Heart failure with preserved ejection fraction:

One or several diseases?

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Beyrouth– Jeudi 11 Avril 2019

DEFINITION OF HEART FAILURE

Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
	2	LVEF <40%	LVEF 40–49%	LVEF ≥50%
	3	–	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).	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).

Diagnosis of heart failure with preserved ejection fraction

- The presence of symptoms and/or signs of HF
- A 'preserved' EF (defined as LVEF ≥50% or 40–49% for HFmrEF)
- Elevated levels of NPs (BNP >35 pg/mL and/or NT-proBNP >125 pg/mL)
- Objective evidence of other cardiac functional and structural alterations underlying HF

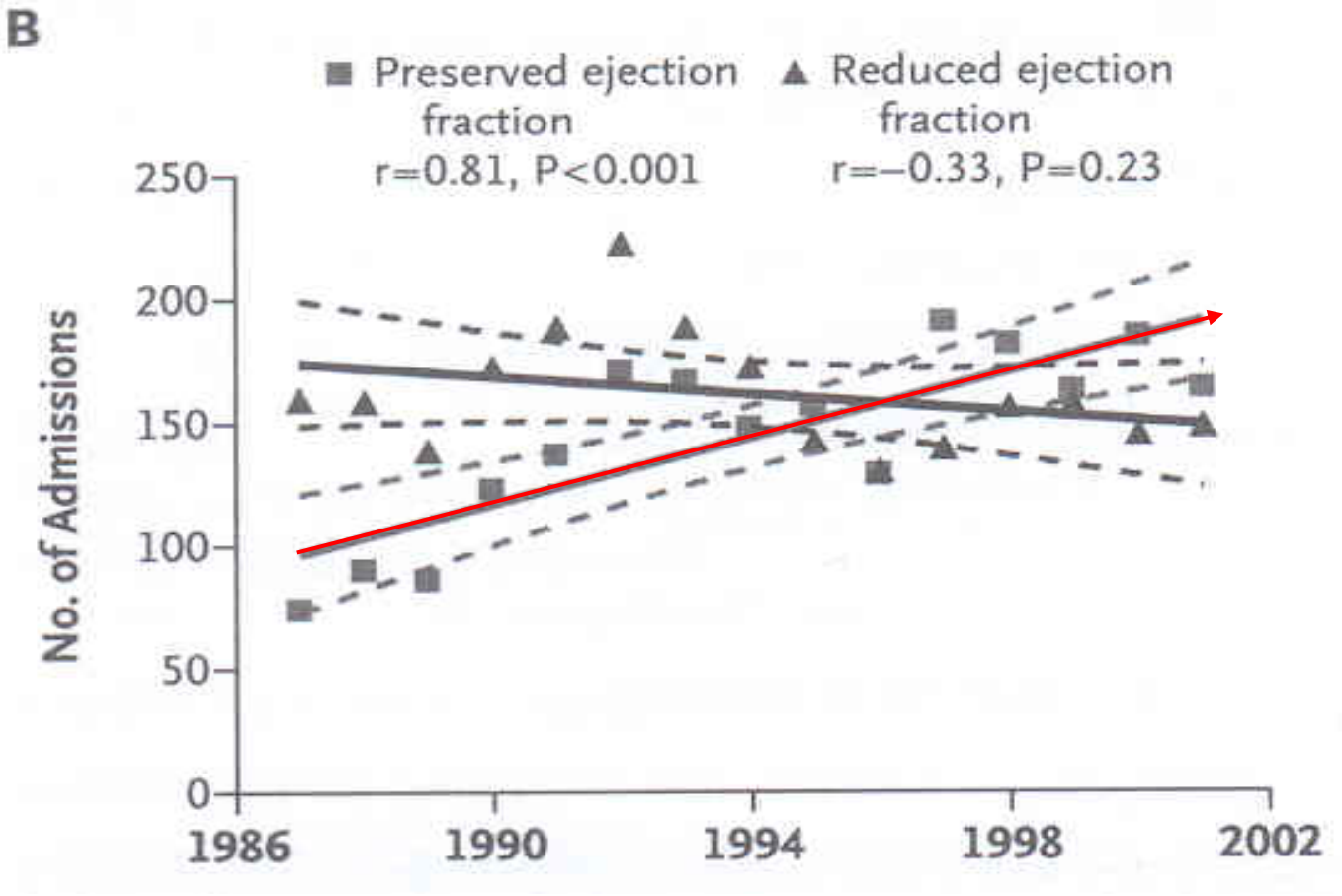
Ponikowski P, *Eur Heart J*. 2016 Jul 14;37(27):2129-200

WHY SUCH A QUESTION ?

Prevalence of 2 types of Heart Failure

Mayo Clinic

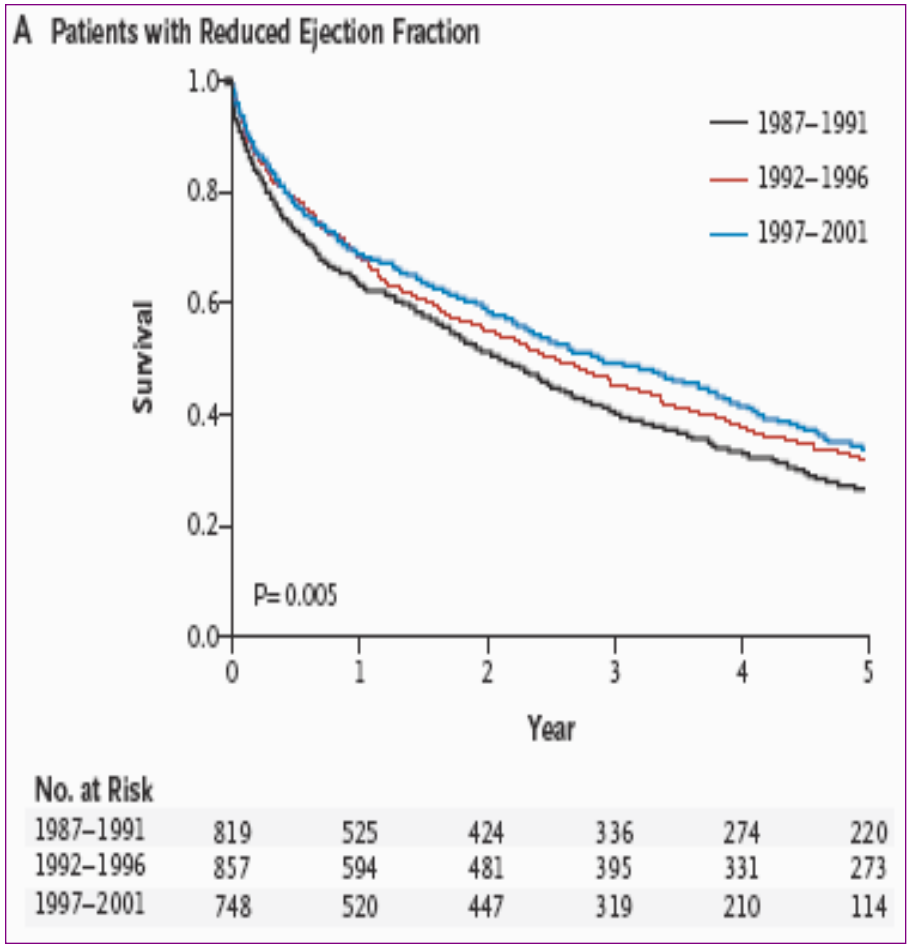
6076 patients → 4596 with EF available
EF < 50% N=2429 EF ≥ 50% N=2167



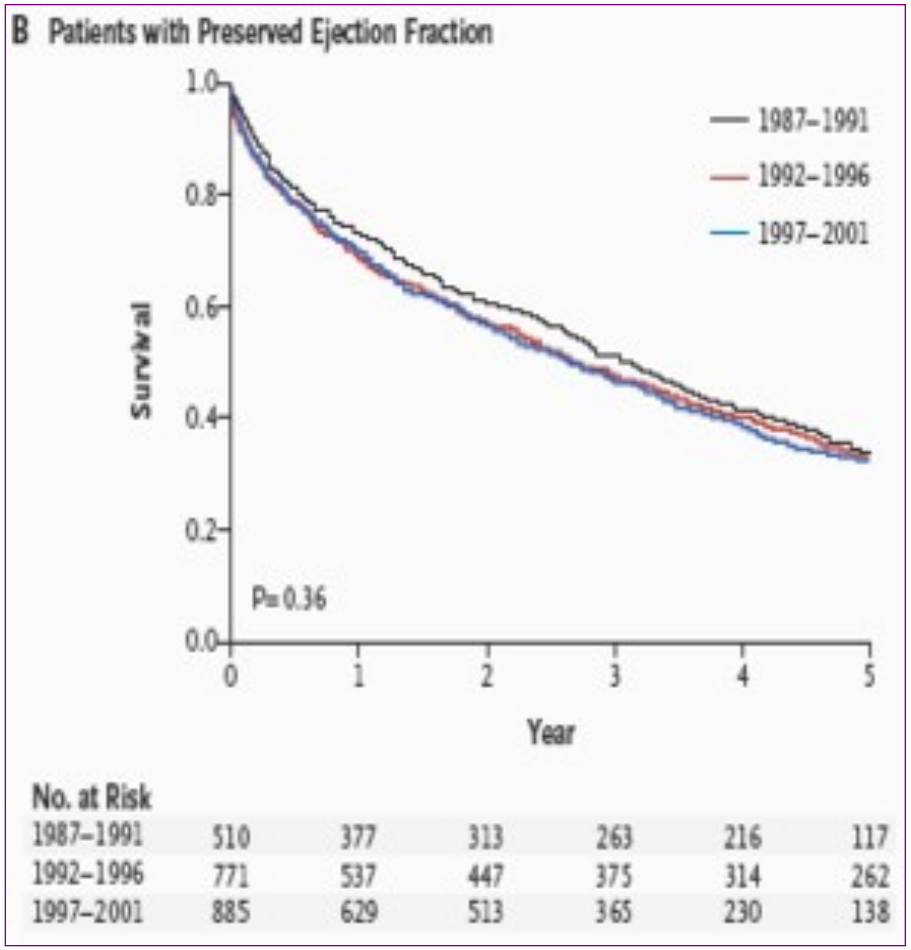
Heart failure Survival

from 1987 to 2001

ICFEr



ICFEp



N.Engl.J. Med 2006;355:251-9

Clinical trials

Trials	Treatment	Endpoints	Results
PEP - CHF 1 000 patients FU 18 months	**Perindopril** *vs* Placebo	Mortality or hospitalisation for HF	**NS**
CHARM - PRESERVED 3 023 patients FU 37 months	**Candesartan** *vs* Placebo	CV Mortality or hospitalisation for HF	**NS**
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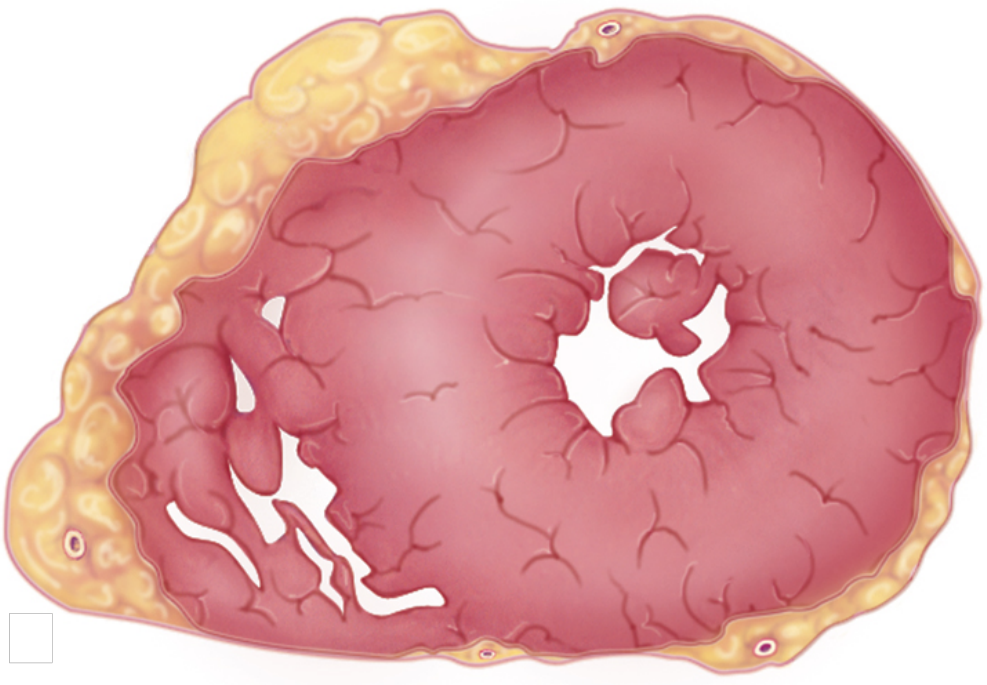
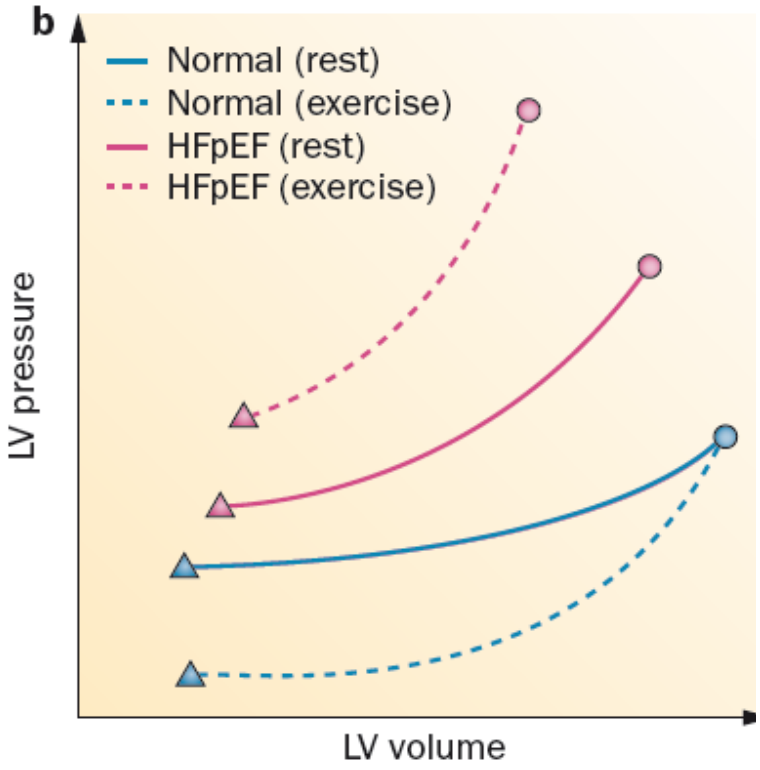
SENIORS 2 135 patients	**Nevibolol** *vs* Placebo	Mortality or CV hospitalisation	**±** **sub-group EF> 35%**

From the classic diastolic dysfunction to An heterogenous syndrome

Diastolic dysfunction

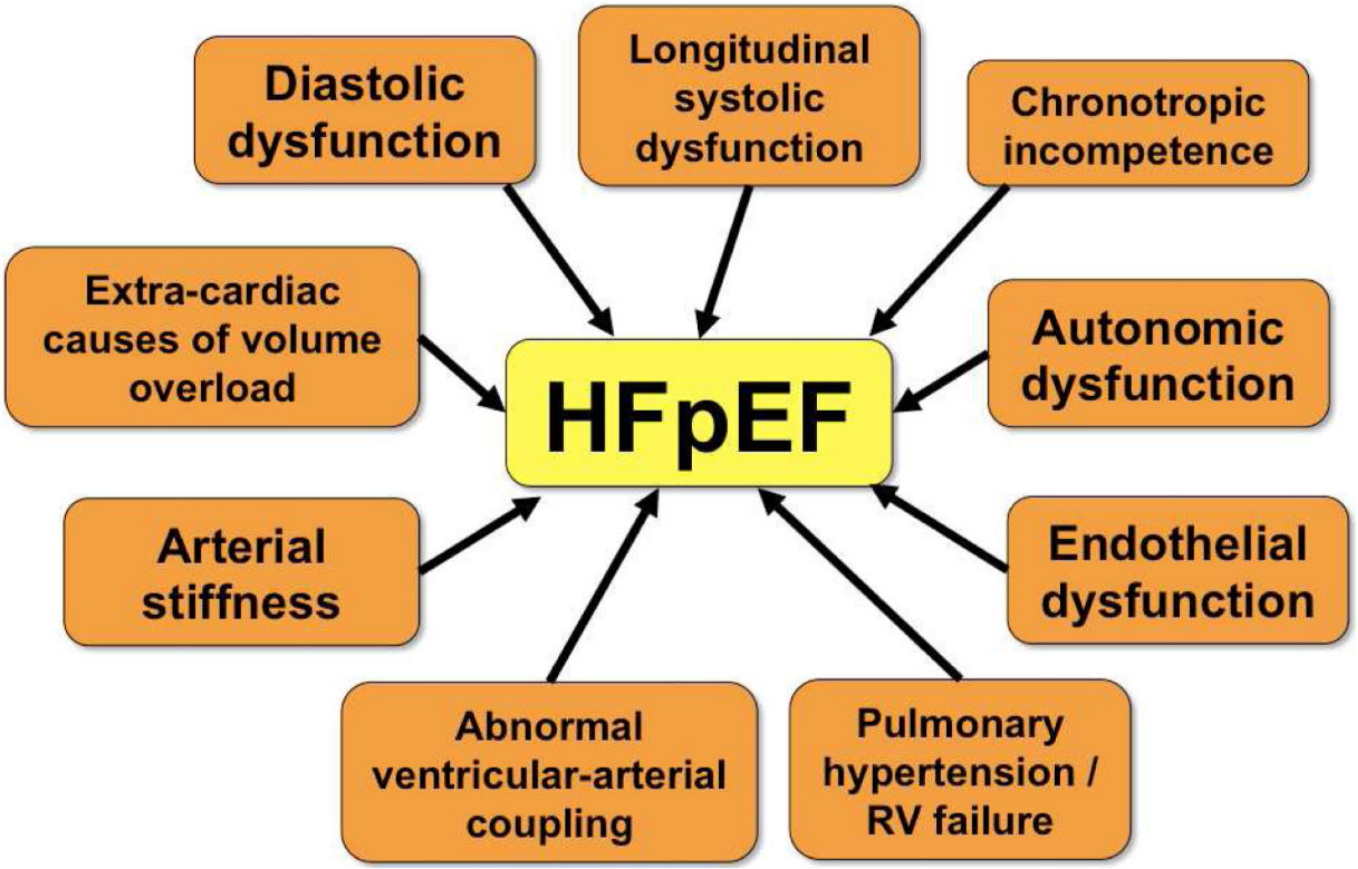




L'ICFEP était historiquement reconnue sous l'entité d'insuffisance cardiaque diastolique

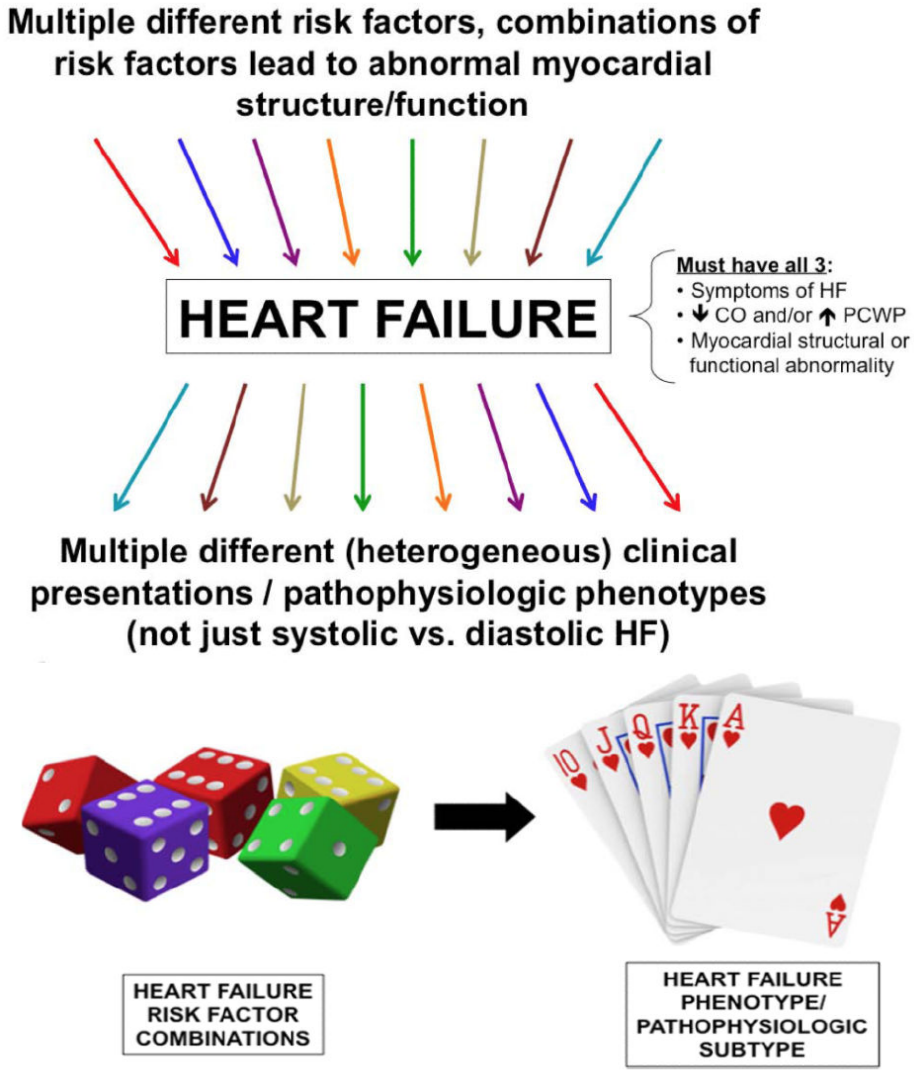
Borlaug BA, *Nat. Rev. Cardiol.2014;* 11, 507–515

Multiple Pathophysiologic Contributors to the Heart Failure with Preserved Ejection Fraction Syndrome



Shah S, *Heart Fail Clin*. 2014 July ; 10(3): 407–418

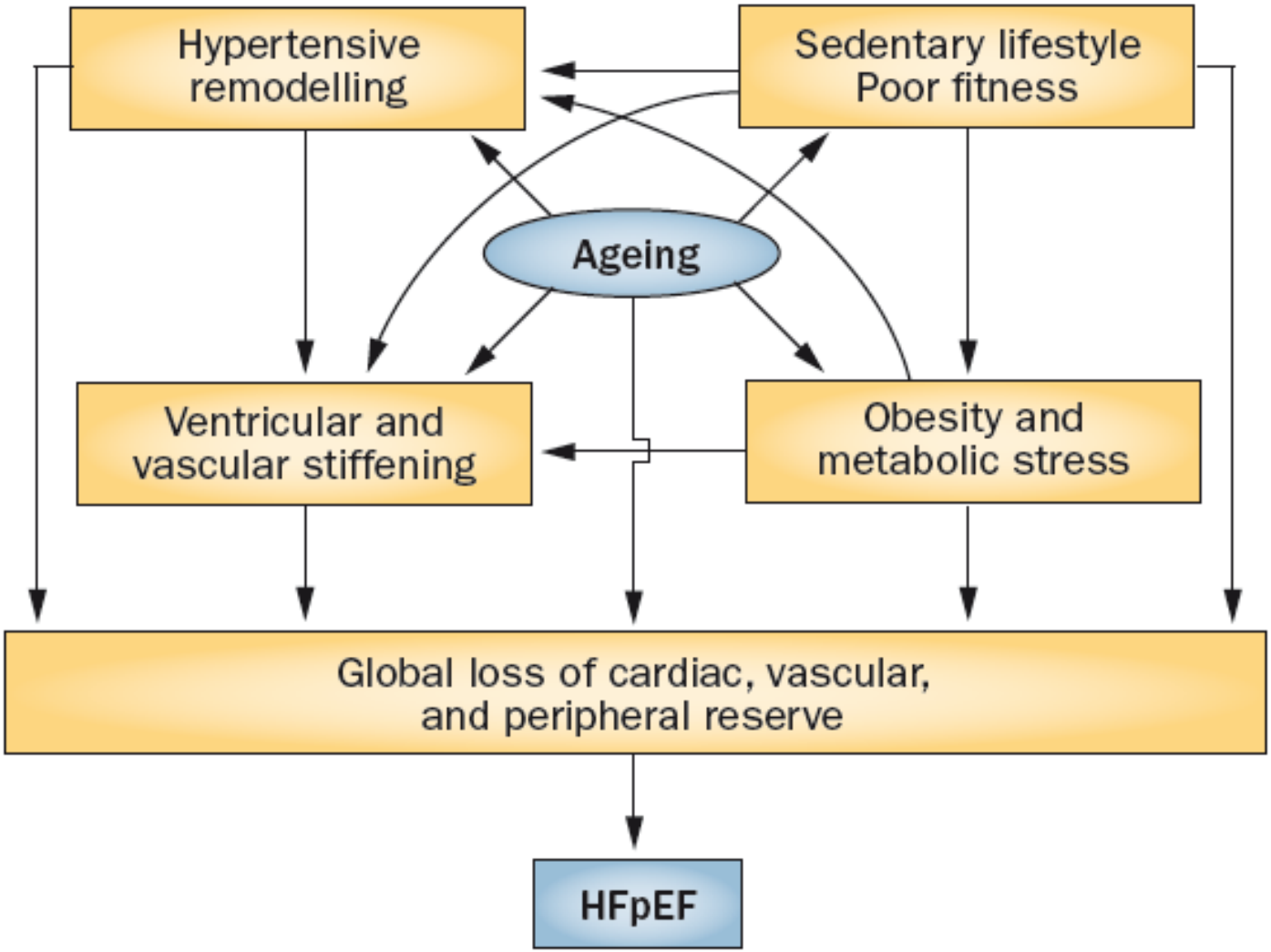
Relationship Between Heart Failure Risk Factor Combinations and Heart Failure Phenotypic Heterogeneity



Shah S, *Heart Fail Clin*. 2014 July ; 10(3): 407–418

SEVERAL ETIOLOGIES

HYPERTENSION, DIABETES, OBESITY



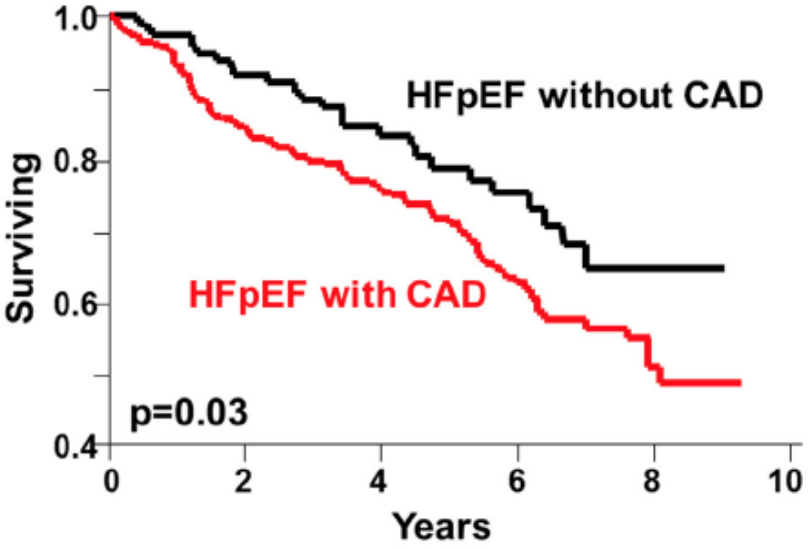
Diabetic

Borlaug BA, *Nat. Rev. Cardiol.2014;* 11, 507–515

CORONARY ARTERY DISEASE

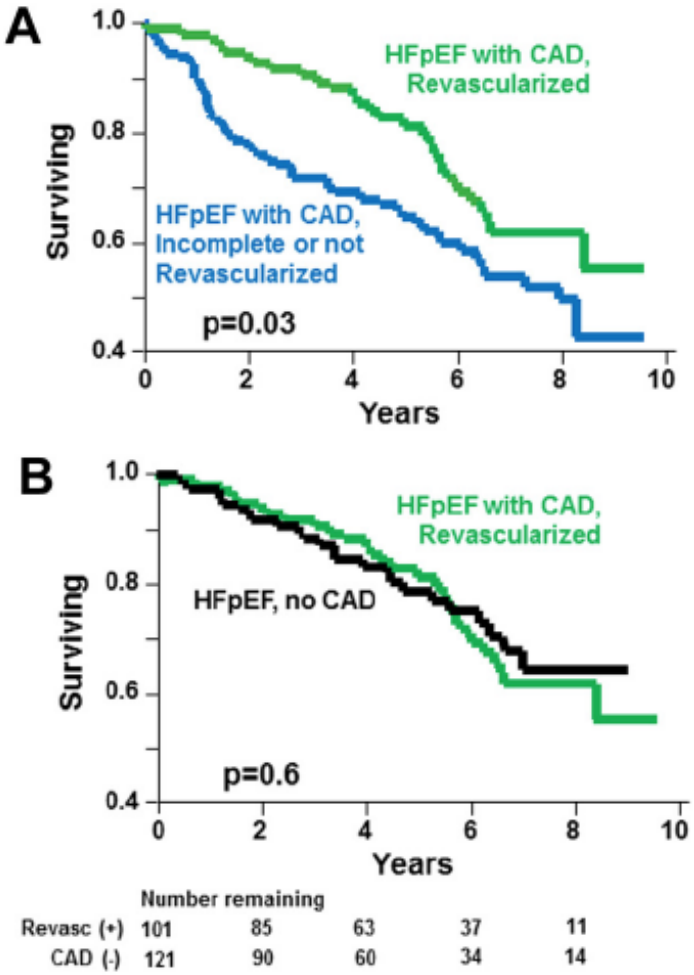
Prévalence de la coronaropathie sur 376 patients avec ICFEP : 68%

Implications of Coronary Artery Disease in Heart Failure With Preserved Ejection Fraction



Number remaining

CAD (-)	121	90	60	34	14
CAD (+)	255	193	129	83	23



Number remaining

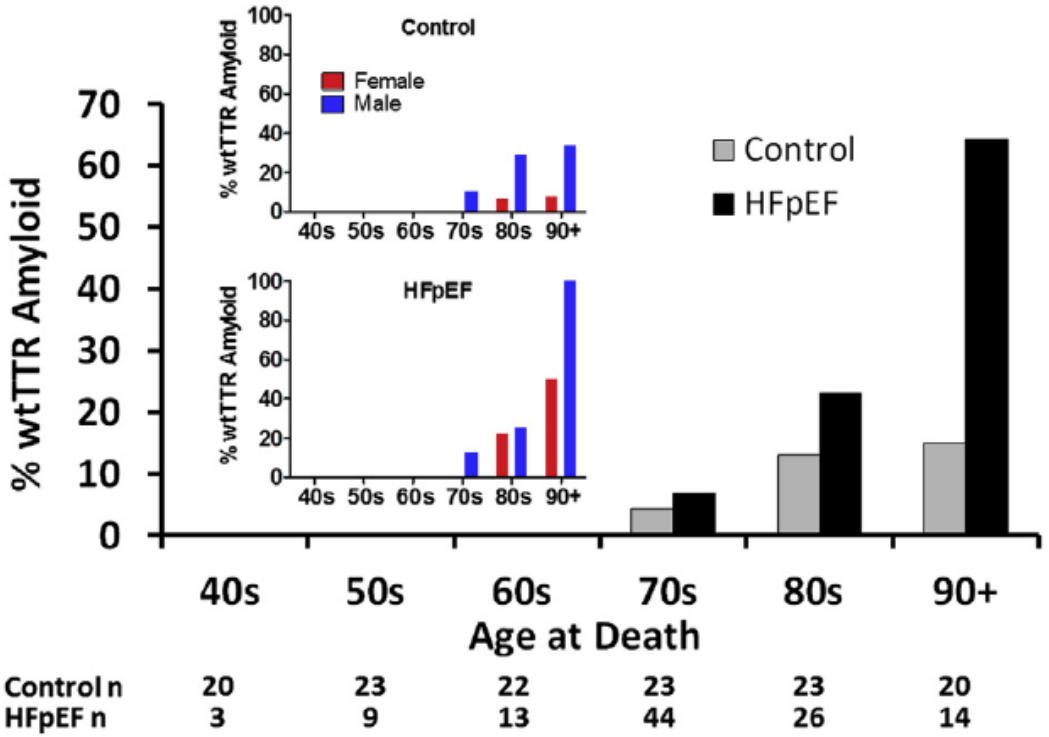
Revasc (+)	101	85	63	37	11
CAD (-)	121	90	60	34	14

Hwang SJ, *J Am Coll Cardiol* 2014;63:2817–27

AMYLOID CARDIOMYOPATHY

Left Ventricular Amyloid Deposition in Patients With Heart Failure and Preserved Ejection Fraction

19% de dépôts amyloïdes sur une série autopsique :
- 1% AL
- 2% non déterminé
- 16% TTR sauvage

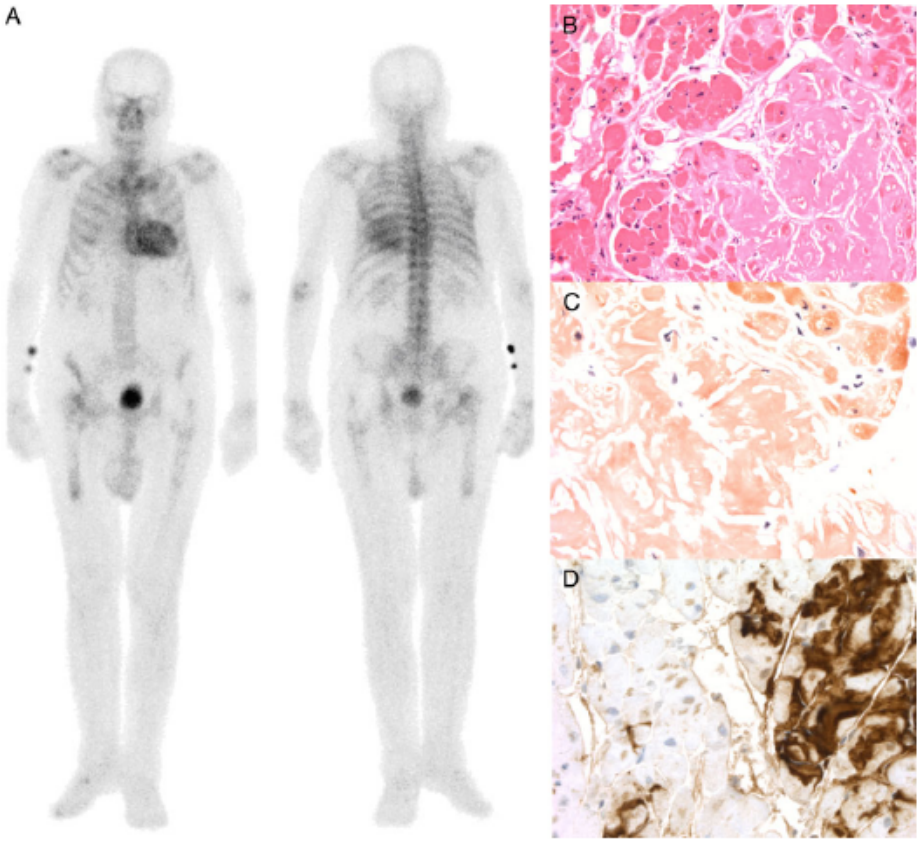


Mohammed SF, *J Am Coll Cardiol HF* 2014;2:113–22

AMYLOID CARDIOMYOPATHY

Wild-type transthyretin amyloidosis as a cause of heart failure with preserved ejection fraction

13% de fixation cardiaque modérée à sévère à la scintigraphie au ^{99m}Tc-DPD dans une population de patients ICFEP de plus de 60 ans avec HVG (SIV > 12 mm)

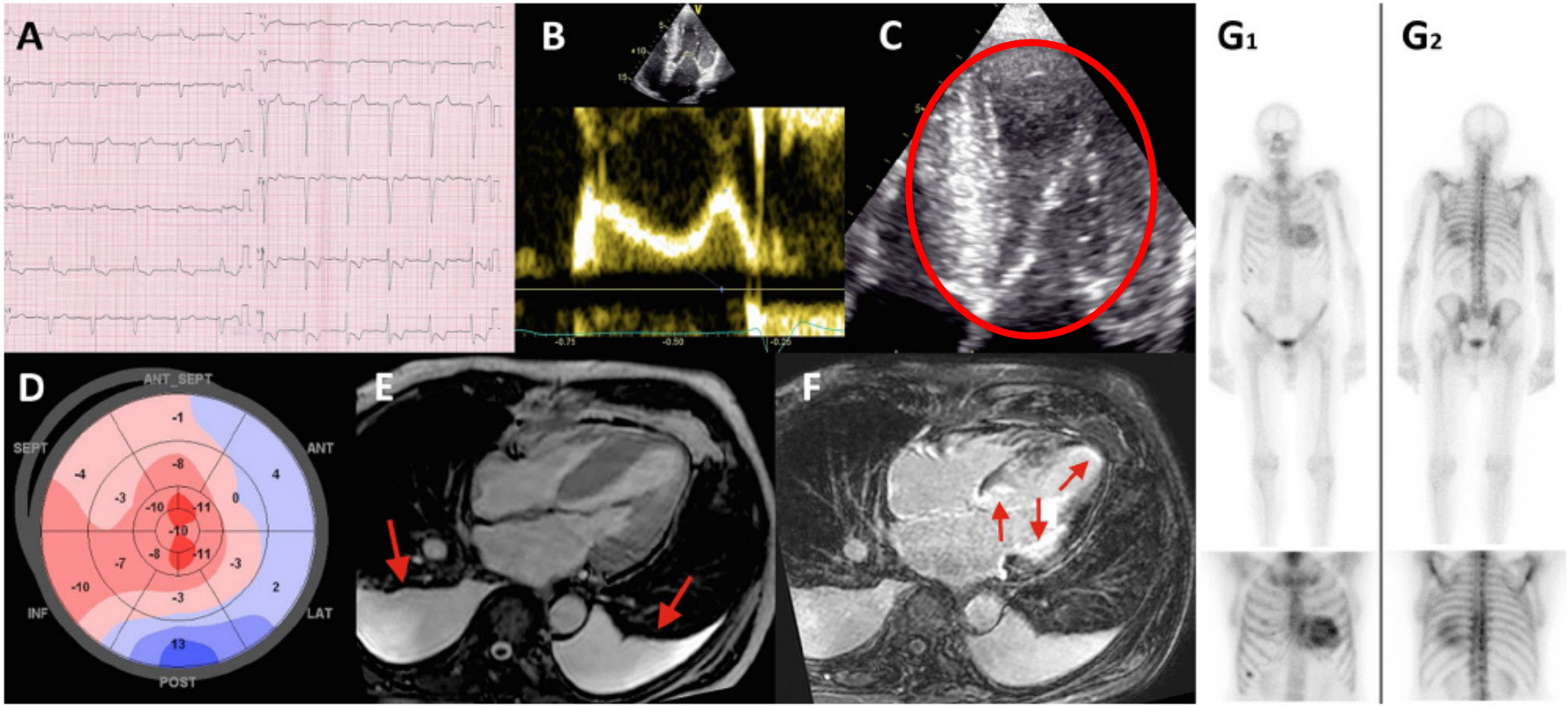


Gonzàlez-Lòpez E, *Eur Heart J.* 2015 Oct 7;36(38):2585-94

AMYLOID CARDIOMYOPATHY

Pilot study for left ventricular imaging phenotype of patients over 65 years old with heart failure and preserved ejection fraction: the high prevalence of amyloid cardiomyopathy

Too often unknown syndrom? **Specific treatment TAFAMIDIS**



Others infiltrative cardiomyopathies (hemochromatosis,…), Fabry cardiomyopath

Bennani-Smires Y, *Int J Cardiovasc Imaging*. 2016; Aurigemma GP, *N Engl J Med* 2004;351:1097-105; Kirk P, *Circulation*. 2009;120:1961-1968;

COMORBIDITIES

ESC 2016 Co-morbidities

- Angina and CAD
- Hypertension
- Valvular heart disease
- Kidney dysfunction (including chronic kidney disease, acute kidney injury, cardio-renal syndrome and prostatic obstruction)
- Hypokalaemia and hyperkalaemia
- Central nervous system (including depression, stroke and autonomic dysfunction)
- Gout and arthritis
- Diabetes
- Hyperlipidaemia
- Obesity
- Sleep disturbance and sleep-disordered breathing
- Lung disease (including asthma and chronic obstructive pulmonary disease)
- Iron deficiency and anaemia
- Erectile dysfunction
- Cancer
- Cachexia and sarcopenia

Eur Heart J 2016. doi: 10,1093/eurheartj/ehw128

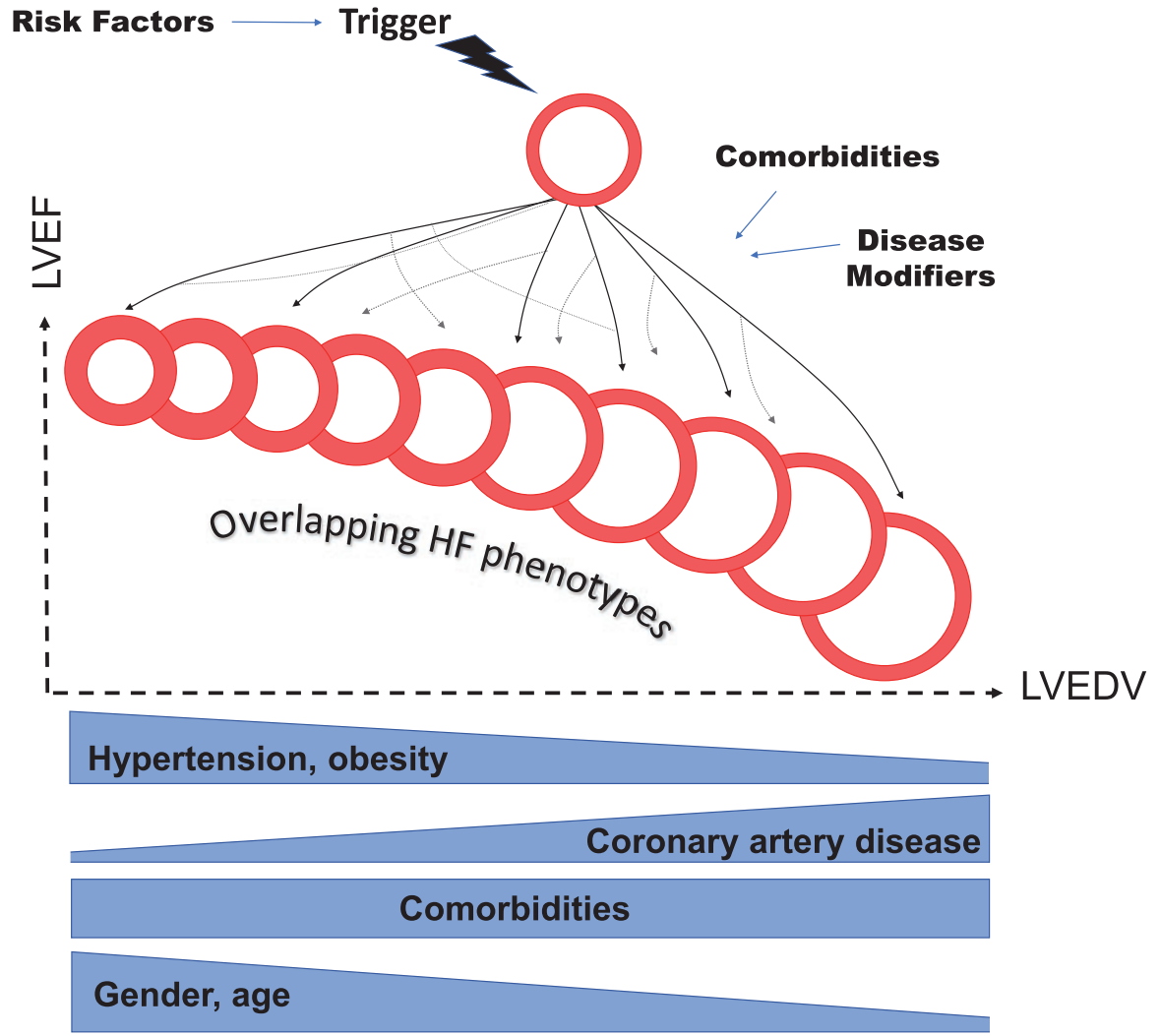
Recommandations ESC 2016 : importances des comorbidités chez les patients insuffisants cardiaques

1) Elles interfèrent avec le processus de diagnostic de l'IC, comme la BPCO qui est une cause confondante de dyspnée
2) Elles aggravent les symptômes et dégradent la qualité de vie
3) Elles contribuent à l'augmentation de la mortalité et des hospitalisations, notamment des réadmissions précoces
4) Elles peuvent affecter l'utilisation des médicaments de l'IC, comme l'insuffisance rénale sévère l'utilisation des bloqueurs du SRAA ou l'asthme qui est une contre-indication relative aux bêtabloquants
5) En constituant pour la plupart un critère d'exclusion des essais, elles limitent le champ d'utilisation et le niveau d'évidence des médicaments de l'IC
6) Leurs traitements peuvent aggraver l'insuffisance cardiaque, comme l'utilisation des AINS au cours des pathologies rhumatologiques
7) Les interactions entre leur traitement et celui de l'IC peuvent diminuer l'efficacité et la sécurité de ces derniers, voire être à l'origine d'effets secondaires comme les bêta-agonistes utilisés dans la BPCO ou l'asthme et les bêtabloquants.

Eur Heart J 2016. doi: 10,1093/eurheartj/ehw128

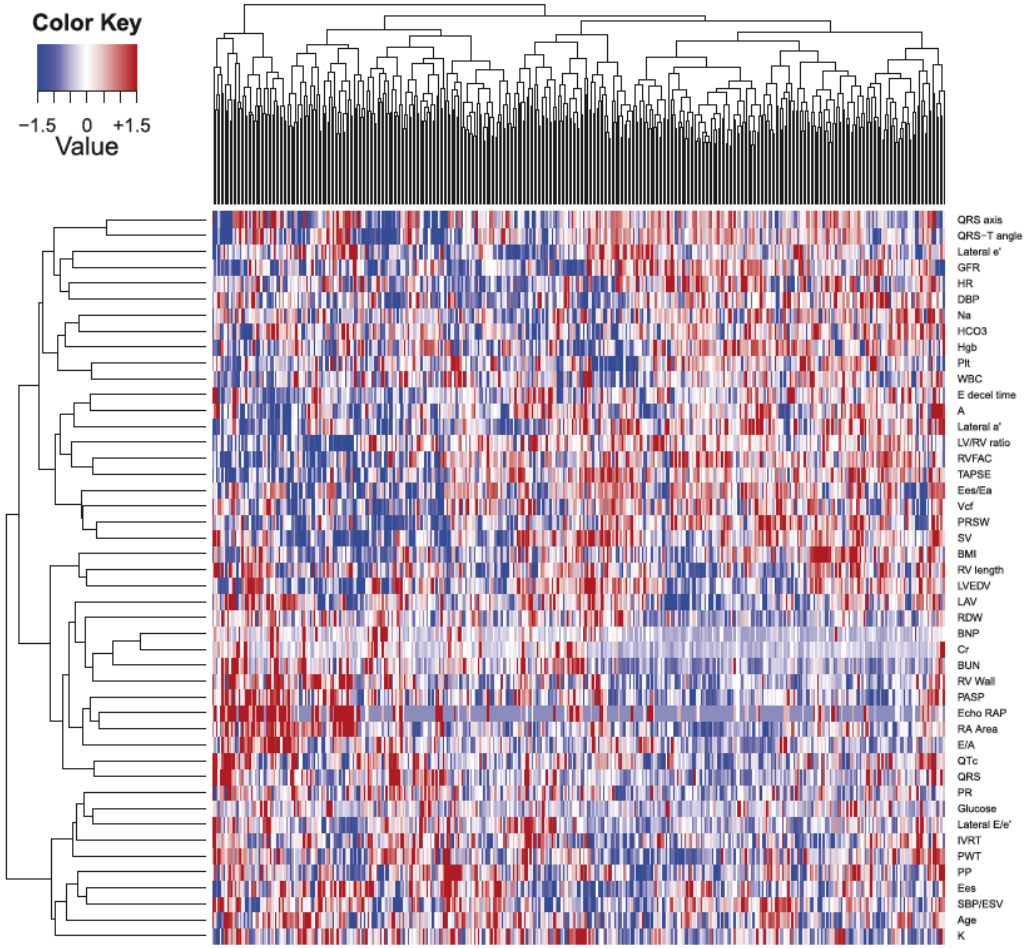
A SOLUTION? PHENOMAPPING

The Heart Failure Spectrum



Triposkiadis et al. EHJ (2019) 00, 1–11

Phenomapping for Novel Classification of Heart Failure With Preserved Ejection Fraction



Shah S, *Circulation*. 2015;131:269-279

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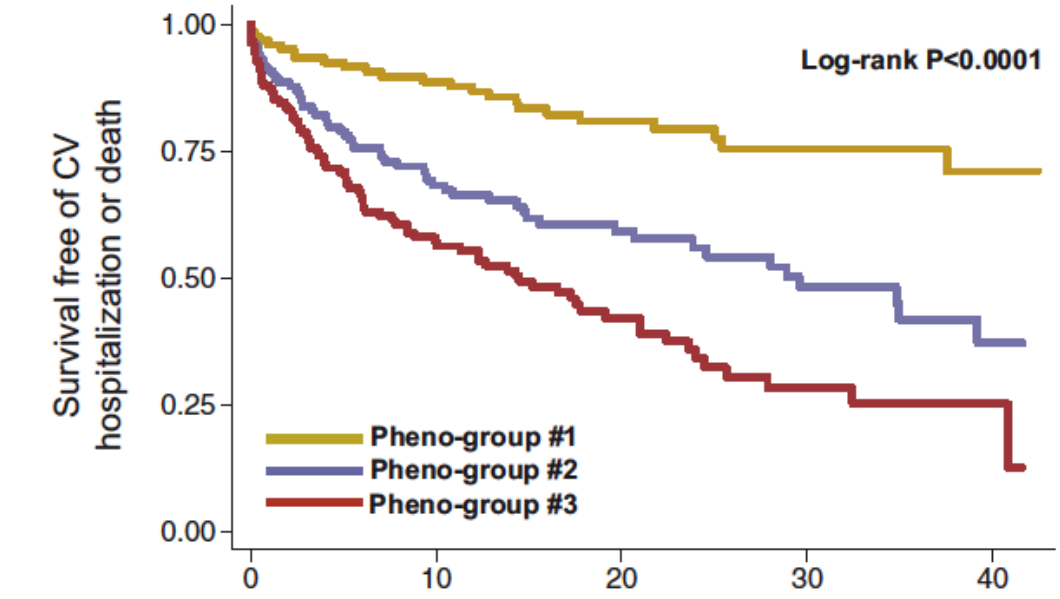
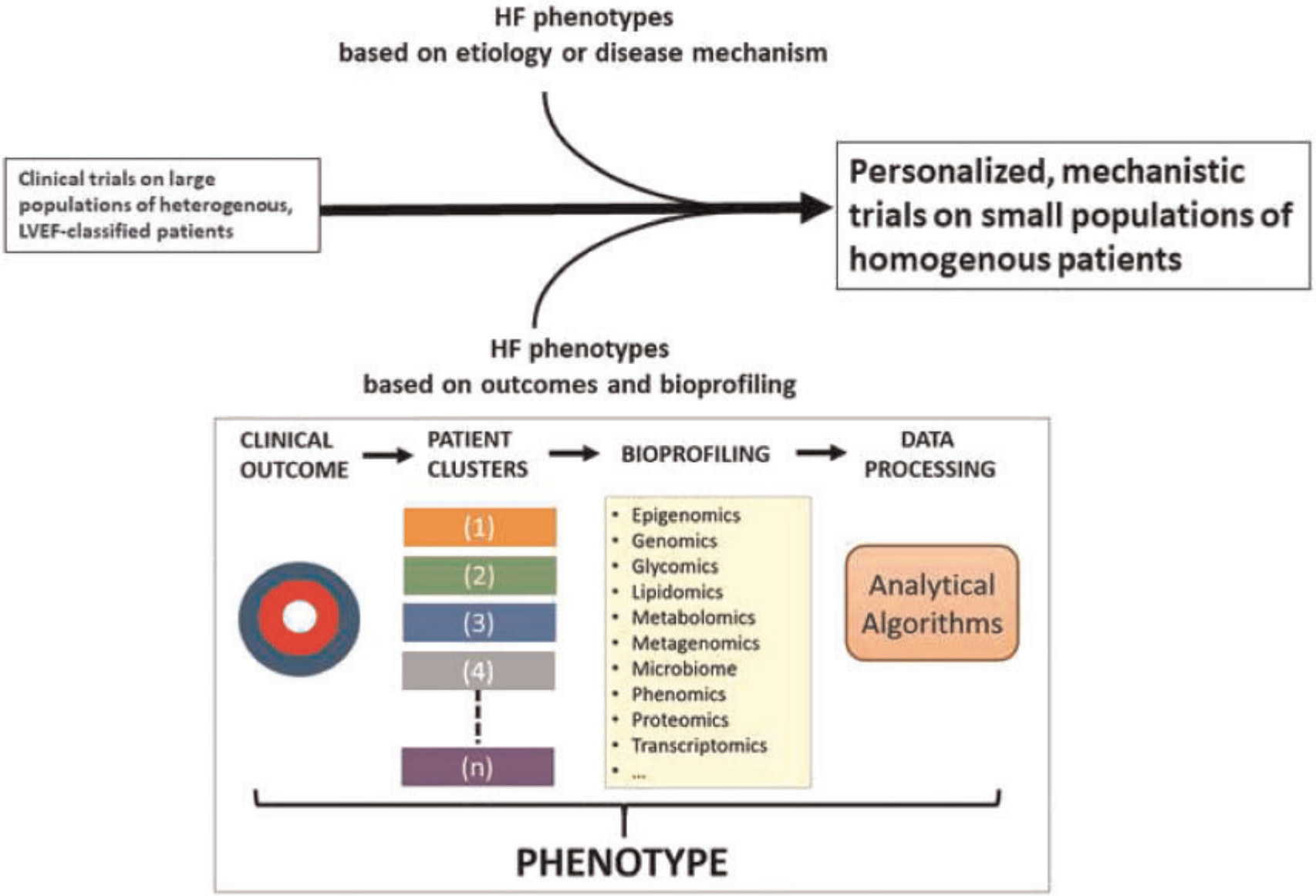


Number at risk					
Pheno-group #1	122	90	57	31	6
Pheno-group #2	133	72	42	24	6
Pheno-group #3	142	65	29	12	3

Shah S, *Circulation*. 2015;131:269-279



Triposkiadis et al. EHJ (2019) 00, 1–11

Conclusions

- ✓ HFpEF is a frequent disease, 50% of all HF, poor outcomes
- ✓ No validated treatment
- ✓ Pathophysiology is different from HFrEF
- ✓ From the classical diastolic dysfunction to an heterogenous syndrome
- ✓ Several etiologies with their own treatments
- ✓ Comorbidities interferences
- ✓ Better classification could be assess with phenomapping to guide clinical trials and hopefully lead to discover specific treatment

Overall, HFpEF is not only a single disease but several disease in one complex syndrom

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BONAMI group

MESAMI group

Academic / Companies fundings

- PHRC
- Conseil Régional MP
- OSEO/BPI, CellForCure
- C4C
- Thoratec
- …

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Back-up slides

TREATMENT ?

Clinical trials

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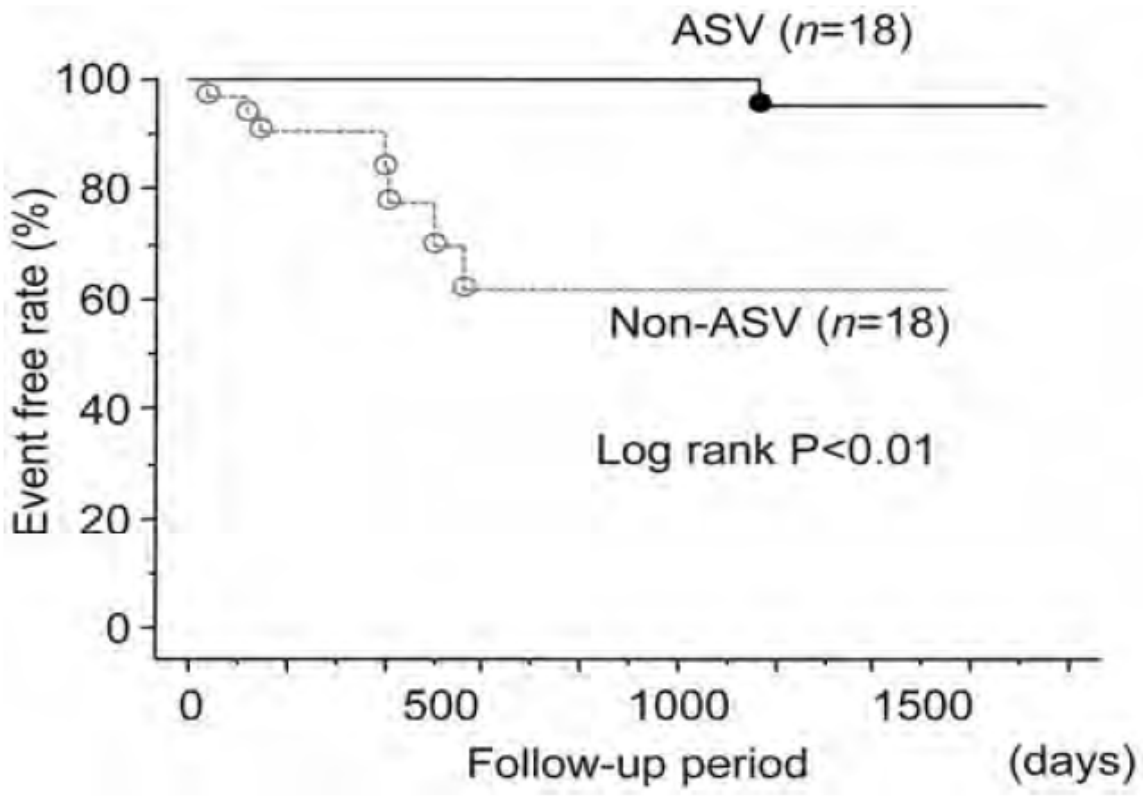
Recommandations ESC 2016 pour le traitement des insuffisances cardiaques à fraction d'éjection préservée ou intermédiaire

Recommandations	Classe	Niveau
Les comorbidités cardiovasculaires et non cardiovasculaires doivent être systématiquement recherchées et traitées par des interventions efficaces et sûres pour améliorer les symptômes, la qualité de vie et/ou le pronostic	I	C
Les diurétiques doivent être utilisés chez les patients congestifs pour améliorer les symptômes et les signes	I	B

Eur Heart J 2016. doi: 10,1093/eurheartj/ehw128

Traitement des apnées du sommeil au cours de l'ICFEp

Effets d'une ventilation servo-assistée sur la mortalité cardiaque et les réhospitalisations pour insuffisance cardiaque chez 36 patients présentant une ICFEp et un SAS

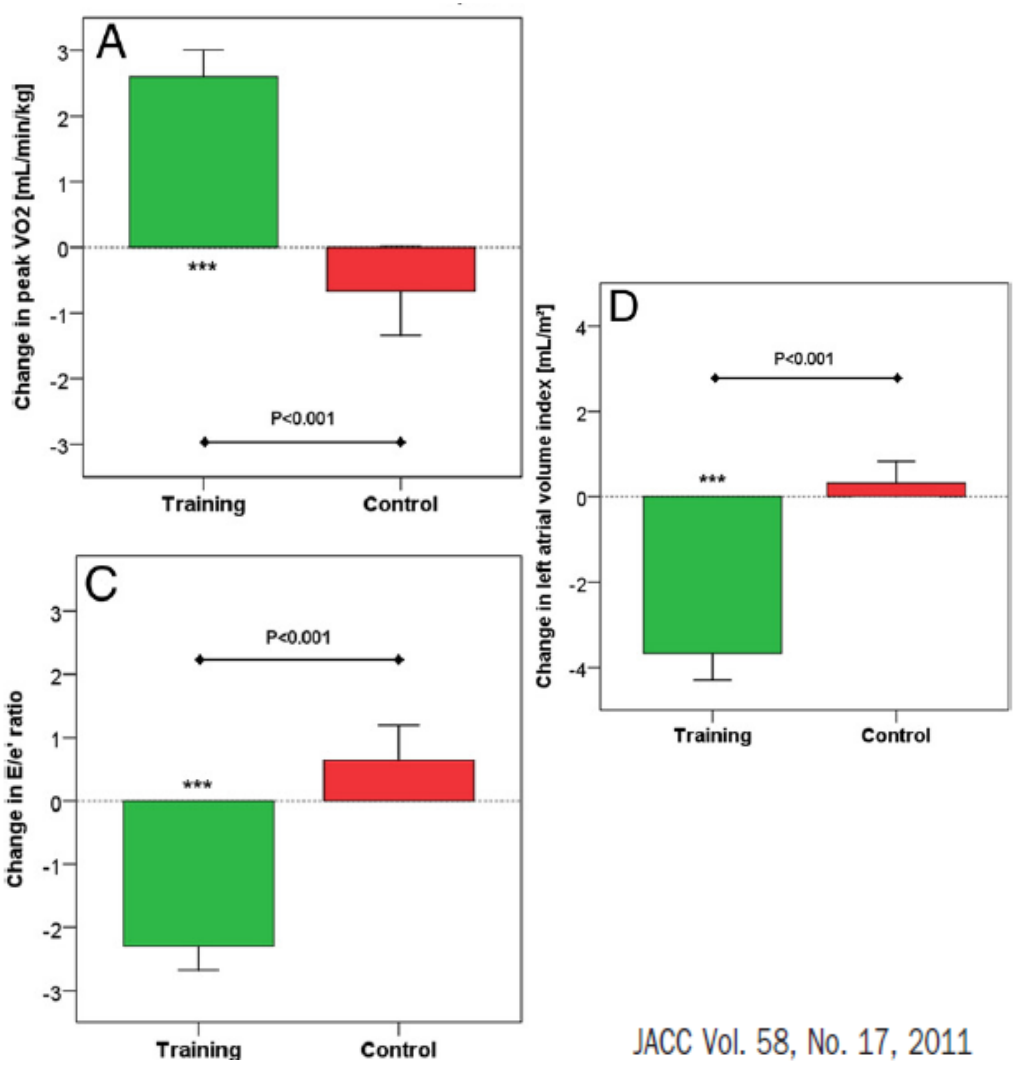


Eur J Heart Fail 2013; 15 : 543-550

Activité physique et ICFEp

Ex-DHF

Intervention	Endurance/resistance training vs control
No. of patients	64
Average age (years)	65
Female (%)	56
LVEF	≥45%
Primary outcome	Changes in NTproBNP
Mean follow-up (weeks)	36



JACC Vol. 58, No. 17, 2011
October 18, 2011:1780–91

Traitement de l'ICFEp : que devons-nous faire ?

Contrôle de la
pré-charge

Vasodilatateurs en aigu (sérélaxine) /diurétiques

Contrôle de la FC :

Agents bradycardisants si FC > 70 bpm
bêtabloquants ou vérapamil si CI
Ivabradine (en l'absence d'angor) ?

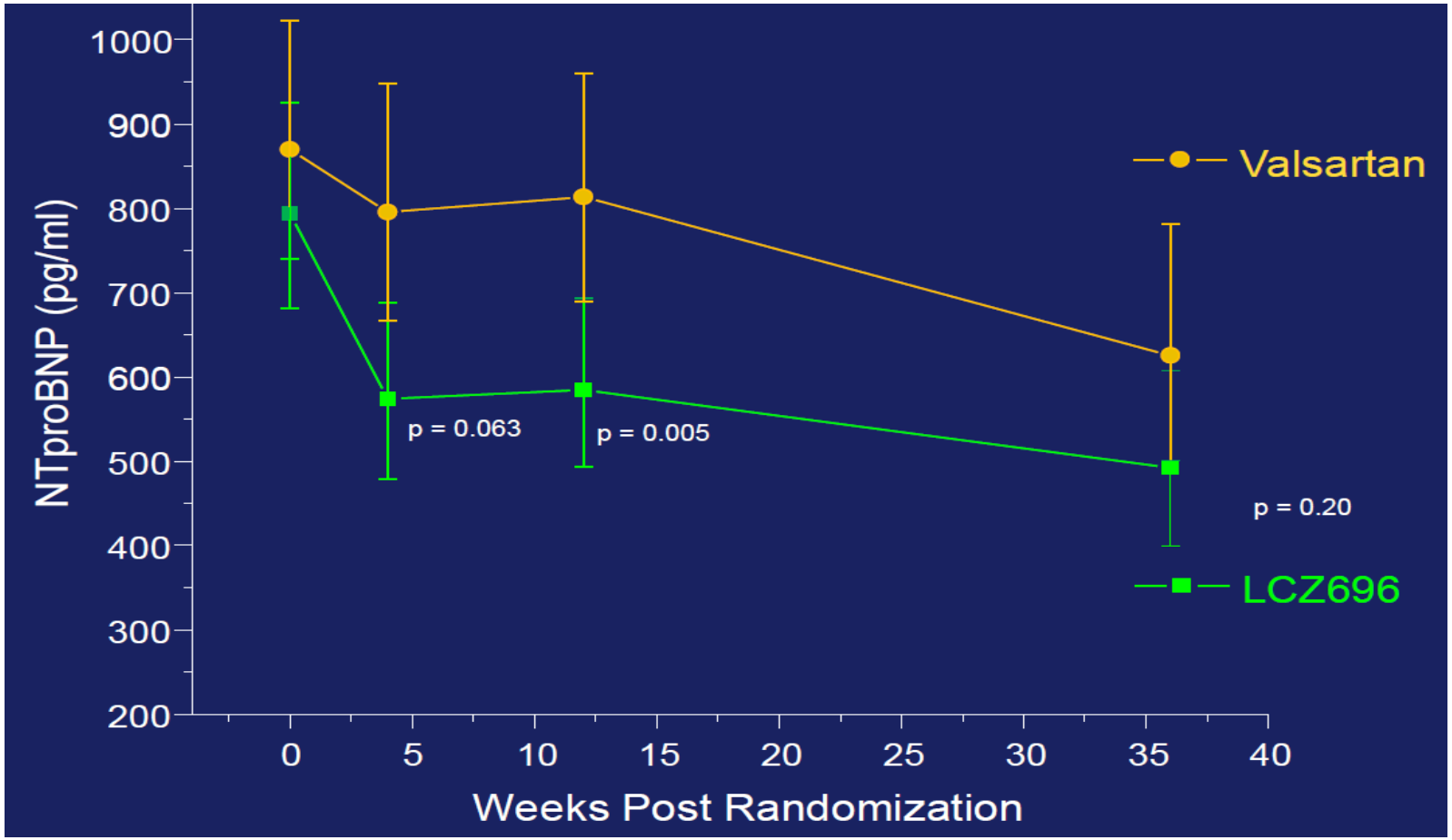
Agents spécifiques

LCZ696 ?

Traitement spécifique de l'ICFEp : mythe ou réalité ?

Effets du LCZ696 (inhibiteur NEP+ARA2) dans l'ICFEp : PARAMOUNT

Critère primaire : modifications du NT-proBNP à 12 semaines

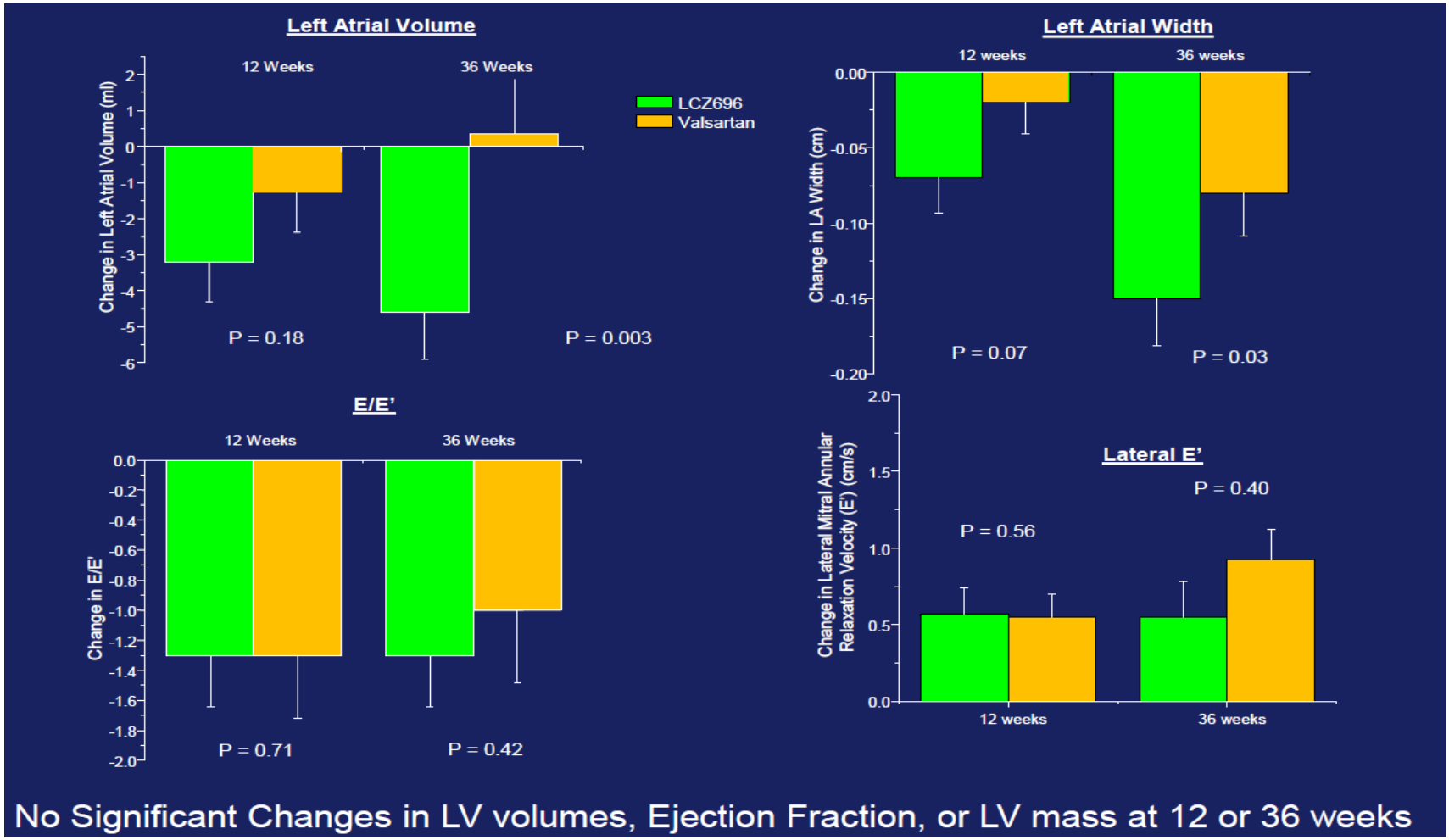


Lancet 2012; 380: 1387–95

Traitement spécifique de l'ICFEp : mythe ou réalité ?

Effets du LCZ696 (inhibiteur NEP+ARA2) dans l'ICFEp : PARAMOUNT

Critères secondaires : modifications des paramètres écho-doppler

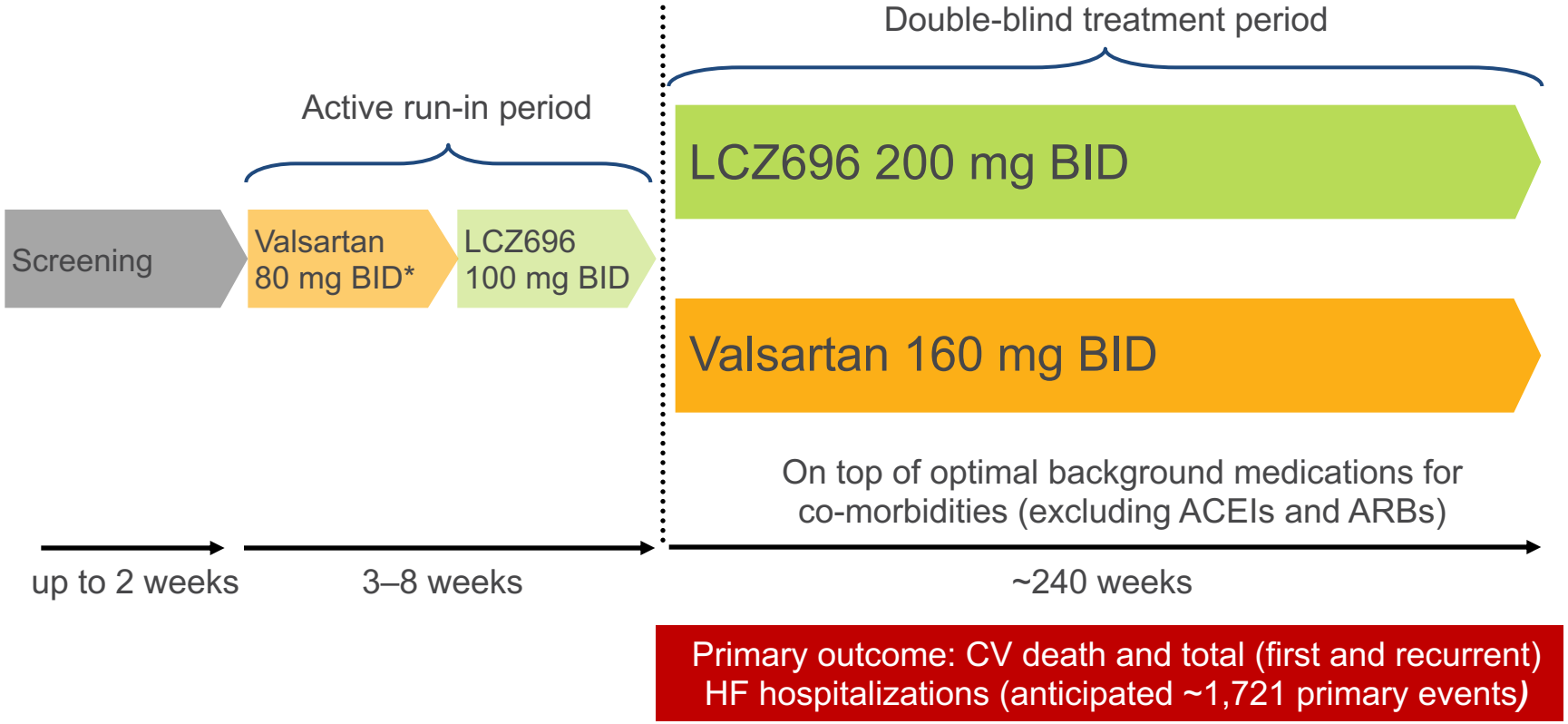


Lancet 2012; 380: 1387–95

PARAGON-HF

Target patient population: ~4,300 patients with symptomatic HF (NYHA Class II–IV) and LVEF ≥45%

Randomization 1:1

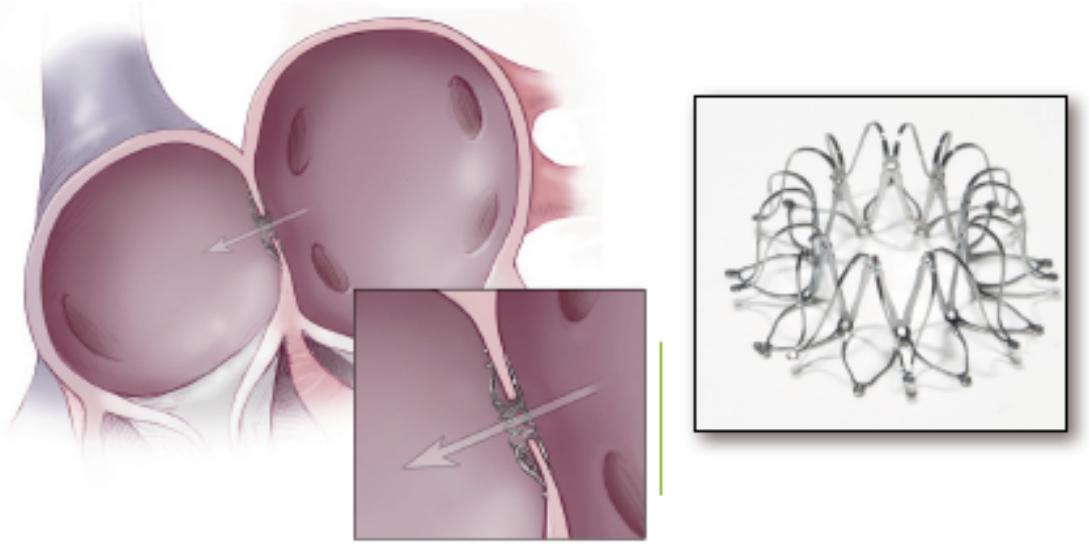


*Valsartan 40 mg BID (up to 2 weeks) followed by valsartan 80 mg BID as an optional starting run-in dose for those patients being treated with less than the minimum dose of ACEI or ARB at Visit 1.

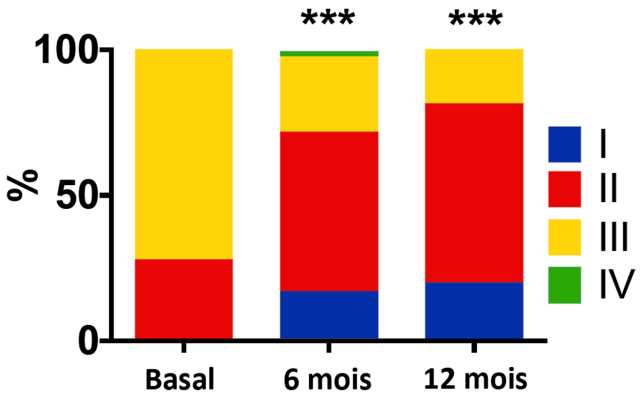
ACEI=angiotensin-converting enzyme inhibitor; ARB=angiotensin receptor blocker; BID=twice daily; CV=cardiovascular; HF=heart failure; LVEF=left ventricular ejection fraction; NYHA=New York Heart Association

Solomon et al. Poster presentation at ESC-HF Congress, 25 May 2013;

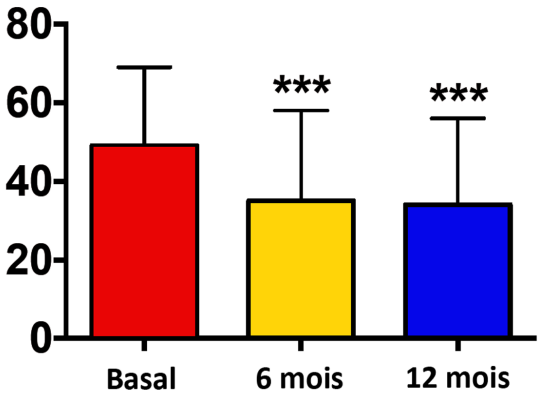
REDUCE LAP HEART FAILURE



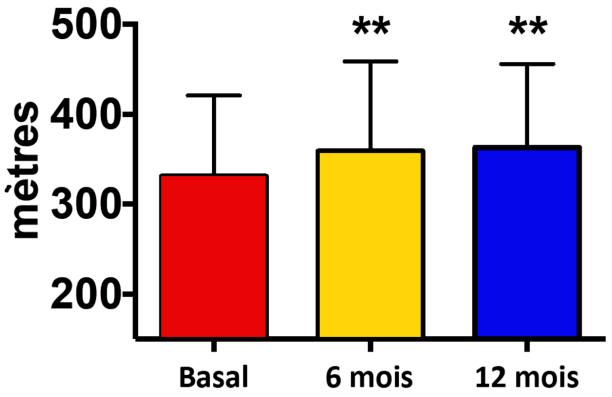
Stade NYHA



Qualité de vie (Minnesota)

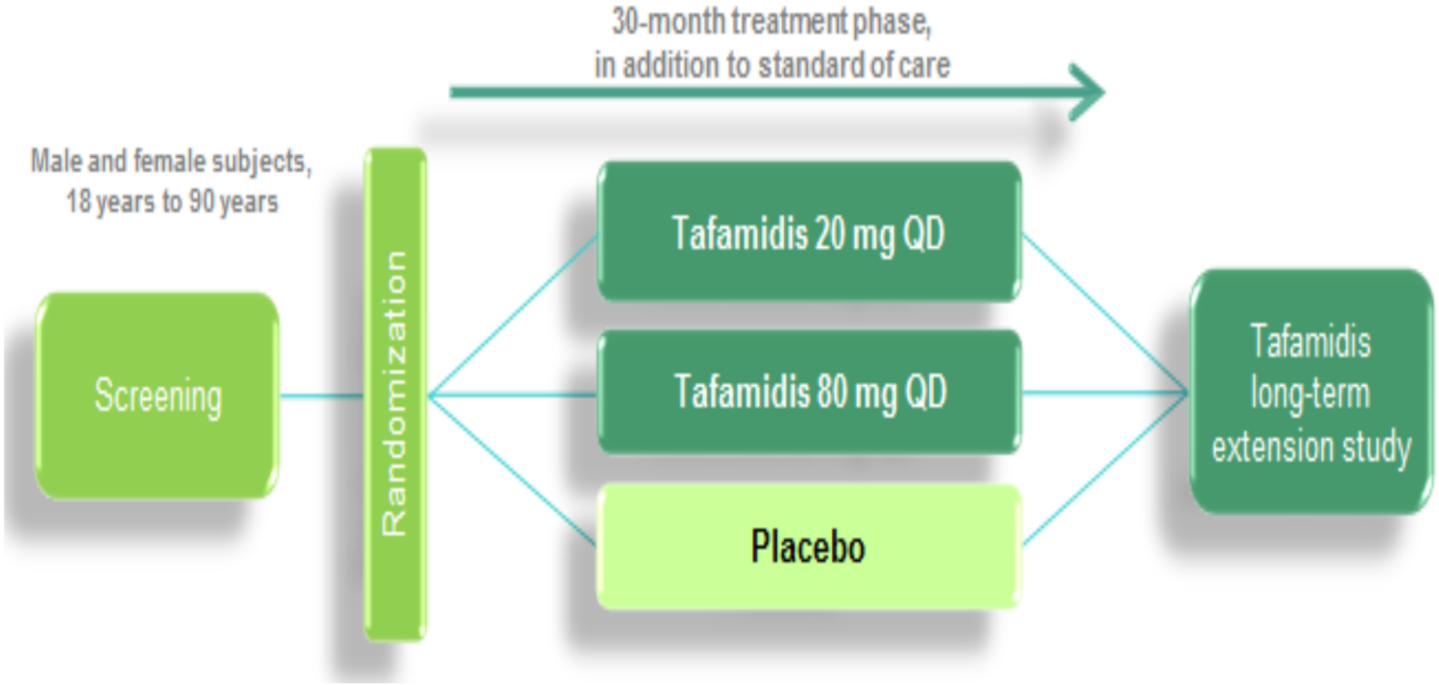


Test de marche des 6 minutes



Kaye MD, *Circ Heart Fail* 2016

ATTR-ACT Study Design



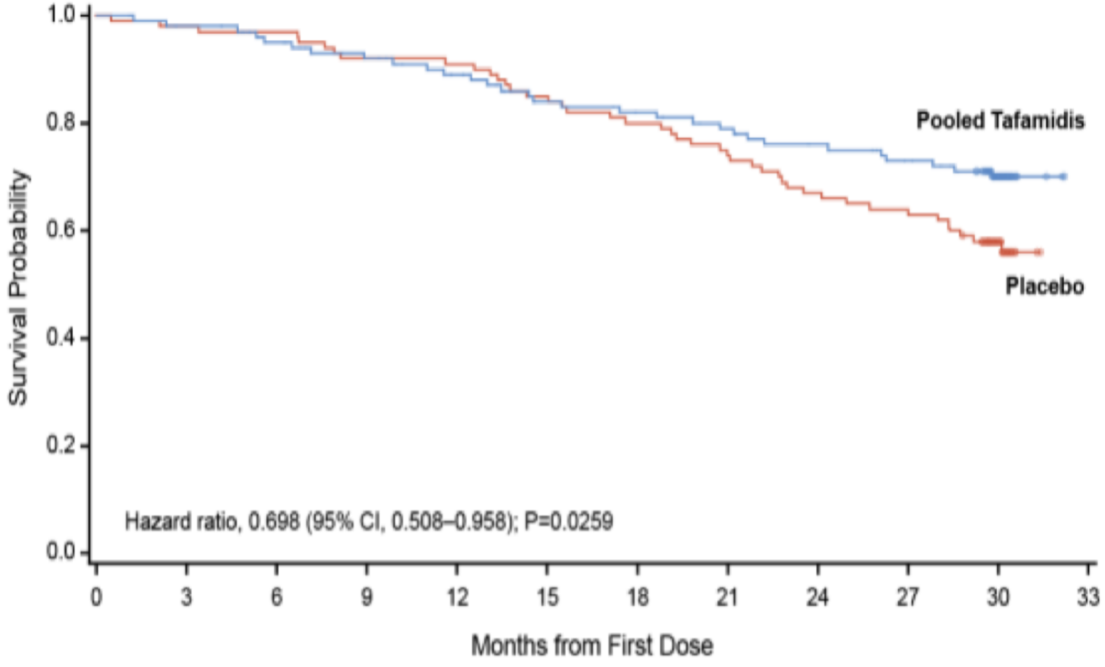
- Patients randomized 2:1:2 to tafamidis 80 mg, tafamidis 20 mg, and placebo
- Stratification for genotype (wild-type or variant) and disease severity (NYHA class)
- A sample size of 400 pts was estimated to give 90% power to detect either a 30% reduction in mortality, or a reduction in the frequency of CV-related hospitalizations from 2.5 to 1.5, or both

All-Cause Mortality Cox Proportional Hazards Model

30% reduction in the risk of all-cause mortality with tafamidis compared with placebo (p=0.0259)*

*Heart transplant and implantation of a cardiac mechanical assist device were treated as death for this analysis

33% reduction (p=0.018) when heart transplant and implantation of a cardiac mechanical assist device were not treated as death



No. at Risk
Patients Remaining at Risk
(Cumulative Events)

Tafamidis	264	259	252	244	235	222	216	209	200	193	99	0
	0	5	12	20	29	42	48	55	64	71	78	78
Placebo	177	173	171	163	161	150	141	131	118	113	51	0
	0	4	6	14	16	27	36	46	59	64	75	76

Conclusions

- ✓ HFpEF is a frequent disease, 50% of all HF, poor outcomes
- ✓ No validated treatment
- ✓ Pathophysiology is different from HFrEF
- ✓ From the classical diastolic dysfunction to an heterogenous syndrome
- ✓ Several etiologies with their own treatments
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Back-up slides

L'algorithme diagnostique

Pour une définition pragmatique de l'ICFEp

IC soupçonnée d'après les symptômes et/ou signes cliniques ± réponse au traitement diurétique

↓

Evaluer la présence d'une cardiopathie par ECG, radiographie et BNP

→ Si ECG et BNP normaux en phase congestive : ICFEp improbable

↓

FEVG ≥ 50 %

→ Si FEVG < 50 % : Présence d'une dysfonction systolique-intermédiaire

↓

Exclure les autres causes de dyspnée:
- Pathologies pulmonaires
- Valvulopathies gauches
- Cardiopathies congénitales
- Péricardite constrictive

→ Si présence : Diagnostic d'ICFEp impossible

↓

ICFEp possible

↓

Présence de facteurs étiologiques :
- Hypertension artérielle
- Diabète
- Obésité
- Syndrome d'apnée du sommeil

→ Exclure des co-morbidités :
- Hyperthyroïdie
- Insuffisance rénale sévère
- Maladies hépatiques (cirrhose)
- Autres surcharges hydriques primitives

↓

Echocardiographie
- Masse VG augmentée
- Dilatation de l'oreillette gauche (> 34 mL/m²)
- Présence d'une dysfonction diastolique

→ Exclure les ICA sans modifications structurales ou hémodynamiques:
- Poussée d'HTA sans cardiopathie hypertensive
- FA sur cœur sain

↓

IC diastolique

Treatment for HFpEF: what should we do?

Contrôle de la
pré-charge

Vasodilatateurs en aigu (sérélaxine) /diurétiques

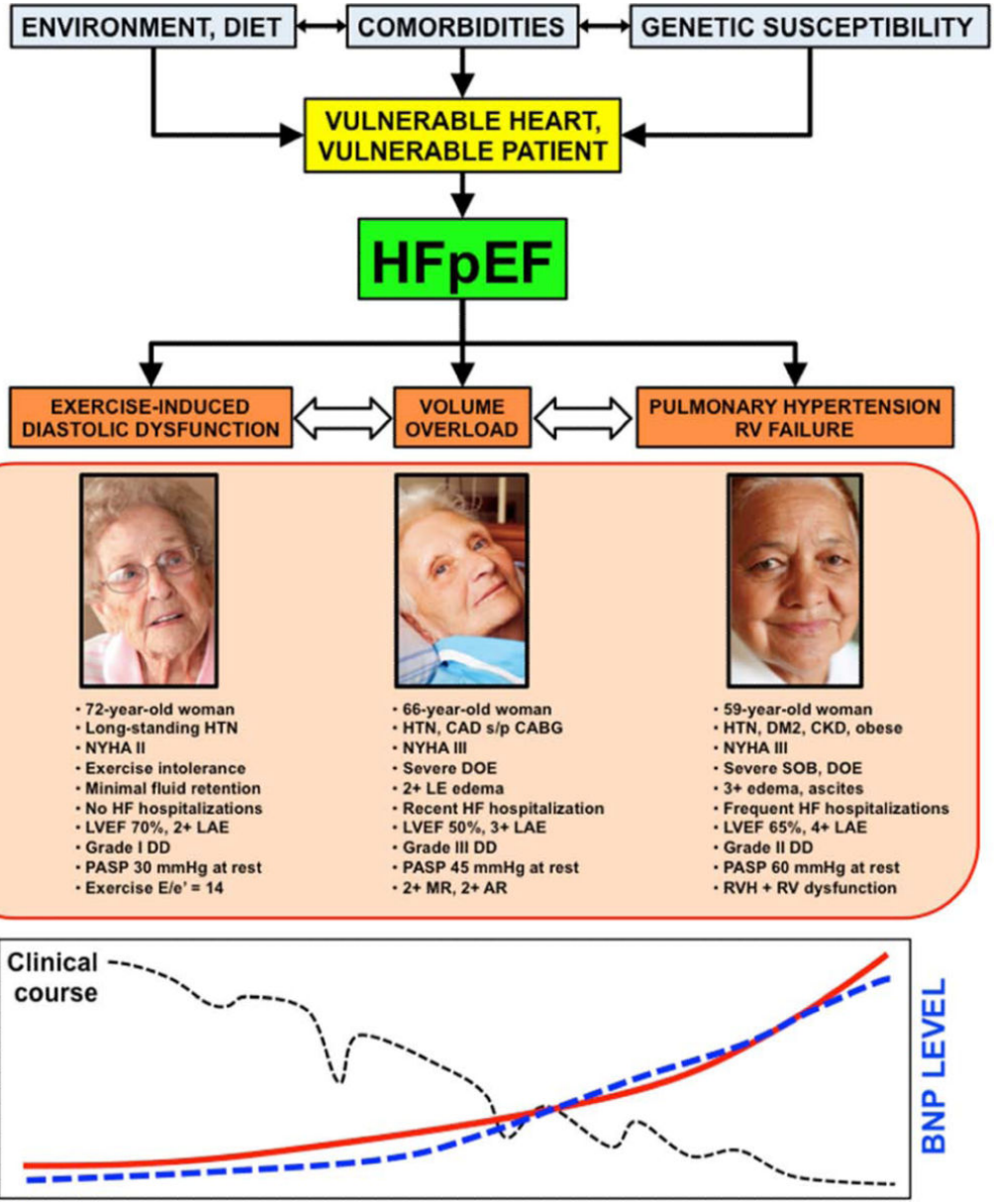
Clusters of Patients

Contrôle de la FC :

Agents bradycardisants si FC > 70 bpm
bêtabloquants ou vérapamil si CI
Ivabradine (en l'absence d'angor) ?

Agents spécifiques

LCZ696 ?


ENVIRONMENT, DIET
COMORBIDITIES
GENETIC SUSCEPTIBILITY
VULNERABLE HEART, VULNERABLE PATIENT
HFpEF
EXERCISE-INDUCED DIASTOLIC DYSFUNCTION
VOLUME OVERLOAD
PULMONARY HYPERTENSION RV FAILURE
SAMPLE PATIENTS
• 72-year-old woman
• Long-standing HTN
• NYHA II
• Exercise intolerance
• Minimal fluid retention
• No HF hospitalizations
• LVEF 70%, 2+ LAE
• Grade I DD
• PASP 30 mmHg at rest
• Exercise E/e' = 14
• 66-year-old woman
• HTN, CAD s/p CABG
• NYHA III
• Severe DOE
• 2+ LE edema
• Recent HF hospitalization
• LVEF 50%, 3+ LAE
• Grade III DD
• PASP 45 mmHg at rest
• 2+ MR, 2+ AR
• 59-year-old woman
• HTN, DM2, CKD, obese
• NYHA III
• Severe SOB, DOE
• 3+ edema, ascites
• Frequent HF hospitalizations
• LVEF 65%, 4+ LAE
• Grade II DD
• PASP 60 mmHg at rest
• RVH + RV dysfunction
RISK PROFILE
Clinical course
BNP LEVEL

Recommandations ESC 2016 : définition de l'insuffisance cardiaque à fraction d'éjection réduite, intermédiaire et préservée

Types d'IC		ICFEr	ICFEi	ICFEp
Critères	1	Symptômes ± Signes cliniques d'IC		
	2	FEVG < 40 %	FEVG 40-49 %	FEVG ≥ 50 %
	3	-	1. Taux de peptides natriurétiques élevés : BNP ≥ 35 pg/mL ou NT-proBNP ≥ 125 pg/mL 1. Au moins un des facteurs additionnels : a) Une anomalie structurelle cardiaque : HVG, dilatation OG (> 34 mL/m²) a) Une dysfonction diastolique : E/e' ≥ 13 ou e' < 9 cm/s	

Eur Heart J 2016. Doi: 10.1093/eurheartj/ehw128

Diagnostic de l'ICFEp

Echocardiographie doppler

Fraction d'éjection

FEVG < 50% => Insuffisance Cardiaque Systolique (40-49% Intermédiaire)

FEVG ≥ 50 % => Insuffisance Cardiaque à Fraction d'Ejection Préservée

Masse ventriculaire gauche et taille de l'oreillette gauche

- ✓ Une HVG échographique ou un remodelage concentrique du ventricule gauche sont associés à une altération de la fonction diastolique.
- ✓ Une dilatation de l'oreillette gauche (> 34 mL/m²) en l'absence de fibrillation atriale et d'anomalie de la valve mitrale peut indiquer l'existence d'une altération de la fonction de remplissage.

Paramètre de fonction diastolique

- ✓ Onde e' < 9 cm/s
- ✓ E/e' > 15 ou ≥ 13

Juillière Y et al. Arch Mal Coeur 2006;99:279-286

Clinical Characteristic	Group 1 (n=128)	Group 2 (n=120)	Group 3 (n=149)	*P* Value
Age, y	60.7±13.6	65.7±11.3	67.3±13.1	<0.001
Female, n (%)	86 (67)	81 (68)	82 (55)	0.049
Race, n (%)				0.32
White	72 (56)	58 (48)	77 (52)	
Black	42 (33)	54 (45)	56 (37)	
Other	14 (11)	8 (7)	16 (11)	
NYHA functional class, n (%)				0.17
I	25 (20)	11 (9)	13 (9)	
II	61 (48)	40 (33)	56 (38)	
III	38 (30)	64 (53)	78 (52)	
IV	3 (2)	5 (4)	2 (1)	
Comorbidities, n (%)				
Coronary artery disease	54 (42)	58 (48)	75 (50)	0.38
Hypertension	84 (66)	108 (90)	112 (75)	<0.001
Hyperlipidemia	65 (51)	75 (62)	73 (49)	0.06
Diabetes mellitus	12 (9)	63 (52)	50 (34)	<0.001
Obesity	65 (51)	84 (70)	55 (37)	<0.001
Chronic kidney disease	8 (6)	41 (34)	79 (53)	<0.001
Atrial fibrillation	17 (13)	26 (22)	64 (43)	<0.001
Chronic obstructive pulmonary disease	43 (34)	46 (38)	56 (38)	0.70
Obstructive sleep apnea	35 (27)	60 (50)	46 (31)	<0.001

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Shah S, *Circulation*. 2015;131:269-279

Clinical Characteristic	Group 1 (n=128)	Group 2 (n=120)	Group 3 (n=149)	*P* Value
Vital signs and laboratory data				
Heart rate, bpm	77.2±14.5	74.7±14.9	71.6±12.6	0.004
Systolic blood pressure, mm Hg	122.4±16.6	129.2±19.0	123.0±22.7	0.011
Diastolic blood pressure, mm Hg	73.3±10.2	70.1±10.2	67.3±13.6	<0.001
Pulse pressure, mm Hg	49.1±12.4	59.2±16.9	55.7±19.6	<0.001
Body mass index, kg/m^2	31.2±7.3	37.0±10.7	28.9±7.4	<0.001
Serum sodium, mEq/L	139.0±3.0	138.4±2.6	137.9±2.9	0.01
Blood urea nitrogen, mg/dL	13.7±4.5	24.4±11.8	33.6±19.9	<0.001
Serum creatinine, mg/dL	0.9±0.2	1.3±0.4	2.3±2.2	<0.001
Estimated GFR, mL·min^{-1}·1.73 m^{-2}	79.5±21.2	53.8±17.6	43.9±27.3	<0.001
Fasting glucose, mg/dL	98.4±15.6	153.2±85.2	111.5±29.2	<0.001
Hemoglobin, g/dL	12.5±1.7	11.8±1.8	11.4±1.9	<0.001
B-type natriuretic peptide, pg/mL	72 (26–161)	188 (83–300)	607 (329–1138)	<0.001

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Shah S, *Circulation*. 2015;131:269-279

Parameter	Group 1 (n=128)	Group 2 (n=120)	Group 3 (n=149)	*P* Value
ECG				
PR interval, ms	166.6±29.6	174.2±29.8	183.3±53.5	0.007
QRS duration, ms	93.8±21.0	91.3±13.6	112.7±33.3	<0.001
QTc interval, ms	450.6±35.2	449.8±34.0	464.6±48.9	0.005
QRS axis, degrees	10.7±39.0	20.4±38.4	−4.2±60.7	<0.001
QRS-T angle, degrees	42.6±41.7	53.4±44.0	86.6±54.0	<0.001
Invasive hemodynamics (n=216)				
Right atrial pressure, mm Hg	10.5±4.6	15.3±6.5	14.6±6.8	<0.001
Pulmonary artery systolic pressure, mm Hg	42.4±12.0	55.9±15.4	56.7±19.7	<0.001
Pulmonary artery diastolic pressure, mm Hg	21.7±6.3	28.2±7.7	26.5±9.1	<0.001
Mean pulmonary artery pressure, mm Hg	28.8±7.7	35.9±9.9	36.6±11.7	<0.001
Pulmonary capillary wedge pressure, mm Hg	19.9±6.3	24.6±8.3	23.7±9.7	0.002
Pulmonary vascular resistance, Wood units	1.2±2.5	2.8±4.6	2.3±3.7	0.043
Cardiac output, L/min	6.1±2.1	6.5±2.1	5.8±2.3	0.15

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Parameter	Group 1 (n=128)	Group 2 (n=120)	Group 3 (n=149)	*P* Value
Echocardiography				
LV end-diastolic volume, mL	81.2±23.4	84.2±24.0	84.6±32.3	0.56
LV end-systolic volume, mL	31.6±12.1	33.1±12.1	35.4±19.2	0.12
Relative wall thickness	0.47±0.11	0.49±0.09	0.56±0.20	<0.001
LV mass index, g/m^2	89.1±22.6	96.4±26.3	122.0±47.3	<0.001
Left atrial volume index, mL/m^2	29.1±11.1	31.5±10.6	40.9±16.7	<0.001
LV ejection fraction, %	61.8±5.6	61.2±6.5	60.0±7.1	0.05
Stroke volume, mL	84.8±22.9	88.6±32.0	80.7±31.3	0.09
Cardiac output, L·min^{-1}·m^{-2}	6.5±2.0	6.6±2.5	5.8±2.6	0.006
Pulmonary artery systolic pressure, mm Hg	35.3±9.7	43.5±14.6	51.2±16.3	<0.001
Right atrial pressure, mm Hg	6.0±2.7	6.9±3.5	9.8±4.7	<0.001
E velocity, cm/s	93.2±28.6	103.2±34.5	118.2±40.9	<0.001
A velocity, cm/s	82.8±22.5	93.1±26.3	81.6±38.7	0.01
E/A ratio	1.2±0.5	1.1±0.4	1.7±1.0	<0.001
Tissue Doppler e' velocity, cm/s	9.3±3.2	7.5±2.1	7.9±3.4	<0.001
E/e' ratio	11.2±3.7	15.2±6.4	18.6±10.6	<0.001
Diastolic dysfunction grade, n (%)				<0.001
Normal diastolic function	21 (16)	9 (8)	2 (1)	
Grade I (mild) diastolic dysfunction	15 (12)	16 (13)	12 (8)	
Grade II (moderate) diastolic dysfunction	60 (47)	56 (47)	43 (29)	
Grade III (severe) diastolic dysfunction	23 (18)	31 (26)	83 (56)	
Indeterminate diastolic function	9 (7)	8 (7)	9 (6)	
RV basal diameter, cm	3.6±0.6	3.8±0.5	4.2±0.8	<0.001
RV end-diastolic area index, cm/m^2	12.4±2.1	12.7±2.4	16.2±4.7	<0.001
RV end-systolic area index, cm/m^2	6.7±1.5	7.2±1.5	9.9±3.4	<0.001
RV wall thickness, cm	0.46±0.03	0.50±0.07	0.56±0.11	<0.001
RV fractional area change	0.46±0.06	0.43±0.05	0.40±0.08	<0.001
TAPSE, cm	2.2±0.6	2.1±0.6	1.7±0.6	<0.001

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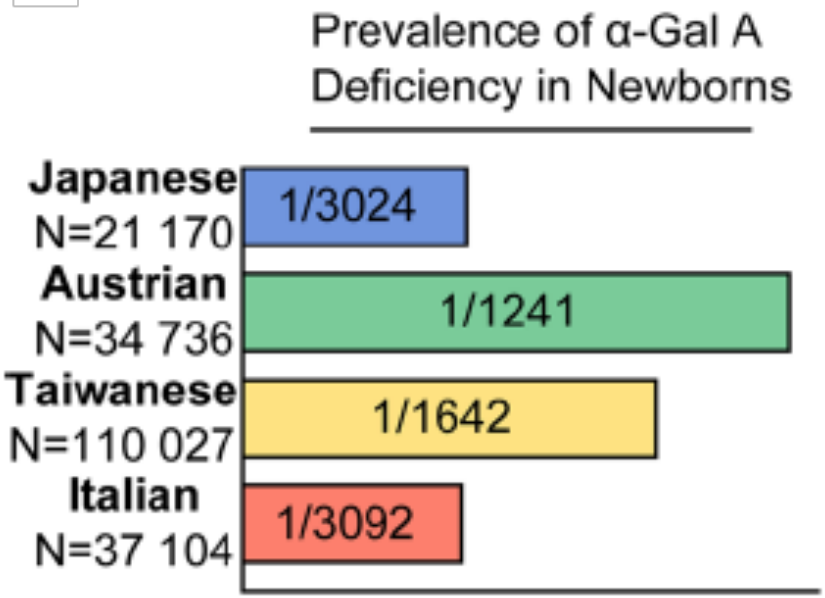
Shah S, *Circulation*. 2015;131:269-279

LA MALADIE DE FABRY ?

Anderson-Fabry cardiomyopathy: prevalence, pathophysiology, diagnosis and treatment

Cardiopathie de surcharge par déficit en α-Galactosidase A (enzyme lysosomale intervenant dans le voies d'épuration intra-cellulaires)



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