

XI Reunión. Estado del Arte en  
**INSUFICIENCIA CARDIACA**

PRÁCTICA CLÍNICA Y MODELOS ORGANIZATIVOS

Sede: Hotel Meliá MaríaPita, A Coruña

**A CORUÑA** 27-28 SEPTIEMBRE 2024



XI Meeting. State of the Art in  
**HEART FAILURE**

CLINICAL PRACTICE AND ORGANIZATIONAL MODELS

Venue: Hotel Meliá MaríaPita, A Coruña

#ACoruñaHF2024

**A CORUÑA** 27-28 SEPTEMBER 2024

# Diffuse myocardial fibrosis in chronic heart failure: Potential diagnostic and therapeutic implications



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Centro de Investigación Biomédica en Red  
**Enfermedades Cardiovasculares**



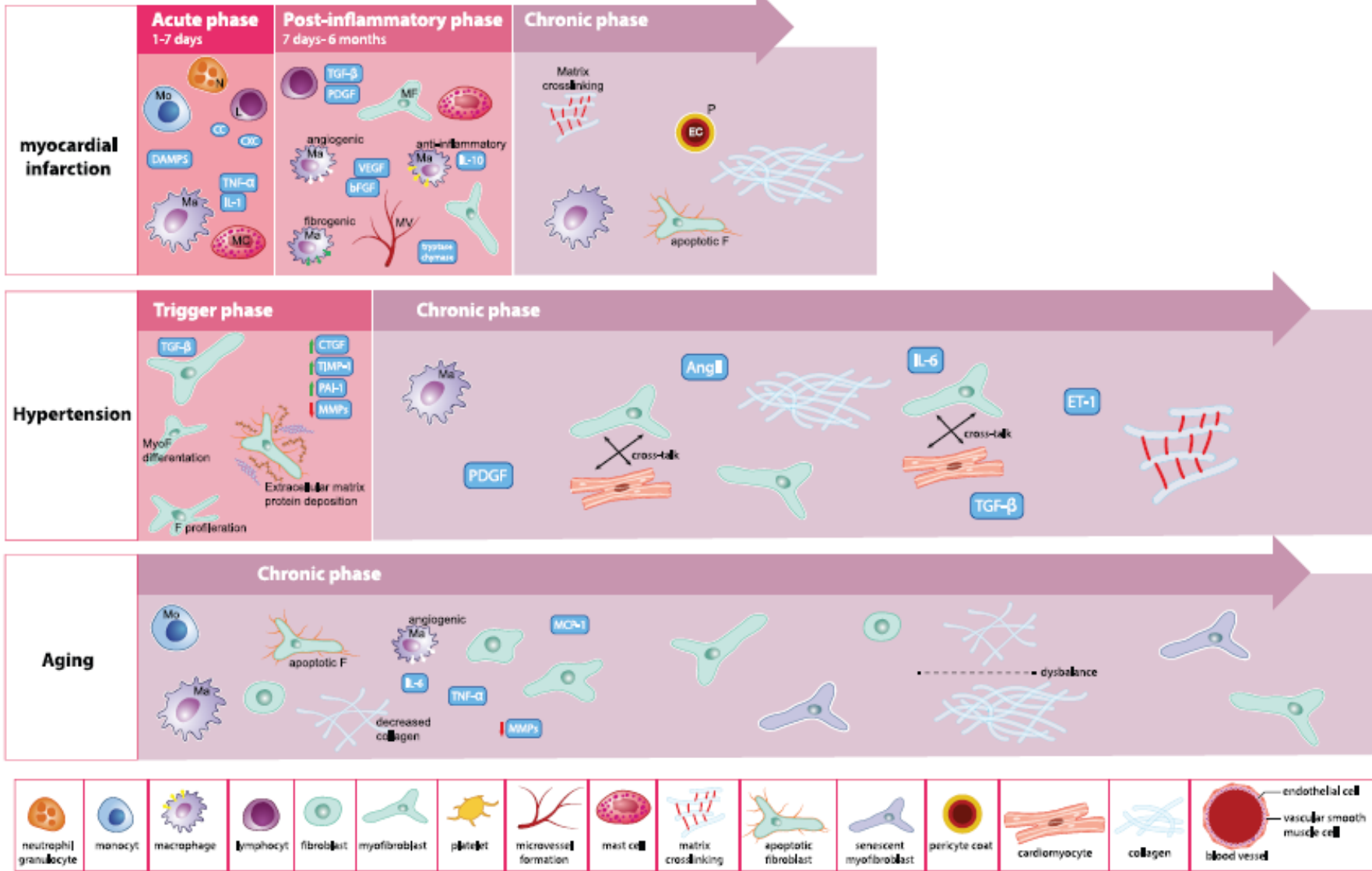
ÁREA SANITARIA  
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**ciber | CV**



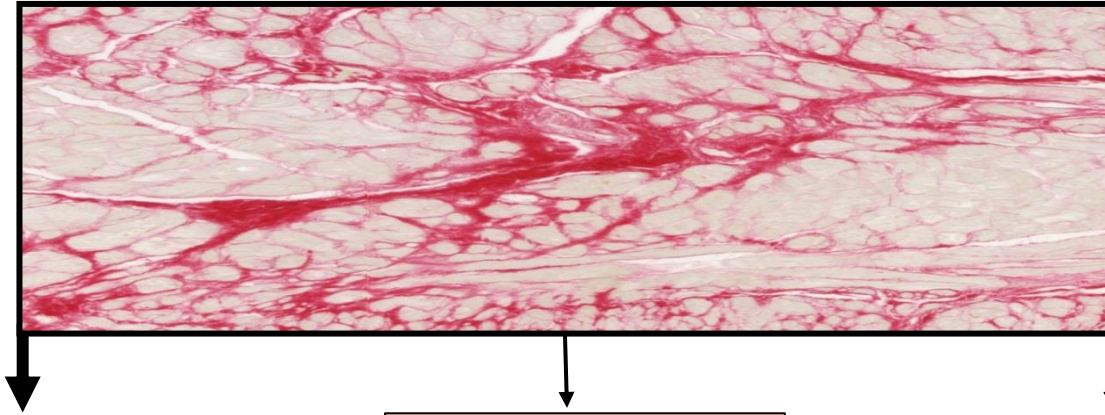
# Heterogeneity and dynamics of myocardial fibrosis



**One size does not fit all**

(de Boer RA et al. Eur J Heart Fail 2019;21:272-85)

# Pathophysiological impact of myocardial fibrosis



*Alterations of myocardial physical properties*

*Alterations of cellular interactions and tissue architecture*

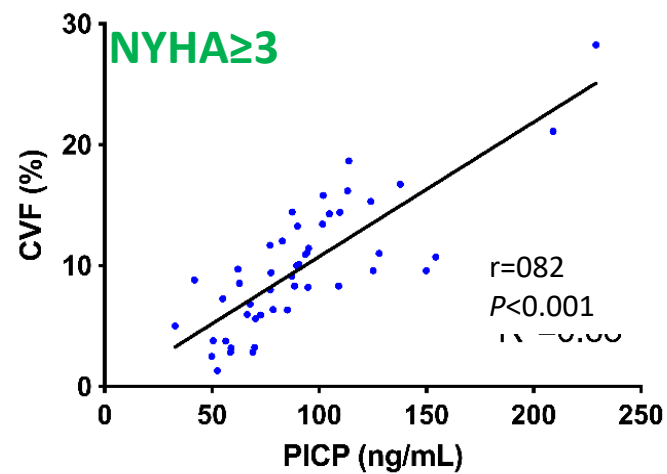
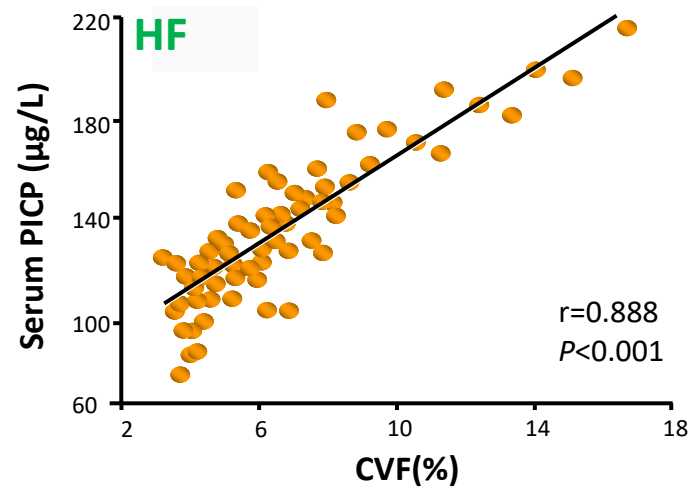
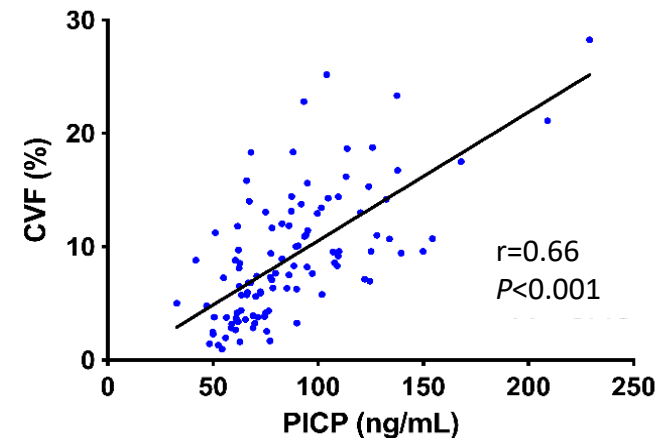
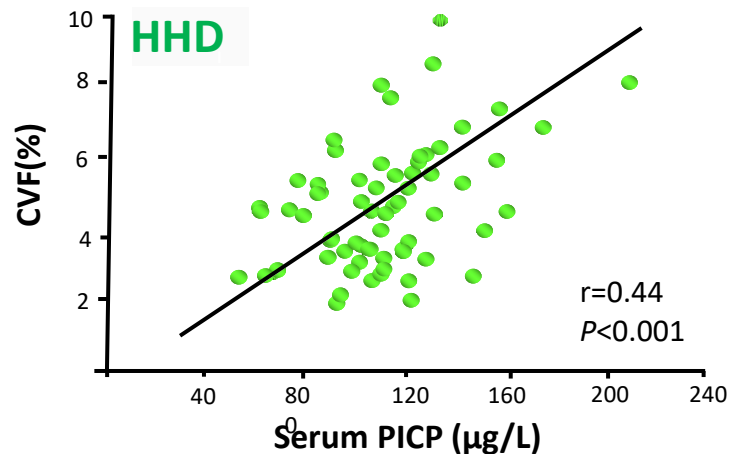
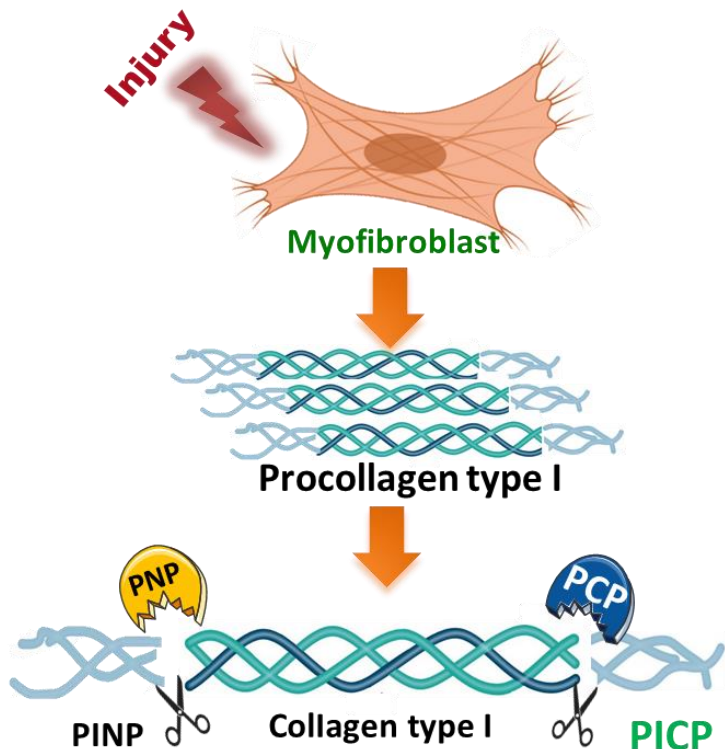
*Alterations of ECM reservoir function*

(González A et al, *J Am Coll Cardiol* 2018;71:1696-1706)

# PICP: A Biomarker of collagen synthesis – Association with myocardial fibrosis

## PICP and CVF in hypertension

## PICP and CVF in DCM - HFrEF

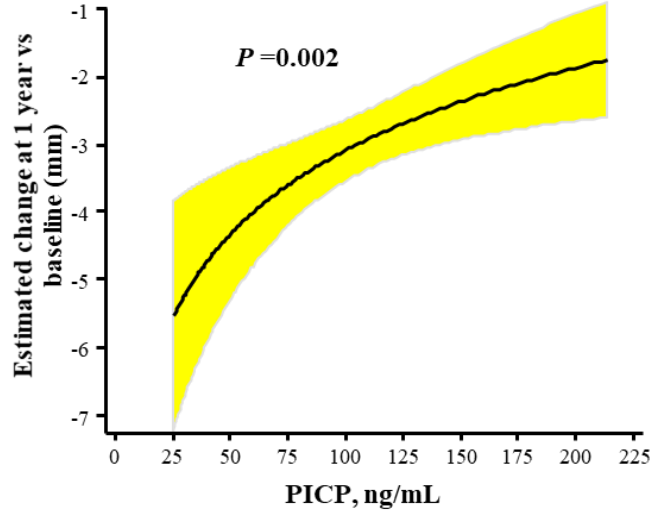


(Querejeta R et al, *Circulation* 2000;101:1729-35;  
López B et al, *JACC* 2004;43:2028-34)

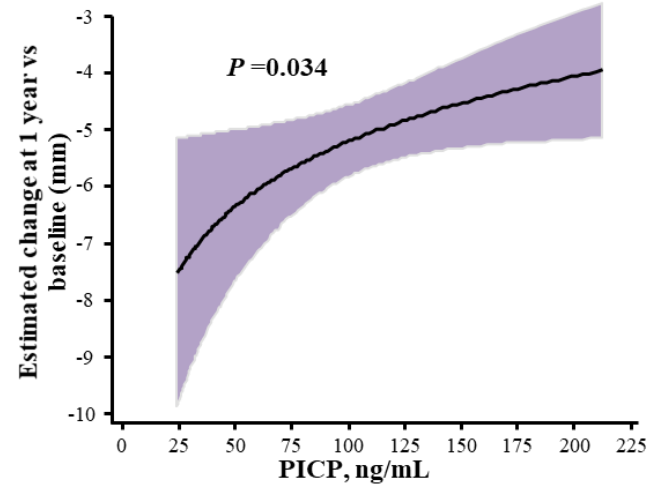
(Raafs AG et al. *Eur J Heart Fail* 2021;23:933-44)

# Fibrosis and LV reverse remodelling after 1-year guideline-guided therapy in HF patients with LVEF<50% (n=665)

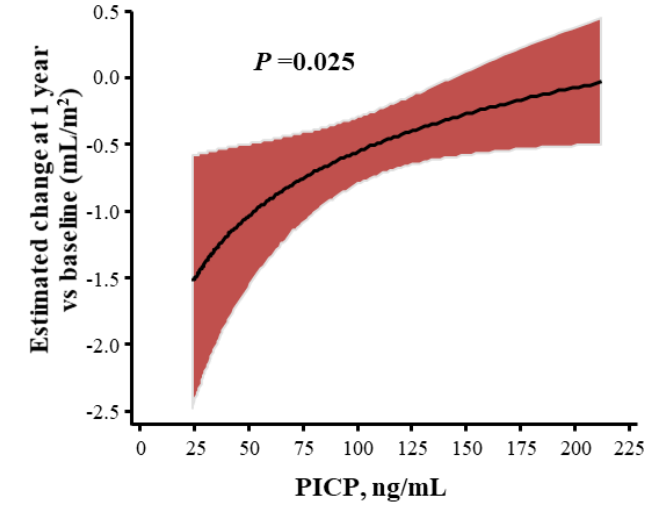
### LV end-diastolic diameter



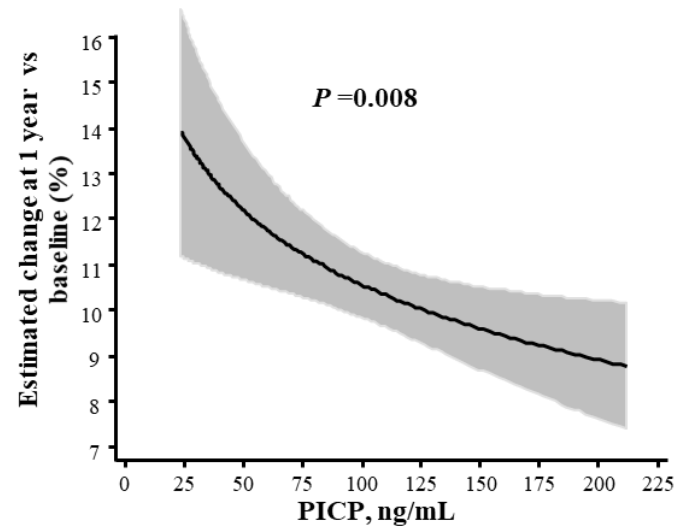
### LV end-systolic diameter



### Left atrial volume index



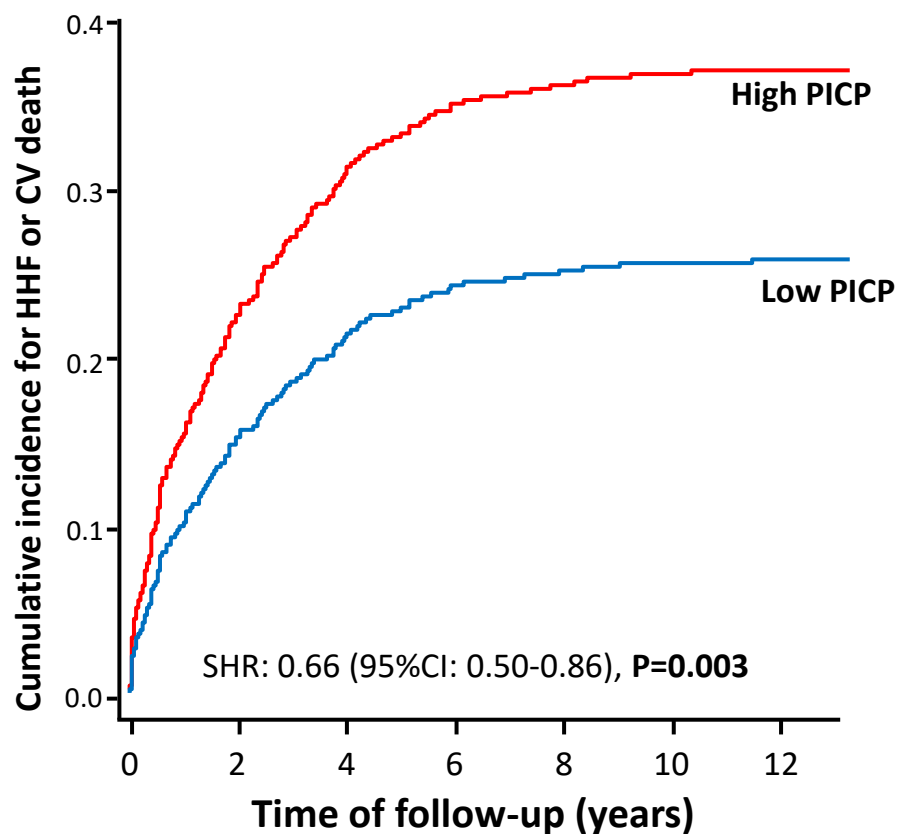
### LV ejection fraction



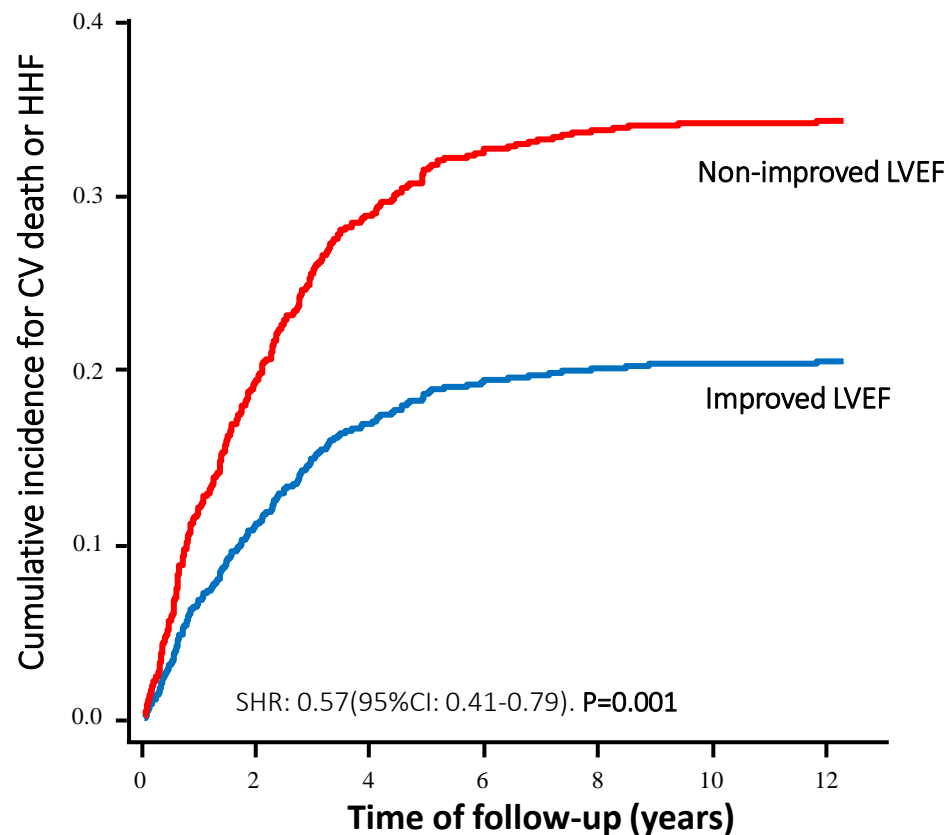
(Ravassa S et al. *JACC Heart Failure* 2023;11:58-72)

# Fibrosis and cardiovascular outcomes in HF patients with LVEF<50% (n=1034)

## HF hospitalization and CV death



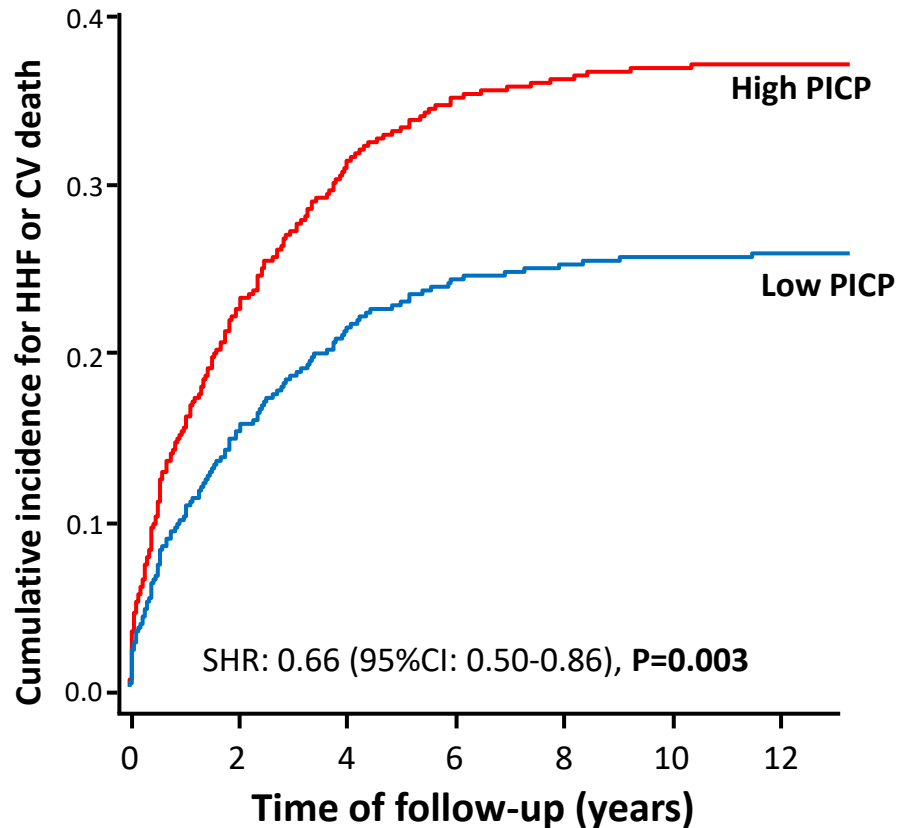
## LVEF improvement



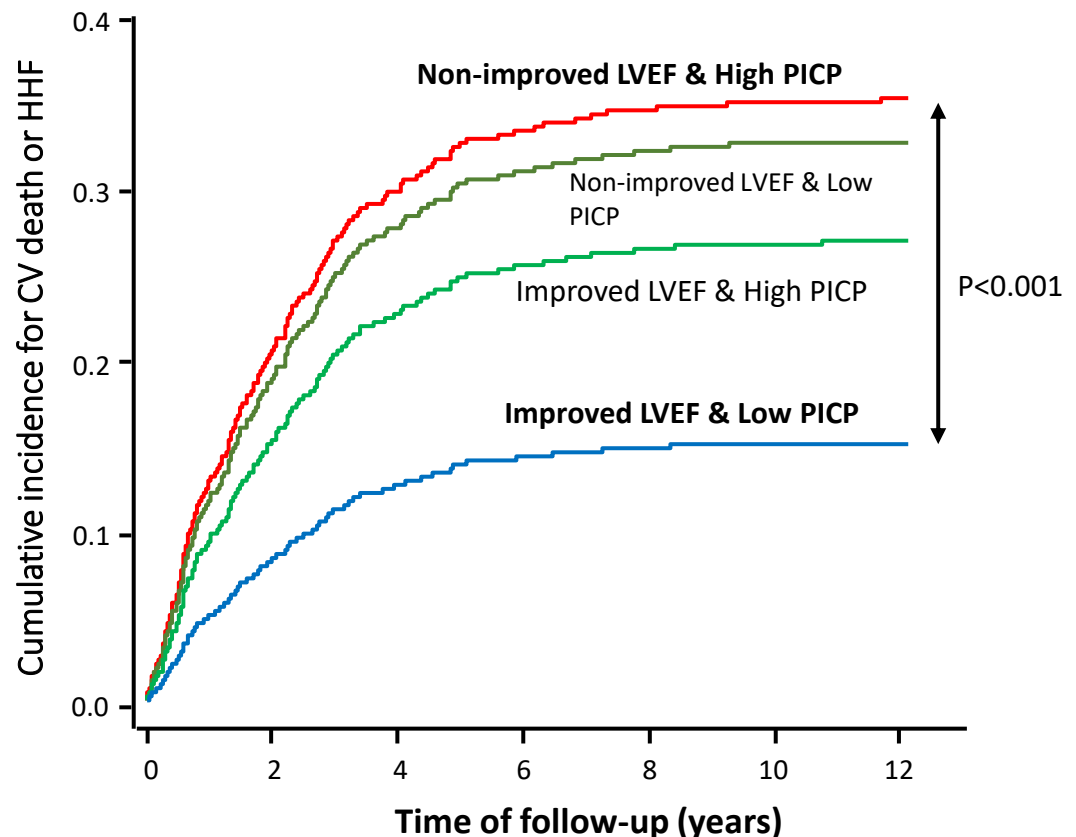
(Ravassa S et al. *JACC Heart Failure* 2023;11:58-72)

# Fibrosis and cardiovascular outcomes in HF patients with LVEF<50% (n=1034)

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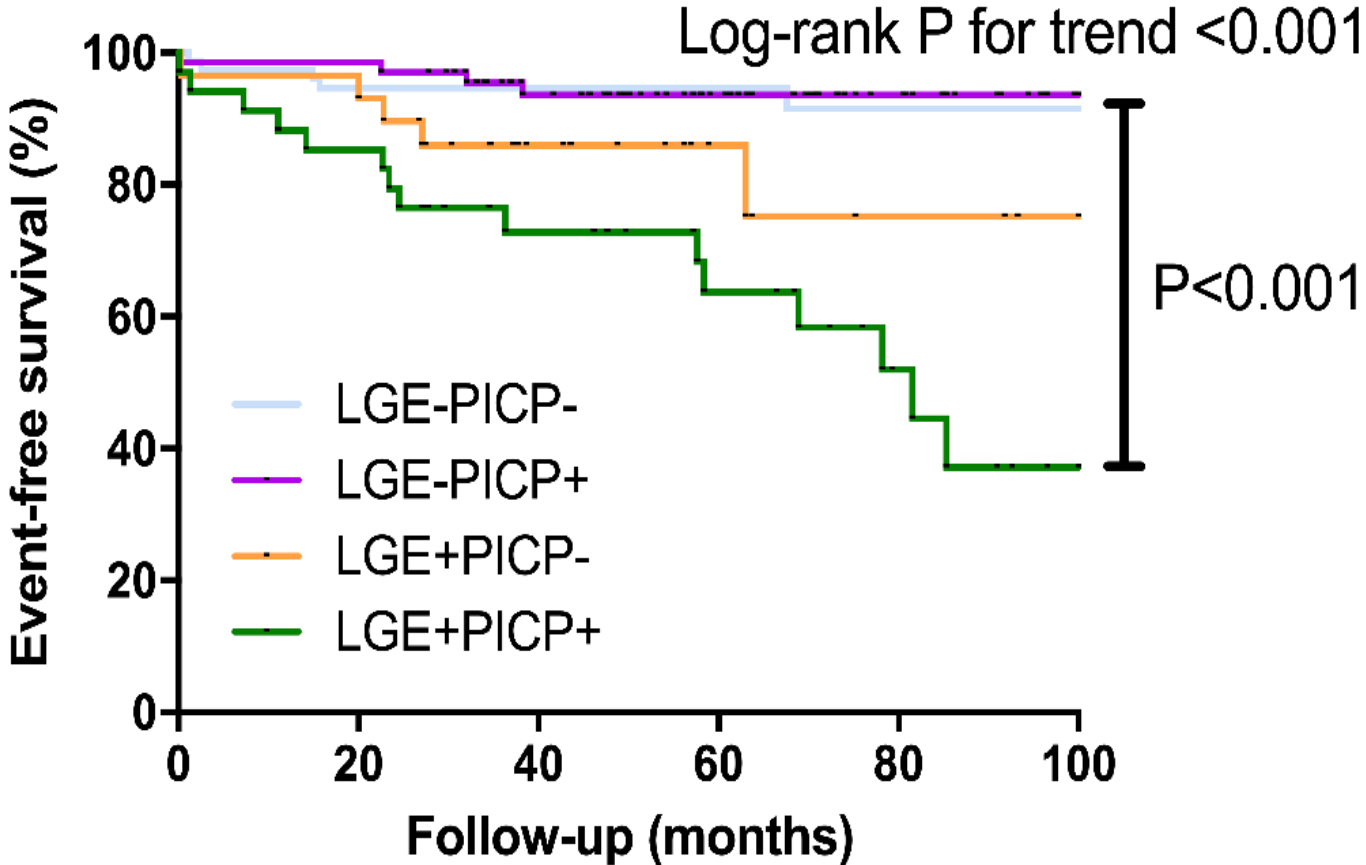


## Combination of LVEF improvement and low PICP



(Ravassa S et al. *JACC Heart Failure* 2023;11:58-72)

# Fibrosis and cardiovascular outcomes in patients with dilated cardiomyopathy (n=209)



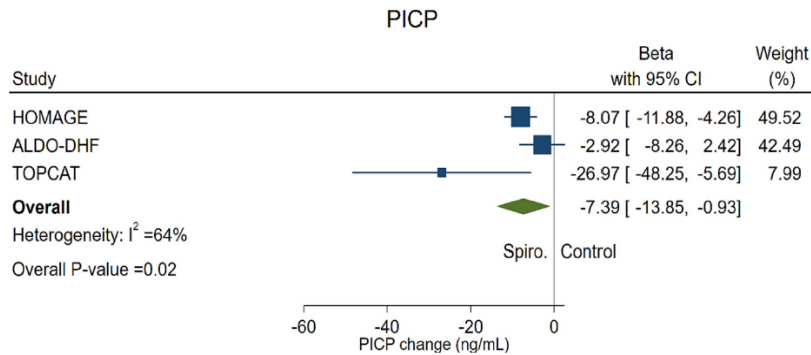
(Raafs AG et al. *Eur J Heart Fail* 2021;23:933-944)



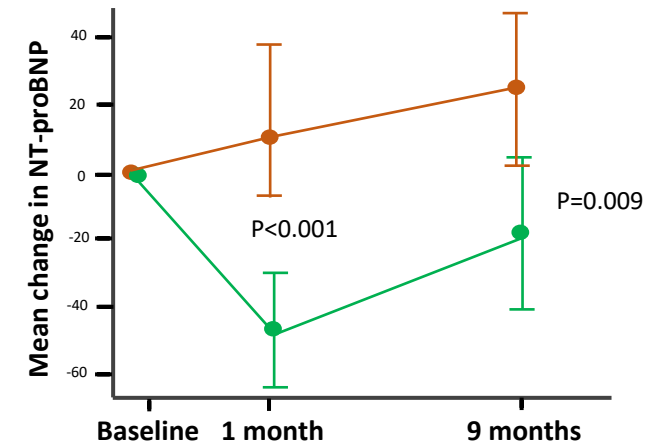
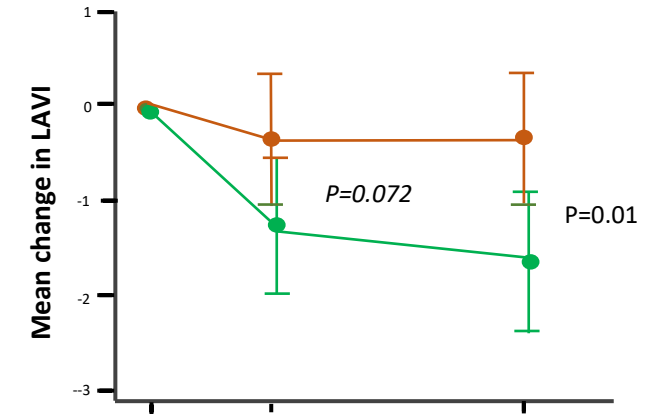
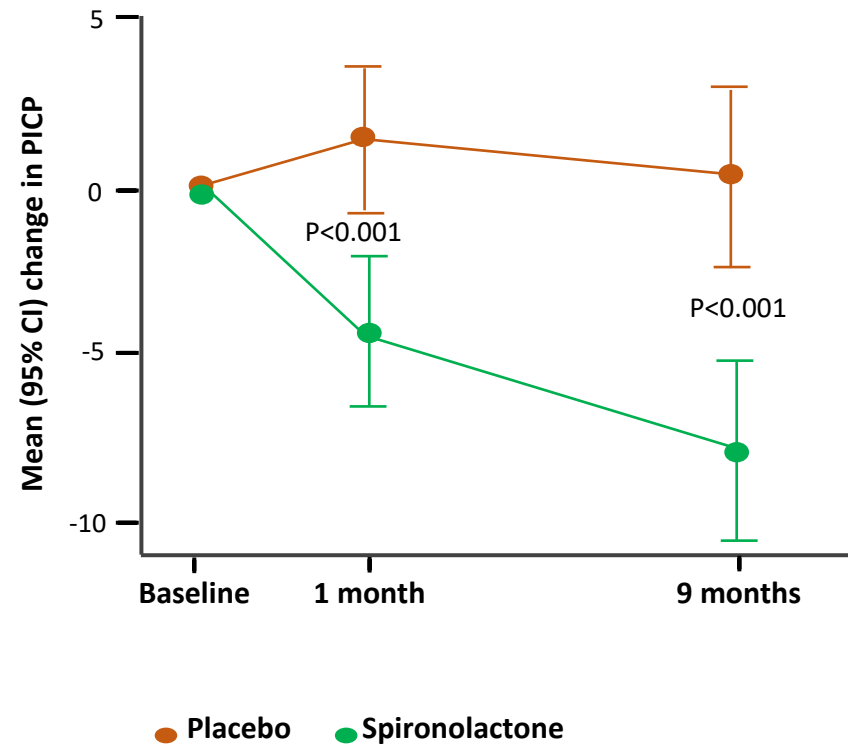
# Anti-fibrotic effects of HF therapy: MRAs

## Spirolactone in patients at risk of HF: HOMAGE Trial

### Mineralocorticoid receptor antagonists



### Changes in PICP

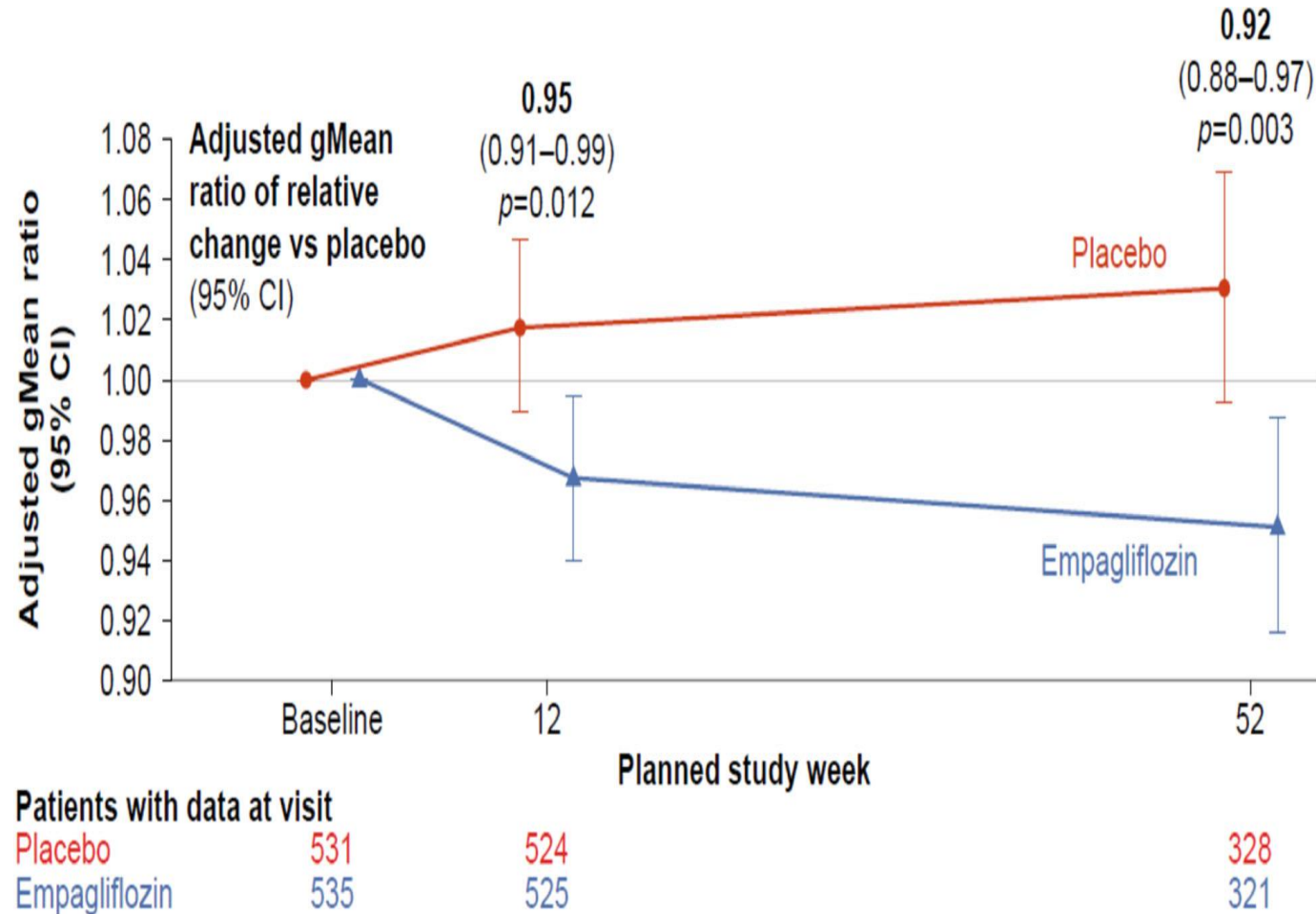


(Ferreira JP et al. *Int J Cardiol* 2023;377:86-88)

(Cleland JGF et al. *Eur Heart J* 2021;42:684-696)

# Anti-fibrotic effects of HF drugs: iSGLT2

## Empagliflozin in HF: The EMPEROR Trials



(Ferreira JP et al. *Eur J Heart Fail* 2024;26:274-284-944)

# Collagen quantity and cross-linking



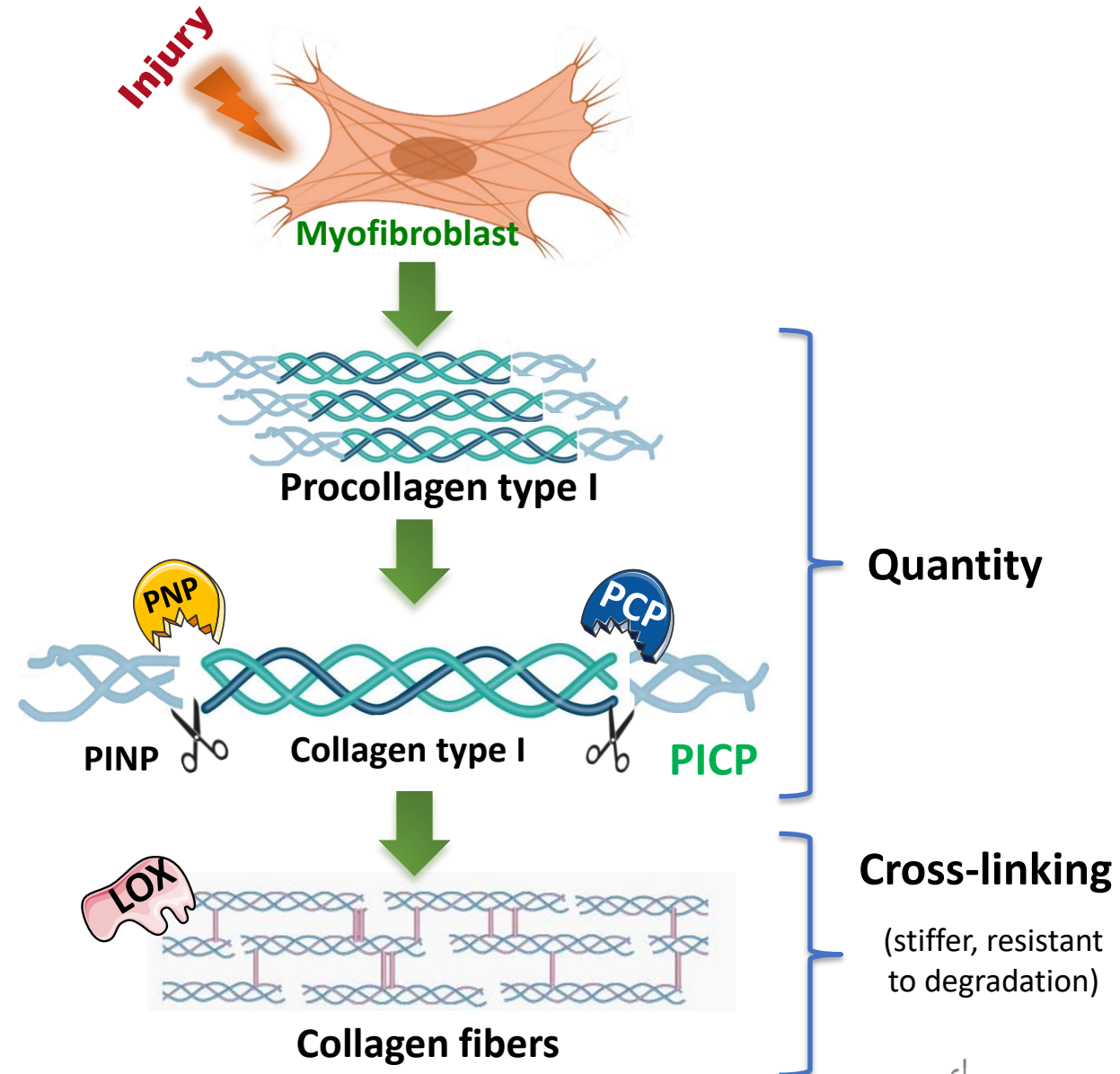
Quantity is not all that matters...

(Collagen molecules)

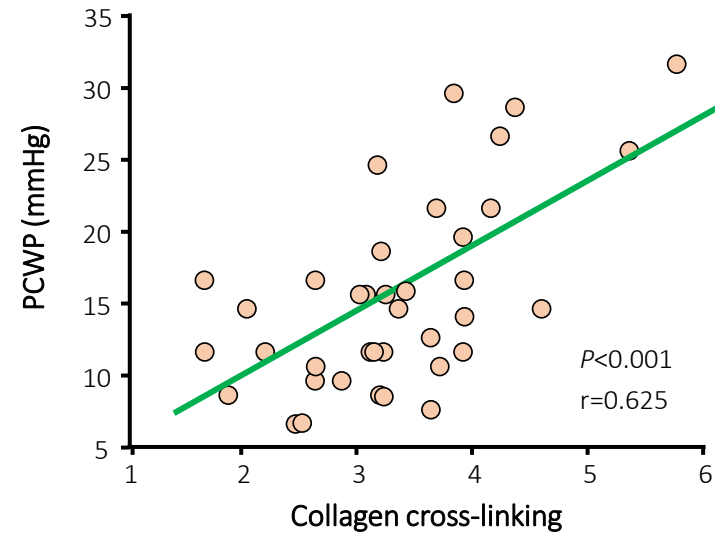
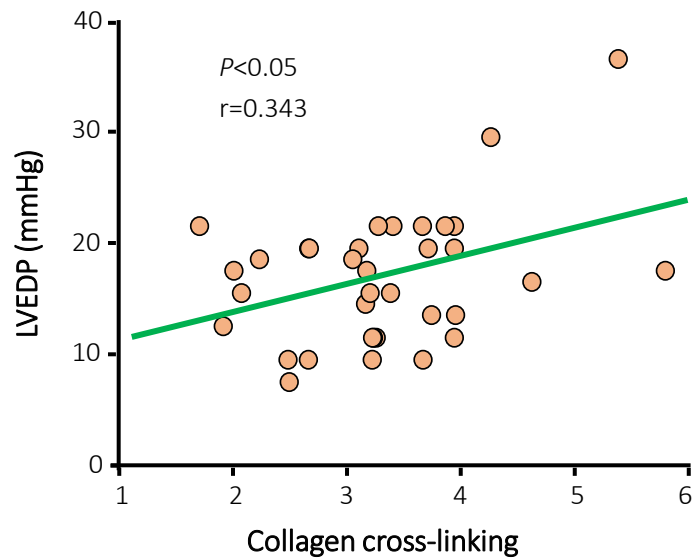
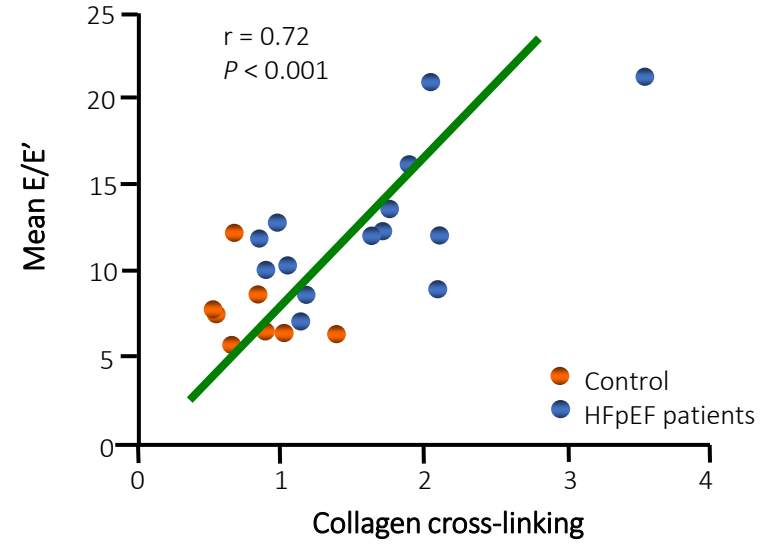
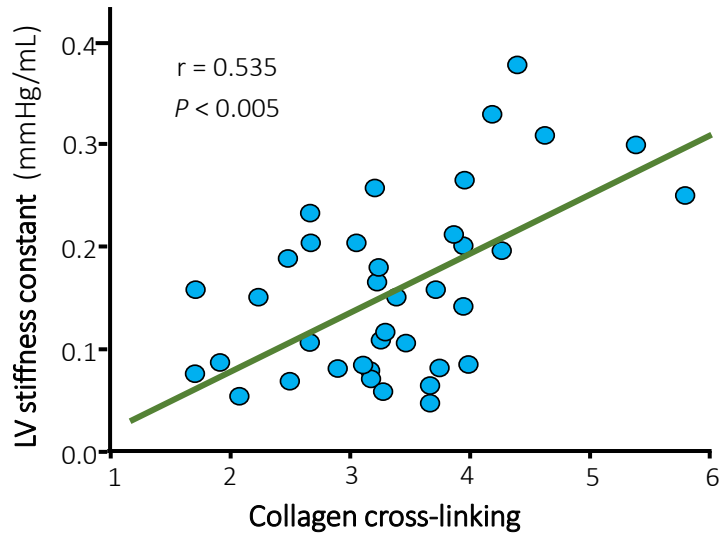


... quality is also important

(Collagen cross-linking)

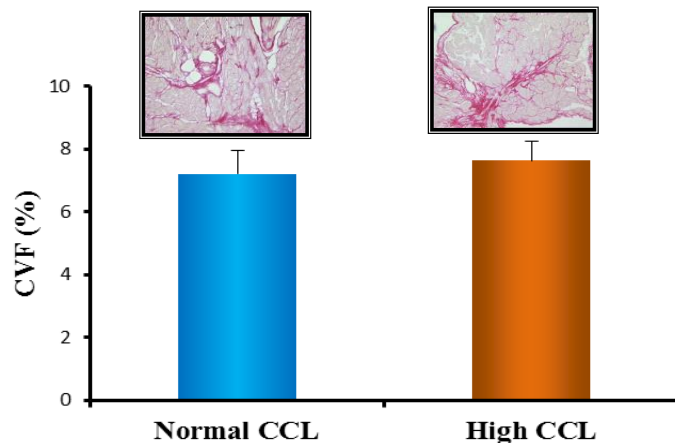
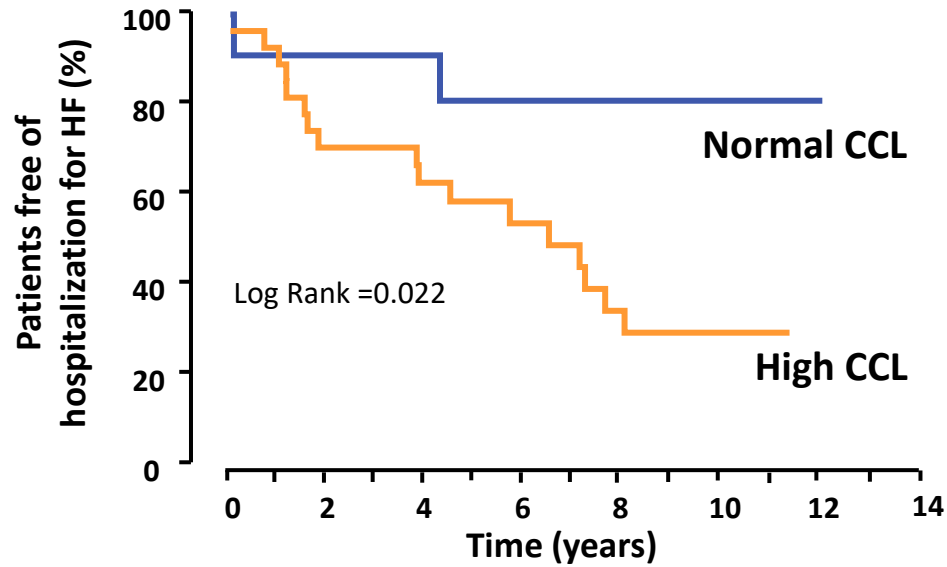


# Association of collagen cross-linking with diastolic dysfunction in HF patients

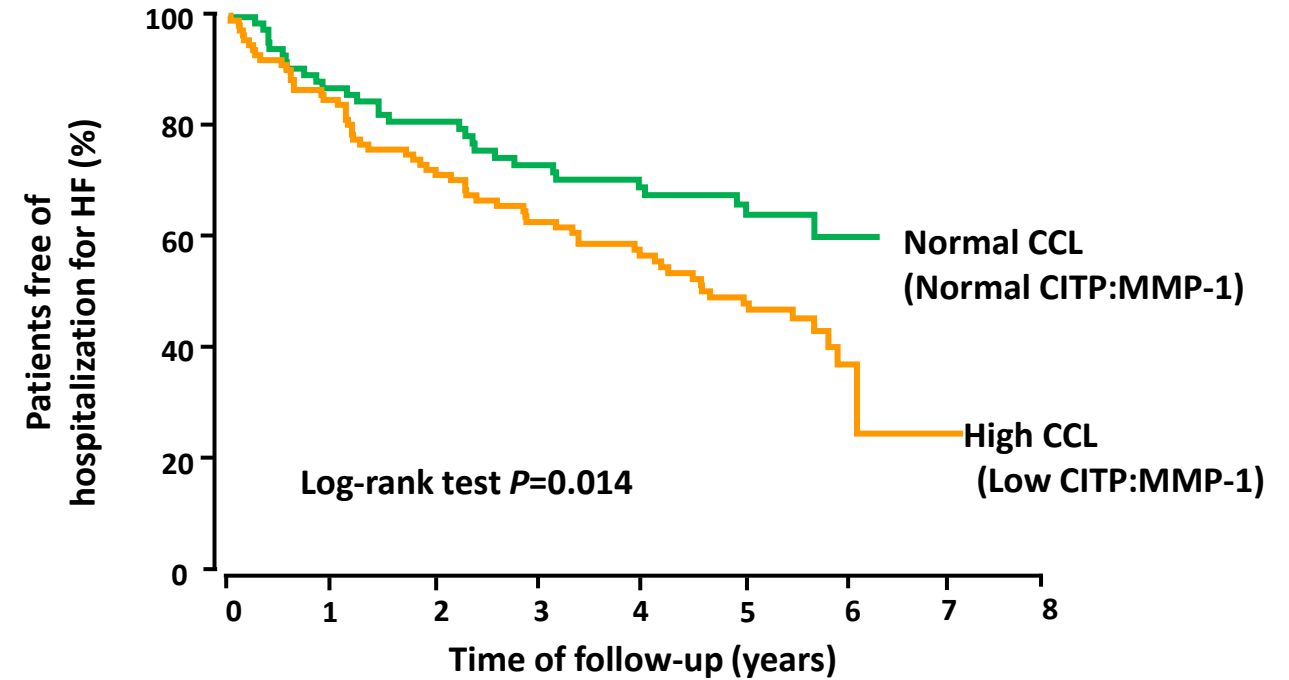


# Impact of collagen cross-linking in heart failure patients

## Hospitalization for HF



## Non-invasive assessment hypertensive HF patients (n=234)



### Adjusted Hazard ratio

**2.22** (95% CI 1.37-3.59,  $P<0.01$ )

(Including the co-variables age, sex, SBP, eGFR, LVMI, LVEF, NT-proBNP and treatment)

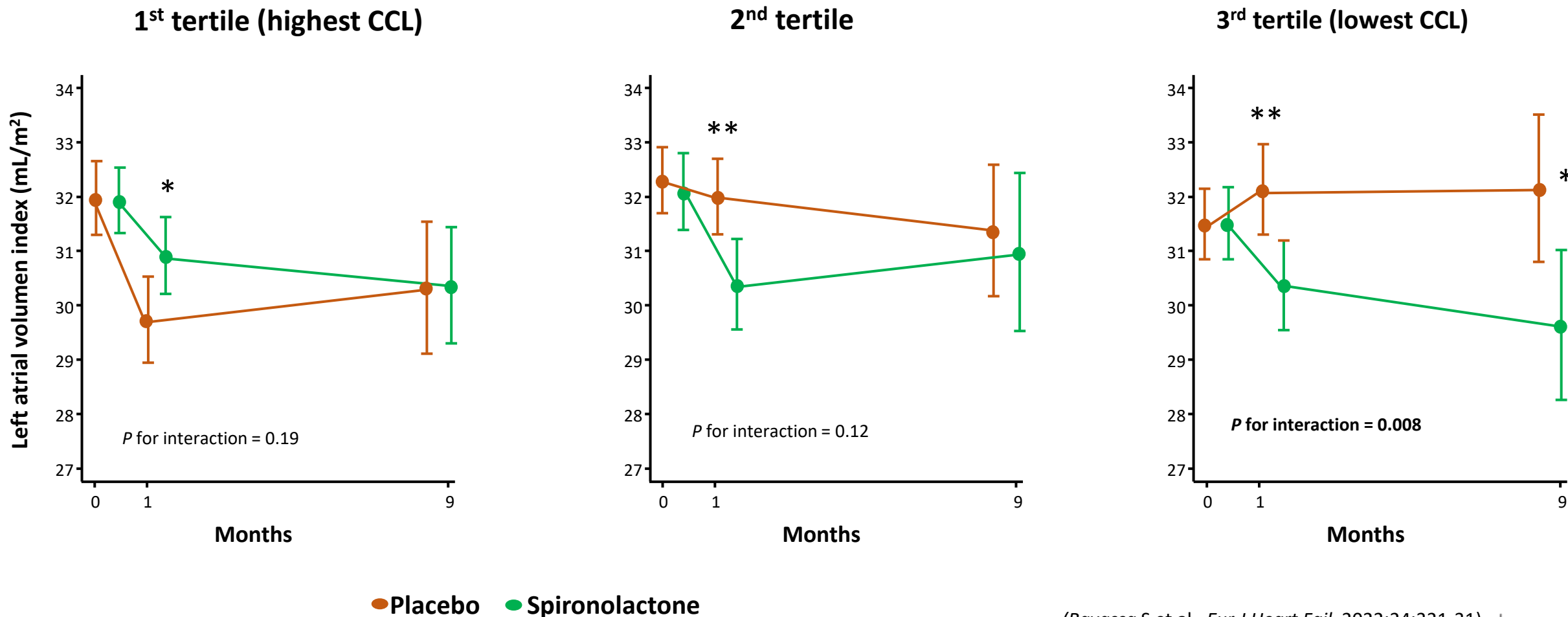
(López B et al, *J Am Coll Cardiol* 2016;67:251-260)

# Selecting responders for available anti-fibrotic drugs: MRAs



## Impact of CCL in spironolactone in patients at risk of HF : The HOMAGE trial

### Changes in LAVI by baseline CITP:MMP-1 tertiles

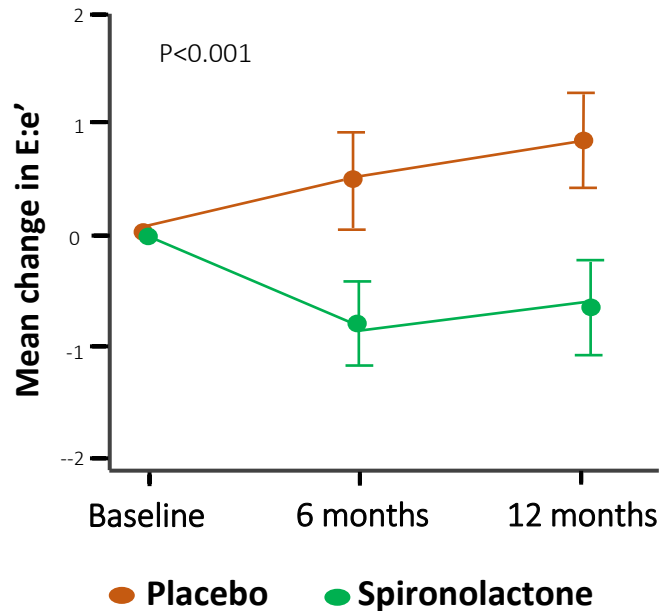


(Ravassa S et al. *Eur J Heart Fail.* 2022;24:321-31)

# Selecting responders for available anti-fibrotic drugs: MRAs

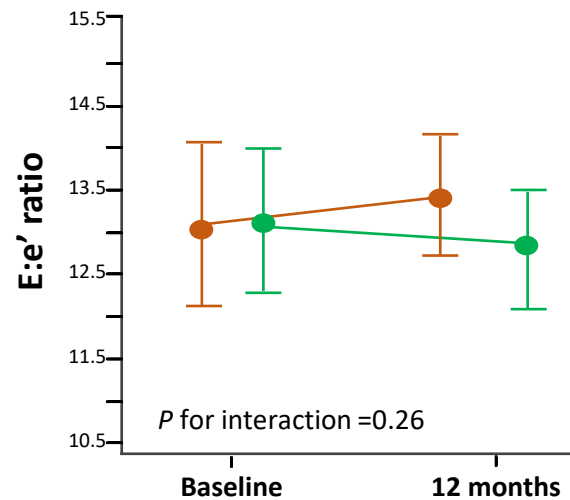
## Impact of CCL in spironolactone in HFpEF: The Aldo-DHF trial

### Changes in E:e' ratio

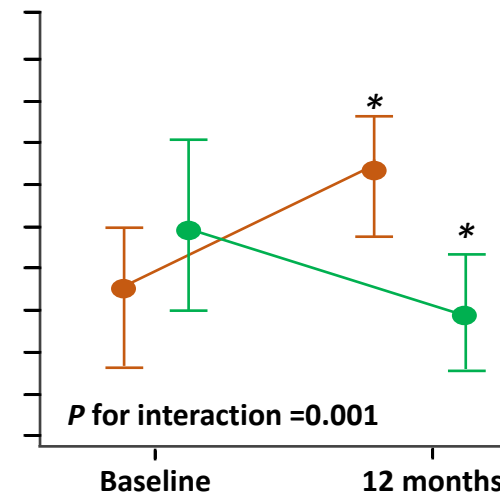


### Changes in E:e' ratio by baseline CITP:MMP-1 tertiles

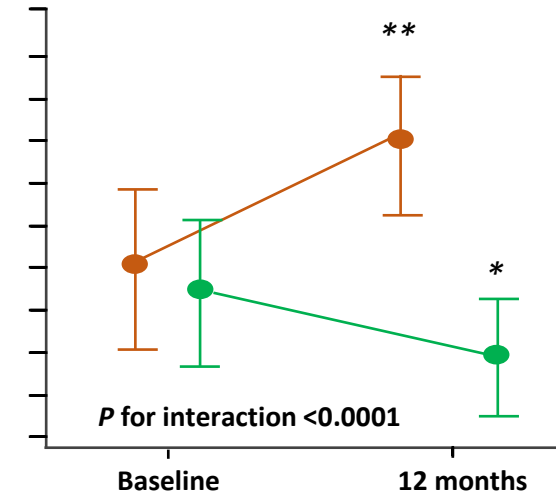
#### First tertile: High CCL



#### Second tertile



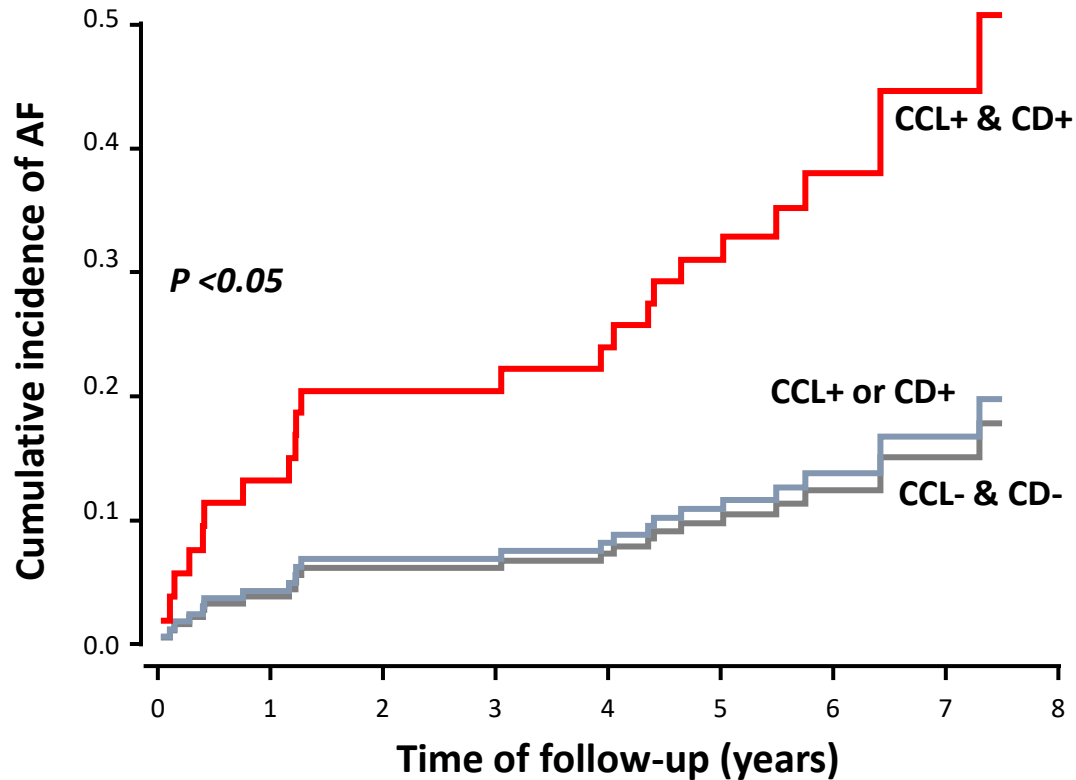
#### Third tertile: Low CCL



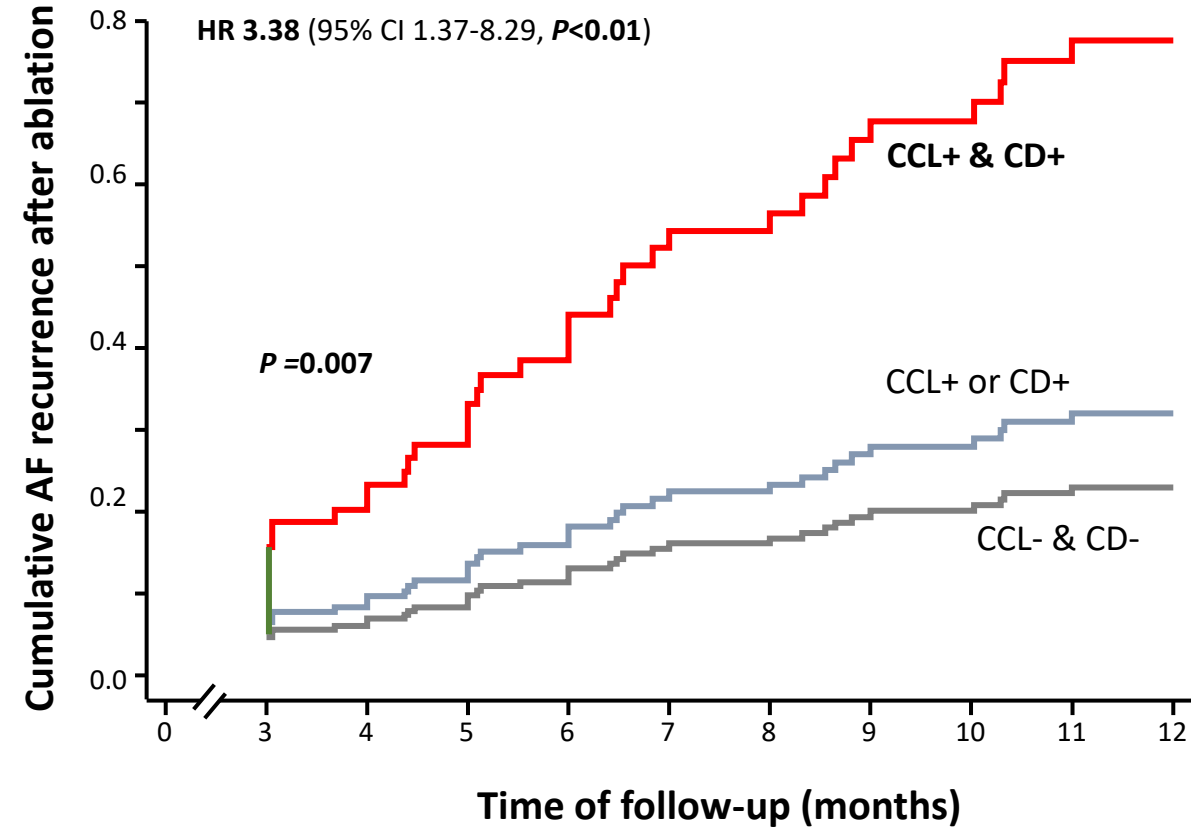
(Edelmann F et al. *JAMA* 2013;309:781-91; Ravassa S et al. *Eur J Heart Fail* 2018;20:1290-9)

# Prognostic value of combined PICP and CITP:MMP-1 in HF: Atrial fibrillation

## Atrial fibrillation onset in hypertensive HF patients (5.5 years follow-up)



## Atrial fibrillation recurrence after ablation (1 year follow-up)

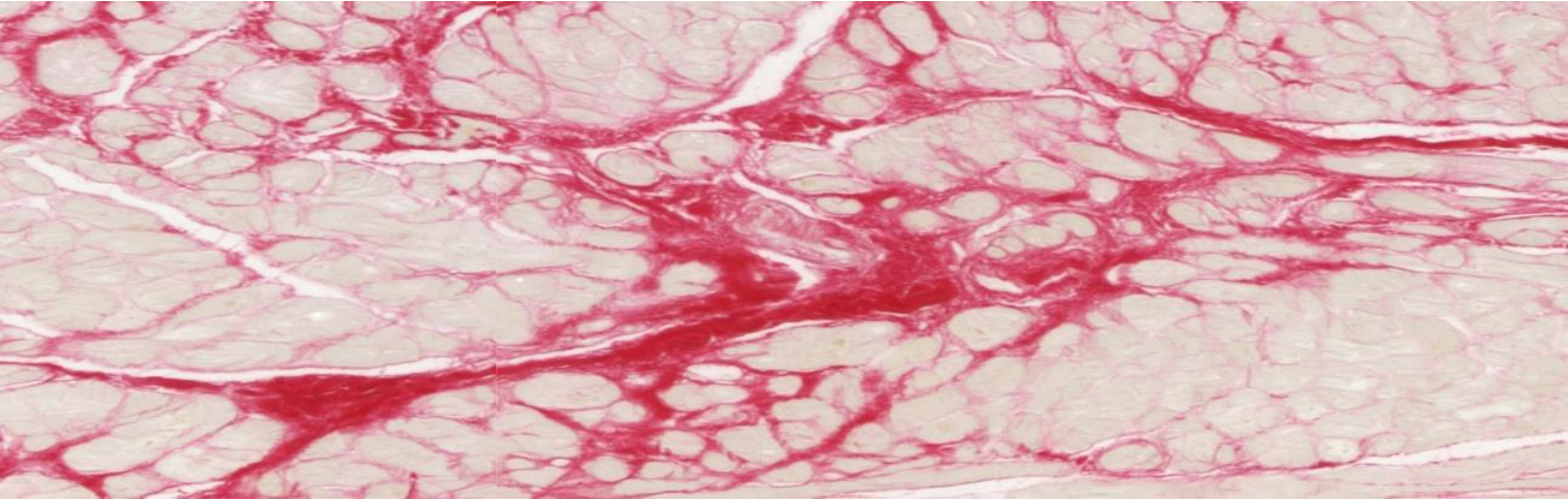


(Ravassa S et al. J Am Coll Cardiol 2019; 73:1398-410)



## Take home messages

- **Diffuse myocardial fibrosis (DMF)** is a common feature in chronic heart failure.
- **Collagen quantity and cross-linking** have an impact on the pathophysiological consequences of DMF.
- **DMF** is associated with an impairment in cardiac function and with adverse clinical prognosis.
- DMF is a **dynamic** process.
- **Circulating biomarkers** can be useful to track the phenotype of diffuse myocardial fibrosis.





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