From Infarction to Heart Failure

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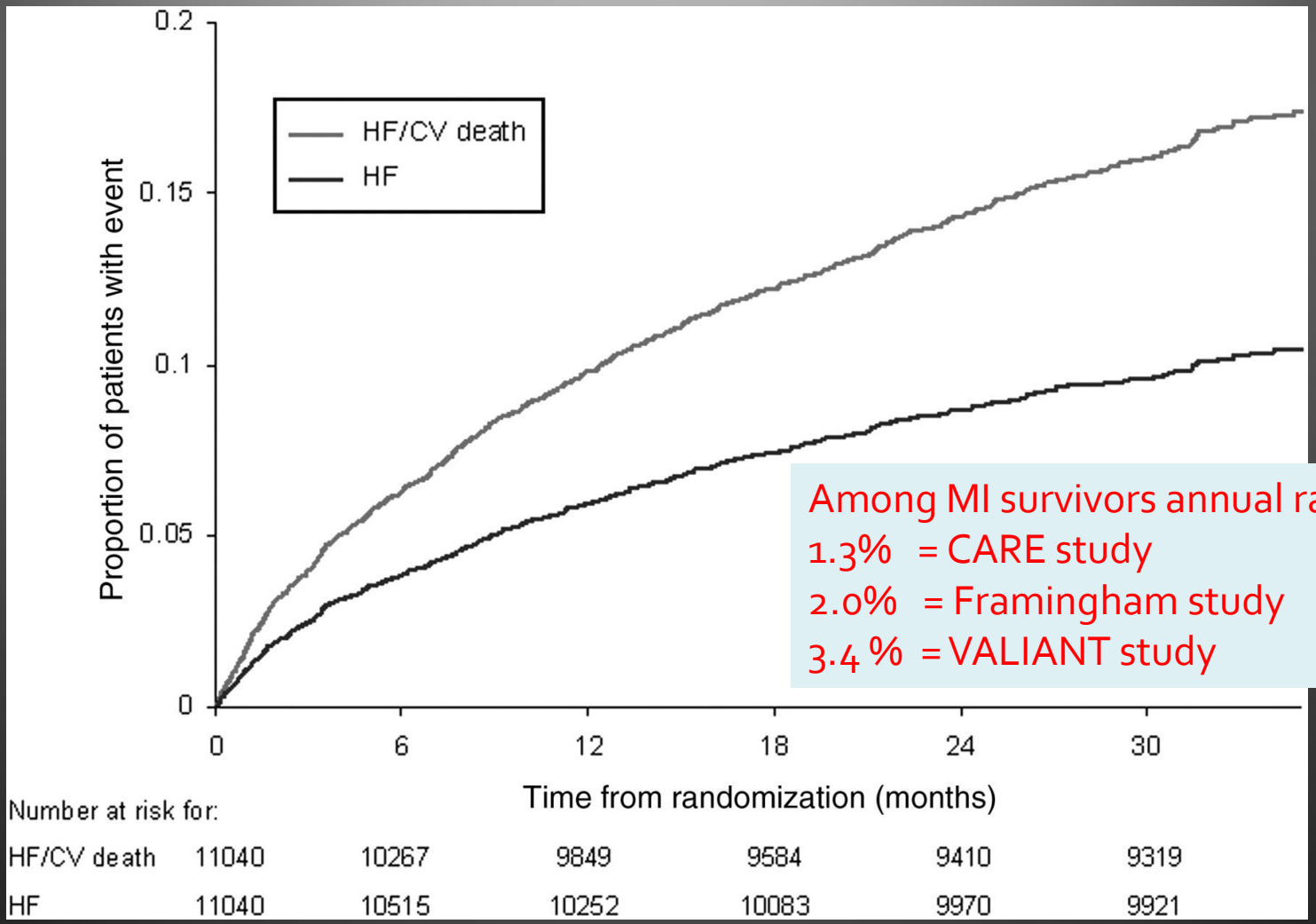
Facts about Heart Failure and CAD

- Approximately 10% to 20% of patients with ACS have concomitant acute HF at admission
- Approximately 10% of them develop HF in-hospital.
- Approximatly 40 % of de novo HF caused by ACS

Heart failure hospitalization and cardiovascular death or heart failure hospitalization among stable myocardial infarction survivors without prior chronic heart failure.



Among MI survivors annual rate of HF
1.3% = CARE study
2.0% = Framingham study
3.4 % = VALIANT study

Lewis E F et al. Eur Heart J 2008;29:748-756

European Heart Journal

Facts about Heart Failure and CAD

- **Chronic Heart Failure**
  Underlying CAD was found in more than 50% (65 %) (KorHF = 52.3%, Thai ADHERE 46%)
- **40-50% of patient after infarction have LV dysfunction**
- **Readmission caused by ACS in about 25% (ATLAS)**
- **50% of sudden cardiac death in ICM have acute MI on autopsy(ATLAS)**

Ischemic Cardiomyopathy:
How to prevent and Manage it

Table 2 Independent predictors of heart failure, and heart failure or death in stable, MI survivors ($n = 8582$)

Predictor	HF			HF or CV death	
	HR (95% CI)	χ^2 test	*P*	HR (95% CI)	*P*
Baseline predictors					
Diabetes	1.71 (1.47–1.98)	51.1	<0.001	1.52 (1.37–1.69)	<0.001
Age (1 year increase)	1.03 (1.02–1.04)	43.8	<0.001	1.02 (1.01–1.03)	<0.001
Prior MI	1.63 (1.41–1.89)	43.4	<0.001	1.63(1.45–1.83)	<0.001
History of PAD	1.60 (1.32–1.95)	22.5	<0.001	1.53 (1.30–1.79)	<0.001
LVEF (5% decrease)	1.07 (1.03–1.11)	14.4	<0.001	1.09 (1.07–1.13)	<0.001
New LBBB	1.67 (1.28–2.19)	13.9	<0.001	1.72 (1.38–2.14)	<0.001
Race					
Black	1.84 (1.31–2.59)	12.4	<0.001	1.56 (1.17–2.07)	0.003
Other	1.41 (0.98–2.03)	3.5	0.06	1.04 (0.75–1.44)	0.807
Killip Class					
III	1.37 (1.15–1.64)	11.8	<0.001	1.44 (1.25–1.67)	<0.001
IV	1.42 (1.11–1.82)	8.0	0.005	1.31 (1.07–1.61)	0.009
GFR (10 cc/min increase)[a]	1.08 (1.03–1.12)	11.0	<0.001	1.12 (1.08–1.16)	<0.001
History of chronic lung disease	1.43 (1.16–1.77)	10.9	<0.001	1.38 (1.16–1.64)	<0.001
Clinical evidence of HF	1.32 (1.12–1.56)	10.7	0.001	1.27 (1.12–1.45)	<0.001
History of hypertension	1.28 (1.10–1.48)	10.7	0.001	1.32 (1.17–1.48)	<0.001
Pulse pressure (10 mm increase)[b]	0.44 (0.27–0.72)	10.5	0.001	0.50 (0.33–0.76)	0.001
BMI (1 kg/m^2 increase)[c]	1.01 (1.00–1.02)	8.3	0.004	1.01 (1.00–1.02)	0.024
Atrial fibrillation post-MI	1.20 (0.99–1.46)	3.6	0.06	1.25 (1.08–1.46)	0.004

Eldrin F lewis et al, European Heart Journal (2008) 29, 748–756

Post-infarct Left Ventricular Remodeling

Early phase (within 72 hours)
Late phase (beyond 72 hours).

From: HEART FAILURE: A COMPANION TO BRAUNWALD'S HEART DISEASE, SECOND EDITION 2011

Early phase (infarct expansion)

In the infarcted regions,

Wall thinning as a result of the loss of myocytes, collapse of the intercellular space, and stretching of surviving myocytes.

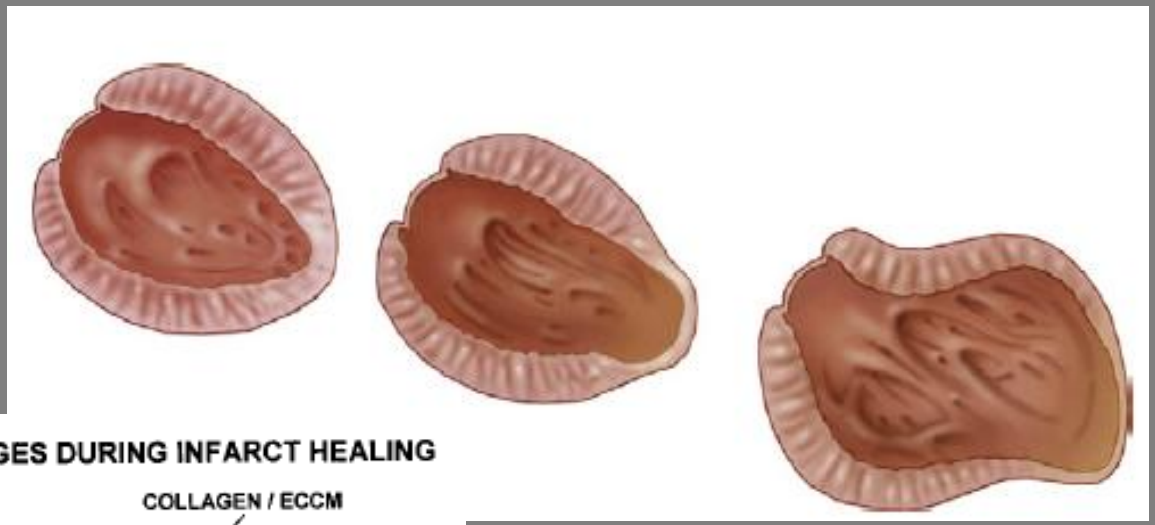
In the noninfarcted regions,

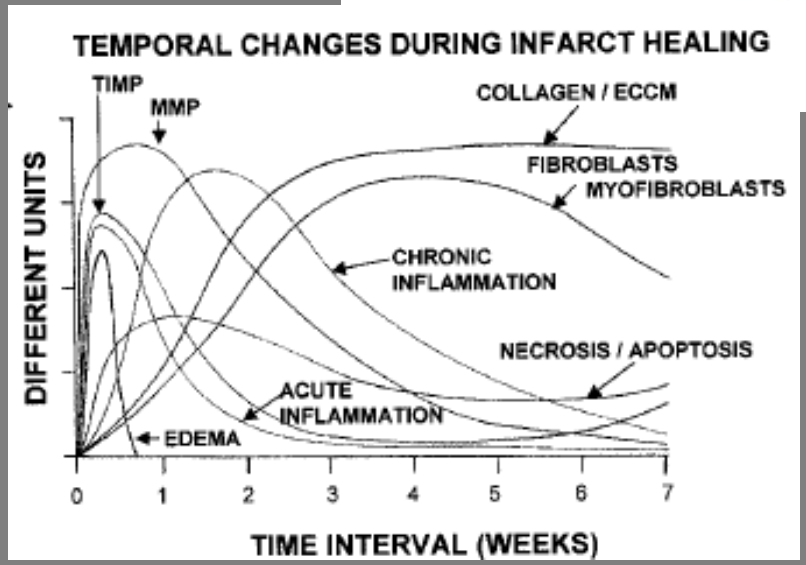
The myocardium thins because of a decrease in the number of myocytes across the wall.

From: HEART FAILURE: A COMPANION TO BRAUNWALD'S HEART DISEASE, SECOND EDITION 2011

Late progressive LV remodeling

involving predominantly the noninfarcted segments.





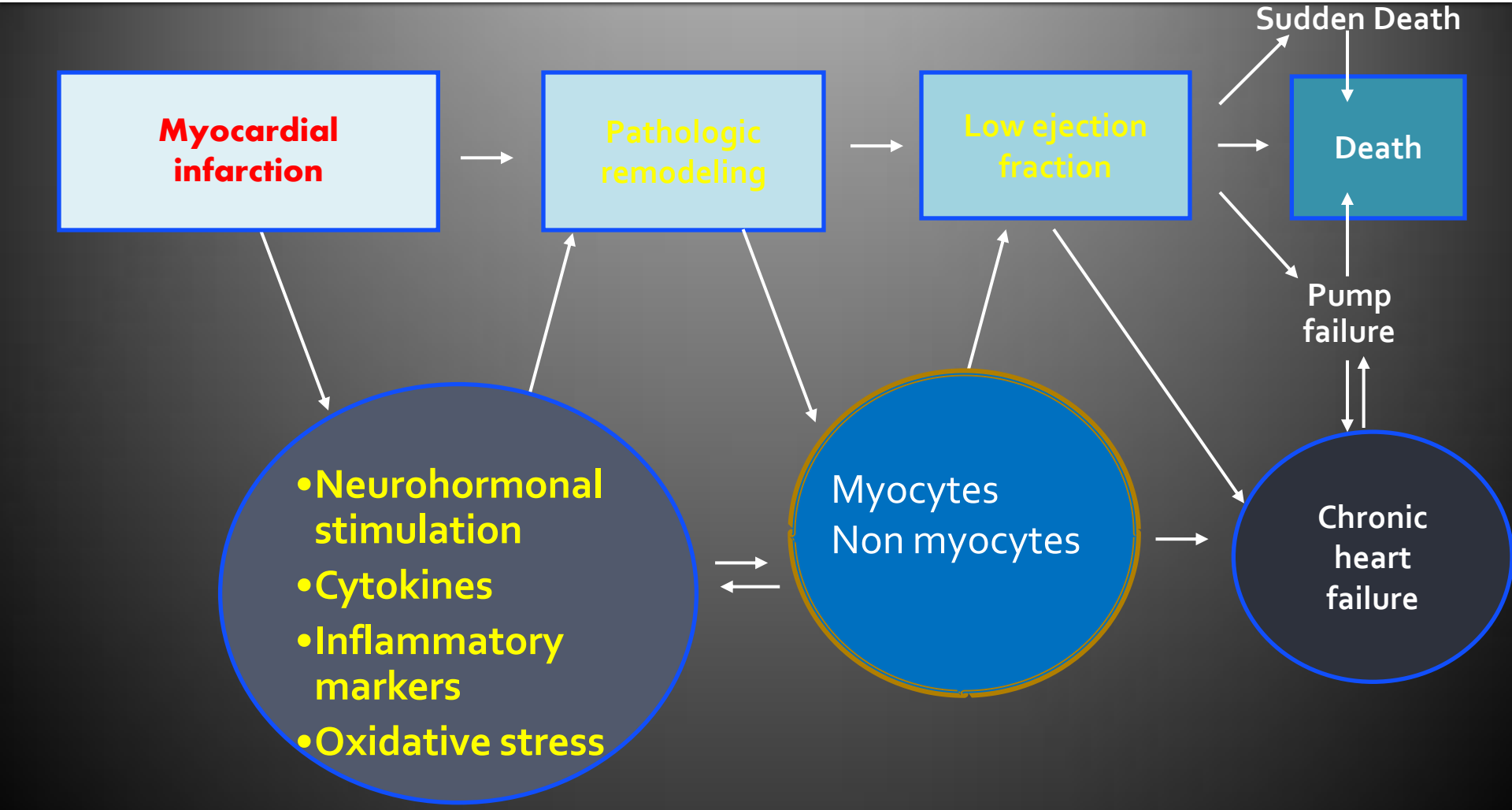
Changes in

Myocytes,

Nonmyocyte (Extracellular matrix),

Neurohormones and cytokines.

Pathologic Progression of CV Disease leading to HF



Adapted from Cohn JN. *N Engl J Med*. 1996;335:490–498.

Alterations in myocyte compartment

-  Myocyte hypertrophy
  - Increase myocyte length >width
-  Myocyte death (necrosis, apoptosis)
- Myocyte structural proteins Changes
- Myocyte hyperplasia ?

Alterations in non myocyte compartment

- Extracellular matrix remodeling
  - Matrix protein, signaling molecules and cell types
-  Myocardial fibrosis (?RAAS)
  - Reparative fibrosis(scar), reactive fibrosis
-  Coronary microvasculature

Effect of RAAS

- Increase myocyte and fibroblast protein synthesis (myocyte hypertrophy and fibrosis)
- Increase vessel permeability
- Growth factor activation
- Metalloproteinase activation
- Vasoconstriction and water retension
- Oxidative stress (ROS)
- Cytotoxic

Neurohormones and other Modulators

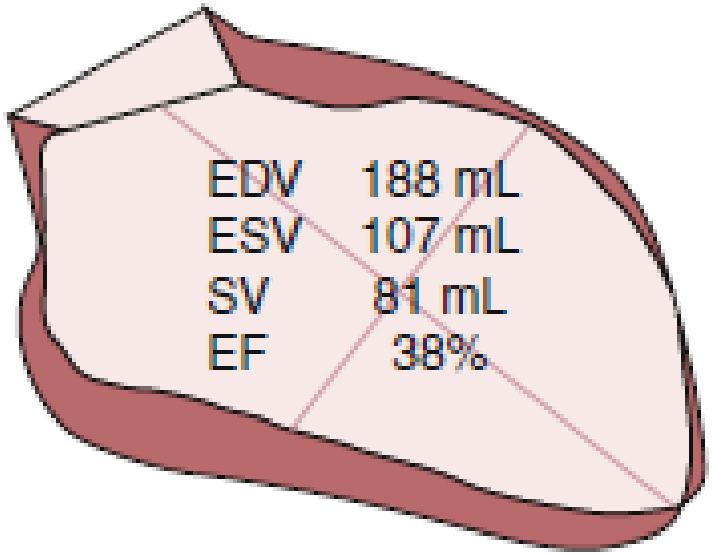
- Rennin Angiotensin System (RAAS)
- Adrenergic system
- Inflammatory markers: cytokines (TNF, IL-1, IL-6)
- Oxidative stress (ROS)

- Hibernation and stunnin g
  - Apoptosis, fibrosis,progressive LVSD
- Endothelial dysfunction(decrease NO)
  - vasoconstriction, smooth muscle migration and proliferation, increased lipid deposition

CHANGES IN GLOBAL STRUCTURE AND FUNCTION

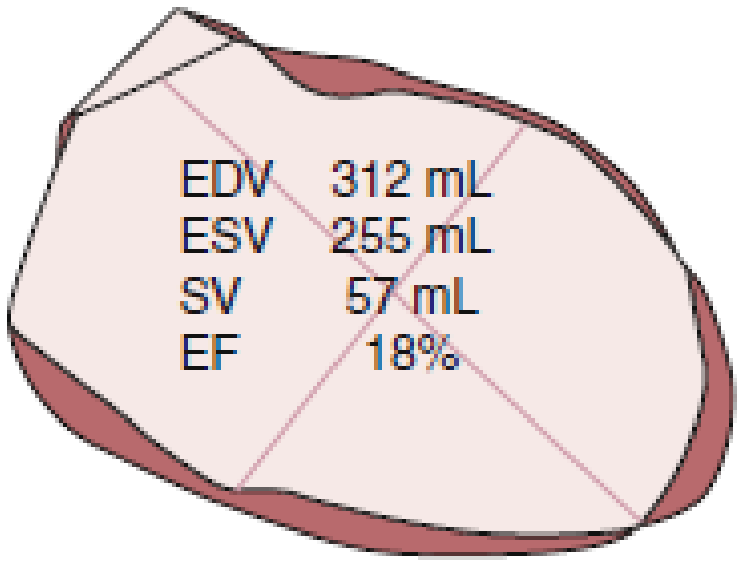
- LV geometry alters from ellipse to a mechanically disadvantageous shape (spherical or globular)
- Results:
  - an increase in wall stress, an abnormal distribution of fiber shortening, an increase in oxygen consumption and abnormal myocardial bioenergetics
- The spherical shape of the LV leads to dilation of the AV valve ring and stretching of the papillary muscles, resulting in functional mitral regurgitation
- The high LV end-diastolic volume and pressure promote subendocardial ischemia that aggravates LV dysfunction and neurohormonal activation,
- Thus a downward spiral of worsening heart failure

March 1996

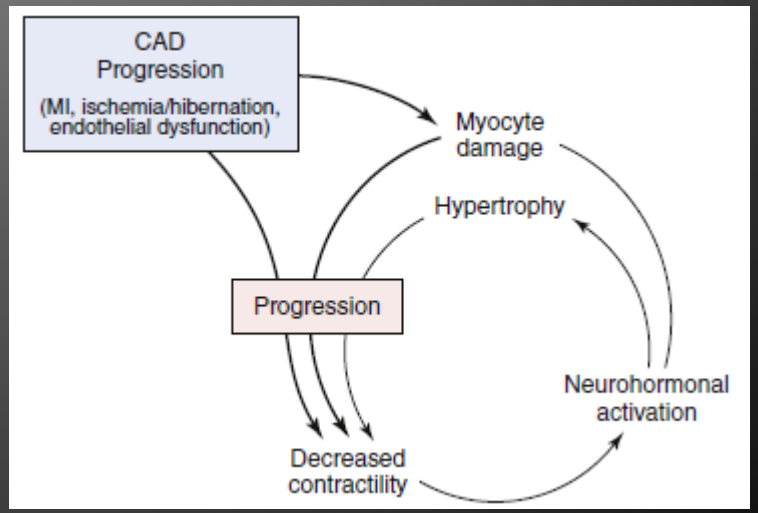


ECHO LV Mass 206 g
Mass/vol, 1.1; no MR

April 1998



ECHO LV Mass 288 g
Mass/vol, 0.9; 3+ MR



From: HEART FAILURE: A COMPANION TO BRAUNWALD'S HEART DISEASE, SECOND EDITION 2011

HFSA 2010 Practice Guideline

HF and Ischemic Disease

- *Evaluation for CAD*
- *Recommendation 13.1*
- **Assessment for risk factors for CAD is recommended in all patients with chronic HF regardless of LVEF.**

Strength of Evidence = A

TABLE 36–1 Advantages and Disadvantages of Different Cardiac Imaging Modalities for Detecting Myocardial Viability

Imaging Technique	Advantages	Disadvantages
Cardiac SPECT	• Well-established • Widely available • Lower cost • High sensitivity • Observational outcome literature • Commonly first choice	• Depth-dependent attenuation correction • Moderate specificity • Lower spatial resolution (in comparison with PET and CMR imaging)
Cardiac PET with CT	• Acceptable spatial resolution • Best molecular sensitivity • Use of natural occurring elements • Quantitative capabilities • Rapid patient throughput • Depiction of flow, metabolism, function, and coronary anatomy in the same session	• High radiation dose • High cost • Poorer availability • Dependence of FDG uptake on the patient's metabolic state
CMR imaging	• Increasingly available • Best noninvasive definition of myocardial structure • Moderate sensitivity and specificity • Depiction of structure, function, perfusion, and scar in the same session • No radiation	• Contraindicated or used with caution in patients with renal failure • Limited outcome literature (in patients with viability imaging and severe left ventricular dysfunction) • Contraindicated in patients with metallic objects and devices • Heart rate and rhythm not visualized
Stress echocardiography with dobutamine	• Availability • No radiation • High specificity	• Lower sensitivity • High interobserver and intercenter variation • Accuracy reduced by severity of resting dysfunction • Moderate observational literature (no randomized trials)

Comparison of noninvasive imaging techniques for assessment of myocardial viability in patients with heart failure. Although stress echocardiography with dobutamine, cardiac magnetic resonance (CMR) imaging, cardiac single photon emission computed tomography (SPECT), and cardiac positron emission tomography (PET) with computed tomography (CT) all are helpful and validated techniques for assessment of myocardial viability, each has its particular advantages and disadvantages.

FDG, fluorodeoxyglucose.

(From Camici PG, Prasad SK, Rimoldi OE. Stunning, hibernation, and assessment of myocardial viability. *Circulation* 2008:117:103-114.)

BOX 8–1 Pharmacological, Device, and Surgical Methods That Lead to Reverse Remodeling

Pharmacological Reverse Remodeling

β-blockers*
ACE inhibitors*
Angiotensin receptor blockers*
Aldosterone antagonists*
Hydralazine/isosorbide*

Device-based Reverse Remodeling

Mechanical circulatory assist devices
- Pulsatile*
- Continuous*

Cardiac resynchronization therapy*
Cardiac support devices

Surgical Reverse Remodeling

Myocardial revascularization
Partial ventriculectomy
Surgical ventricular reconstruction (SVR)
Mitral valve repair

Conclusion.

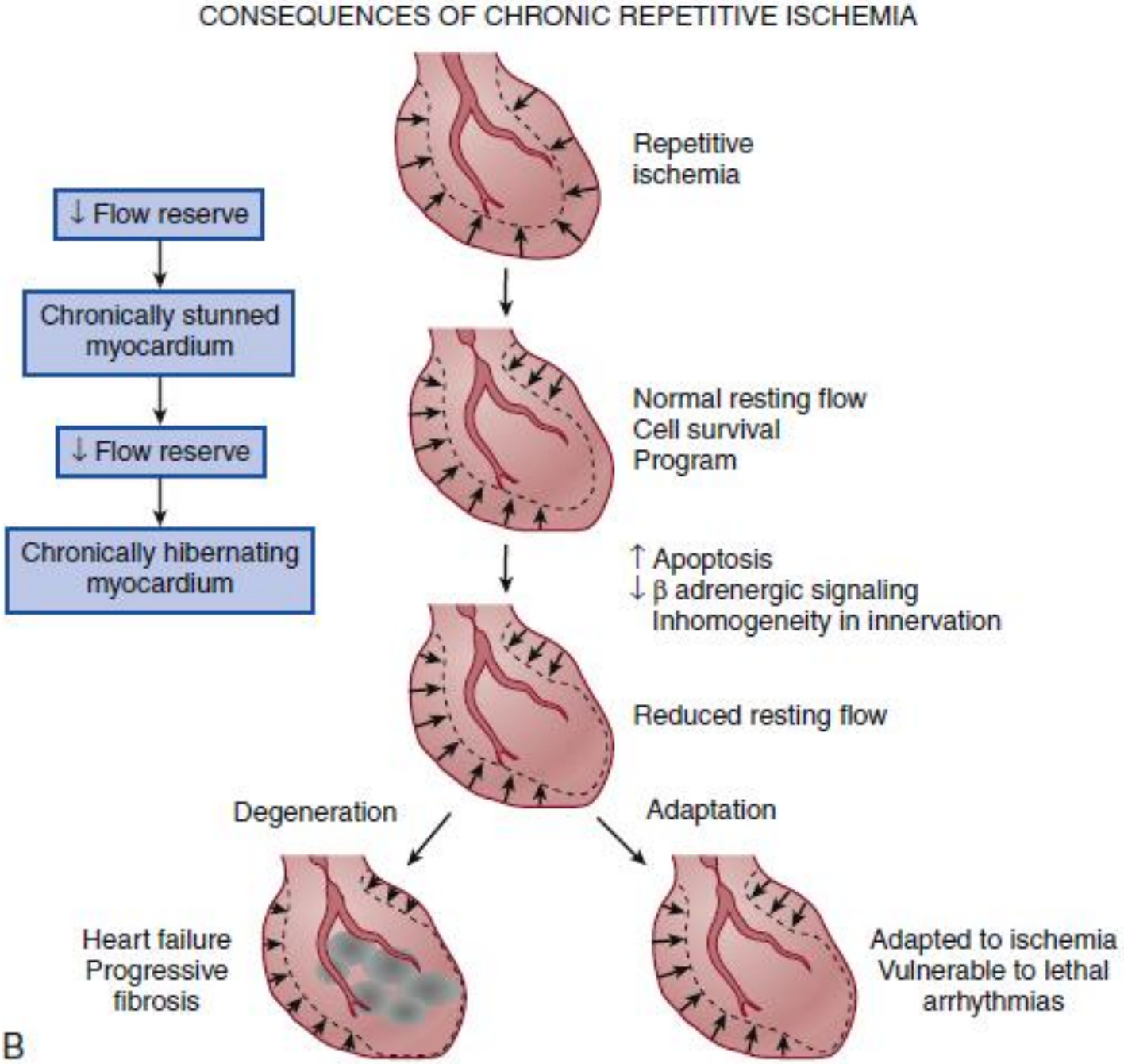
- Chronic Heart failure after Myocardial infarction is explained by process of remodelling
- Cardiac remodelling is a complex process involves multiple modalities and numbers of morphological changes
- The process may be adaptive, but in the long run, remodeling would be the onset of progressive ventricular dysfunction and heart failure.

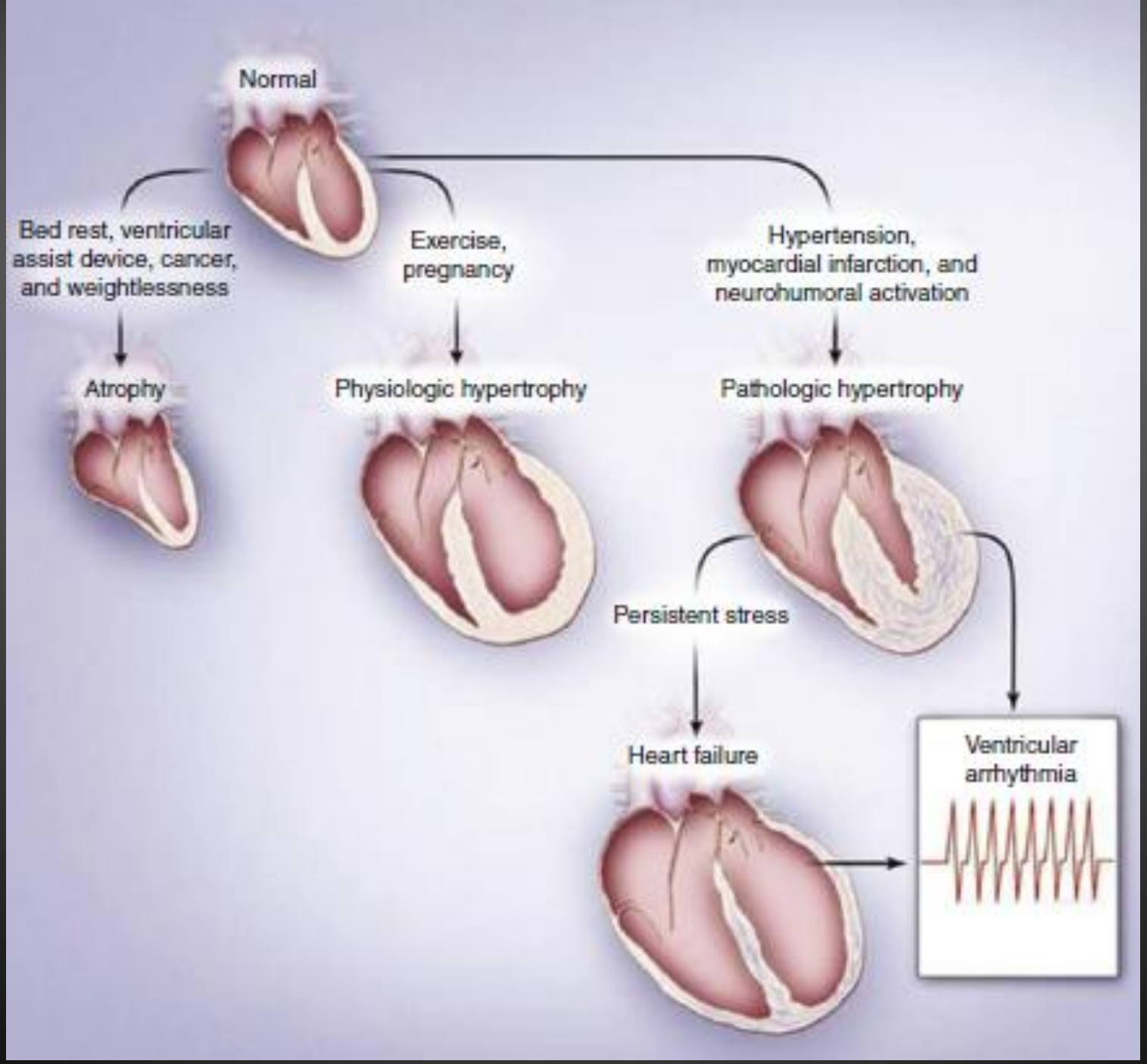
6th Asian Pacific Congress of Heart Failure

APCHF 2012

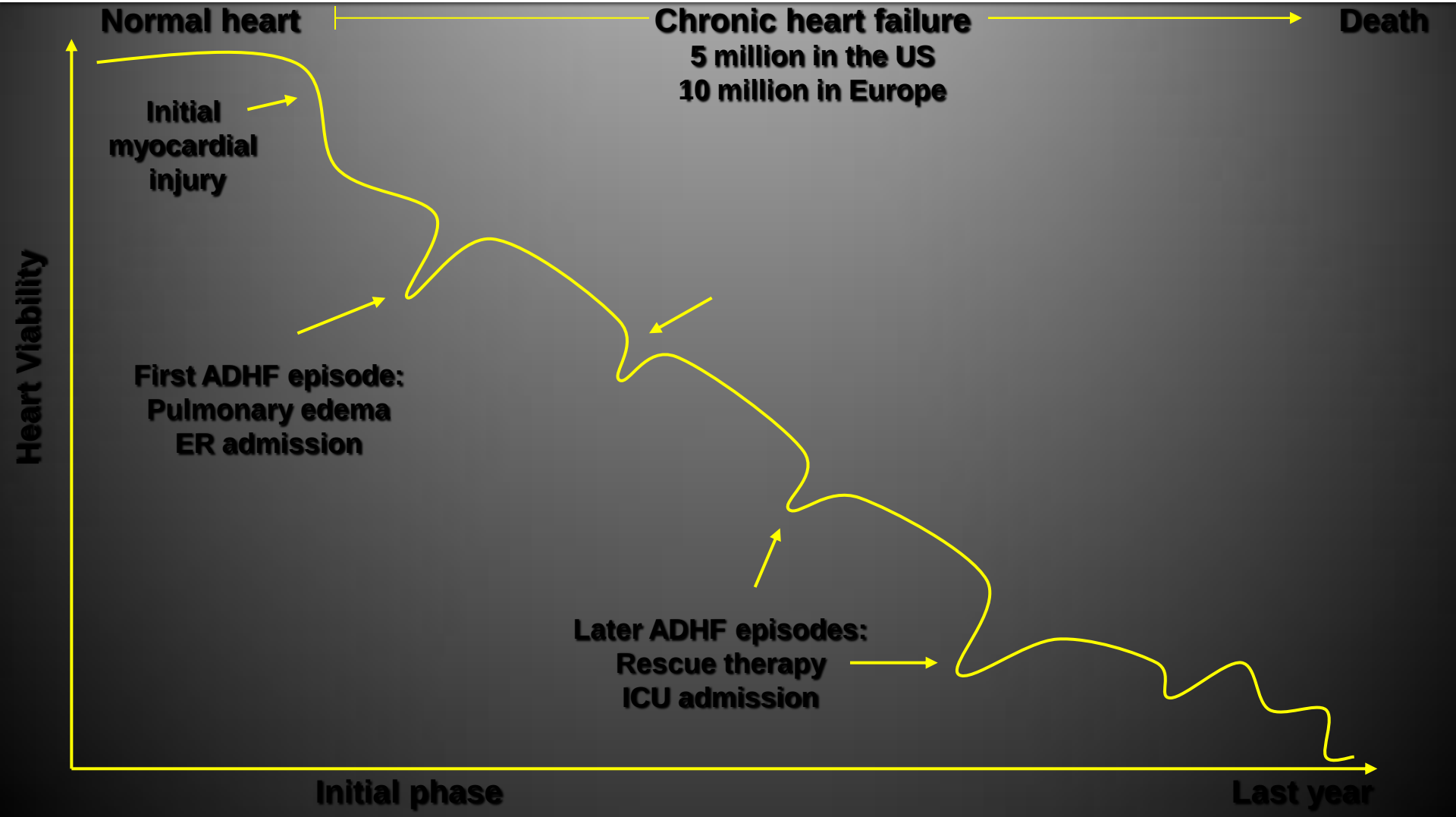
February 3-5, 2012

Le Méridien Chiang Mai Hotel
Thailand


CONSEQUENCES OF CHRONIC REPETITIVE ISCHEMIA
↓ Flow reserve
Chronically stunned myocardium
↓ Flow reserve
Chronically hibernating myocardium
Repetitive ischemia
Normal resting flow
Cell survival
Program
↑ Apoptosis
↓ β adrenergic signaling
Inhomogeneity in innervation
Reduced resting flow
Degeneration
Adaptation
Heart failure
Progressive fibrosis
Adapted to ischemia
Vulnerable to lethal arrhythmias
B


Normal
Bed rest, ventricular assist device, cancer, and weightlessness
Exercise, pregnancy
Hypertension, myocardial infarction, and neurohumoral activation
Atrophy
Physiologic hypertrophy
Pathologic hypertrophy
Persistent stress
Heart failure
Ventricular arrhythmia

Natural History of Chronic and Acute Heart Failure



Gheorghiade M. Am J Cardiol. 2005;96(suppl 6A):1-4G.