Understanding Heart Failure
HFrEF and Advanced Heart Failure

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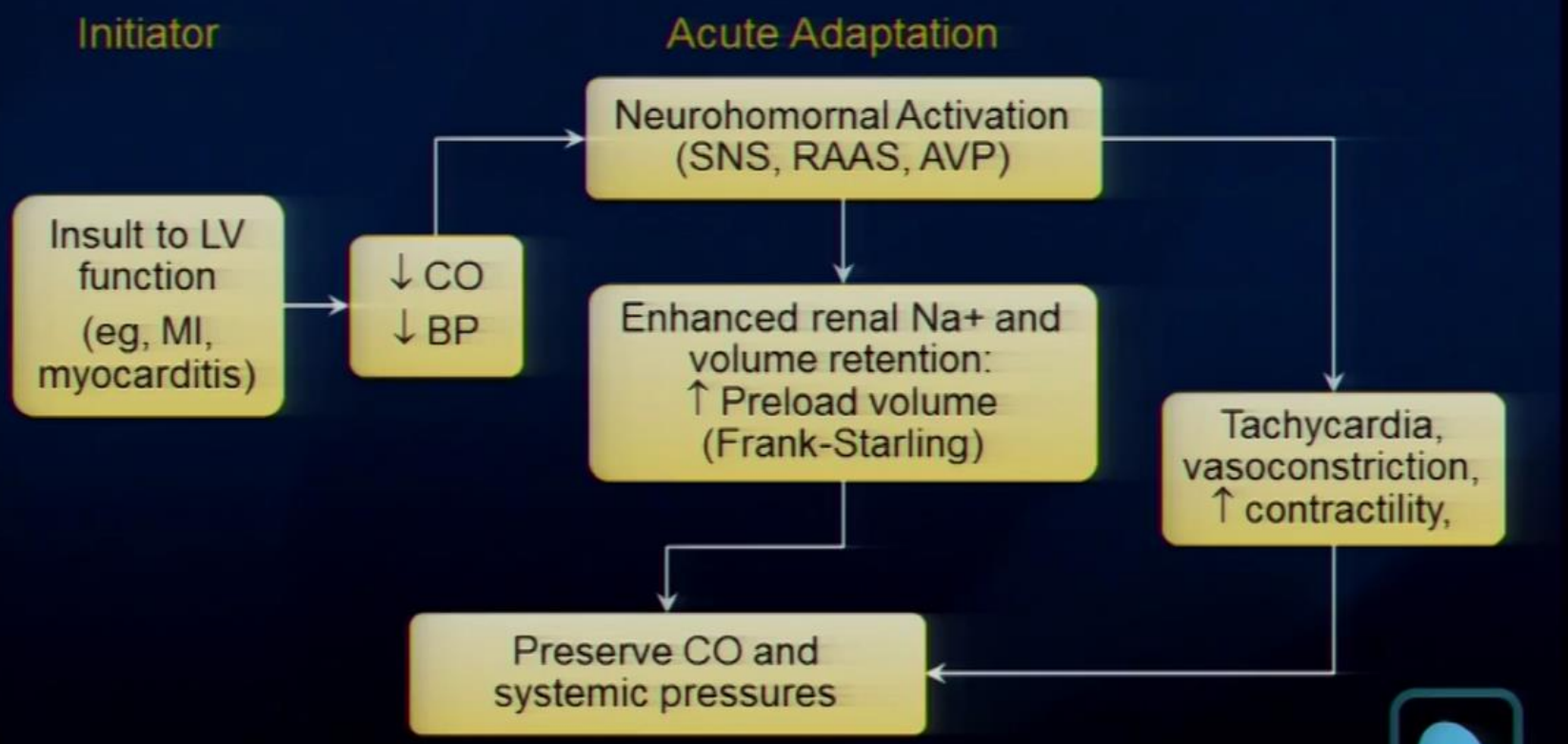
Objectives

- Review pathophysiology of HFrEF
- Briefly touch on Guidelines
- Understand the of concept Advanced Heart Failure and recognize it

Clinical Vignette

- 70 y/o female with CMY related chemotherapy (breast Ca)
- Increasing symptoms of HF
- Admissions: 4/16, seen in the office 5/3, set up for BiV 7/17 (cancelled due to lab abnl)
- Admitted 8/23/16, seen 9/15, readmitted 9/23 had BiV, readmitted 10/31, discharged and presented at an outside hospital 2 days later and transferred to local hospital
- 11/16 my introduction to her
- 12/16
- ……..

Integrated Systems Response to Systolic Dysfunction



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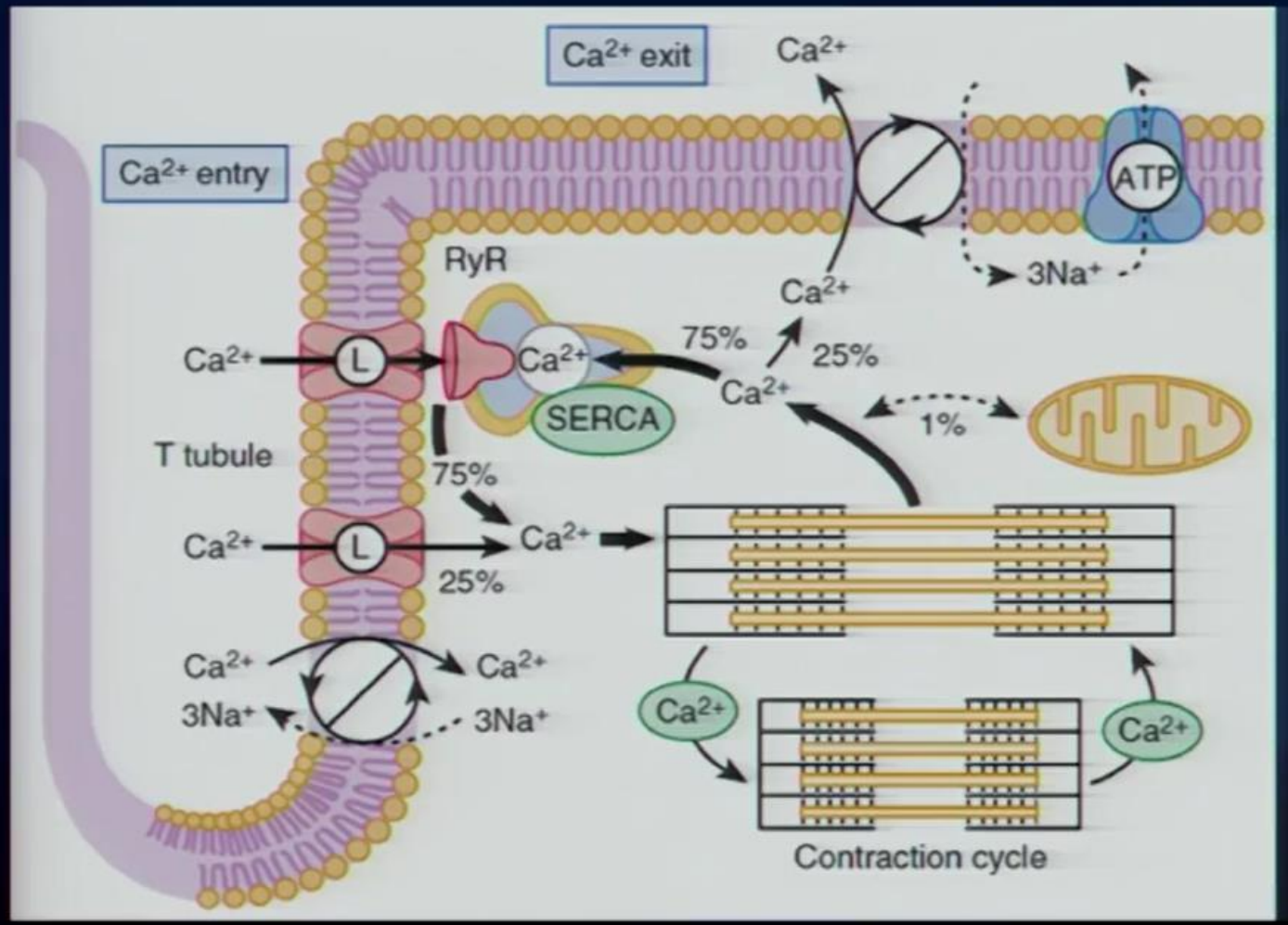
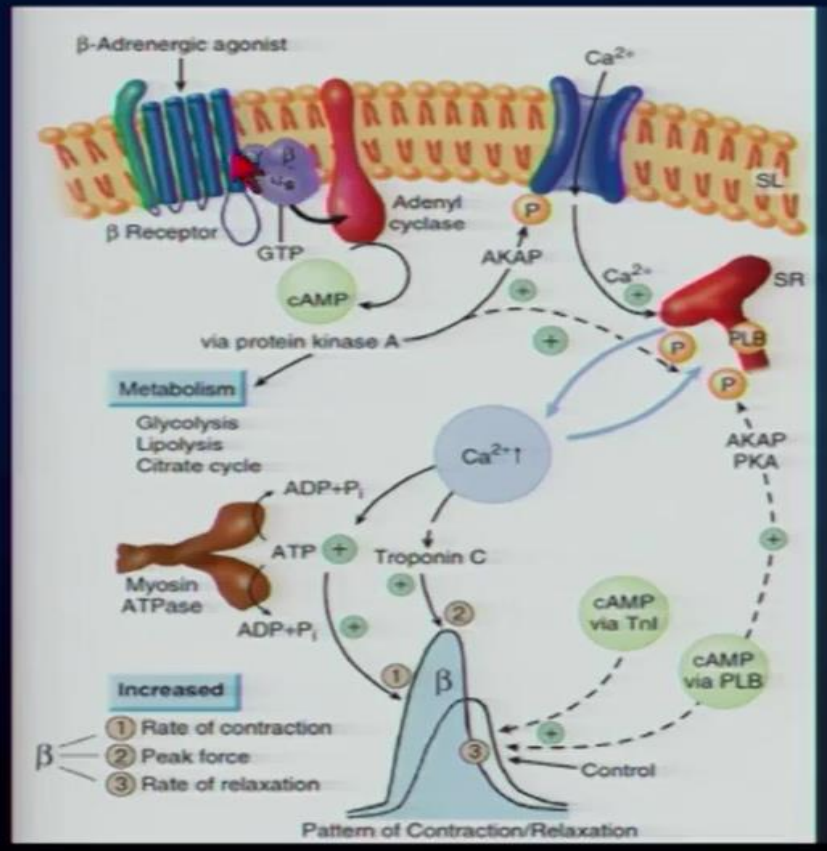
CHF

Excitation-Contraction Coupling in HF



Bers & Borlaug *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*, 11th Ed

Abnormalities in β-AR Density and Coupling



	ALPHA, MEDIATED	BETA MEDIATED
Electrophysiologic effects	±	++ Conduction Pacemaker Heart rate – AP duration
Myocardial mechanics	±	++ Contractility, lusitropy Stroke volume Cardiac output
Myocardial metabolism	± Glycolysis	++ O_2 uptake ↑ ATP
Signal systems	GPCR, can activate PKC and MAPK	GPCR, activates cAMP and PKA
Coronary arterioles	++ Constriction	+ Direct dilation +++ Indirect dilation (metabolic)
Peripheral arterioles	+++ Constriction SVR ↑ SBP ↑	+ Dilation SVR ↓ SBP ↓

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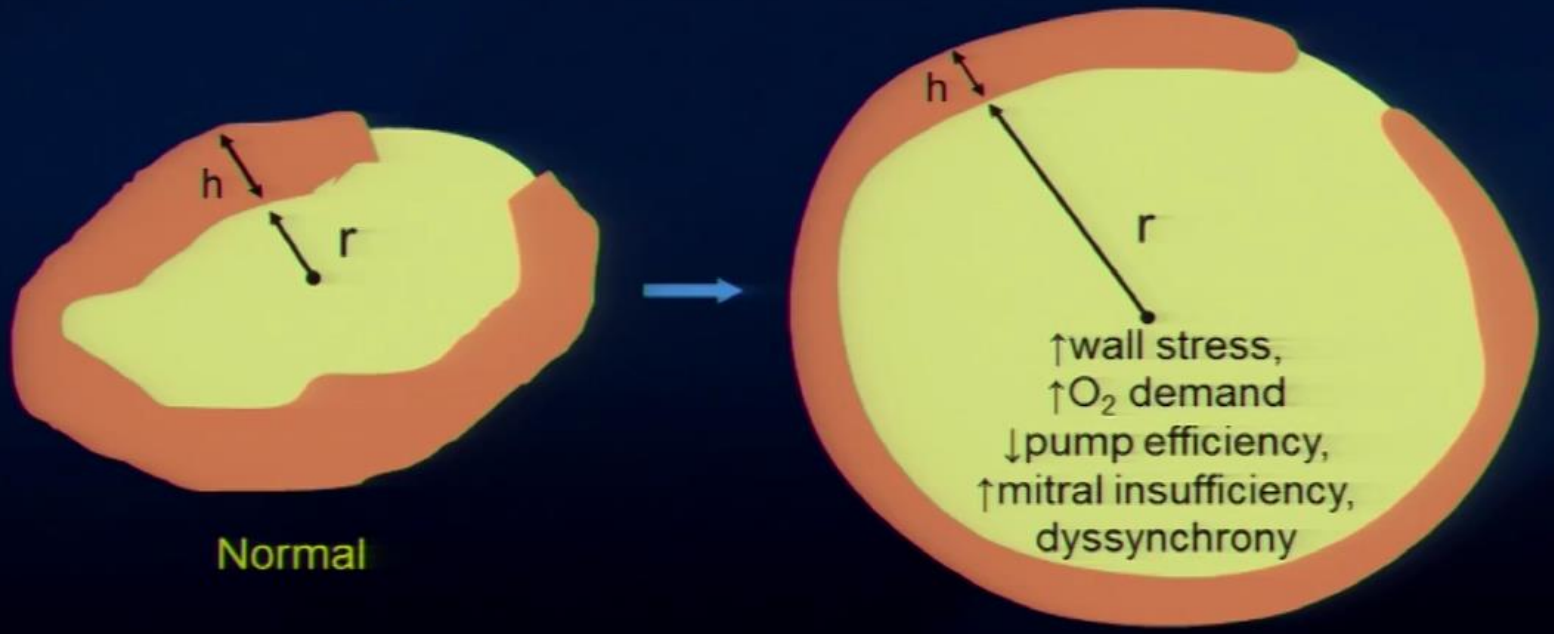
Bers & Borlaug *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*, 11th Ed

Chronic NH Hyper-Activation and LV Overfilling Lead to Eccentric LV Remodeling

Laplace's Law: Wall stress ~ P*r/2h



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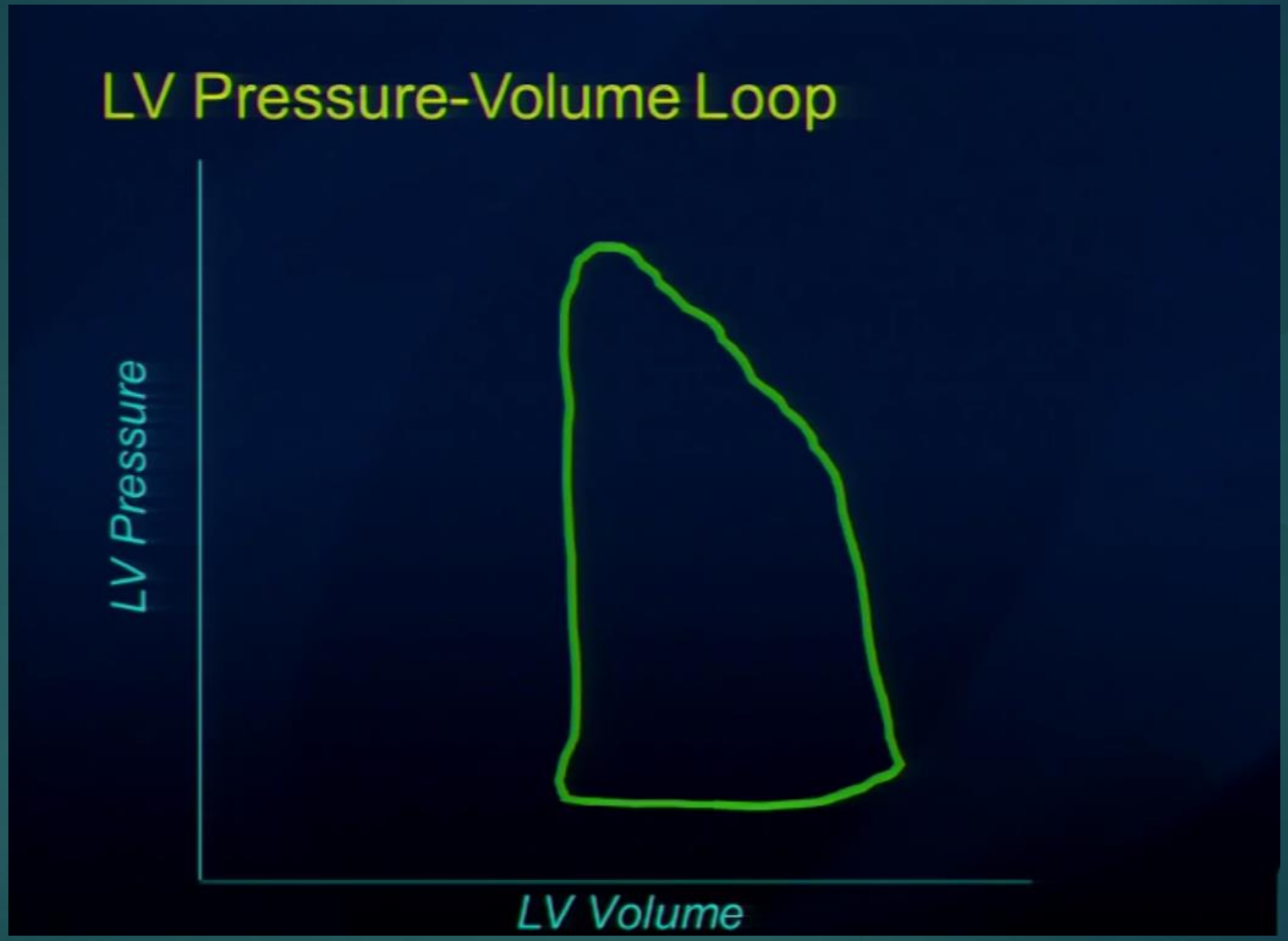
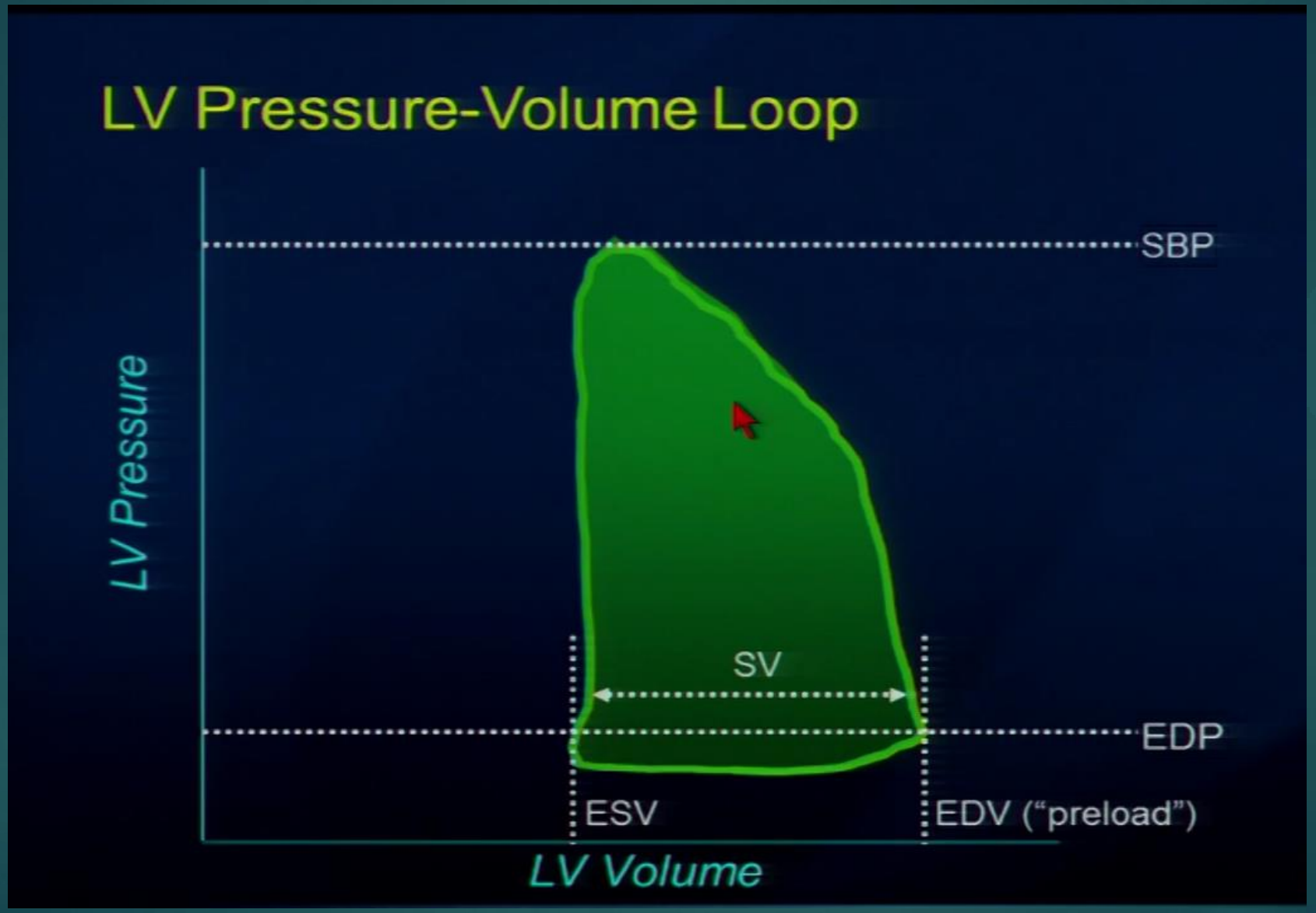
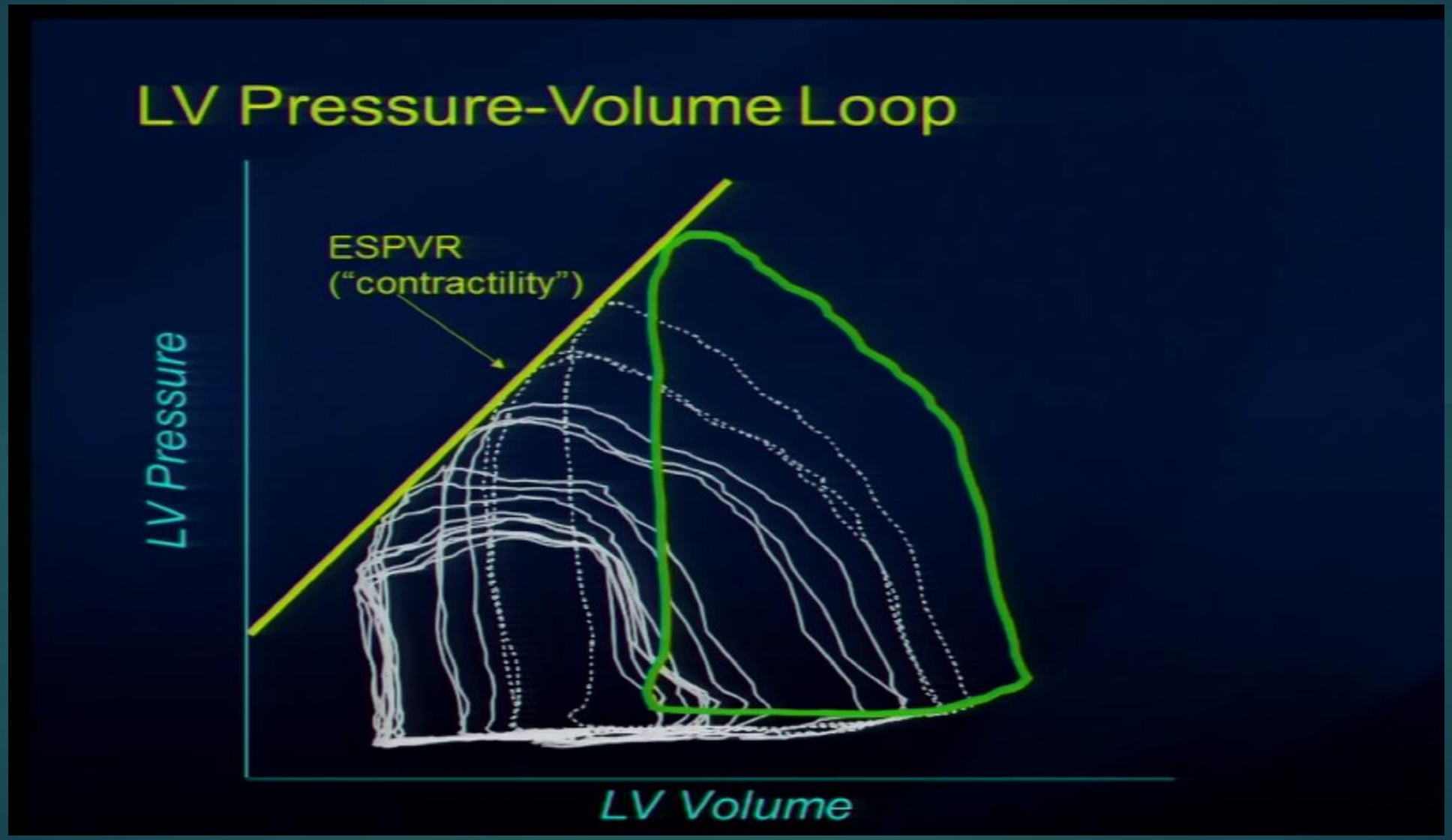
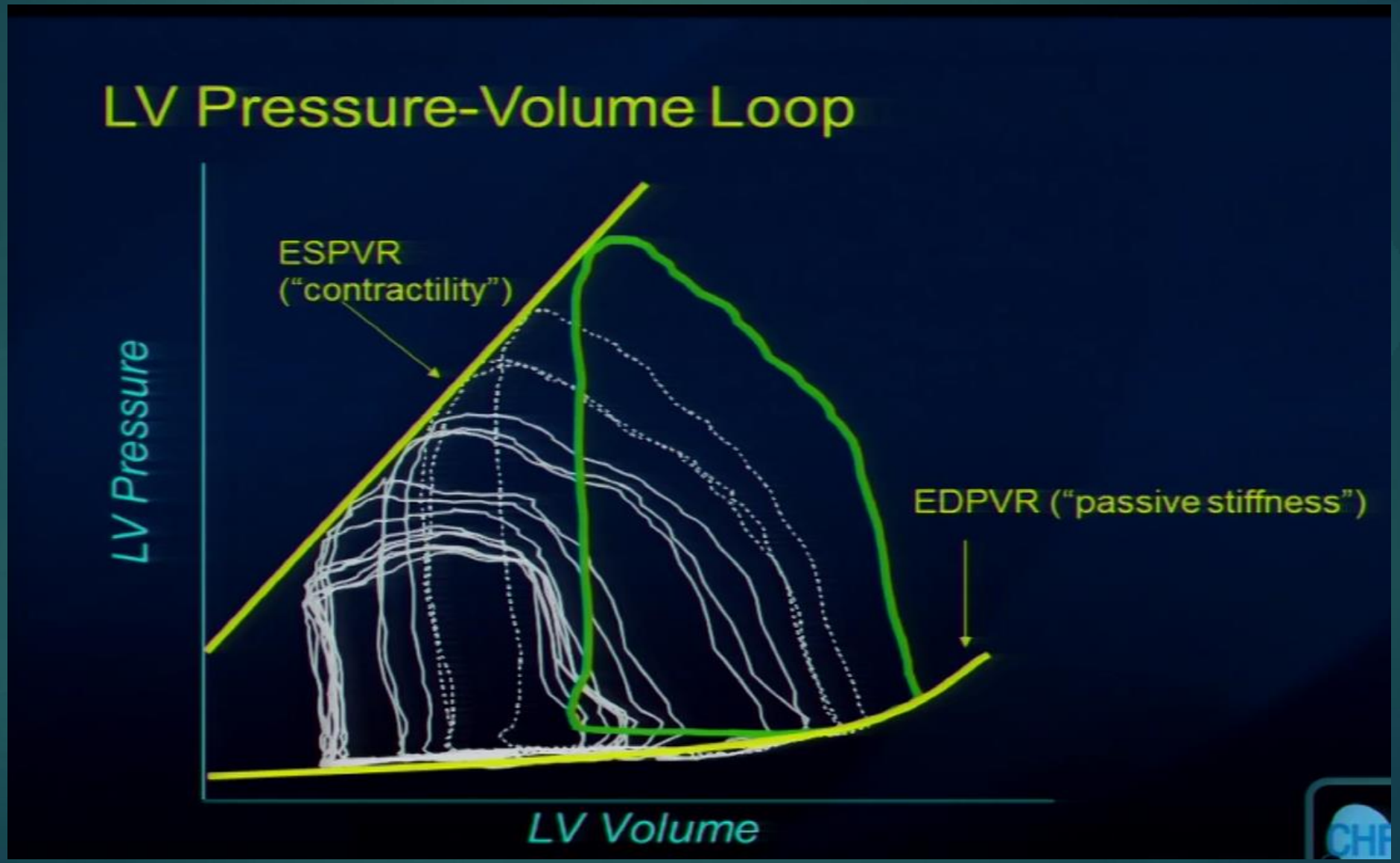
Neurohormonal Derangements

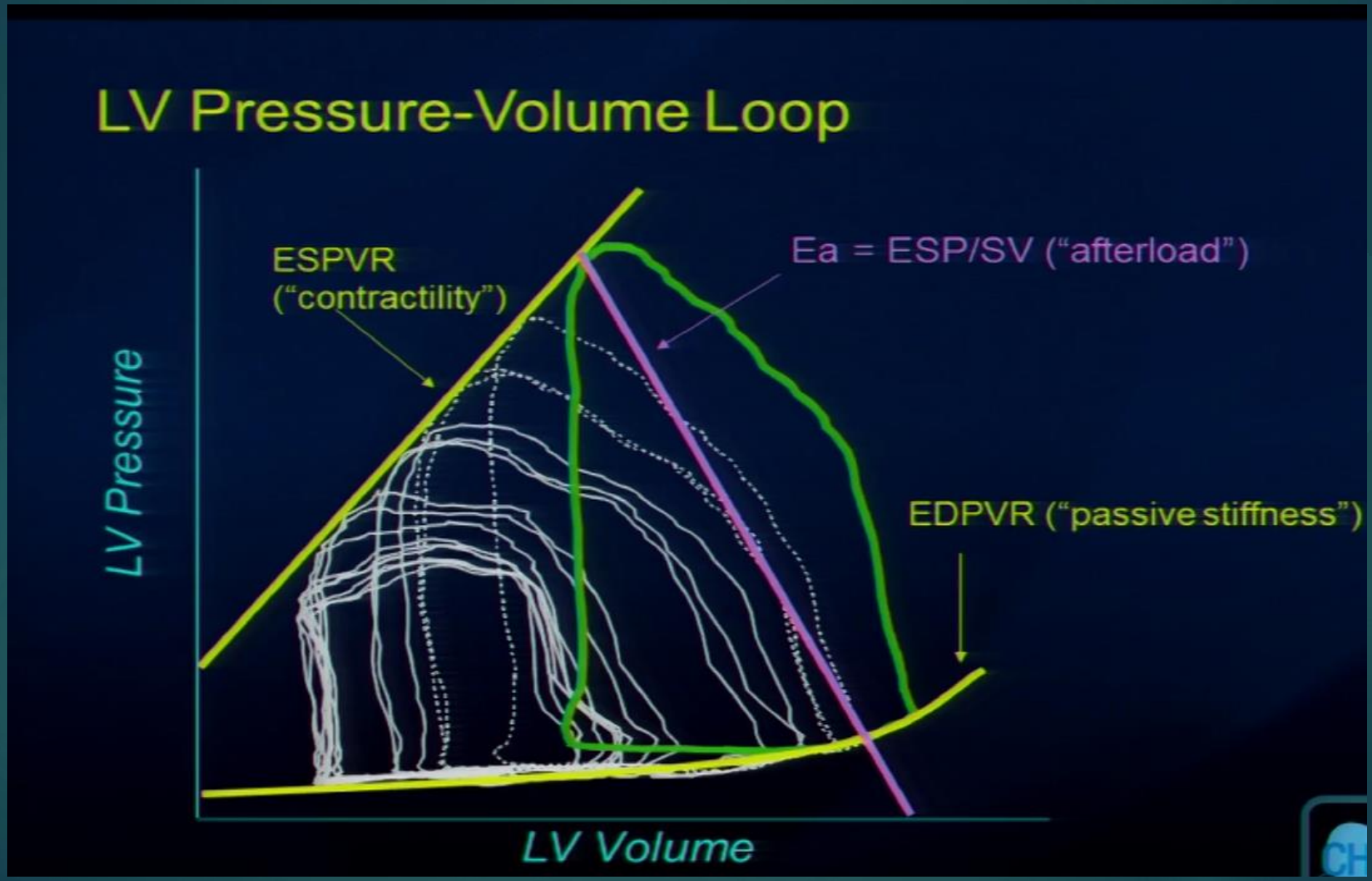
Pro-Remodeling	Anti-Remodeling
Norepinephrine (NE) Angiotensin II (Ang II) Aldosterone (aldo) Endothelin (ET) Vasopressin (AVP	Natriuretic peptides (NP) Nitric Oxide (NO) Prostacyclin (PGI_2)
Stimulate hypertrophy, remodeling, fibrosis, apoptosis, fetal gene expression, contractile abnormalities	Anti-hypertrophic Anti-proliferative Vasodilatory
Lead to vasoconstriction, sodium and fluid retention retention, endothelial dysfunction	Relax ventricular loading Conditions, promote Diuresis, anti-remodeling, Enhance endothelium

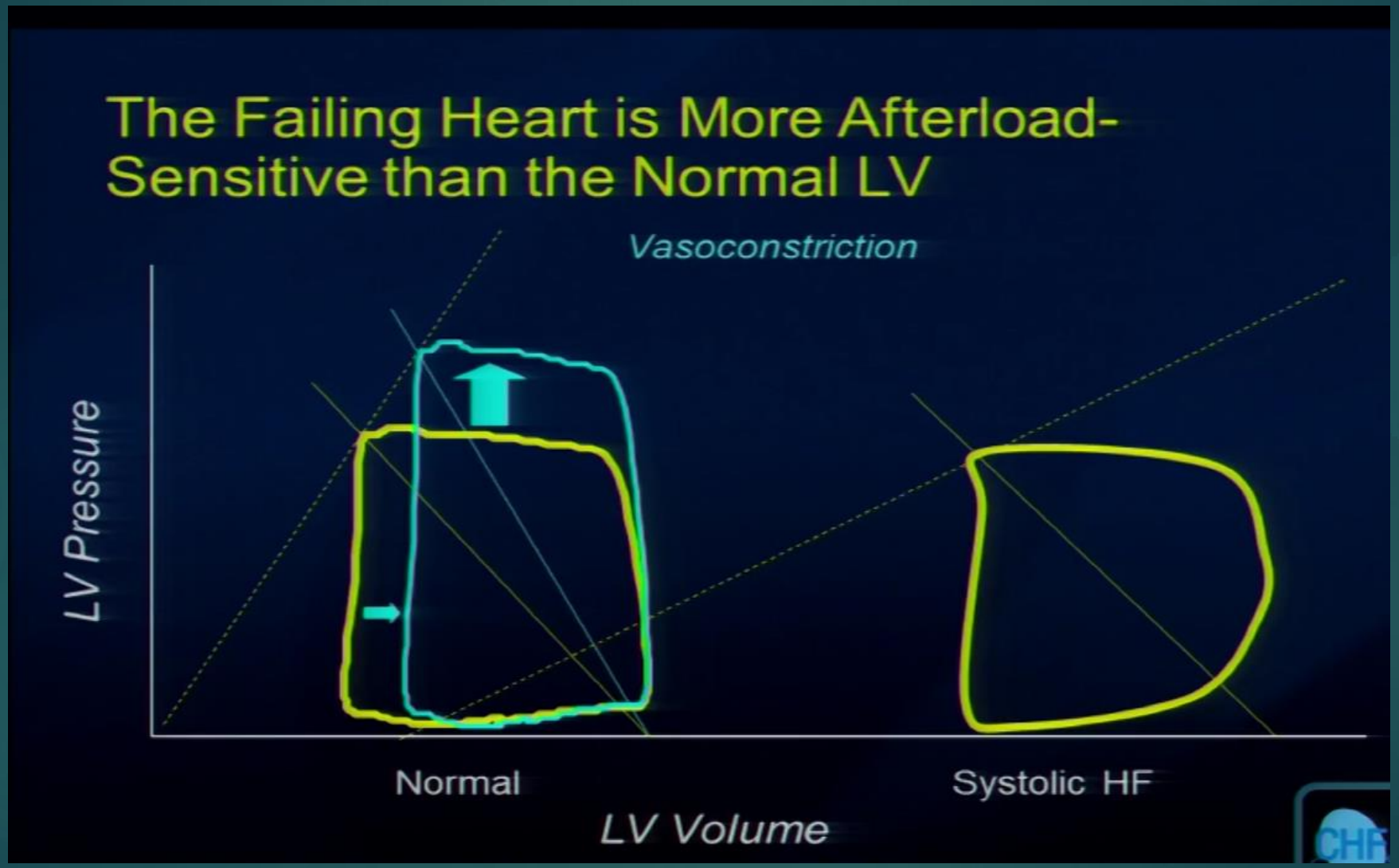

LV Pressure-Volume Loop
LV Pressure
LV Volume

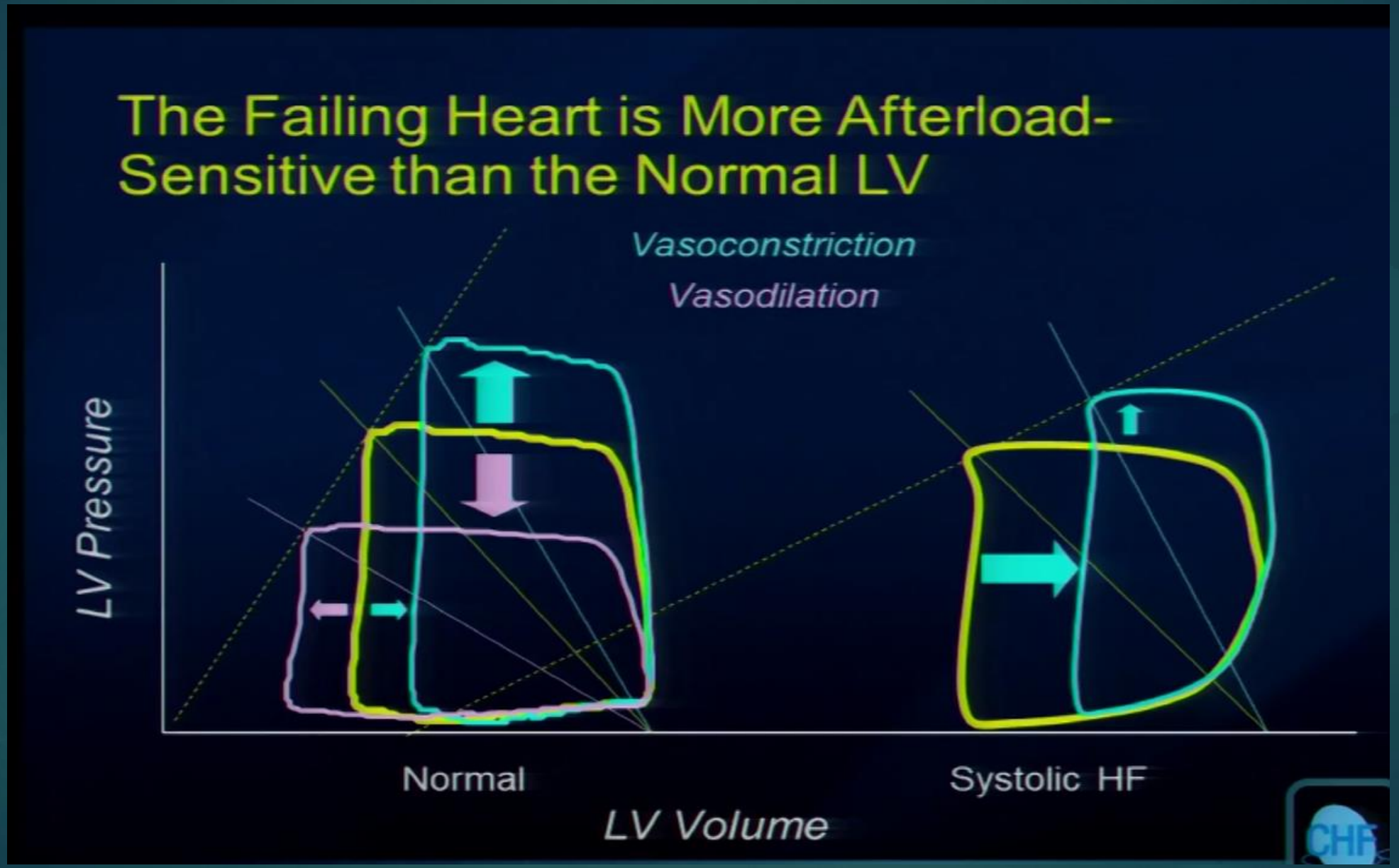

LV Pressure-Volume Loop
SBP
LV Pressure
SV
EDP
ESV
EDV ("preload")
LV Volume

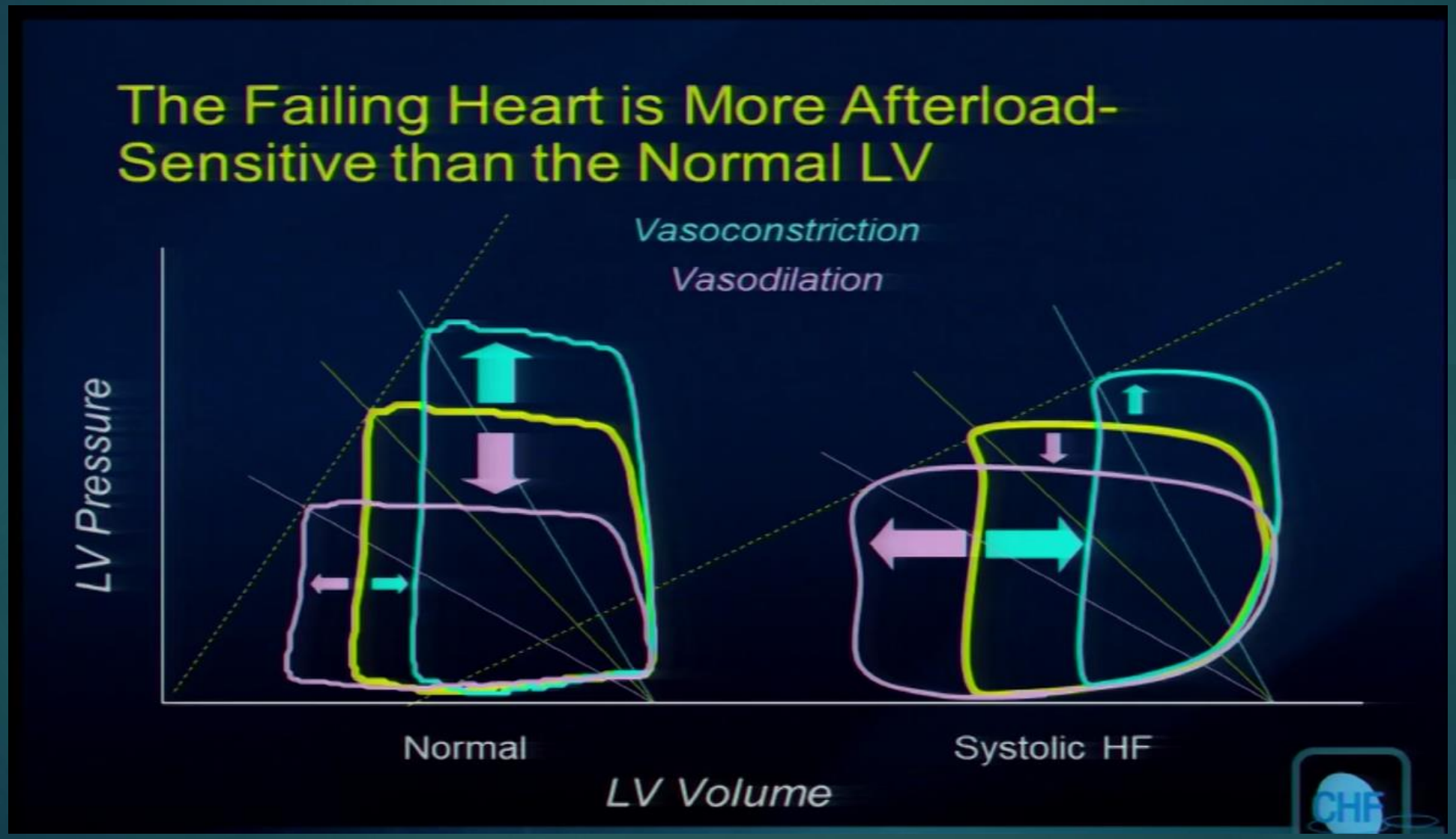

LV Pressure-Volume Loop
ESPVR
("contractility")
LV Pressure
LV Volume

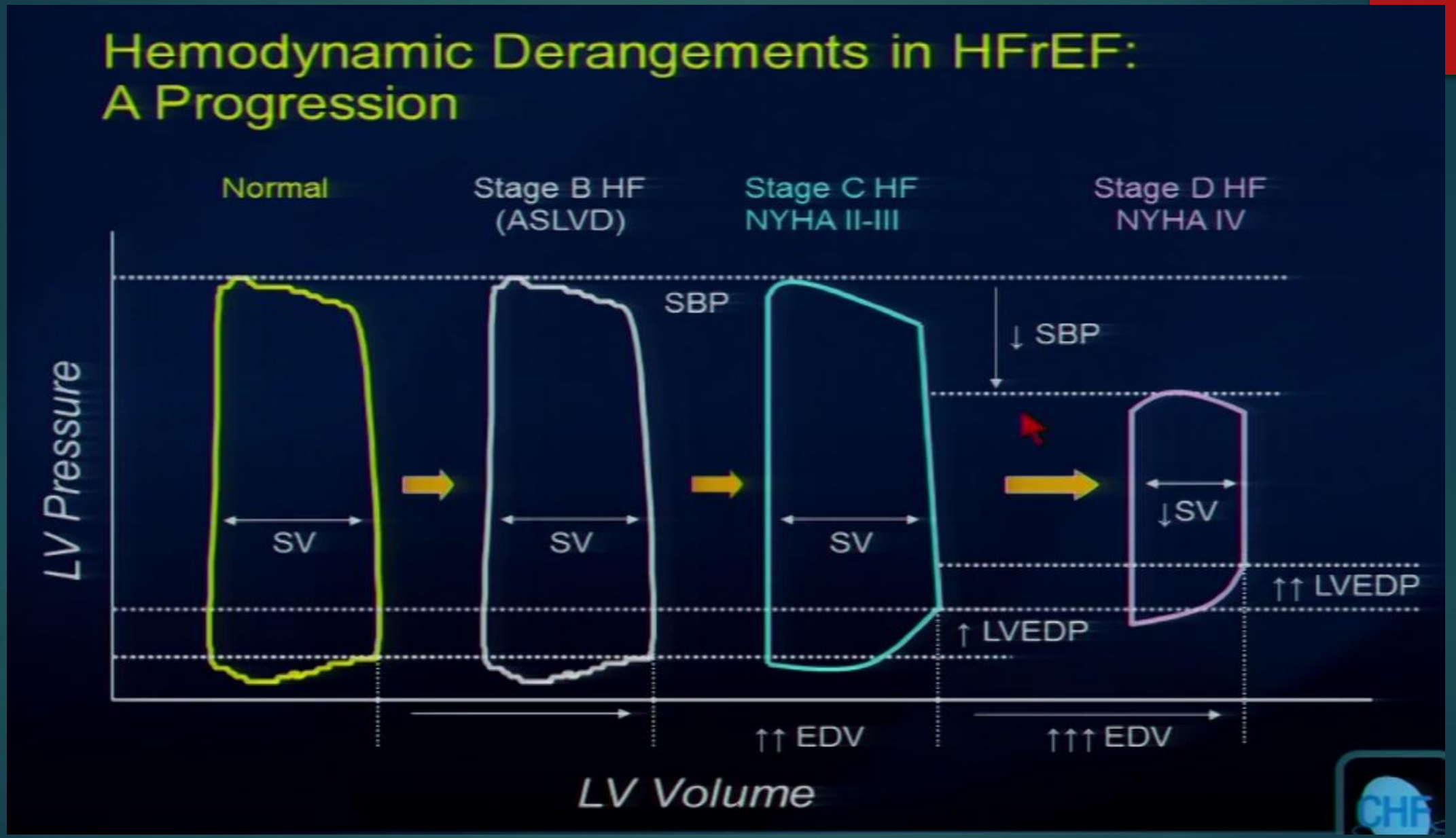

LV Pressure-Volume Loop
ESPVR
("contractility")
EDPVR ("passive stiffness")
LV Pressure
LV Volume

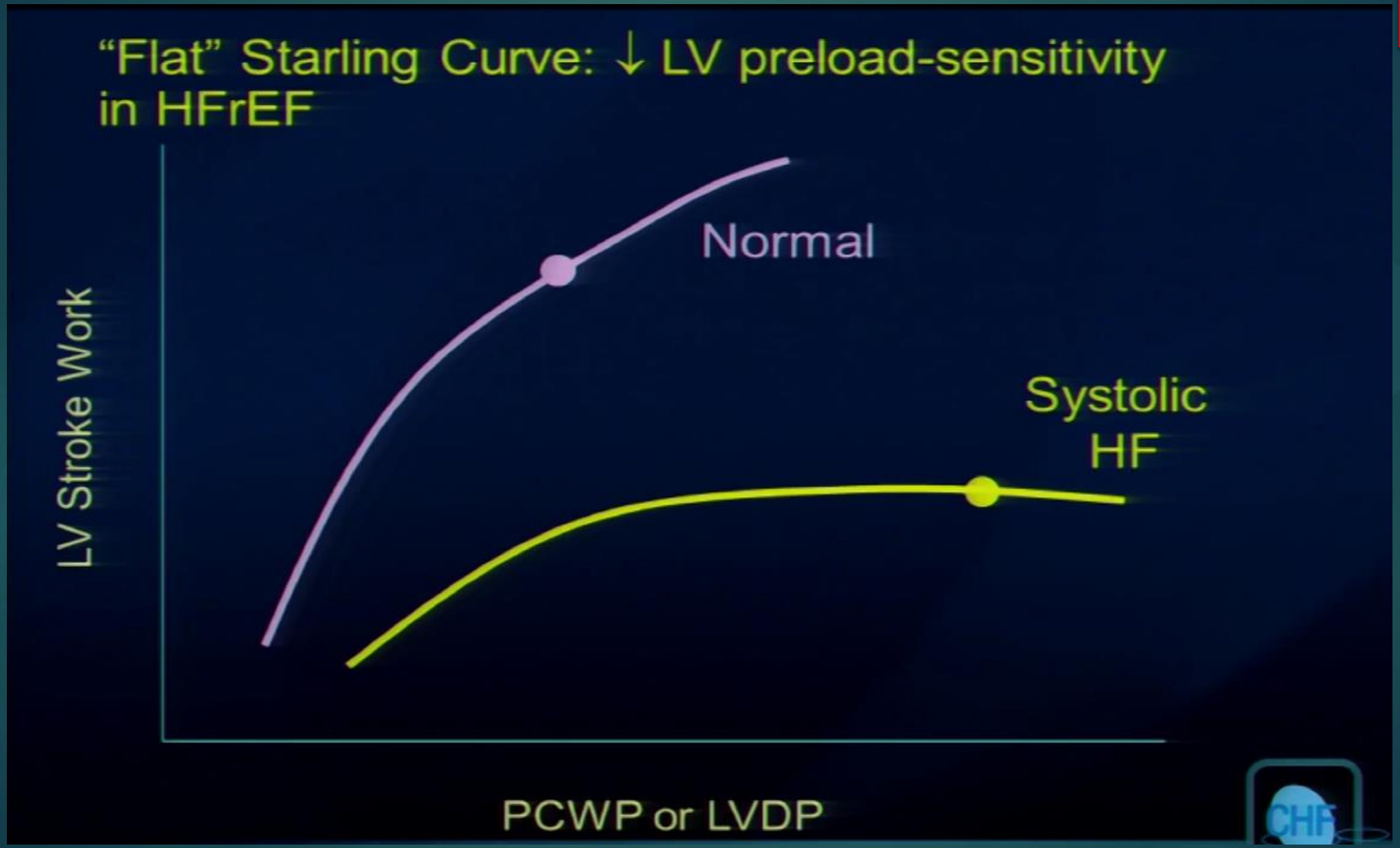

LV Pressure-Volume Loop
ESPVR
("contractility")
Ea = ESP/SV ("afterload")
EDPVR ("passive stiffness")
LV Pressure
LV Volume

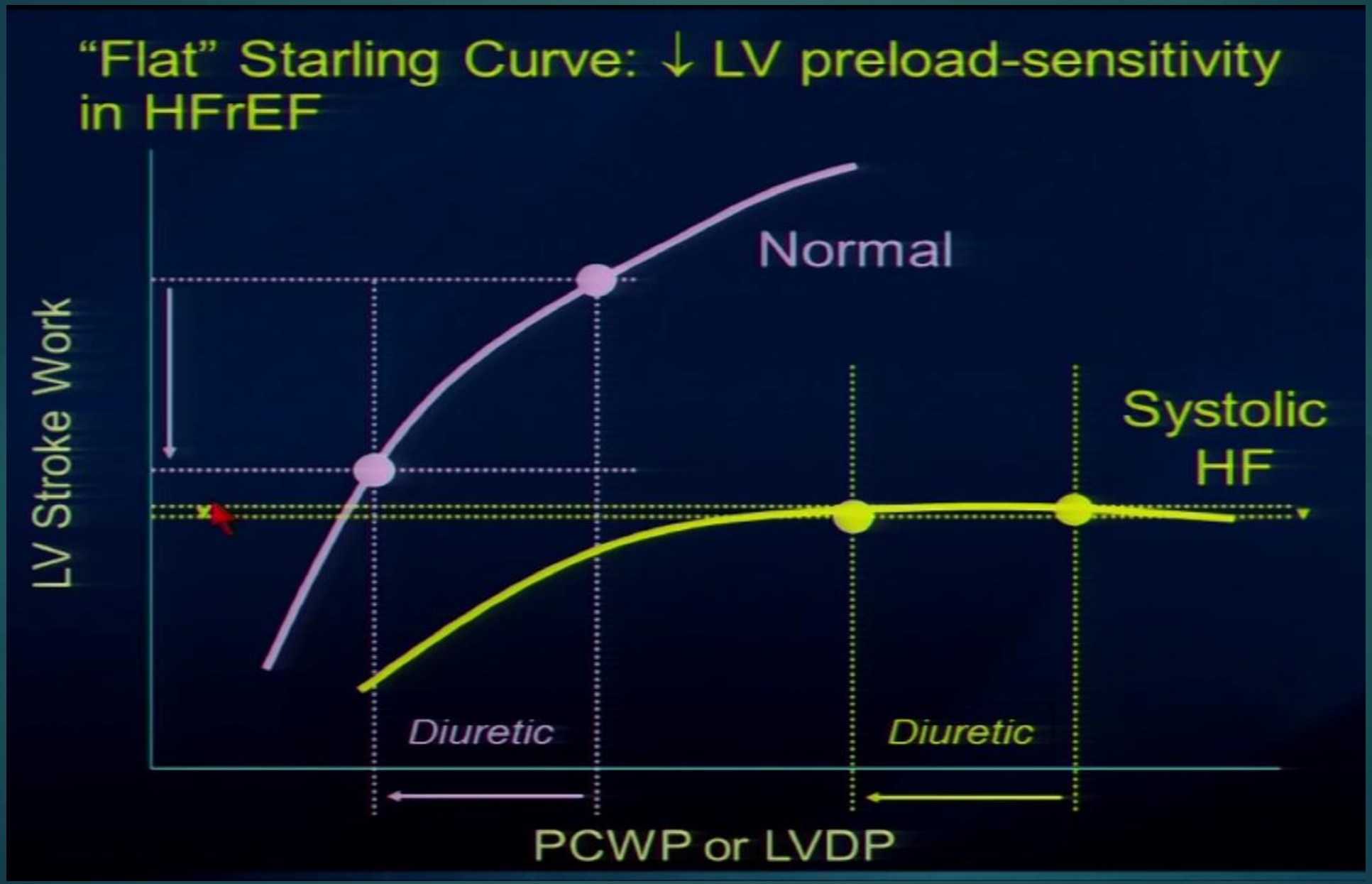

The Failing Heart is More Afterload-Sensitive than the Normal LV
Vasoconstriction
LV Pressure
Normal
Systolic HF
LV Volume

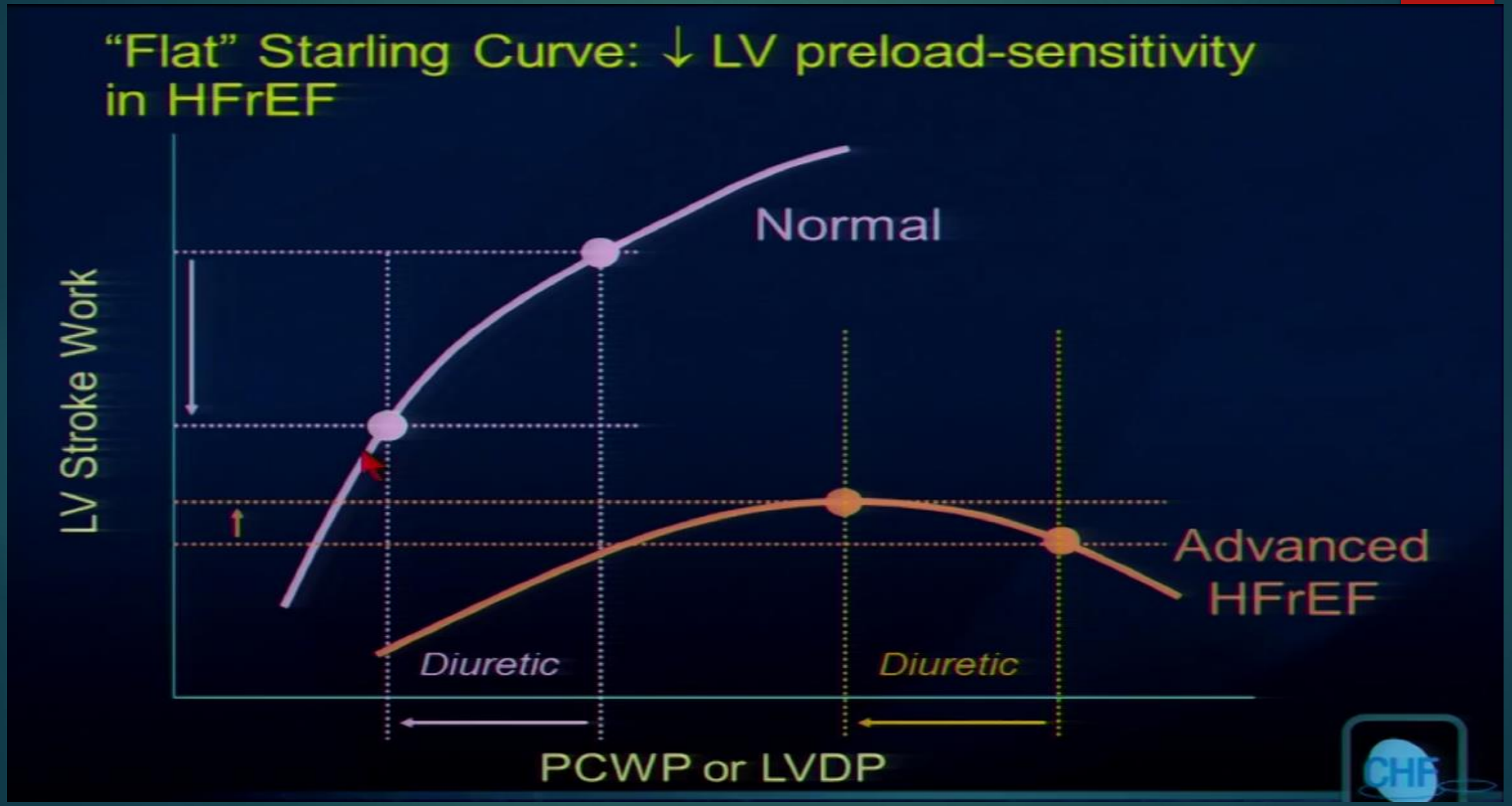

The Failing Heart is More Afterload-Sensitive than the Normal LV
Vasoconstriction
Vasodilation
LV Pressure
Normal
Systolic HF
LV Volume
CHF

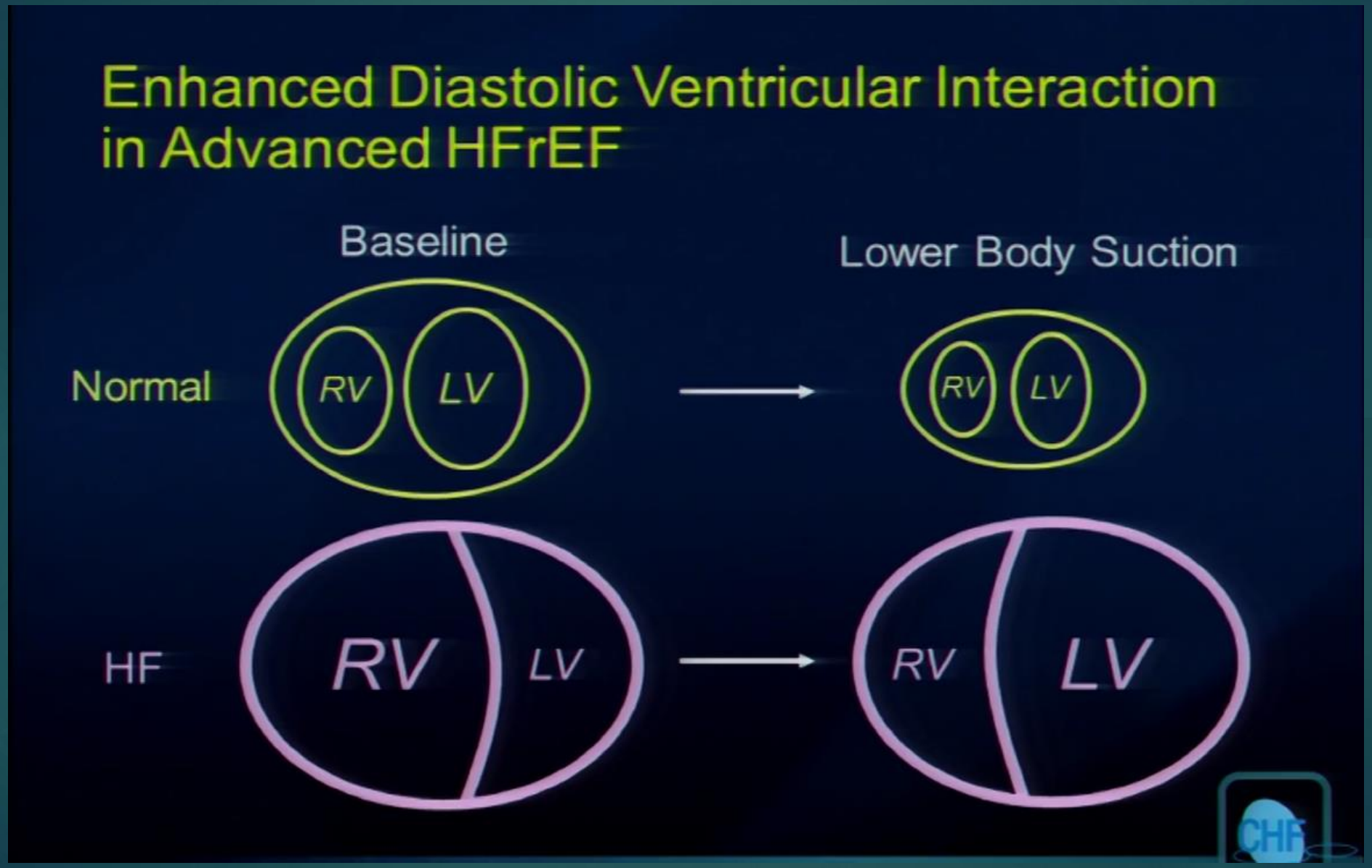

The Failing Heart is More Afterload-Sensitive than the Normal LV
Vasoconstriction
Vasodilation
LV Pressure
Normal
Systolic HF
LV Volume
CHF

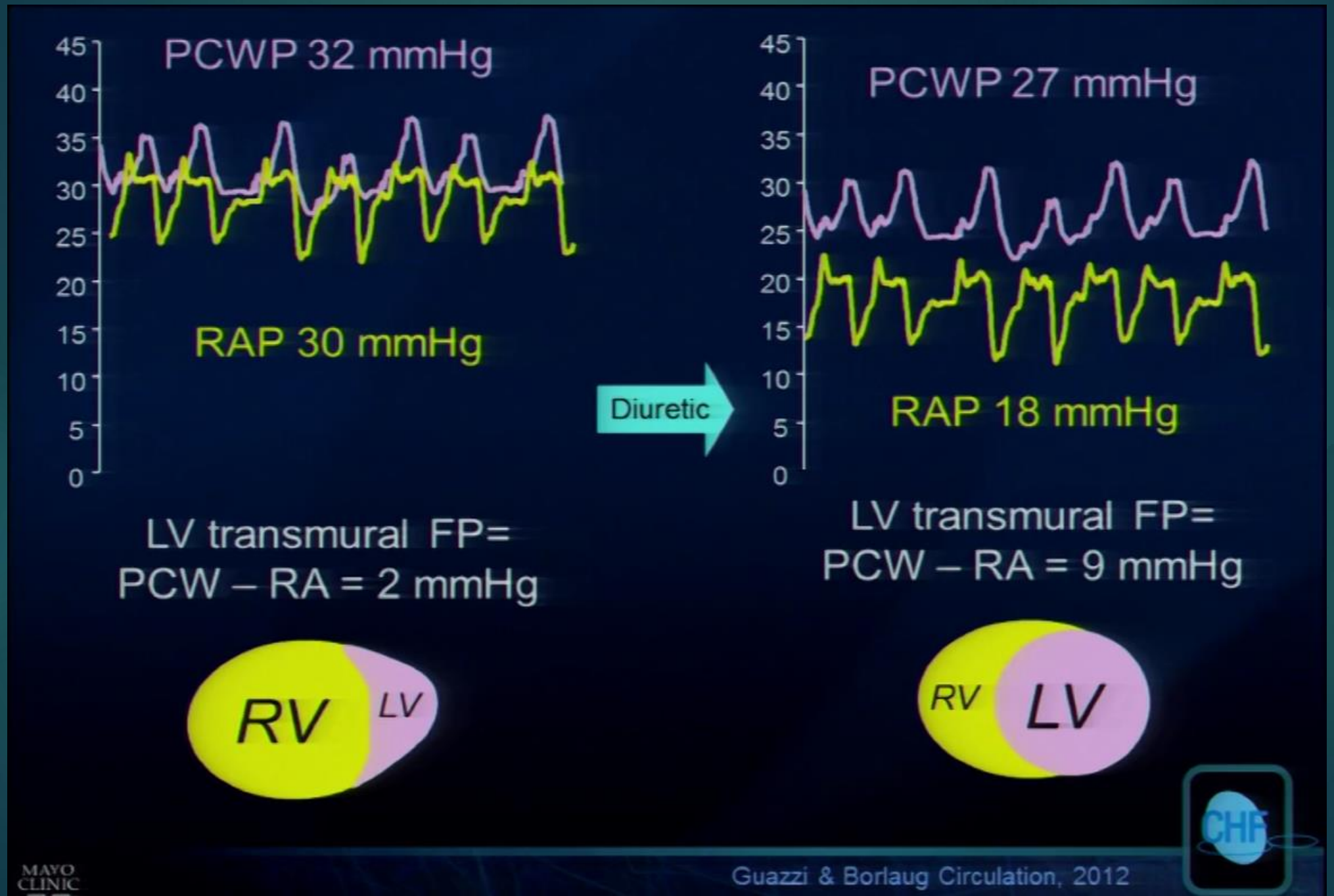

Hemodynamic Derangements in HFrEF:
A Progression
Normal
Stage B HF
(ASLVD)
Stage C HF
NYHA II-III
Stage D HF
NYHA IV
SBP
↓ SBP
SV
SV
SV
↓SV
↑↑ LVEDP
↑ LVEDP
↑↑ EDV
↑↑↑ EDV
LV Pressure
LV Volume


"Flat" Starling Curve: ↓ LV preload-sensitivity in HFrEF
Normal
Systolic HF
LV Stroke Work
PCWP or LVDP


"Flat" Starling Curve: ↓ LV preload-sensitivity in HFrEF
Normal
Systolic HF
LV Stroke Work
Diuretic
Diuretic
PCWP or LVDP


"Flat" Starling Curve: ↓ LV preload-sensitivity in HFrEF
Normal
LV Stroke Work
Advanced HFrEF
Diuretic
Diuretic
PCWP or LVDP


Enhanced Diastolic Ventricular Interaction in Advanced HFrEF
Baseline
Lower Body Suction
Normal
RV
LV
RV
LV
HF
RV
LV
RV
LV
CHF


PCWP 32 mmHg
RAP 30 mmHg
45
40
35
30
25
20
15
10
5
0
Diuretic
PCWP 27 mmHg
RAP 18 mmHg
LV transmural FP=
PCW – RA = 2 mmHg
LV transmural FP=
PCW – RA = 9 mmHg
RV
LV
RV
LV
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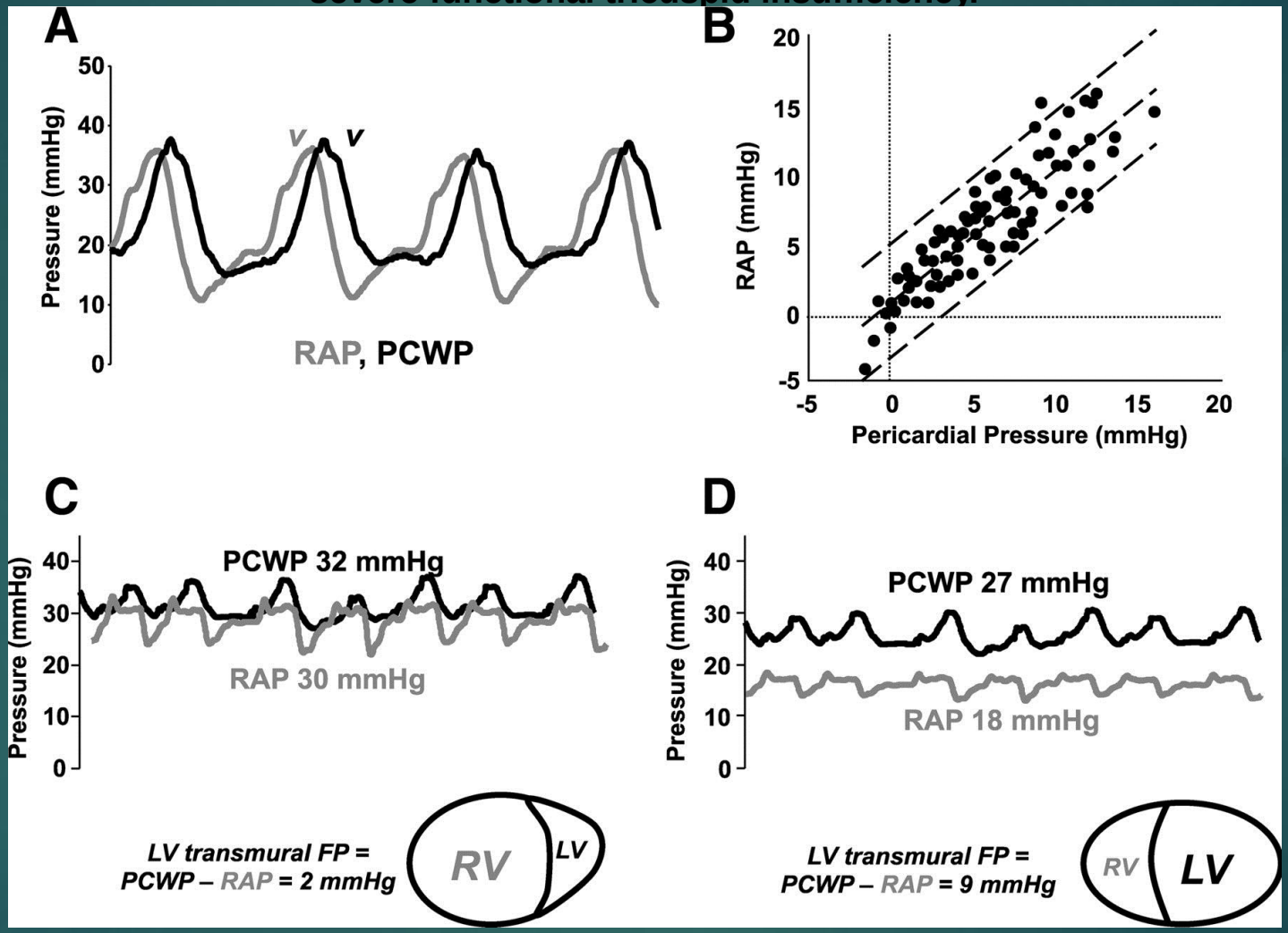
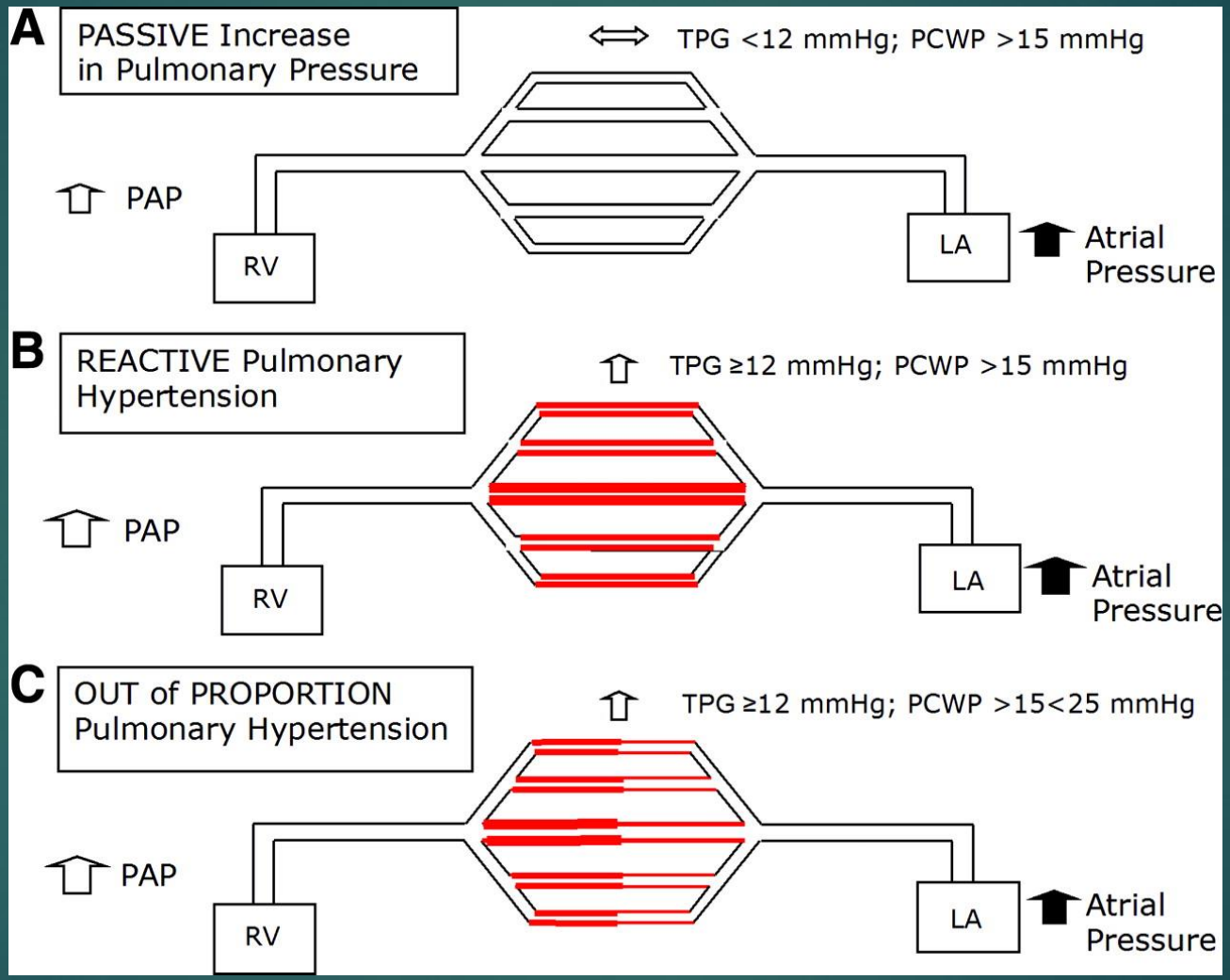
Guazzi & Borlaug Circulation, 2012
CHF

Ventricular interdependence in right heart failure from group 2 PH. A, typical equalization in RAP and PCWP from enhanced interdependence in a patient with biventricular HF, group 2 PH, and severe functional tricuspid insufficiency.



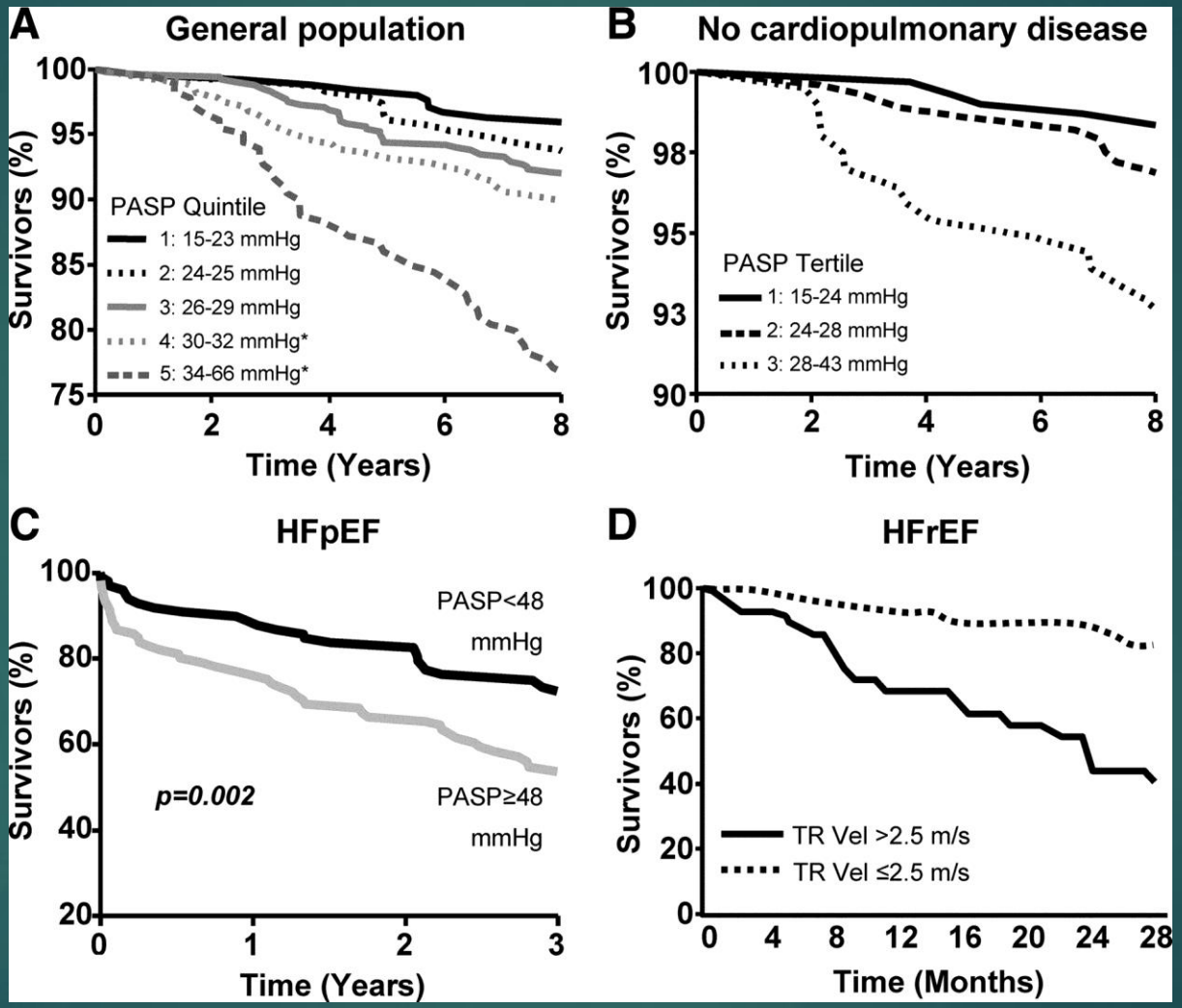
Marco Guazzi, and Barry A. Borlaug Circulation. 2012;126:975-990

Diagram showing the various hemodynamic stages observed in group 2 PH. A, Passive.



Marco Guazzi, and Barry A. Borlaug Circulation. 2012;126:975-990

Pulmonary artery systolic pressure (PASP) estimates are a risk factor for death.



Marco Guazzi, and Barry A. Borlaug Circulation. 2012;126:975-990

American Heart Association

Extracardiac Sequelae

- Hepatic Congestion/dysfunction/ascites
- Anemia/iron deficiency
- Endothelial Dysfunction
- Oxidative Stress
- Sleep disordered breathing

Cardiorenal Interactions

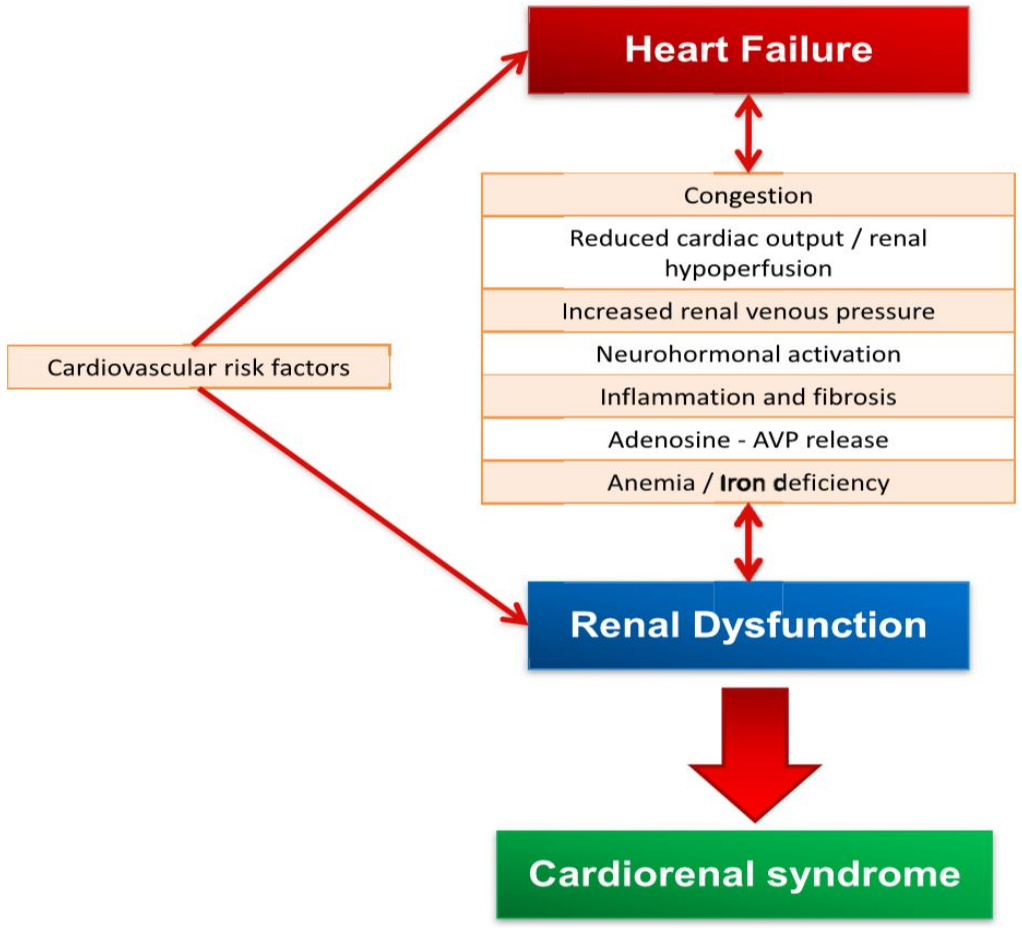
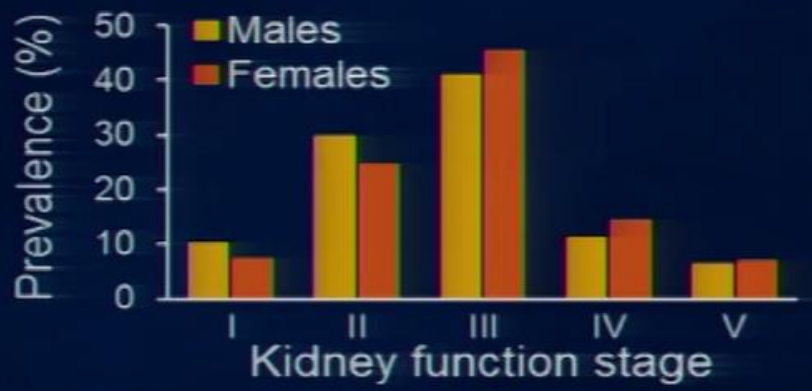
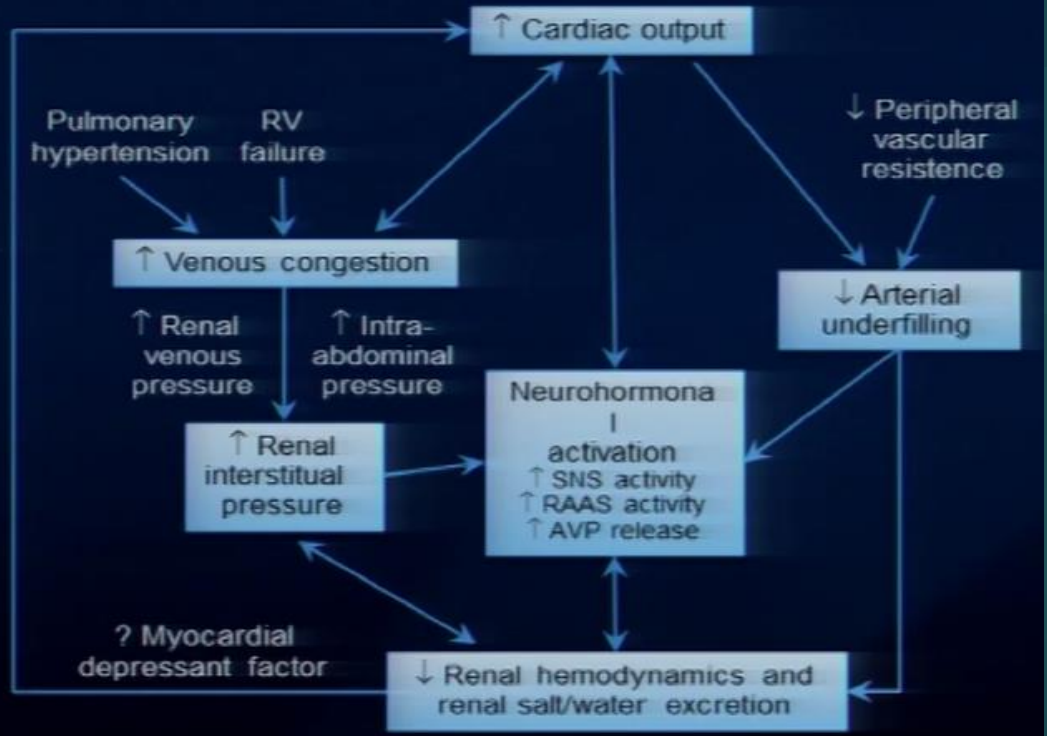


Fig. 1. Pathophysiological mechanisms of CRS.

Renal Dysfunction in HF



Heywood J Card Fail, 2005



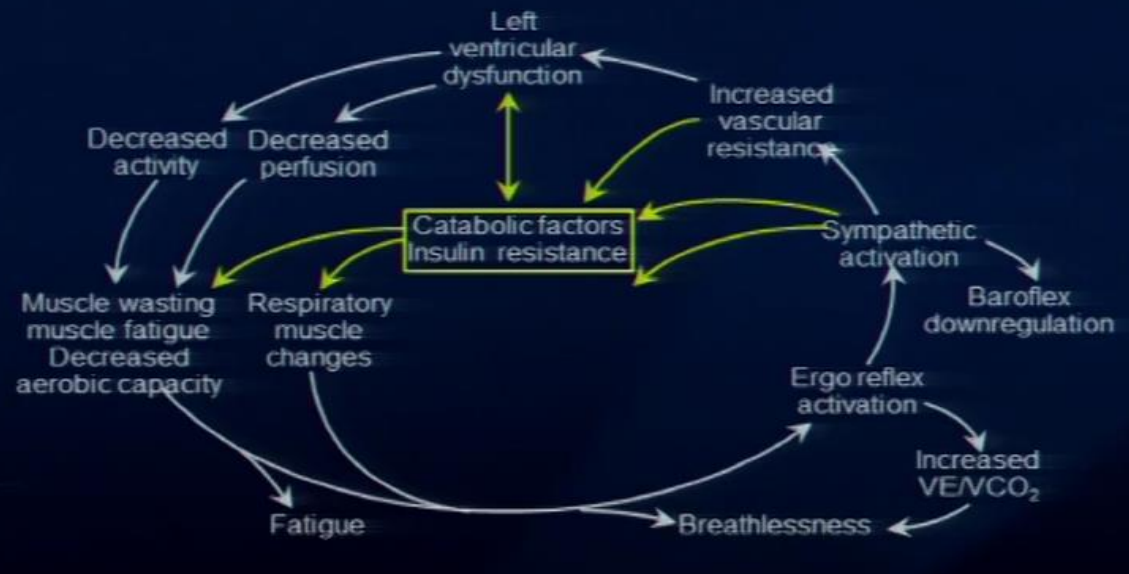
Tang & Mullens Heart 2010

Consensus Conference of Acute Dialysis Quality Initiative Group classification of cardiorenal syndromes

Type	Pathophysiology	Consequences
Type 1	Acute worsening heart function	Kidney injury and/or dysfunction
Type 2	Chronic abnormalities in heart function	Kidney injury and/or dysfunction
Type 3	Acute worsening of kidney function or AKI	Heart injury and/or dysfunction
Type 4	CKD	Heart injury and/or dysfunction
Type 5	Systemic conditions	Simultaneous injury and/or dysfunction of heart and kidney

Alterations in Skeletal Muscle

Skeletal Muscle Δ in HF	
Fiber type	
I	↓
Iia	↓
Iib	↑
Krebs cycle	↓
Ox Phos	↓
Lipid oxidation	↓
Capillary density	↓/↔
Mitochondria	↓



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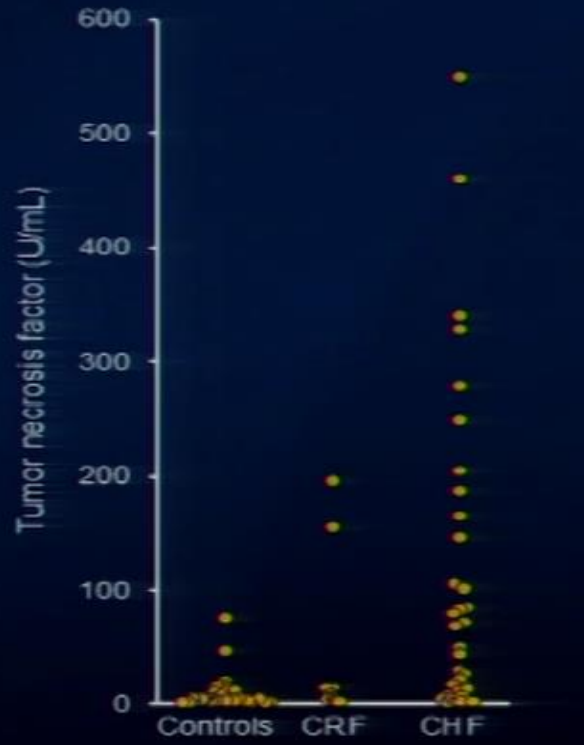
Clark J Am Coll Cardiol, 1996

CHF

HF = A Systemic Inflammatory Disease



Levine: New Engl J Med, 1990

	Healthy volunteers (n=14)	CHF no oedema (n=20)	CHF oedema (n=20)
Endotoxin (EU/mL)	0.46 (0.21)	0.37 (0.23)	0.74 (0.45)
LBP (g/mL)	9.6 (4.9)	10.4 (5.3)	12.1 (6.0)
Lipopolysaccharide/ log LBP ratio	0.54 (0.20)	0.44 (0.30)	0.75 (0.49)
TNFα (pg/mL)	24.6 (8.9)	25.8 (7.9)	36.6 (12.3)
Soluble TNF receptor-1 (pg/mL)	708 (213)	1077 (529)	1922 (1399)
Soluble TNF receptor-2 (pg/mL)	1465 (835)	2096 (1360)	3143 (1690)
Soluble CD14 (ng/mL)	3456 (583)	3674 (454)	4243 (688)
Procalcitonin (ng/mL)	87 (16)	106 (73)	145 (94)
Interleukin-6 (pg/mL)	2.0 (0.4)	4.3 (5.5)	14.7 (17.3)
C-reactive (mg/L)	5.6 (1.7)	9.5 (9.5)	19.7 (17.1)

Niebauer: Lancet, 1999

Untoward effects of inflammatory mediators in heart failure

- Left-ventricular dysfunction
- Pulmonary oedema
- Cardiomyopathy
- Reduced blood flow in leg
- Left-ventricular remodeling
- β-receptor uncoupling from adenylate cyclase
- Activation of the fetal gene programme
- Alterations of the extracelluar matrix

Mann: Lancet, 1999

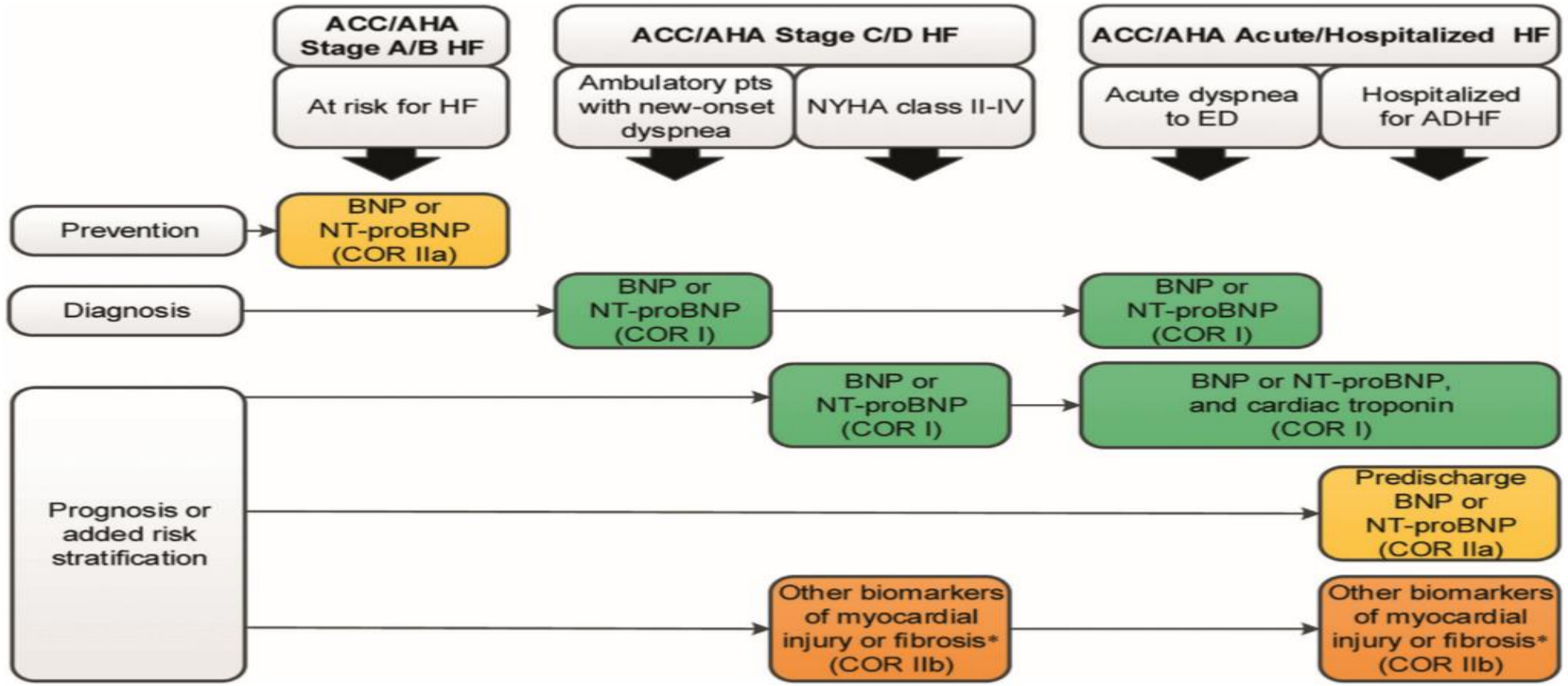
Clinical Assessment

Figure 1. Two-Minute Assessment of Hemodynamic Profile

Diagram indicating 2 × 2 table of hemodynamic profiles for patients presenting with heart failure. Most patients can be classified in a 2-minute bedside assessment according to the signs and symptoms shown although in practice some patients may be on the border between the warm-and-wet and cold-and-wet profiles. This classification helps guide initial therapy and prognosis for patients presenting with advanced heart failure. Although most patients presenting with hypoperfusion also have elevated filling pressures (cold and wet profile), many patients present with elevated filling pressures without major reduction in perfusion (warm and wet profile). Patients presenting with symptoms of heart failure at rest or minimal exertion without clinical evidence of elevated filling pressures or hypoperfusion (warm and dry profile) should be carefully evaluated to determine whether their symptoms result from heart failure. Reprinted with permission from Dr Stevenson.

Biomarkers

FIGURE 1 Biomarkers Indications for Use



Colors correspond to COR in Table 1.

*Other biomarkers of injury or fibrosis include soluble ST2 receptor, galectin-3, and high-sensitivity troponin.

ACC indicates American College of Cardiology; AHA, American Heart Association; ADHF, acute decompensated heart failure; BNP, B-type natriuretic peptide; COR, Class of Recommendation; ED, emergency department; HF, heart failure; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; and pts, patients.

Causes of Elevated Natriuretic Peptide Levels

TABLE 2 Selected Potential Causes of Elevated Natriuretic Peptide Levels (38–41)

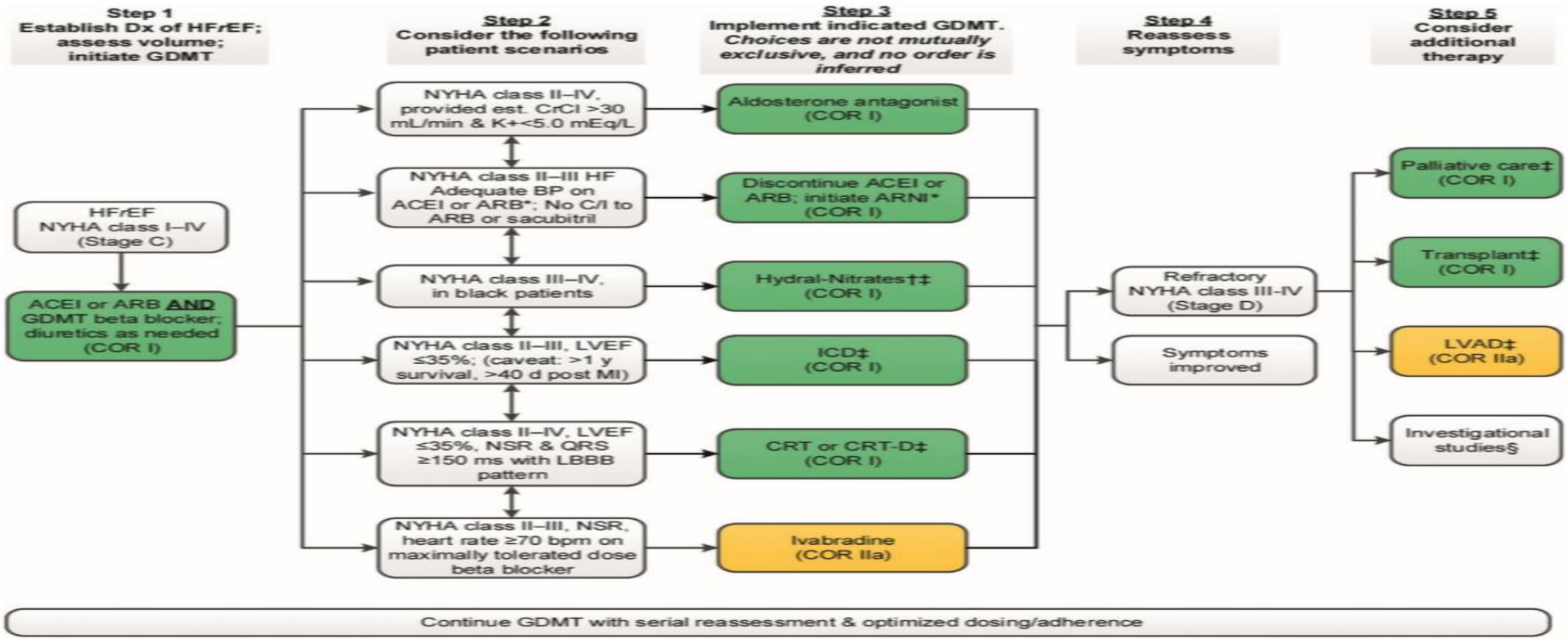
Cardiac
HF, including RV syndromes
Acute coronary syndromes
Heart muscle disease, including LVH
Valvular heart disease
Pericardial disease
Atrial fibrillation
Myocarditis
Cardiac surgery
Cardioversion
Toxic-metabolic myocardial insults, including cancer chemotherapy
Noncardiac
Advancing age
Anemia
Renal failure
Pulmonary: obstructive sleep apnea, severe pneumonia
Pulmonary hypertension
Critical illness
Bacterial sepsis
Severe burns

Modified from Table 8 of the 2013 HF guideline (9).

HF, indicates heart failure; LVH, left ventricular hypertrophy; and RV, right ventricular

ACC/AHA/HFSA focused updated guidelines for HF

FIGURE 2 Treatment of HF*r*EF Stage C and D



Colors correspond to COR in Table 1. For all medical therapies, dosing should be optimized and serial assessment exercised.
*See text for important treatment directions.
†Hydral-Nitrates green box: The combination of ISDN/HYD with ARNI has not been robustly tested. BP response should be carefully monitored. ‡See 2013 HF guideline (9).
§Participation in investigational studies is also appropriate for stage C, NYHA class II and III HF.
ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor-blocker; ARNI, angiotensin receptor-neprilysin inhibitor; BP, blood pressure; bpm, beats per minute; C/I, contraindication; COR, Class of Recommendation; CrCl, creatinine clearance; CRT-D, cardiac resynchronization therapy–device; Dx, diagnosis; GDMT, guideline-directed management and therapy; HF, heart failure; HF*r*EF, heart failure with reduced ejection fraction; ICD,

Advanced HF is the presence of progressive and/or persistent severe symptoms of heart failure despite optimized medical, surgical and device therapy

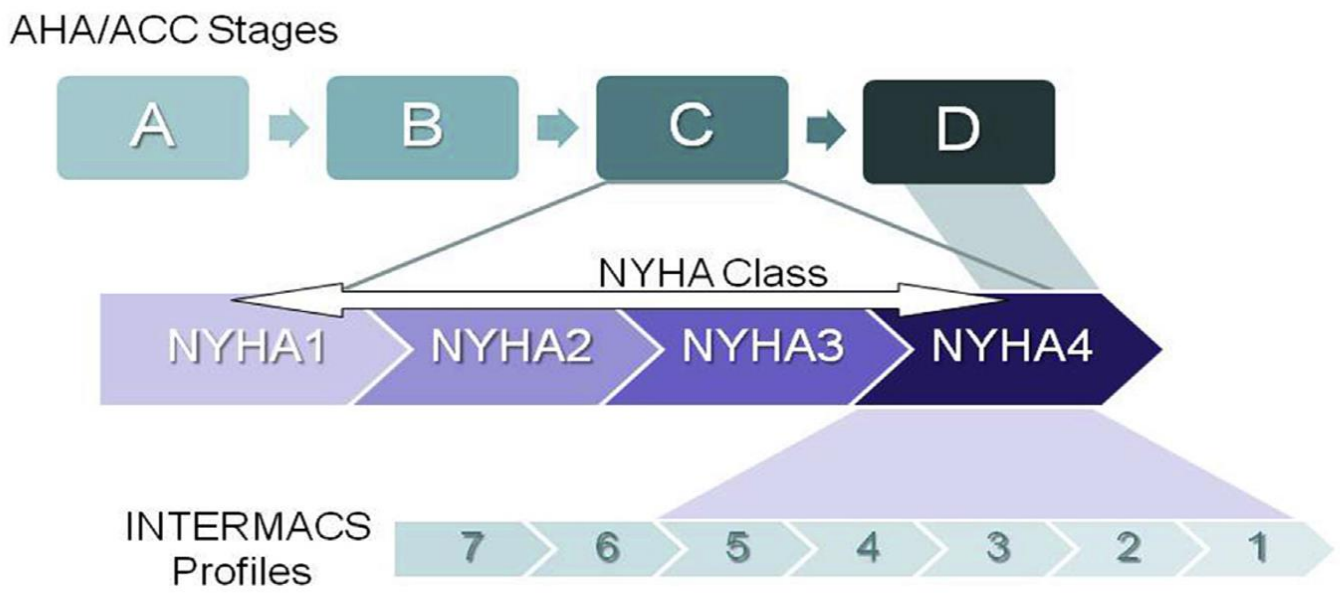


Fig. 1. Classification schemes for heart failure severity. Overlapping classification systems provide complementary descriptive and prognostic information for patients with advanced heart disease. NYHA classifies dynamic functional limitation, the American Heart Association/American College of Cardiology-Stages of Heart Failure highlight antecedent risk factors and disease progression, while the INTERMACS patient profiles integrate symptom burden and ongoing measures use to treat evolving shock.

Interagency Registry for Mechanically Assisted Circulatory Support patient profiles

Patient Profile Official Shorthand
1 "Crash and burn"
2 "Sliding fast" on inotropes
3 "Stable" on continuous inotropes
4 Resting symptoms on oral therapy at home
5 "Housebound", comfortable at rest but symptoms with minimum activities of daily living
6 "Walking wounded", activities of daily living possible by meaningful activity limited
7 Advanced NYHA class III

Adapted from Stevenson LW, Pagani FD, Young JB, et al. INTERMACS profiles of advanced heart failure. J Heart Lung Transplant 2009;28(6):537

Definition of Advanced Heart Failure

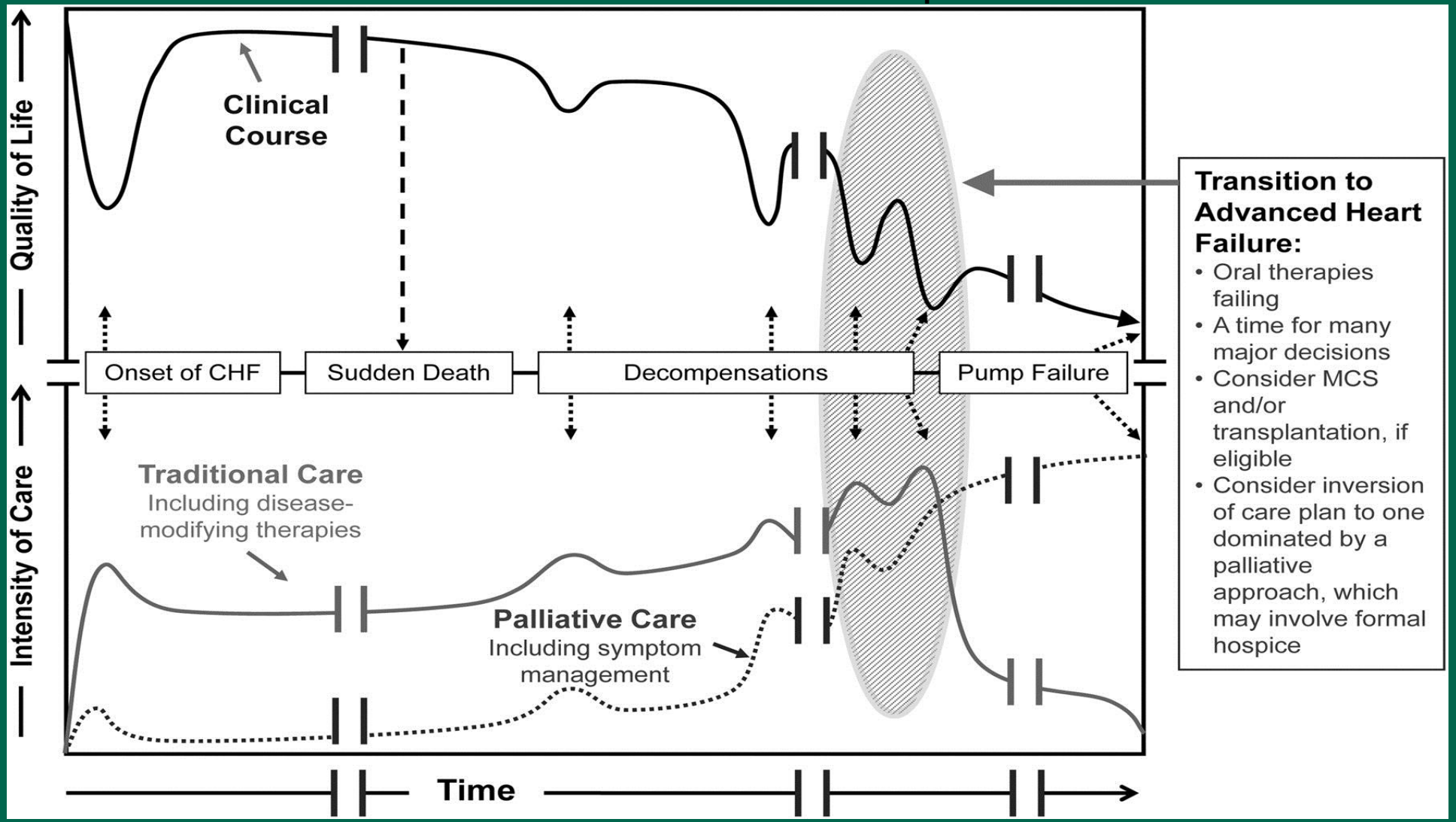
1.Moderate to severe symptoms of dyspnea and/or fatigue at rest or with minimal exertion (NYHA functional class III or IV)
2.Episodes of fluid retention and/or reduced cardiac output
3.Objective evidence of severe cardiac dysfunction demonstrated by at least 1 of the following:
    1. Left ventricular ejection fraction <30%
    2. Pseudonormal or restrictive mitral inflow pattern by Doppler
    3. High left and/or right ventricular filling pressures, or
    4. Elevated B-type natriuretic peptide
4.Severe impairment of functional capacity as demonstrated by either inability to exercise, 6-min walk distance <300 m, or peak oxygen uptake <12 to 14 mL · g^{-1} · min^{-1}
5.History of at least 1 hospitalization in the past 6 mo
6.Characteristics should be present despite optimal medical therapy

Table 1
Definition of Advanced HF Across Cardiovascular Societies

Definition of Advanced HF Across Cardiovascular Societies

	Refractory symptoms					*Exercise Intolerance*	*Objective evidence of severe cardiac dysfunction*			
	Severe Symptoms	Multiple Hospitalizations	Optimal Therapy	Inotropic Support	Fluid Retention and/or Peripheral Hypoperfusion	Severe Functional Capacity Impairment†‖	Reduced Ejection Fraction	Doppler Echo‡	Hemodynamics§	Elevated Natriuretic Peptides
ACC/AHA	x	x	x			x	x			
HFSA	x	x	x	x		x				
ESC	x	x	x		x	x	x	x	x	x

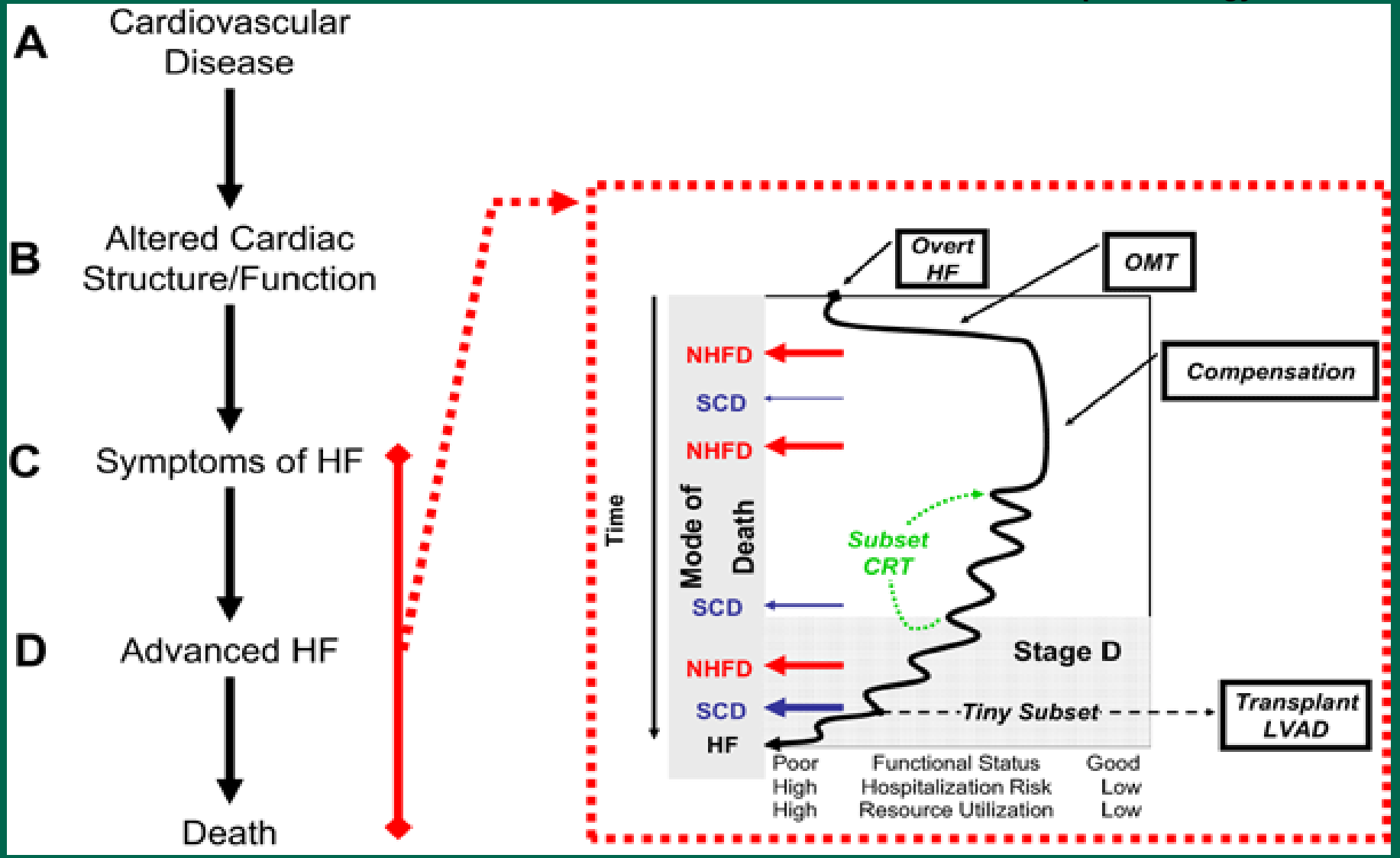
A depiction of the clinical course of heart failure with associated types and intensities of available therapies.



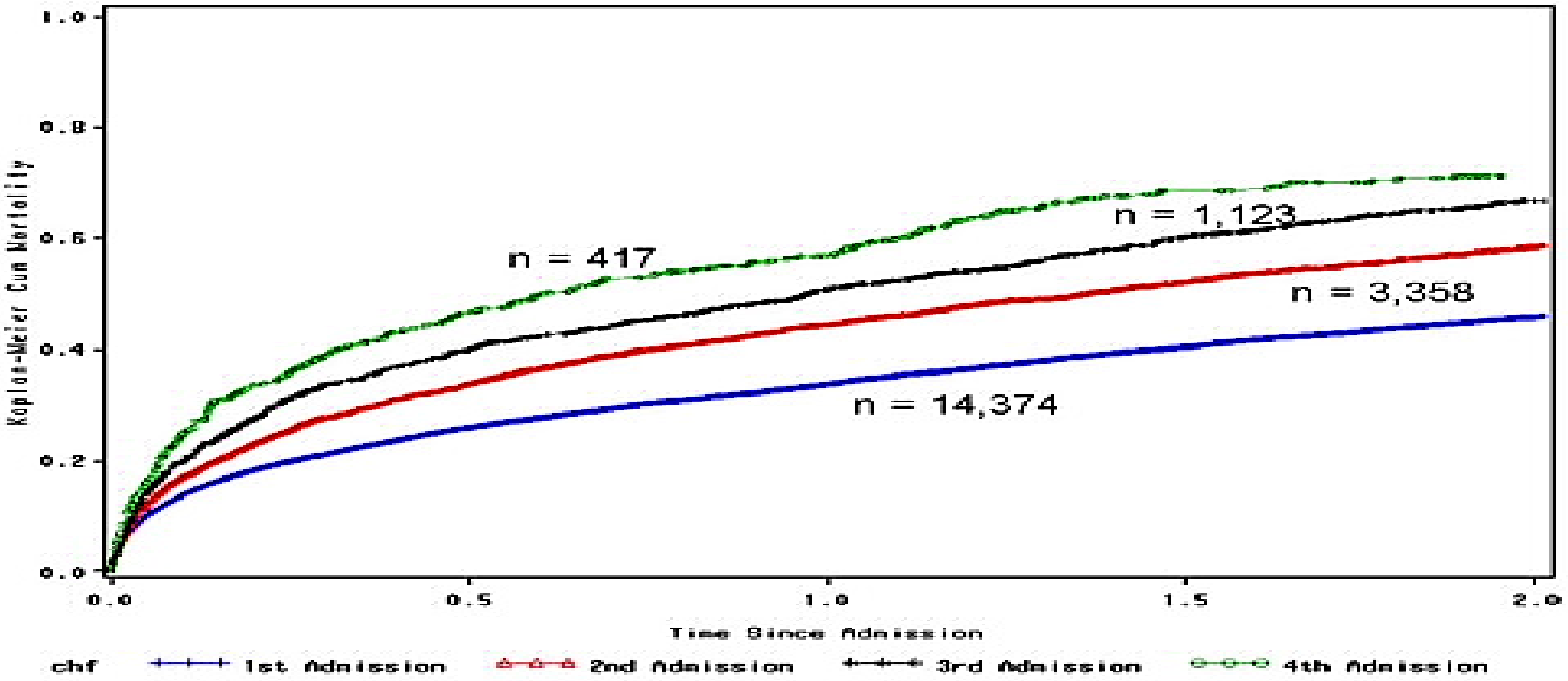
Larry A. Allen et al. Circulation. 2012;125:1928-1952

American Heart Association.

Who Has Advanced Heart Failure? Definition and Epidemiology



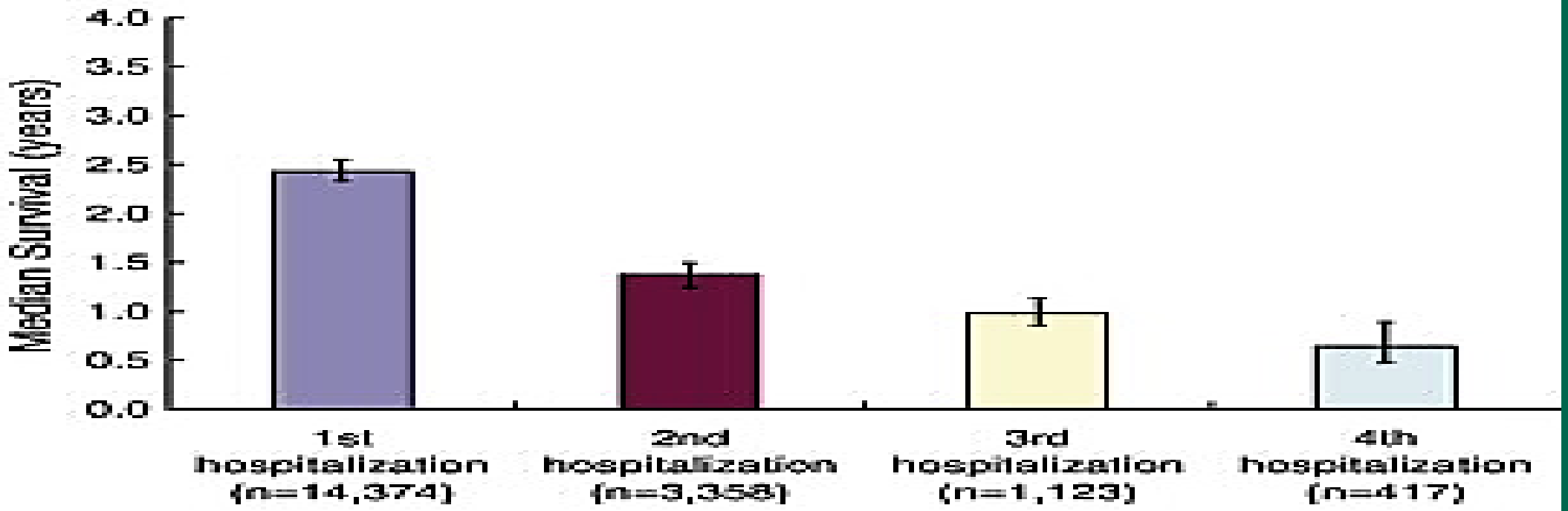
Congestive Heart Failure
Volume 17, Issue 4, pages 160-168, 21 JUL 2011 DOI: 10.1111/j.1751-7133.2011.00246.x
http://onlinelibrary.wiley.com/doi/10.1111/j.1751-7133.2011.00246.x/full#f1



Kaplan-Meier cumulative mortality curve for all-cause mortality after each subsequent hospitalization for HF.

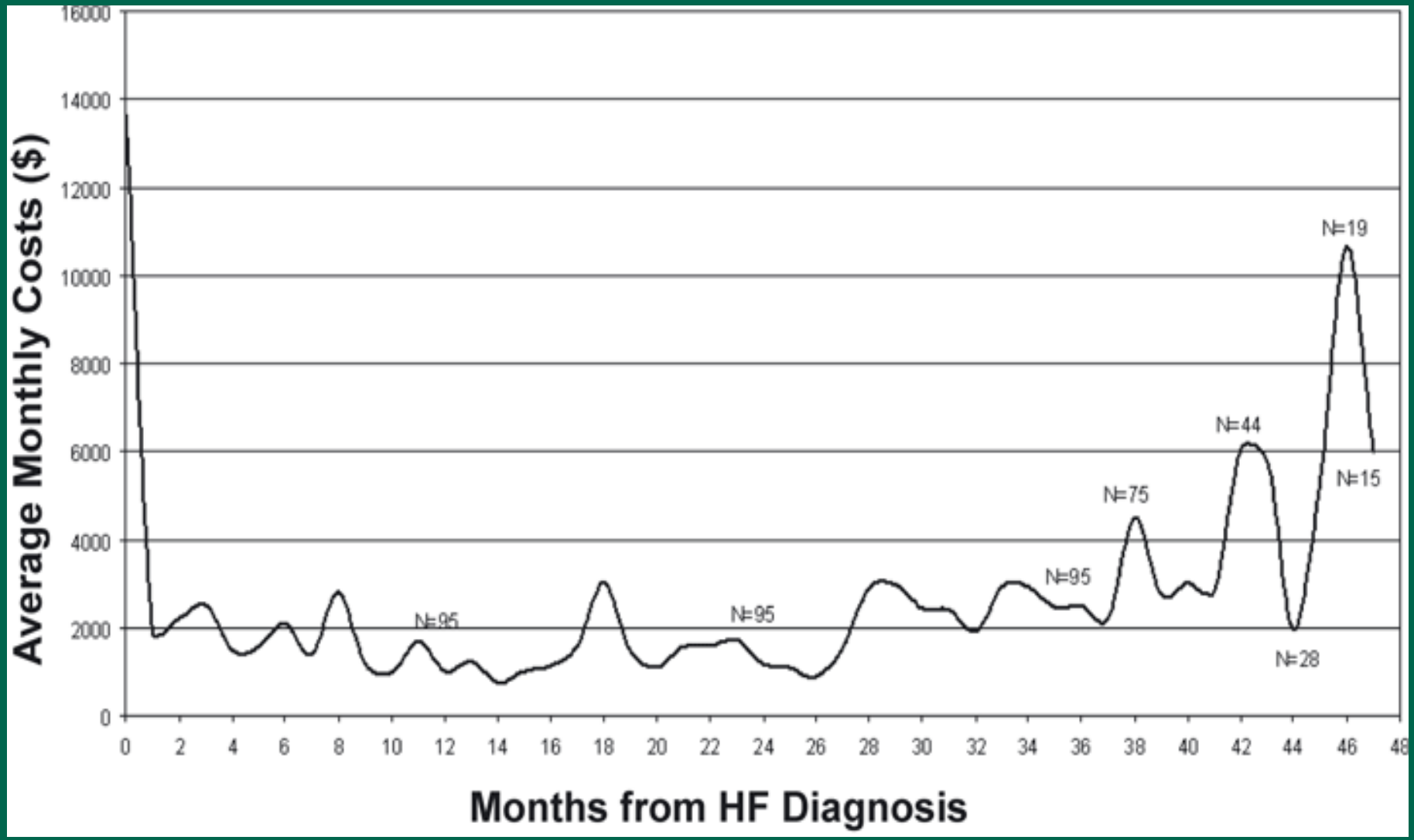
Impact of recurrent heart failure hospitalization on mortality. Median survival (50% mortality) with 95% confidence limits in patients with heart failure after each heart failure hospitalization. (From Setoguchi S, Stevenson LW, Schneeweiss S. Repeated hospitalizations predict mortality in the community population with heart failure. Am Heart J 2007;154(2):262;)

Figure 2



Median survival (50% mortality) and 95% confidence limits in patients with HF after each HF hospitalization.

Who Has Advanced Heart Failure? Definition and Epidemiology



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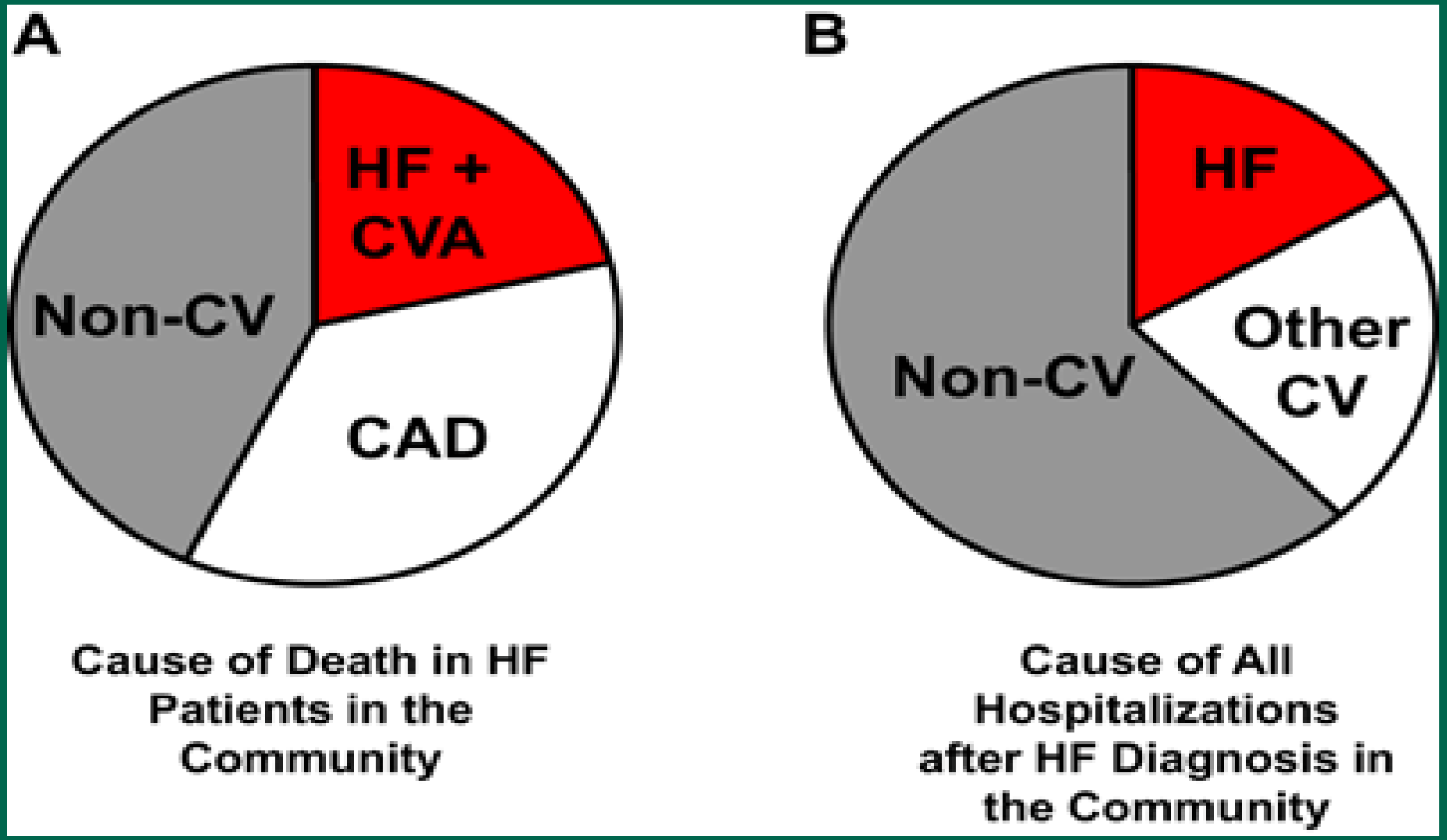

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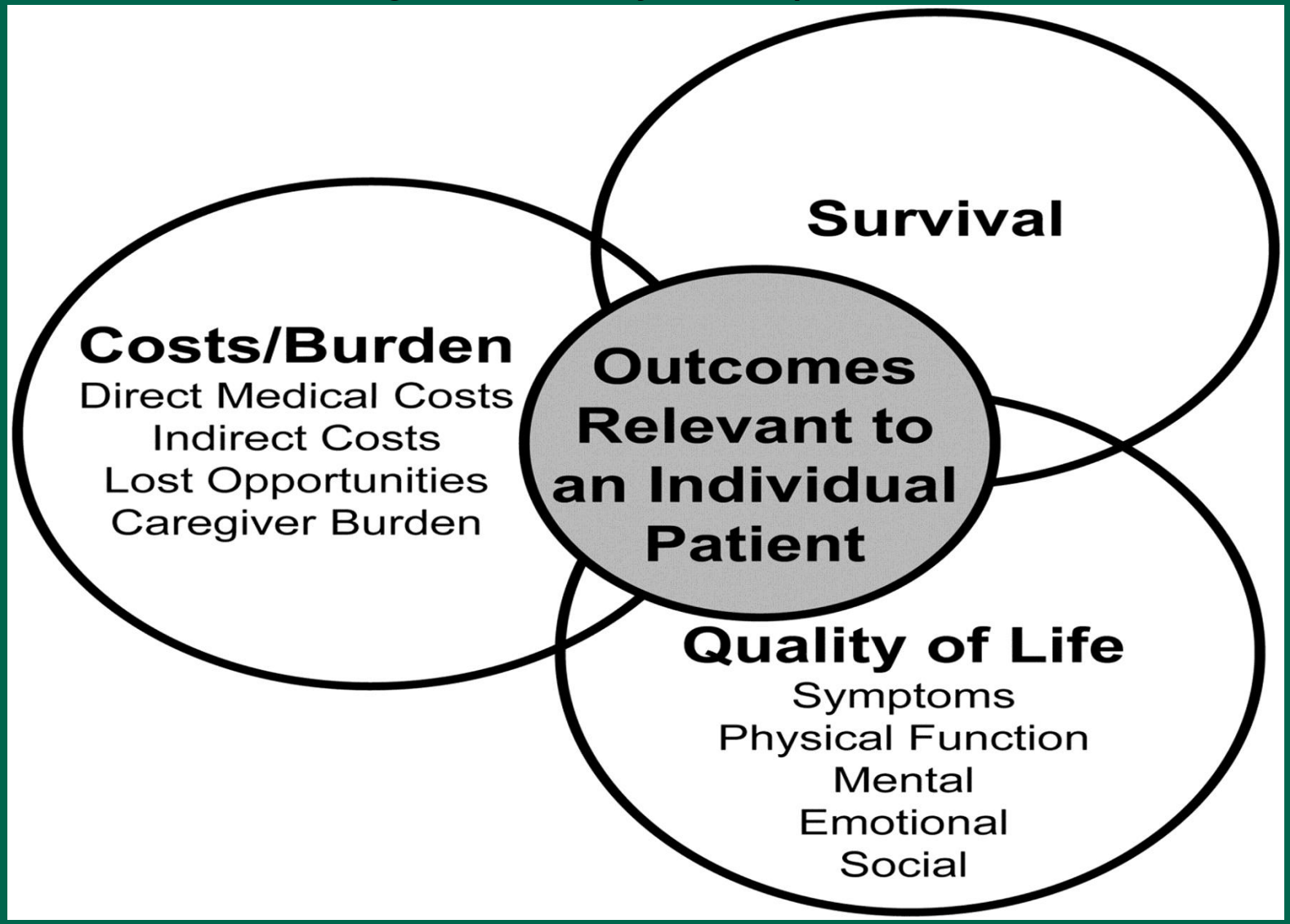
Prognosis is not only about expectations for survival.



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American Heart Association

Our study suggests that the number of HF hospitalizations may serve as an integrated measure of severity over time. Throughout the progression of HF, many decisions need to be individualized in light of all available information. The number of hospitalizations does not replace consideration of multiple factors such as age, cardiac and renal function, functional status, and comorbidities. However, the current study suggests that the number of HF hospitalizations may be useful to triage patients for the therapies that benefit most at different stages of the disease. Perhaps most importantly, repeated rehospitalizations for HF should trigger individualized discussion with the patient and family about the goals of care for the limited time remaining.

Prognostic Factors

Systolic blood pressure	High admission blood pressure is associated with lower mortal postdischarge Readmission rate: 30% at 90 d for both normotensive and hypertensive patient
CHD	Associated with 2-fold increase in postdischarge mortality compared with patients with primary cardiomyopathy. IN CHD patients there is an imcreased post discharge mortality in reponse to short term intravenous milrinone compared with placebo
Troponin release	30–70% of patients hospitalized with AHFS have detectable plasma levels of cardiac troponin. Associated with a 2-fold increase in post discharge mortality and a 3-fold increase in rehospitalization
BUN	BUN and BUN/creatinine ratio appear to be better prognostic indicators than creatinine Relatively minor increase in BUN is associated with 2- to 3-fold increase in postdischarge mortality
Hyponatremia	&25% of patients with AHFS have mild hyponatremia, associated with a 2- 3 fold increase in in-hospitality and post discharge mortality
Natriuretic peptides	Levels correlate weakly with elevated LV filling pressures. Increased levels are associated with higher postdischarge mortality and repeated hospitalizations
PCWP	Reduction in PCWP during hospitalization, but not an increase in the cardiac output, has been associated with improved postdischarge survival. Reduction in PCWP with agents such as mirinone and dobutamine is associated with worse outcomes
Functional capacity	6-minute walk test is emerging as an important predictor of postdischarge outcomes
Other prognostic factors	LVEF, anemia, diabetes mellitus, new sustained arrhythmias, and nonuse of neurohormonal antagonists

Precipitants for Decompensated Heart failure

- Nonadherence
  - Medication noncompliance
  - Dietary indiscretion
- Arrhythmias
  - Atrial fibrillation/atrial flutter
  - Ventricular tachycardia
- Infection
- Ischemia
- Valvular disease
  - Mitral regurgitation
  - Aortic stenosis
- Thyroid disease
- Renal failure
- Anemia
- Medications: TZD's, NSAIDs, prednisone, CCB's, antiarrhythmics
- Substance abuse/use cocaine, ETOH
- PE/COPD exacerbation/uncontrolled HTN/Overaggressive BB titration

Tailored Therapy in Advanced Heart Failure

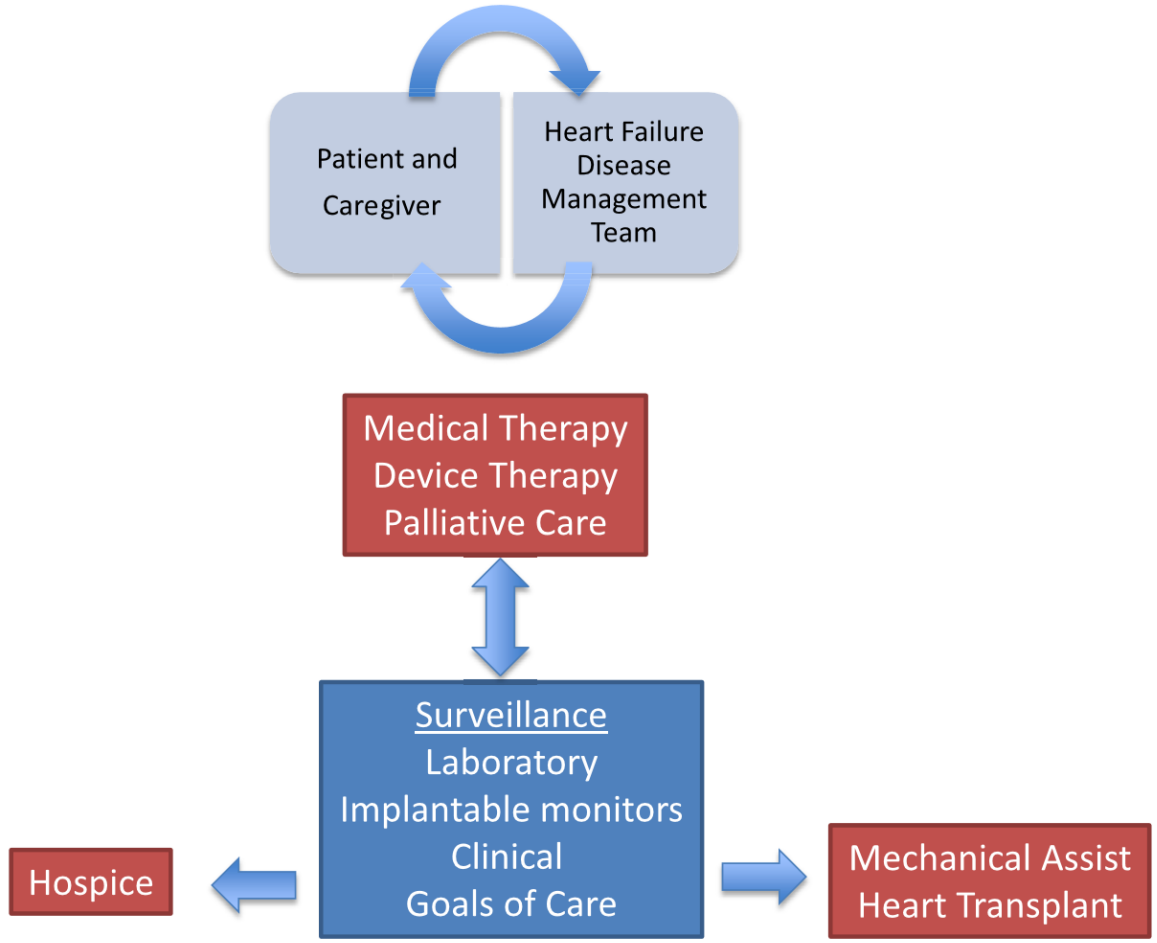


Fig. 1. Dyadic relationship between patient and HF team to engage in shared decision making and monitoring to inform advanced therapy options.

Heart failure medical trials enrolling New York Heart Association class III–IV patients

Trial	NYHA Class	Drug	Mortality Relative Risk Reduction (%)
CONSENSUS	IV	Enalapril	31
CIBIS II	III-IV	Bisoprolol	34
COPERNICUS	IV	Carvedilol	35
RALES	III-IV	Spironolactone	30
A-HeFT	III-IV	ISDN/Hydralazine	43

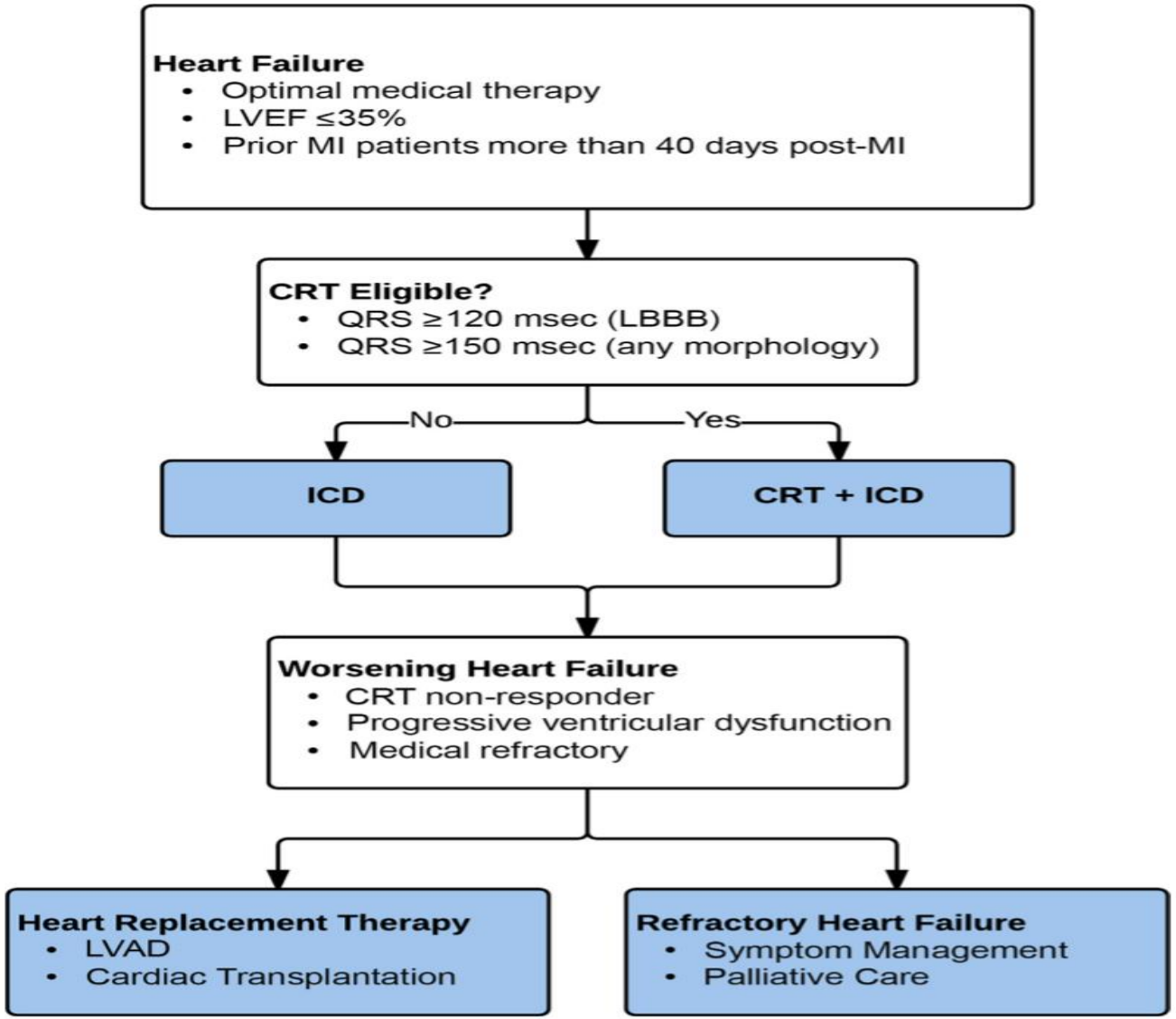


Fig. 1. Cardiac implanted electronic device algorithm in management of heart failure with reduced ejection fraction. Initial evaluation starts with identification of patients who benefit from implantable cardioverter defibrillator (ICD) for primary prevention. These patients should be on optimal medical therapy as part of their treatment strategy. A waiting period of 40 days applies for patients who have a reduced ejection fraction as a result of a myocardial infarction before they qualify for an ICD. Patients with wide QRS duration should be considered for a cardiac resynchronization therapy (CRT). LBBB, left bundle branch block; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; MI, myocardial infarction.

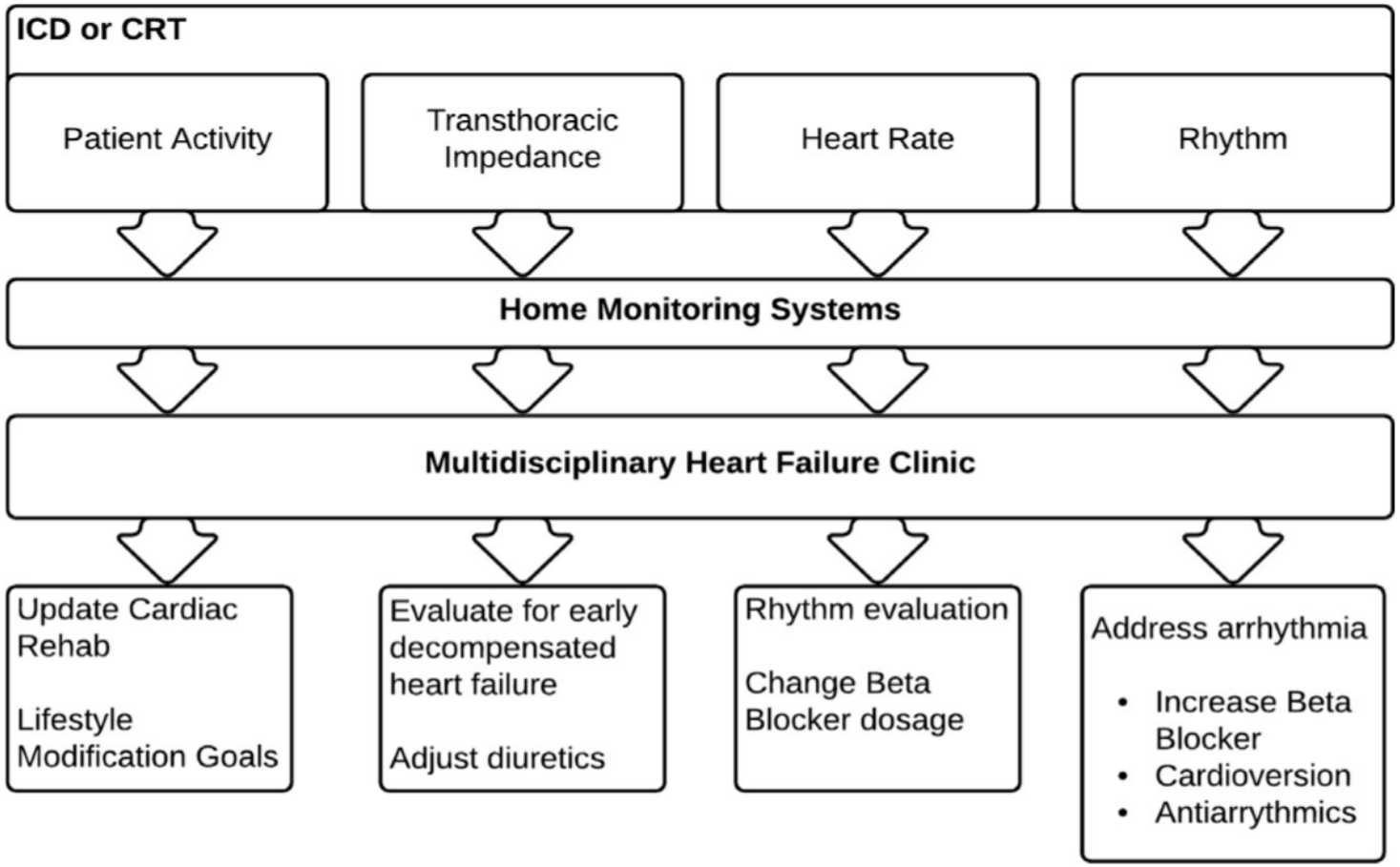


Fig. 4. Remote monitoring strategies for heart failure care. Home monitoring systems for implanted cardiac electrical devices provide remote transmission of rhythm analysis, baseline electrocardiograph, transthoracic impedance, and patient activity. Commercially available devices at home can provide patient data to upload to the Internet or can be web-connected directly. The flow of information can feed into a multidisciplinary heart failure clinic and can provide the opportunity to make adjustments to home medications (ie, beta-blockers or diuretics) or prompt a request for the patient to seek unscheduled medical evaluation. CRT, cardiac resynchronization therapy; ICD, implantable cardioverter-defibrillator.

Suggested hemodynamic goals in advanced HF

- Goal Hemodynamic Parameter
- Maintain blood pressure: SBP 80–90 mm Hg, MAP 65 mm Hg
- Decrease right-sided filling pressures: CVP <8 mm Hg
- Decrease left-sided filling pressures: PCW <16 mm Hg
- Decrease peripheral resistance: SVR 1000–1200 dyne/s/cm5 Decrease
- pulmonary resistance: Mean PA 25% reduction, PVR <3 WU, TPG <15 mm Hg
- Increase cardiac output: Cardiac index 2.2 L/min/m2

Selected Prognostic Models in Heart failure

	Key Covariates	Outcome
Ambulatory		
Heart Failure Survival Score23	Peak $\dot{V}o_2$, LVEF, serum sodium, mean BP, HR, ischemic etiology, QRS duration/morphology	All-cause mortality
Seattle Heart Failure Model22 (depts.washington.edu/shfm)[22a]	NYHA function class, ischemic etiology, diuretic dose, LVEF, SBP, sodium, hemoglobin, percent lymphocytes, uric acid, and cholesterol	All-cause mortality, urgent transplantation, or LVAD implantation
Hospitalized		
EVEREST Risk Model22	Age, diabetes, h/o stroke, h/o arrhythmia, β-blocker use, BUN, sodium, BNP, KCCQ scores	The combined end point of mortality or persistently poor quality of life (KCCQ <45) over the 6 mo after discharge
EFFECT29	Age, SBP, respiratory rate, sodium, hemoglobin, BUN, h/o CVA, h/o dementia, h/o COPD, h/o cirrhosis, h/o cancer	30-d and 1-y mortality
ADHERE28	BUN, SBP, serum creatinine	In-hospital mortality
ESCAPE Discharge Score31	BNP, cardiopulmonary resuscitation or mechanical ventilation during hospitalization, BUN, sodium, age >70 y, daily loop diuretic dose, lack of β-blocker, 6-min walk distance	6-mo mortality

Triggers for Formally Assessing Prognosis and Having Conversations About Goals of Care and Voluntary Advance Care Planning

Routine
"Annual Heart Failure Review" with a scheduled clinic visit
Event-driven "milestones" that should prompt reassessment
Increased symptom burden and/or decreased quality of life
Significant decrease in functional capacity
Loss of ADLs
Falls
Transition in living situation (independent to assisted or LTC)
Worsening heart failure prompting hospitalization, particularly if recurrent(57)
Serial increases of maintenance diuretic dose
Symptomatic hypotension, azotemia, or refractory fluid retention necessitating neurohormonal medication underdosing or withdrawal(58)
Circulatory-renal limitations to ACEI/ARB
Decrease or discontinuation of β-blockers because of hypotension
First or recurrent ICD shock for VT/VF(59)
Initiation of intravenous inotropic support
Consideration of renal replacement therapy
Other important comorbidities: new cancer, etc
Major "life events": death of a spouse

Indicators of advanced heart failure that should trigger consideration of referral for evaluation of advanced therapies

- Need for intravenous inotropic therapy for symptomatic relief or to maintain end-organ function
- Peak VO2 <14 mL/kg/min or less than 50% predicted
- 6 minute walk distance less than 300 m
- 2 heart failure hospitalizations in 12 months
- Worsening right heart failure and secondary pulmonary hypertension
- Diuretic refractoriness associated with worsening renal function
- Circulatory-renal limitations to RAAS inhibition or beta-blocker therapy
- Progressive/persistent NYHA functional class III-IV symptoms
- Increased 1-year mortality (eg, >20%–25%) predicted by heart failure survival models
- Progressive renal or hepatic end-organ dysfunction
- Persistent hyponatremia (serum sodium <134 mEq/L)
- Cardiac cachexia
- Inability to perform activities of daily living

Abbreviations: NYHA, New York Heart Association; RAAS, renin angiotensin aldosterone system; VO2, oxygen uptake. Adapted from Stewart GC, Givertz MM. Mechanical circulatory support for advanced heart failure: patients and technology in evolution. Circulation 2012;125:1311; with permission.

HF clinic

- Disease Management Clinic
- Multidisciplinary team
- Work up of advanced HF patients
- CPET
- Amyloid clinic
- CardioMems

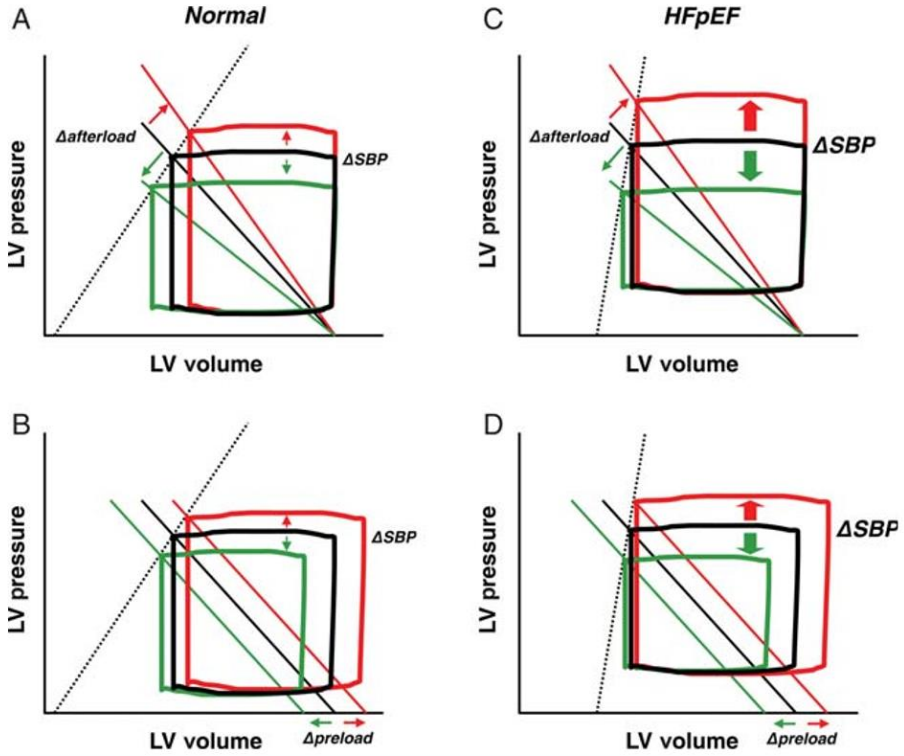
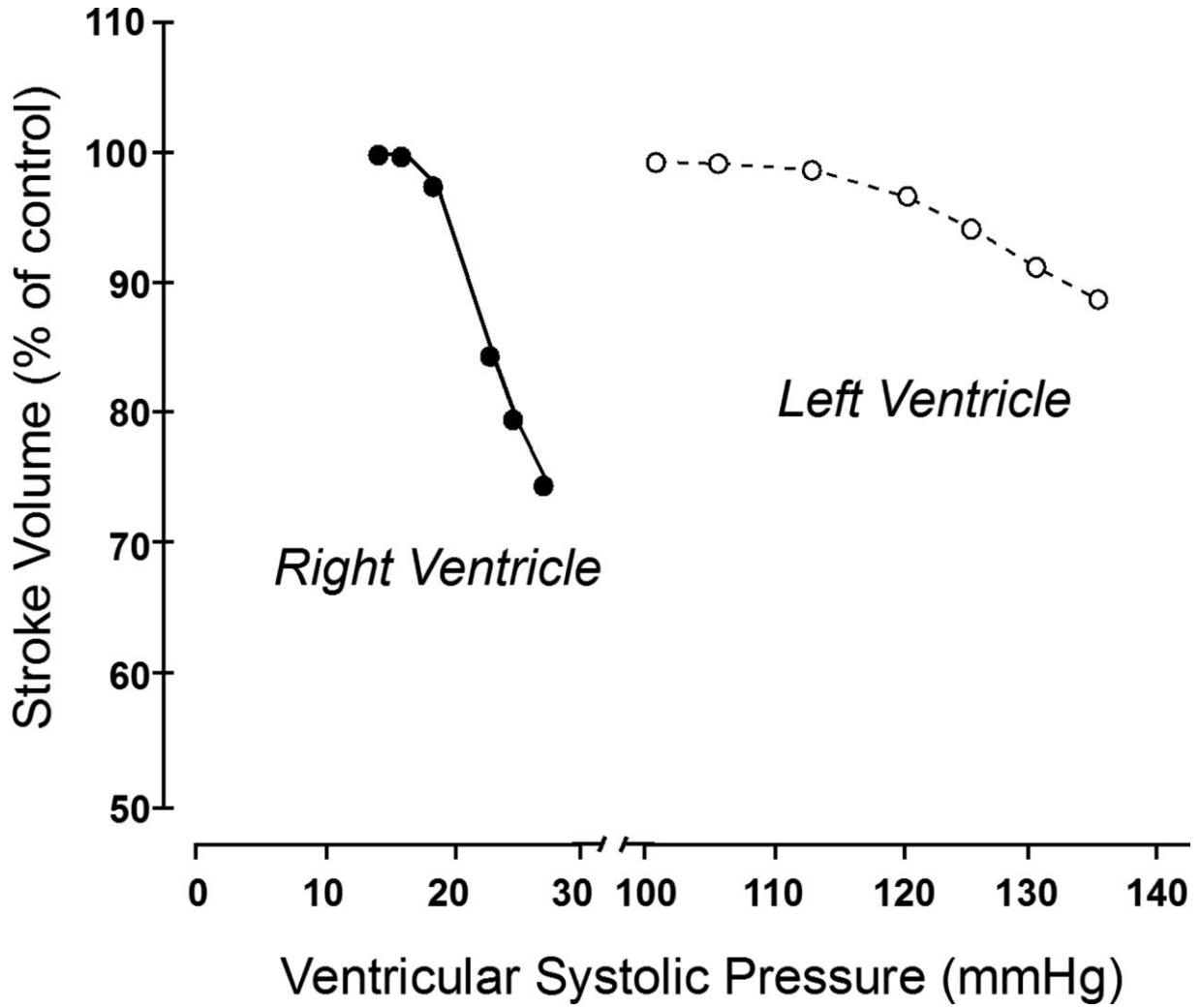


Figure 3 Compared with normal controls (*A* and *B*), the slope of the end-systolic pressure–volume relationship (end-systolic elastance; Ees, dotted lines) is increased in heart failure with preserved ejection fraction (HFpEF) (*C* and *D*). This leads to exaggerated increases and decreases in blood pressure for the same change in afterload (A and C) or preload (B and D) in HFpEF, accounting for the greater predilection for hypertensive crisis and/or hypotension and azotemia with over-diuresis or overly vigorous vasodilation.

Enhanced afterload sensitivity of the right ventricle compared with the left.



Marco Guazzi, and Barry A. Borlaug Circulation. 2012;126:975-990