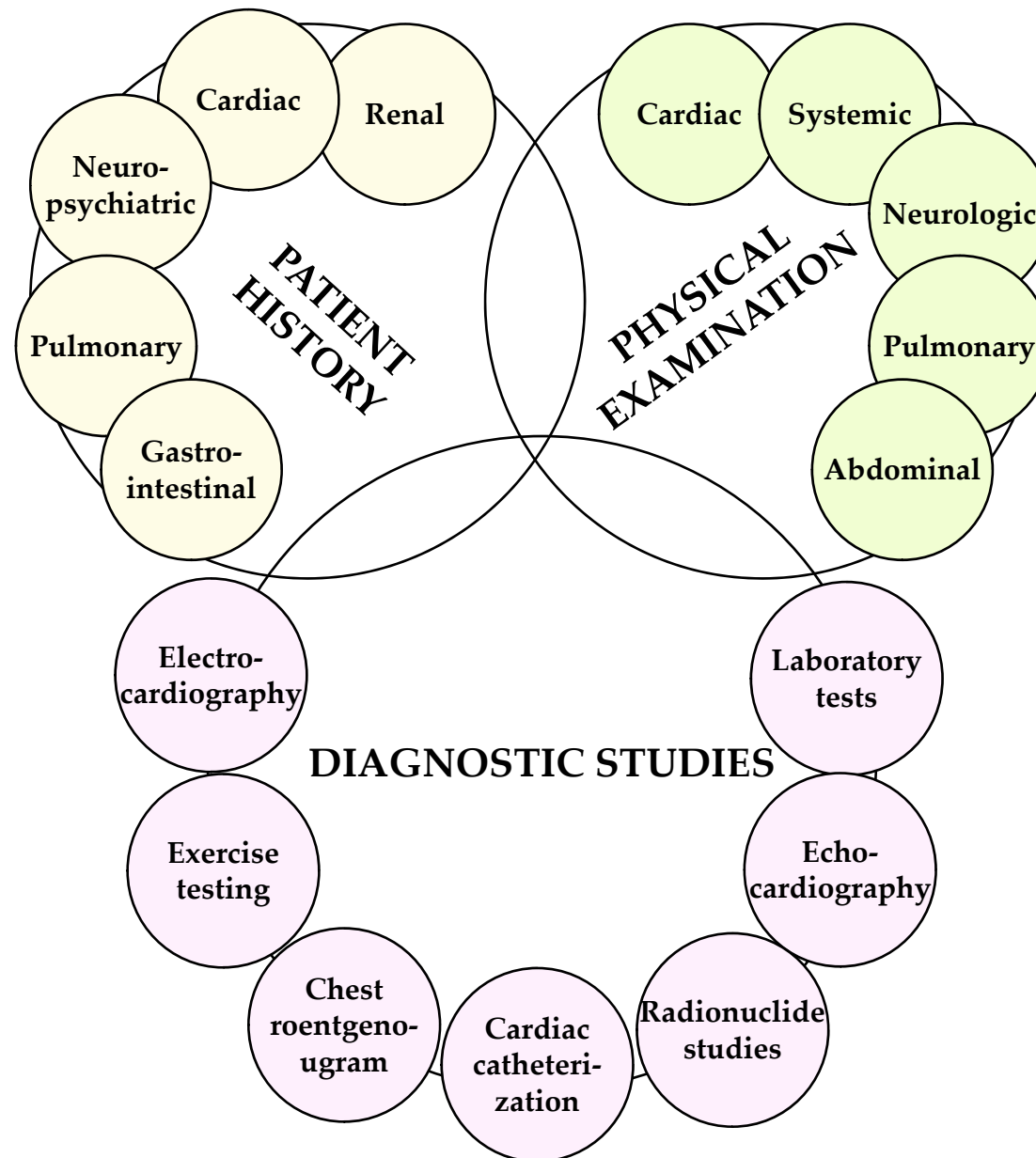


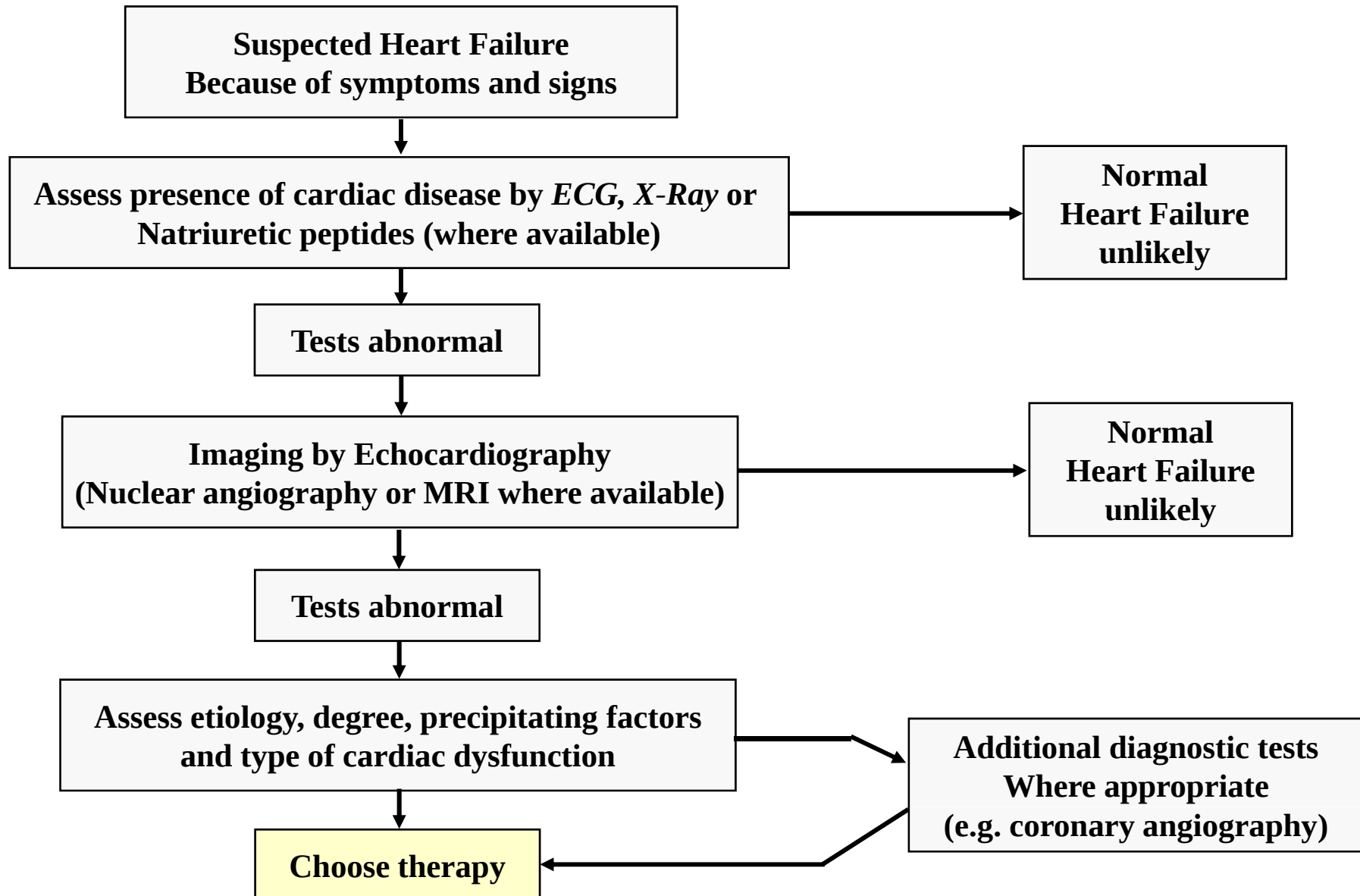
# Standard Laboratory Markers

울산의대 서울 아산병원 심장내과  
김 재 중

# Assessment of Heart Failure



# Algorithm for the Diagnosis of Heart Failure



# Chest X-ray in Heart failure

## *What we have to see*

- ① Cardiothoracic ratio
  - ② Cardiac chamber size and shape
  - ③ Pulmonary vascularity and congestion
  - ④ Pleural effusion
  - ⑤ Mass lesions or infiltrates
  - ⑥ Mediastinal configuration
  - ⑦ Great-vessel abnormality
  - ⑧ Vascular/cardiac calcifications
-

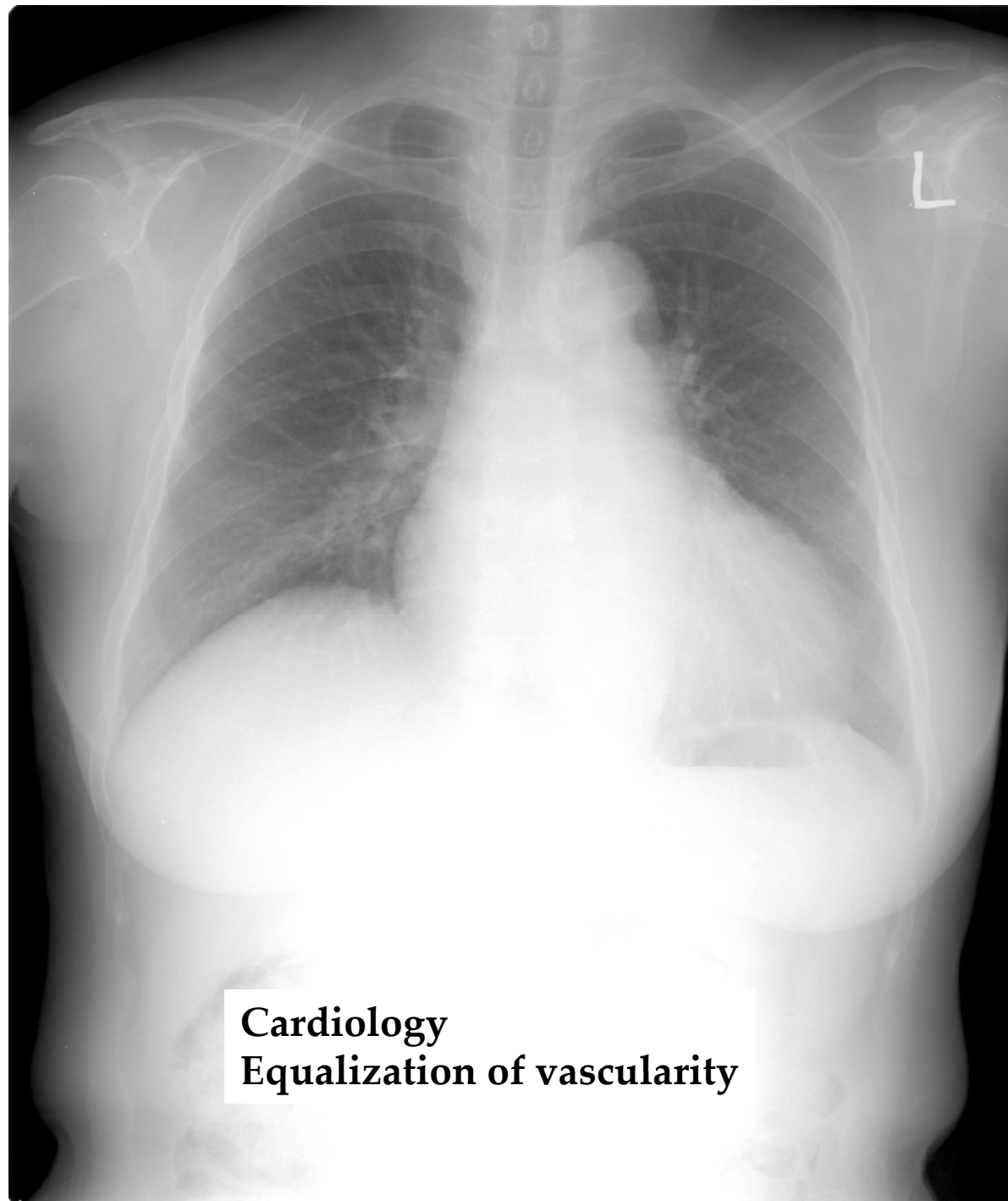
# Chest X-ray in Heart failure

- The chest X-ray should be part of the initial diagnostic work-up in heart failure
  - A high predictive value
    - ❑ Only achieved by interpretation of the X-ray in the context of clinical findings and ECG abnormalities
  - Increased cardiac size (CT ratio $>0.5$ ) and the presence of pulmonary venous congestion
    - ❑ Useful indicator of abnormal cardiac function with decreased LVEF and/or elevated LV filling pressure
  - CT ratio and heart volume determined on the plain film
    - ❑ Relatively specific but insensitive indicator of increased LVEDV
-

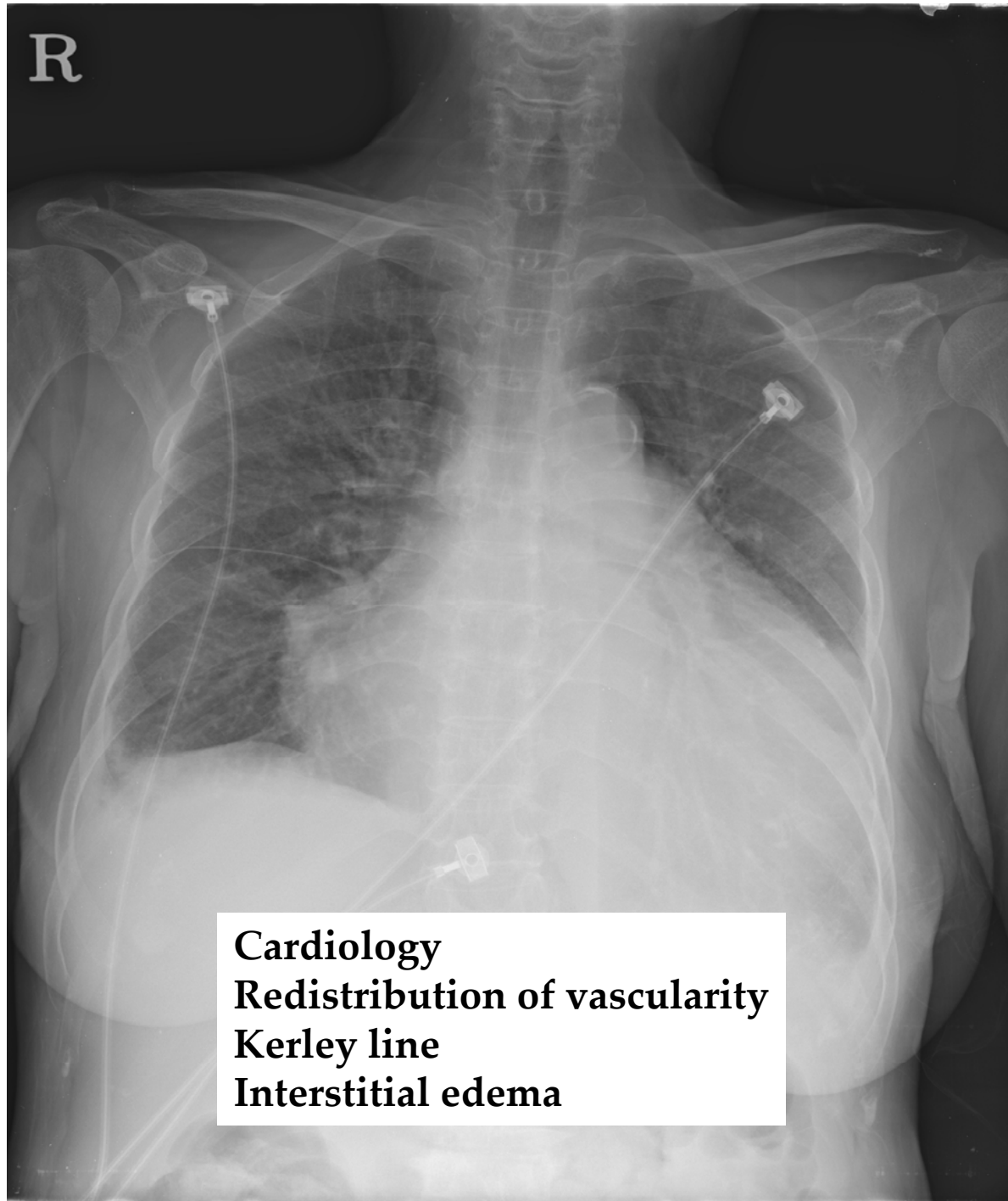
# Chest X-ray in Heart failure

## *Pulmonary congestion*

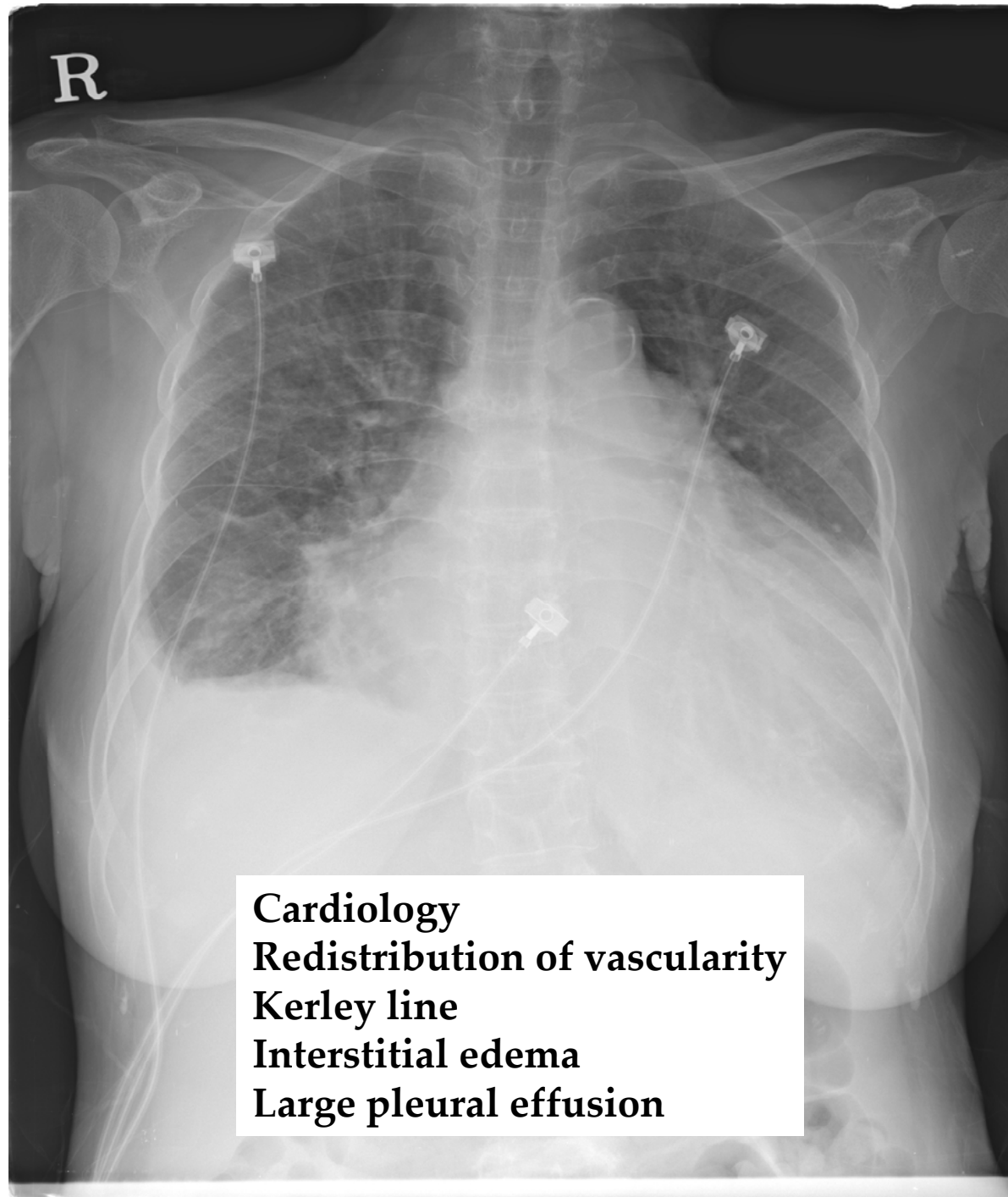
- 1) PCWP 13-17mmHg
    - equalization in size of vessels at the apices and bases due to compression of pulmonary vessels in the lower lobes
  - 2) PCWP 18-23mmHg
    - actual pulmonary vascular redistribution
  - 3) PCWP 20-25mmHg
    - develop interstitial pulmonary edema
  - 4) PCWP > 25mmHg
    - alveolar edema in “butterfly pattern” and pleural effusion
- The relationship between radiological signs and hemodynamic findings
    - Depend on the duration as well as the severity
-



**Cardiology**  
**Equalization of vascularity**



**Cardiology**  
**Redistribution of vascularity**  
**Kerley line**  
**Interstitial edema**

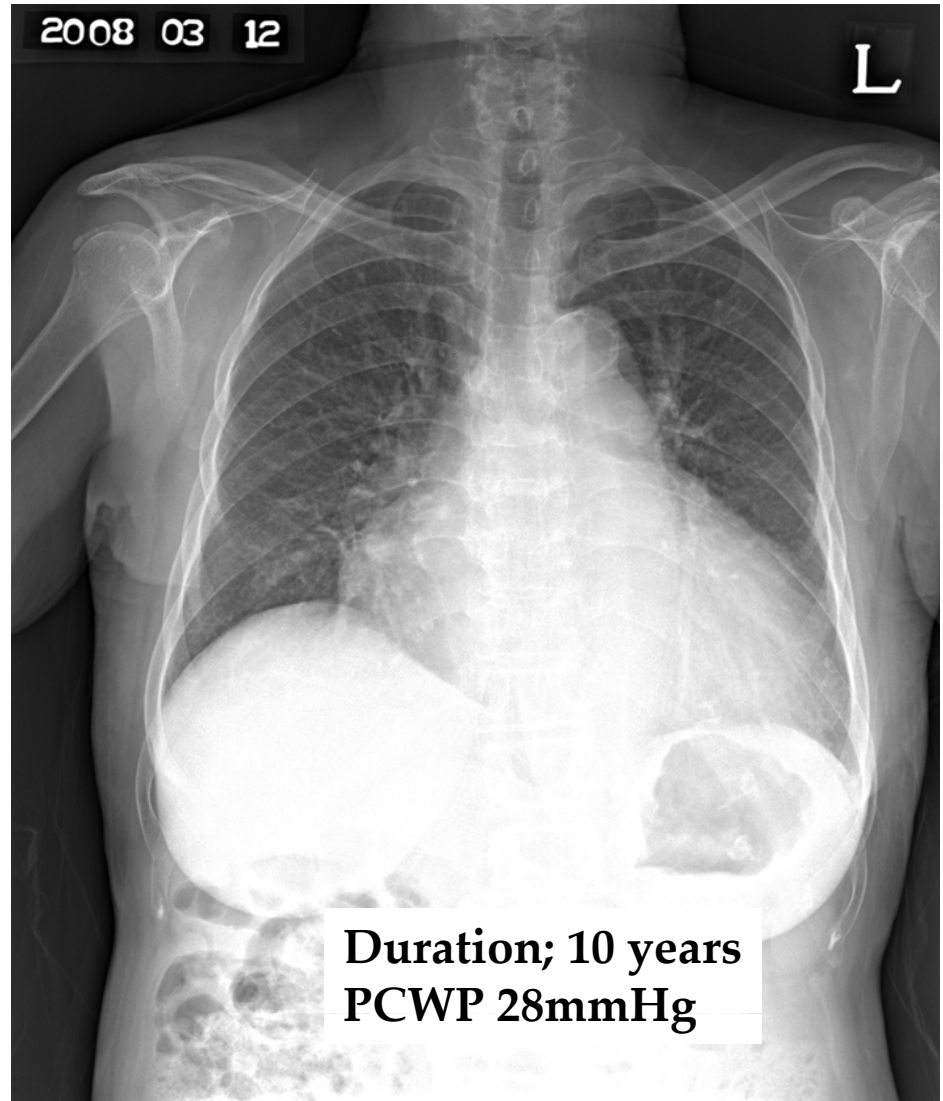
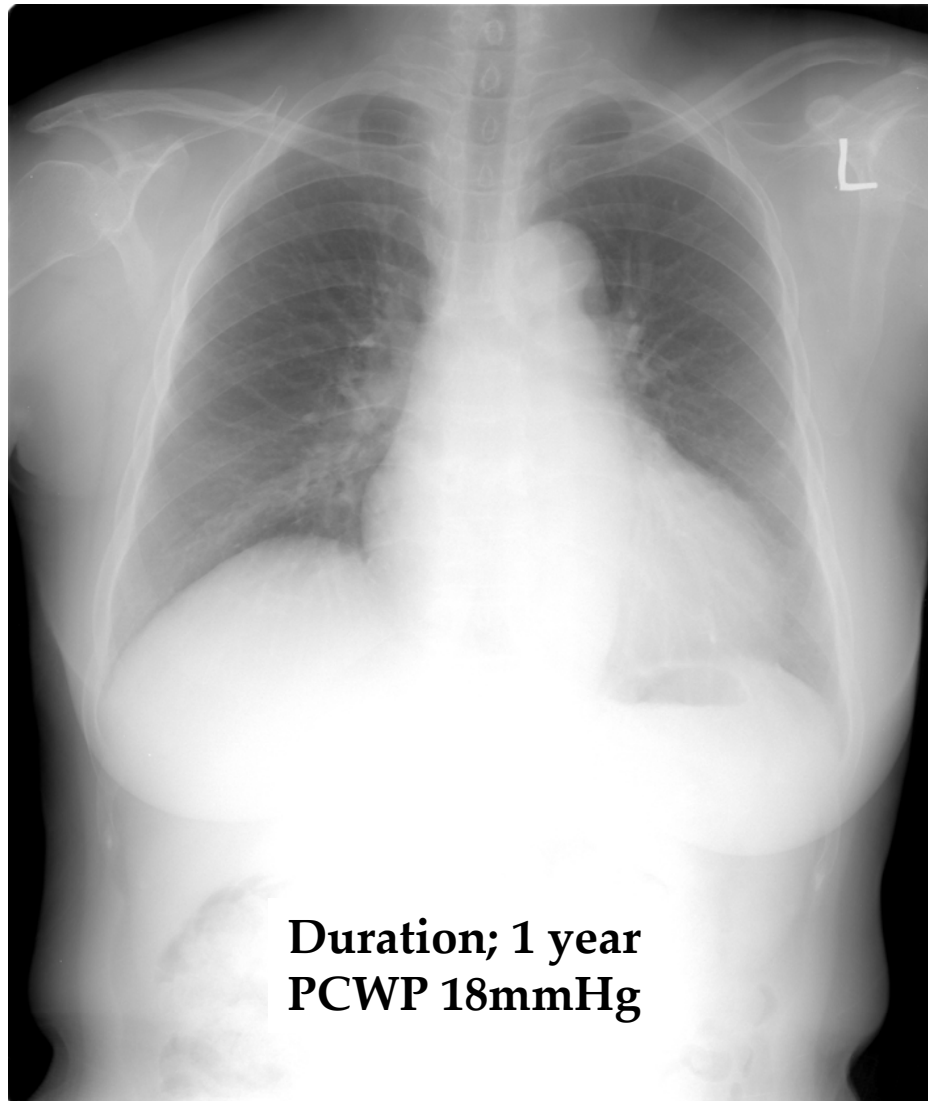


**Cardiology**  
**Redistribution of vascularity**  
**Kerley line**  
**Interstitial edema**  
**Large pleural effusion**



**Alveolar pulmonary edema  
-"Butterfly pattern"**

# Redistribution of Pulmonary Vascularity

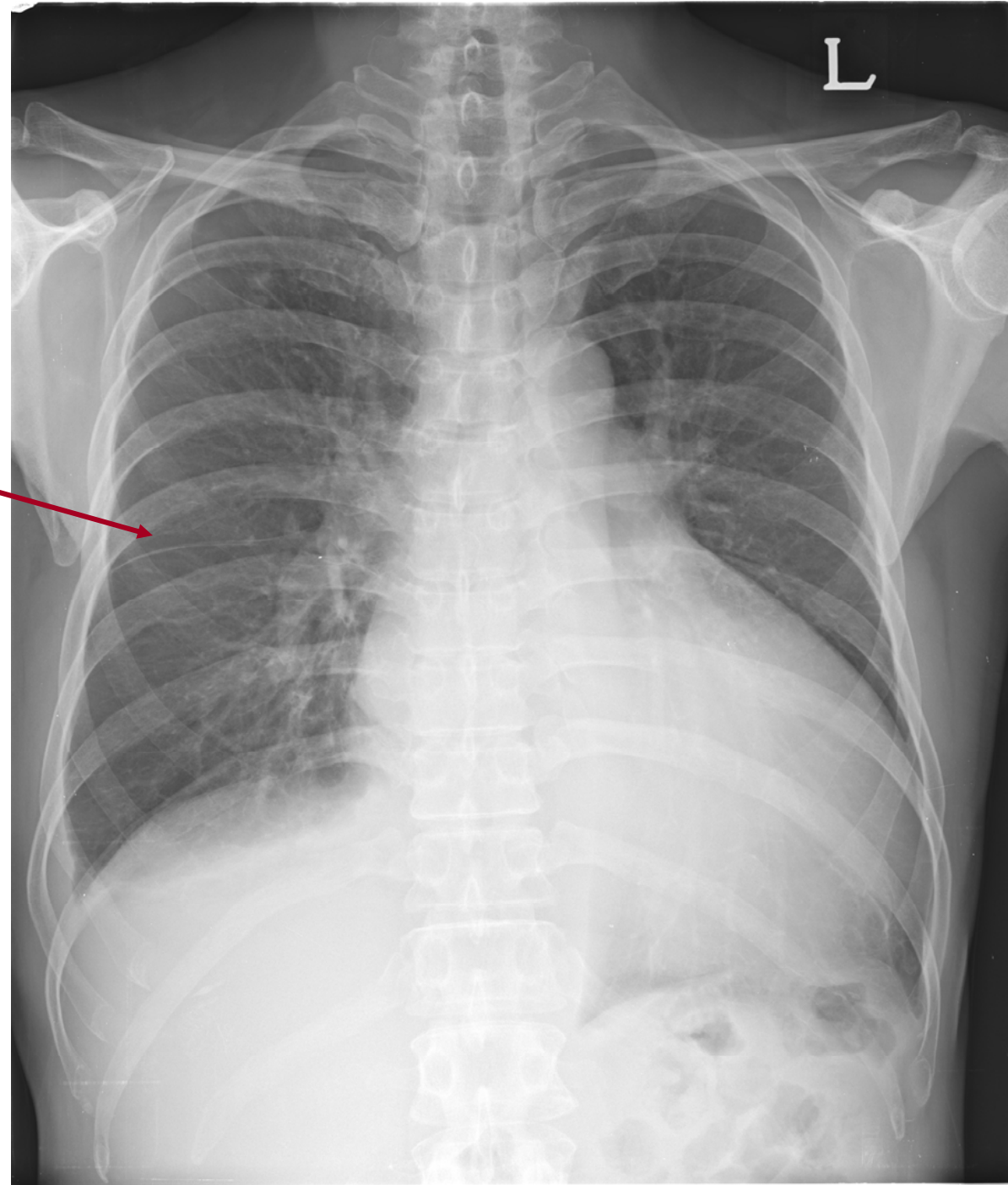


# Chest X-ray in Heart failure

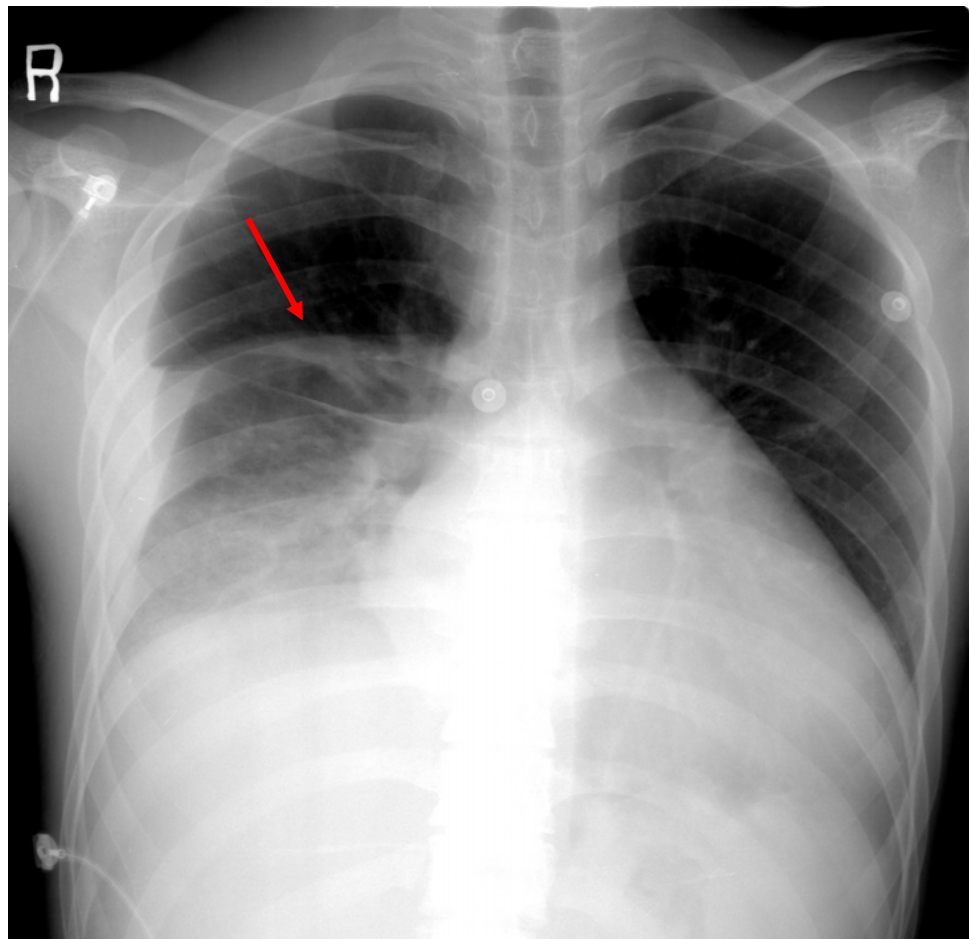
## *Patterns of Interstitial Edema*

- 1) Septal : sharp Linear densities of interlobular interstitial edema – Kerley line
  - 2) Perivascular : loss of sharpness of the central and peripheral vessels
  - 3) Subpleural : spindle-shaped accumulation of fluid between the lung and adjacent pleural surface
-

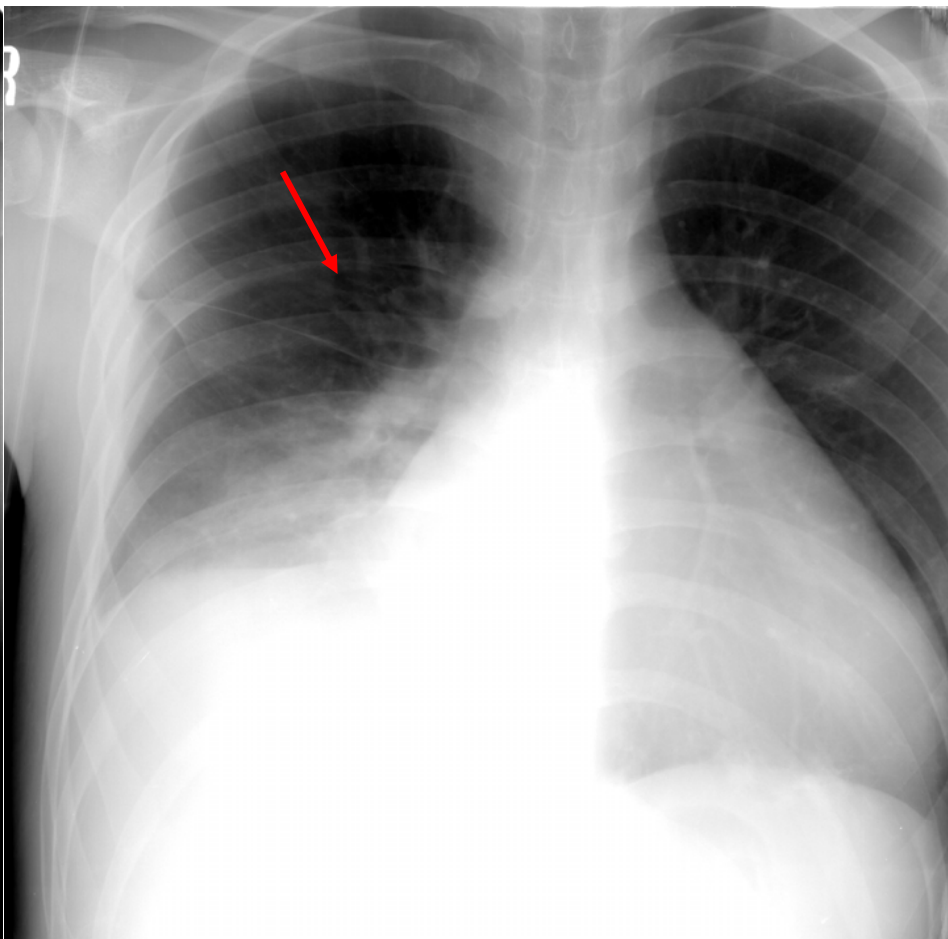
**Kerley line**



1997.04.25



1997.04.27



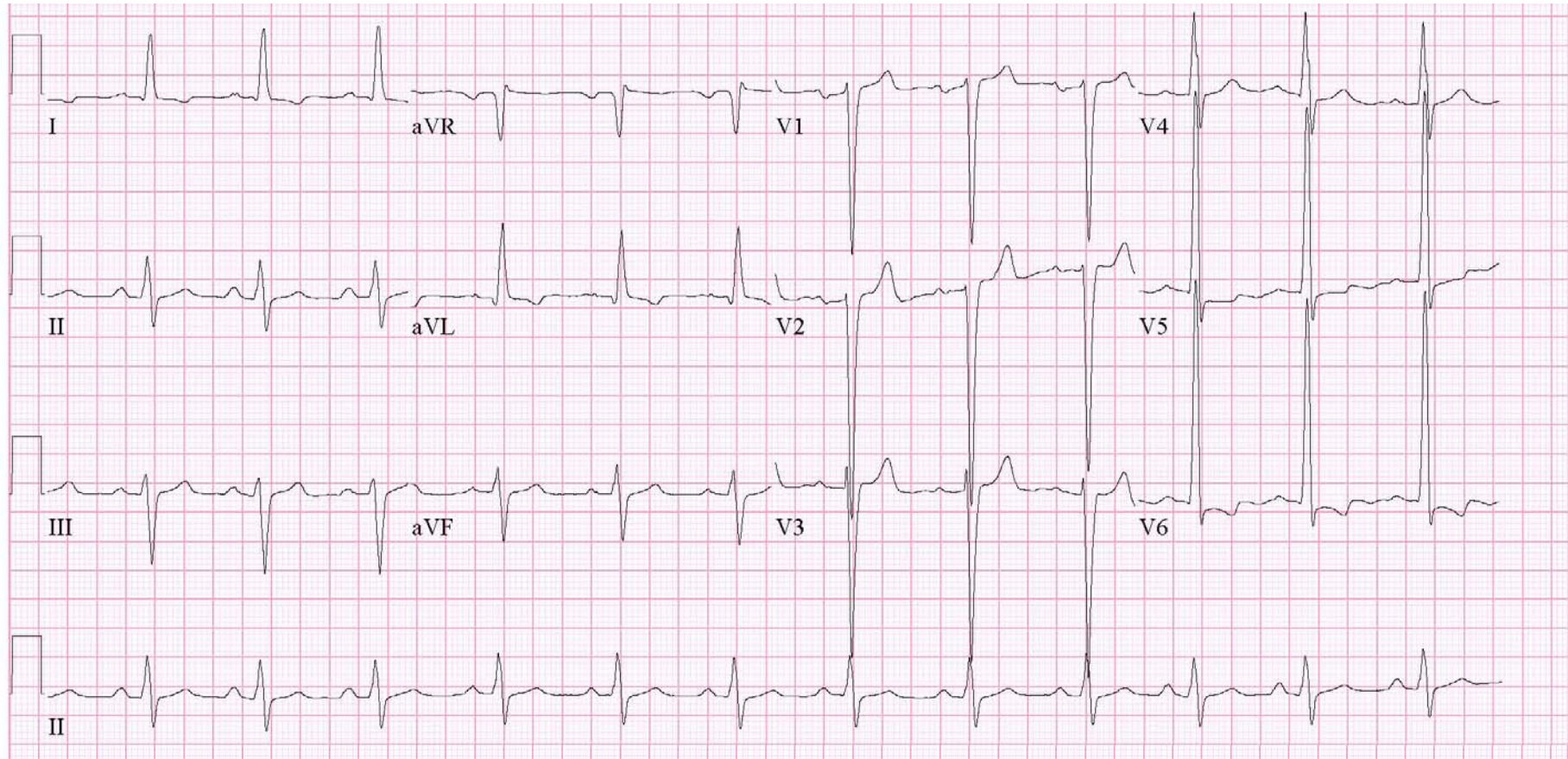
# ECG in Heart failure

## *What we have to see*

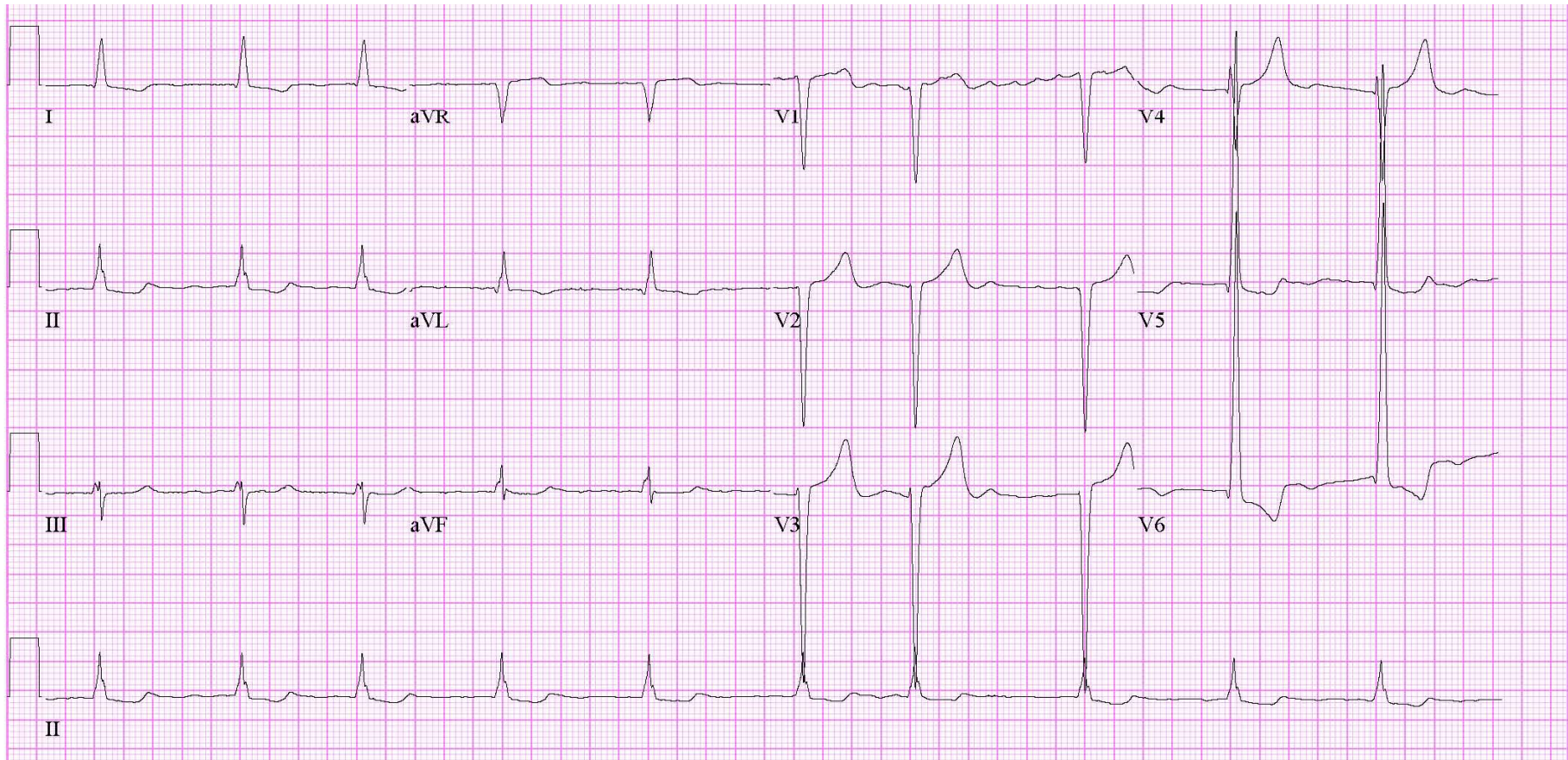
- ① Rhythm: Atrioventricular coupling, atrial fibrillation, ventricular arrhythmias
  - ② Heart rate
  - ③ Evidence of ventricular hypertrophy
  - ④ Q-waves
  - ⑤ P mitrale/ pulmonale
  - ⑥ Interventricular conduction disturbances (QRS duration, AV block)
  - ⑦ QRS voltage
  - ⑧ Digitalis effects
  - ⑨ Metabolic ST-T wave changes
-

# ECG in Heart failure

- The normal ECG suggests that the diagnosis of CHF should be carefully reviewed
    - ❑ Negative predictive value of normal ECG to exclude LV systolic dysfunction → >90%
  - Presence of anterior Q-wave and a LBBB in patients with ischemic heart disease
    - ❑ A good predictors of a decreased LVEF
  - ECG signs of LA enlargement of LV hypertrophy
    - ❑ May be associated with LV systolic as well as diastolic dysfunction
    - ❑ Low predictive value
  - Co-existence of clinical symptoms and signs of heart failure
    - ❑ Increase diagnostic contribution of ECG abnormalities
-

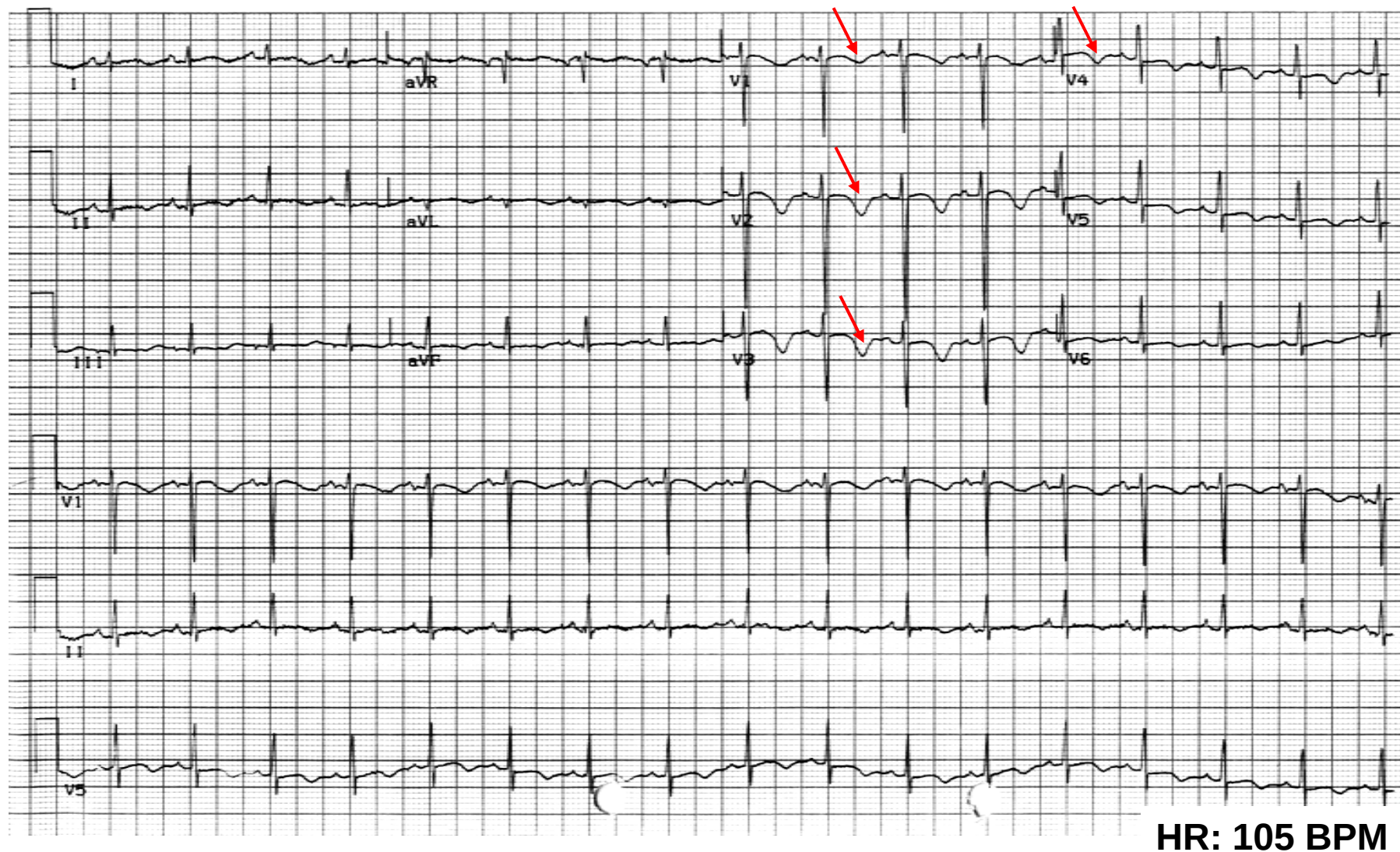


**M/35, DCMP**  
**Markedly cardiomyopathy**  
**LVEF 27%**

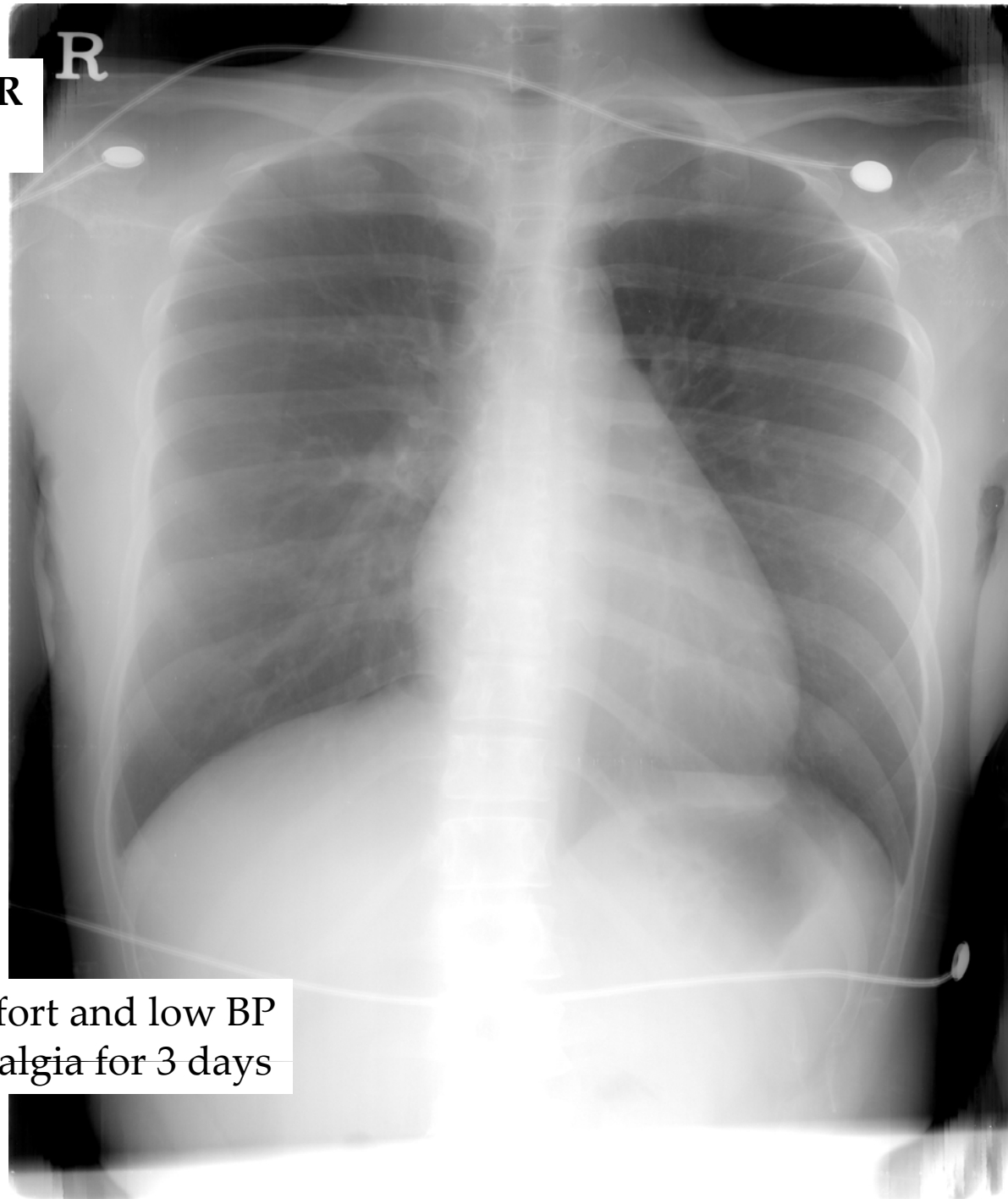


**M/84, Severe AR**  
**Markedly cardiomegaly**  
**LVEF 44%**

# ECG in patient with fever, chest pain and heart failure

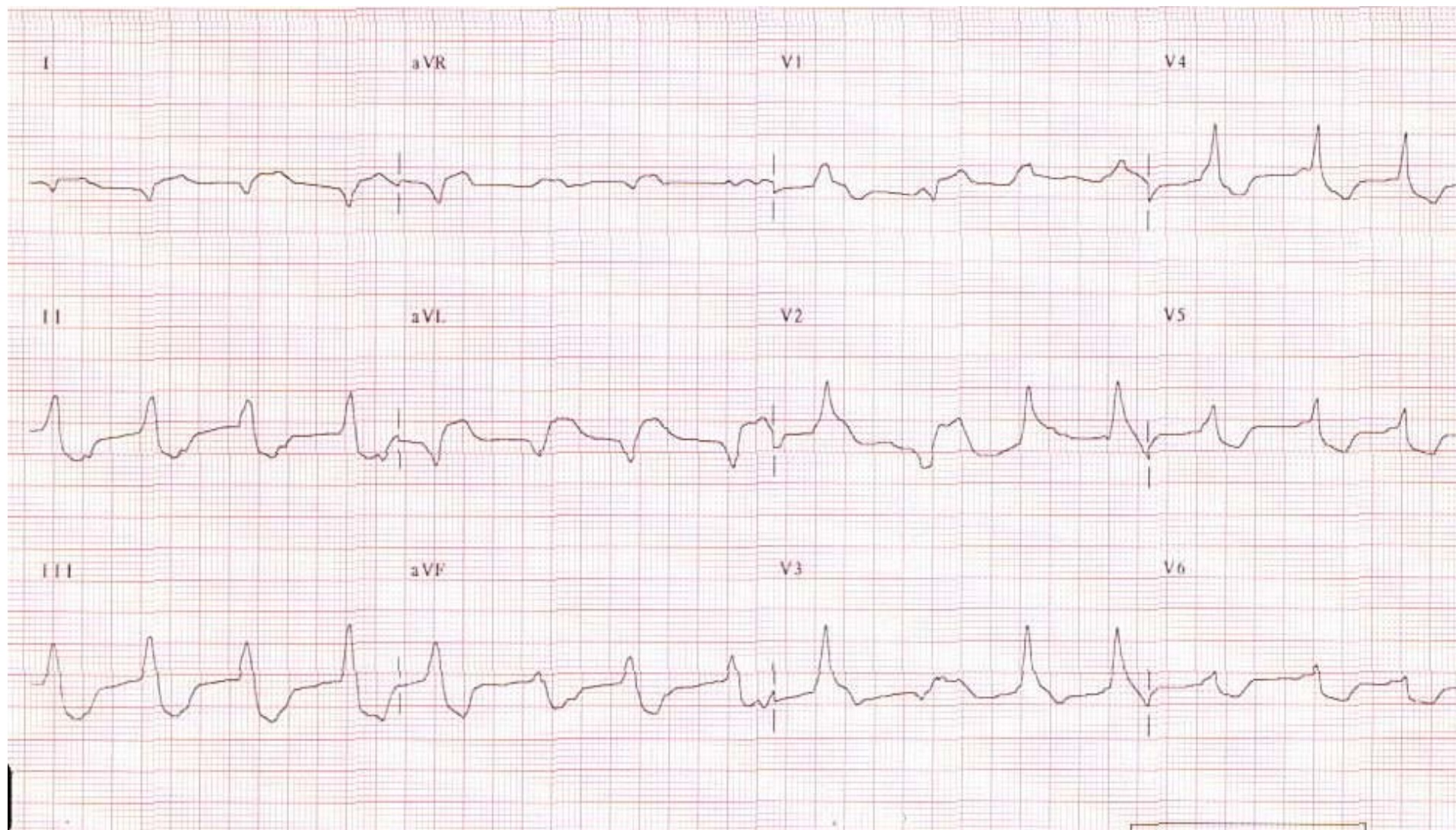


Chest PA at ER  
14:05

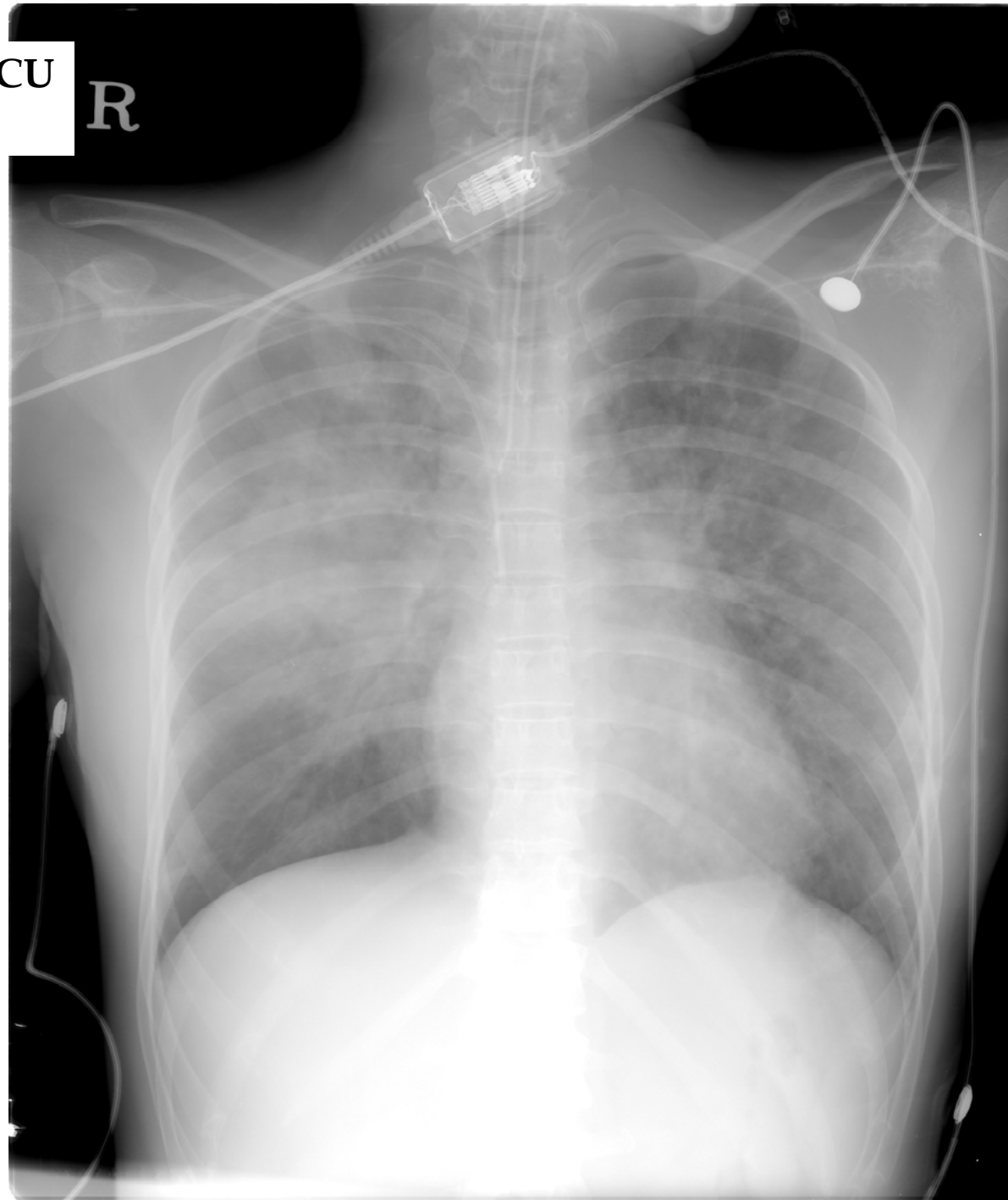


Chest discomfort and low BP  
Fever and myalgia for 3 days

**ECG at ER**  
**14:27**



Chest PA at CCU  
16:17



---

# Standard Laboratory Tests

The following laboratory investigations are recommended as part of a routine diagnostic evaluation of patients with heart failure

- CBC, serum electrolytes, creatinine, glucose and hepatic enzymes, urinalysis
- Additional test; CRP, TSH, serum uric acid, BUN
- In acute exacerbation, myocardial biomarkers for MI

*(ESC guidelines for the diagnosis and treatment of chronic heart failure, 2005)*

---

# Hyponatremia in Heart failure

## ■ Etiology

- ① Prolonged sodium restriction
- ② Intensive diuretic therapy
- ③ Inability to excrete free water (dilutional hyponatremia)
- ④ Elevated circulating levels of arginin vasopressin
- ⑤ Activation of renin-angiotensin system
- ⑥ Excessive sodium and water intake

## ■ Indicate severe heart failure

- May associated poor prognosis



# Potassium in CHF

## Hypokalemia

- Etiology
  - Common adverse effect of treatment with diuretics
  - Secondary hyperaldosteronism
- May cause
  - Fatal arrhythmias
  - Increase risk of digitalis toxicity

## Hyperkalemia

- May complicate therapy with ACE-I, ARBs and aldosterone antagonist
  - Serum K<sup>+</sup> 5.0-5.5 mEq/L ; 50% reduction  
    > 5.5 mEq/L ; stop aldosterone antagonist
-

## Other Common Electrolytes and Acid-Base Abnormalities in HF

- Hypomagnesemia
    - Due to diuretic use or hyperaldosteronism
    - Risk of sudden cardiac death, esp. with hypokalemia
  - Hyperuricemia
    - Due to renal dysfunction or thiazides use
  - Hypophosphatemia
    - Due to alcohol use or poor nutrition
  - Metabolic alkalosis with elevated CO<sub>2</sub> level
    - Often coupled to hypokalemia
    - Difficulty to wean from ventilator
-

# Renal Dysfunction in Heart failure

- Etiology
    - ❑ Secondary to reduction in renal blood flow and GFR
    - ❑ Altered balance of vasoconstrictor and vasodilator
    - ❑ Comorbidities such as DM and HT
    - ❑ Medication affecting renal blood flow
      - ACE-I, ARBs, NSAIDs, COX-2 inhibitors
  - Elevated serum creatinine, BUN and decreased GFR
    - ❑ Associated poor prognosis
  - Cardio-renal syndrome
    - ❑ Patients in whom symptoms of heart failure cannot be relieved despite aggressive management with IV diuretics, vasodilators and inotropic drugs
-

# CBC in Heart failure

- To see hemoglobin level, WBC count and ESR
  - Anemia
    - Poorer prognosis than normal Hct level
    - May aggravated heart failure symptoms and ischemia
  - Leukocytosis
    - Acute MI, endocarditis, myocarditis, pulmonary embolism
    - With elevated ESR
      - Suggest associated infection
-

# Other tests in Heart failure

## Liver function test

- Abnormal LFT due to hepatic congestion
    - ❑ Increased total bilirubin up to 15-20mg%
    - ❑ Increased AST and ALT up to 10 times of normal values
    - ❑ Elevated ALP and prolonged prothrombin time
    - ❑ Rapidly ameliorated by successful treatment
  - Hypoalbuminemia
    - ❑ Suggest cardiac cirrhosis or due to cardiac cachexia
-

# Other tests in Heart failure

## Thyroid function test

- Hyper- or hypothyroidism can precipitate or aggravate ventricular dysfunction or clinical HF
  - Thyrotoxicosis; frequently associated rapid Af
-

# Variables Relevant to Prognosis of heart Failure Patients

---

## Clinical assessment

NYHA class

syncope

angina pectoris

## Hemodynamics

LVEF, RVEF

PAP, PCWP

PAP-PCWP

CI

## Heart failure etiology

## Demographics

gender

race

age

## Comorbidities

## Metabolic

## Exercise Testing

metabolic assessment

BP response

HR response

peak VO<sub>2</sub>

anaerobic threshold

VE/VCO<sub>2</sub>

## Cytokines

TNF- $\alpha$ , IL-1, IL-6, IL-10

ESR

## Endomyocardial biopsy

inflammatory state

degree of fibrosis

infiltrative processes

## EKG

## Chest X-RAY

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# Prognostic Variables of HF

## Comorbidities

- ❑ Diabetes
  - ❑ *Systemic hypertension (better ?)*
  - ❑ Pulmonary hypertension
  - ❑ Sleep apnea
  - ❑ Obesity/cachexia (body mass)
  - ❑ Renal insufficiency
  - ❑ Hepatic abnormalities
  - ❑ COPD
-

# Renal Dysfunction in Heart failure

## **As poor prognosis**

- Below CCr <70mL/min (Dries DL, 2000)
  - BUN  $\geq$  43mg% (Fonarow GC, 2005)
  - Worsening renal function ( $\geq$  0.5mg%) in ADHF (Smith KJ, 2003)
  - Worsening renal function in chronic heart failure (Dries DL, 2000)
-

---

# Prognostic Variables of HF

## Metabolic

- ❑ Serum sodium
  - ❑ Thyroid dysfunction
  - ❑ Anemia
  - ❑ Acidosis/alkalosis
-

# Hyponatremia in Heart failure

- A simple, inexpensive, and easy-to-obtain marker
  - Serum  $\text{Na}^+$  falls as PRA and vasopressin increase
  - Serum  $\text{Na}^+$  130mEq/L or less vs > 130mEq/L
    - 1-year survival <20% vs 50% (*Lee WH, 1986*)
-

# Thyroid function in Heart failure

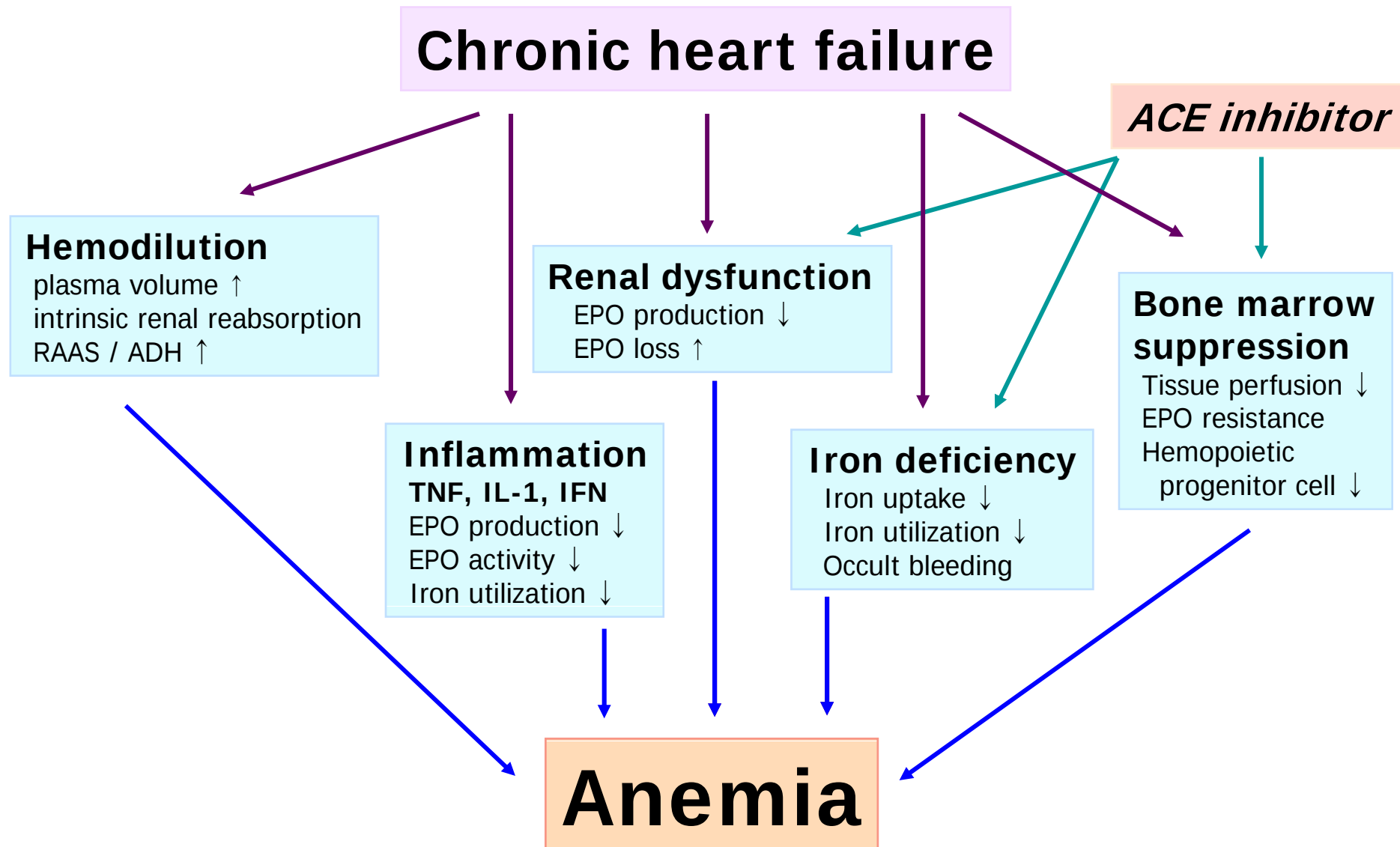
## Thyroid function test

- ❑ Low T-3 or T-3 index, increased reversed T-3 and normal TSH level
  - ❑ Higher short-term mortality (*Hamilton MA, 1990*)
-

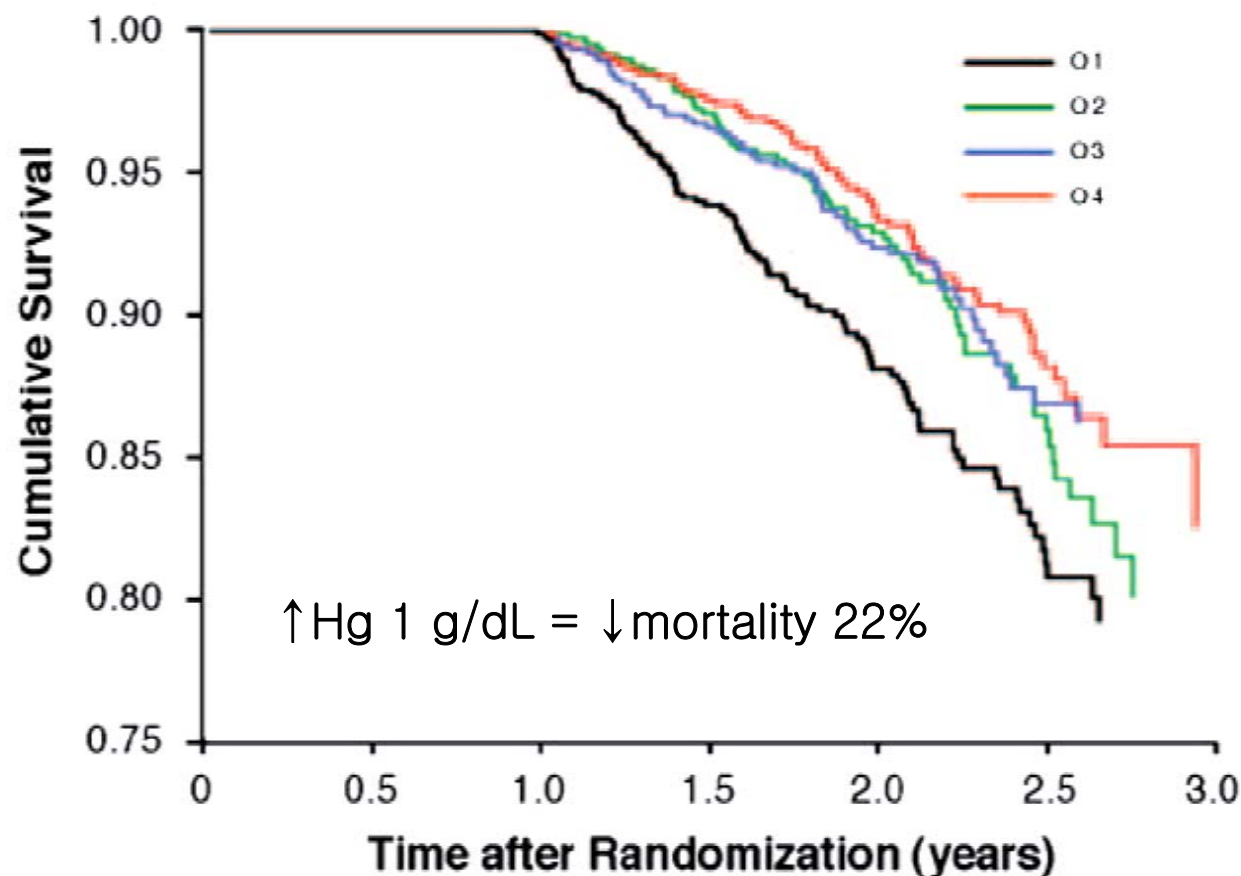
# Prevalence of Anemia in HF

- 2.72 – 69.7%
  - Such variance associated with
    - Differences in the definition of anemia
    - Substantial differences in population studied
    - A lack of information about correctable causes of anemia
    - No control for differences in true anemia vs dilutional anemia
-

# Mechanisms of Anemia in HF



# Changes of Hb & Prognosis



## Val-HeFT

Q1: Hb 14.2 → 12.6  
(-6.3 ~ -0.9)

Q2: Hb 13.9 → 13.4  
(-0.8 ~ -0.2)

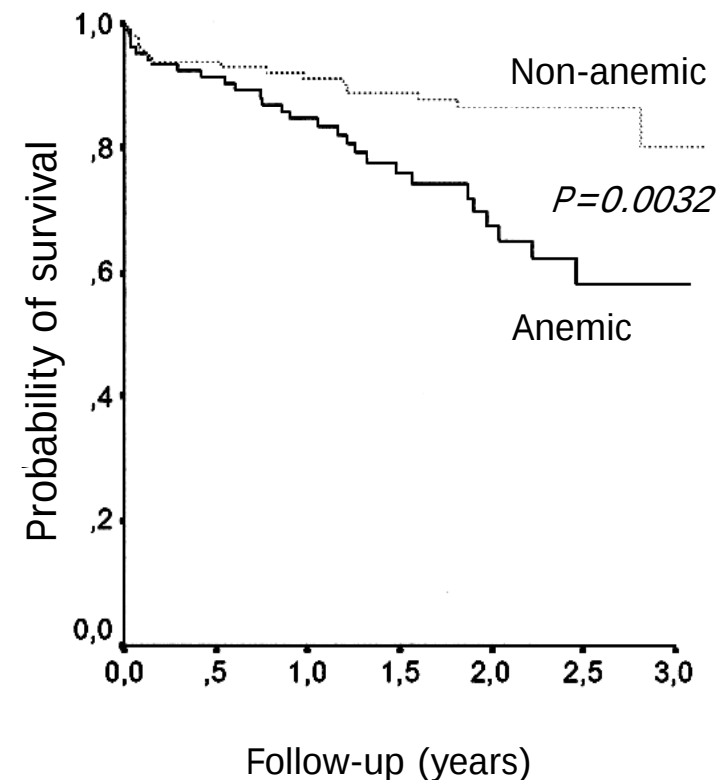
Q3: Hb 13.7 → 13.8  
(-0.1 ~ 0.4)

Q4: Hb 13.3 → 14.4  
(0.5 ~ 6.8)

# Anemia in Diastolic HF

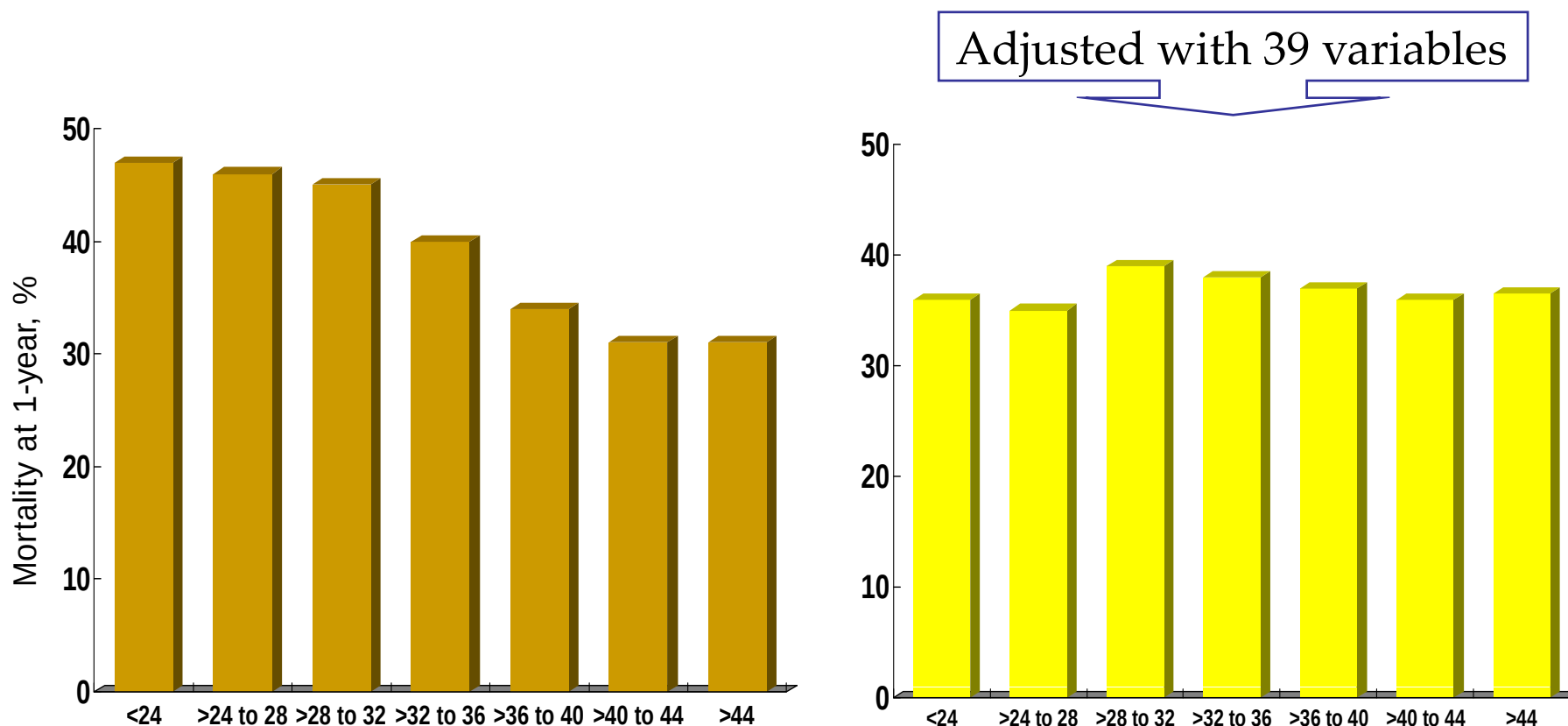
- CHF with LVEF  $\geq 50\%$
- WHO criteria
- Anemia : 46% (97 / 210)

| Variable | RR (CI95%)          | p     |
|----------|---------------------|-------|
| Age      | 1.042 (1.003-1.082) | 0.035 |
| Ischemic | 1.417 (0.708-2.836) | 0.599 |
| Male     | 1.618 (0.823-3.179) | 0.163 |
| DM       | 0.764 (0.343-1.701) | 0.510 |
| NYHA IV  | 1.112 (0.589-2.101) | 0.744 |
| ACEI     | 0.513 (0.263-1.002) | 0.051 |
| CKD      | 0.628 (0.328-1.203) | 0.161 |
| Anemia   | 2.647 (1.308-5.357) | 0.007 |



Shamagian LG et al. Heart 2005

# Hct and Outcomes in CHF



Anemia may be *a predominantly a marker* rather than a mediator of increased mortality risk

Kosiborod M et al. Arch Intern Med 2005;165:2237-44

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# Prognostic Variables of HF

## Chest X-Ray

### ■ Congestion

- ❑ Evidence of volume overload
- ❑ Independent predictor of mortality  
(*Kelly TL, 1990; Madsen BK, 1994*)

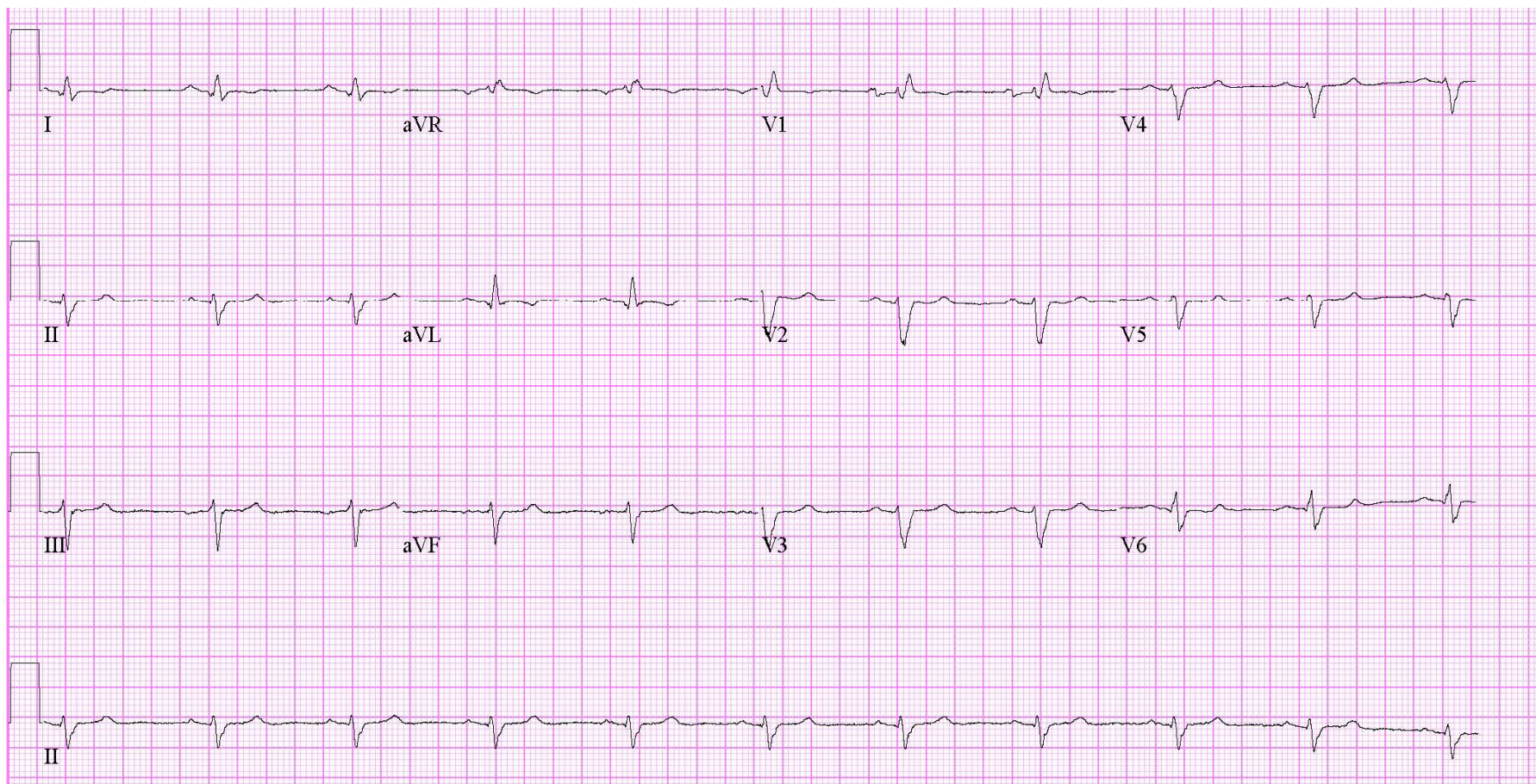
### ■ Cardiothoracic ratio

- ❑ Independent predictors of survival in V-HeFT and others (*Fuster V, 1981*)
  - ❑ A poor correlation with LVEF
-

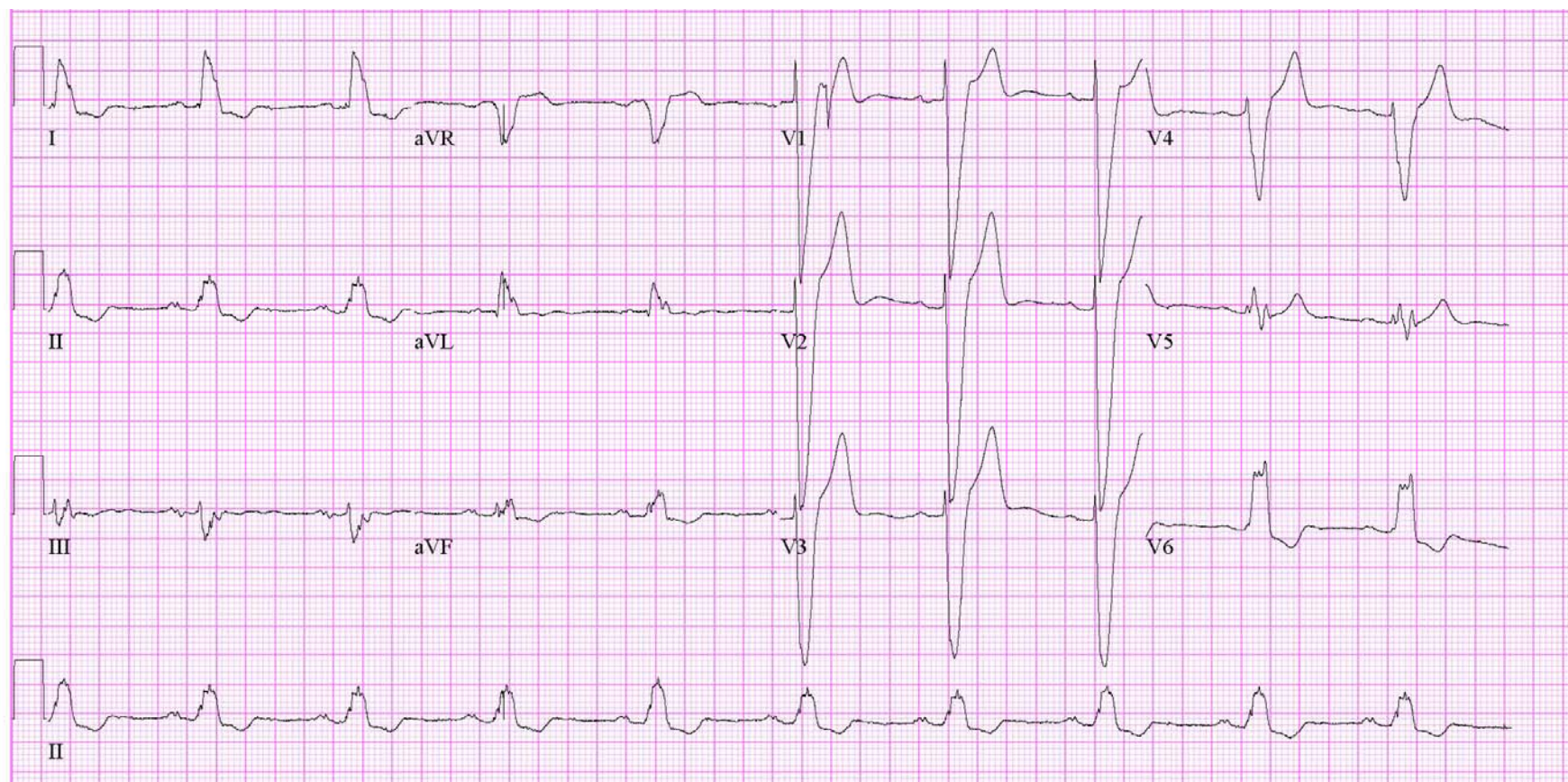
# Prognostic Variables of HF

## EKG

- ❑ Rhythm (atrial fibrillation or ventricular arrhythmias)
  - Af ; *Rockman HA 1989, Middlekauf HR 1991*
  - Frequent PVCs, couplets, NSVT; *DeMaria R 1992*
- ❑ Voltage
- ❑ Signal-averaged EKG (T-wave alternans)
  - Low sensitivity
  - May be useful in ischemic heart disease
- ❑ QT interval (QT dispersion)
- ❑ HR variability
  - More powerful makers than QT dispersion
- ❑ QRS width



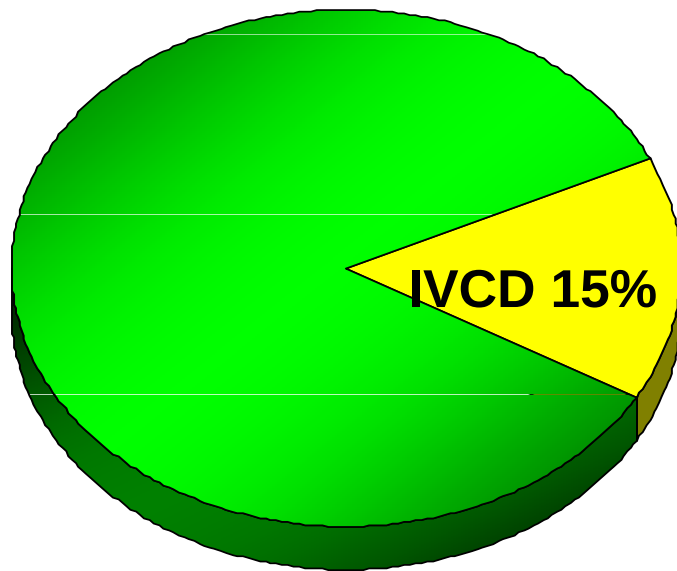
**M/48, Cardiac amyloidosis**  
**LV hypertrophy in Echo.**  
**LVEF 55%**



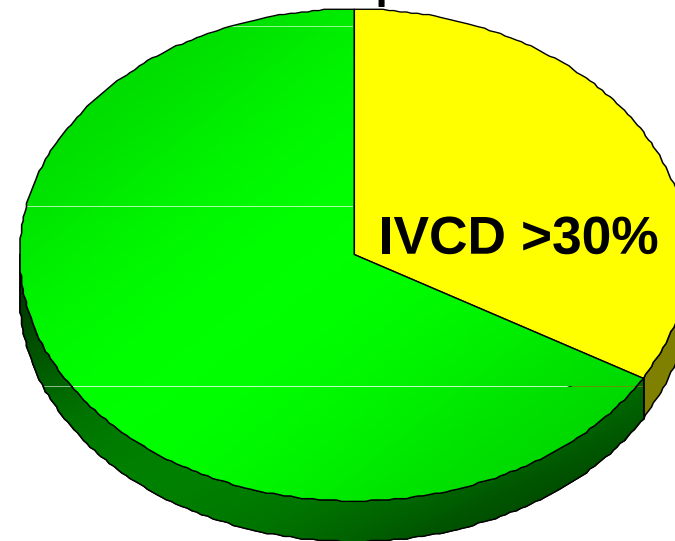
**F/64, DCMP**  
**Markedly cardiomegaly**  
**LVEF 25%**

# Prevalence of Inter- or Intraventricular Conduction Delay

General HF Population



Moderate to Severe HF Population



Havranek E, Masoudi F, Westfall K, et al. *Am Heart J* 2002;143:412-417  
Schoeller R, Andresen D, Buttner P, et al. *Am J Cardiol.* 1993;71:720-726  
Aaronson K, Schwartz J, Chen T, et al. *Circulation* 1997;95:2660-2667  
Farwell D, Patel N, Hall A, et al. *Eur Heart J* 2000;21:1246-1250

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# Ventricular Dyssynchrony

## ■ Ventricular Dyssynchrony



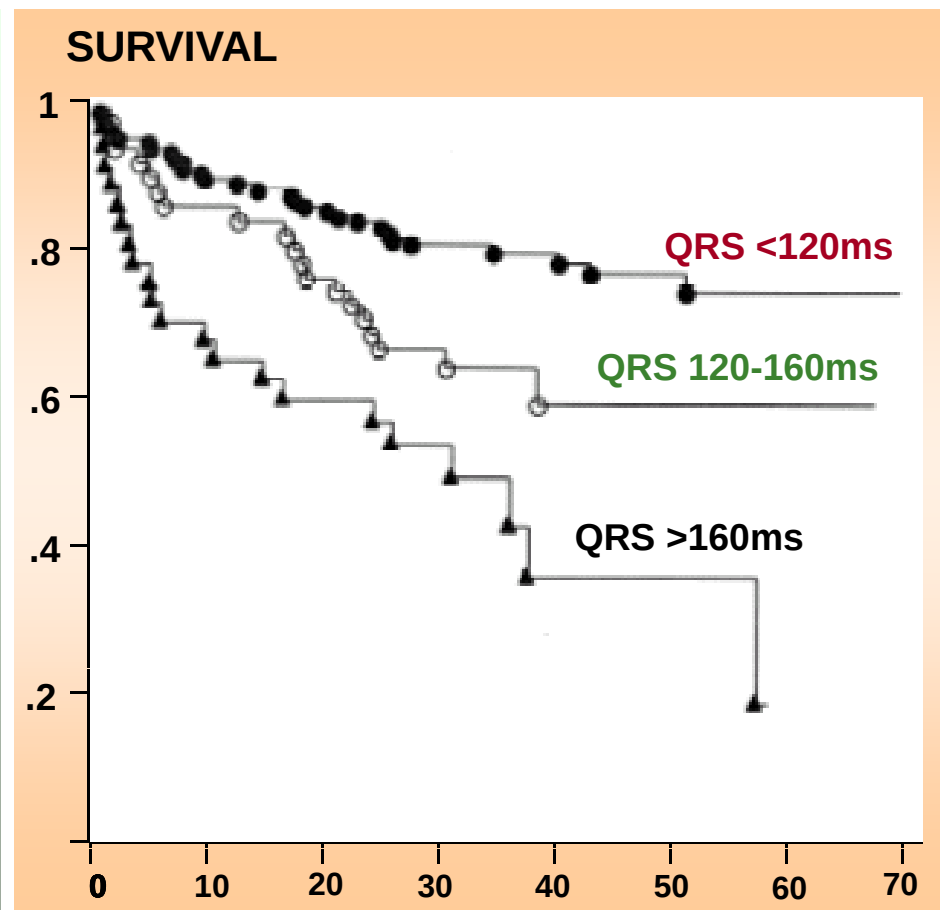
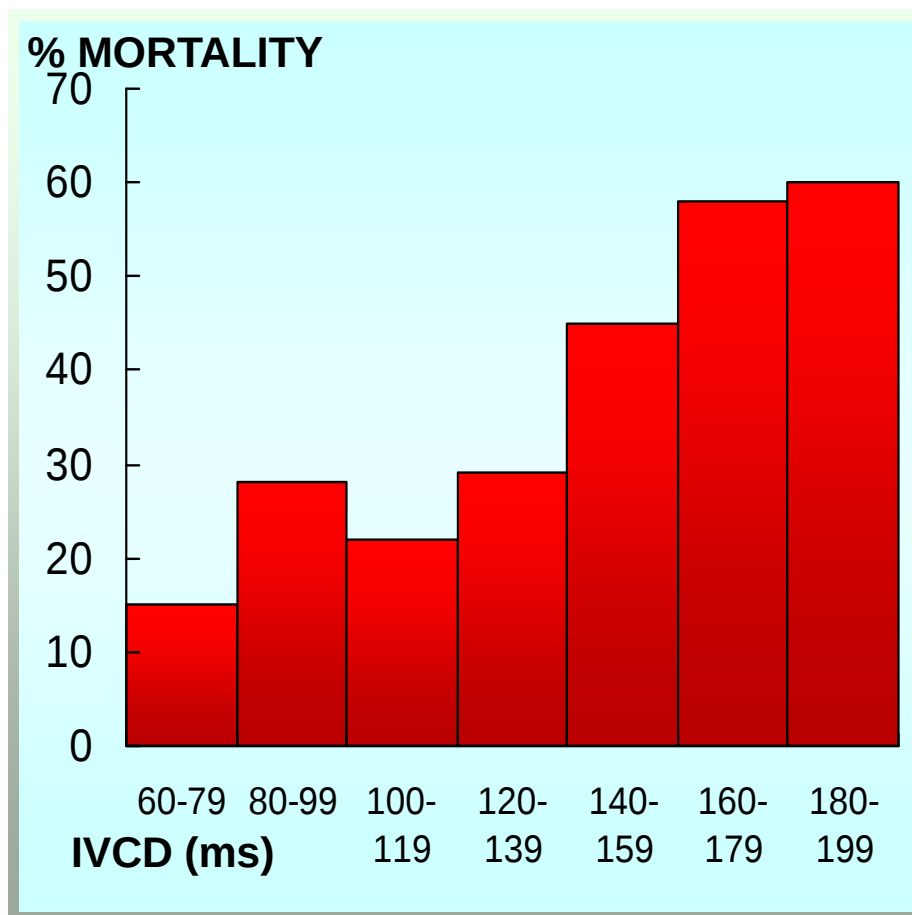
- ❑ **Electrical:** Inter- or Intraventricular conduction delays typically manifested as left bundle branch block
- ❑ **Structural:** disruption of myocardial collagen matrix impairing electrical conduction and mechanical efficiency
- ❑ **Mechanical:** Regional wall motion abnormalities with increased workload and stress—compromising ventricular mechanics

*Tavazzi L. Eur Heart J 2000;21:1211-1214*

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# IVCD as Prognostic Factor

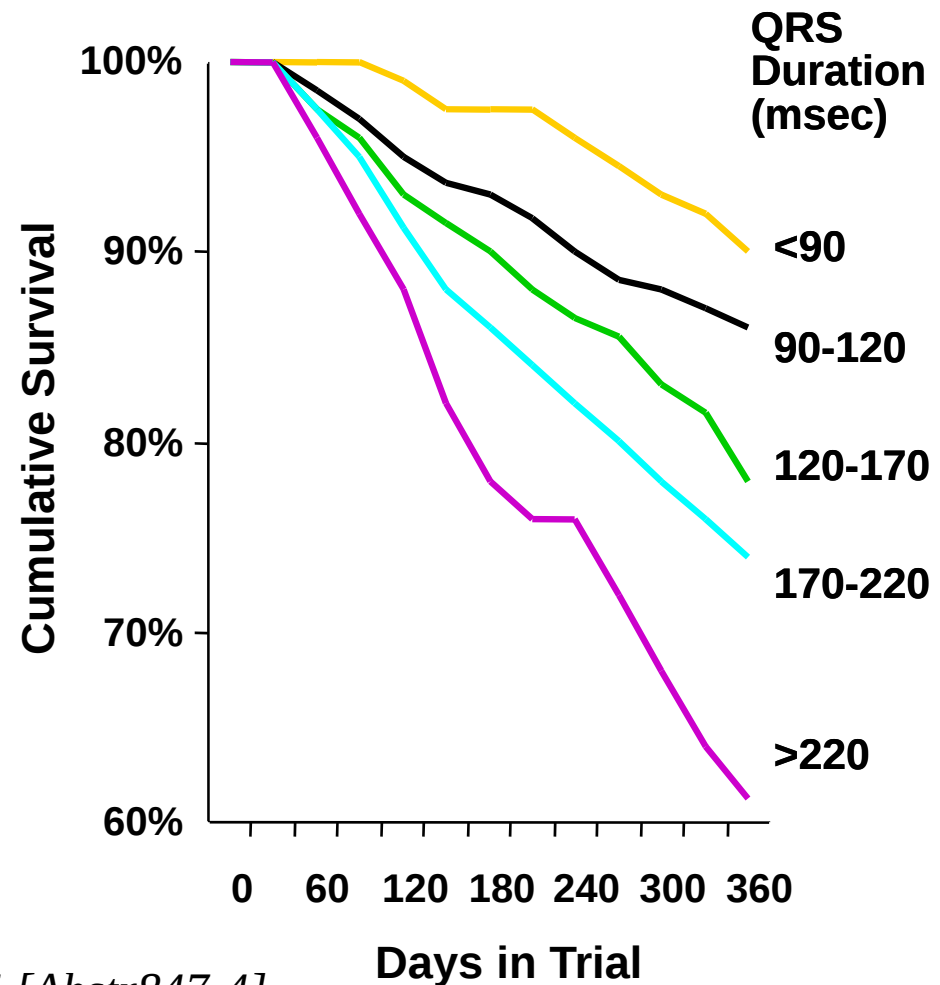
*Shamim W, et al. Int J Cardiol 1999;70:171-8.*



# Wide QRS –Mortality Increase

## VEST study analysis

- NYHA Class II-IV patients
- 3,654 ECGs digitally scanned
- Age, creatinine, LVEF, heart rate, and QRS duration found to be independent predictors of mortality
- *Relative risk of widest QRS group; 5 times greater than narrowest*



Gottipaty V et al. JACC 1999;33(2) :145 [Abstr847-4]

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# Standard Laboratory Tests

The following laboratory test be obtained routinely in patients being evaluated for heart failure

- Serum electrolytes, BUN, serum creatinine, glucose, calcium and magnesium, lipid profile, CBC, LFT, urinalysis, TFT
- ECG and chest X-ray are recommended in all patients with heart failure or being evaluated for heart failure

*(HFSA 2006 comprehensive heart failure practice guideline)*

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# Requiring Lab for Heart Failure

- Plasma BNP or NT-proBNP
- CBC
- Serum electrolytes, BUN, creatinine,  $Mg^{++}$ ,  $Ca^{++}$ , uric acid
- Liver function test
- Lipid levels
- Hemoglobin A1c
- Urinalysis
- Thyroid function test
- hs-CRP
- ABGA
- Prothrombin time

# Minimal Required Tests in HF

- CBC
  - Metabolic profile
    - Serum electrolyte
    - BUN, serum creatinine
  - Biochemistry
    - Uric acid, calcium, magnesium, phosphorus
    - Liver function test
  - Urinalysis
  - BNP level
-

# Monitoring Recommendations in ADHF

| Frequency              | Value                   | Specifics                                                                                                                            |
|------------------------|-------------------------|--------------------------------------------------------------------------------------------------------------------------------------|
| <i>At least daily</i>  | Weight                  | Determine after voiding in the morning<br>Account for possible increased food intake due to improved appetite                        |
| <i>At least daily</i>  | Fluid intake and output |                                                                                                                                      |
| <i>More than daily</i> | Vital signs             | Including orthostatic blood pressure                                                                                                 |
| <i>At least daily</i>  | Signs                   | Edema<br>Ascites<br>Pulmonary rales<br>Hepatomegaly<br>Increased jugular venous pressure<br>Hepatojugular reflux<br>Liver tenderness |

# Monitoring Recommendations in ADHF

| Frequency             | Value          | Specifics                                                                          |
|-----------------------|----------------|------------------------------------------------------------------------------------|
| <i>At least daily</i> | Symptoms       | Orthopnea<br>Paroxysmal nocturnal dyspnea<br>Nocturnal cough<br>Dyspnea<br>Fatigue |
| <i>At least daily</i> | Electrolytes   | Potassium<br>Sodium                                                                |
| <i>At least daily</i> | Renal function | BUN<br>Serum creatinine                                                            |

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# Standard Laboratory Makers

- For diagnosis of heart failure
  - For differential diagnosis of underlying etiology
  - For monitoring of treatment
  - For prognosis
-

2008 년 5월 2일 서울 아산 병원

경청해 주셔서 감사합니다!



# Cardio-Renal-Anemia syndrome

