Challenges in Management of Symptomatic and Stable Heart Failure in Asian Population

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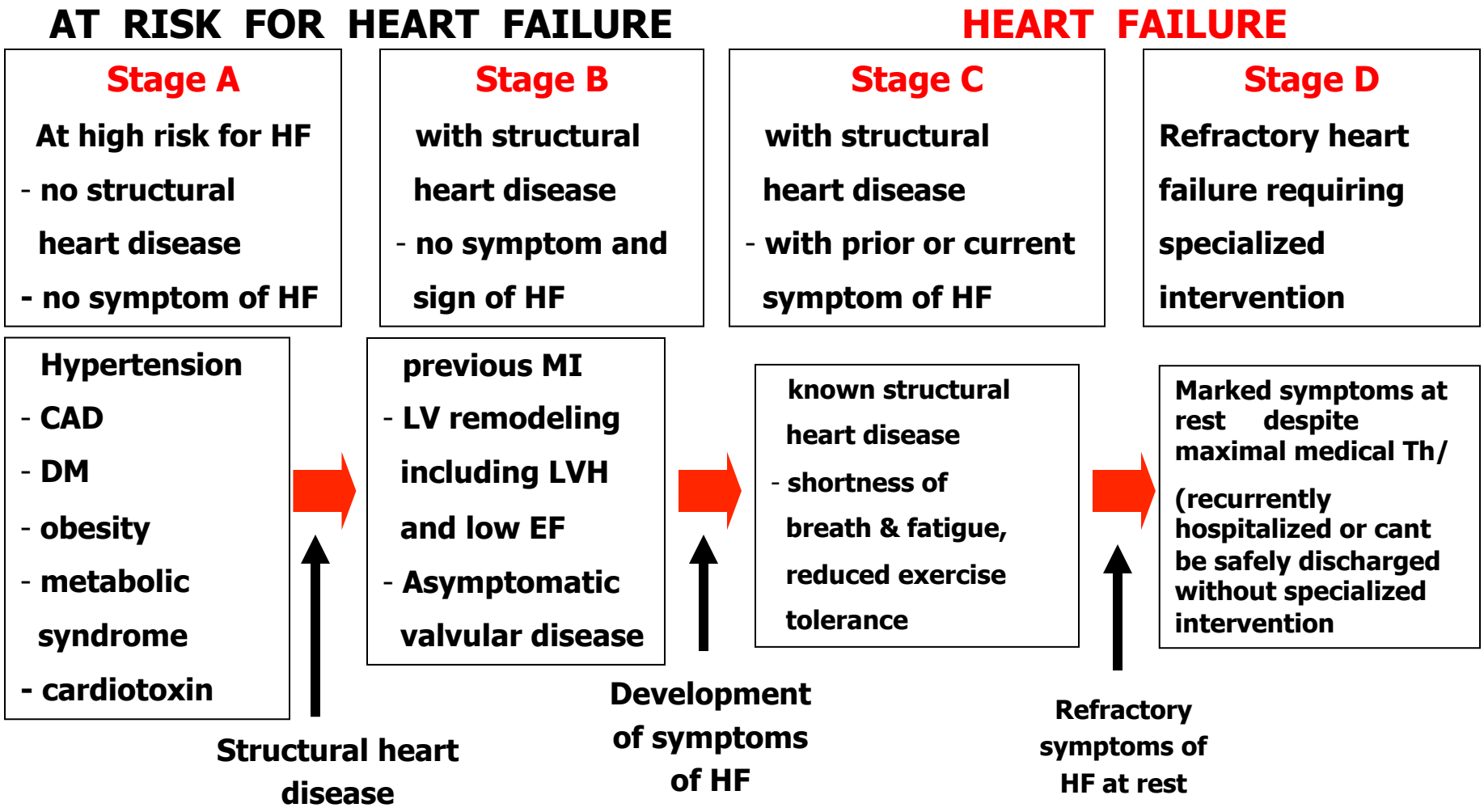
Definition of heart failure[1,2]

- "HF is a **clinical syndrome** characterized by typical symptoms (e.g. breathlessness, ankle swelling and fatigue) that may be accompanied by signs (e.g. elevated jugular venous pressure, pulmonary crackles and peripheral oedema) caused by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and/or elevated intracardiac pressures at rest or during stress"[1] (ESC 2016)

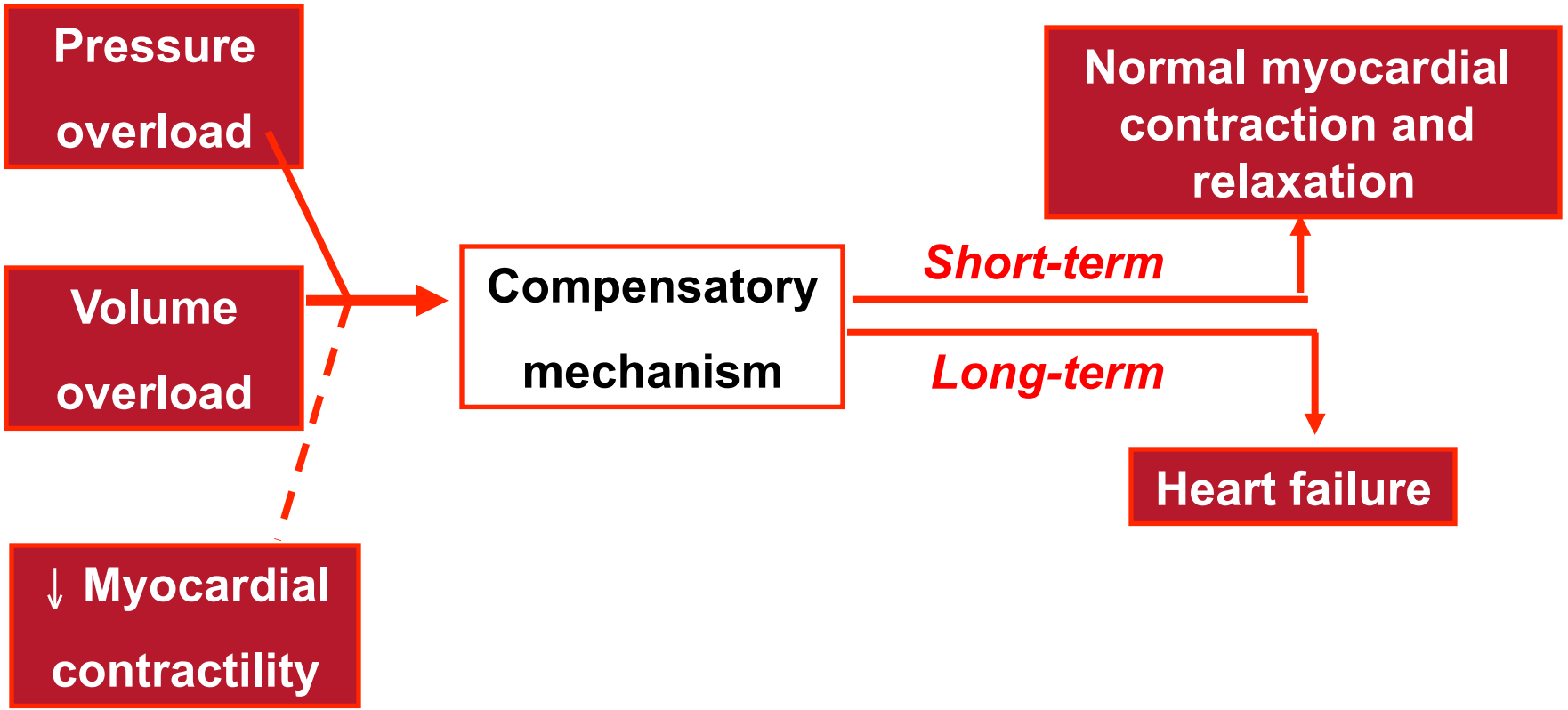
- "Heart failure is a complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood"[2] (ACCF/AHA 2013)

AHA=Heart Association; ACCF=American College of Cardiology Foundation; ESC=European Society of Cardiology

1. Ponikowski et al. Eur Heart J. 2016;37:2129–200; 2. Yancy et al. JACC 2013;62:e147–e239


AT RISK FOR HEART FAILURE
HEART FAILURE
Stage A
At high risk for HF
- no structural heart disease
- no symptom of HF
Stage B
with structural heart disease
- no symptom and sign of HF
Stage C
with structural heart disease
- with prior or current symptom of HF
Stage D
Refractory heart failure requiring specialized intervention
Hypertension
- CAD
- DM
- obesity
- metabolic syndrome
- cardiotoxin
previous MI
- LV remodeling including LVH and low EF
- Asymptomatic valvular disease
known structural heart disease
- shortness of breath & fatigue, reduced exercise tolerance
Marked symptoms at rest despite maximal medical Th/
(recurrently hospitalized or cant be safely discharged without specialized intervention
Structural heart disease
Development of symptoms of HF
Refractory symptoms of HF at rest

MECHANISM OF HEART FAILURE



MECHANISM OF COMPENSATION

HORMONAL MEDIATORS

Vasoconstrictors	Vasodilators	Growth factors
Noradrenaline	Atrial Natriuretic Peptide	Insulin
Renin / Angiotensin II	Prostaglandin E2	Tumor Necrosis Factor Alpha
Vasopresin	Endothelin Derived Releasing Factor	Cytokines
Endothelin	Cholecystokinin Gene Related Peptide	Angiotensin II

Cardiac dysfunction triggers the activation of three compensatory neurohormonal systems

Cardiac structure/function abnormality

↓

Activation of compensatory mechanisms to maintain cardiac output and organ perfusion[1]

Activated in response to reduced cardiac output[1]

Short-term effects are beneficial in early HF[1]

Long-term activation exerts unfavourable effects[1,3]

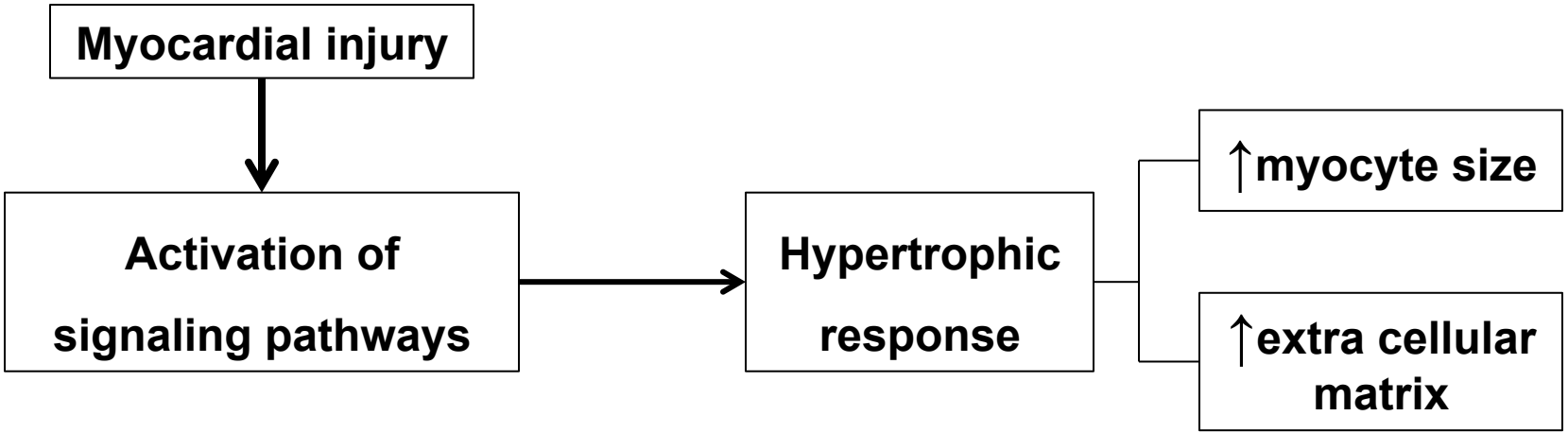
Release of NPs in response to cardiac stress[2]

Opposes the actions of the RAAS[2] and SNS[4,5]

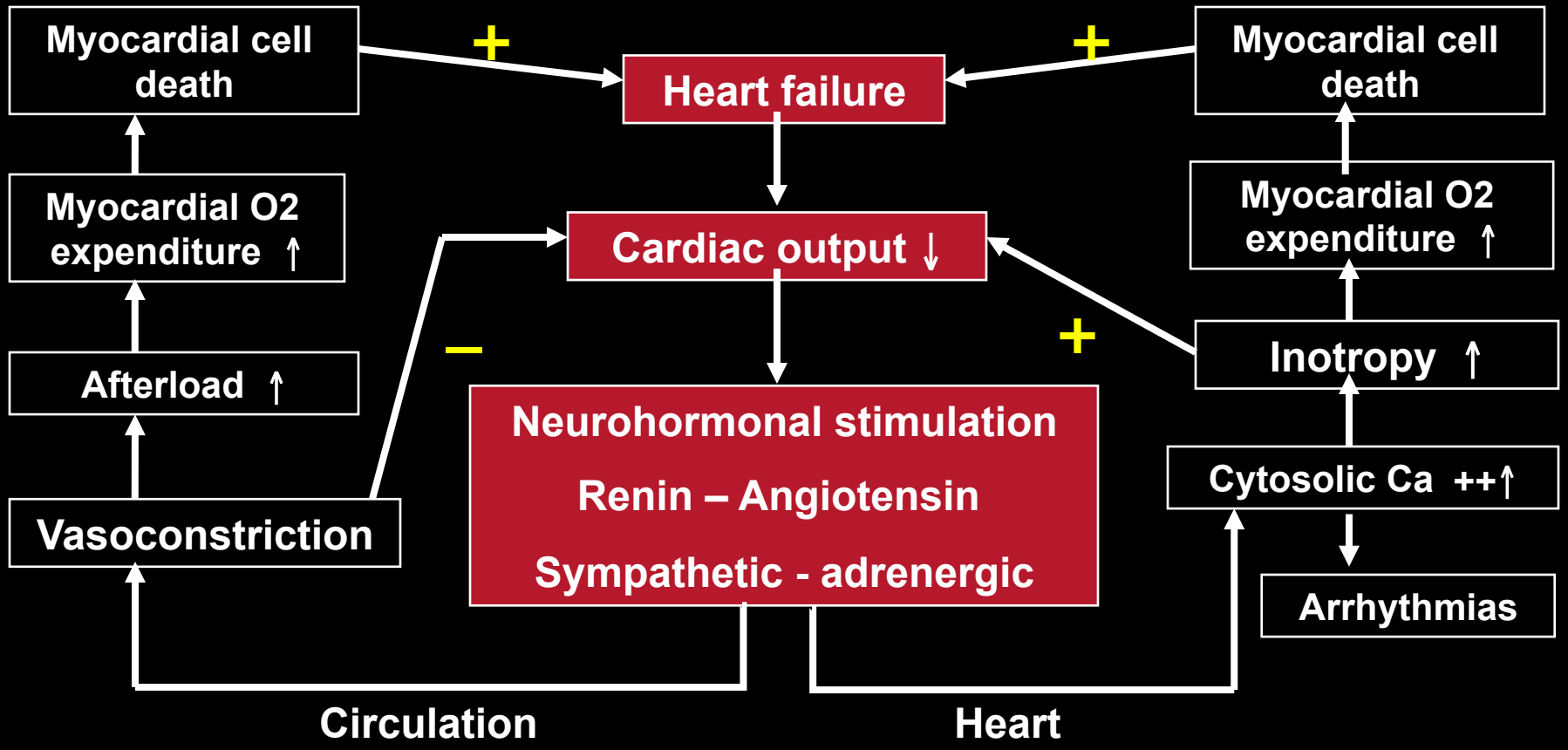
NP=natriuretic peptide; RAAS=renin angiotensin aldosterone system;SNS=sympathetic nervous system

1. Francis et al. Ann Intern Med 1984;101:370–7; 2. Clerico et al. Am J Physiol Heart Circ Physiol 2011;301:H12–H20;
3. Von Lueder et al. Circ Heart Fail 2013;6:594–605 4. Luchner & Schunkert. Cardiovasc Res 2004;63:443–9;
5. Thygesen et al. Eur Heart J 2012;33:2001–6

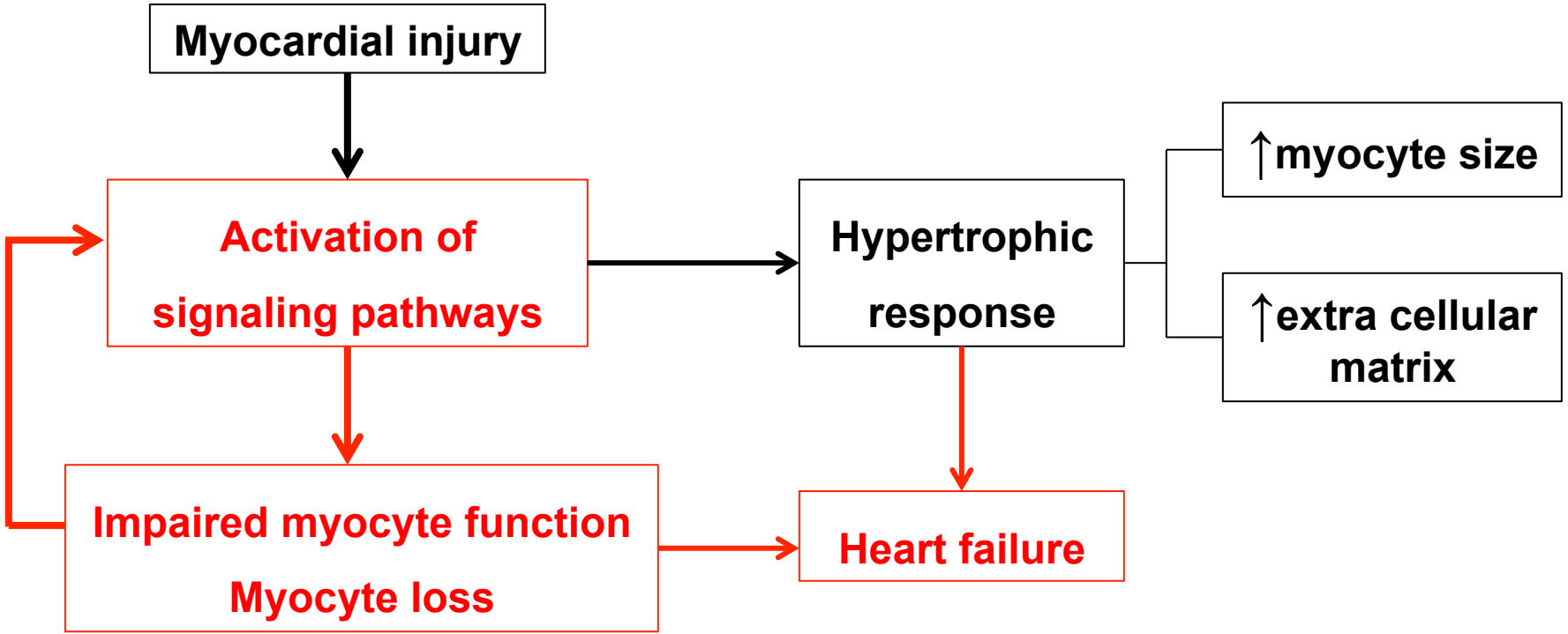
Molecular Basis Hypertrophy



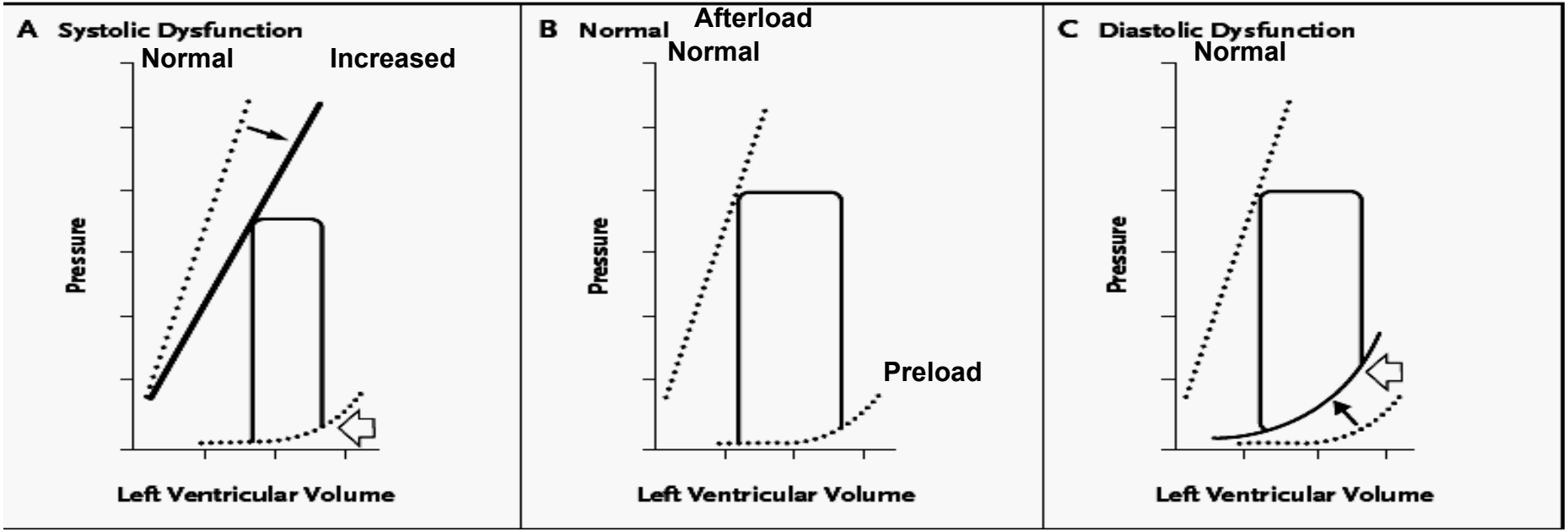
DISEASE PROGRESSION OF HEART FAILURE



Molecular Basis of Heart Failure



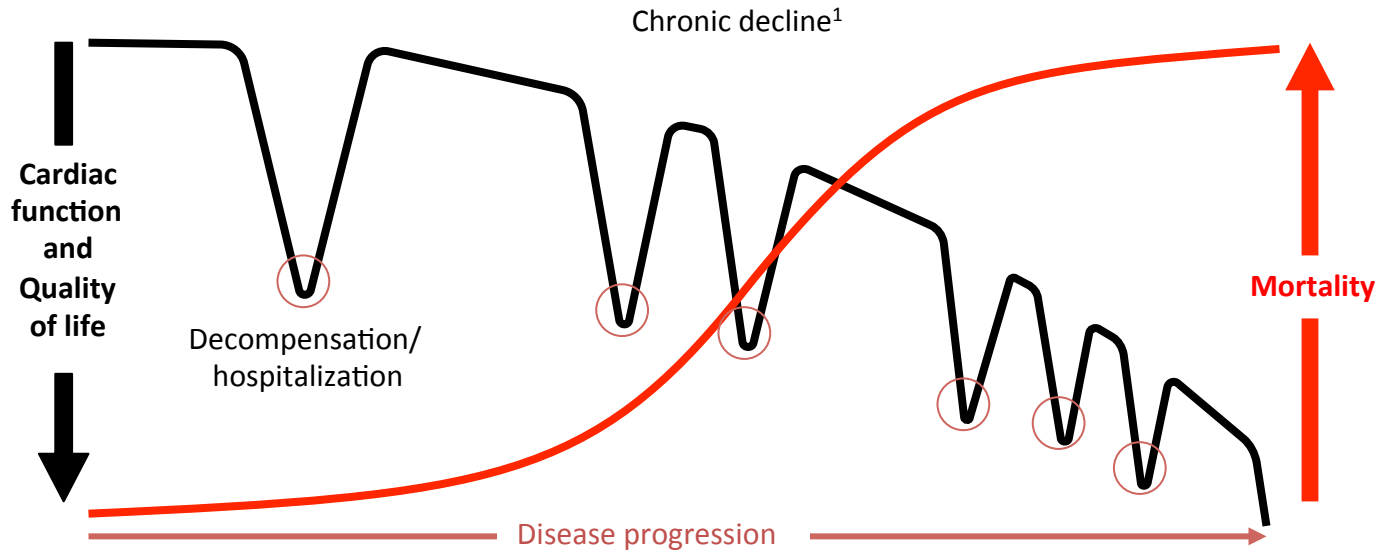
LV Pressure-Volume Loops in Systolic and Diastolic Dysfunction



Aurigemma GP, Gaasch WH. N Engl J Med 2004;351:1097-1105

Due to the progressive nature of HF, patients cannot be perceived as 'stable'

Frequency of decompensation and risk of mortality increase,[1–5] with acute events and sudden death occurring at any time



1. Adapted from Gheorghiade et al. Am J Cardiol 2005;96:11G–17G; 2. Ahmed et al. Am Heart J 2006;151:444–50; 3. Gheorghiade and Pang. J Am Coll Cardiol 2009;53:557–73; 4. Holland et al. J Card Fail 2010;16:150–6; 5. Muntwyler et al. Eur Heart J 2002;23:1861–6

Guideline recommended treatment goals in heart failure[1,2]

HF=heart failure

1. Ponikowski et al. Eur Heart J 2016;37:2129–200; 2. Yancy et al. Circulation 2016;134:e282–93

HEART FAILURE IN ASIA

Cardiovascular Disease Burden in Epidemiological Transition as a cause of the Heart Failure Pandemic in Asia

- Industrialization and urbanization played a significant role in shifting the major causes of death and disability from nutritional deficiencies and infectious diseases to degenerative diseases including CVD.
- Urbanization inevitably increases consumption of high-calorie foods, while it reduces physical activity and energy expenditure.
- Industrialization also makes people sedentary, particularly in rural areas.
- Thus, along with the introduction of high-fat diets, smoking, and sedentary lifestyles, non-communicable diseases are predominating, with the highest mortality caused by CVD, particularly in the younger generation.

ESC HEART FAILURE
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Table 1. Prevalence of Stage A HF cardiovascular risk factors in Southeast Asian nations compared with the United Kingdom and United States of America (from the World Health Organization Global Status Report 2014)

Country	World Bank Income Group Classification	Prevalence in population aged 18+ years (crude adjusted estimates with 95% Confidence Interval)				
		insufficient physical activity	Current tobacco smoking[a]	Overweight[b]	Raised blood glucose[c]	Raised blood pressure[d]
Brunei	High	—	15.8 (6.7–26.6)	47.8 (40.7–54.3)	11.2 (5.1–17.1)	19.3 (12.4–26.3)
Cambodia	Low	9.7 (8.7–10.8)	21.3 (16.0–27.5)	16.4 (12.7–20.2)	6.8 (3.6–10.3)	24.4 (17.8–30.9)
Indonesia	Lower middle	22.8 (18.0–28.1)	36.5 (29.9–45.3)	24.4 (19.9–28.9)	8.0 (4.0–11.8)	23.3 (17.7–29.1)
Laos	Lower middle	9.0 (7.4–10.8)	—	16.6 (13.1–20.6)	6.4 (3.4–9.4)	24.1 (18.3–30.4)
Malaysia	Upper middle	51.6 (46.3–56.8)	23.6 (17.2–30.7)	37.3 (31.9–42.6)	9.9 (5.5–14.2)	22.1 (16.4–27.8)
Myanmar	Low	9.0 (7.4–10.9)	22.6 (15.6–29.7)	17.4 (13.4–21.2)	6.3 (2.8–9.5)	23.7 (17.7–30.4)
Philippines	Lower middle	14.4 (3.3–42.2)	27.0 (21.5–32.3)	22.3 (18.1–26.6)	6.0 (2.7–9.2)	22.1 (16.2–28.2)
Singapore	High	33.7 (31.3–36.1)	15.6 (12.6-19.6)	34.6 (30.1–38.9)	9.8 (6.1–13.9)	14.1 (10.0–17.9)
Thailand	Upper middle	14.6 (13.4–16)	—	31.6 (26.7–36.7)	10.9 (6.3–15.5)	21.3 (15.8–26.9)
Vietnam	Lower middle	23.6 (16.2–32.5)	24.3 (19.8–29.5)	20.4 (16.2-24.6)	6.0 (3.1–8.9)	22.2 (16.3–28.3)
United Kingdom	High	40.0 (38.6–41.4)	19.9 (16.2–23.5)	66.7 (63.4–70.3)	10.1 (6.9–13.7)	15.2 (11.9–18.6)
United States of America	High	35.0 (32.5–37.6)	18.0 (14.9–21.1)	69.6 (66.0–73.5)	10.5 (6.6–13.9)	13.4 (10–17.1)

[a]In the population aged 15+ years.
[b]Body mass index ≥25 kg/m^2.
[c]Fasting glucose ≥7.0 mmol/L or on medications for raised blood glucose or with history of diabetes.
[d]Systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg.

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Public awareness of heart failure symptoms is dangerously low

- Delaying hospital treatment by as little as 4–6 hours after symptoms of heart failure appear can increase the chances of death, yet px typically do not seek treatment for hours or even days after developing symptoms.
- In low- and middle-income countries such as Indonesia, px may not seek treatment straight away because they live far from a hospital or lack health insurance, but ignorance of heart failure symptoms is also a major reason for delay.
- More patients exhibiting severe clinical signs and symptoms.

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Underutilization of baseline heart failure medications such as Aspirin, ACEI, ARB, Beta Blocker and Lipid therapies

- Reasons :
  - Side effects of Aspirin ?
  - AKI after ACEi ?
  - Worsening symptoms of HF after BBs ?
  - How about lipid targetted ?
  - How about others co-morbidities ?

Heart failure in the elderly in Asia

- Management of elderly HF patients is an emerging issue along with prolongation of life expectancy, not only in developed countries such as Japan, Hong Kong, South Korea, and Singapore, but also in other Asian developing countries.
- In the elderly population, HF conditions are more likely to **depress appetite** and gastrointestinal functions and **decrease muscle volumes** and physical activity, resulting in **malnutrition and frailty**, both of which are associated with a poor prognosis of HF.

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TEN PATHWAYS AND PRINCIPLES TO GUIDE OPTIMAL THERAPY

1. Target doses are associated with best outcomes
2. When facing clinical scenarios that limit the ability to use target doses of all relevant therapies, a top priority should be to address the factor(s) limiting Guidline Directed Medical Treatment of HF.

- Scenario 1: Worsening renal function or hyperkalemia.
- Action:
  - Use less than target doses of ACEI/ARB/ARNI
  - Discontinue aldosterone antagonist if estimated creatinine clearance <30 cc/min or serum K >5.5 mEq/dL.

- Scenario 2: Symptomatic hypotension.
- Action: re-asses!
  - May cause by overdiuresis, other vasoactive medication, autonomic dysfunction, or taking multiple medications together.
  - After excluding other causes of hypotension, use best-tolerated doses of GDMT.

- **Low dose ACEI still have acceptable survival benefit even in the setting of renal insufficiency and marginal blood pressure**

3. Optimal SNS modulation with target doses of beta blocker appears to have the best effect on HFrEF outcomes

   (**Reduce cardiovascular mortality, pump failure mortality, and sudden cardiac death**)

Scenario: Patient is able to tolerate target doses B-Blocker and less ACEI/ARB

Action: Use target doses of beta blocker and, as necessary and if needed, lower doses of RAAS blockade

4. Not all medications that lower heart rate impact outcomes equally
5. African-American patients experience further benefit from the use of HYD/ISDN therapy
6. Primary prevention device therapy and cardiac resynchronization therapy should only be considered **after consistent use of optimal doses** of all medications for **3 to 6 months**

7. Symptomatic congestion should be treated adequately with diuretics irrespective of other therapies

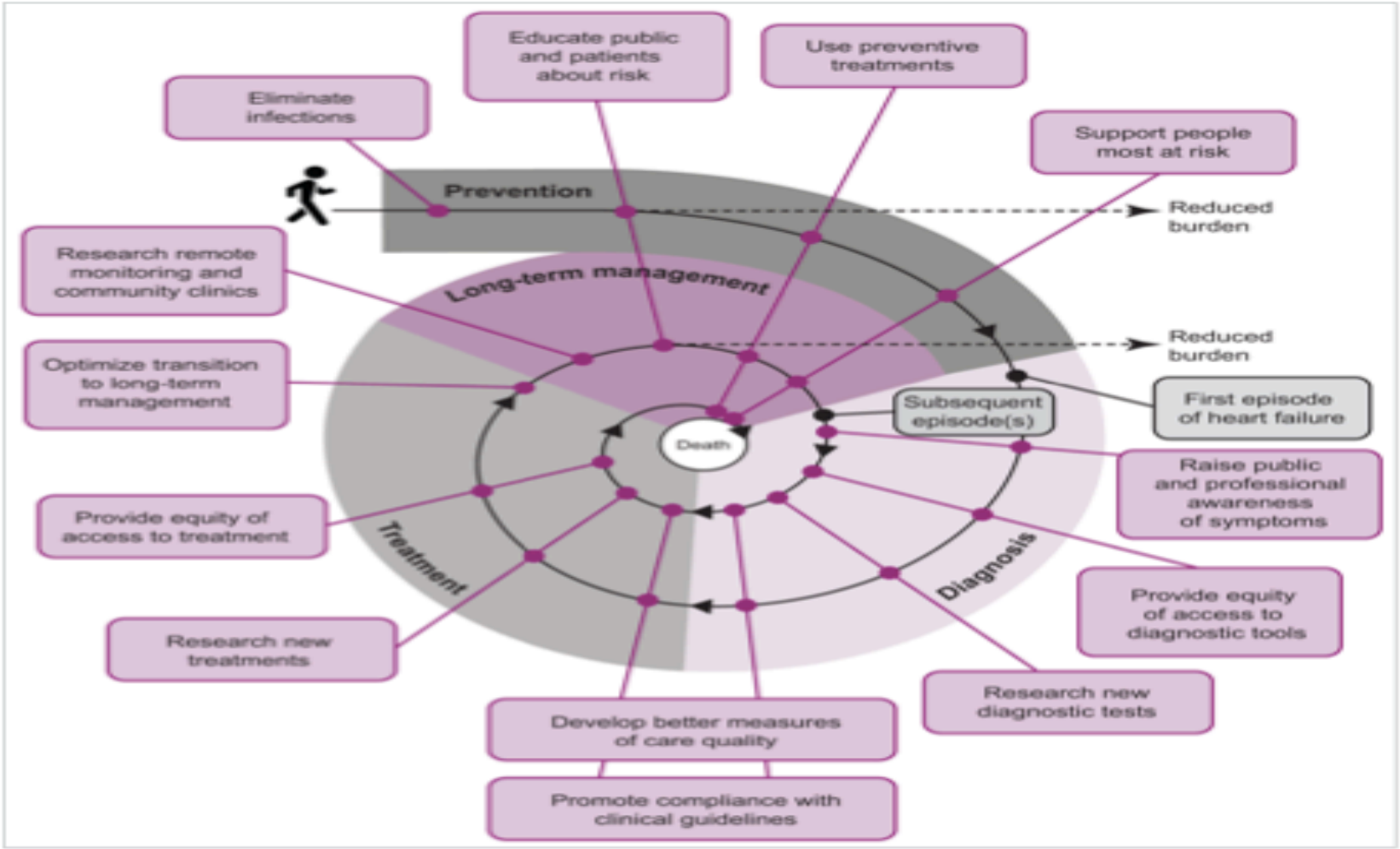
   - Pulmonary artery catheterization if needed

8. Optimize team-based care

9. Tolerability and side effects in part depend on how and when the therapy is prescribed.
   - Start at low doses and up-titrate based on tolerability
10. Focus on both the patient symptoms and functional capacity as well as improving cardiac function

Conclusion

- Heart Failure in Indonesia becomes an epidemic due to uncontrolled risk factors, lack of compliance, suboptimal care. Health education and preventive measures should be more intensive.
- Although now the Indonesia Universal Health Coverage helps many poor sick patients in seeking medical treatment, but the referral system and the available essential drugs were limited.
- This makes the mortality and readmission rate still high. Indonesia Universal Health system and Ina Case Based Group missed management.
- Urgent revision needed to help Indonesia Universal Health insurance.


Educate public and patients about risk
Use preventive treatments
Eliminate infections
Support people most at risk
Prevention
Reduced burden
Research remote monitoring and community clinics
Long-term management
Reduced burden
Optimize transition to long-term management
Subsequent episode(s)
First episode of heart failure
Death
Raise public and professional awareness of symptoms
Provide equity of access to treatment
Treatment
Diagnosis
Provide equity of access to diagnostic tools
Research new treatments
Research new diagnostic tests
Develop better measures of care quality
Promote compliance with clinical guidelines

THANKYOU