Duration of Heart Failure, Cardiac Dysfunction and Remodeling, and Response to Atrial Shunt Treatment in HFpEF and HFmrEF

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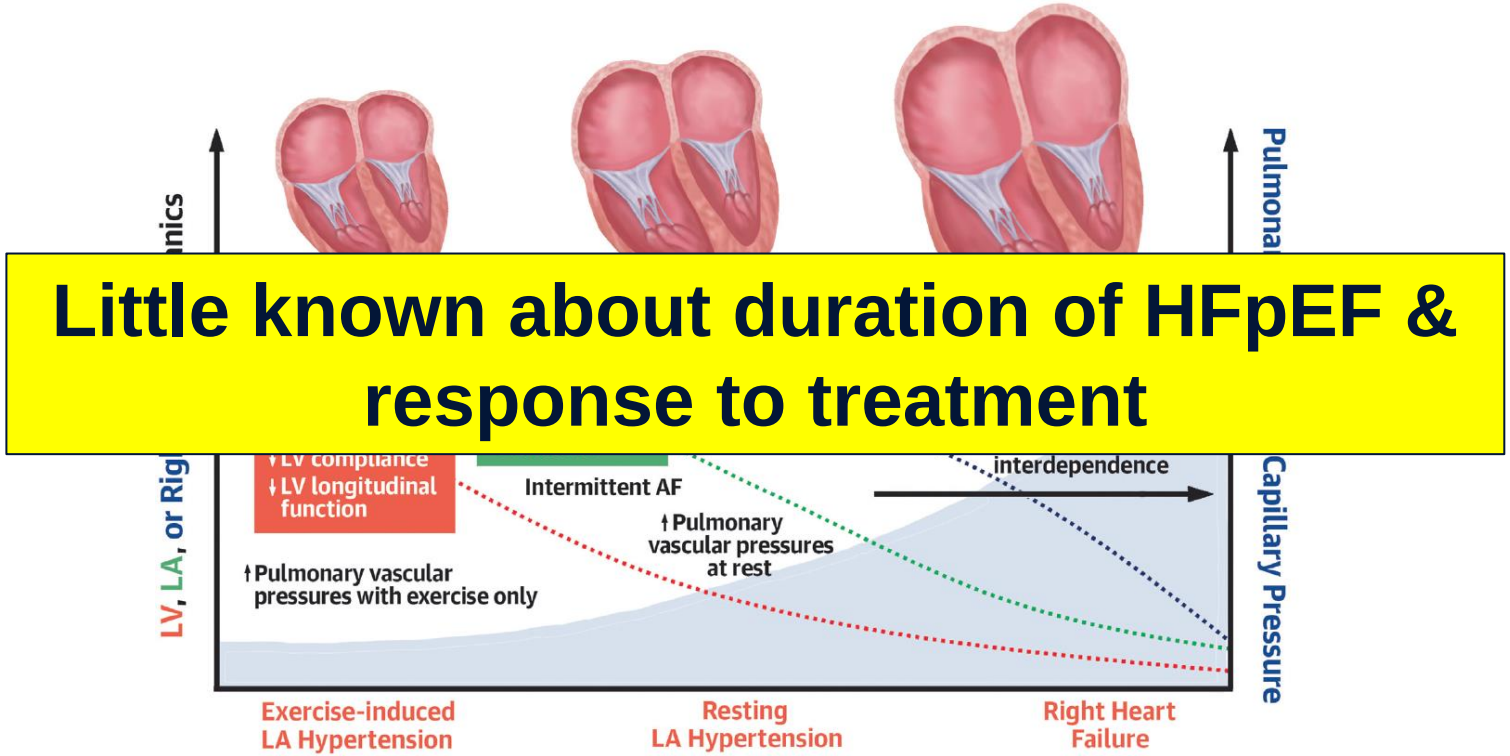
Longitudinal Disease Progression in HFpEF



Little known about duration of HFpEF & response to treatment

Borlaug, Sharma, Shah, Ho *J Am Coll Cardiol* 2023

Hypothesis

- Longer duration of HFpEF/HFmrEF would be associated with more severe cardiac remodeling and dysfunction.

- That individuals with shorter duration would have better outcomes, greater responsiveness to treatment, and more favorable responses to atrial shunt.

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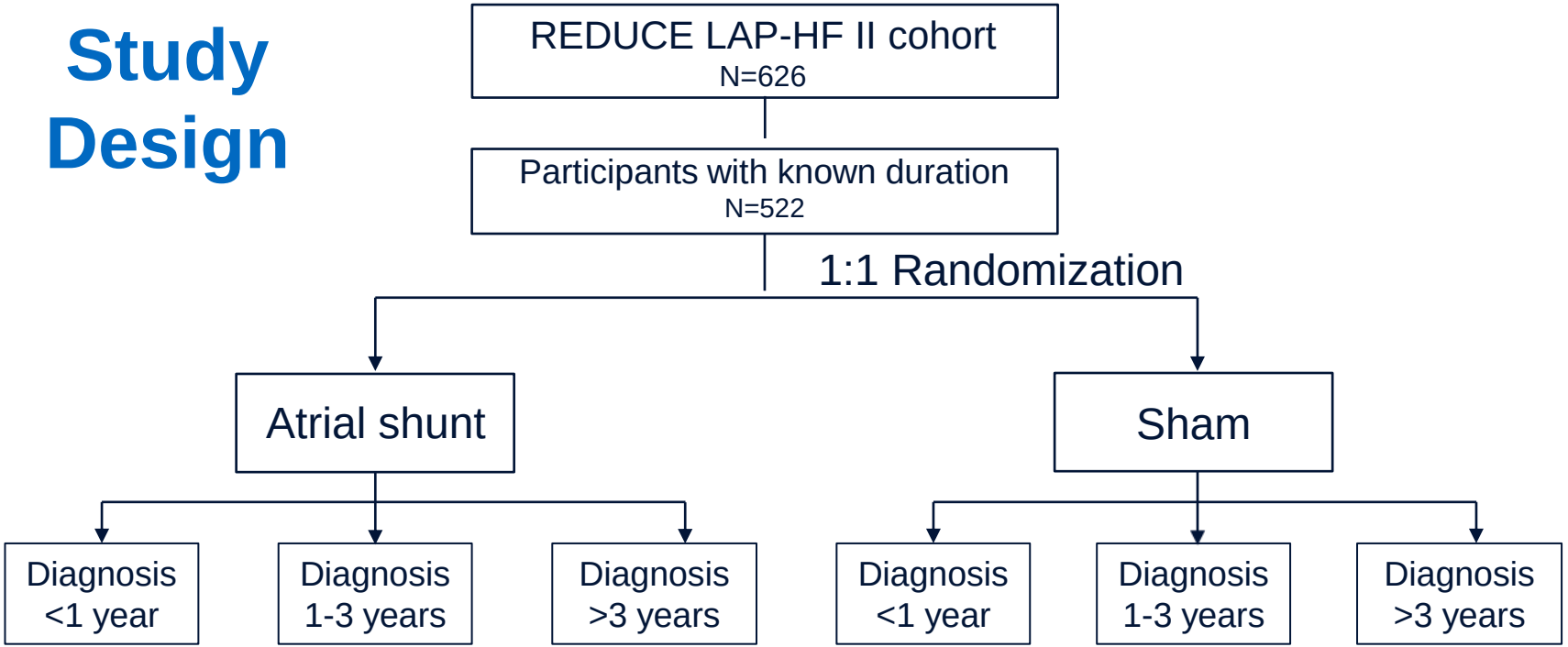
Study Design



Primary endpoint: hierarchical composite endpoint of cardiovascular death or nonfatal ischemic stroke, heart failure hospitalization, and change in health status (MITT analysis)

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Baseline Characteristics

	Diagnosis <1 year N=211 (40%)	Diagnosis 1-3 years N=152 (29%)	Diagnosis >3 years N=159 (31%)	p-value
Age, years	72 (66-77)	72 (65-77)	73 (66-78)	0.89
Female sex	148 (70.1%)	96 (63.2%)	86 (54.1%)	0.007
Body mass index, kg/m^2	31.4 (27.2-36.9)	32.1 (27.9-36.9)	32.8 (28.0-37.2)	0.49
Hypertension	180 (86.1%)	135 (88.8%)	142 (89.3%)	0.60
Ischemic heart disease	21 (10.0%)	26 (17.3%)	34 (21.4%)	0.009
AF or AFL	104 (49.3%)	83 (54.6%)	96 (60.4%)	0.11

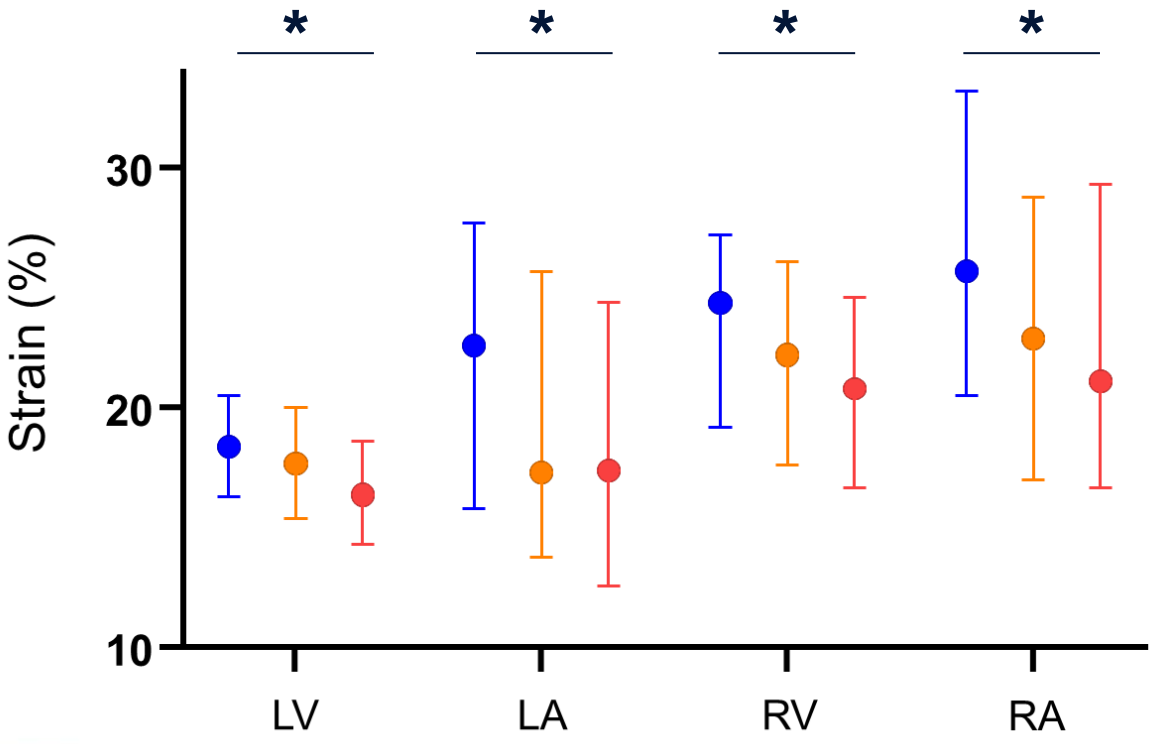
Baseline Characteristics

	Diagnosis <1 year N=211	Diagnosis 1-3 years N=152	Diagnosis >3 years N=159	p-value
NYHA class III	153 (73.2%)	112 (75.7%)	129 (81.6%)	0.16
KCCQ-OSS	46.6 (28.6-65.6)	43.5 (27.5-62.8)	46.6 (32.0-63.5)	0.65
HFpEF (EF ≥50%)	157 (87.7%)	113 (83.1%)	108 (75.5%)	0.016
Estimated GFR	58.4 (44.0-69.0)	56.0 (39.0-69.0)	55.0 (43.6-63.0)	0.21
NT-proBNP, pg/ml	267 (137-605)	548 (251-1085)	536 (252-1214)	<0.001

Baseline Cardiac Structure/Function

	Diagnosis <1 year N=211	Diagnosis 1-3 years N=152	Diagnosis >3 years N=159	p-value
LV mass index (g/m²)	77.1 (63.9-91.6)	79.7 (66.2-100.2)	86.5 (71.4-106.3)	<0.001
LA volume index (ml/m²)	29.5 (24.0-36.2)	29.9 (24.2-37.7)	34.0 (26.4-40.9)	0.004
RV end-diastolic volume (ml)	40.0 (30.5-51.0)	45.0 (34.0-58.0)	47.0 (36.6-62.0)	0.006
RV s' velocity (cm/s)	12.0 (10.0-14.0)	11.0 (9.0-14.0)	11.0 (9.0-13.0)	0.002
RA volume index (ml/m²)	22.6 (17.7-28.7)	24.5 (18.8-32.1)	27.2 (21.0-36.5)	<0.001

Greater Biventricular & Biatrial Dysfunction w Longer duration



- Diagnosis <1 year
- Diagnosis 1-3 years
- Diagnosis >3 years

*p<.001

Resting Hemodynamics at Baseline

	Diagnosis <1 year N=211	Diagnosis 1-3 years N=152	Diagnosis >3 years N=159	p-value
Systolic BP (mmHg)	145 (130-159)	142 (127-157)	143 (128-156)	0.54
Right atrial pressure (mmHg)	9 (6-11)	9 (6-12)	9 (7-12)	0.19
Mean PA pressure (mmHg)	24 (21-29)	26 (22-33)	27 (23-33)	0.012
PCWP (mmHg)	16 (13-22)	17 (14-22)	18 (15-23)	0.027
Resting PCWP≥15	135 (64.9%)	106 (70.7%)	119 (75.8%)	0.078
Cardiac output (L/min)	5.2 (4.4-6.2)	5.1 (4.4-6.2)	5.1 (4.3-6.2)	0.62
PVR (WU)	1.4 (1.1-2.0)	1.6 (1.1-2.1)	1.6 (1.0-2.2)	0.43

Baseline Hemodynamics during exercise

	Diagnosis <1 year N=211	Diagnosis 1-3 years N=152	Diagnosis >3 years N=159	p-value
Right atrial pressure (mmHg)	17 (14-22)	17 (14-22)	18 (15-23)	0.18
Mean PA pressure (mmHg)	45 (40-52)	45 (40-51)	47 (40-52)	0.58
PCWP (mmHg)	33 (28-38)	34 (29-41)	35 (31-42)	0.051
Cardiac output (L/min)	8.2 (6.6-10.5)	8.0 (6.3-9.9)	7.8 (6.2-9.7)	0.38
PVR, WU	1.3 (0.9-2.0)	1.3 (0.8-1.9)	1.4 (0.8-2.0)	0.86
Peak workload (Watts)	40 (20-60)	40 (20-60)	40 (20-60)	0.59

Efficacy Outcomes (MITT) for overall cohort

Subgroup	Variable	Statistic	Atrial Shunt	Sham Control	Win Ratio (95% CI)	P-value*
Diagnosis <1 year	Composite primary endpoint	Win ratio	—	—	1.18 (0.85, 1.64)	0.32
	CV death/non-fatal stroke	Rate per 100 patient-years	1.91	1.00	—	0.26
	HF event**	Rate per 100 patient-years	10.2	15.5	—	0.36
	ΔKCCQ-OSS at 12 months	Mean (95% CI)	14.2 (10.1-18.2) (n=95)	10.1 (6.6-13.6) (n=111)	—	0.11

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Diagnosis 1-3 years	Composite primary endpoint	Win ratio	—	—	1.04 (0.71, 1.53)	0.83
	CV death/non-fatal stroke	Rate per 100 patient-years	4.09	3.48	—	0.69
	HF event**	Rate per 100 patient-years	15.7	17.7	—	0.39
	ΔKCCQ-OSS at 12 months	Mean (95% CI)	8.8 (4.0-13.5) (n=78)	7.9 (2.9-13.9) (n=66)	—	0.72

Efficacy Outcomes (MITT) for overall cohort

Subgroup	Variable	Statistic	Atrial Shunt	Sham Control	Win Ratio (95% CI)	P-value*
Diagnosis <1 year	Composite primary endpoint	Win ratio	—	—	1.18 (0.85, 1.64)	0.32
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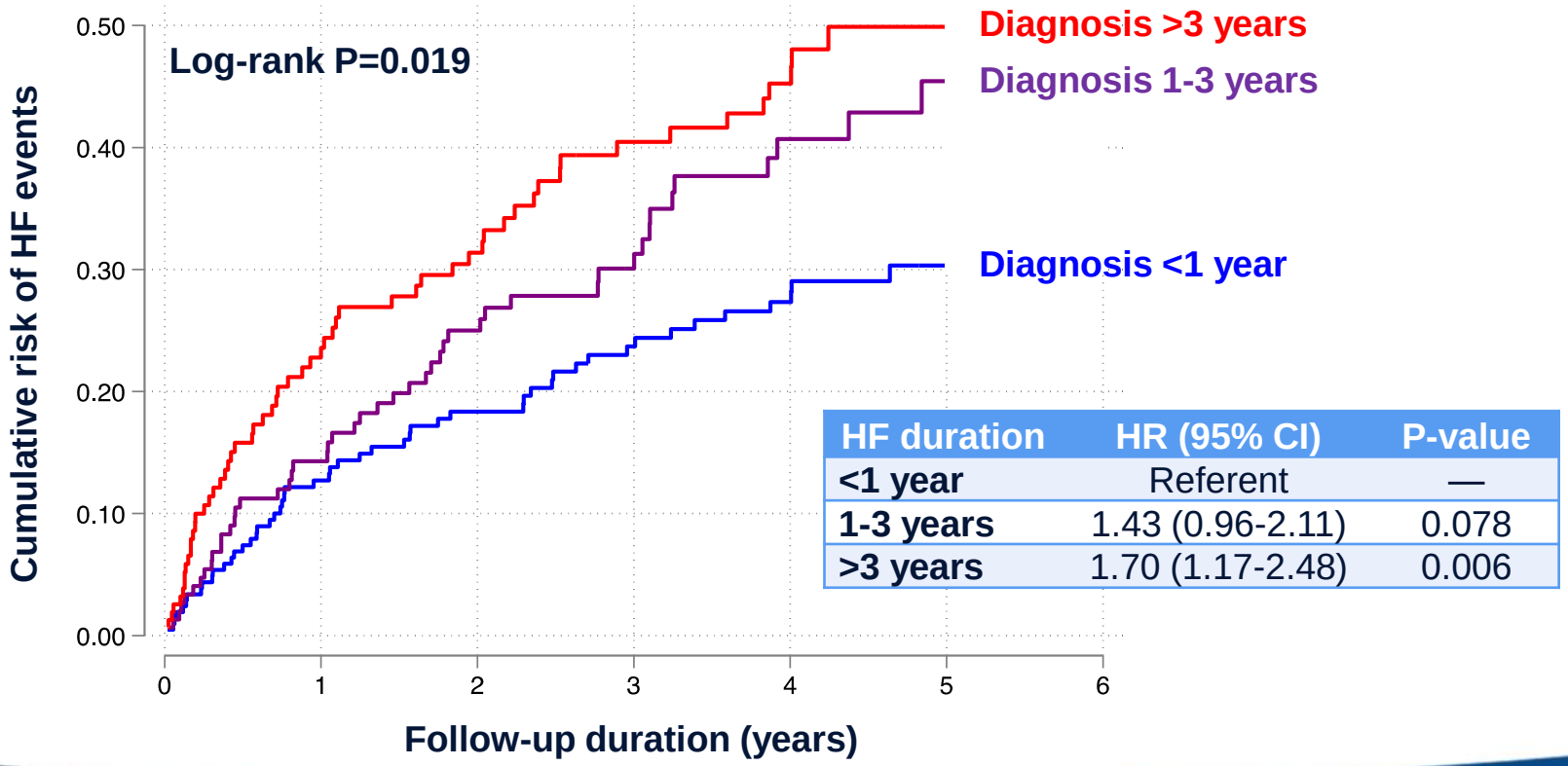
	HF event**	Rate per 100 patient-years	15.7	17.7	—	0.39
	ΔKCCQ-OSS at 12 months	Mean (95% CI)	8.8 (4.0-13.5) (n=78)	7.9 (2.9-13.9) (n=66)	—	0.72
Diagnosis >3 years	Composite primary endpoint	Win ratio	—	—	0.83 (0.57, 1.20)	0.31
	CV death/non-fatal stroke	Rate per 100 patient-years	3.70	1.63	—	0.10
	HF event**	Rate per 100 patient-years	22.2	19.0	—	0.31
	ΔKCCQ-OSS at 12 months	Mean (95% CI)	7.8 (2.6-12.9) (n=67)	9.4 (5.0-13.8) (n=81)	—	0.71

Association of HF duration with HF events



HF duration	HR (95% CI)	P-value
<1 year	Referent	—
1-3 years	1.43 (0.96-2.11)	0.078
>3 years	1.70 (1.17-2.48)	0.006

Conclusion

- In HFpEF/HFmrEF, longer duration of diagnosis is associated with:
  - Greater cardiac remodeling
  - More severe cardiac dysfunction & adverse hemodynamics
  - Higher risk of worsening HF
- Duration of HF does not modify the response to atrial shunt therapy in patients with HFpEF/HFmrEF.
- Earlier diagnosis of HFpEF/HFmrEF may increase the potential for interventions that delay or arrest disease progression

Thank you

ESC European Society of Cardiology
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RESEARCH ARTICLE

Biatrial myopathy in heart failure with preserved ejection fraction

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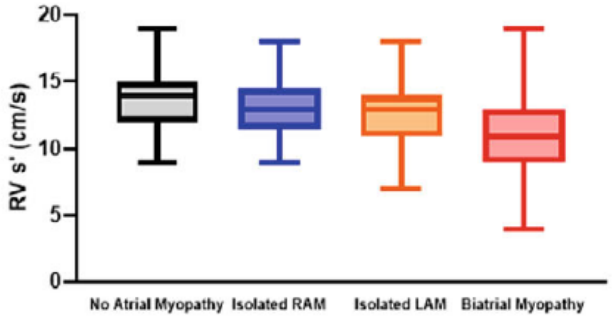
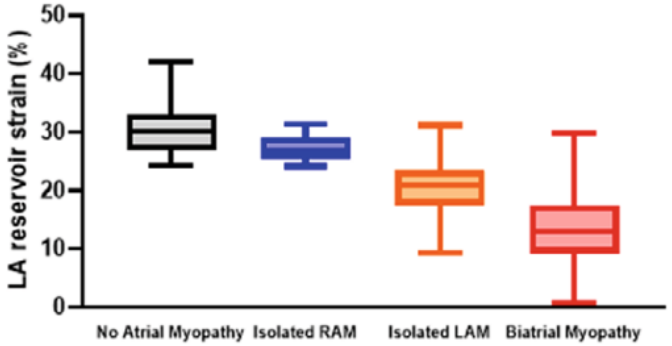
	No atrial myopathy ($n = 125$)	Isolated RAM ($n = 20$)	Isolated LAM ($n = 147$)	Biatrial myopathy ($n = 184$)	*p*-value
Age (years)	62 ± 12	60 ± 10	69 ± 9	74 ± 9	<0.0001
Female sex, *n* (%)	72 (58)	9 (45)	82 (56)	103 (56)	0.9
Body mass index (kg/m^2)	34.6 ± 7.2	33.3 ± 9.9	33.3 ± 7.8	31.2 ± 5.9	0.0004
Comorbidities, *n* (%)					
Obesity	92 (74)	14 (70)	95 (65)	102 (55)	0.01
Hypertension	115 (92)	19 (95)	137 (93)	177 (96)	0.4
Atrial fibrillation (none/paroxysmal/persistent)	93/7/0%	90/5/5%	71/25/4%	27/17/55%	<0.0001
Medications, *n* (%)					
Renin–angiotensin system inhibitors	58 (46)	11 (55)	68 (46)	91 (49)	0.8
Beta-blockers	58 (46)	7 (35)	91 (62)	121 (66)	0.002
Diuretics	60 (48)	9 (45)	73 (50)	133 (72)	<0.0001
Laboratories					
Haemoglobin (g/dl)	13.1 ± 1.4	14.0 ± 1.6	12.9 ± 1.7	12.9 ± 1.7	0.02
Estimated GFR (ml/min/1.73 m^2)	71 ± 19	69 ± 19	64 ± 19	56 ± 19	<0.0001
NT-proBNP (pg/ml)	90 (52–193)	110 (30–311)	277 (115–664)	959 (395–2059)	<0.0001

26% **4%** **31%** **39%**





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CLINICAL RESEARCH
Heart failure/cardiomyopathy

Deterioration in right ventricular structure and function over time in patients with heart failure and preserved ejection fraction

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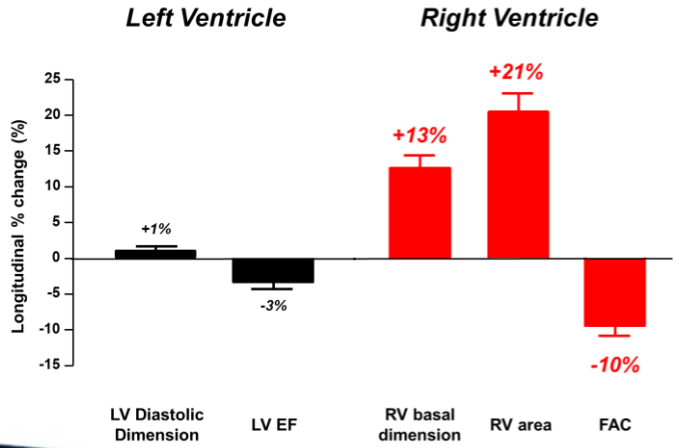
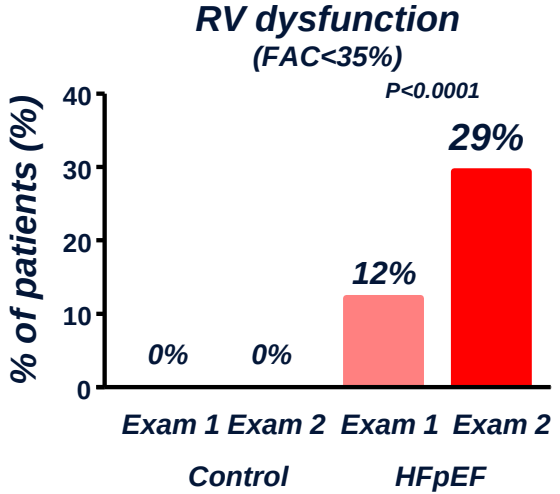
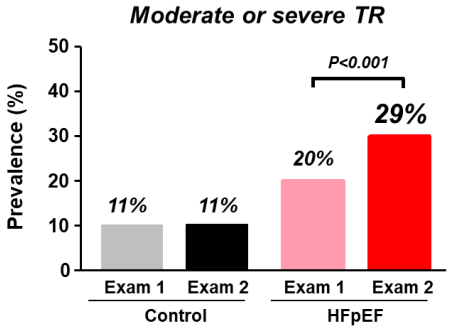
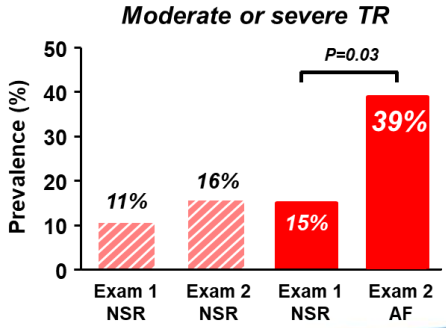
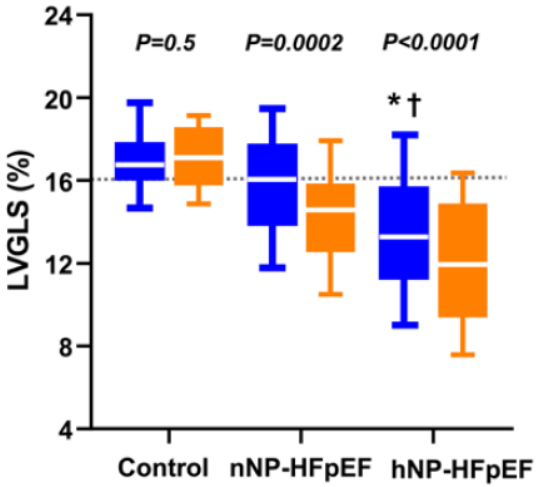


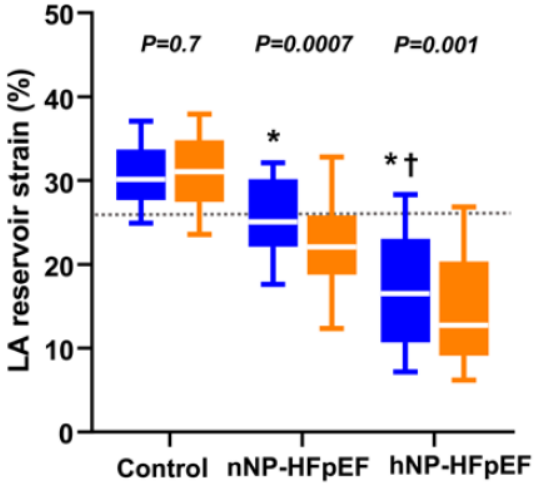


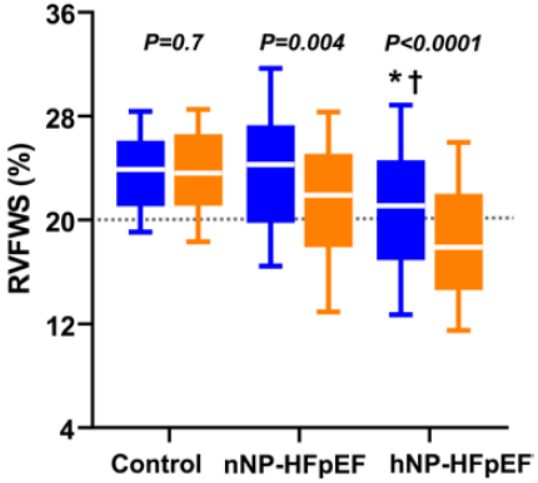




Worsening Biventricular and Atrial Mechanics over time







Little known about duration of HFpEF & response to treatment

Sorimachi...Borlaug *Circulation* 2022