Right Ventricular Dysfunction & Pulmonary Hypertension in HFpEF

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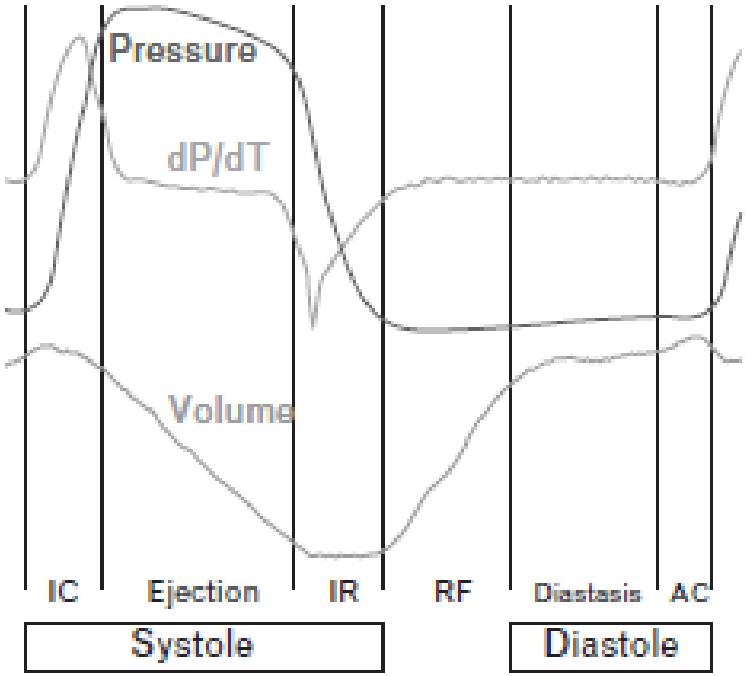
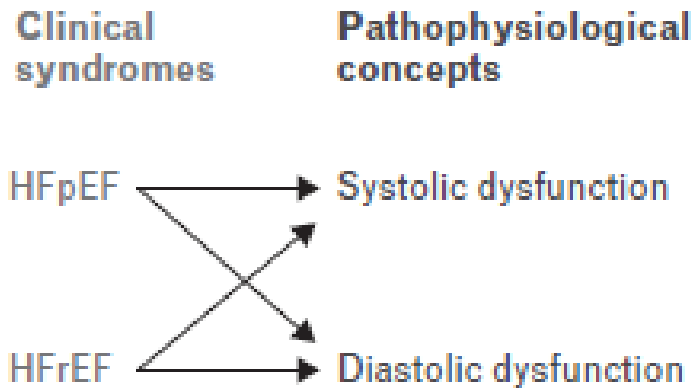
CONCEPTUAL FRAMEWORK OF DIASTOLIC DYSFUNCTION & HEART FAILURE WITH PRESERVED EJECTION FRACTION (HFpEF)

- **Heart failure (HFpEF & HFrEF) is a clinical syndrome**





Systolic dysfunction (SD)=
- LV dysfunction during contraction or relaxation
- Abnormal systolic time intervals

Diastolic dysfunction (DD)=
- Decreased LV compliance
- Increased LVEDP

SYSTOLIC vs. DIASTOLIC Dysfunction

- **Classification of heart failure patients into systolic and diastolic heart failure, based solely on ejection fraction, is artificial.**
- **Almost all patients with HFrEF and HFpEF have at the same time a certain degree of systolic and diastolic dysfunction**
- **'Diastolic dysfunction' in descriptions of pathophysiological mechanisms, considering that diastolic dysfunction occurs in both HFrEF and HFpEF.**

Current diagnostic criteria of HFpEF

1) Clinical signs or symptoms of heart failure
2) Ejection fraction higher than 50%
3) Signs of diastolic dysfunction

- Heart failure is the m/c cause of pul. HTN and among patients with HFpEF, pulmonary hypertension is a common finding.
- Pul.HTN correlates better with indices of diastolic function than systolic function and more pronounced with higher LV filling pressure.

PATHOPHYSIOLOGY OF PULMONARY HYPERTENSION INDUCED BY DIASTOLIC DYSFUNCTION

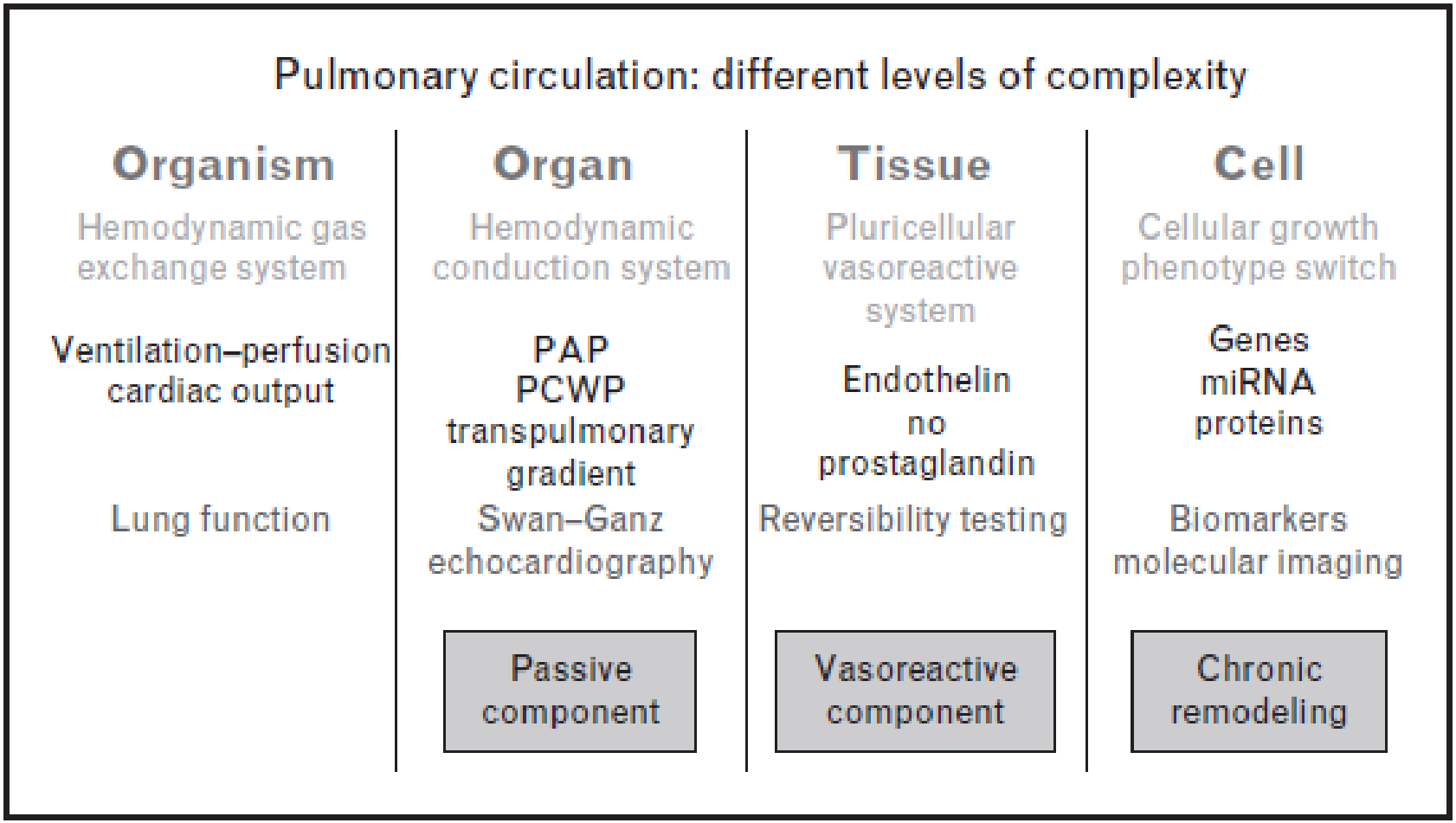
- **Pulmonary vasculature is characterized by low resistance, low pressure & high distensibility.**

- **Two main components:**

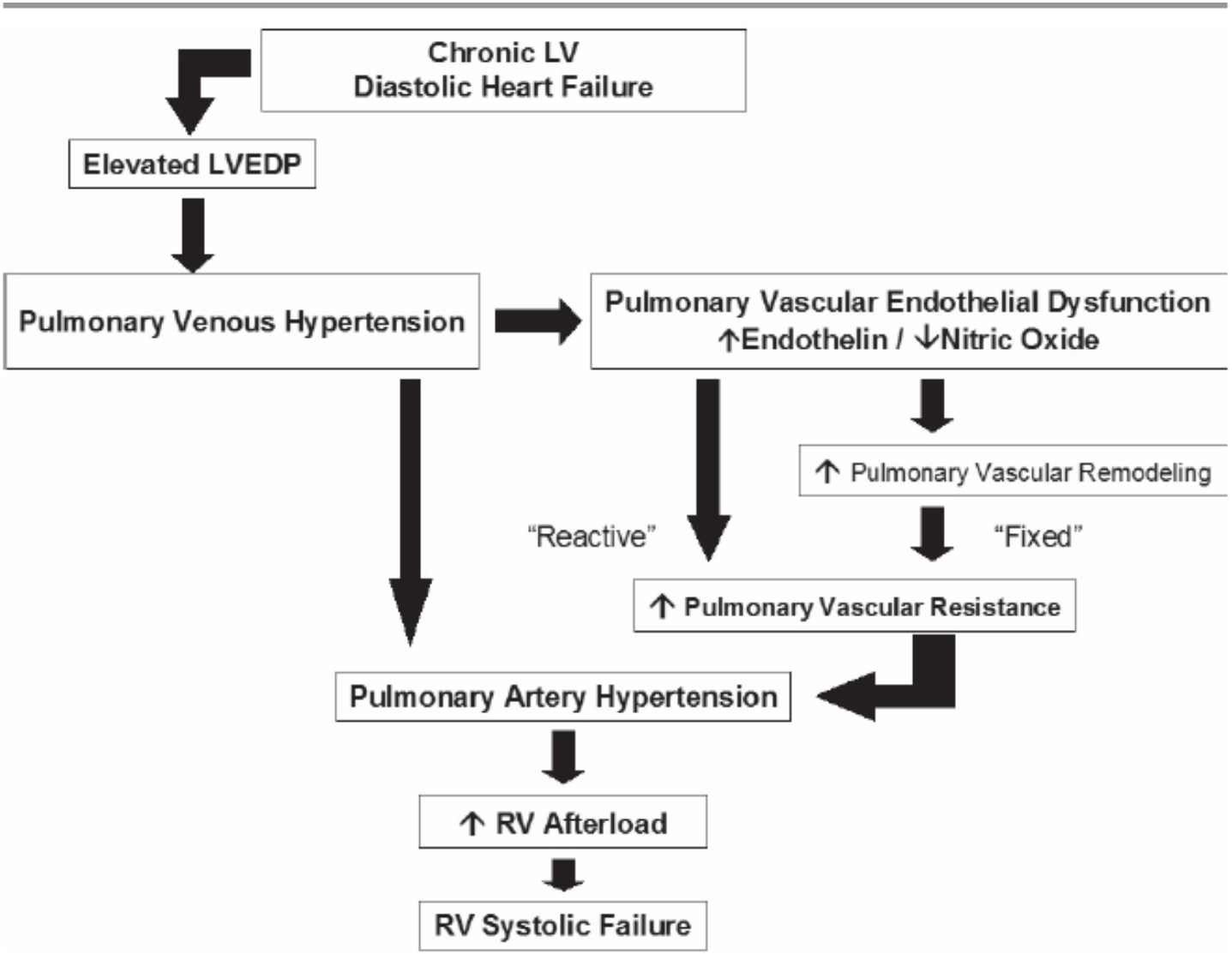
① **Hydrostatic component consisting of passive transmission of increased LVEDP**

② **Reactive component consisting of pulmonary vasoconstriction and vascular remodelling**

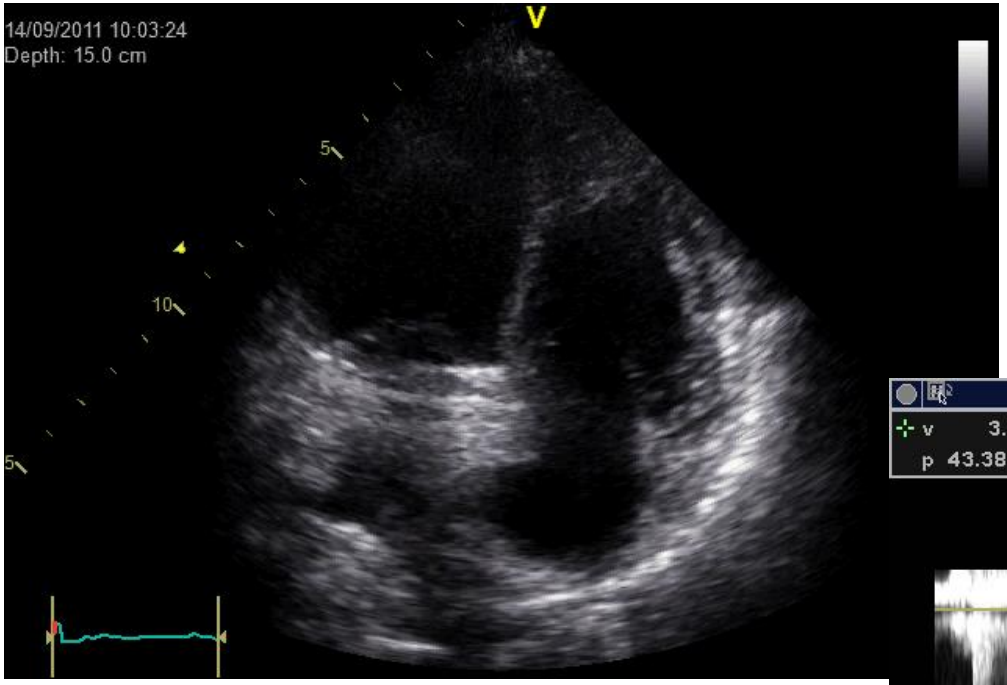
PATHOPHYSIOLOGY OF PULMONARY HYPERTENSION IN THREE DIFFERENT COMPONENTS

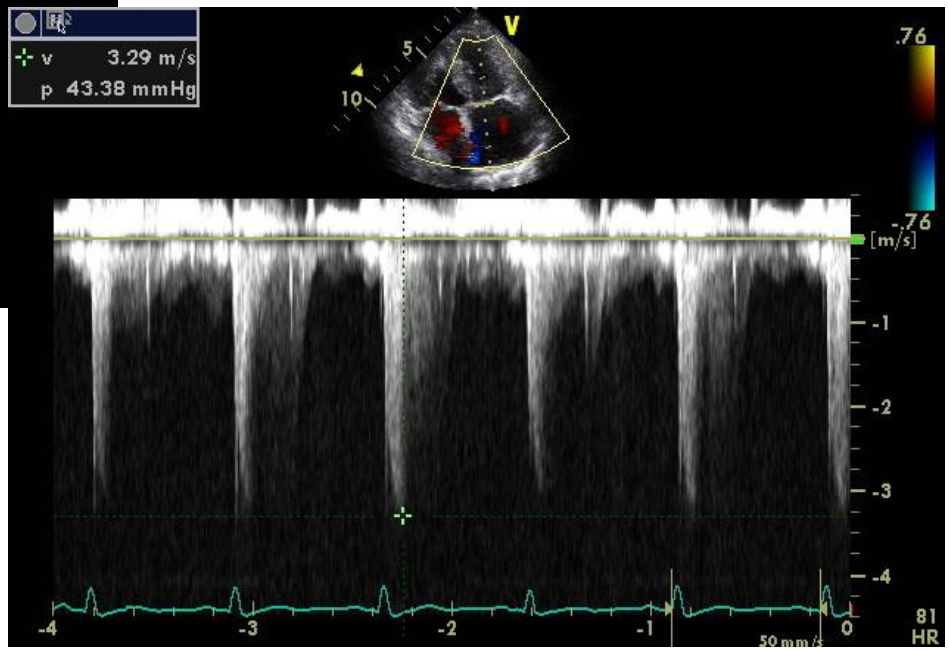


Proposed relationship between LV diastolic dysfunction, pulmonary venous hypertension, and pulmonary artery hypertension



Typical finding of pulmonary hypertension due to diastolic dysfunction.





(1) Hydrotic passive component (hemodynamic level)

- An increased LVEDP due to increased stiffness of the left ventricle

➔Increased filling pressures lead to increased pulmonary venous pressures that lead to a passive increase in PAP

- Pulmonary venous hypertension (postcapillary pulmonary hypertension) arises from most commonly associated with HFpEF and the incidence increases with increasing LVEDP

(1) Hydrotic passive component (hemodynamic level)

➔ **passive postcapillary pulmonary hypertension :**

① **increased mean PAP (mPAP >25mmHg) based on increased pulmonary capillary wedge pressure (PCWP >15mmHg)**

② **a normal transpulmonic gradient (mPAP-PCWP <12mmHg)**

- **During exercise, in normal patients, LVEDP increases minimally with increased end diastolic volumes.**
- **In patients with HFpEF, LVEDP increases dramatically during exercise with only limited increases in end diastolic volumes**

(2) Reactive component (intercellular signaling, tissue level)

- **Diastolic dysfunction induces not only a passive increase in PAP but also a reactive increase in some patients.**
- **Reactive pulmonary vasoconstriction is mediated by endothelin, nitric oxide, multiple comorbidities, including lung diseases that increase PAP**

① transpulmonic gradient is increased (mPAP-PCWP >12mmHg)

② an increased PCWP, leading to a higher mPAP than might be expected from passive transmission of PCWP alone.

(3) Cellular physiology (Cell level)

- **Pulmonary remodeling is influenced by properties of the endothelial and vascular smooth muscle cells themselves, their genes, proteins, and microRNAs :**

① miRNAs are small noncoding RNAs that regulate protein translation of one or multiple messenger RNAs

➔ increasing or decreasing miRNAs is a novel and promising therapeutic strategy for patients with pulmonary hypertension (ex. miR-21, miR-204…)

INTERACTION BETWEEN LEFT AND RIGHT VENTRICLES AND THE DEVELOPMENT OF HEART FAILURE

- **Both ventricles are connected not only by the pulmonary vasculature but also by the interventricular septum.**

- **Patients with HFpEF show subendocardial systolic and diastolic dysfunction of the right ventricle similar to the dysfunction of the left ventricle**

➔ **similar pathophysiological process originates in both ventricles at the same time.**

Role of the interventricular septum

- **Both ventricles are connected not only by the pulmonary vasculature but also by the interventricular septum.**

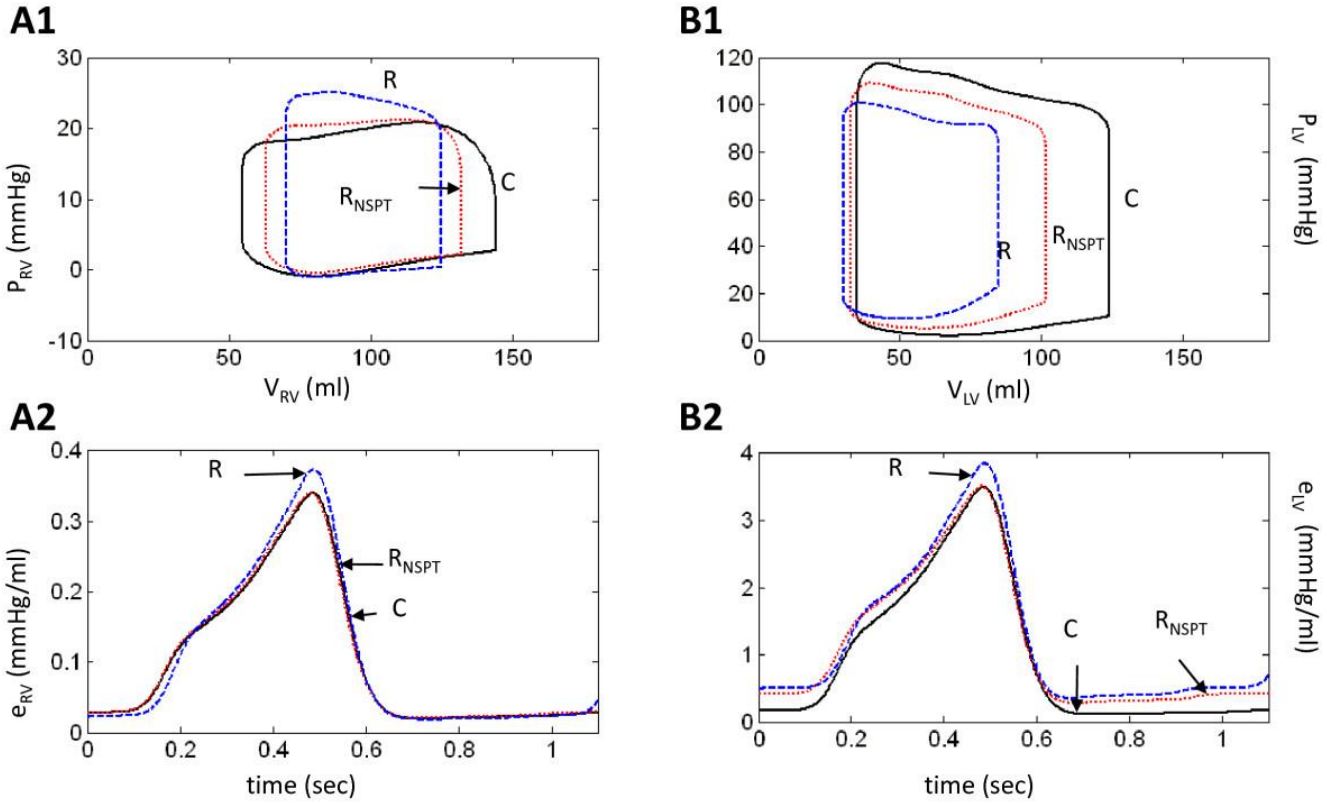
- **Left ventricular diastolic dysfunction leads to**

➔ **a loss of the septal role in right ventricular ejection and to delayed opening of the pulmonic valve**

➔ **abnormal septal performance that interferes with mechanical synchrony of ventricles during systole**

Role of the interventricular septum

Simulated ventricular function curves of normal physiology (control, C), increased LV wall *and* septal stiffness (R), and increased LV wall but *normal* septal stiffness (R_{NSPT}).



Theor Biol Med Model 2011;8:14.

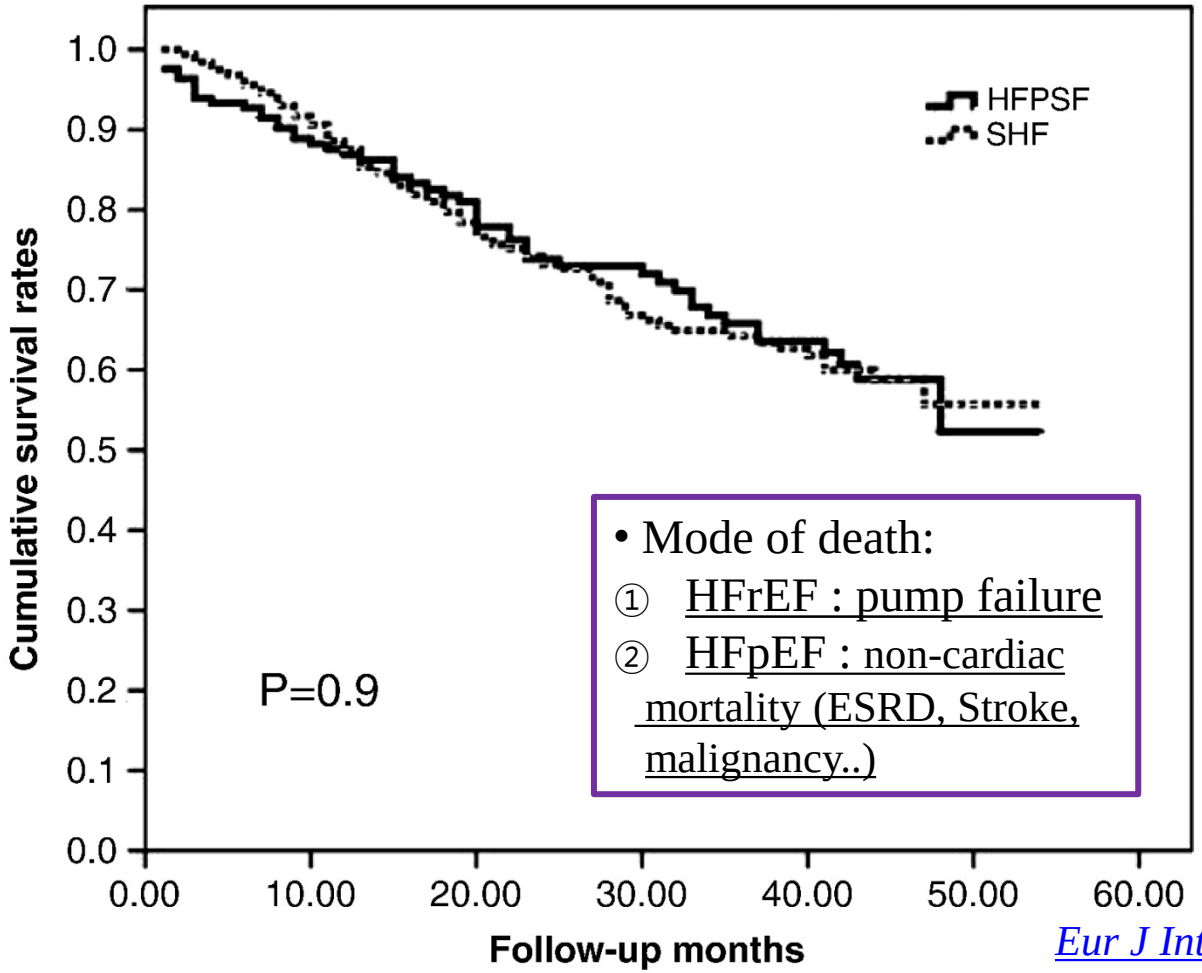
Development of left ventricular failure in patients with pulmonary hypertension

- **Pulmonary hypertension has developed because of hydrostatic and reactive transmission of elevated left ventricular filling pressures.**

- **The reverse model in a rat :**
  primary pulmonary hypertension and right ventricular heart failure that left ventricular diastolic dysfunction develops as a result of ventricular interdependence and neurohumoral activation

NATURAL HISTORY OF PULMONARY HYPERTENSION AND HEART FAILURE WITH PRESERVED EJECTION FRACTION

- **Mortality rates of patients with HFpEF are similar to those of patients with HFrEF**



- 317(66%) patients : LVEF was <40%
- 164(34%) patients: LVEF≥40% (HFpEF).

- Mode of death:
  ① HFrEF : pump failure
  ② HFpEF : non-cardiac mortality (ESRD, Stroke, malignancy..)

Eur J Intern Med. 2011;22(1):53-6.

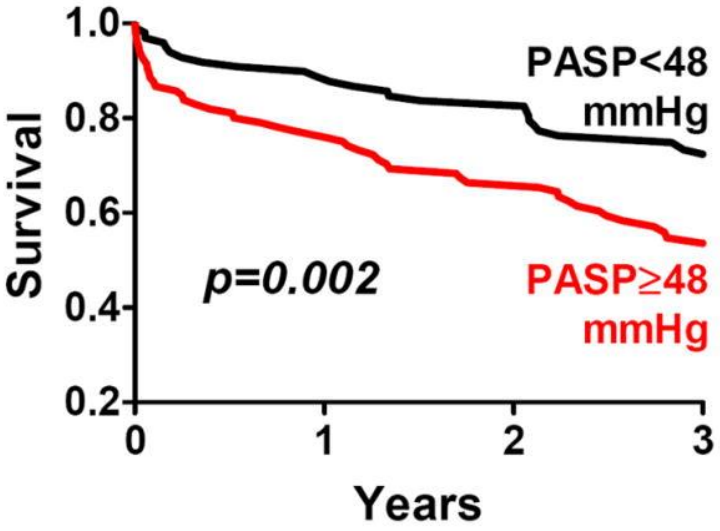
NATURAL HISTORY OF PULMONARY HYPERTENSION AND HEART FAILURE WITH PRESERVED EJECTION FRACTION

- **Poor prognosis :**

① **Pulmonary hypertension** in patients with HFpEF

② Patients with **renal dysfunction** have **higher mortality** than patients with **HFrEF**

③ **LVEDP > 25mmHg, high BMI, atrial arrhythmias, age > 80 years, COPD, Having DOE**



Number remaining				
PASP<48 mmHg	98	86	80	44
PASP≥48 mmHg	105	78	67	38

J Am Coll Cardiol. 2009;53(13):1119-26

CONCLUSION

- Pulmonary hypertension is a common finding in patients with HFpEF, is a predictor of poor prognosis, and the incidence increases with higher LVEDP.

- The pathophysiology of pulmonary hypertension in HFpEF can be explained by passive hydrostatic transmission of LV filling pressures, reactive vasoconstriction, and remodeling of pulmonary arteries.

- Preventive measures and earlier and more effective treatment of heart failure will lead to a slower progression of the vicious circle of heart failure

진도 여객선 희생자들 모두 명복을 빕니다....