

ΘΕΡΑΠΕΙΑ ΤΗΣ ΚΑΡΔΙΑΚΗΣ ΑΝΕΠΤΑΡΚΕΙΑΣ ΜΕ ΔΙΑΤΗΡΗΜΕΝΟ ΚΑΙ ΕΝΔΙΑΜΕΣΟ ΚΛΑΣΜΑ ΕΞΩΘΗΣΗΣ - ΝΕΩΤΕΡΑ ΔΕΔΟΜΕΝΑ

Dr ΑΛΕΞΙΑ ΣΤΑΥΡΑΤΗ

ΚΑΡΔΙΟΛΟΓΟΣ

ΔΙΕΥΘΥΝΤΡΙΑ ΕΣΥ, ΚΑΡΔΙΟΛΟΓΙΚΟ ΤΜΗΜΑ Γ.Ν.Θ

‘Γ.ΠΑΠΑΝΙΚΟΛΑΟΥ’



CONFLICT OF INTEREST

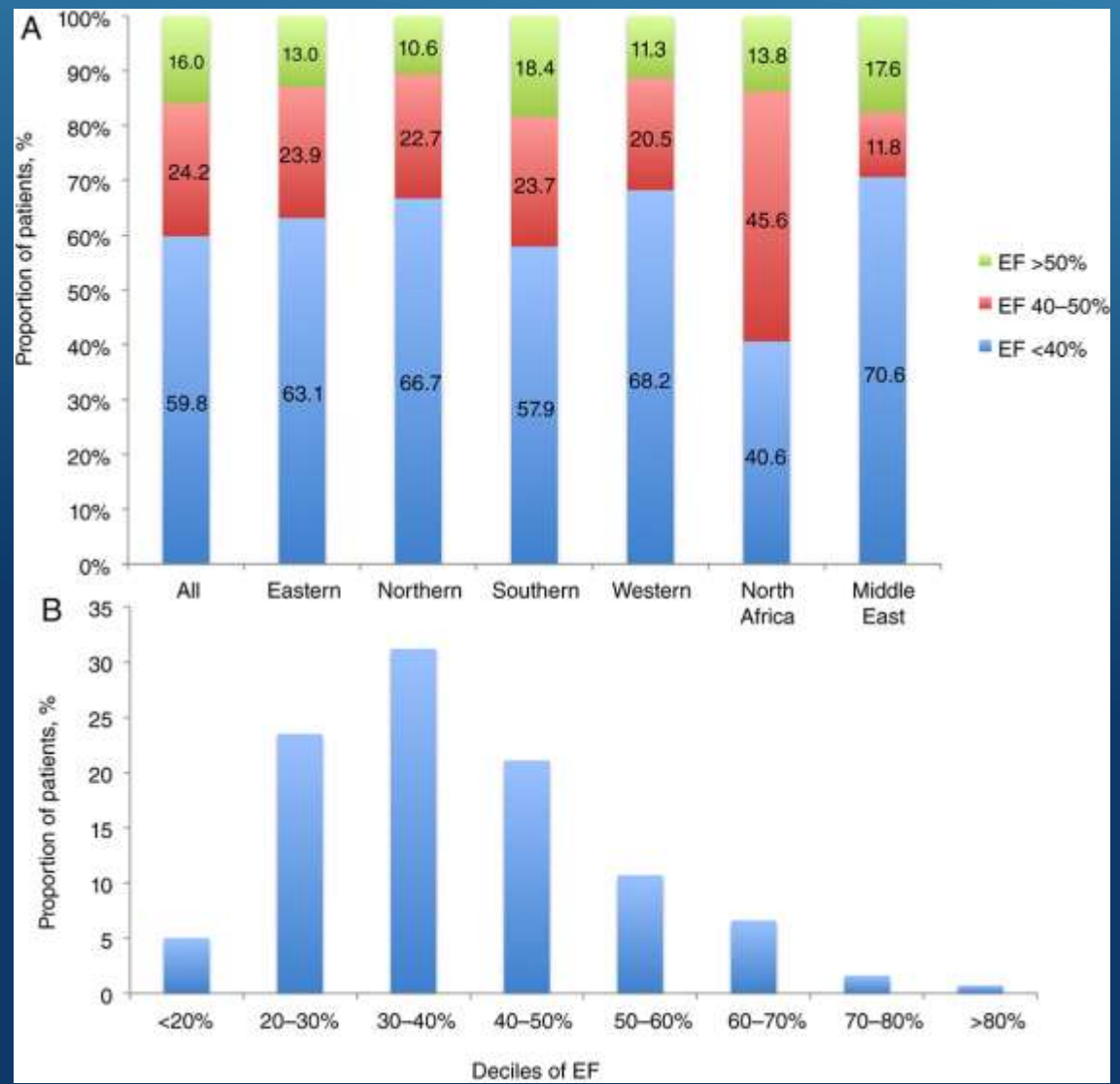
Nothing to Declare

A decorative graphic consisting of several parallel white lines of varying thicknesses, slanted diagonally from the bottom-left towards the top-right, set against a blue gradient background.

HF : DEFINITION

		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs	Symptoms ± Signs	Symptoms ± Signs
	2	LVEF <40%	LVEF 40-49%	LVEF ≥ 50%
	3	-	1.Elevated levels of natriuretic peptides. 2.At least one additional criterion: a.relevant structural heart disease (LVF and/or LAE); b.diastolic dysfunction (for details see Section 4.3.2.).	1.Elevated levels of natriuretic peptides. 2.At least one additional criterion: a.relevant structural heart disease (LVF and/or LAE); b.diastolic dysfunction (for details see Section 4.3.2.).

EPIDEMIOLOGY AND ONE-YEAR OUTCOMES IN PATIENTS WITH CHRONIC HEART FAILURE AND PRESERVED, MID-RANGE AND REDUCED EJECTION FRACTION: THE ESC HEART FAILURE LONG-TERM REGISTRY



(A) Geographic distribution of 9134 heart failure patients stratified by ejection fraction (EF).

(B) Distribution of patients by deciles of EF.

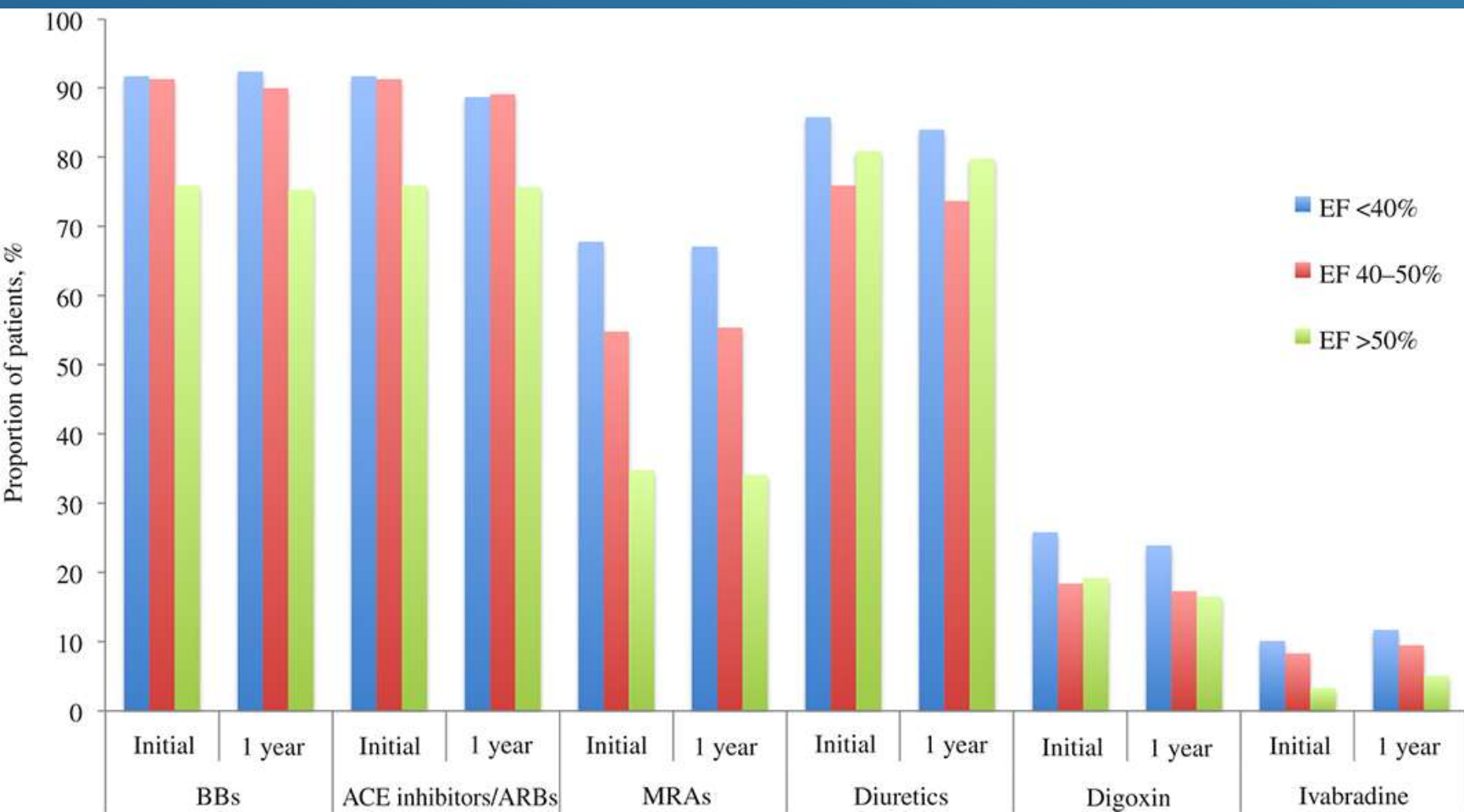
CHARACTERISTICS OF HOSPITALIZATIONS FOR HEART FAILURE WITH PRESERVED EJECTION FRACTION

- ▶ Among 388,442,396 discharge records reviewed from 2003-2012, there were 5,046,879 hospitalizations with acute heart failure
- ▶ Among those hospitalized with acute heart failure, **46%** (n = 2,329,391) of patients had **HFpEF** and 54% (n = 2,717,48) had HFrEF

EPIDEMIOLOGY AND ONE-YEAR OUTCOMES IN PATIENTS WITH CHRONIC HEART FAILURE AND PRESERVED, MID-RANGE AND REDUCED EJECTION FRACTION: THE ESC HEART FAILURE LONG-TERM REGISTRY

	All (n = 9134)	EF <40% (n = 5460)	EF 40–50% (n = 2212)	EF >50% (n = 1462)	P-value ^a
1. ^a P-values for differences among EF <40%, EF 40–50% and EF >50%.					
All-cause death, %	8.1	8.8	7.6	6.3	0.005
Cardiovascular death, %	52.1	53.5	50.6	47.2	0.504
Non-cardiovascular death, %	23.2	20.1	27.8	30.7	0.059
Unknown, %	24.7	26.3	21.6	21.9	0.393
All-cause hospitalization, %	28.1	31.9	22.0	23.5	<0.001
HF hospitalization, %	12.4	14.6	8.7	9.7	<0.001
All-cause death or HF hospitalization, %	18.6	21.2	15.0	14.6	<0.001

EPIDEMIOLOGY AND ONE-YEAR OUTCOMES IN PATIENTS WITH CHRONIC HEART FAILURE AND PRESERVED, MID-RANGE AND REDUCED EJECTION FRACTION: THE ESC HEART FAILURE LONG-TERM REGISTRY



Pharmacological treatments administered in 9134 heart failure patients at entry and at 1 year of follow-up according to ejection fraction (EF) category. ACE, angiotensin-converting enzyme; ARBs, angiotensin receptor blockers; BB, beta-blockers; MRAs, mineralocorticoid receptor antagonists.

CENTRAL ILLUSTRATION: Characterization of HFpEF, HFmrEF, and HFrEF

	Characteristics			Outcomes		Guideline-Directed Medical Therapies				
	Older Age	Male Sex	CAD	Morbidity	Mortality	ACEI	ARB	ARNI	BB	MRA
HFpEF (LVEF > 50%)	+++	+	++	++	++	X	✓ (IIB)	?	X	✓ (IIB)
HFmrEF (LVEF 40-50%)	++	++	+++	++/+++	++	?	✓ (IIB)	?	?	✓ (IIB)
HFrEF (LVEF < 40%)	+	+++	+++	+++	+++	✓ (I)	✓ (I)	✓ (I)	✓ (I)	✓ (I)

Hsu, J.J. et al. J Am Coll Cardiol HF. 2017;5(11):763-71.

MYTH

- ▶ HFpEF or HFmrEF is very benign compared with HFrEF
- 
- A decorative graphic consisting of several parallel white lines of varying lengths, slanted diagonally from the bottom right towards the top right, located in the lower right quadrant of the slide.

MYTH?

- ▶ There is no Evidenced Based Treatment for HFpEF or HFmrEF
- 

WHAT HAVE WE LEARNED ABOUT HEART FAILURE WITH MID-RANGE EJECTION FRACTION ONE YEAR AFTER ITS INTRODUCTION?

- ▶ In the past years, several pharmaceutical interventions that showed to be beneficial in HFrEF patients have shown **neutral effects** in trials specifically targeting HFpEF
- ▶ Incomplete understanding of HFpEF pathophysiology, heterogeneity of the patient population, inadequate diagnostic criteria, poor matching of therapeutic mechanisms and primary pathophysiological processes
- ▶ Interestingly, **several retrospective analyses that have now been published suggest that patients with mid-range EF might benefit** from these drugs including angiotensin receptor blockers (ARBs), beta-blockers and MRAs

WHAT HAVE WE LEARNED ABOUT HEART FAILURE WITH MID-RANGE EJECTION FRACTION ONE YEAR AFTER ITS INTRODUCTION?

- ▶ **CHARM programme:** Candesartan showed a positive treatment effect for left ventricular EFs of up to 50%.
- ▶ **Swedish Heart Failure registry:** ACE inhibitors and ARBs were overall associated with reduced all-cause mortality in HFpEF. There was a strong signal toward a stronger association in HFmrEF (HR 0.85, 95% CI 0.76-0.95) than in HFpEF (HR 0.95, 95% CI 0.87-1.04).
- ▶ **Beta-blockers in the CHART-2 study :** Use of beta-blockers was associated with improved survival in HFrEF and HFmrEF, but not in HFpEF.
- ▶ **The Beta-Blockers in Heart Failure Collaborative Group:** 18 637 patients, beta-blockers improved mortality in sinus rhythm in all EF categories up to and including 40-49% (HFmrEF), but not in $\geq 50\%$.
- ▶ **The TOPCAT trial:** Patients with an EF between 45-55% showed an estimated benefit from spironolactone treatment which disappeared in patients with EFs $>55\%$.

Treatment of patients with heart failure with preserved ejection fraction and heart failure with mid-range ejection fraction

Recommendations	Class	Level
it is recommended to <u>screen patients with HFpEF or HFmrEF</u> for both <u>cardiovascular and noncardiovascular co-morbidities</u> , which, if present, should be treated provided safe and effective interventions exist to improve symptoms, well-being and/or prognosis.	I	C
<u>Diuretics</u> are recommended in congested patients with HFpEF or HFmrEF in order to alleviate symptoms and signs.	I	B

RECOMMENDATIONS FOR STAGE C HFpE

COR	LOE	Recommendations	Comment/Rationale
I	B	Systolic and diastolic blood pressure should be controlled in patients with HFpEF in accordance with published clinical practice guidelines to prevent morbidity	2013 recommendation remains current.
I	C	Diuretics should be used for relief of symptoms due to volume overload in patients with HFpEF.	2013 recommendation remains current.
IIa	C	Coronary revascularization is reasonable in patients with CAD in whom symptoms (angina) or demonstrable myocardial ischemia is judged to be having an adverse effect on symptomatic HFpEF despite GDMT	2013 recommendation remains current.
IIa	C	Management of AF according to published clinical practice guidelines in patients with HFpEF is reasonable to improve symptomatic HF.	2013 recommendation remains current
IIa	C	The use of beta-blocking agents, ACE inhibitors, and ARBs in patients with hypertension is reasonable to control blood pressure in patients with HFpEF	2013 recommendation remains current.
IIb	B-R	In appropriately selected patients with HFpEF (with EF \geq 45%, elevated BNP levels or HF admission within 1 year, estimated glomerular filtration rate $>$ 30 mL/min, creatinine $<$ 2.5 mg/dL, potassium $<$ 5.0 mEq/L), aldosterone receptor antagonists might be considered to decrease hospitalizations	NEW: Current recommendation reflects new RCT data.

HFPEF AND MRAS

- ▶ The **TOPCAT trial** investigated the aldosterone antagonist **spironolactone** in patients with HFpEF and demonstrated no reduction in the composite primary outcome of cardiovascular death, aborted cardiac arrest or hospitalization for heart failure. However, spironolactone **slightly reduced the risk of heart failure hospitalizations compared to placebo**. In addition, subgroup analysis demonstrated that the primary outcome was met in the patients with elevated natriuretic peptides at baseline.
- ▶ In the mechanistic **Aldo-DHF trial** in patients with HFpEF, **spironolactone reduced E/e'**, an estimate of LV filling pressures, and led to improvements in cardiac structure (i.e. reduction in LV mass index) and **reduction in NT-proBNP levels**, but failed to improve symptoms or exercise capacity

RECOMMENDATIONS FOR STAGE C HFPE

I Ib	B	The use of ARBs might be considered to decrease hospitalizations for patients with HFpEF	2013 recommendation remains current.
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III: No Benefit	B-R	Routine use of nitrates or phosphodiesterase-5 inhibitors to increase activity or QoL in patients with HFpEF is ineffective	NEW: Current recommendation reflects new data from RCTs.
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III: No Benefit	C	Routine use of nutritional supplements is not recommended for patients with HFpEF.	2013 recommendation remains current.
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2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure

NITRATE - SILDENAFIL

- ▶ **NEAT-HF_pEF** (Nitrate's Effect on Activity Tolerance in Heart Failure With Preserved Ejection Fraction) trial randomized **110 patients with EF \geq 50%** on stable HF therapy, to **either isosorbide mononitrate or placebo** and found **no beneficial effects on activity levels, QoL, exercise tolerance, or NT-proBNP levels.**
- ▶ The **RELAX** trial randomized **216 patients with EF \geq 50%** on stable HF therapy and with reduced exercise tolerance (peak observed VO_2 $<$ 60% of predicted) to **sildenafil or placebo**. This study **did not show improvement in oxygen consumption or exercise tolerance.**

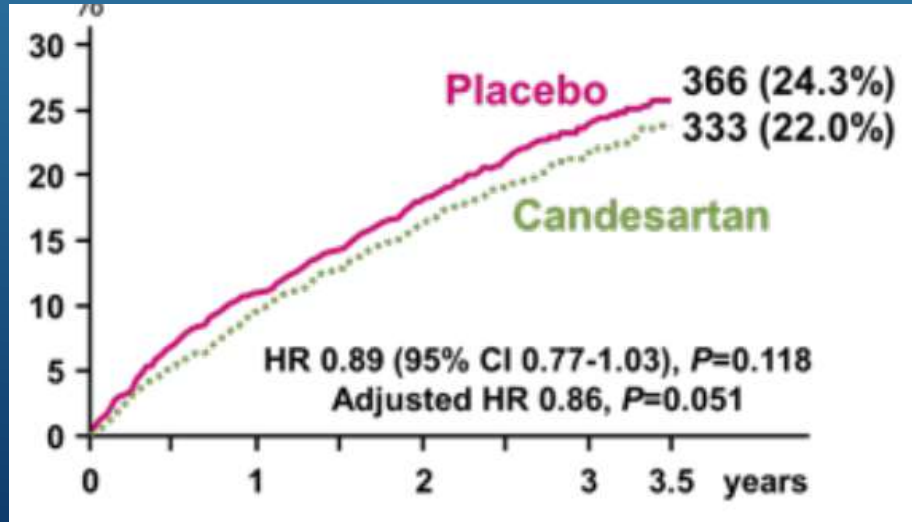
RECOMMENDATION FOR HYPERTENSION IN STAGE C HFPEF

COR	LOE	Recommendation	Comment/Rationale
I	C-LD	Patients with HFpEF and persistent hypertension after management of volume overload should be prescribed GDMT titrated to attain systolic blood pressure less than 130 mm Hg	NEW: New target goal blood pressure based on updated interpretation of recent clinical trial data.

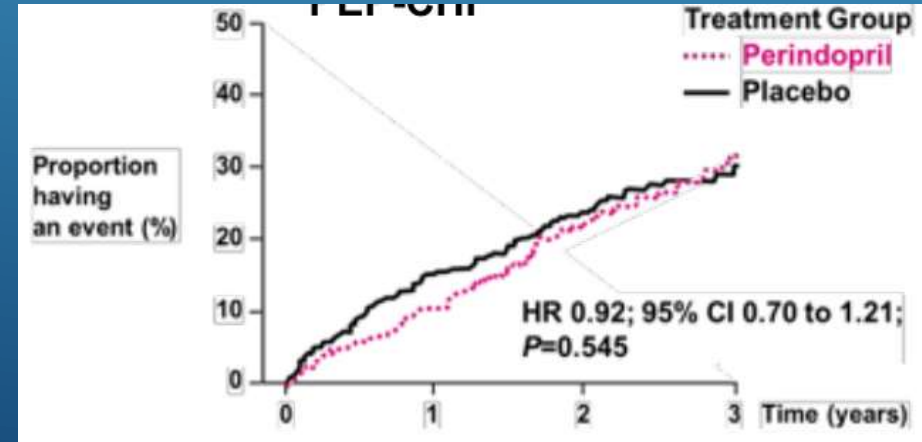
- **RAAS inhibition with ACE inhibitor, ARB (especially mineralocorticoid receptor antagonists), and possibly ARNI would represent the preferred choice.** A shared decision-making discussion with the patient influenced by physician judgment should drive the ultimate choice of antihypertensive agents.

RAAS INHIBITION - OUTCOMES TRIALS IN HFPEF

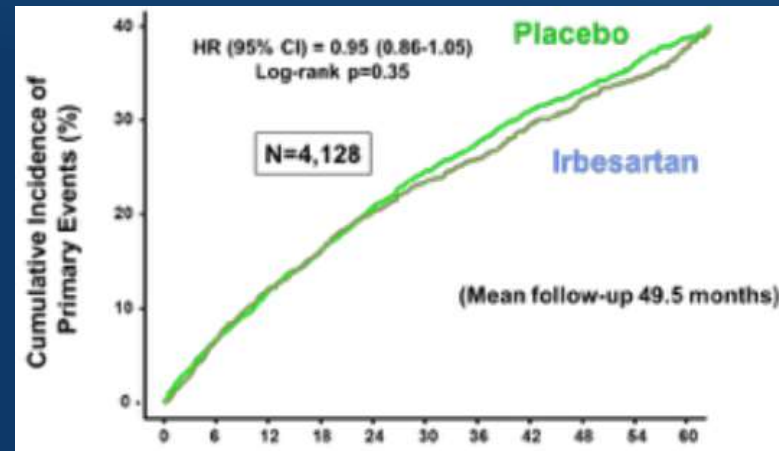
CHARM-Preserved



PEP-CHF



I-PRESERVE



B-BLOCKERS

- ▶ Data from the **SENIORS** trial suggest that **nebivolol might be as useful in patients with HFpEF** as it was for patients with HFrEF, and observational data from the **Swedish Heart Failure Registry** also suggest that **β -blockers may be beneficial in HFpEF**
- ▶ **Nebivolol is currently being tested** in a phase 4 trial for its potential effect on PVR and 6-minute walk distance in patients with PH-HFpEF (ClinicalTrials.gov NCT02053246).
- ▶ Previously, **carvedilol** resulted in **significant improvement in E/A ratio** in patients with HFpEF from the SWEDIC trial. Carvedilol has also been demonstrated to improve RV systolic function in patients with HFrEF, yet any **effect on the RV in HFpEF is currently unknown**.

Effect of carvedilol on diastolic function in patients with diastolic heart failure and preserved systolic function. Results of the Swedish Doppler-echocardiographic study (SWEDIC)[☆]

A. Bergström^a, B. Andersson^b, M. Edner^c, E. Nylander^a, H. Persson^c, U. Dahlström^{a,*}

Effects of carvedilol on heart failure with preserved ejection fraction: the Japanese Diastolic Heart Failure Study (J-DHF)

Kazuhiro Yamamoto^{1*}, Hideki Origasa², and Masatsugu Hori³ on behalf of the J-DHF Investigators

Beta-Blockade With Nebivolol in Elderly Heart Failure Patients With Impaired and Preserved Left Ventricular Ejection Fraction

Data From SENIORS (Study of Effects of Nebivolol Intervention on Outcomes and Rehospitalization in Seniors With Heart Failure)

Association Between Use of β -Blockers and Outcomes in Patients With Heart Failure and Preserved Ejection Fraction

Lars H. Lund, MD, PhD; Lina Benson, MSc; Ulf Dahlström, MD, PhD; Magnus Edner, MD, PhD; Leif Friberg, MD, PhD

EFFICACY OF BETA-BLOCKERS IN HEART FAILURE ACCORDING TO LEFT VENTRICULAR EJECTION FRACTION

AN INDIVIDUAL PATIENT LEVEL ANALYSIS OF DOUBLE-BLIND RANDOMISED TRIALS

DIPAK KOTECHA, MBCHB PHD MRCP FESC FHEA ON BEHALF OF

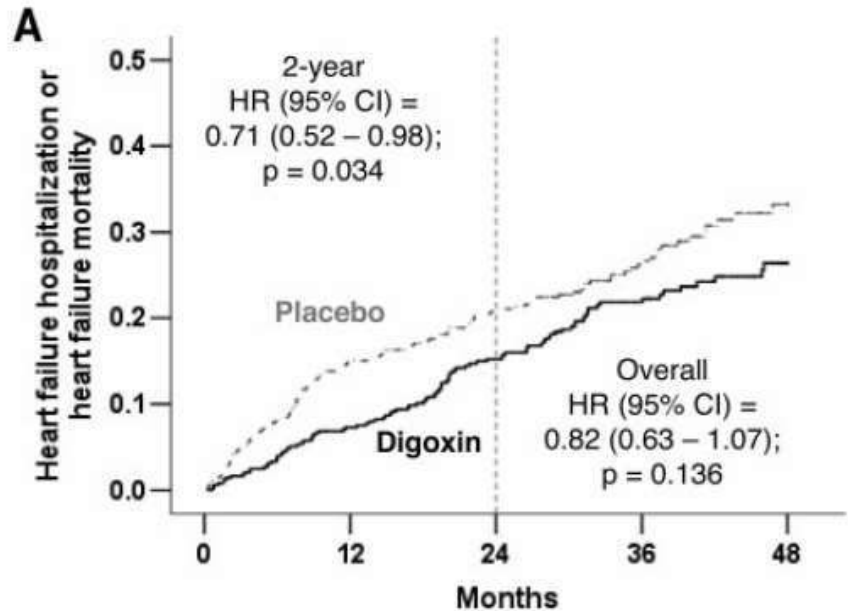
THE BETA-BLOCKERS IN HEART FAILURE COLLABORATIVE GROUP

EFFICACY OF BETA-BLOCKERS IN HEART FAILURE ACCORDING TO LEFT VENTRICULAR EJECTION FRACTION

- ▶ Beta-blockers improve LVEF and **reduce cardiovascular mortality in patients with heart failure in sinus rhythm and LVEF <40% or 40-49%**
- ▶ Too few patients in double-blind RCTs to comment on heart failure with LVEF $\geq 50\%$.
- ▶ Disconnect in AF patients warrants further investigation * - no consistent evidence of prognostic benefit with betablockers

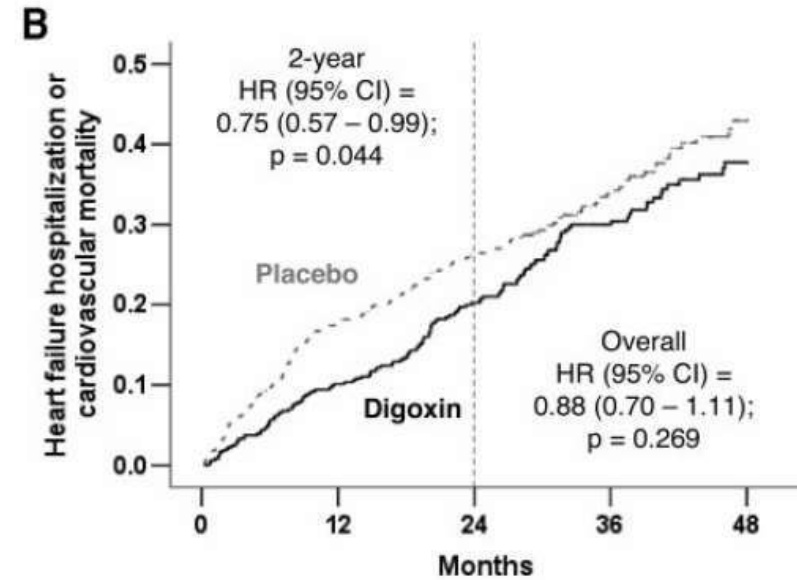
Effects of Digoxin on Morbidity and Mortality in Diastolic Heart Failure

The Ancillary Digitalis Investigation Group Trial



Number of patients at risk

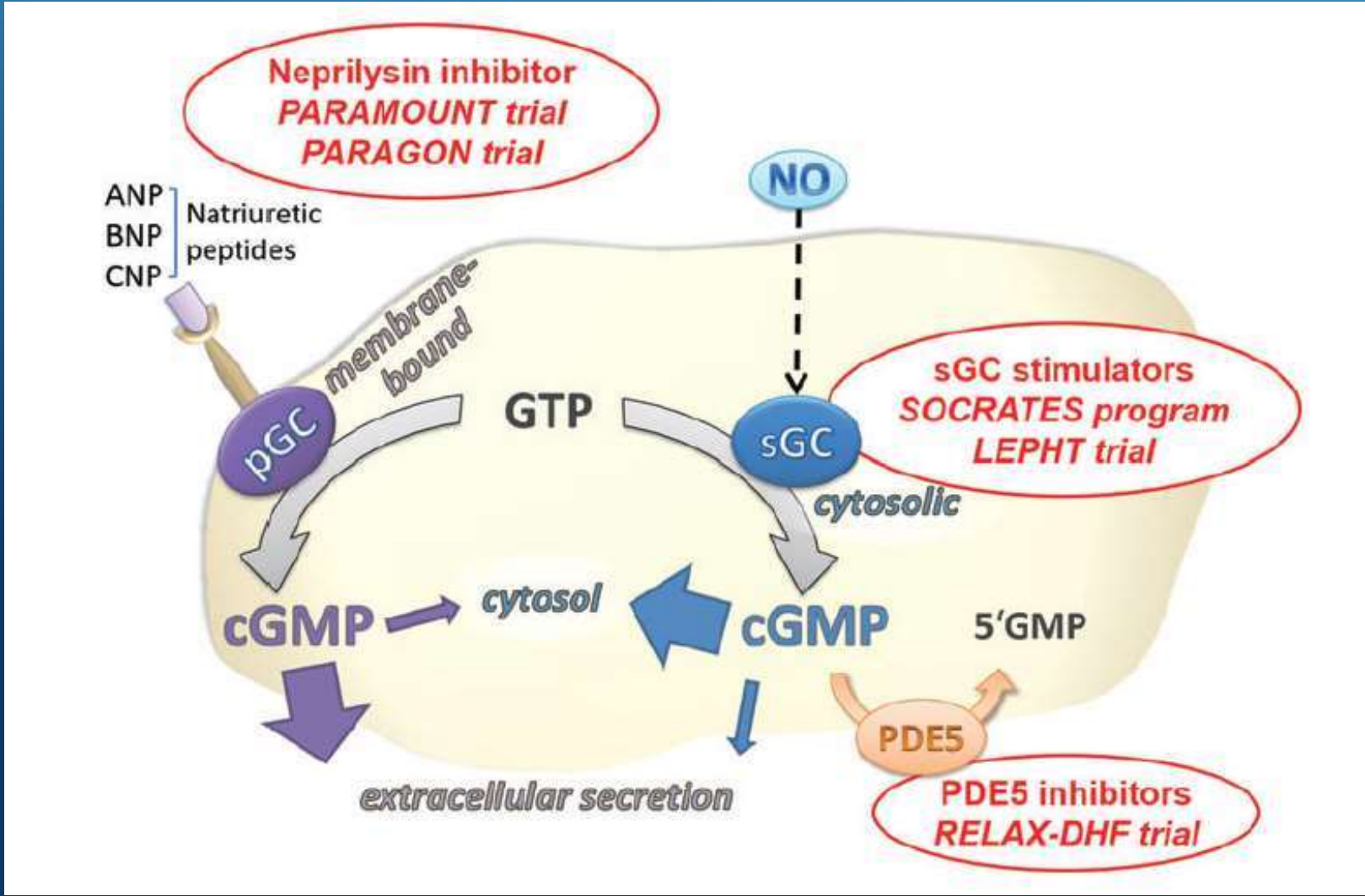
	0	12	24	36	48
Placebo	496	408	366	240	84
Digoxin	492	440	387	248	98



Number of patients at risk

	0	12	24	36	48
Placebo	496	408	366	240	84
Digoxin	492	440	387	248	98

NO- CGMP- PKG PATHWAY



SOCRATES-PRESERVED: PRIMARY RESULTS

- ▶ 2 Phase II, randomized, parallel-group, placebo-controlled, double-blind, dose finding phase IIb studies of 4 dose regimens of the oral sGC stimulator **vericiguat** over 12 weeks
- ▶ **No reduction in log-NT-proBNP or in LAV** at week 12 compared with placebo
- ▶ **Riociguat**: DILATE-1, neutral results

HFPEF AND ARNIS

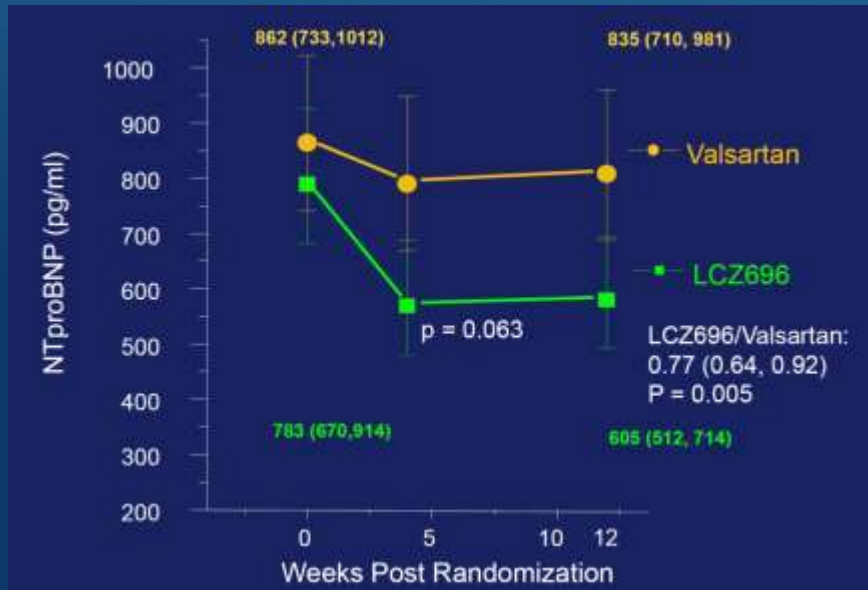
- ▶ **Sacubitril/valsartan** is an angiotensin receptor neprilysin inhibitor that has been proven to improve outcomes in patients with HFrEF.

PARAGON-HF EFFICACY AND SAFETY OF LCZ696 COMPARED TO VALSARTAN, ON MORBIDITY AND MORTALITY IN HEART FAILURE PATIENTS WITH PRESERVED EJECTION FRACTION

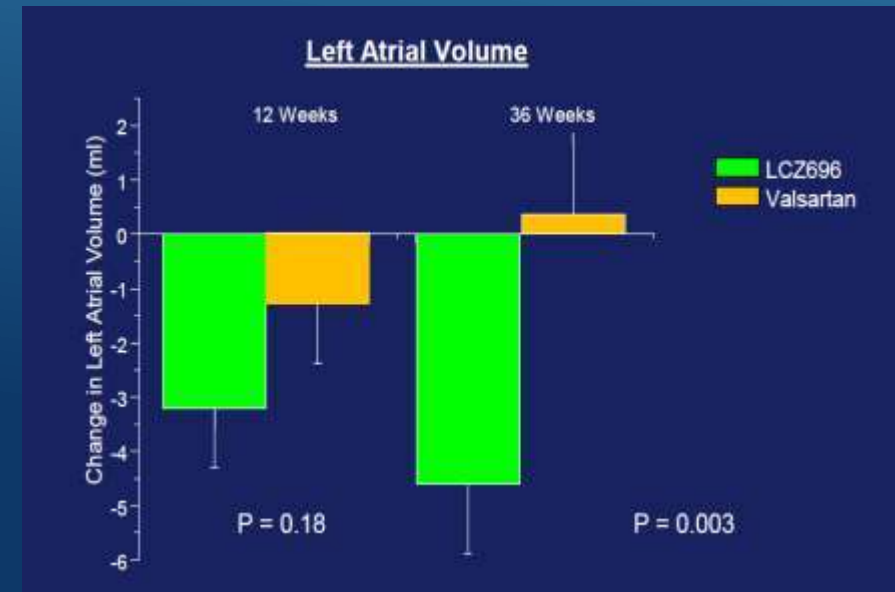
- ▶ A randomized, double-blind, parallel group, active-controlled, event-driven trial comparing the long-term efficacy and safety of valsartan and sacubitril/valsartan in patients with chronic HFpEF (left ventricular ejection fraction $\geq 45\%$), New York Heart Association functional class II to IV symptoms, elevated natriuretic peptides, and evidence of structural heart disease
- ▶ PARAGON-HF will determine whether sacubitril/valsartan is superior to angiotensin receptor blockade alone in patients with chronic symptomatic HFpE

PARAMOUNT TRIAL THE ANGIOTENSIN RECEPTOR NEPRILYSIN INHIBITOR LCZ696 IN HEART FAILURE WITH PRESERVED EJECTION FRACTION

NT proBNP

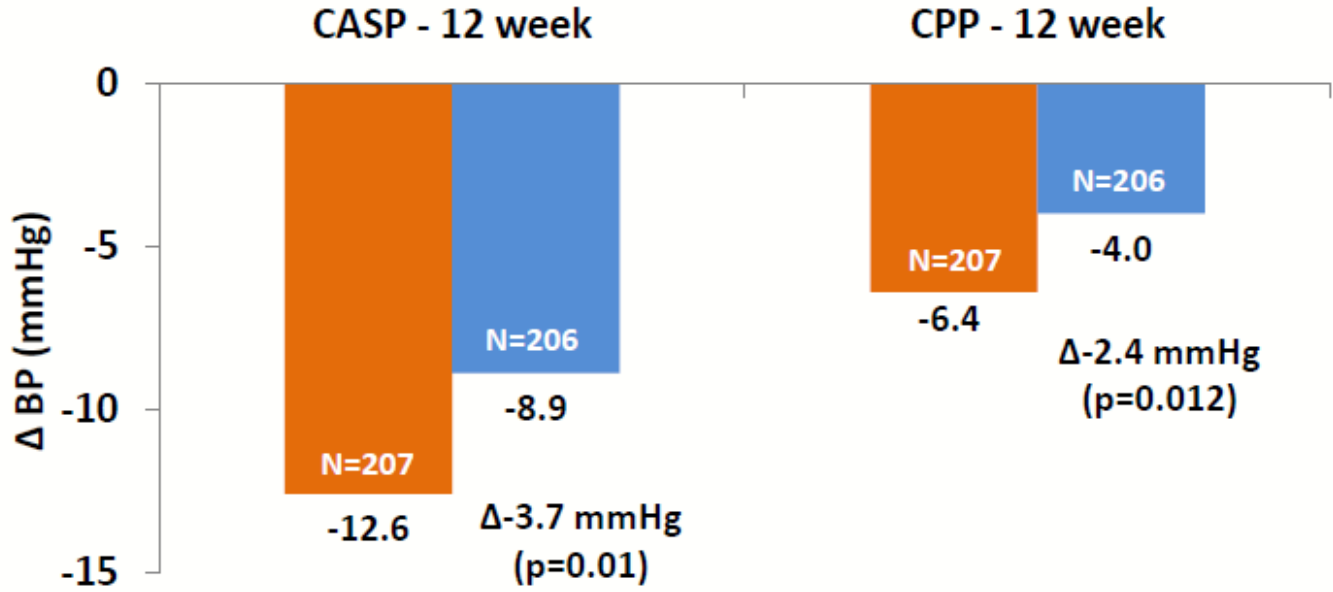


Left atrial volume



PRINCIPAL RESULTS OF THE PROSPECTIVE COMPARISON OF ANGIOTENSIN RECEPTOR NEPRILYSIN INHIBITOR WITH ANGIOTENSIN RECEPTOR BLOCKER MEASURING ARTERIAL STIFFNESS IN THE ELDERLY (PARAMETER) STUDY

Primary and key secondary outcomes:
Change from baseline in mean CASP and CPP at Week 12



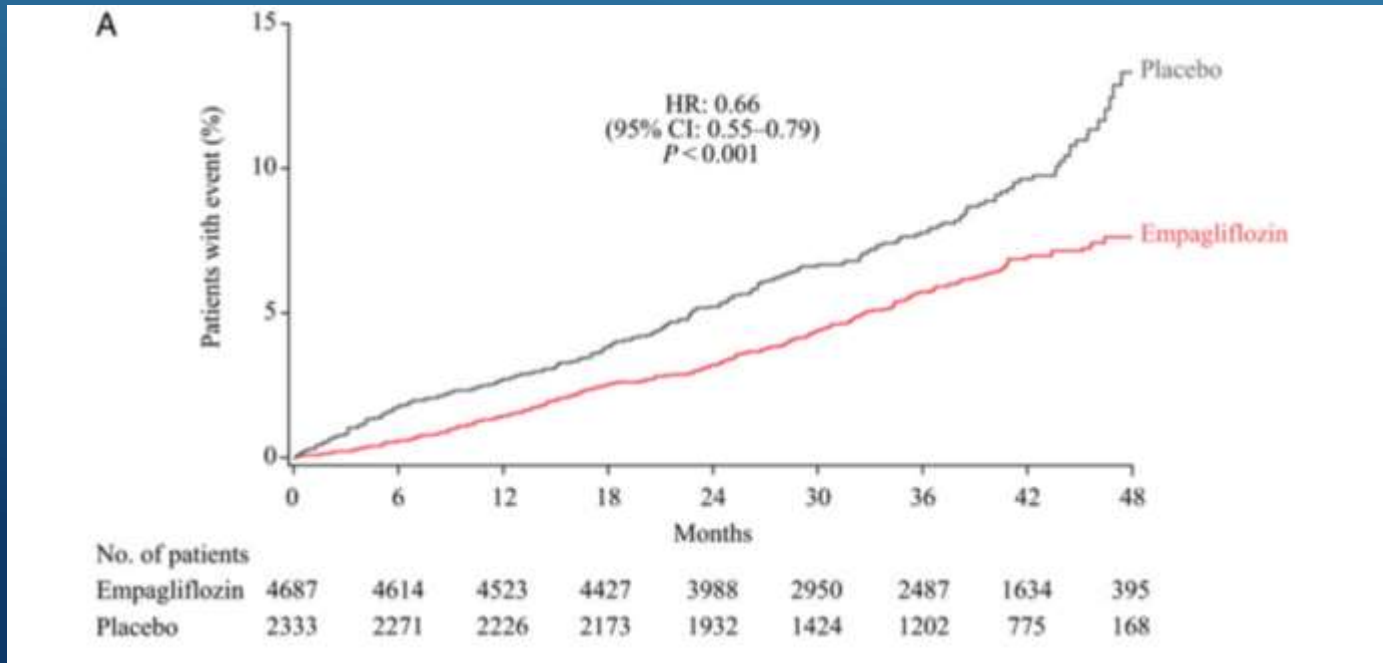
HFPEF AND RANOLAZINE

- ▶ There is **preliminary evidence** from two small studies that it **might have a potential in PAH**. In one small open-label pilot study in 11 patients with symptomatic PAH, ranolazine was demonstrated to be safe and associated with **improvement in functional class, reduction in RV size, and improvement in RV strain during exercise**.
- ▶ In another non randomized pilot study in 10 patients with HFpEF and **isolated post-capillary PH, mean PA pressure and PCWP significantly decreased, PVR remained unchanged, and 6-minute walking distance increased, during 6-month treatment with ranolazine (1000 mg daily)**.
- ▶ Clearly, **further evidence** in adequately powered, prospective studies is needed to investigate the effects of ranolazine on prognostic endpoints in **PH-HFpEF**.

EFFECT OF IVABRADINE IN PATIENTS WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION: **THE EDIFY** RANDOMIZED PLACEBO-CONTROLLED **TRIAL**

- ▶ **Aims** : This randomized, double-blind, placebo-controlled trial assessed whether heart rate (HR) reduction with **ivabradine** improves cardiac function in heart failure with preserved ejection fraction (**HFpEF**).
- ▶ **Methods and results** : 179 patients in New York Heart Association (NYHA) classes II and III, in sinus rhythm, with HR of ≥ 70 b.p.m., NT-proBNP of ≥ 220 pg/mL (BNP ≥ 80 pg/mL) and left ventricular ejection fraction of $\geq 45\%$. Patients were followed for 8 months on the change and assessed for **three co-primary endpoints: echo-Doppler E/e' ratio, distance on the 6-min walking test (6MWT), and plasma NT-proBNP concentration.**
- ▶ **Conclusions** : In patients with HFpEF, HR reduction with ivabradine did not improve outcomes. These findings **do not support the use of ivabradine in HFpEF.**

HEART FAILURE HOSPITALIZATIONS REDUCED SUBSTANTIAL WITH THE SGLT-2 INHIBITOR EMPAGLIFOZIN



CONCLUSION:

In patients with type 2 diabetes and high cardiovascular risk, empagliflozin reduced heart failure hospitalization and cardiovascular death, with a consistent benefit in patients with and without baseline heart failure.

FAIR-HFPEF DESIGN

- ▶ Design: Multicentre, randomized (1:1), double-blind, placebo-controlled
- ▶ Main inclusion criteria:
 - ▶ - NYHA class II / III, **LVEF \geq 45%**, SR, BNP/NT-proBNP $>100/ >300$ pg/mL or MRproANP >120 mmol/L (if in AF, twice), 6MWT < 450 m
 - ▶ - **Iron deficiency**: serum ferritin <100 μ g/L or TSAT $<20\%$
 - ▶ - **Hb: 9.0-14.0g/dl**
- ▶ Primary endpoint
 - ▶ - Change in 6MWT at week 24

HEART FAILURE WITH PRESERVED EJECTION FRACTION AND ATRIAL FIBRILLATION

- ▶ There are no treatments for patients with HFpEF and AF that have been shown to improve prognosis, aside from **anticoagulation**
- ▶ **Rate control** is suggested in elderly, symptomatic patients to reduce symptomatic burden, improve ventricular filling time and prevent decongestion
- ▶ **Rhythm control** in patients with HFpEF, especially in an advanced stage with older age and multi-morbidity, is **rather challenging**, yet **ongoing studies** with early rhythm control strategies in HFpEF may hold promise in this regard
- ▶ **Catheter ablation in HFpEF** was associated with improved diastolic function in patients who maintained sinus rhythm (?)
- ▶ **Early rhythm control strategies**, which are currently under investigation, may increase the beneficial effects on symptom burden and may potentially improve prognosis.
- ▶ **Implantable cardiac devices** may also affect the prognosis in patients with HFpEF, with and without AF

RACE 3

RISK FACTOR DRIVEN UPSTREAM THERAPY IN
EARLY ATRIAL FIBRILLATION
THE **R**OUTINE VERSUS **A**GGRESSIVE UPSTREAM
RHYTHM **C**ONTROL FOR PREVENTION OF **E**ARLY
PERSISTENT ATRIAL FIBRILLATION IN HEART
FAILURE STUDY

RACE 3 : FLOWCHART

Patients with early persistent AF and HF



Causal treatment of AF and HF



Risk factor driven upstream

Conventional

Upstream therapy consists of:

- 1) Mineralocorticoid receptor antagonist
- 2) Statin 3
- 3) ACE-inhibitors
and/or angiotensin-receptor blockers
- 4) Cardiac rehabilitation:
-physical activity
-dietary restrictions

ECV after 3 weeks



Guideline-recommended rhythm and rate control



7-day Holter at 1-year

RACE 3 : CONCLUSION AND IMPLICATION

- ▶ The RACE 3 study shows that risk factor driven upstream therapy, including treatment of risk factors and change of lifestyle, is effective and feasible to improve maintenance of sinus rhythm in patients with early persistent AF and HF
- ▶ The effect of upstream therapy on reduction of risk factors and cardiovascular diseases, instead of atrial remodeling, was favourable

HEART FAILURE WITH PRESERVED EJECTION FRACTION AND ATRIAL FIBRILLATION

- ▶ **The VIP-HF** (Ventricular tachyarrhythmia detection by Implantable Loop Recording in Patients with Heart Failure and Preserved Ejection Fraction) **registry** is due to report its results in **late 2018**
- ▶ Whether cardiac resynchronization therapy (**CRT**) is beneficial in HFpEF with and without AF needs to be determined
- ▶ Substudies of CRT trials have shown that patients with less severe LV dysfunction (LVEF >35%) appeared to derive clinical and structural benefit from resynchronization
- ▶ The value of CRT in HFpEF patients with AF needs to be explored in future trials.

RIGHT HEART DYSFUNCTION AND FAILURE IN HEART FAILURE WITH PRESERVED EJECTION FRACTION: MECHANISMS AND MANAGEMENT

- ▶ RVD is present in at least 20% and potentially up to 30-50% of patients with HFpEF
- ▶ The high prevalence of RVD and its potent prognostic consequences in HFpEF support the development of **treatment strategies targeting the right side in HFpEF**
- ▶ Until now, many previous attempts have demonstrated **neutral results**
- ▶ **Class III recommendation for PAH-approved treatment for patients with PH due to left heart disease**

RIGHT HEART DYSFUNCTION AND FAILURE IN HEART FAILURE WITH PRESERVED EJECTION FRACTION: MECHANISMS AND MANAGEMENT

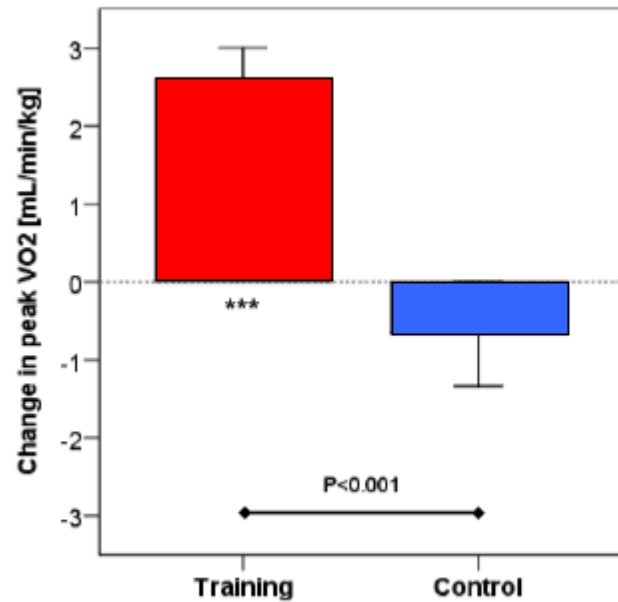
- ▶ A cornerstone in the current management of symptomatic patients with HFpEF, particularly those with signs of right heart failure, is **adequate volume management**
- ▶ **Excessive volume overload** is a major driver of **decompensation**, deterioration of RV function and multi-organ dysfunction.
- ▶ In clinical practice, in many patients with RVD-HFpEF diuretics are not given in sufficiently high dosages to ensure decongestion /euvolaemia, and early identification of patients who are at risk for diuretic resistance is important.
- ▶ In addition, patients should be counselled to **avoid excessive fluid and salt intake**.

HFPEF AND EXERCISE

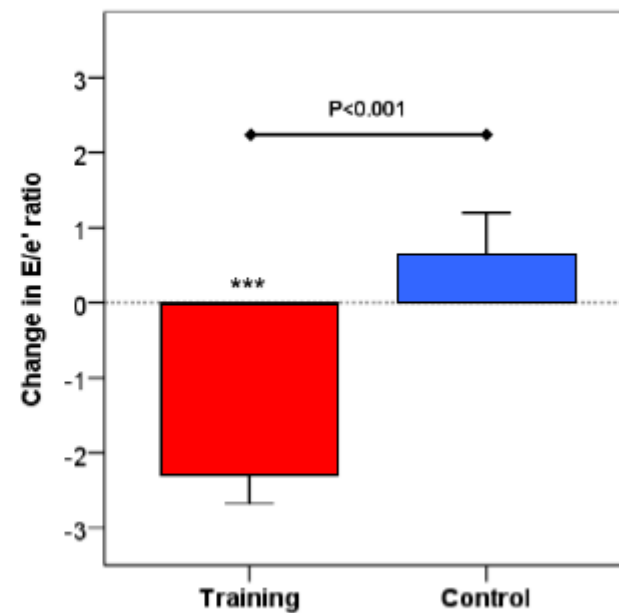
- ▶ **Obese, older patients** with stable HFpEF benefit from **caloric restriction and aerobic exercise training**. It is recommended to encourage regular aerobic exercise training in all patients with heart failure, to improve their functional capacity and symptoms (class IA recommendation).

EXERCISE TRAINING IN HFPEF - EX-DHF-P STUDY

Peak VO₂



E/e' ratio



REVERSING THE CARDIAC EFFECTS OF SEDENTARY AGING IN MIDDLE AGE—A RANDOMIZED CONTROLLED TRIAL IMPLICATIONS FOR HEART FAILURE PREVENTION

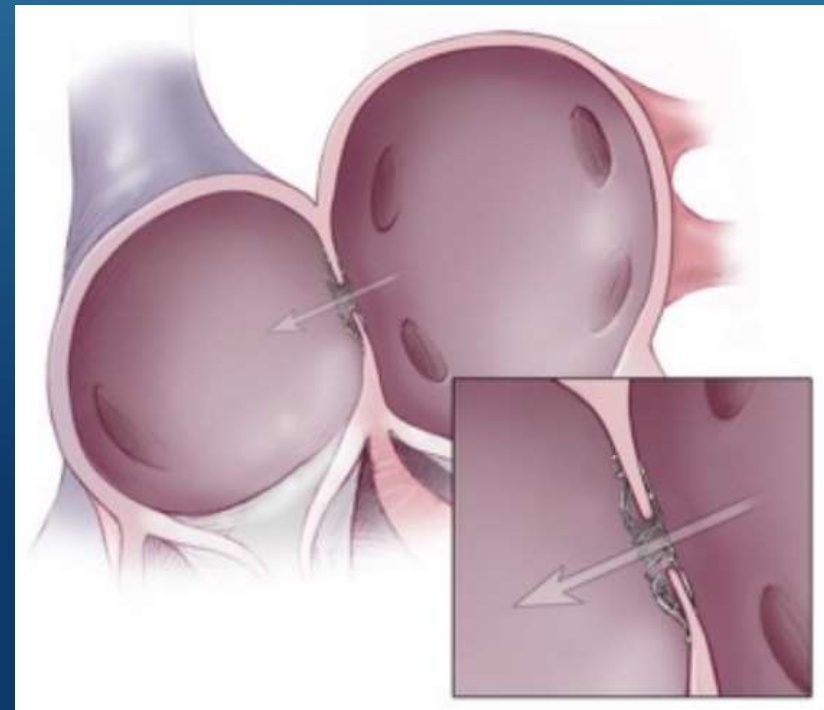
- ▶ Sixty-one (48% male) healthy, sedentary, middle-aged participants (53±5 years) were randomly assigned to either 2 years of exercise training (n=34) or attention control (control; n=27).
- ▶ In previously sedentary healthy middle-aged adults, 2 years of exercise training improved maximal oxygen uptake and decreased cardiac stiffness.
- ▶ Regular exercise training may provide protection against the future risk of heart failure with a preserved ejection fraction by preventing the increase in cardiac stiffness attributable to sedentary aging

Monitoring of pulmonary artery pressures using a wireless implantable haemodynamic monitoring system (CardioMems) may be considered in symptomatic patients with HF with previous HF hospitalization in order to reduce the risk of recurrent HF hospitalization.

IIb

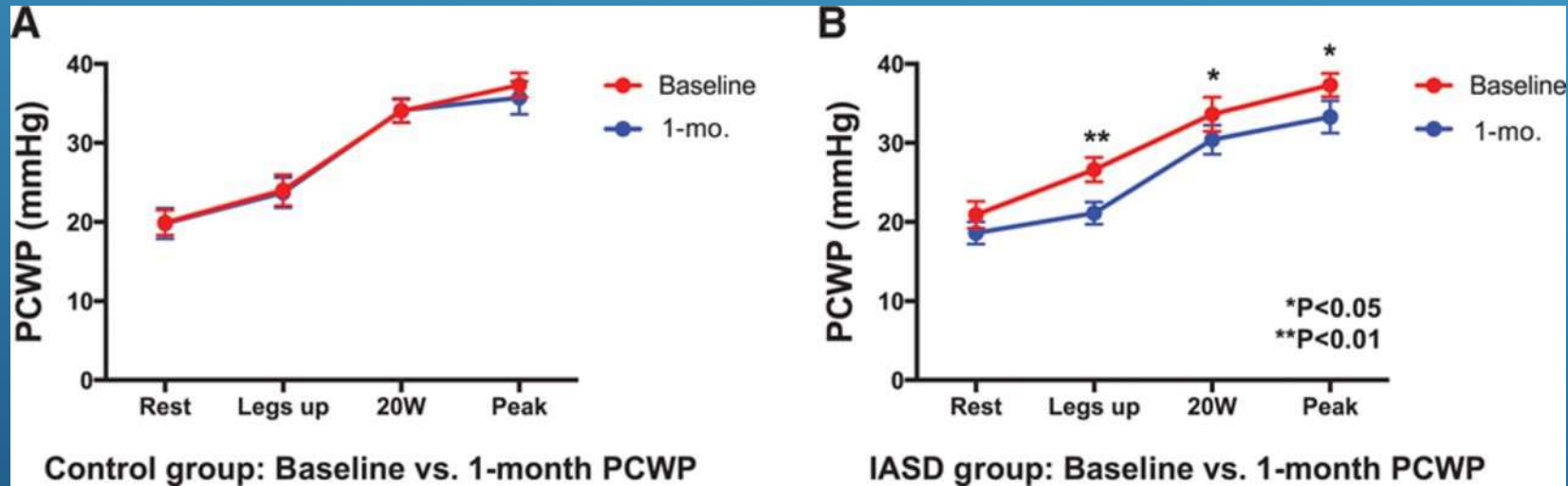
B

INTER-ATRIAL SHUNT DEVICE



- The use of a transcatheter interatrial shunt device was safe and reduced left atrial pressures during exercise and thus demonstrated potential efficacy in patients with HFpEF.
- Whether the observed haemodynamic effects, and the sudden **change from pressure to volume overload of the right heart**, will be beneficial during longer follow-up in patients with HFpEF remains to be evaluated.

Transcatheter Interatrial Shunt Device for the Treatment of Heart Failure With Preserved Ejection Fraction (**REDUCE LAP-HF I**)



Pulmonary capillary wedge pressure during exercise hemodynamic testing: baseline versus 1-month postrandomization, stratified by treatment group.

Conclusions: In patients with HF and EF $\geq 40\%$, **IASD treatment reduces PCWP during exercise**. Whether this mechanistic effect will translate into sustained improvements in symptoms and outcomes requires further evaluation.

CONCLUSIONS

- ▶ Heart failure with preserved or mean range ejection fraction is a **major and growing public health problem**, the most common form of HF in patients older than 65 years.
- ▶ The **ideal treatment** modality for HFpEF should be one that is able to **relieve symptom but also provide mortality and morbidity benefit**.
- ▶ To date, there are **no approved therapies** available for reducing mortality or hospitalizations for these patients.
- ▶ The **failure to develop successful therapies** for the management of HFpEF may be because of the **poor understanding of the pathophysiology** of HFpEF, **inadequate** standardization of the HFpEF **diagnosis**, and the lack of strict definition and **inadequate differentiation** of disease subtypes.

CONCLUSIONS

- ▶ In addition, HFpEF is likely a **systemic syndrome**, with **multi-factorial pathophysiology**, underlying **age-related changes**, frequent **multiple chronic co-morbidities**, **multi-organ involvement**, and **clinical heterogeneity**.
- ▶ These concepts have led to the proposal of **key phenotypes in HFpEF**, with each phenotype having somewhat distinct pathophysiological and treatment implications
- ▶ **Advances in diagnostic algorithms, imaging, and invasive assessment** will allow for more accurate and earlier diagnosis
- ▶ Diastolic dysfunction **CANNOT** account for the disorder and abnormalities of **systole are becoming more recognized**
- ▶ Diuretics remain the only recommended therapy for HFpEF
- ▶ **Designing therapies to match specific patient phenotypes may prove to be a more effective approach**



**ΚΑΡΔΙΟΧΕΙΡΟΥΡΓΙΚΟ
ΚΕΝΤΡΟ
ΒΟΡΕΙΑΣ ΕΛΛΑΔΑΣ**

