

Atrial Dysfunction in Patients with AF and HF

Cross Specialty 1: Joint Symposium with Heart Failure

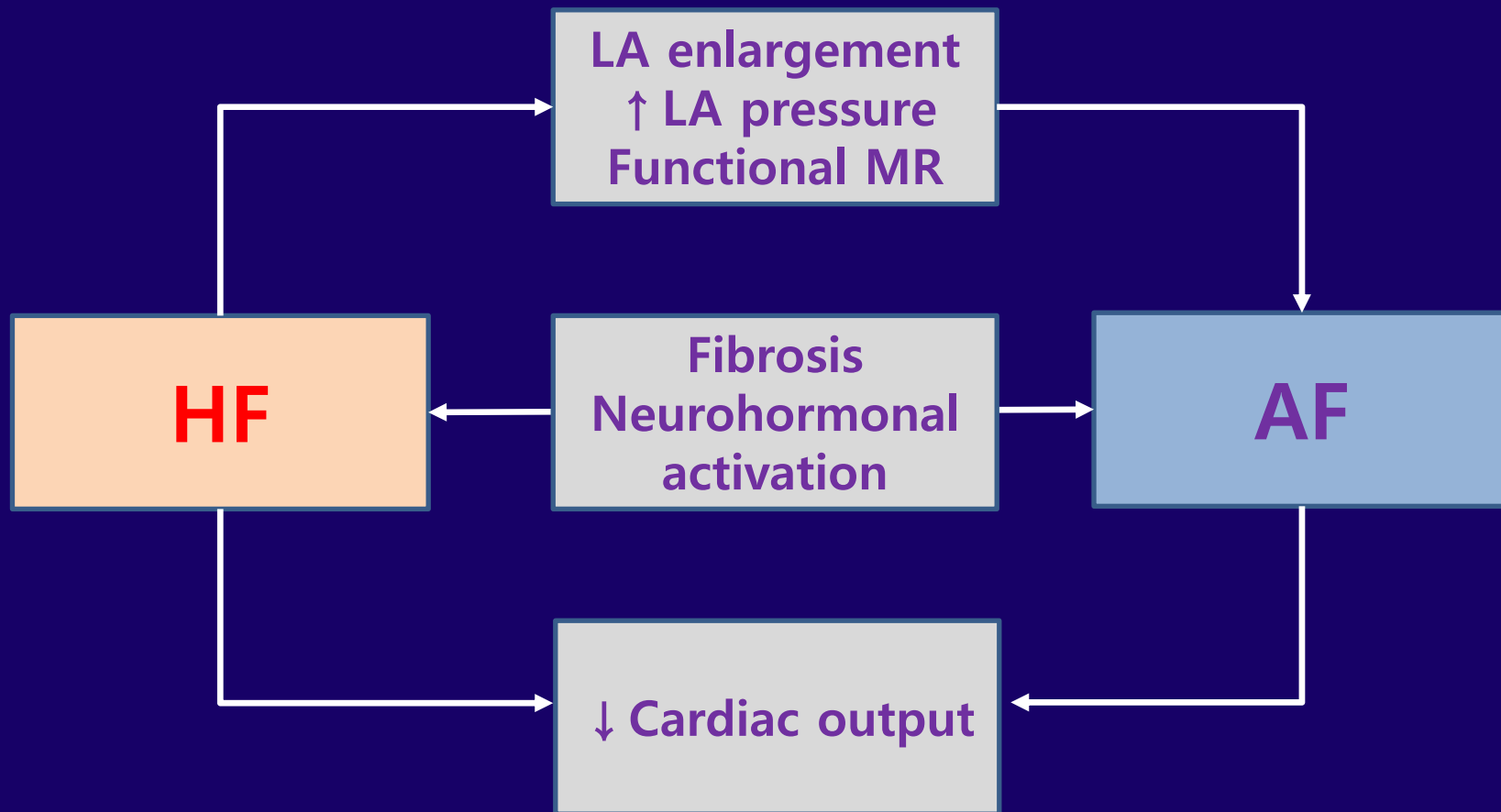
KHRS 2021

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CHUNGBUK NATIONAL UNIVERSITY HOSPITAL



Mutual Promotion between HF and AF



A meta-analysis of the prognostic significance of atrial fibrillation in chronic heart failure

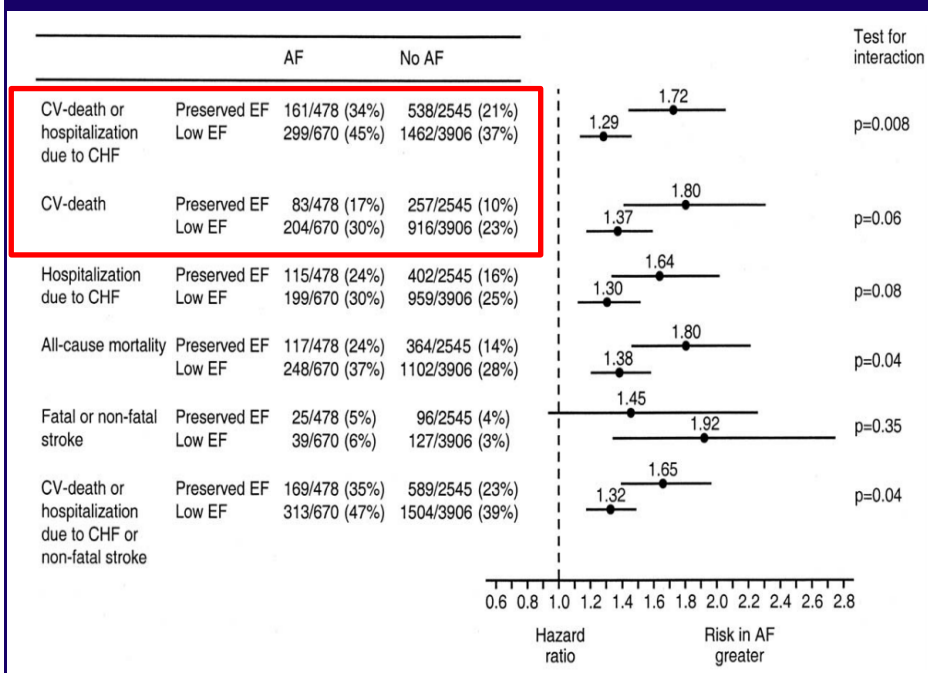
Mamas A. Mamas.

Table I Summary of randomized controlled studies

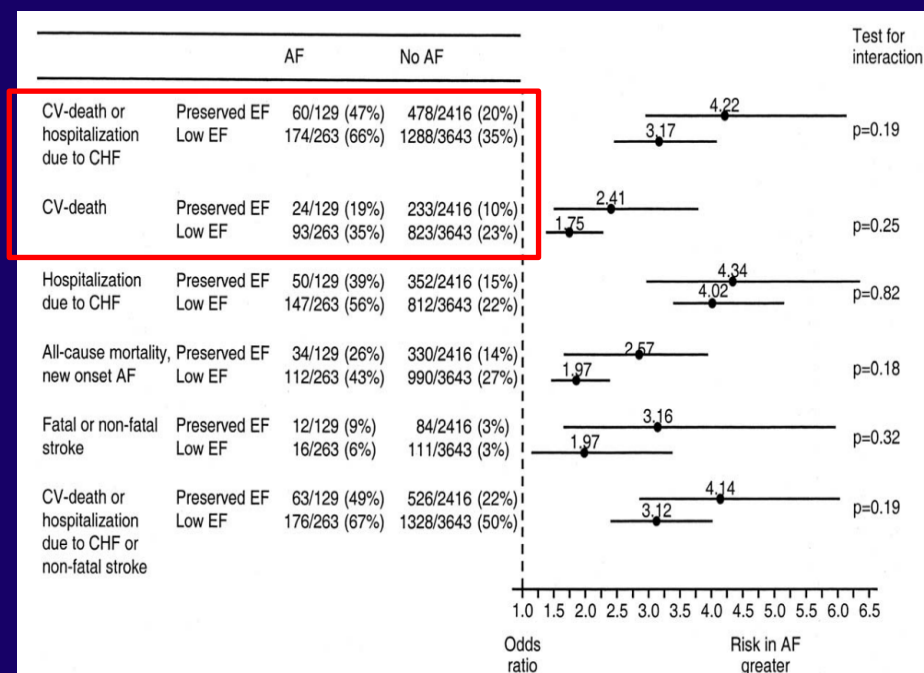
Author	Setting	Number	LV systolic function inclusion	Mean follow-up	% AF	Number (%) of deaths		P-value
						SR	AF	
Carson <i>et al.</i> ⁷	V-HEFT I & II	1427	LVEF < 45%	2.5 years	19	480/1221 (39)	75/206 (36)	NS
Dries <i>et al.</i> ⁶	SOLVD	6517	LVEF < 35%	2.8 years	6	1395/8098 (23)	149/419 (34)	<0.0001
Mathew <i>et al.</i> ¹³	DIG	7788	All LVEF included	3.1 years	11	2231/6922 (32)	375/866 (43)	<0.0001
Crijns <i>et al.</i> ¹⁵	PRIME II	409	LVEF < 35%	3.4 years	21	153/325 (47)	50/84 (60)	<0.05
Swedberg <i>et al.</i> ¹⁶	COMET	3029	LVEF < 35%	4.8 years	20	874/2429 (36)	258/600 (43)	<0.0005
Olsson <i>et al.</i> ¹⁰	CHARM	7601	All LVEF included	3.1 years	15	1466/6451 (23)	365/1148 (32)	<0.001
Pederson <i>et al.</i> ¹⁴	DIAMOND	3587	LVEF < 35%	N/A	24	1951/2661 (73)	634/818 (77)	<0.001

Effect of AF on Prognosis according to HF subtype

Prior AF



New onset AF

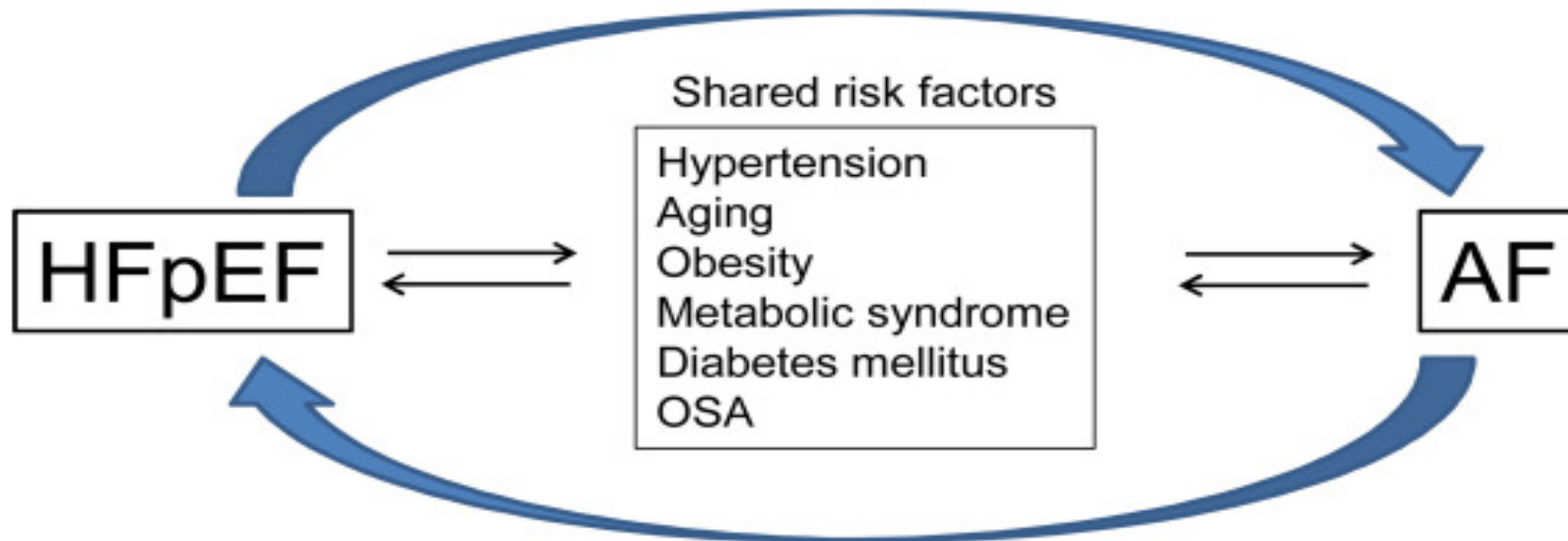


Topic

Impact of AF on Prognosis in HFpEF
Through LA myopathy

Mutual Promotion between HFpEF and AF

- Atrial structural remodeling
- Atrial electrical remodeling
- Calcium handling impairment
- Neurohormonal activation
- Oxidative stress/inflammation



- Tachycardia
- Irregularity
- Loss of atrial kick
- Functional MR, TR

HFpEF Diagnostic Criteria

2016 ESC

HFpEF
Symptoms ± Signs ^a
LVEF ≥50%
1. Elevated levels of natriuretic peptides ^b ; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).

2019 New consensus



European Society
of Cardiology

European Heart Journal (2019) 40, 3297–3317

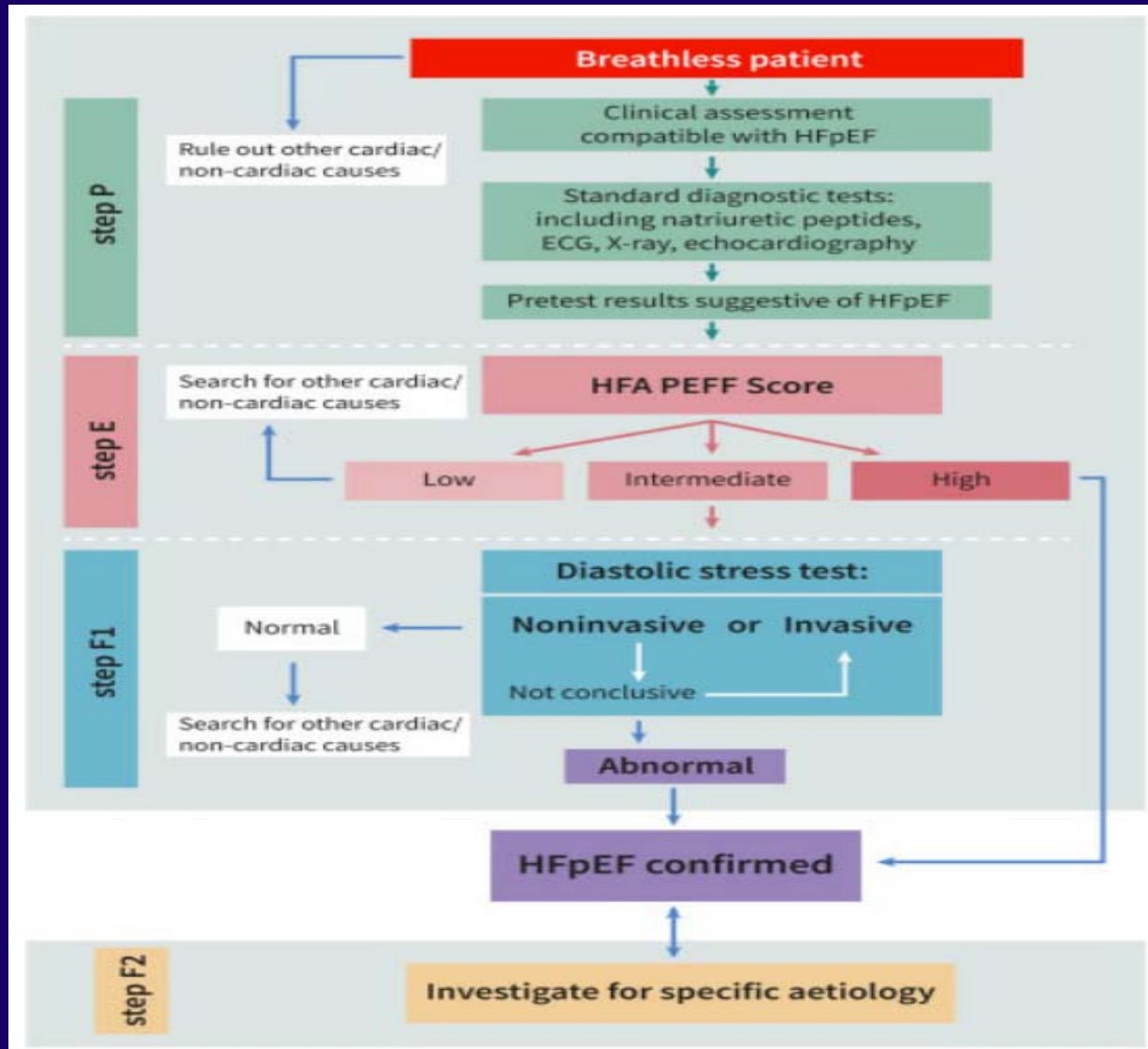
doi:10.1093/eurheartj/ehz641

FASTTRACK CLINICAL RESEARCH

Heart failure/cardiomyopathy

How to diagnose heart failure with preserved ejection fraction: the HFA-PEFF diagnostic algorithm: a consensus recommendation from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC)

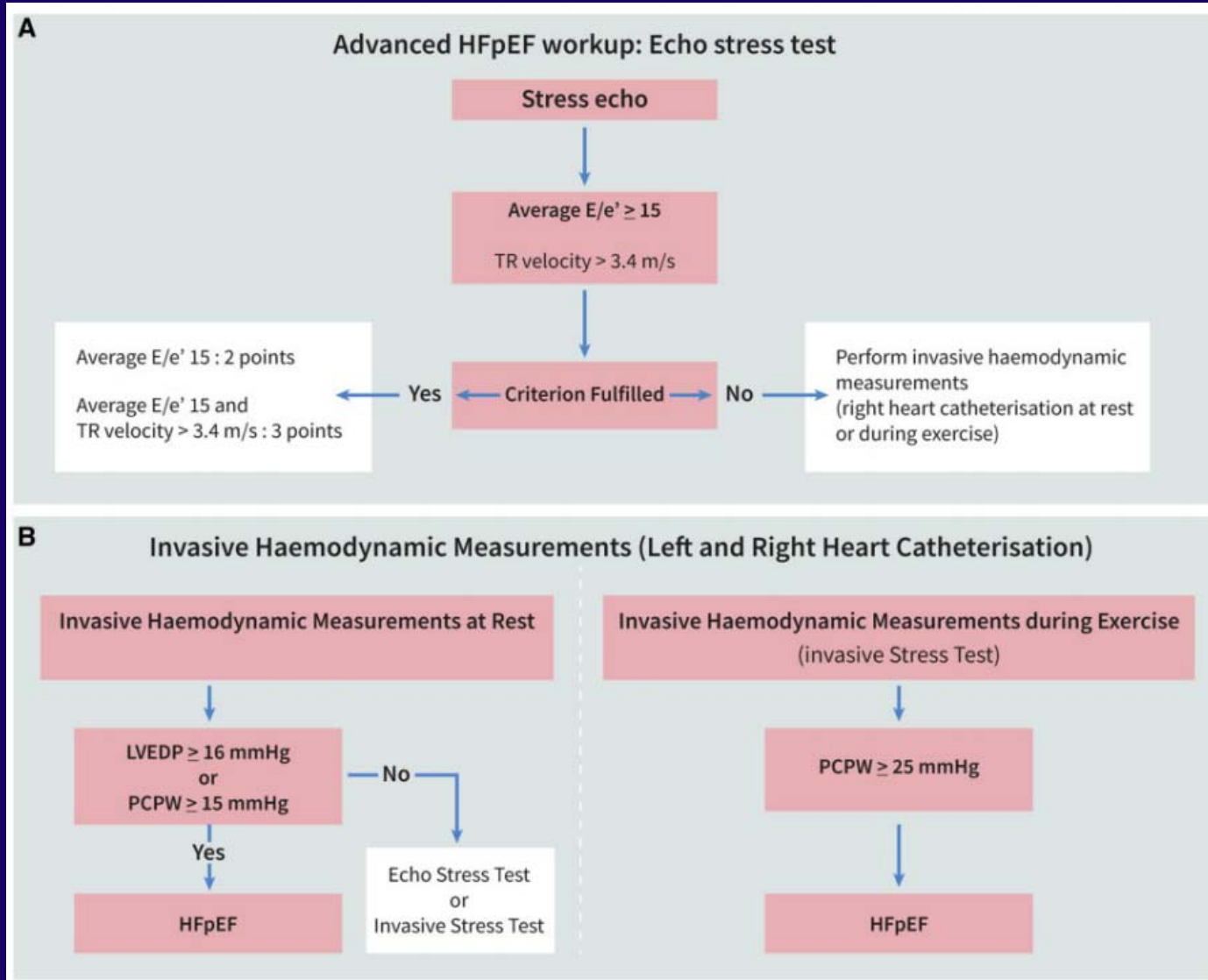
HFpEF Diagnostic Criteria



HFA PEFF Score






	Functional	Morphological	Biomarker (SR)	Biomarker (AF)
Major	septal $e' < 7$ cm/s or lateral $e' < 10$ cm/s or Average $E/e' \geq 15$ or TR velocity > 2.8 m/s (PASP > 35 mmHg)	LAVI > 34 ml/m ² or LVMI $\geq 149/122$ g/m ² (m/w) and RWT $> 0,42$ #	NT-proBNP > 220 pg/ml or BNP > 80 pg/ml	NT-proBNP > 660 pg/ml or BNP > 240 pg/ml
Minor	Average $E/e' 9-14$ or GLS $< 16\%$	LAVI 29-34 ml/m ² or LVMI $> 115/95$ g/m ² (m/w) or RWT $> 0,42$ or LV wall thickness ≥ 12 mm	NT-proBNP 125-220 pg/ml or BNP 35-80 pg/ml	NT-proBNP 365-660 pg/ml or BNP 105-240 pg/ml
Major Criteria: 2 points		≥ 5 points: HFpEF		
Minor Criteria: 1 point				

HFpEF Diagnostic Criteria

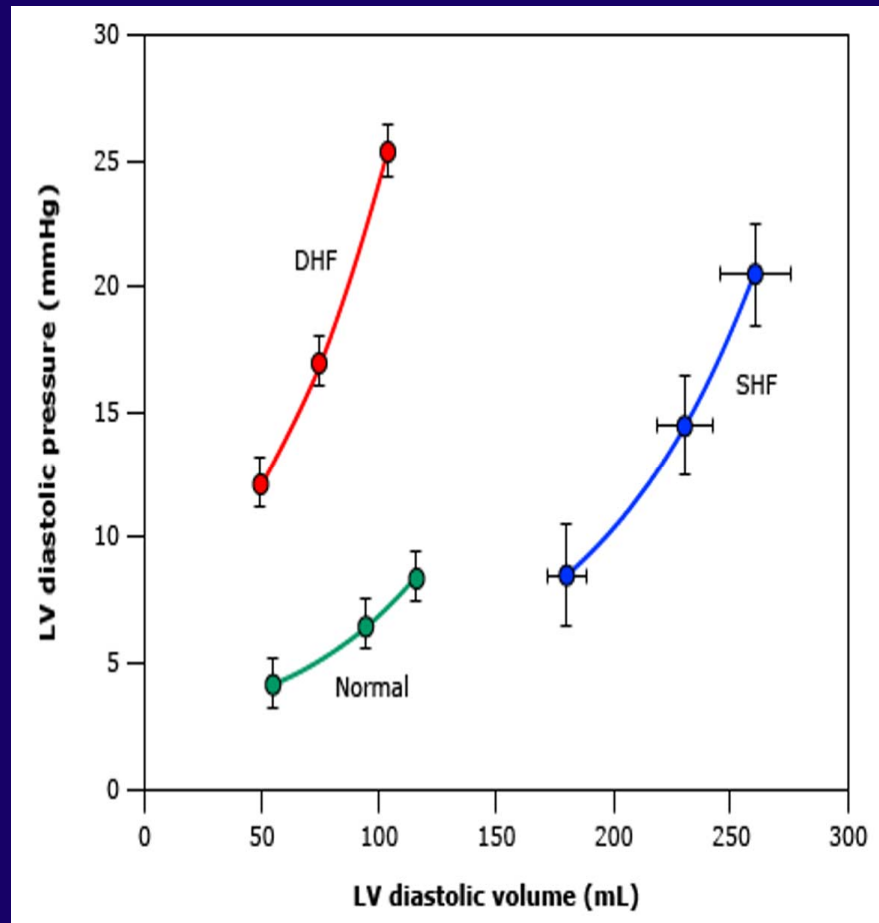


HFrEF vs HFpEF

Pattern of LV remodeling

		Left ventricular mass	
		Normal	Increased
Left ventricular geometry	Normal		
	Concentric	 Concentric remodeling	 Concentric hypertrophy
	Eccentric	 Eccentric remodeling	 Eccentric hypertrophy

LV distensibility

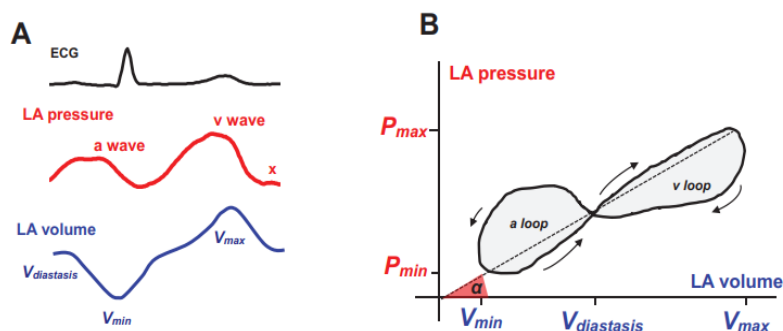


Left Atrial Remodeling: HFpEF vs HFrEF

MAYO CLINIC

- 198 pts
- 40 control: 101PEF: 97 REF
- Rt side catheterization

	Controls, n=40	HFpEF, n=101	HFrEF, n=97	PValue
LA stiffness, mm Hg/mL	0.30±0.20	0.79±0.75*	0.48±0.44†	<0.0001



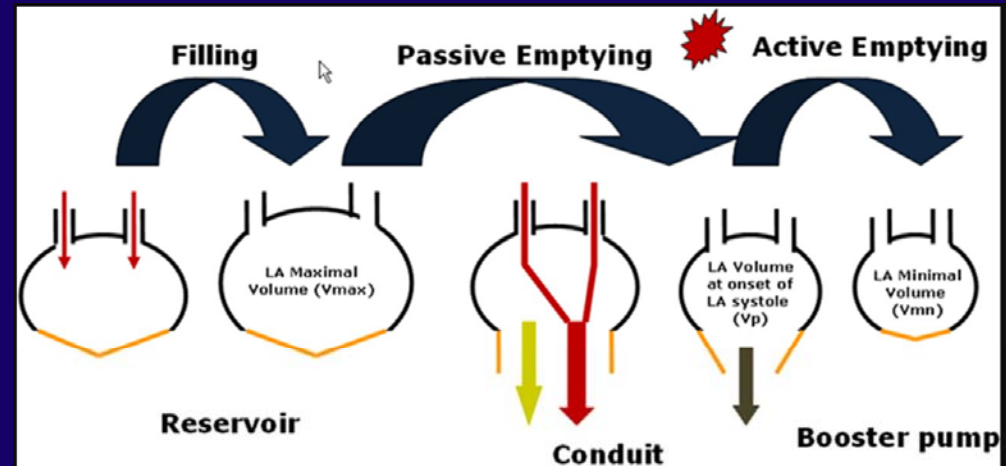
C

$$\text{Total LA EF} = \frac{V_{\max} - V_{\min}}{V_{\max}}$$

$$\text{Active LA EF} = \frac{V_{\text{diastasis}} - V_{\min}}{V_{\text{diastasis}}}$$

$$\text{Passive LA EF} = \frac{V_{\max} - V_{\text{diastasis}}}{V_{\max}}$$

$$\text{LA stiffness} = \alpha$$

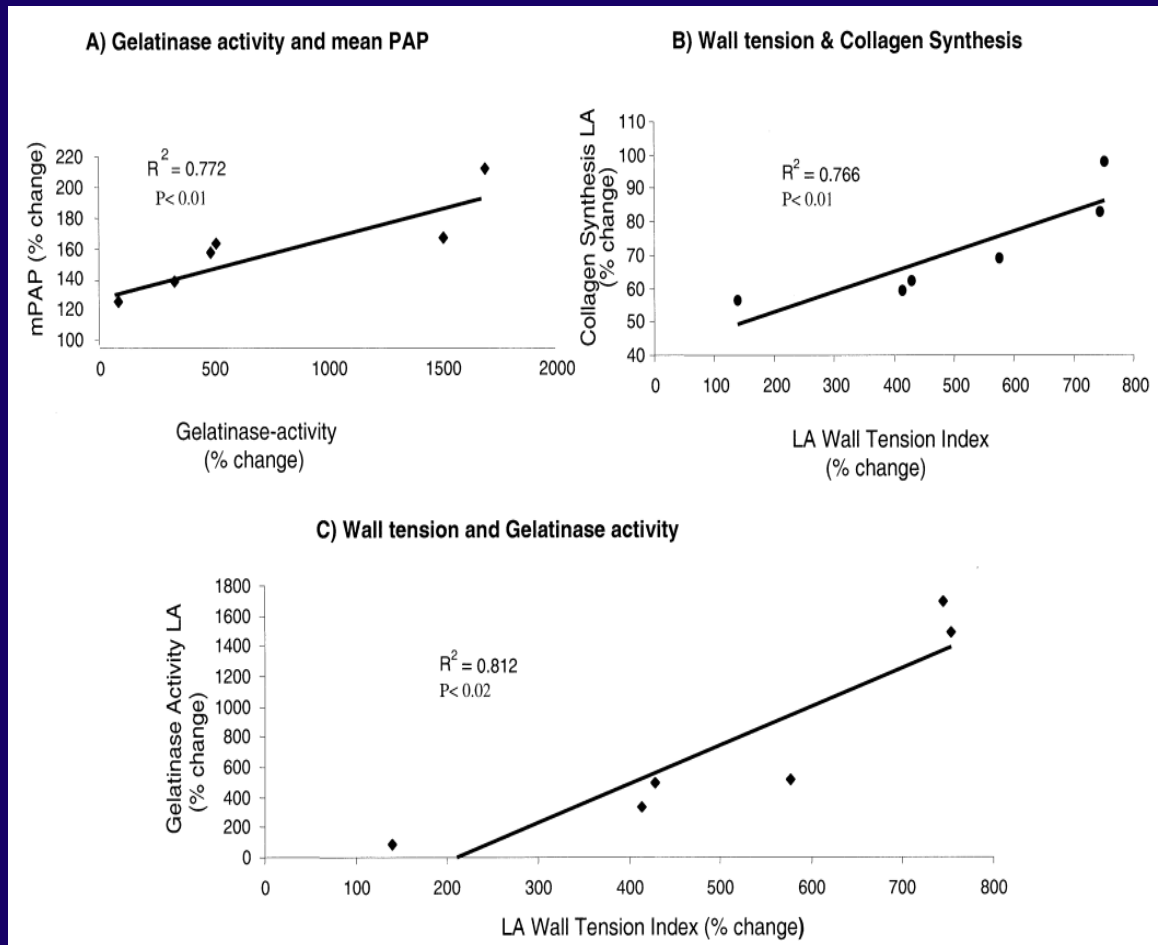


LA reservoir function
= Expansion index
= (LA_{max}-LA_{min}) / LA_{min}

Mechanism of Left Atrial Stiffness

Canine model

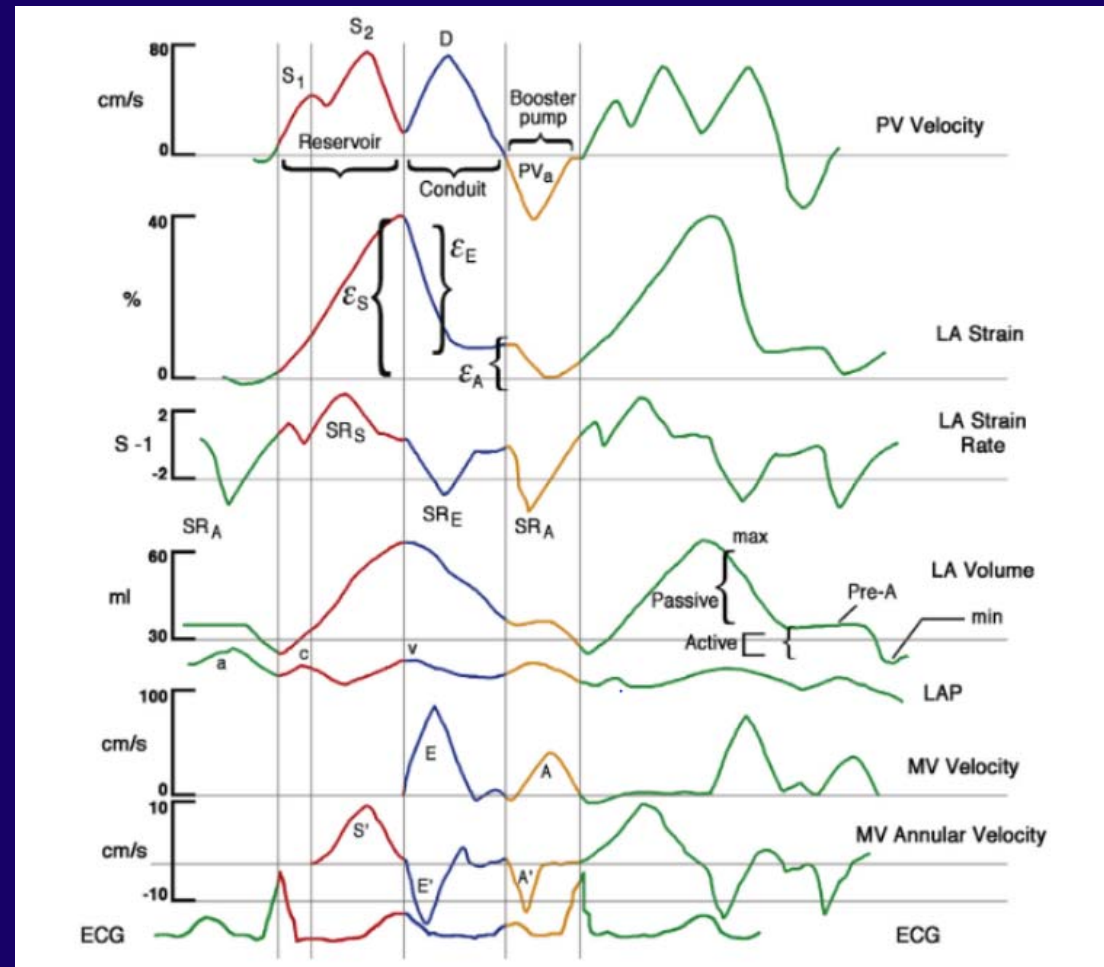
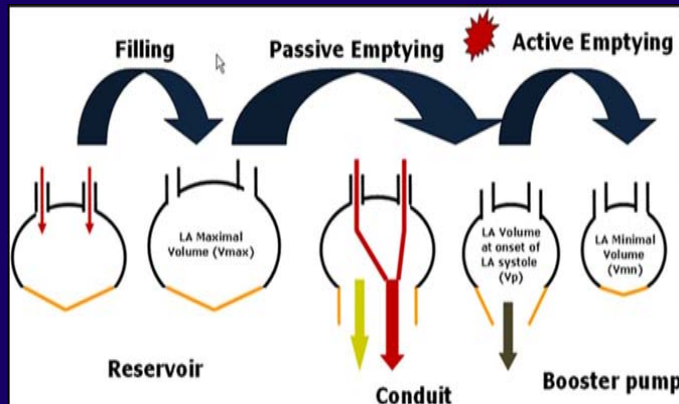
- RV pacing (240 bpm) for 3 weeks
- according to LA wall tension
 - gelatinase activity
 - Collagen synthesis



Non-Invasive Analysis of Left Atrial Function

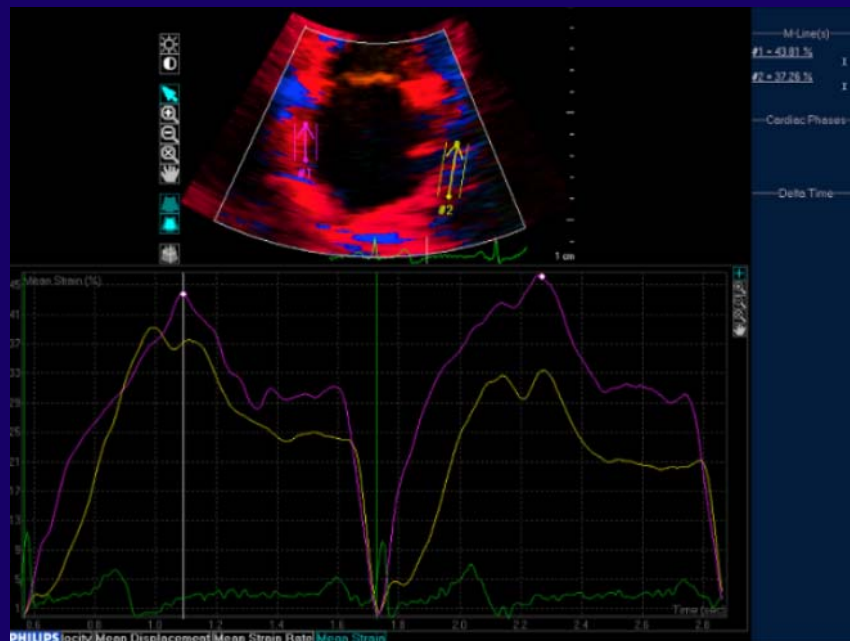
LA function

- Volume analysis
- Spectral Doppler of trans-mitral, pulmonary venous, and LAA appendage flow
- Tissue doppler and deformation analysis (strain and strain rate)

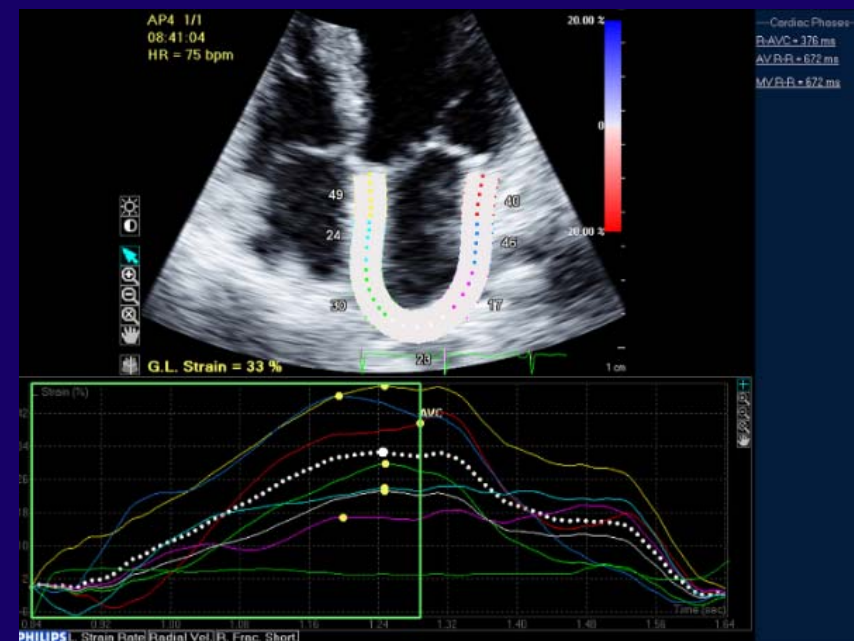


Methods of LA Strain

Tissue doppler imaging



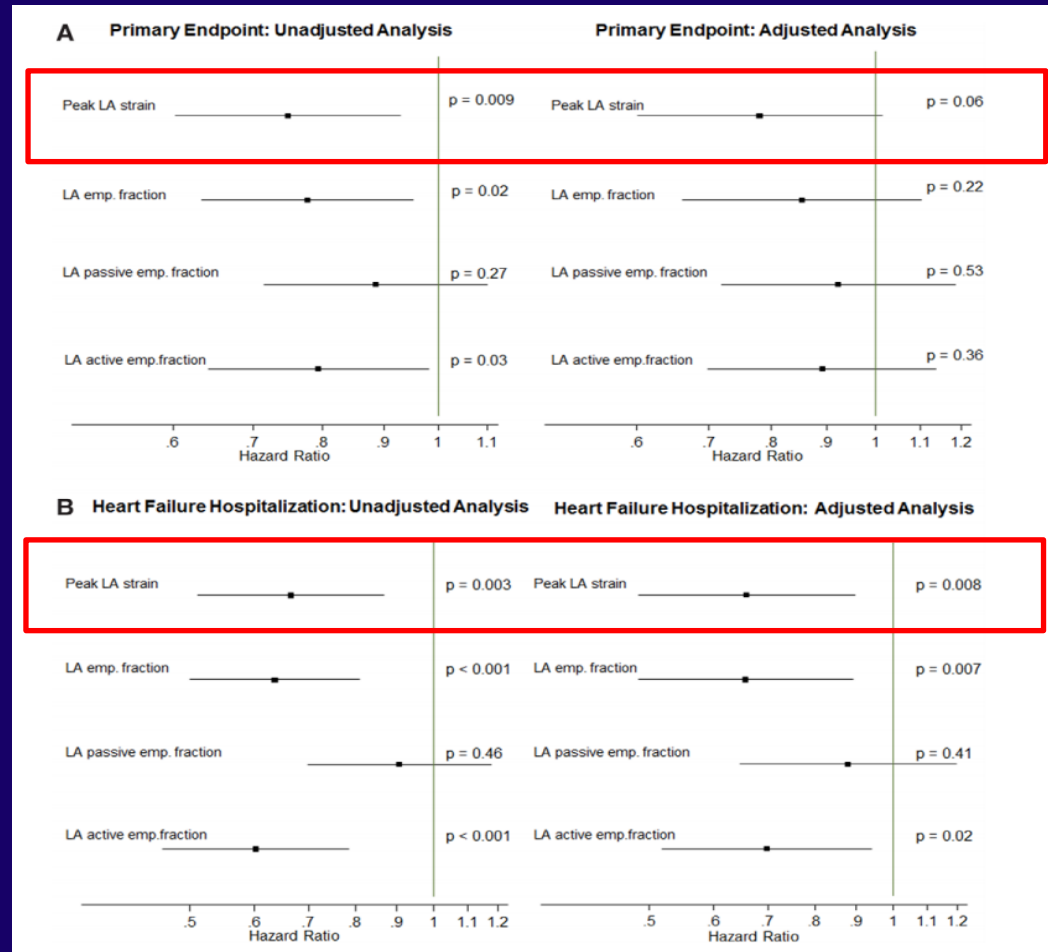
Speckle tracking imaging



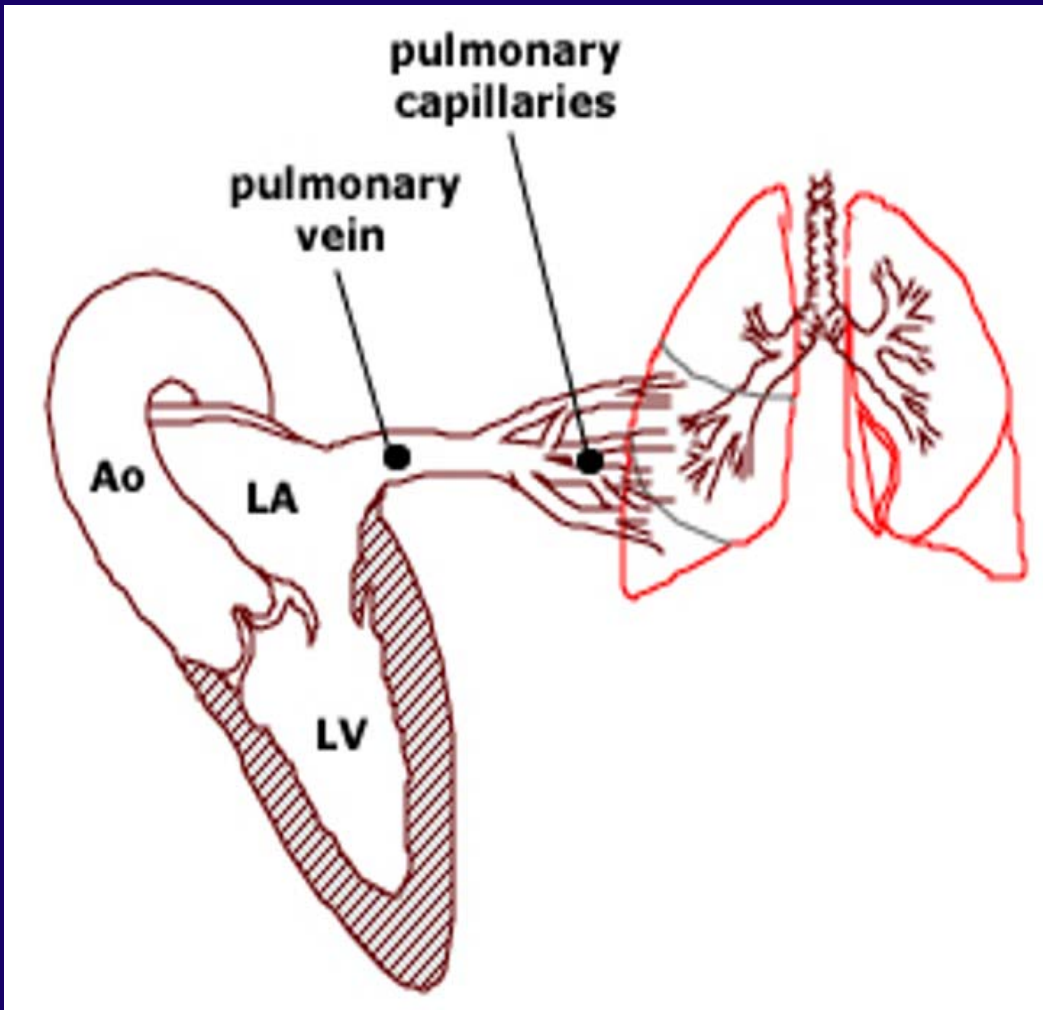
Relationship of LA strain and prognosis in HFpEF

TOPCAT Trial

- 357 HFpEF
- Strain
 - LA (peak LA strain)
 - LV longitudinal strain
- Primary Endpoint
 - Cardiac death
- Secondary Endpoint
 - Hospitalization d/t HF



Common Chamber during Diastole



Left Atrium

- Buffering pressure and flow oscillation between LV and pulmonary vasculature.
- LV stiffness → Impaired LA function → LA myopathy → remodeling of pulmonary vasculature -> pulmonary hypertension

**Atrial fibrillation
= absence of atrial
kick**

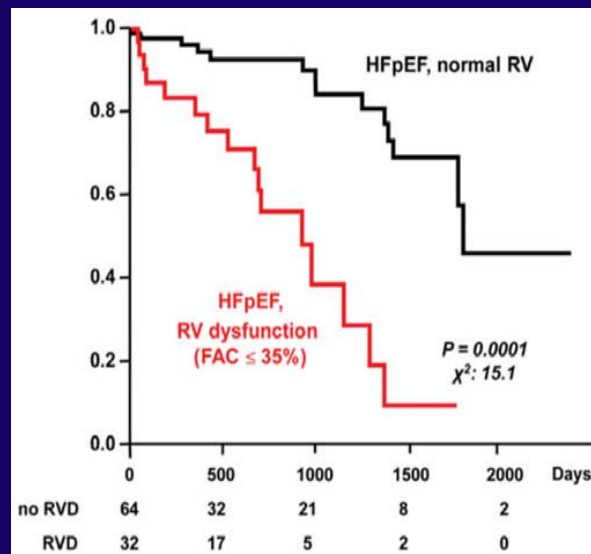
Right heart dysfunction in heart failure with preserved ejection fraction

Vojtech Melenovsky^{1,2*}, Seok-Jae Hwang¹, Grace Lin¹, Margaret M. Redfield¹, and Barry A. Borlaug¹

MAYO CLINIC

- 96 PEF
- 46 control
- RV dysfunction
 - RV fractional change (below 35% vs. above 35%)

Survival



Predictor for RVD

Odd ratio

- Male: 8.0 (2.9-26)
- **AF: 4.0 (1.5-11)**
- LVEF: 2.0 (1.2-3.5)
- CAD: 3.1 (1.2-7.1)
- SBP: 0.6 (0.4-0.9)

Atrial Dysfunction in Patients With Heart Failure With Preserved Ejection Fraction and Atrial Fibrillation



Yogesh N.V. Reddy, MBBS, MSc,^a Masaru Obokata, MD, PhD,^a Frederik H. Verbrugge, MD, PhD,^{a,b} Grace Lin, MD,^a Barry A. Borlaug, MD^a

**MAYO
CLINIC**

- 285 PEF
- 146 control
- Rt side catheterization
- TTE

TABLE 1 Demographics and Clinical Characteristics

	Control Subjects (n = 146)	HFpEF _{no-AF} (n = 181)	HFpEF _{parox-AF} (n = 49)	HFpEF _{perm-AF} (n = 48)	p Value
Age, yrs	56 ± 15*	66 ± 11*	71 ± 7	75 ± 6	<0.0001
Female	60	62	61	60	0.90
BMI, kg/m ²	28.3 ± 5.6	33.8 ± 7.4†‡	32.9 ± 7.9†	30.7 ± 5.7	<0.0001
Hemoglobin, g/dl	12.9 ± 1.3*	12.3 ± 1.5	12.2 ± 1.5	11.8 ± 1.6	<0.0001
Diabetes	14	30	35	21	<0.0001
Hypertension	84	94	100	98	0.0001
COPD	8	12	12	10	0.70
Laboratories and chest radiography					
NT-proBNP, pg/ml	69 (31-127)*	195 (68-557)*	613 (296-1,061)*	1,859 (969-3,051)*	<0.0001
Creatinine, mg/dl	0.9 ± 0.2*	1.1 ± 0.4	1.2 ± 0.4	1.2 ± 0.4	<0.0001
eGFR, ml/min/1.73 m ²	73 ± 18*	61 ± 17	58 ± 20	55 ± 20	<0.0001
Cardiomegaly	4	16	31	62	<0.0001
Lung congestion	0	3	4	19	<0.0001
Medication					
Beta-blocker	29	51	47	75	<0.0001
ACE inhibitor or ARB	24	41	39	58	<0.0001
Diuretic	23	43	55	65	<0.0001
MRA	6	10	16	27	0.0008
Digoxin	2	1	2	23	<0.0001
Anticoagulation	5	7	33	75	<0.0001

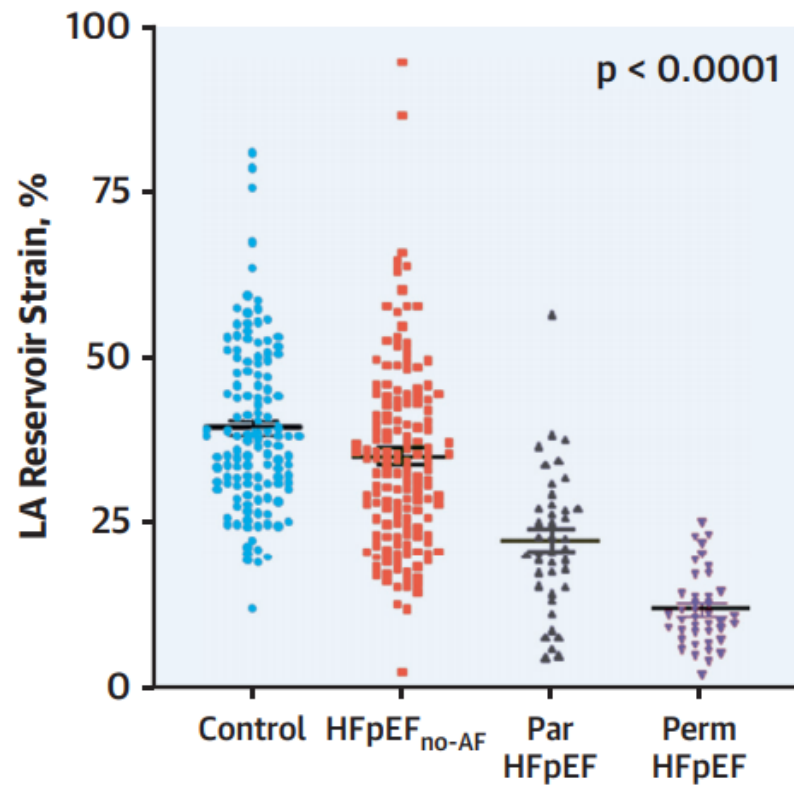
LV strain, no AF vs. PAF vs. PerAF

TABLE 2 Cardiac Structure and Function

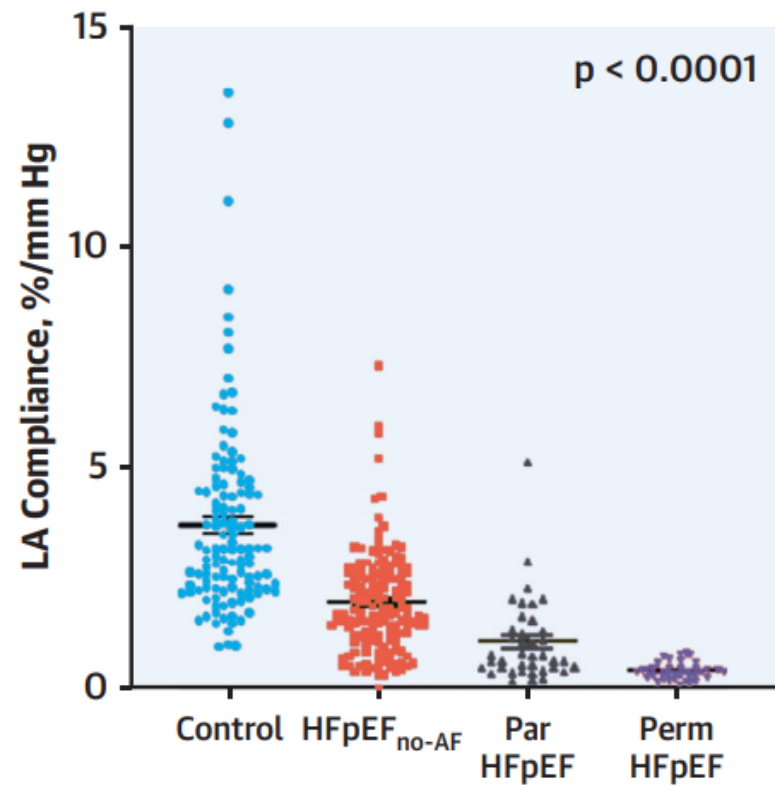
	Control Subjects (n = 146)	HFpEF _{no-AF} (n = 181)	HFpEF _{parox-AF} (n = 49)	HFpEF _{perm-AF} (n = 48)	p Value
LV structure and function					
LA volume index, ml/m ²	28 ± 8*	33 ± 9*	41 ± 12*	56 ± 15*	<0.0001
LVEDD, mm	48 ± 5	48 ± 5	49 ± 6	49 ± 6	0.20
EF, %	63 ± 5	64 ± 6	62 ± 7	61 ± 6†	0.005
LV mass index, g/m ²	84 ± 19*	90 ± 21	98 ± 26	97 ± 27	<0.000
LV GLS, %	16 ± 3	16 ± 3	15 ± 3‡	14 ± 4†‡	<0.000
LV stiffness β, mm Hg/ml	0.42 ± 0.11	0.47 ± 0.15‡	0.46 ± 0.14	0.47 ± 0.12‡	0.009
E/e'	9 ± 4*	13 ± 7	14 ± 6	16 ± 6‡§	<0.0001
Septal a', cm/s	10 ± 2	9 ± 3	7 ± 3*	–	<0.0001

LA Reservoir Dysfunction

A



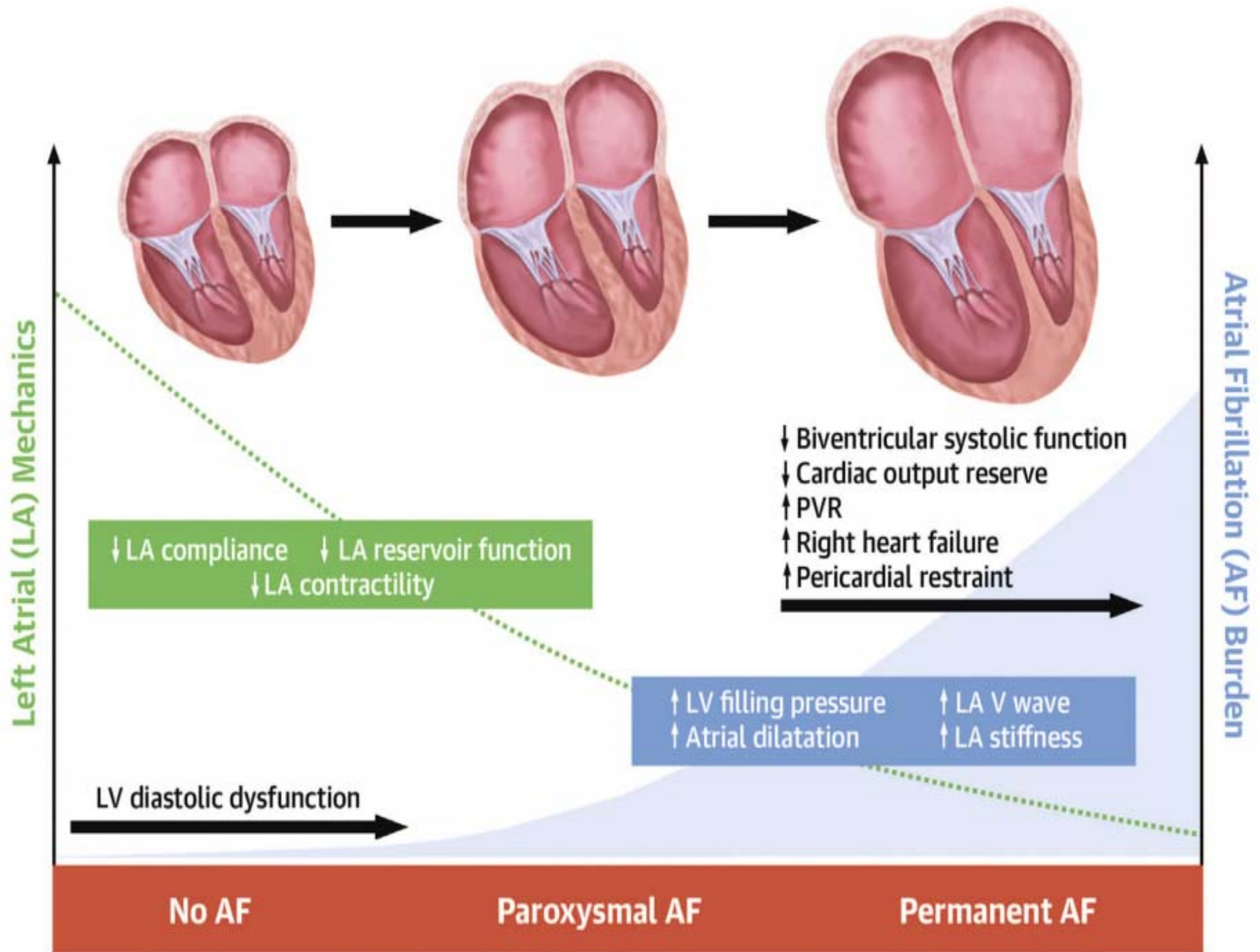
B



Resting Hemodynamics

TABLE 3 Resting Hemodynamics

	Control Subjects (n = 146)	HFpEF _{no-AF} (n = 181)	HFpEF _{parox-AF} (n = 49)	HFpEF _{perm-AF} (n = 48)	p Value
Pressure data, mm Hg					
PCWP, mean	9 ± 3*	15 ± 5	16 ± 6	19 ± 6††	<0.0001
Peak a-wave	12 ± 4*	19 ± 6	20 ± 6	—	<0.0001
Nadir x-descent	8 ± 3*	14 ± 5*	16 ± 6*	18 ± 5*	<0.0001
Peak v-wave	12 ± 5*	21 ± 10*	26 ± 12*	31 ± 11*	<0.0001
Nadir y-descent	8 ± 3*	14 ± 5*	16 ± 6	18 ± 5††	<0.0001
RA mean	5 ± 2*	9 ± 4	10 ± 4	12 ± 5*	<0.0001
PA mean	17 ± 4*	25 ± 7*	28 ± 10	31 ± 9	<0.0001
PA systolic	28 ± 7*	38 ± 11§	43 ± 15	47 ± 14	<0.0001
LVTMP	4 ± 2*	6 ± 4	7 ± 4	7 ± 4	<0.0001
RA/PCWP	0.57 ± 0.21	0.61 ± 0.20	0.59 ± 0.15	0.64 ± 0.17	0.08
PCWP/LVEDV	0.08 ± 0.04*	0.14 ± 0.06	0.15 ± 0.06	0.17 ± 0.07††	<0.0001
LVTMP/LVEDV	0.04 ± 0.03*	0.06 ± 0.04	0.07 ± 0.05	0.06 ± 0.04	<0.0001

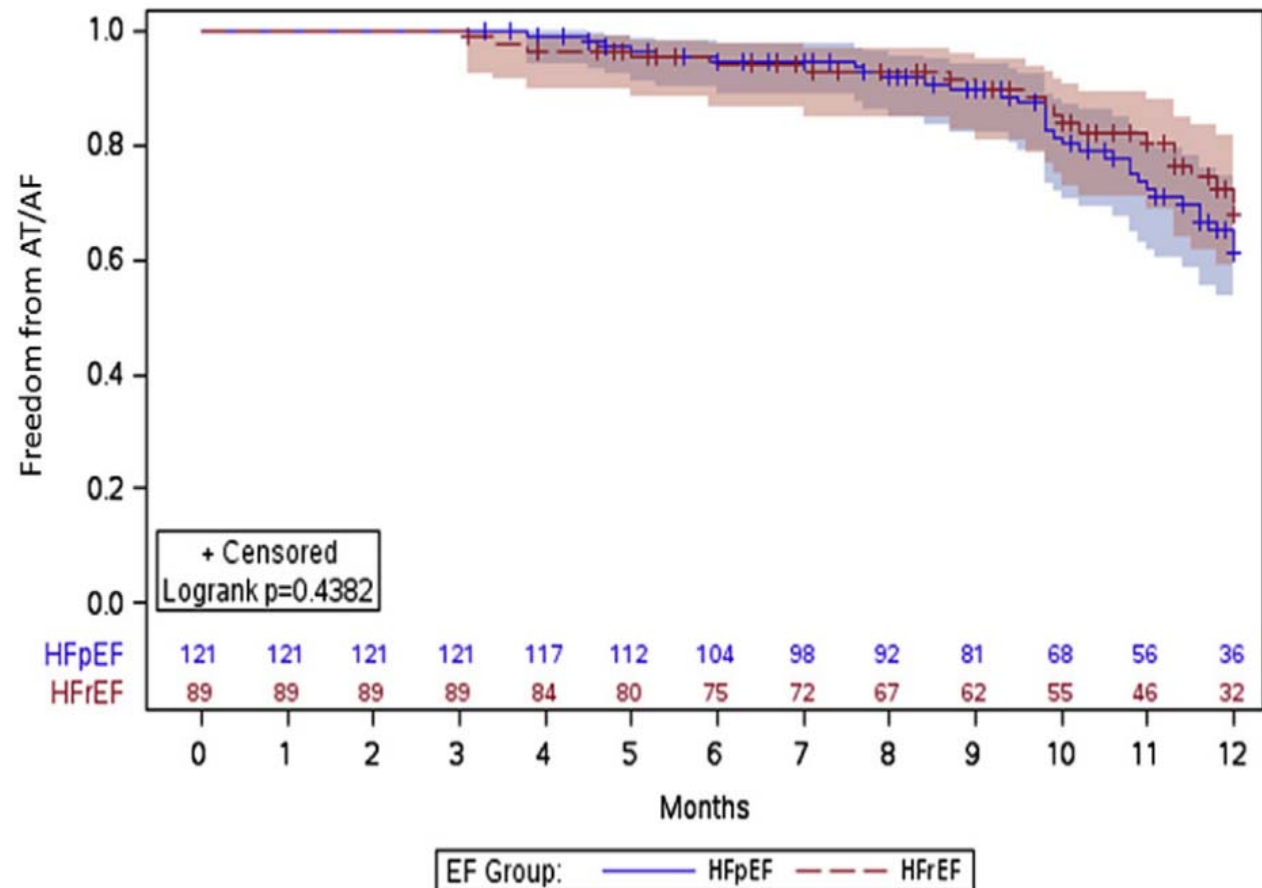


Treatment of AF in HFpEF

Heart Rhythm 2018;15:651–657

DUKE univ.

- 230 pts
- 42% HFrEF
- 58% HFpEF
- 63% PeAF
- AF success rate

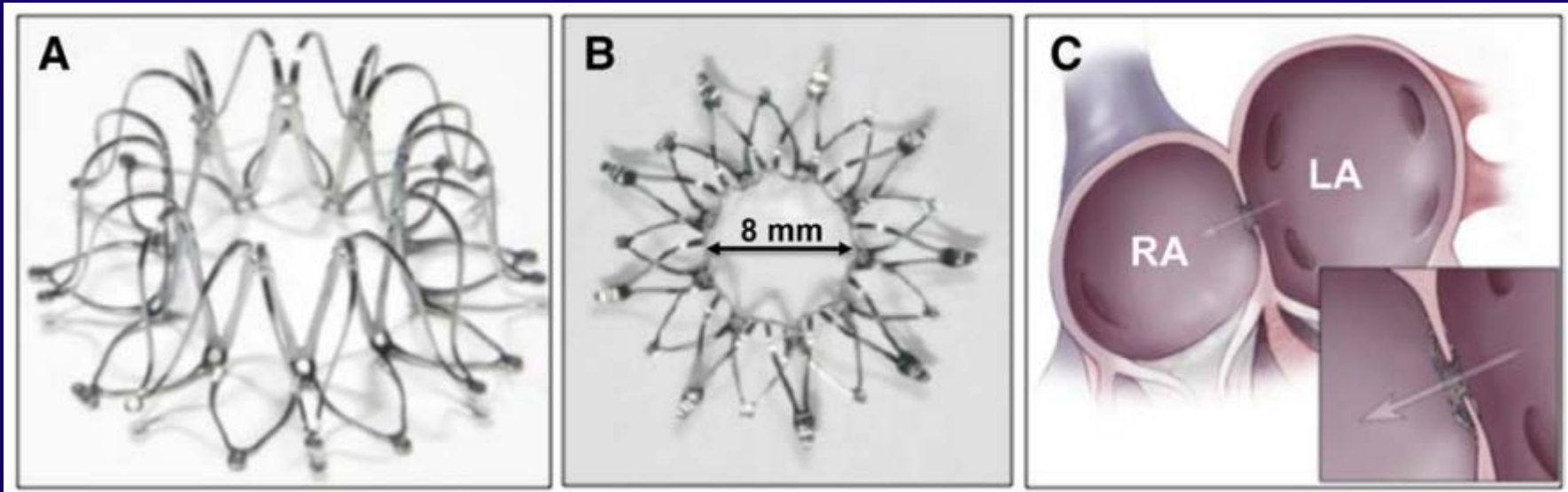


LA myopathy → LA pressure 상승

ORIGINAL RESEARCH ARTICLE

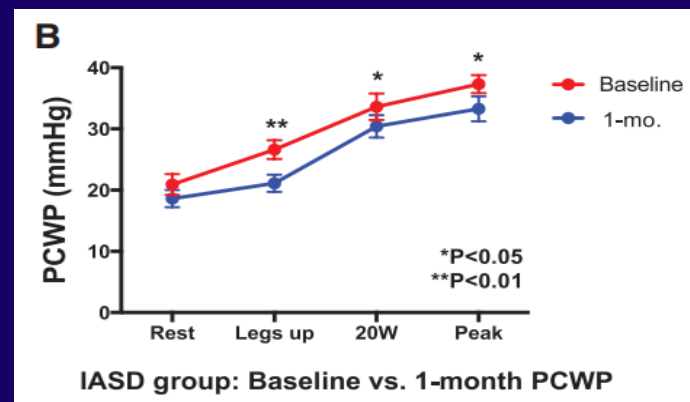
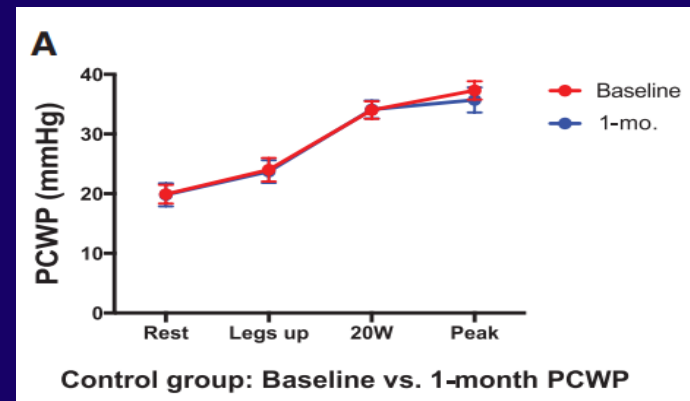
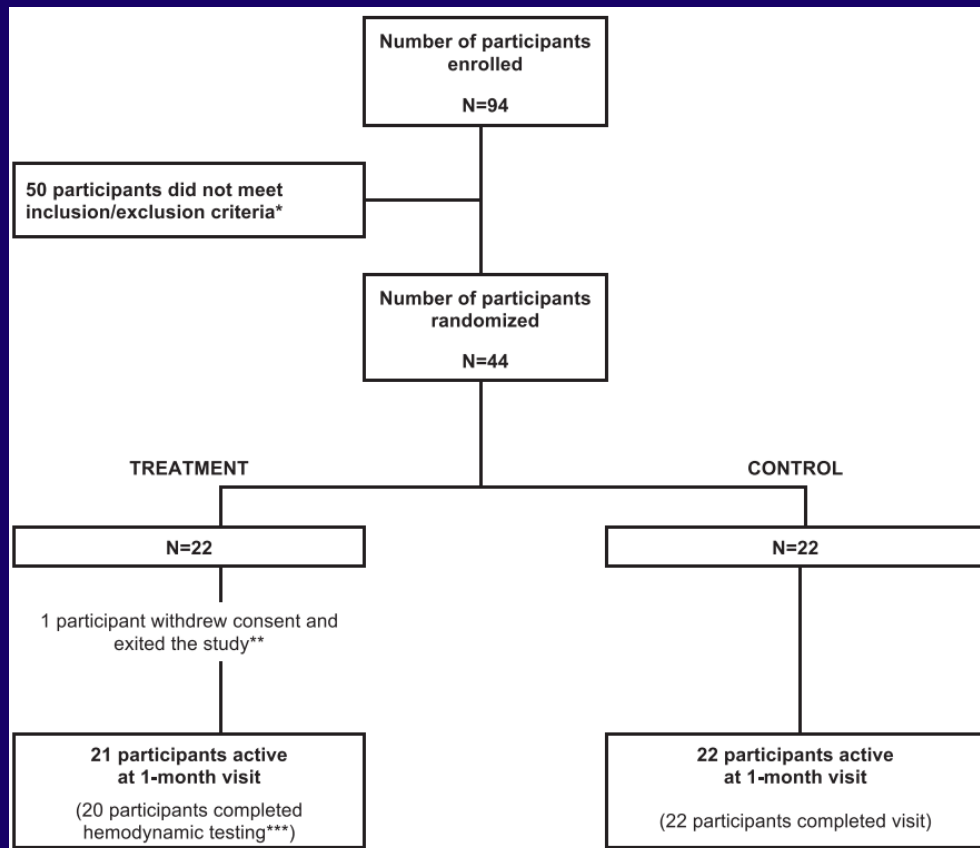
Transcatheter Interatrial Shunt Device for the Treatment of Heart Failure With Preserved Ejection Fraction (REDUCE LAP-HF I [Reduce Elevated Left Atrial Pressure in Patients With Heart Failure])

A Phase 2, Randomized, Sham-Controlled Trial



Transcatheter Interatrial Shunt Device for the Treatment of Heart Failure With Preserved Ejection Fraction (REDUCE LAP-HF I [Reduce Elevated Left Atrial Pressure in Patients With Heart Failure])

A Phase 2, Randomized, Sham-Controlled Trial



Conclusions

- In patients with HFpEF, LV stiffness induced LA remodeling (LA myopathy) and AF.
- However, LA function deteriorates at some point independent of LV and PAF can occur.
- If this situation persists, RA function declines with persistent AF.
- There is a need for research on effective treatment for LA myopathy and AF in HFpEF.

Thank you for your attention.

