

Il ventricolo destro nell'insufficienza cardiaca



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Conflict of interest

Grant for scientific collaboration (advisory board, clinical studies, speaker):

- Actelion
- Acceleron
- Bayer
- Dompè
- Janssen
- GSK
- Lilly
- MSD
- United therapeutics



Epidemiology of Pulmonary hypertension and RV dysfunction in Heart Failure

- A common condition.

Prevalence of PH depends on the population studied:

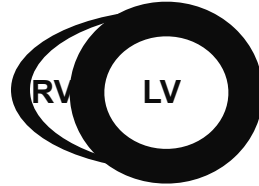
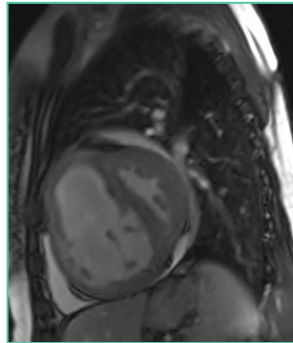
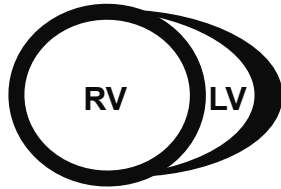
in referral centers, where advanced pts are evaluated for potential heart transplant listing, up to 50% of pts may have RV dysfunction

Why the RV becomes dysfunctional ?

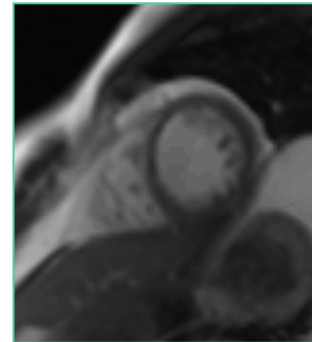
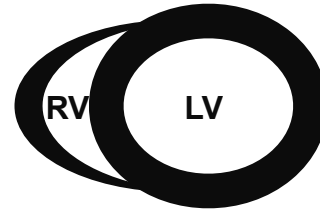
- Geometrical interdependance
- Functional interdependance
- Pathological interdependance

Geometrical interdependence of the ventricles: The interventricular septum

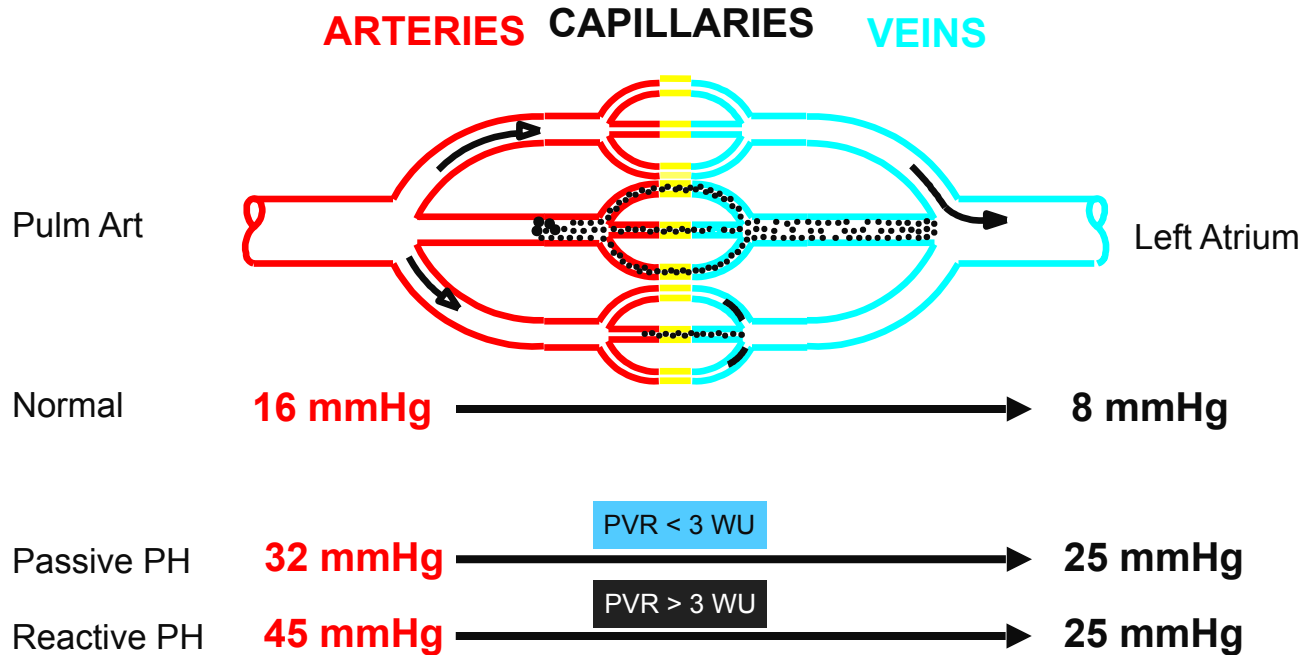
RV Overload: PAH



LV Overload: CHF



Functional interdependence of the ventricles: The pulmonary circulation



Pathologic interdependence

The same pathological process could interest both ventricles:

- Myocarditis
- Infiltrative diseases
- Ischemia (RV infarction)
- Degenerative diseases (diabetes)



What happens in the clinical arena ?

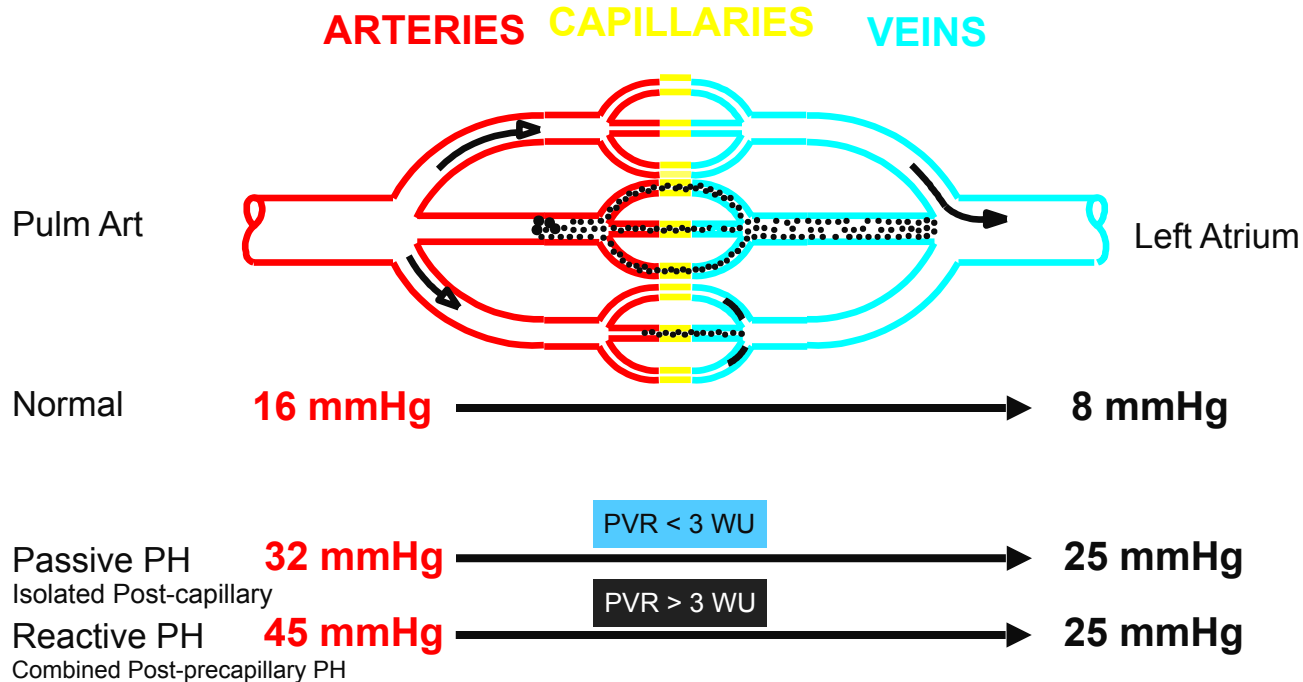
- The RV could be the first ventricle failing and the cause of AHF:
 - Acute pulmonary embolism
 - Acute RV infarction
 - Rapid progression of “chronic PH”

or

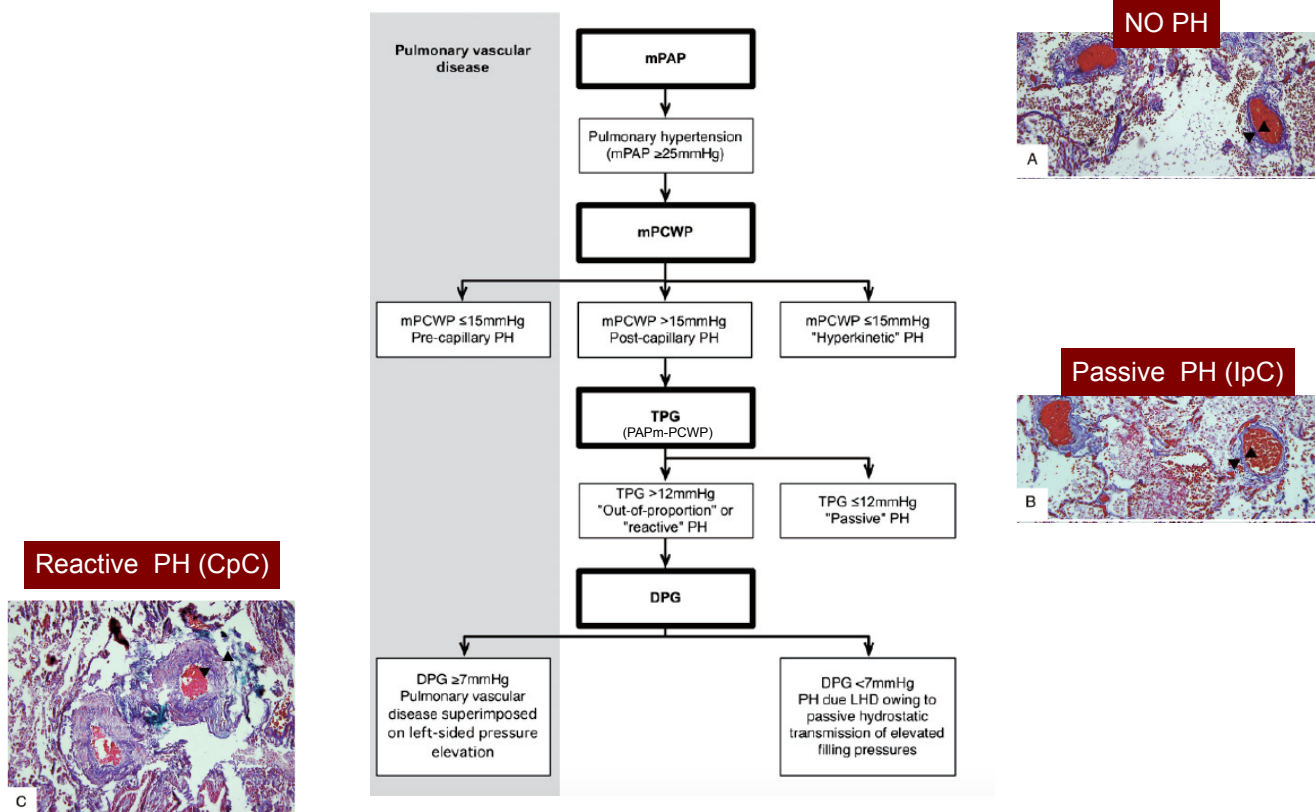
- The RV could be “involved” in a primary LV dysfunction as a consequence of increased pulmonary vascular resistance



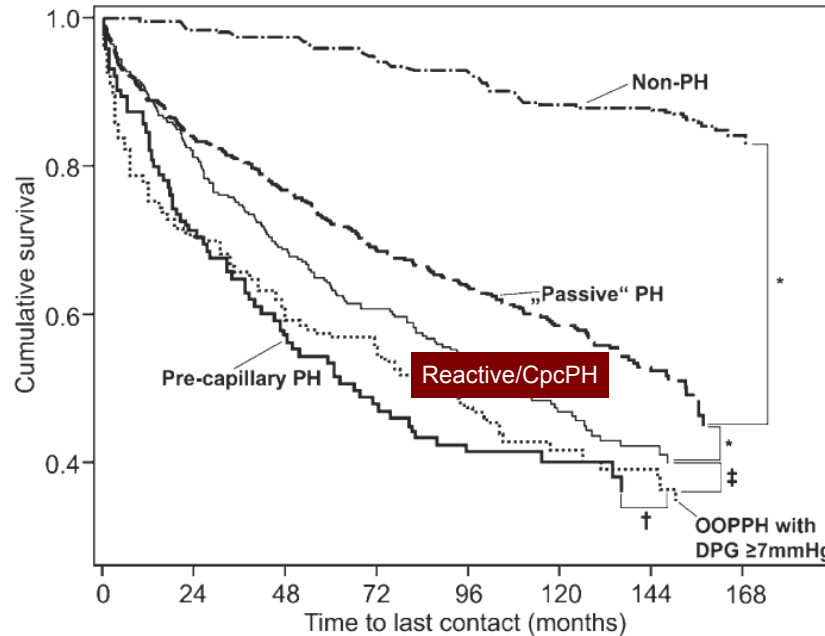
Pulmonary hypertension in left heart disease



The correlation between hemodynamic and histology



Survival according to the type of PH



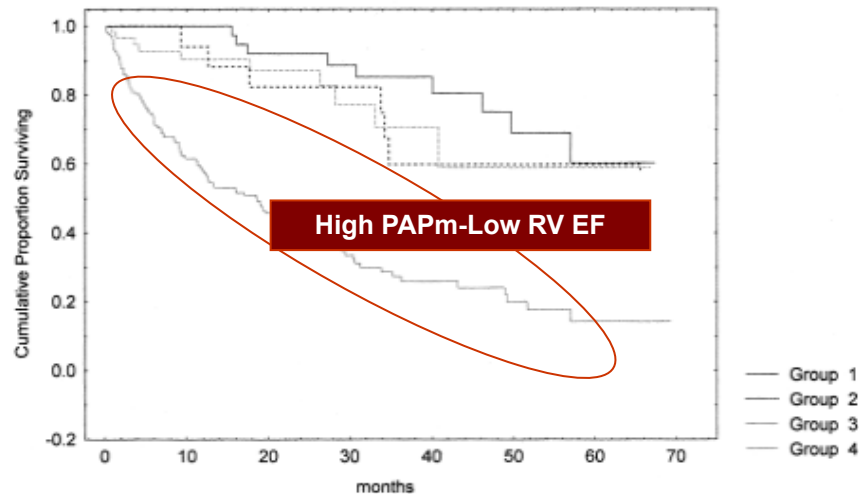
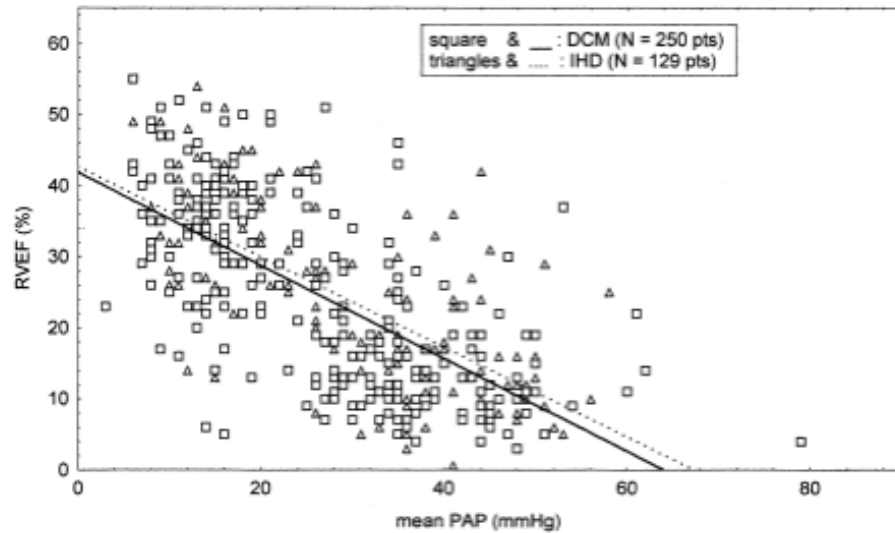
Pulmonary hypertension and RV dysfunction in Heart Failure reduced Ejection Fraction (HFrEF)



Independent and Additive Prognostic Value of Right Ventricular Systolic Function and Pulmonary Artery Pressure in Patients With Chronic Heart Failure

Stefano Ghio, MD, FESC,* Antonello Gavazzi, MD, FESC,* Carlo Campana, MD,*
Corinna Inserra, MD,* Catherine Klersy, MD,† Roberta Sebastiani, MD,* Eloisa Arbustini, MD,‡
Franco Recusani, MD,* Luigi Tavazzi, MD, FESC, FACC*

Pavia, Italy



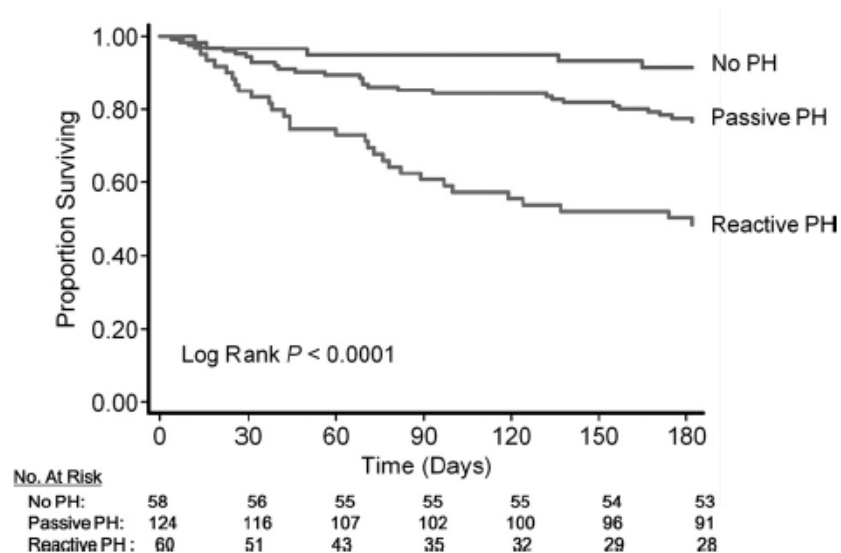
What about Acute Decompensate Heart failure ?



Relationship Between Reactive Pulmonary Hypertension and Mortality in Patients With Acute Decompensated Heart Failure

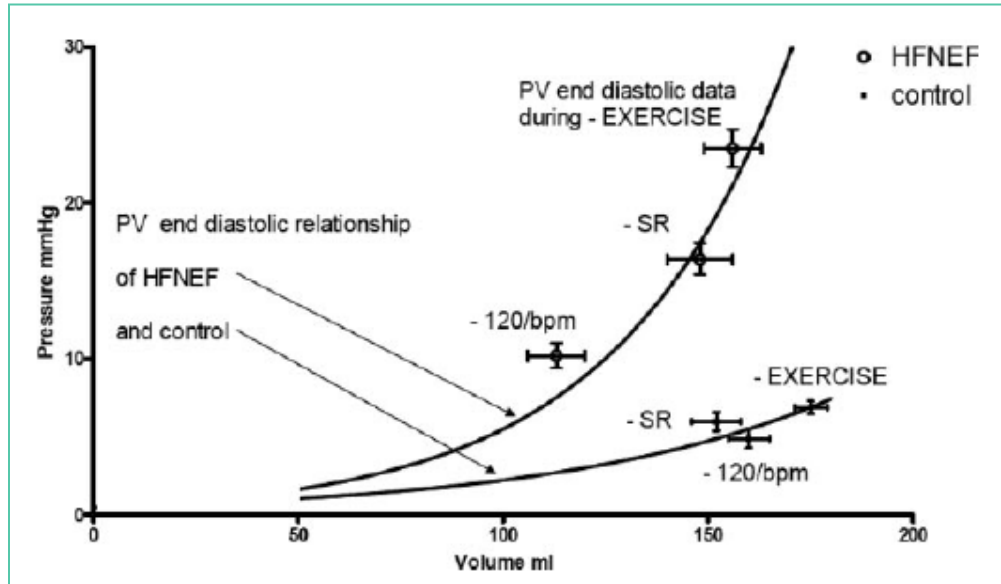
Doron Aronson, MD; Amnon Eitan, MD; Robert Dragu, MD; Andrew J. Burger, MD

Baseline	Final (Posttreatment)		
	No PH	Passive PH	Reactive PH
No PH (n=2)	1 (50)	1 (50)	0 (0)
Passive PH (n=143)	44 (31)	80 (56)	19 (13)
Reactive PH (n=97)	13 (13)	43 (45)	41 (42)
Total	58	124	60



Pulmonary hypertension in Heart Failure with preserved Ejection Fraction (HFpEF)

Diastolic heart failure: Increased LV stiffness and wedge pressure



Pulmonary Hypertension in Heart Failure With Preserved Ejection Fraction

A Community-Based Study

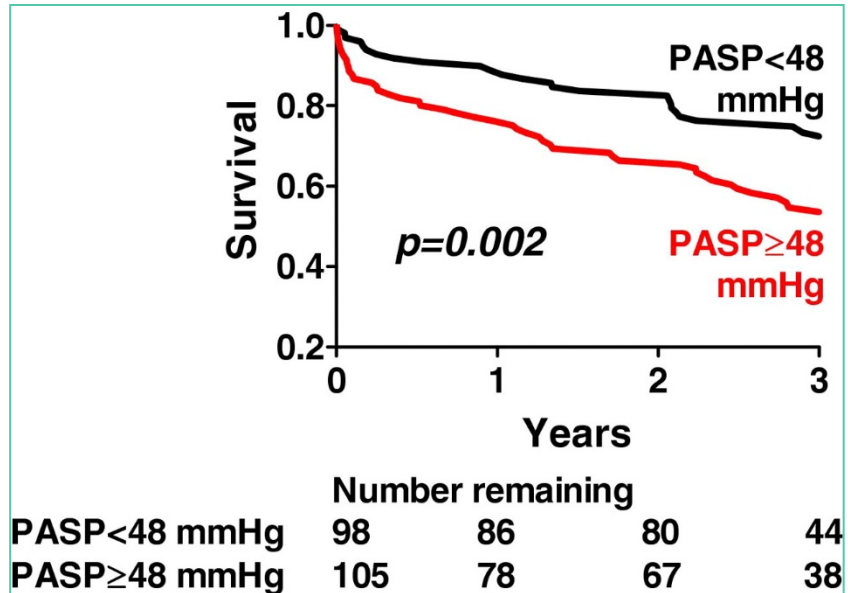
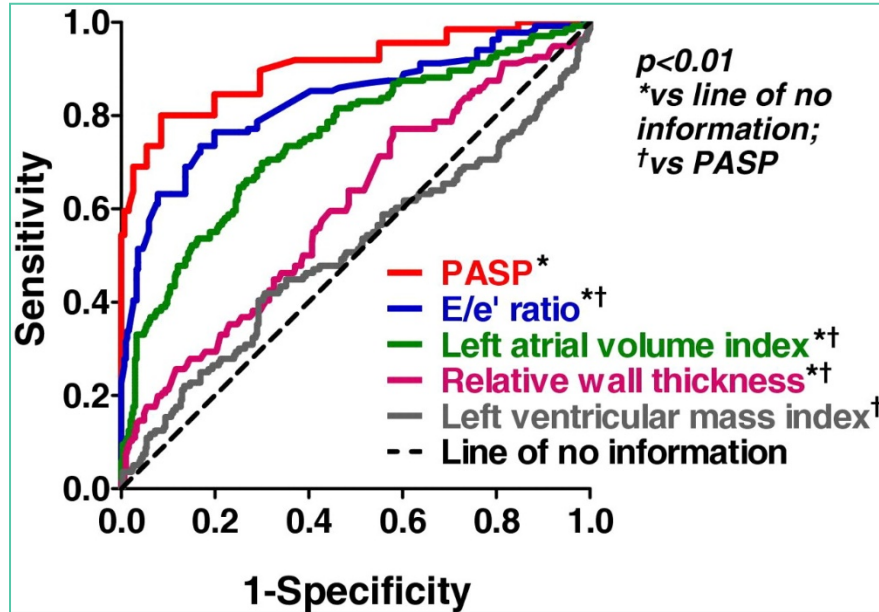
Carolyn S. P. Lam, MBBS,*† Véronique L. Roger, MD, MPH,* Richard J. Rodeheffer, MD,*
Barry A. Borlaug, MD,* Felicity T. Enders, PhD,‡ Margaret M. Redfield, MD*

Rochester, Minnesota; and Singapore, Singapore

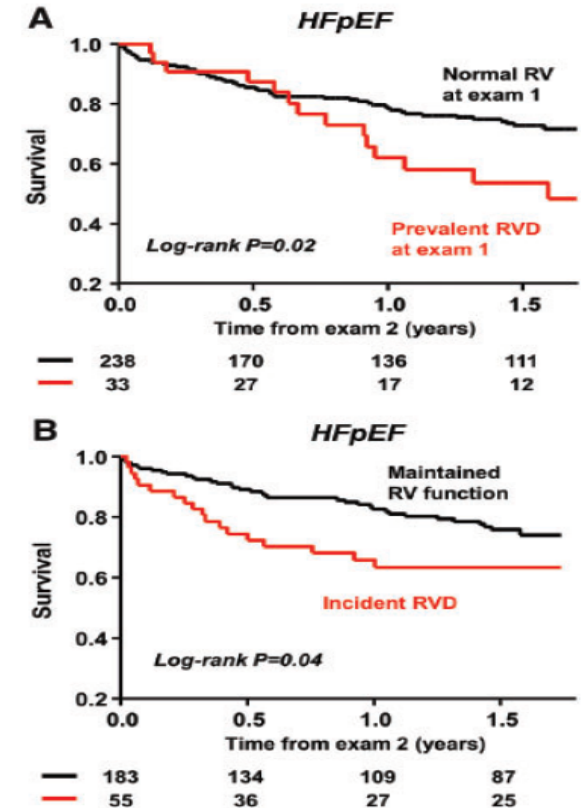
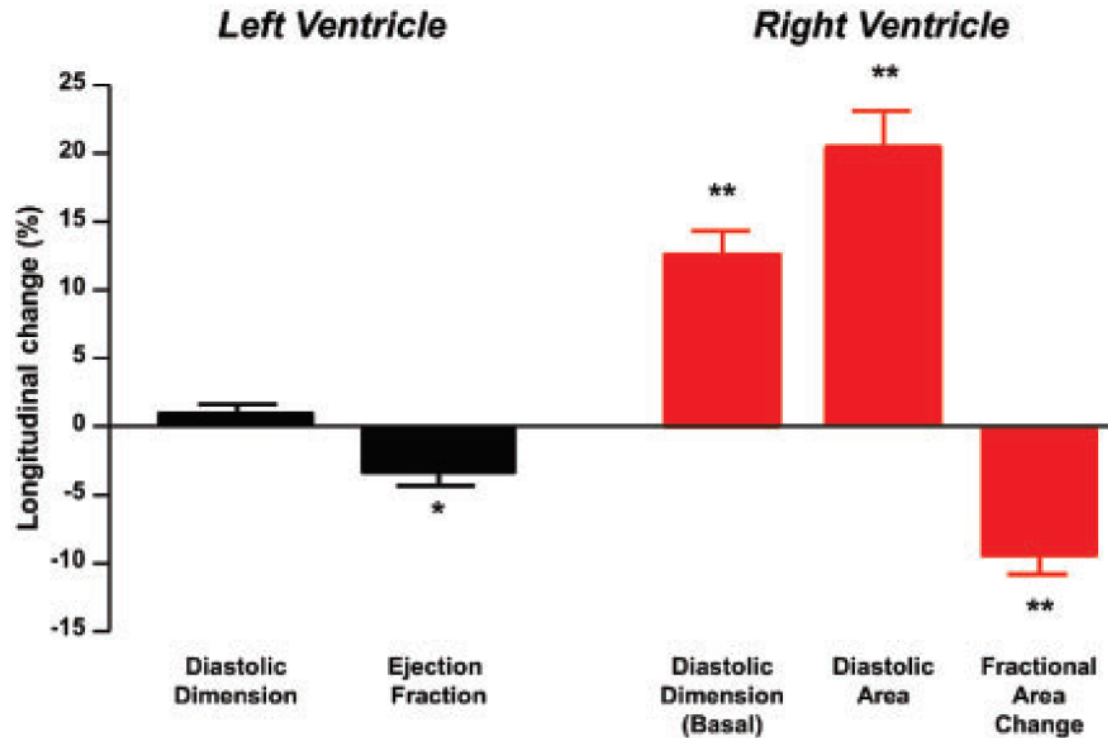
	HTN		HFpEF	
	PH Absent	PH Present	PH Absent	PH Present
N (% group)	432 (92)	38 (8)	34 (17)	169 (83)
PASP, mm Hg	28 ± 4	40 ± 5*	30 ± 3	52 ± 13*
Clinical characteristics				
Age, yrs	67 ± 10	72 ± 9*	74 ± 11	79 ± 12*
Male, %	40	32	47	41
Height, m	1.66 ± 0.10	1.62 ± 0.08*	1.66 ± 0.10	1.65 ± 0.14
Weight, kg	79.6 ± 16.9	75.3 ± 14.5	84.8 ± 17.9	81.6 ± 23.0
BSA, m ²	1.91 ± 0.23	1.83 ± 0.20	1.97 ± 0.24	1.92 ± 0.29
Body mass index, kg/m ²	28.8 ± 5.5	28.8 ± 5.2	30.9 ± 6.3	29.6 ± 7.2
Systolic blood pressure, mm Hg	141 ± 21	153 ± 27*	125 ± 20	134 ± 24*
Diastolic blood pressure, mm Hg	75 ± 11	75 ± 11	69 ± 13	67 ± 14
Pulse pressure, mm Hg	66 ± 18	78 ± 20*	56 ± 18	67 ± 20*
Heart rate, beats/min	65 ± 11	65 ± 13	68 ± 15	71 ± 16
Hypertension, %	100	100	91	97
Atrial fibrillation, %	5	13*	22	31
Coronary artery disease, %	16	21	59	53
Diabetes mellitus, %	10	13	27	34
Chronic kidney disease,† %	29	43	50	51
Chronic obstructive lung disease,‡ %	14	21	29	32
Echocardiographic characteristics				
Ejection fraction, %	65 ± 5	65 ± 7	63 ± 5	62 ± 7
Stroke volume/BSA, ml/m ²	46.8 ± 9.3	48.9 ± 10.5	42.7 ± 10.3	43.2 ± 9.8
Cardiac index, l/min/m ²	3.0 ± 0.7	3.1 ± 0.8	2.8 ± 0.7	3.0 ± 0.8
LV mass/BSA, g/m ²	99.6 ± 22.4	107.4 ± 31.0	99.7 ± 27.2	103.3 ± 30.1
Relative wall thickness	0.42 ± 0.07	0.42 ± 0.08	0.46 ± 0.11	0.45 ± 0.09
LV end-diastolic volume/BSA, ml/m ²	59.2 ± 12.2	60.7 ± 11.1	54.5 ± 11.4	57.4 ± 15.0
E/e' ratio	9.3 ± 3.3	12.8 ± 4.7*	15.7 ± 9.8	19.6 ± 9.6*
PCWP, mm Hg	18 ± 2	20 ± 3*	21 ± 6	24 ± 6*
Left atrial volume/BSA, ml/m ²	26.2 ± 7.8	32.7 ± 8.5*	32.1 ± 11.4	38.1 ± 14.3*



Pulmonary systolic pressure: Impact on diagnosis and survival



Deterioration in RV Structure and Function Over Time in Patients with HFpEF



Key message

Pulmonary Hypertension and RV dysfunction

- are a quite frequent observation in patients with Heart Failure
- RV dysfunction could be determined by several mechanisms, but the most important is the increase in afterload due to the development of pulmonary hypertension (PH)

PH in left heart disease

- is a consequence of post-capillary hypertension, and could be aggravated by a precapillary component
- PH and the related RV dysfunction are important prognostic factors in HFrEF and HFpEF

Always look at the right ventricle !



Pharmacological Studies in Cpc-PH HFpEF

Pulmonary Vasodilator Therapy and **PVR** (primary or secondary EP)

Guazzi et al. Circulation 2021
44 PH-HFpEF randomized
to Sildenafil or Placebo
1-YEAR FOLLOW-UP

PVR primary End-point
PVR from 5.0 WU to 3 WU

Belyaviskiy et al. BMC Cardio Disord 2020
50 PH-HFpEF randomized
to Sildenafil or Placebo
6 MONTHS FOLLOW-UP

PVR primary End-point
PVR from 3.5 WU to 2.5 WU

SPHERE Trial Eur J Heart Fail 2022
80 PH-HFpEF randomized
To Mirabegron or Placebo
4 MONTHS FOLLOW-UP

PVR primary endpoint
from 4.0 WU to 4.09 WU

Ongoing Trials

- **PASSION**
- **RE-PHIRE**
- **CADENCE**

2011

2014

2017

2020

2022

2023

LEPTH Trial Circulation 2013
139 Cp-PH-HFpEF randomized
to Riociguat or Placebo
12 weeks follow-up

PVR secondary End-point
from 8.0 WU to 7.2 WU

DILATE-1 Trial Chest 2014
84 PH-HFpEF randomized
to Riociguat or Placebo
ACUTE

PVR secondary End-point
from 5.0 WU to 3.0 WU

BEATH –HF Circ RES 2019
15 PH-HFpEF randomized
to Albuterol or Placebo
ACUTE

Exercise PVR primary End-point
from 2.2 WU to 1.4 WU

HemoDYNAMIC Trial Circulation 2022
114 PH-HFpEF randomized
to Riociguat or Placebo (only 18 CpC)
12 weeks follow-up

PVR secondary End-point from 3.2 WU to 3. WU



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Positive Long Term



Neutral Long term



Positive Acute



Neutral Acute