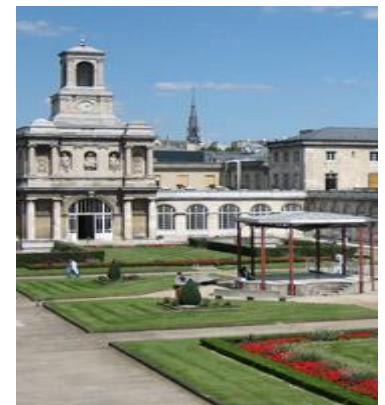


Patient profiling and combination treatment

Damien Logeart
Hôpital Lariboisière, Paris



What is the issue?

Type of HF		HF-rEF	HF- mrEF	HF-pEF
Criteria	1	Symptoms ± Signs	Symptoms ± Signs	Symptoms ± Signs
	2	LVEF ≤ 40%	LVEF 41-49%	LVEF ≥ 50%
	3	<p style="text-align: center;">There is a need to profile HFpEF patients for more specific/efficient therapeutic strategy</p>		

(relatively) homogeneous pathophysiology

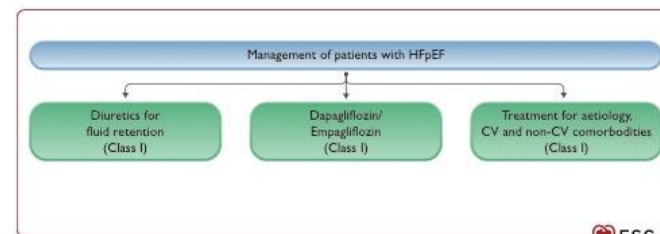


Strong evidence-based medicine for all

Heterogeneous pathophysiology



Lack of evidence-based medicine



To look for secondary HFpEF

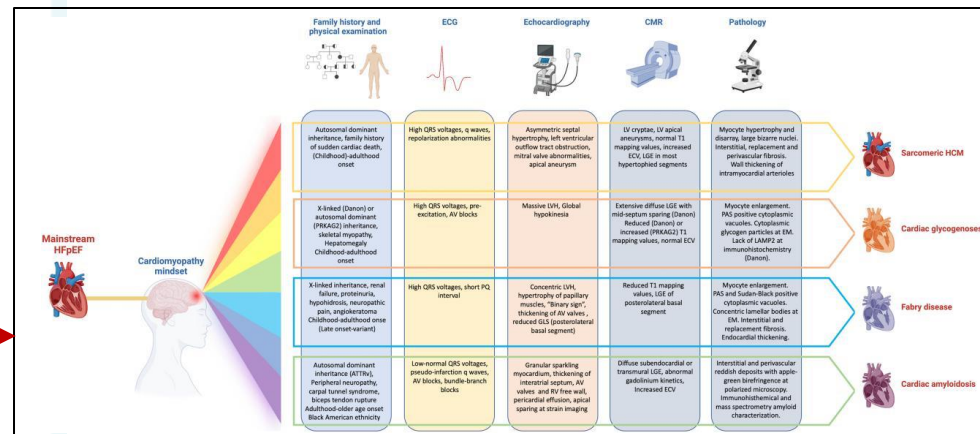
Primary HFpEF

- Age
- Sex
- Type 2 diabetes mellitus
- Obesity
- Sleep apnoea
- Arterial hypertension
- Arterial hypotension
- Pulmonary hypertension
- Chronic obstructive pulmonary disease
- Iron deficiency
- Coronary artery disease
- Atrial fibrillation
- High heart rate
- Chronotropic incompetence
- Atrial functional mitral regurgitation
- Functional tricuspid regurgitation
- Cachexia and sarcopenia
- Very high ejection fraction (>65%/>70%)
- LVEF between 50% and 55%
- HFpEF in patients with cancer

Secondary HFpEF

- Restrictive cardiomyopathies
- Hypertrophic cardiomyopathy
- Constrictive pericarditis
- Valvular heart disease

Keep in mind !



Important phenotypes in primary HFpEF

Primary HFpEF

Age

Sex

Type 2 diabetes mellitus

Obesity

Sleep apnoea

Arterial hypertension

Arterial hypotension

Pulmonary hypertension

Chronic obstructive pulmonary disease

Iron deficiency

Coronary artery disease

Atrial fibrillation

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HFpEF in patients with cancer

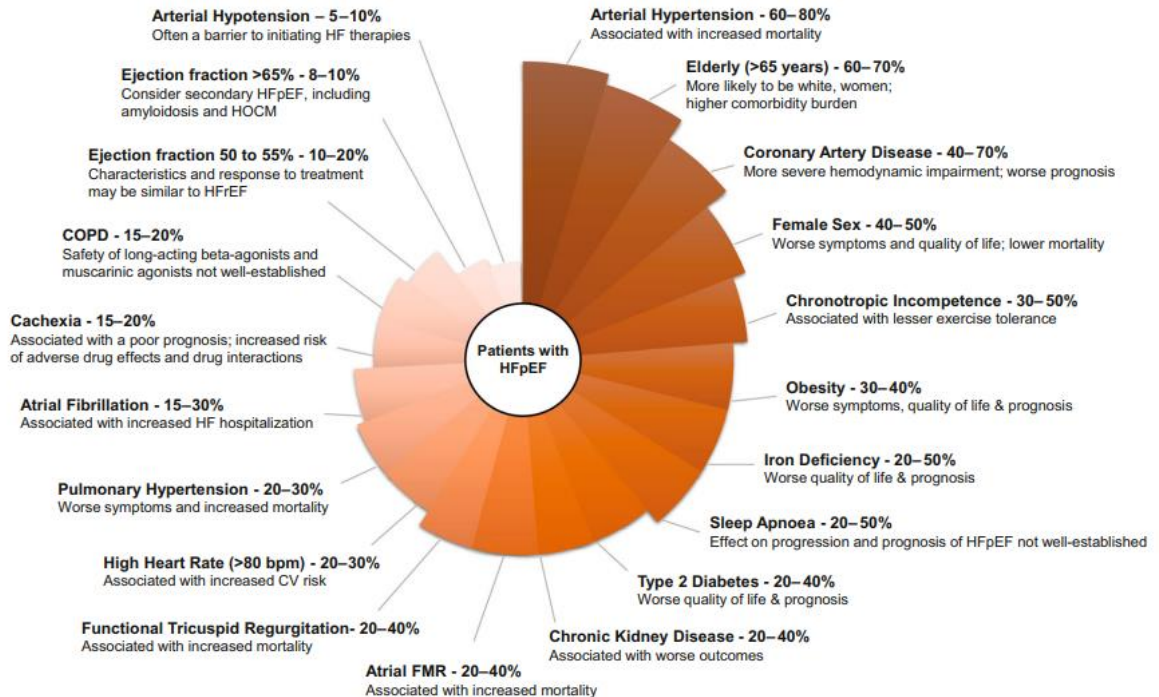
Secondary HFpEF

Restrictive cardiomyopathies

Hypertrophic cardiomyopathy

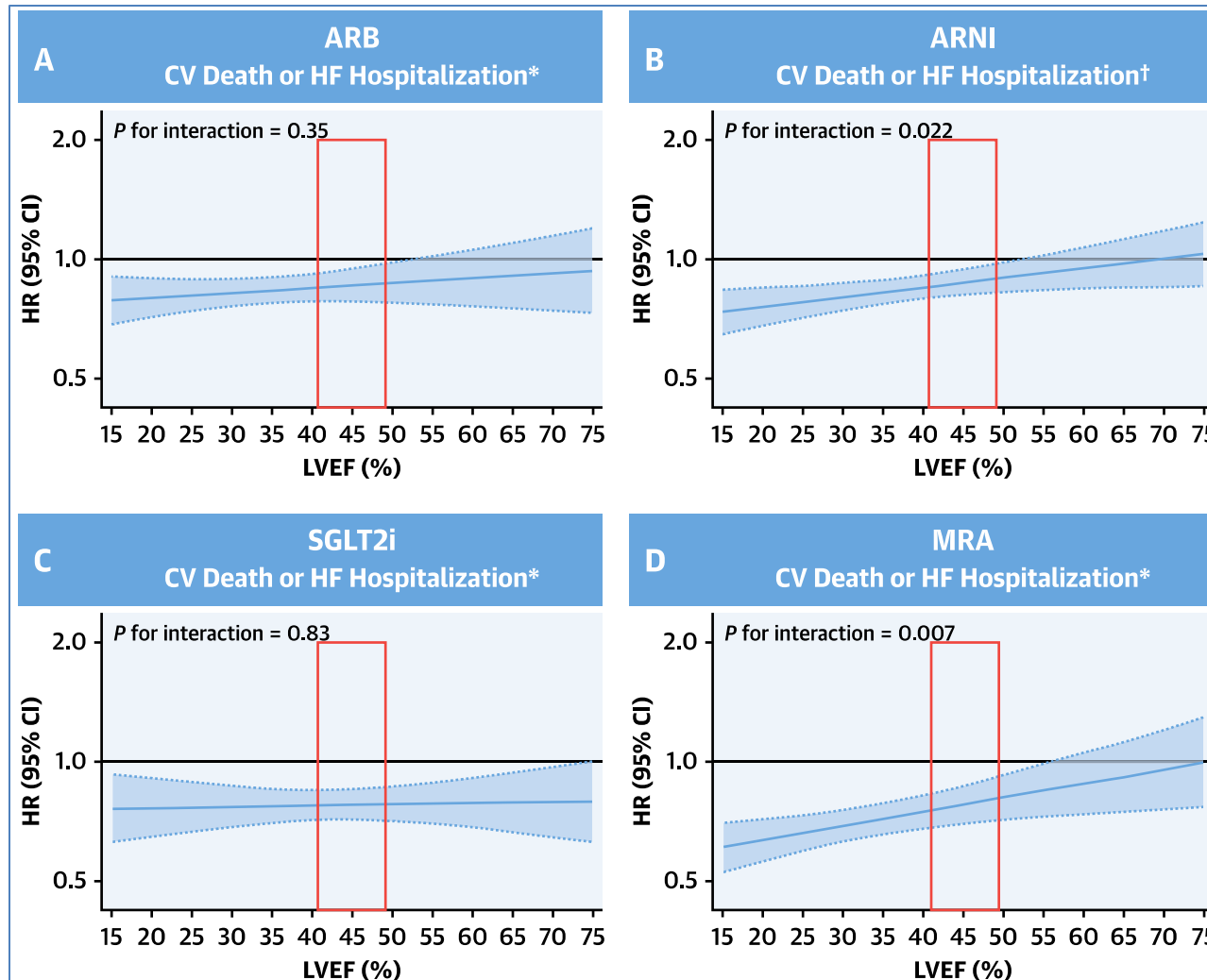
Constrictive pericarditis

Valvular heart disease

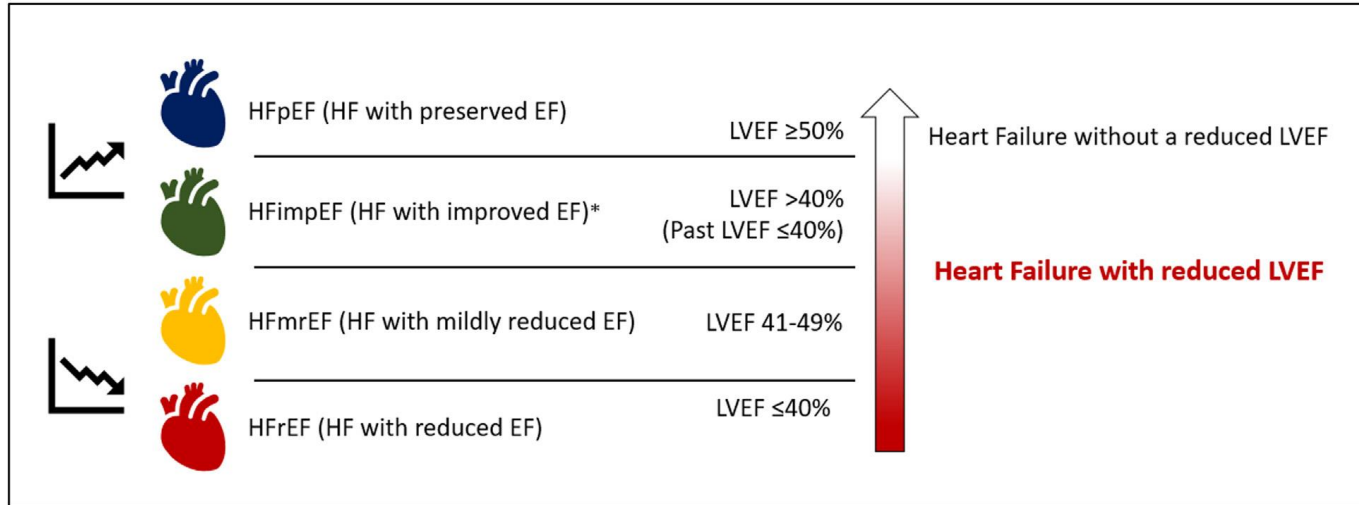


LVEF between 50% and 55%

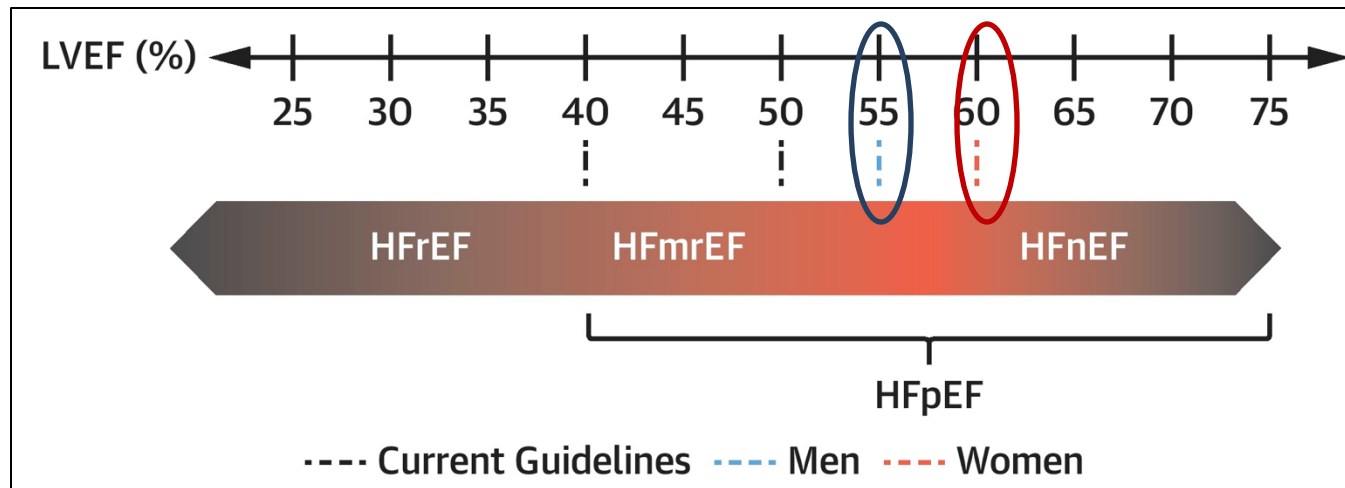
ARB, MRA, ARNi => clinical benefits up to EF 50-55%



Do we have to rethink LVEF threshold for classifying HF and for using EBM-drugs?

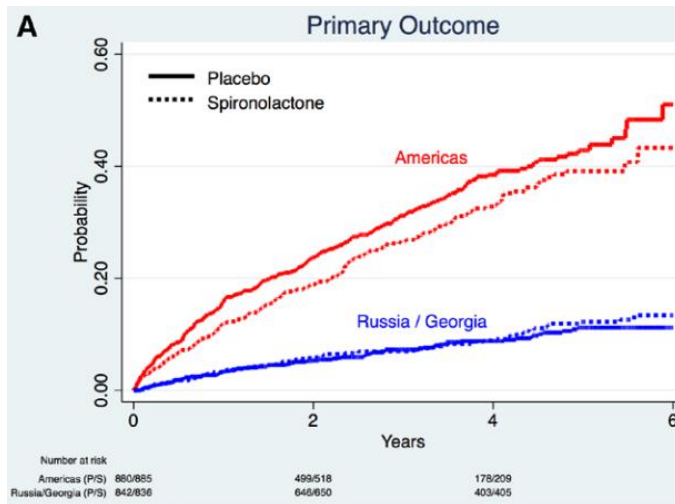
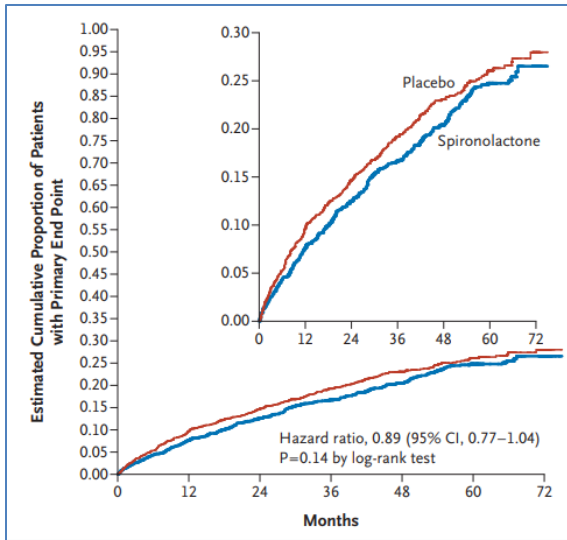


Dimond MG et al. JACC-HF 2024



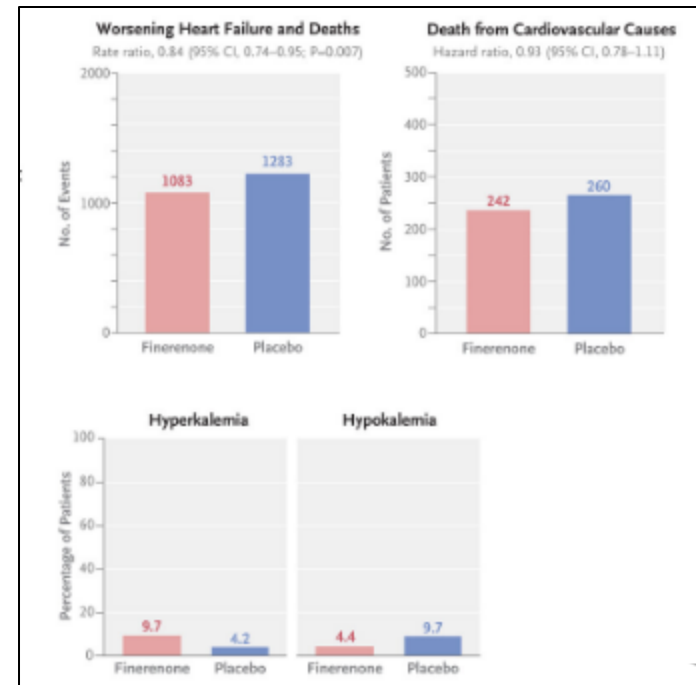
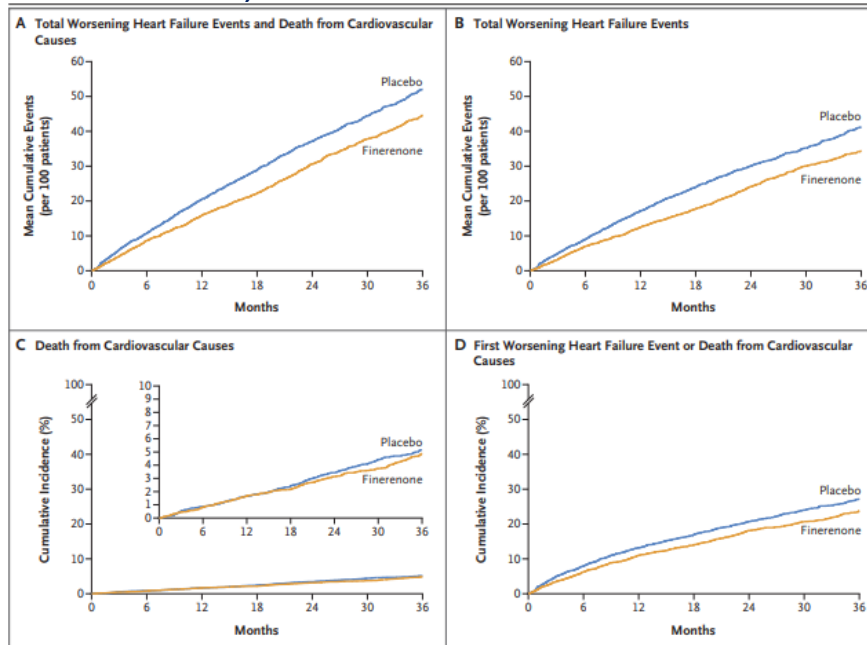
Lam C, Solomon SD. JACC 2021

MRA in HFpEF

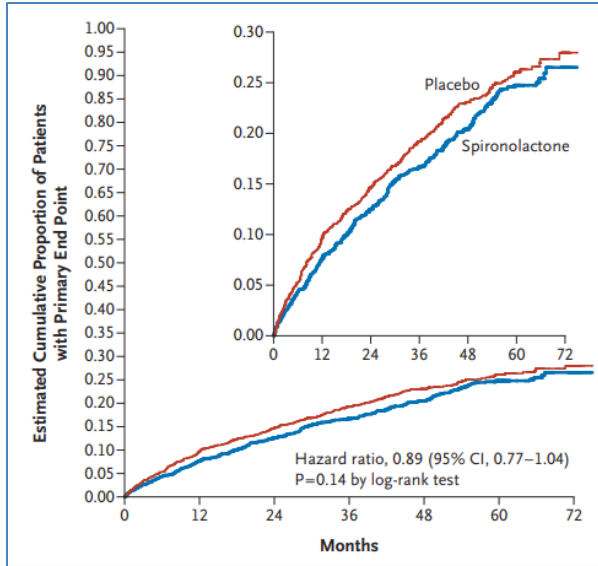


TOPCAT trial, 2014

FINEARTS-HF, NEJM 2024

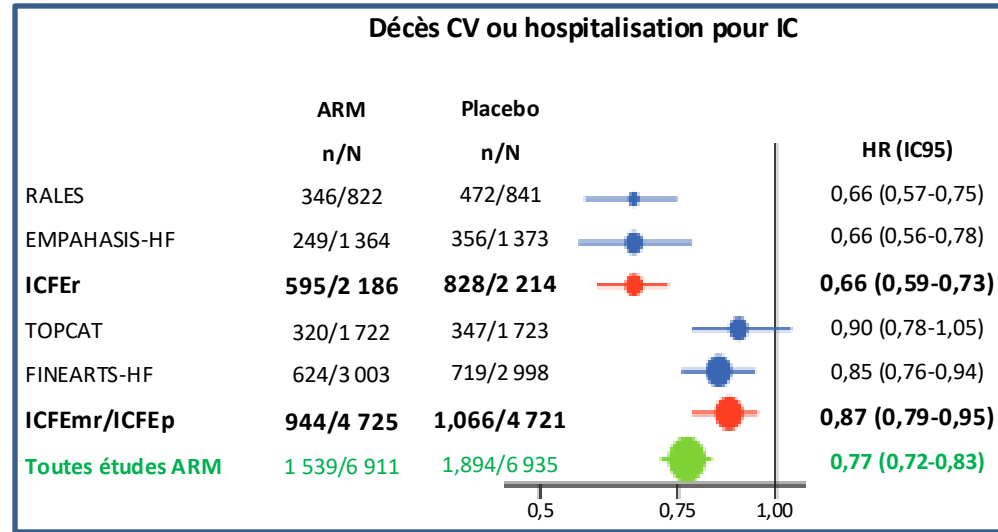


MRA in HFpEF

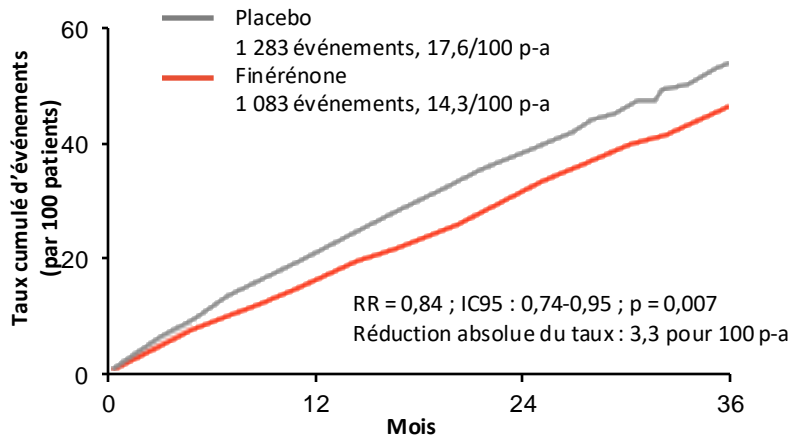


TOPCAT trial, 2014

FINEARTS-HF, NEJM 2024

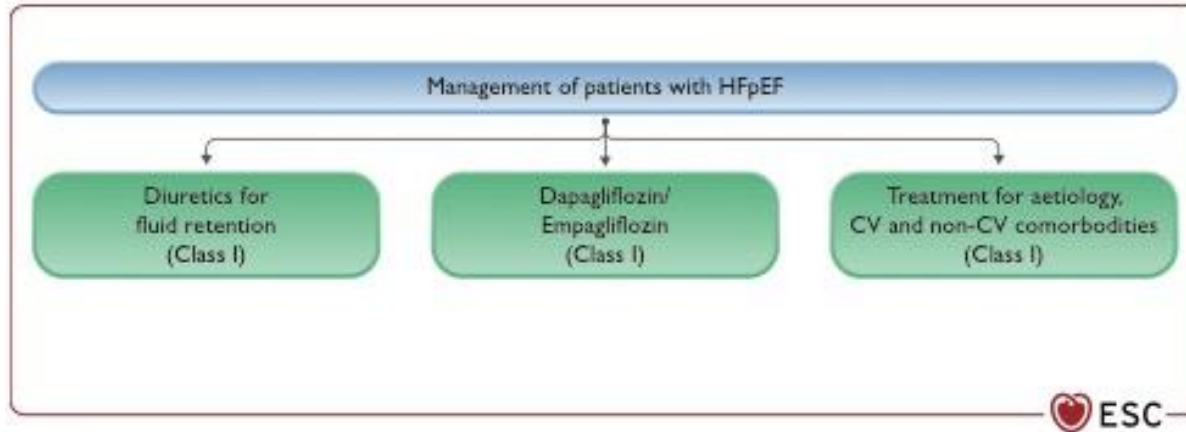


Décès cardiovasculaire et événements IC
(hospitalisations/consultations urgentes)

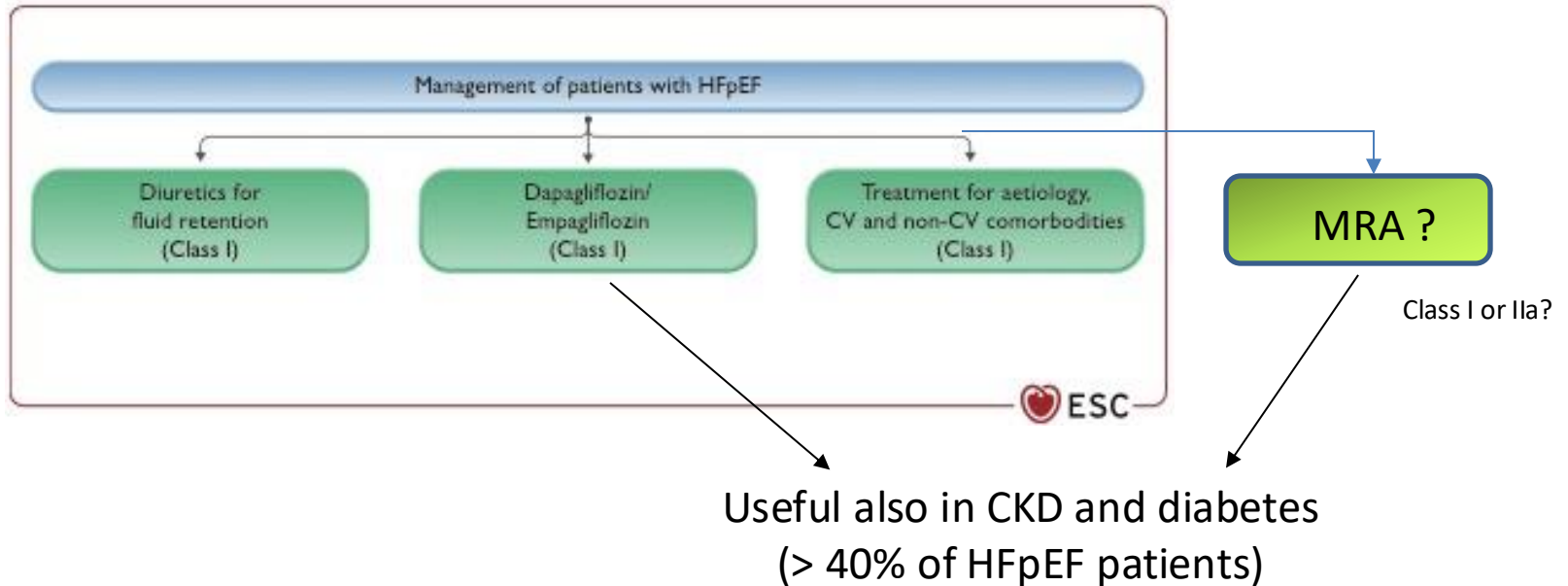


MRA in HFpEF

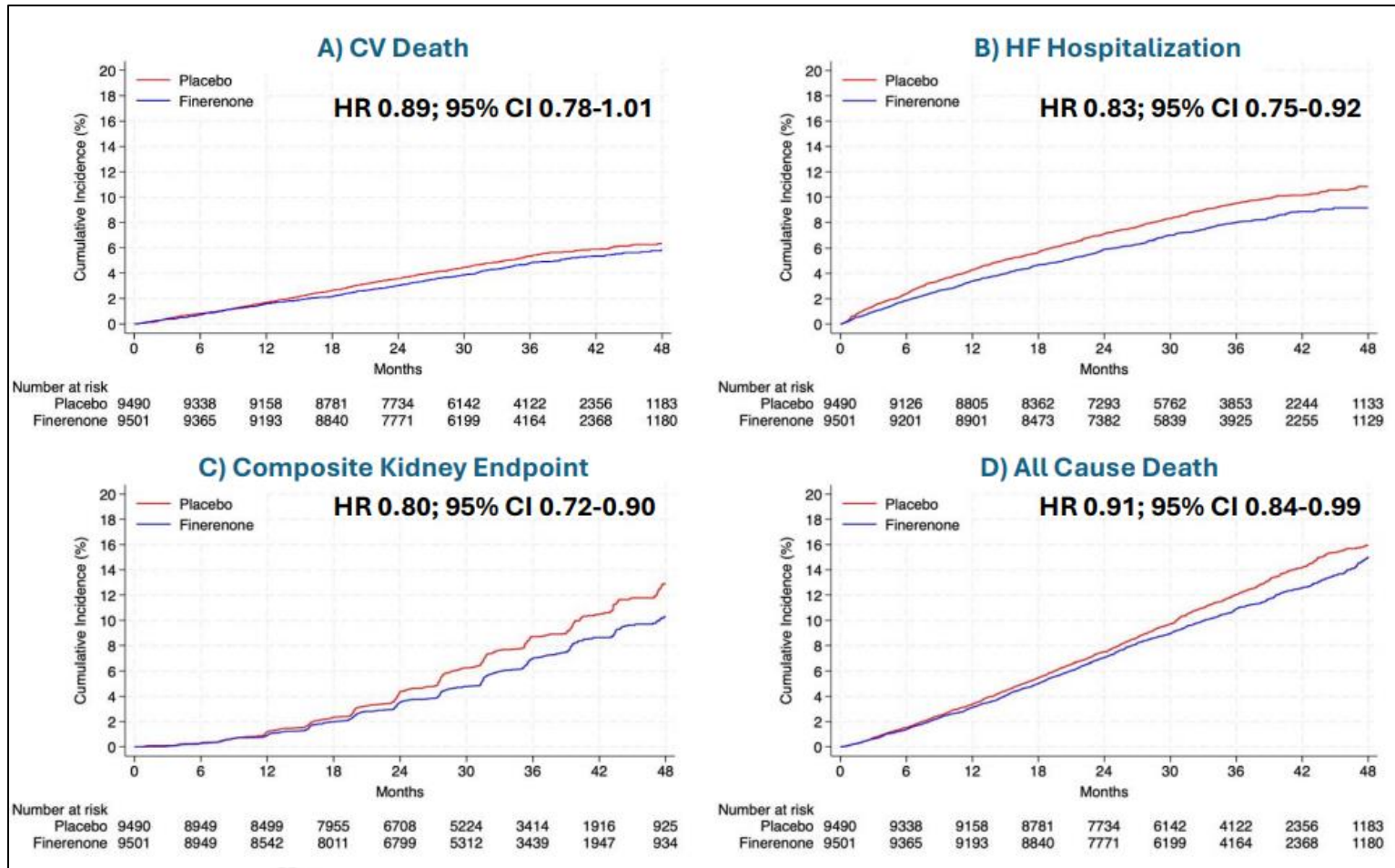
2023 ESC guidelines for HFpEF



Next ESC guidelines for HFpEF ?



MRA : meta-analysis FIDELIO-CKD, FIGARO-CKD, FINEARTS



Vaduganathan M, et al. Finerenone in heart failure and chronic kidney disease with type 2 diabetes: FINE-HEART pooled analysis of cardiovascular, kidney and mortality outcomes. Nat Med. 2024 Sep 1. doi: 10.1038/s41591-024-03264-4.

HFpEF, phenomapping and therapeutic consequences

Clinical Phenogroups in HFpEF: Detailed Phenotypes, Prognosis, and Response to Spironolactone

P1



- Normal LV geometry
- Low arterial stiffness
- Low natriuretic peptides
- Markers of COPD (not genuine HFpEF?)
- Low event rate
- Preferentially enrolled in Russia/Georgia

P2



- Concentric remodeling
- Very stiff arteries
- LA enlargement and AF
- High natriuretic peptides
- Innate immunity activation
- High risk of primary endpoint

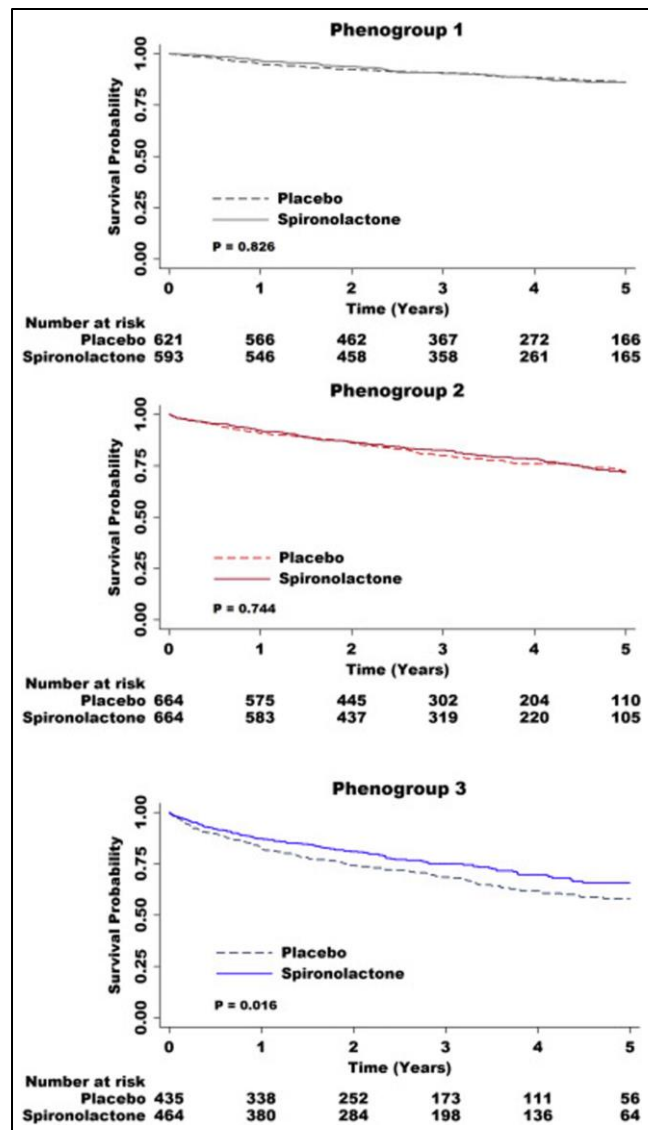
P3



- Obesity/Diabetes
- Inflammation (TNF- α)
- Abnormal metabolism, liver and renal injury/dysfunction
- High renin
- Highest risk of primary endpoint
- Preferential response to spironolactone

Cohen JB et al. JACC-HF 2020

Topcat trial



Important phenotypes in primary HFpEF

Primary HFpEF

Age

Sex

Type 2 diabetes mellitus

Obesity

Sleep apnoea

Arterial hypertension

Arterial hypotension

Pulmonary hypertension

Chronic obstructive pulmonary disease

Iron deficiency

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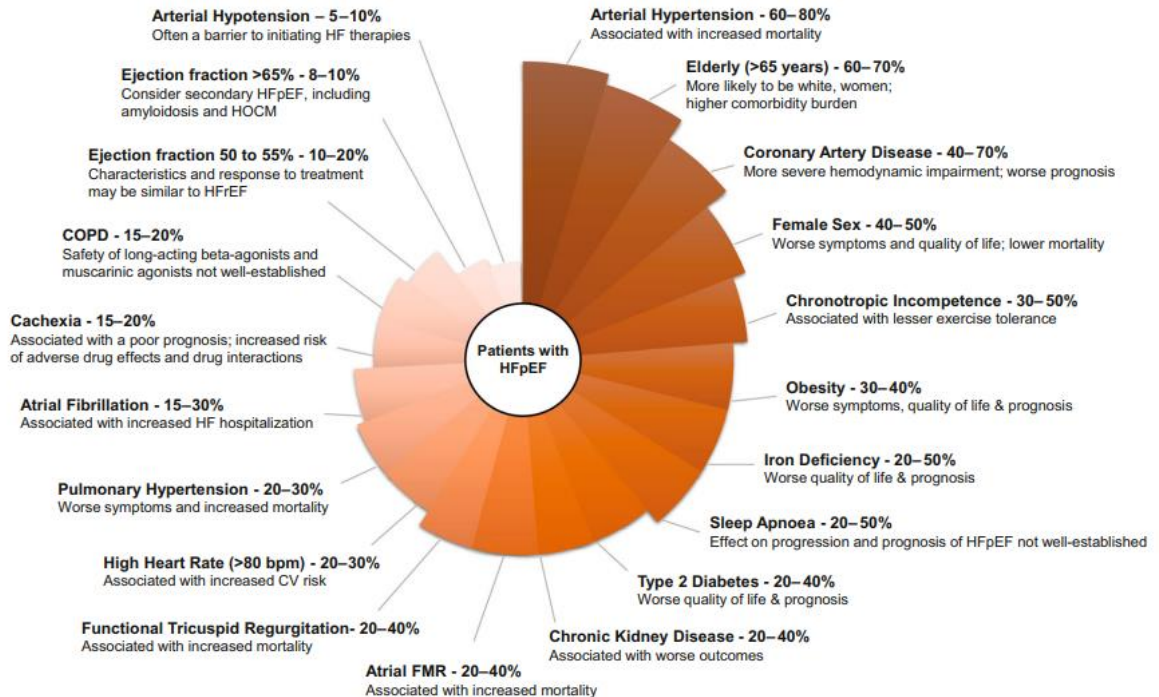
Secondary HFpEF

Restrictive cardiomyopathies

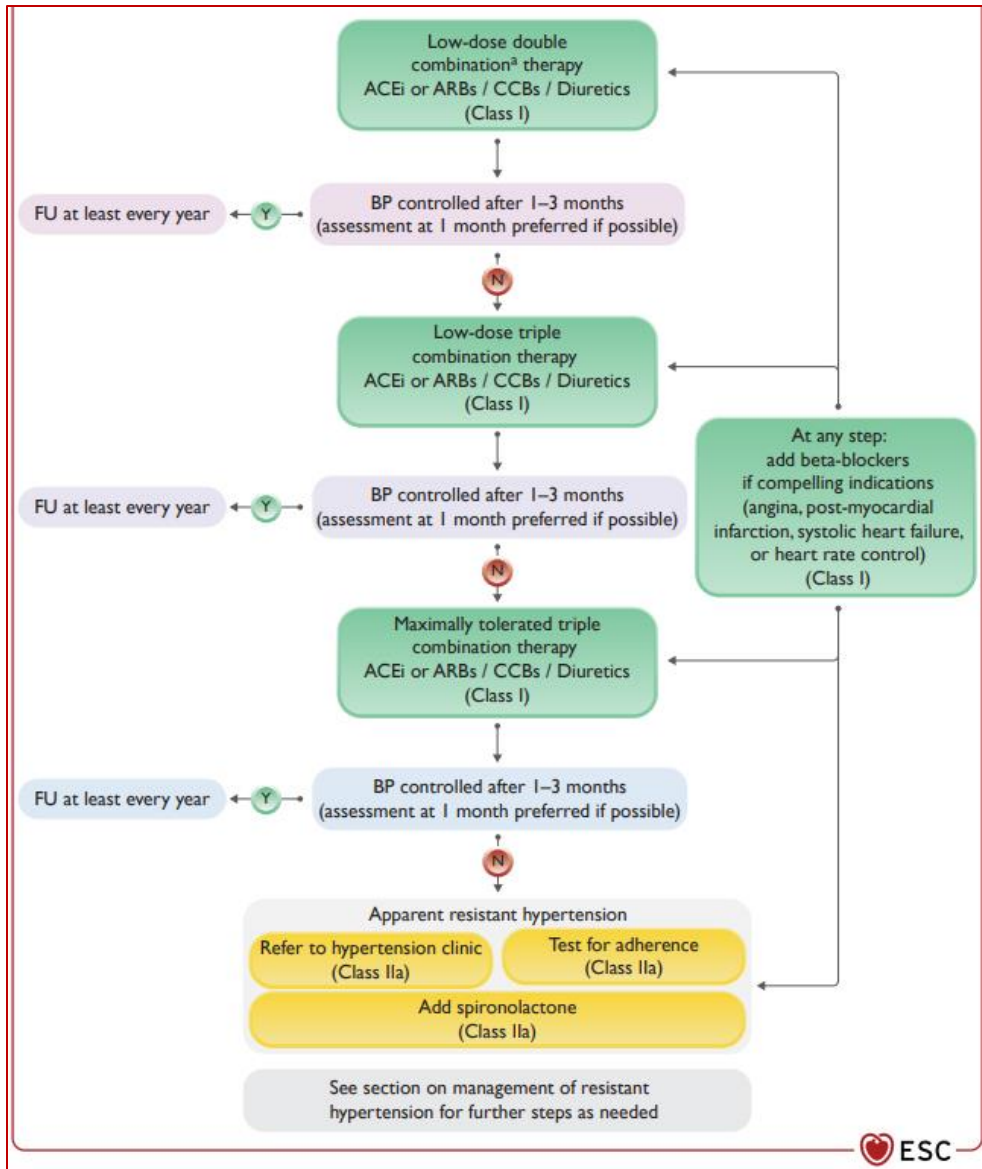
Hypertrophic cardiomyopathy

Constrictive pericarditis

Valvular heart disease



How to deal hypertension in HFpEF



of acute and chronic heart failure

with HFpEF, but the optimal treatment

diabetes, CKD, CAD, valvular heart

ension should be avoided.

elevated blood pressure and hypertension

is treated with BP-lowering therapy for confirmed

BP $\geq 129/70-79$ mmHg,

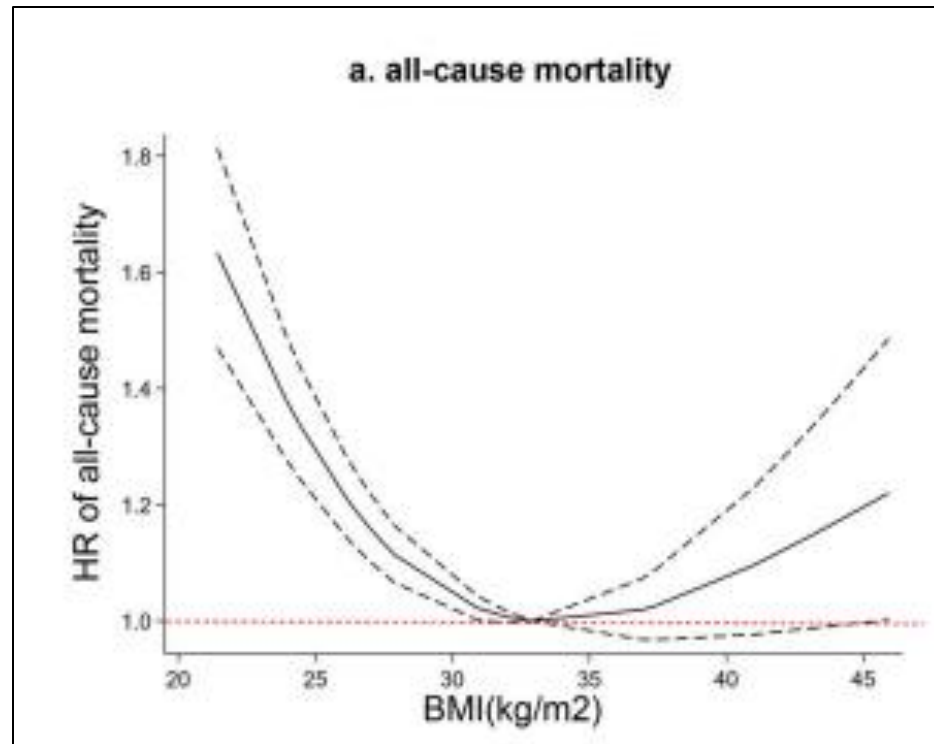
with the confirmation of on-treatment BP.

**Large room for MRA
... and maybe for ARNi**

Obesity and HFpEF : frequent and a deleterious impact

Obesity epidemic: 13% of adults were obese in 2016
(x3 versus 1975)

Obesity in > 25% of HFpEF



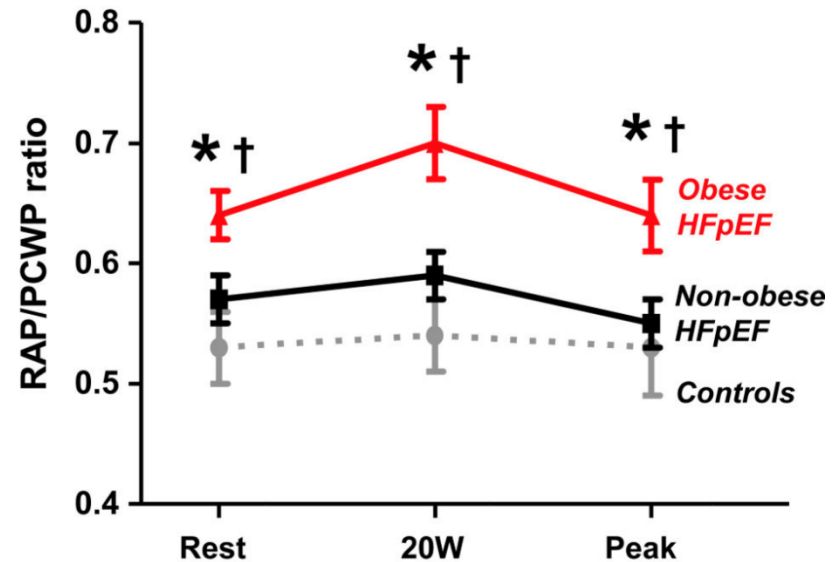
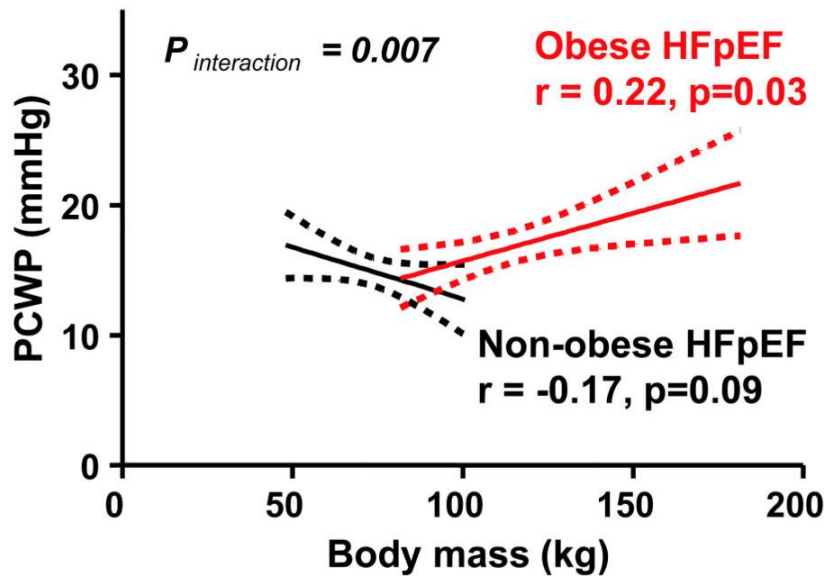
Obesity and HFpEF : frequent and a deleterious impact

Obesity epidemic: 13% of adults were obese in 2016
(x3 versus 1975)

Obesity in > 25% of HFpEF



Obesity and HFpEF: deleterious impact on pathophysiology



Circulation. 2017; 136(1): 6–19.

Obesity and HFpEF : impact of the weight loss

Effects of weight loss in heart failure patients with overweight and obesity: a systematic review and meta-analysis

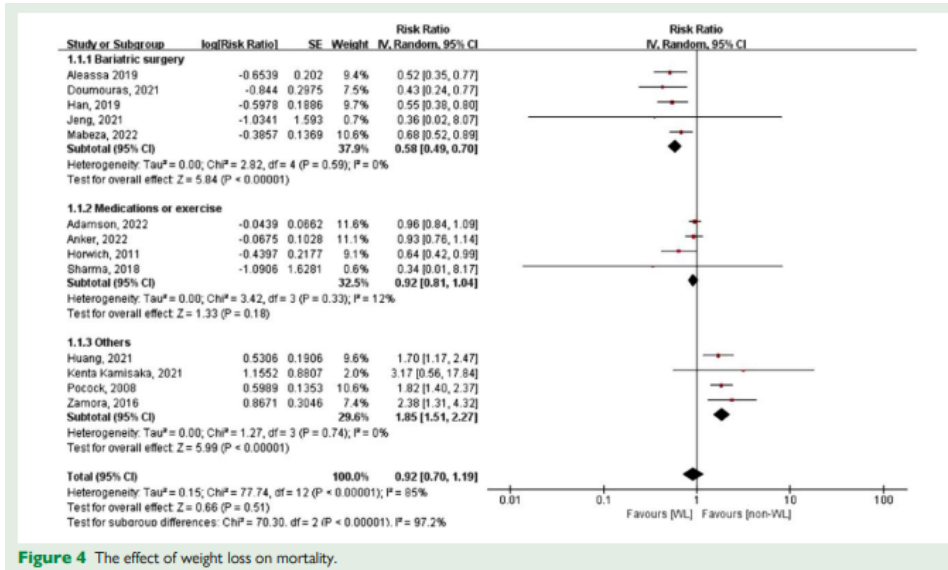


Figure 4 The effect of weight loss on mortality.

Bariatric surgery: positive impact++

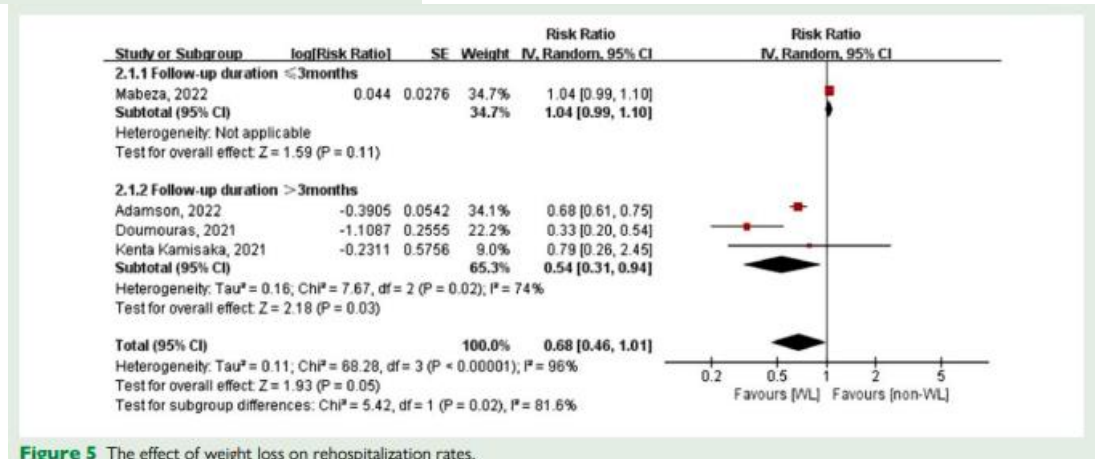


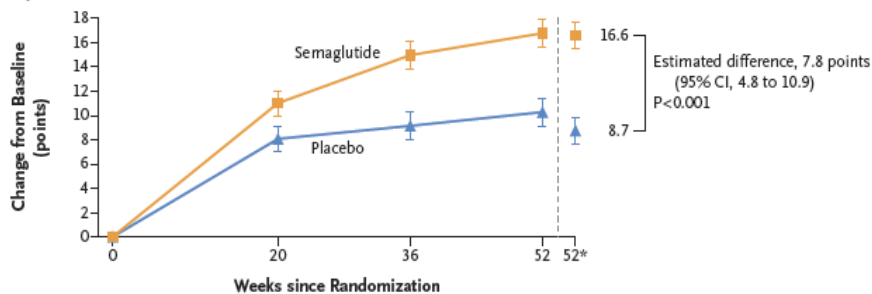
Figure 5 The effect of weight loss on rehospitalization rates.

STEP-HFpEF: semaglutide (GLP1 agonist) in HFpEF and obesity

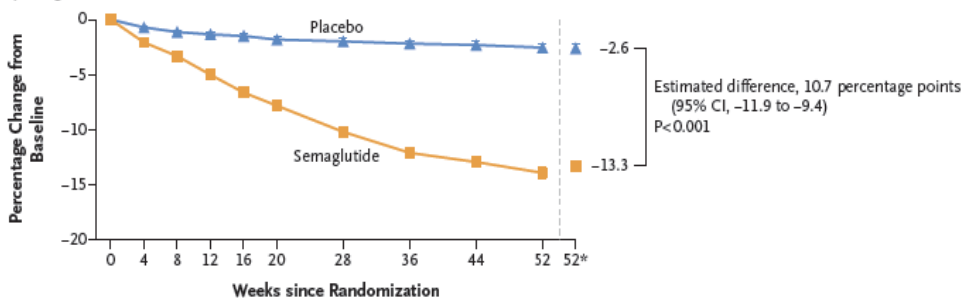
STEP-HFpEF

529 HFpEF
with BMI > 30 (BMI > 35 in 66%)
HbA1c < 6.5%

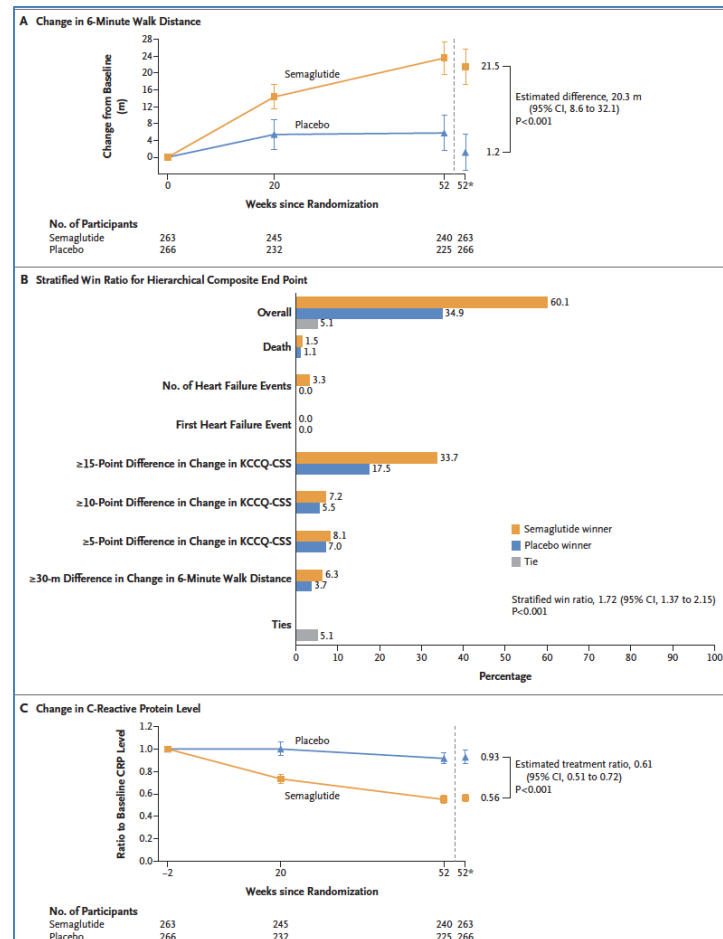
A Change in KCCQ-CSS



B Change in Body Weight



A noter aussi :
1 vs 12 hospit. pour IC au cours du suivi

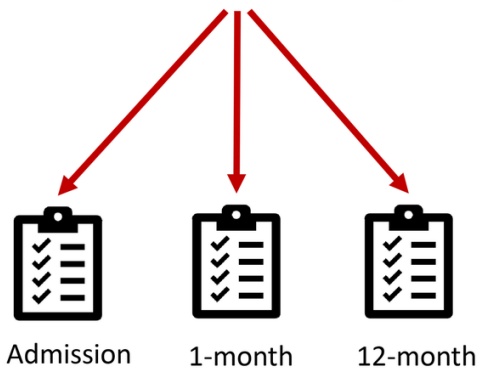


Inflammation in HFpEF: potential target?

1,281 patients with acute heart failure

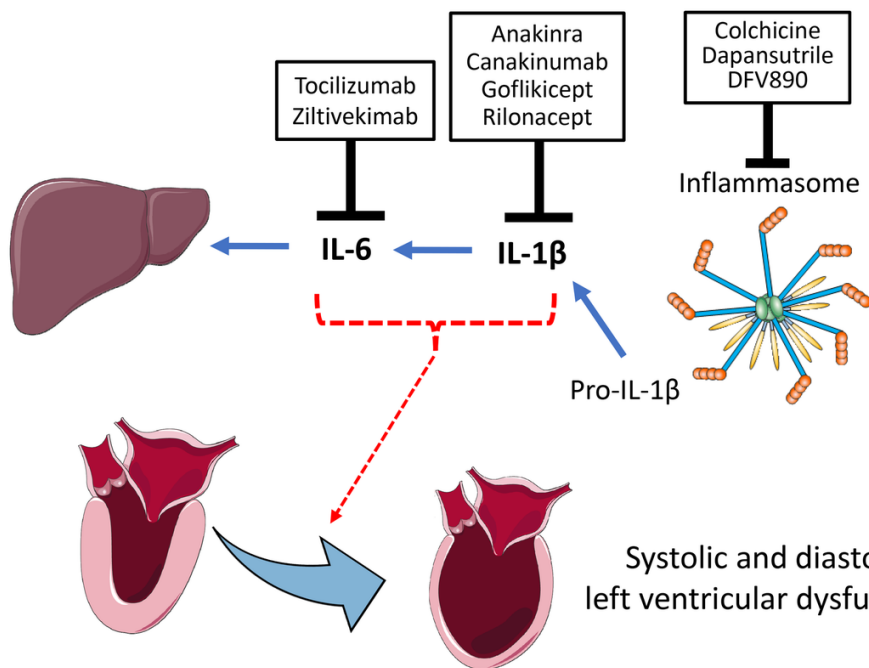


High sensitivity
C-Reactive Protein
(hsCRP)



Admission 1-month 12-month

Long-term
cumulative hsCRP



Systolic and diastolic
left ventricular dysfunction

Patients in the highest quartile of
cumulative hsCRP

- 2.4-fold higher risk of all-cause death
- 2.6-fold higher risk of CV death

Patients with
elevated hsCRP at 3 time points

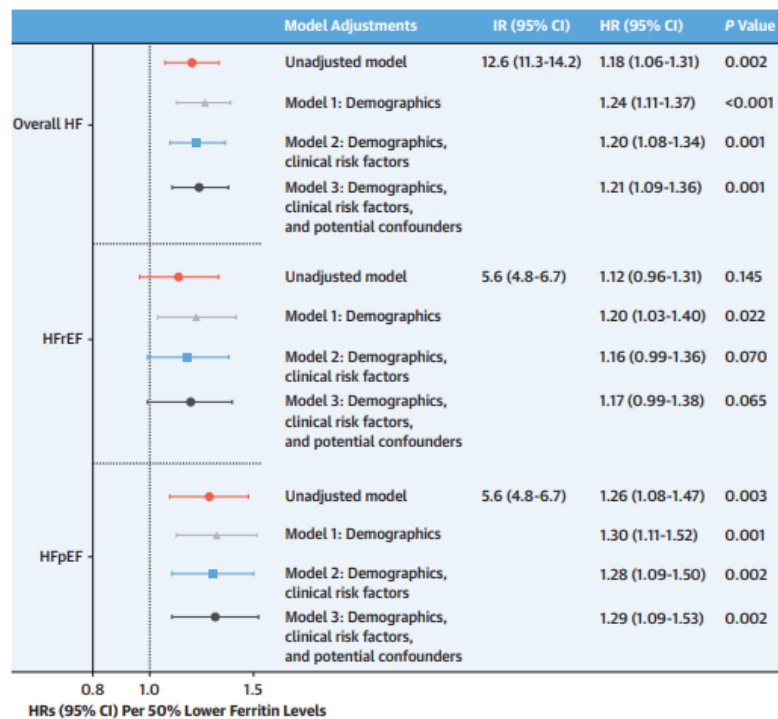
- 2.8-fold higher risk of all-cause death
- 3.1-fold higher risk of CV death

HERMES trial
Ziltivekimab dans HFpEF avec CRP>2

JAHA 2023;12:e031786

Iron deficiency and HFpEF

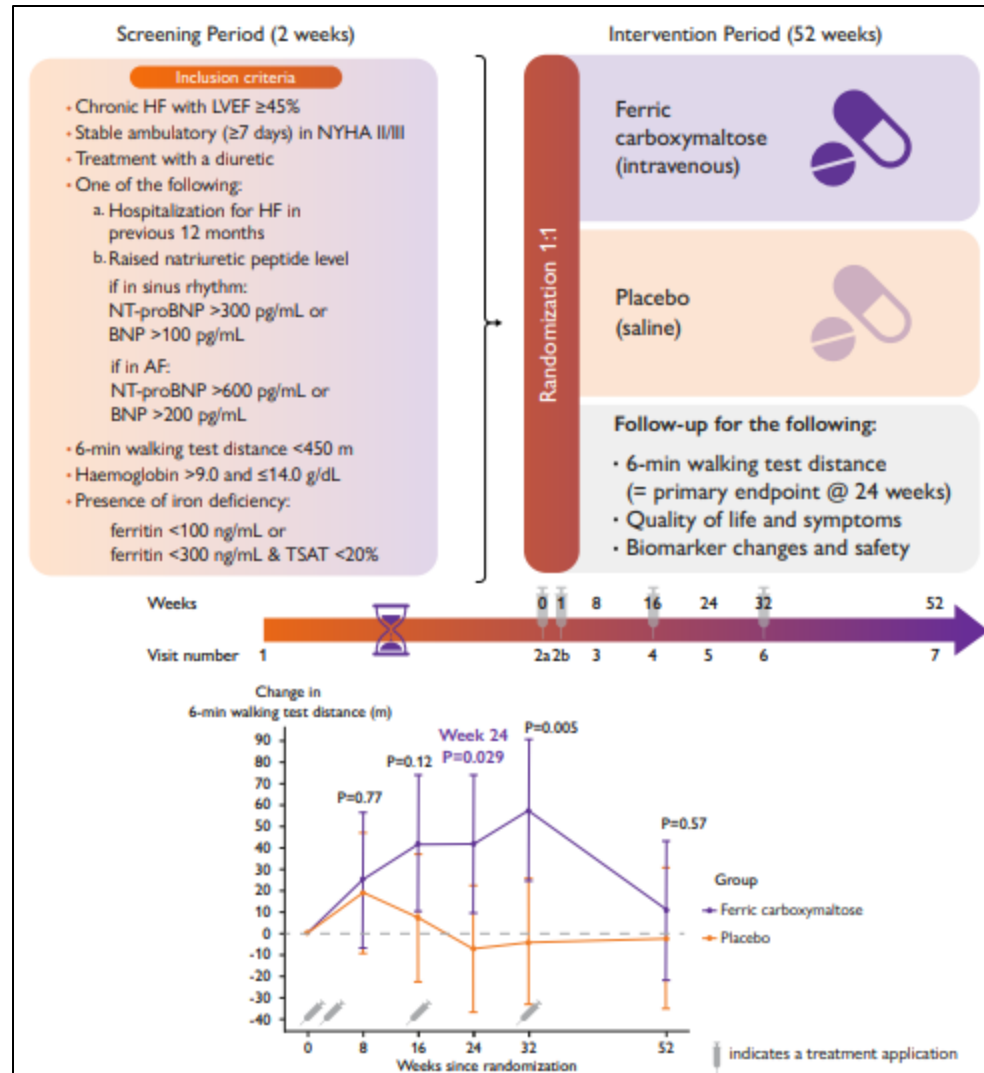
CENTRAL ILLUSTRATION Associations of Plasma Ferritin Light Chain Levels With Incident HF and HF Subtypes



Aboelsaad IAF, et al. J Am Coll Cardiol HF. 2024;12(3):539-548.

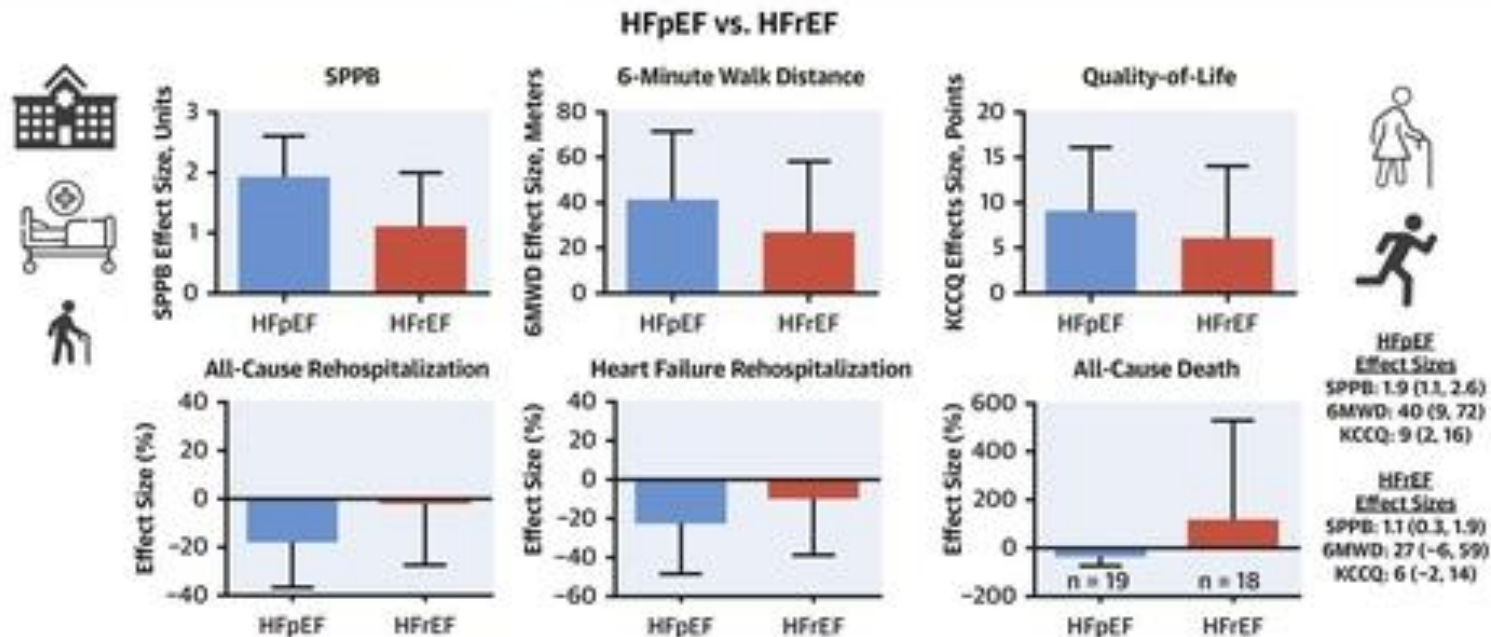
The trial was stopped because of slow recruitment after 39 patients had been included !

Ferric carboxymaltose and exercise capacity in heart failure with preserved ejection fraction and iron deficiency: the FAIR-HFpEF trial



Cardiac rehabilitation

CENTRAL ILLUSTRATION: Novel Rehabilitation Intervention in Older Patients With Acute Decompensated Heart Failure



Compared to patients with HFrEF, those with HFpEF may derive greater benefit from the intervention.

Mentz, R.J. et al. J Am Coll Cardiol HF. 2021;9(10):747-57.

HFpEF and chronotropic insufficiency

Chronotropic insufficiency: very frequent in HF

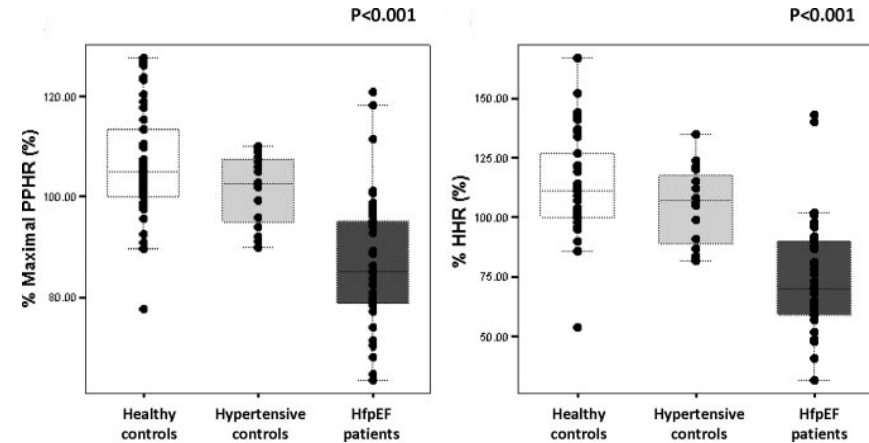
Definition/diagnosis: can be challenging

$$\begin{aligned} \text{Réserve chronotrope} \\ = (\text{FCmax}/\text{FMT}) \times 100 \\ \text{Seuil} \leq 85\% \end{aligned}$$

$$\begin{aligned} \text{Réserve chronotrope relative} \\ [(\text{FCmax} - \text{FCrepos})/(\text{FMT} - \text{FCrepos})] \times 100 \\ \text{Seuil} \leq 80-70\% \end{aligned}$$

Formule de Wilkoff

$$\begin{aligned} \text{FCpalier} &= (220 - \hat{\text{age}} - \text{FCrepos}) \times (\text{METS}_{\text{palier}} - 1) + \text{FC repos} \\ \text{Ratio de réserve chronotrope} &= [(\text{FCpic} - \text{FCrepos})/\text{FCpalier}] \times 100 \\ \text{Seuil} &\leq 80\% \text{ quel que soit le palier} \end{aligned}$$



Circulation Heart Failure 2010

RCT: Effect of Personalized Accelerated Pacing on Quality of Life, Physical Activity, and Atrial Fibrillation in Patients With Preclinical and Overt Heart Failure With Preserved Ejection Fraction

POPULATION

52 Men, 48 Women



Patients with stage B and C heart failure and preserved ejection fraction and pacemakers for ventricular conduction
Median age, 75 (IQR, 69-81) y

SETTINGS / LOCATIONS



1 Academic medical center in Burlington, Vermont

INTERVENTION

107 Patients randomized



57 Usual care (standard lower heart rate)
Pacemaker backup rate remained at standard rate of 60 beats per min



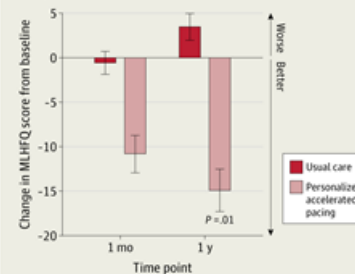
50 Personalized accelerated pacing
Pacemaker backup rate increased to a personalized, moderately accelerated heart rate

PRIMARY OUTCOME

Change in Minnesota Living with Heart Failure Questionnaire (MLHFQ) from baseline to 1 mo and 1 y (score range 0-105 with higher score = worse symptoms)

FINDINGS

The personalized accelerated pacing group had significant improvement in MLHFQ scores at 1-mo and 1-y follow-up compared with usual care



Mean (SD) MLHFQ score change for usual care vs personalized accelerated pacing

1 mo: -0.6 (9.1) vs -10.9 (13.7); P < .001
1 y: 3.5 (10.6) vs -15 (15.5); P < .001

CONCLUSION

**HFrEF: treatments (the 4 fantastic+diuretics)
adapted according to 4 variables: HR/BP/creat/rythm**



CONCLUSION

HFpEF: treatments targeting specific profiles

