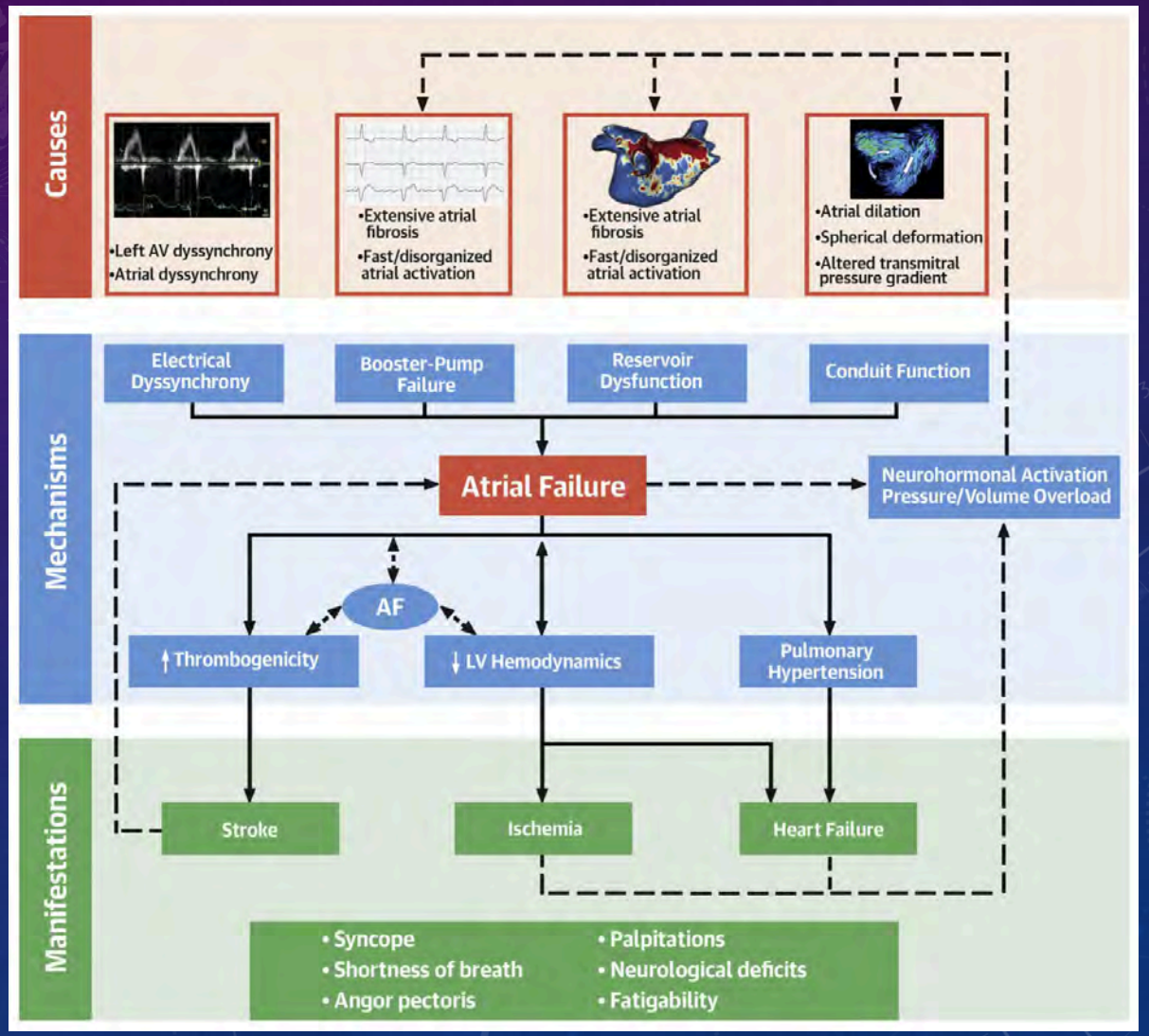



Freed B…Shah SJ. *Circ CV Imaging* 2016

***LA strain is a key determinant of exercise capacity in HFpEF***

# The concept of LA failure/LA myopathy

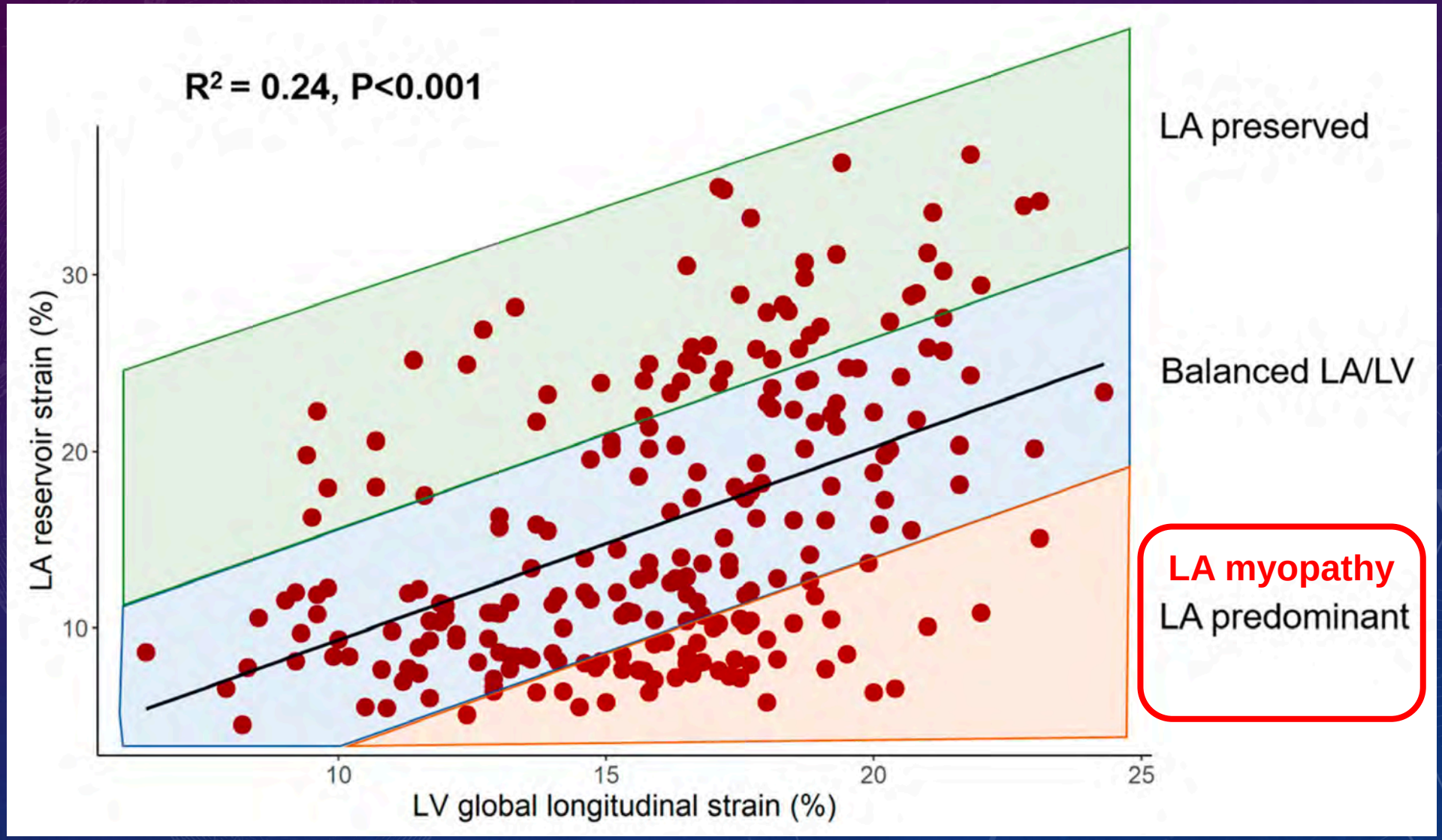



Shen MJ, et al. *JACC BTS* 2019

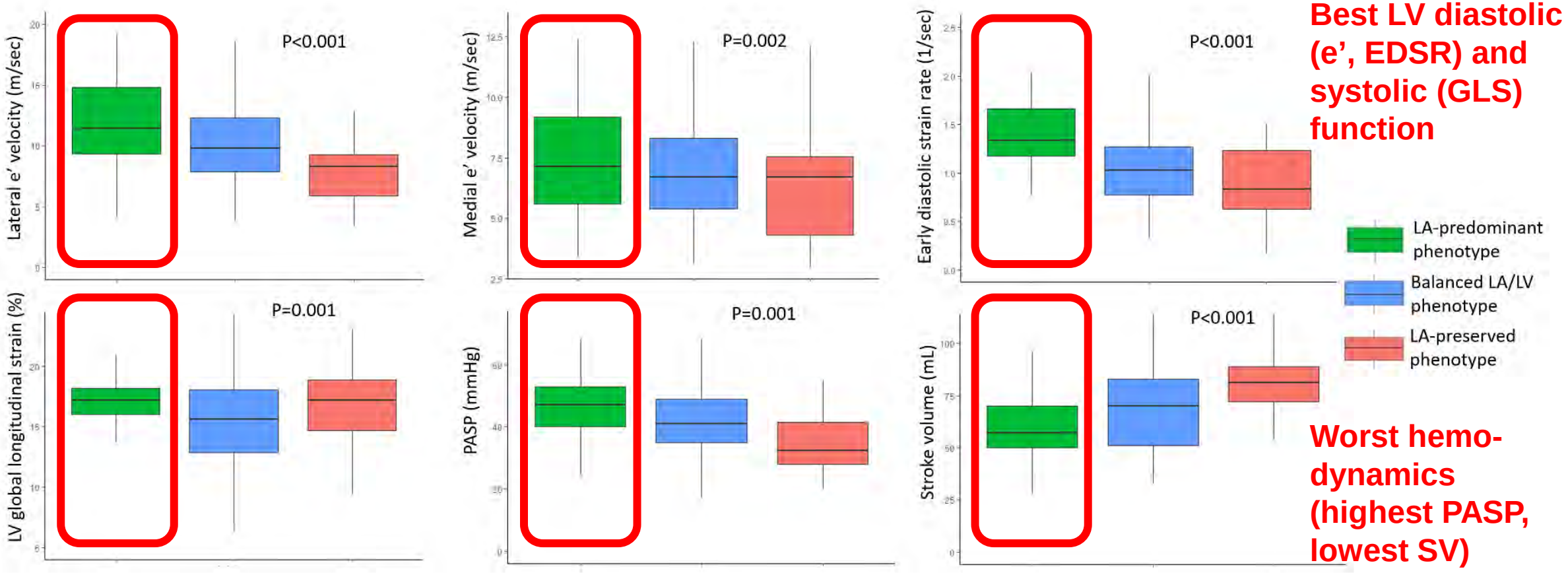
Bisbal F, et al. *JACC* 2020

# LA myopathy in HFpEF




Patel RB…Shah SJ.
*Sci Rep* 2021

# LA myopathy in HFpEF




Patel RB…Shah SJ. *Scientific Reports* 2021

# LA myopathy in HFpEF: Proteomics

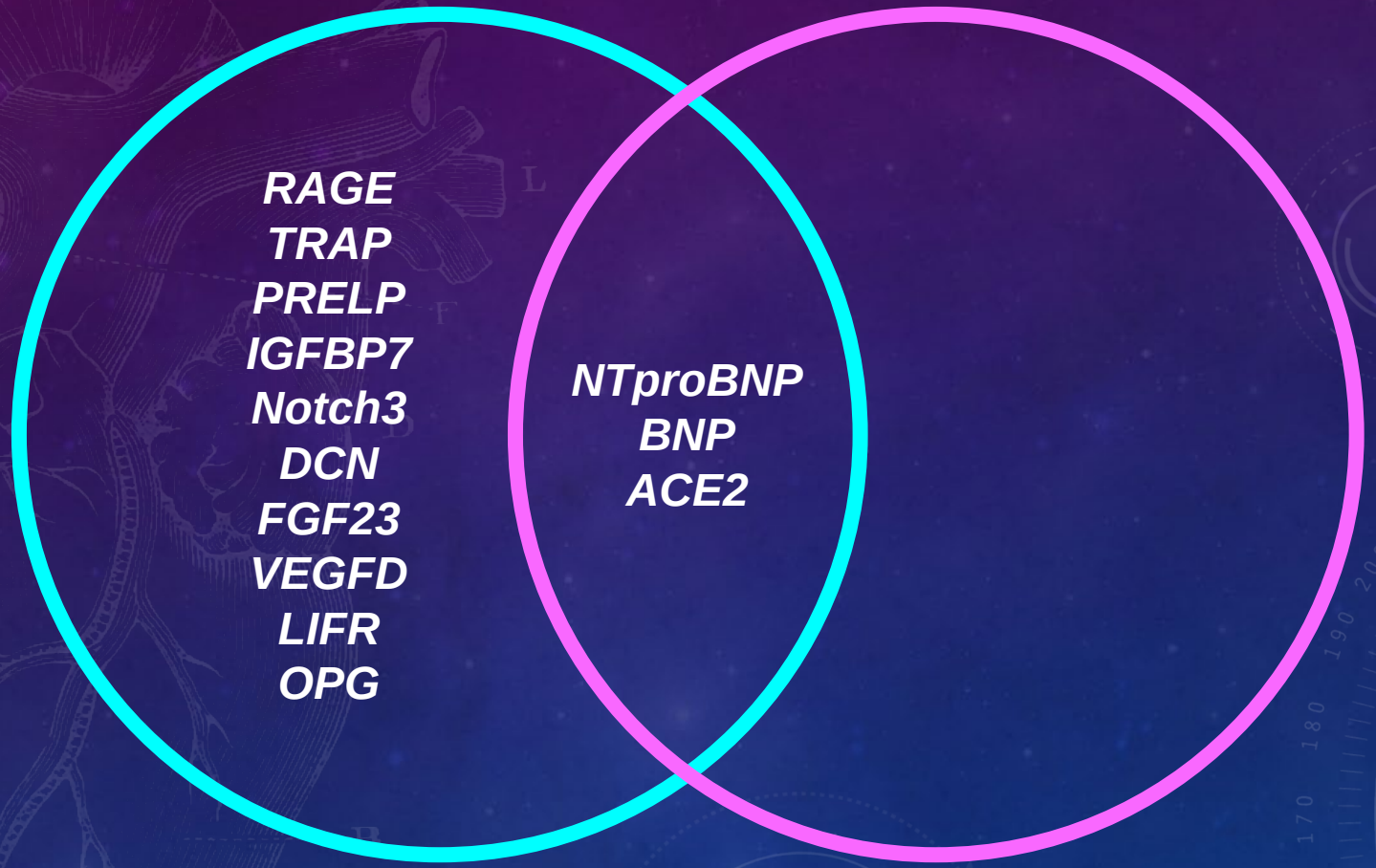
| Protein | PROMIS-HFpEF (n=221) Derivation cohort | | Northwestern-HFpEF (n=99) Validation cohort | |
|---|---|---|---|---|
| | β-coefficient (SE) | FDR-corrected P-value | β-coefficient (SE) | FDR-corrected P-value |
| **NTproBNP** | 0.30 (0.04) | $3.6 \times 10^{-8}$ | **0.28 (0.06)** | **$7.78 \times 10^{-6}$** |
| **BNP** | 0.26 (0.05) | $1.04 \times 10^{-5}$ | **0.23 (0.05)** | **$3.22 \times 10^{-5}$** |
| **HGF** | 0.73 (0.13) | $1.26 \times 10^{-5}$ | -0.02 (0.11) | 0.86 |
| **RAGE** | 0.65 (0.13) | $9.42 \times 10^{-5}$ | **0.44 (0.17)** | **0.01** |
| **PRELP** | 0.95 (0.22) | 0.001 | **1.38 (0.37)** | **0.0003** |
| **PSPD** | 0.37 (0.09) | 0.001 | 0.18 (0.12) | 0.12 |
| **TRAP** | -0.62 (0.15) | 0.002 | **-0.45 (0.18)** | **0.01** |
| **IGFBP7** | 0.50 (0.12) | 0.002 | **0.40 (0.16)** | **0.01** |
| **MMP2** | 0.56 (0.14) | 0.002 | 0.30 (0.16) | 0.15 |
| **Notch3** | 0.60 (0.16) | 0.004 | **0.38 (0.16)** | **0.02** |

FDR = false discovery rate (to correct for multiple comparisons)

Patel RB…Shah SJ. *Scientific Reports* 2021

# LA myopathy in HFpEF: Proteomics

***Proteins identified in PROMIS-HFpEF at FDR-corrected P<0.05 which were validated in the Northwestern HFpEF cohort at P<0.05**




Patel RB…Shah SJ.
*Scientific Reports* 2021

# Case presentation

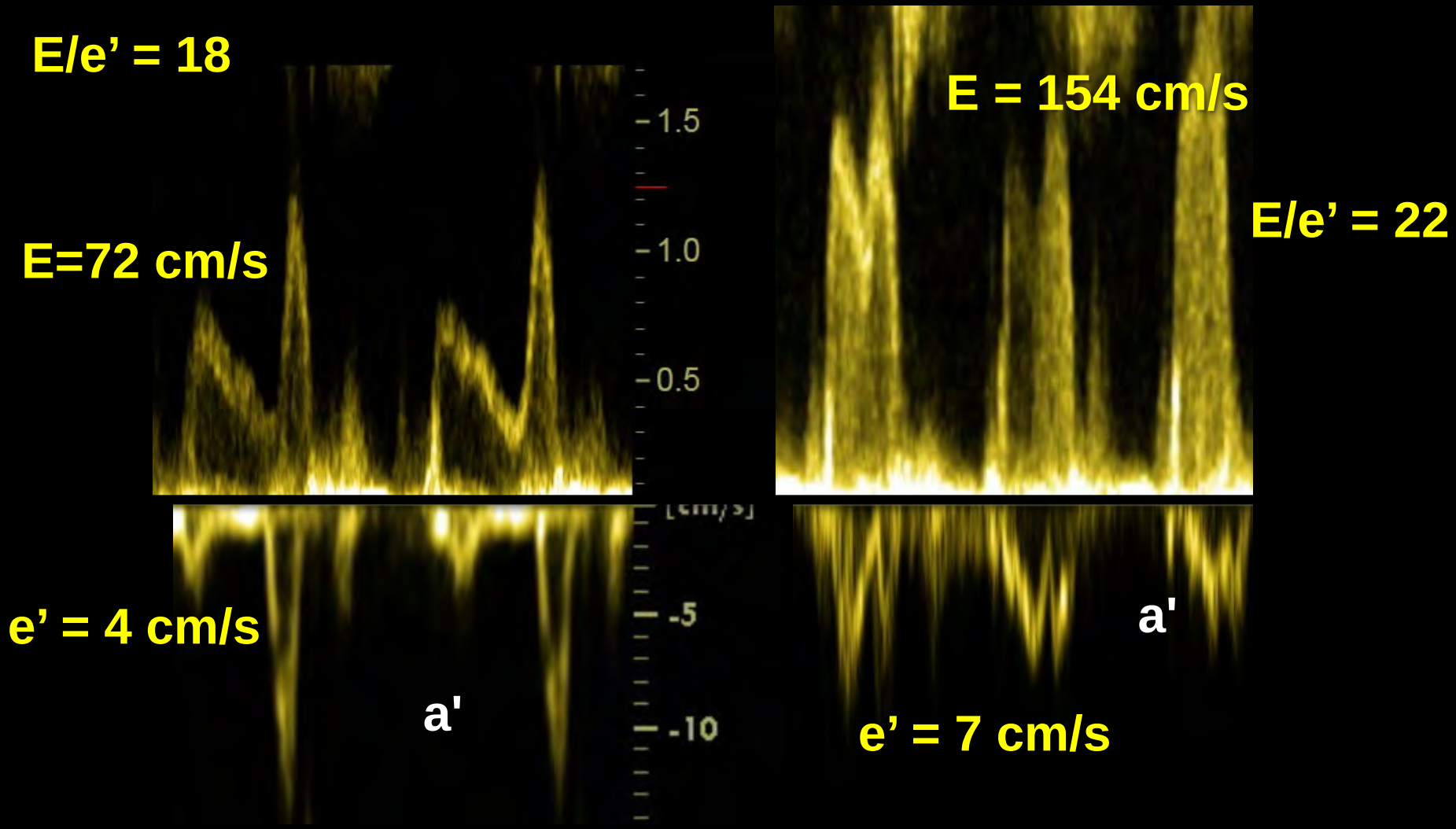
**72-year-old woman w/HFpEF, HTN, obesity, CKD, CAD s/p multiple PCIs, atrial fibrillation s/p ablation, NYHA class 3 with severe exercise intolerance**

**Meds: aspirin, clopidogrel, atorvastatin, bumetanide, spironolactone, isosorbide mononitrate, carvedilol, losartan**

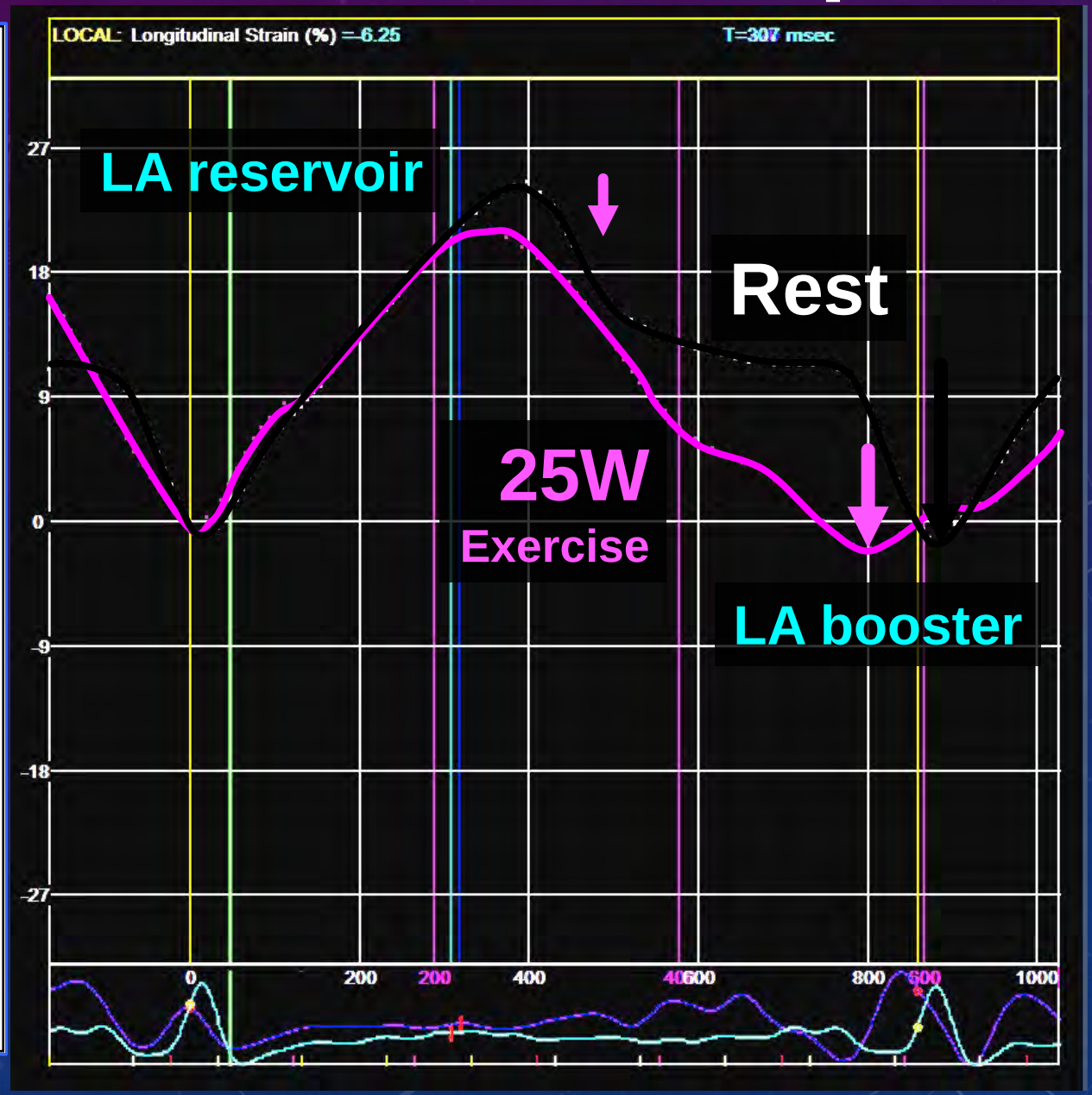
**PEX: BP 122/58, HR 60, RR 12**
**JVP 6 cm, clear lungs, RRR, nl S1 S2, no S3 or S4**
**1/6 holosystolic murmur at the apex, trace lower extremity edema**

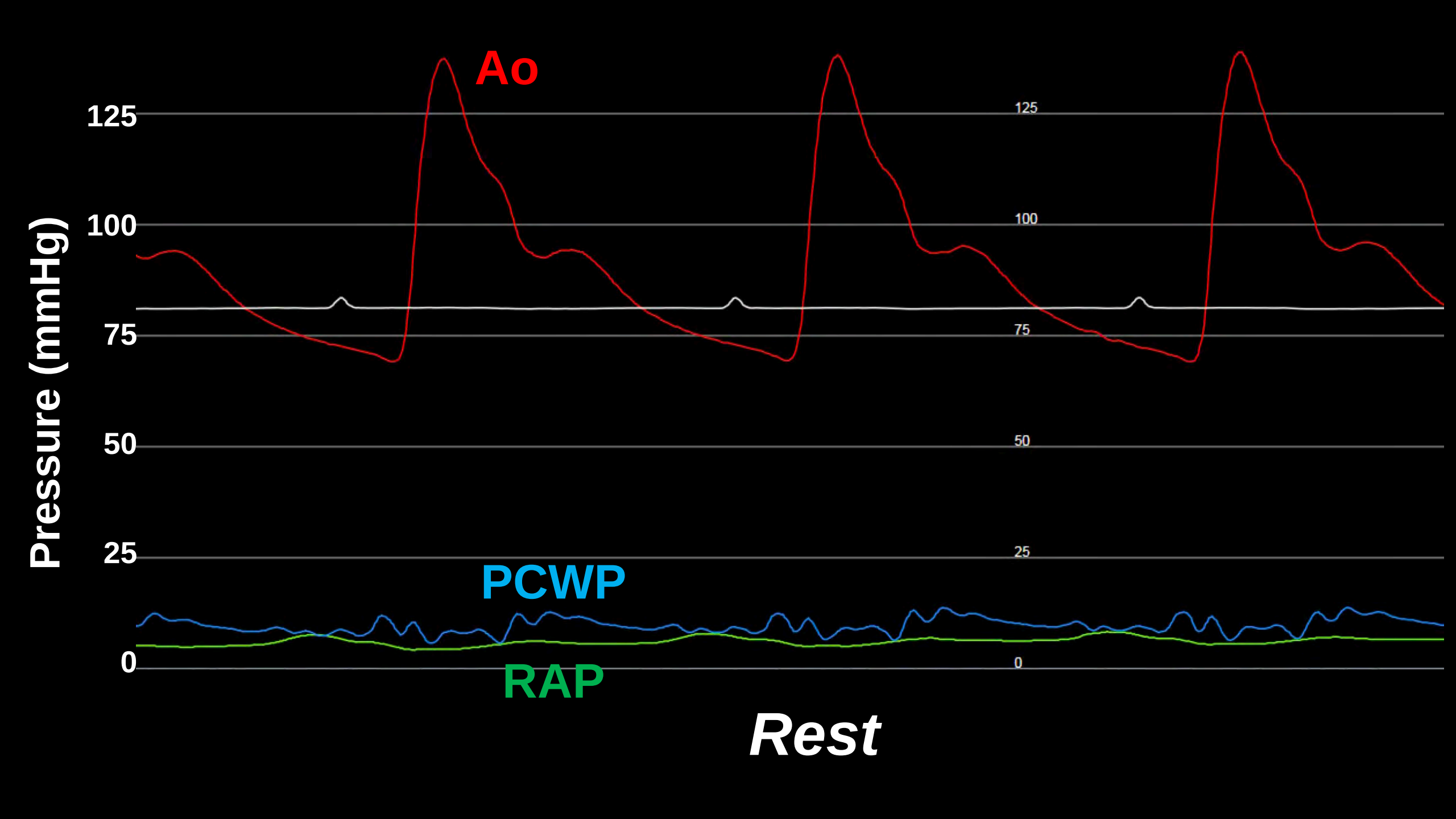
**Labs: Cr 1.4 mg/dl, eGFR 37 ml/min/1.73 $m^2$, NTproBNP 98 pg/ml**
**No evidence of ischemia on recent myocardial perfusion study**

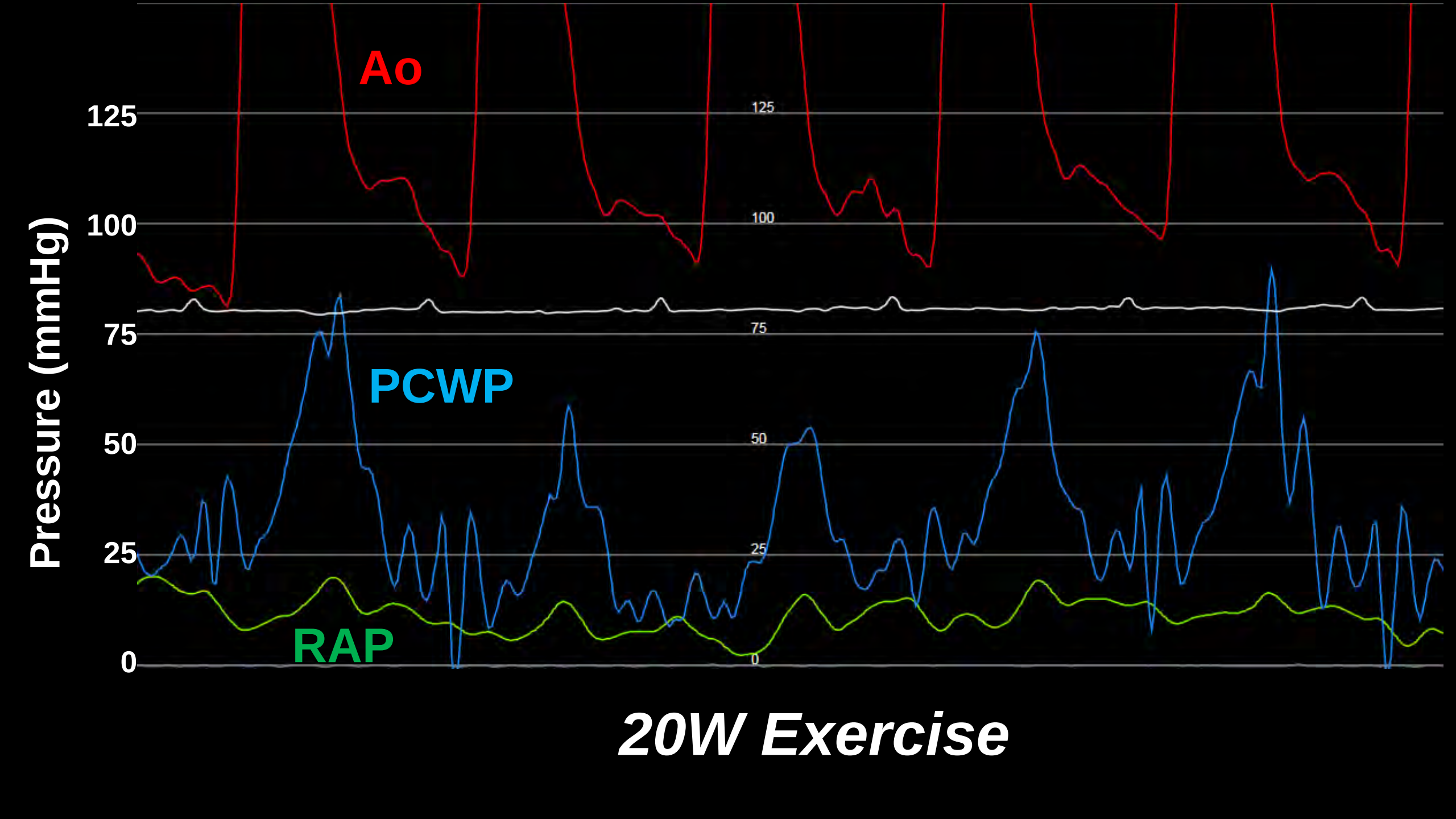
# 72-year-old woman with HFpEF



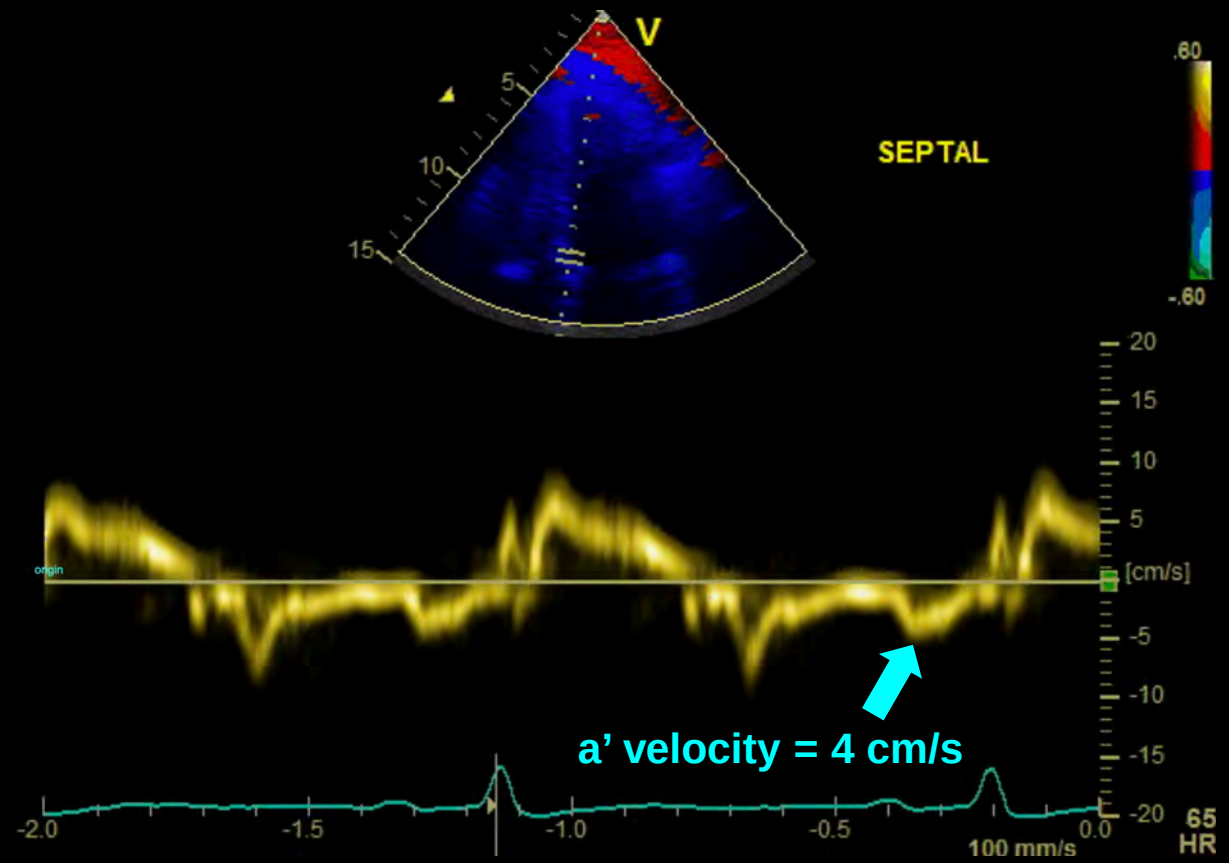
# 72-year-old woman with HFpEF



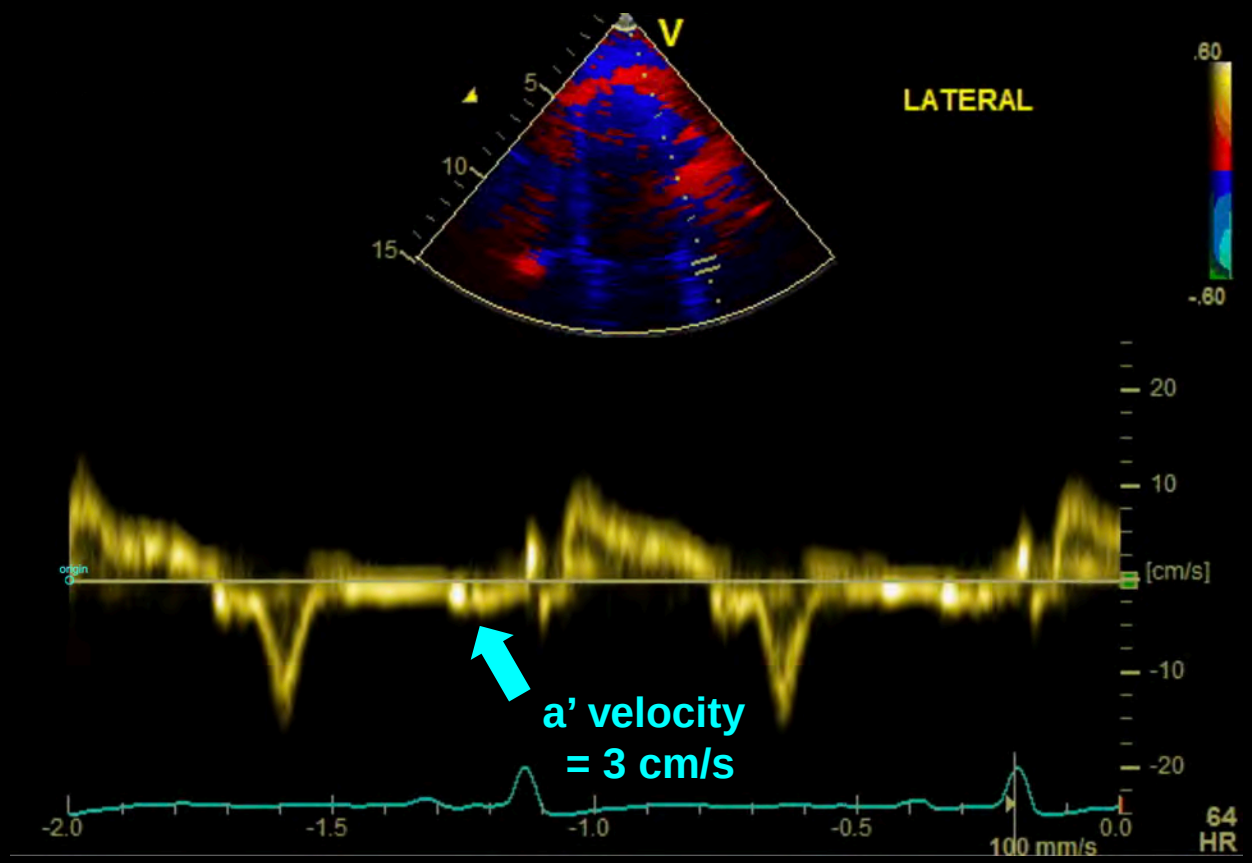

Ao
125
100
75
50
25
0
Pressure (mmHg)
PCWP
RAP
Rest


Ao
PCWP
RAP
Pressure (mmHg)
125
100
75
50
25
0
125
100
75
50
25
0
20W Exercise

# *Left atrial myopathy*

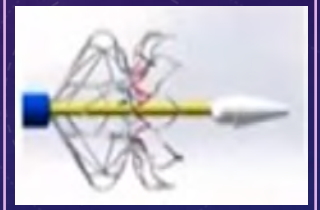



Septal TDI



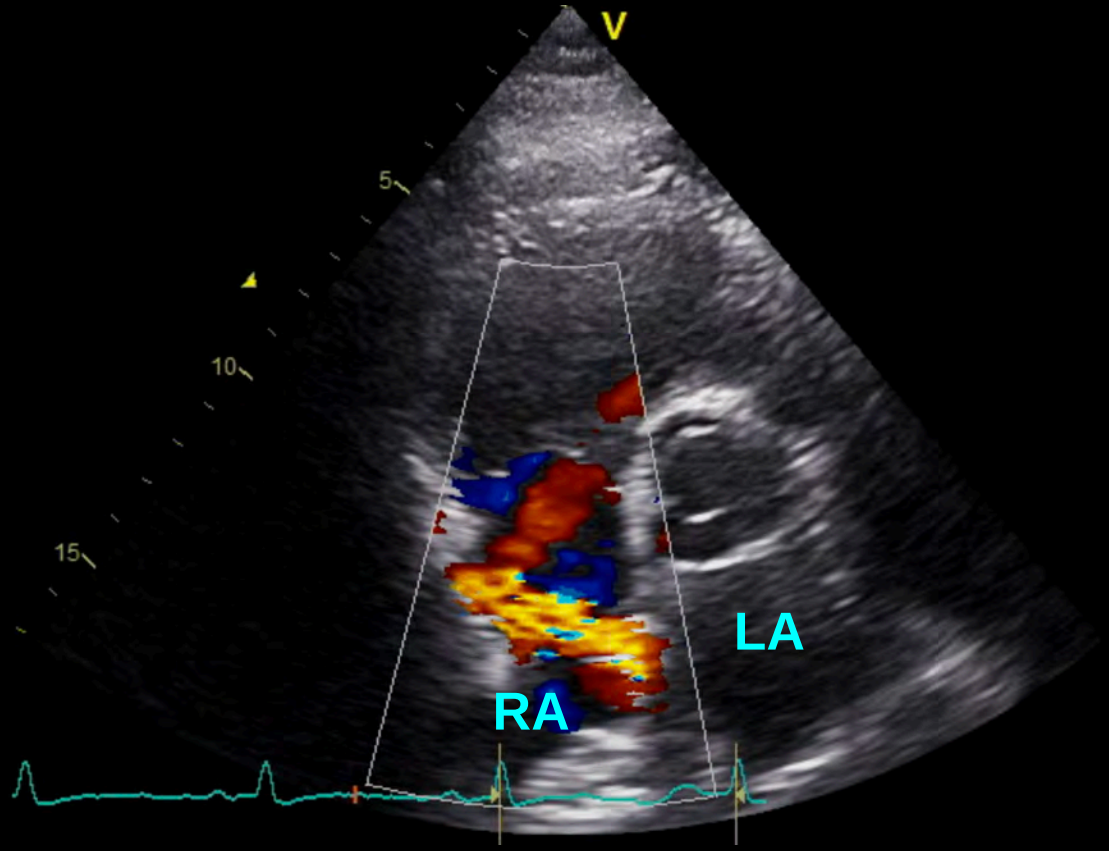

Lateral TDI

# Interatrial shunt devices/procedures

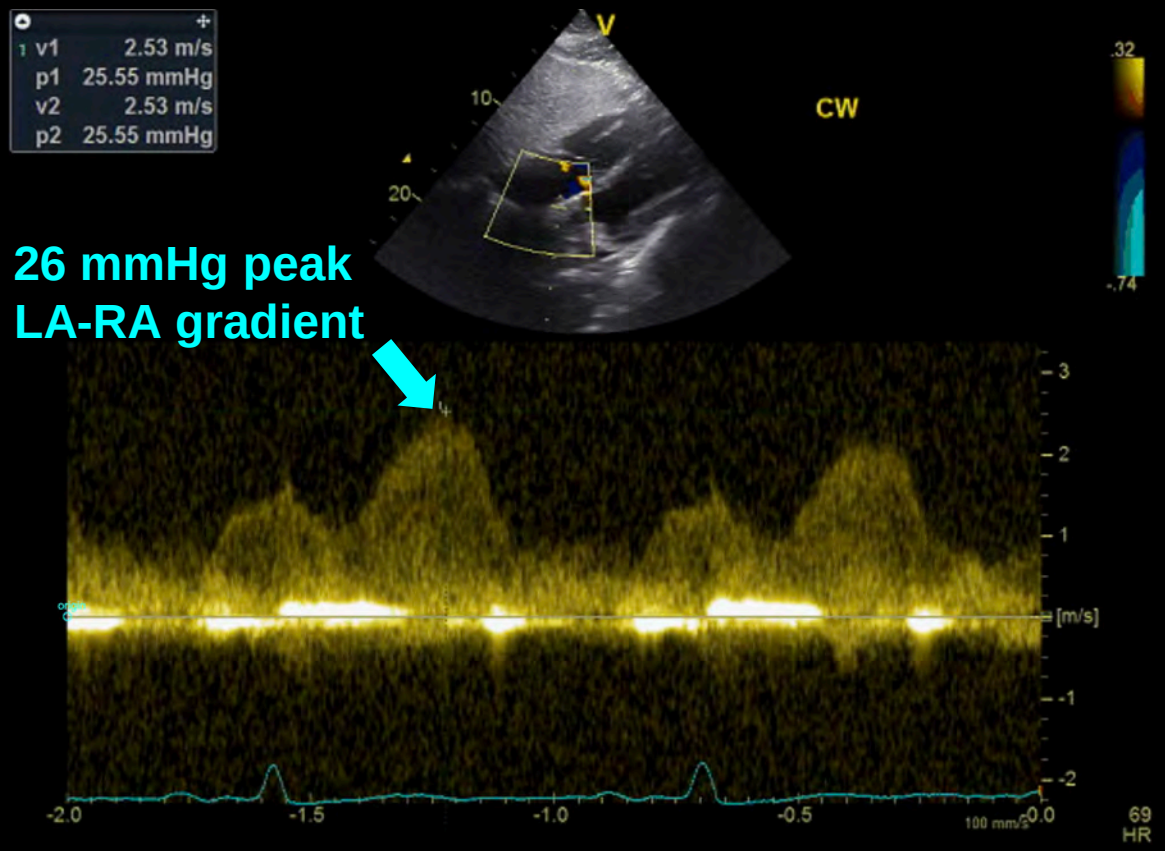
| Device | Corvia | V-Wave | Occlutech | Edwards | Alleviant | NoYA | InterShunt |
|---|---|---|---|---|---|---|---|
| |  |  |  |  |  |  |  |
| **Type** | Implant | Implant | Implant | Implant | Procedure | Procedure | Procedure |
| **Description** | Nitinol stent | Nitinol/PTFE hourglass | Nitinol braid with central orifice | Tubular nitinol device with retention arms | Coring catheter | RF catheter | Cutting catheter |
| **Shunt flow** | LA → RA | LA → RA | LA → RA | LA → CS | LA → RA | LA → RA | LA → RA |
| **Shunt size** | 8 mm | 5.1 mm | 4, 6, 8, 10 mm | 7 mm | 6 mm | 4-12 mm | 4 mm |
| **Development stage** | Phase 3 RCT | Phase 3 RCT | Open-label studies | FIH complete | Animal studies | FIH complete | FIH complete |

*CS = coronary sinus; FIH = first in human

# *3 years after interatrial shunt device placement*




**PSAX Ao valve view**




**CW Doppler across IASD**

# Summary

- The LA is critical to normal cardiovascular homeostasis, especially in the setting of CVD/HF
- The LA has 3 important functions: reservoir, conduit, and booster that we can easily measure with LA strain
- LA reservoir strain is a better measure of the health of the LA than maximal LA volume
- LA myopathy/failure is real! Especially important in HFpEF and may have a unique biochemical profile


Shah Lab – Northwestern University
thank you
sanjiv.shah@northwestern.edu • http://www.hfpef.org • Twitter: @HFpEF