Heart Failure

Managing a Complex Clinical Syndrome
Sixth Annual APRN CE Conference 2019

Ascension

Objectives

1. Identify and discuss the pathophysiology and treatment modalities for heart failure.
2. Review the clinical practice guidelines for the heart failure patient; including ace-inhibitors, beta blockers, diuretics, and new pharmacological options.

Heart Failure Epidemiology

Lifetime Risk	Prevalence	Incidence	Mortality	Hospital Discharges	Cost
20% of Americans ≥ 40 years	~5.7 million	Rose by 800,000 over 5 years	50% within 5 years 1 yr ~ 30%	> 1,000,000 annually	> $30.7 billion annually

- Contributing cause for one in nine deaths
- 1 month readmission rate of 25%
  - 50% at 6 months
- Over half of the total cost of HF care in the US is spent on hospitalizations.

A complex clinical syndrome

Resulting in any structural or functional impairment of ventricular filling or ejection of blood

Disorders of the

- Heart valves and great vessels
- Pericardium, myocardium, endocardium
  - Impaired left ventricular myocardial function

Risk Factors

Hypertension

- Most important modifiable risk factor in the US

Diabetes Mellitus

- Related to obesity and insulin resistance

Metabolic Syndrome

- Any 3 of the following: abdominal adiposity, hypertriglyceridemia, low high-density lipoprotein, hypertension and fasting hyperglycemia

Atherosclerotic Disease

- Coronary, cerebral or peripheral

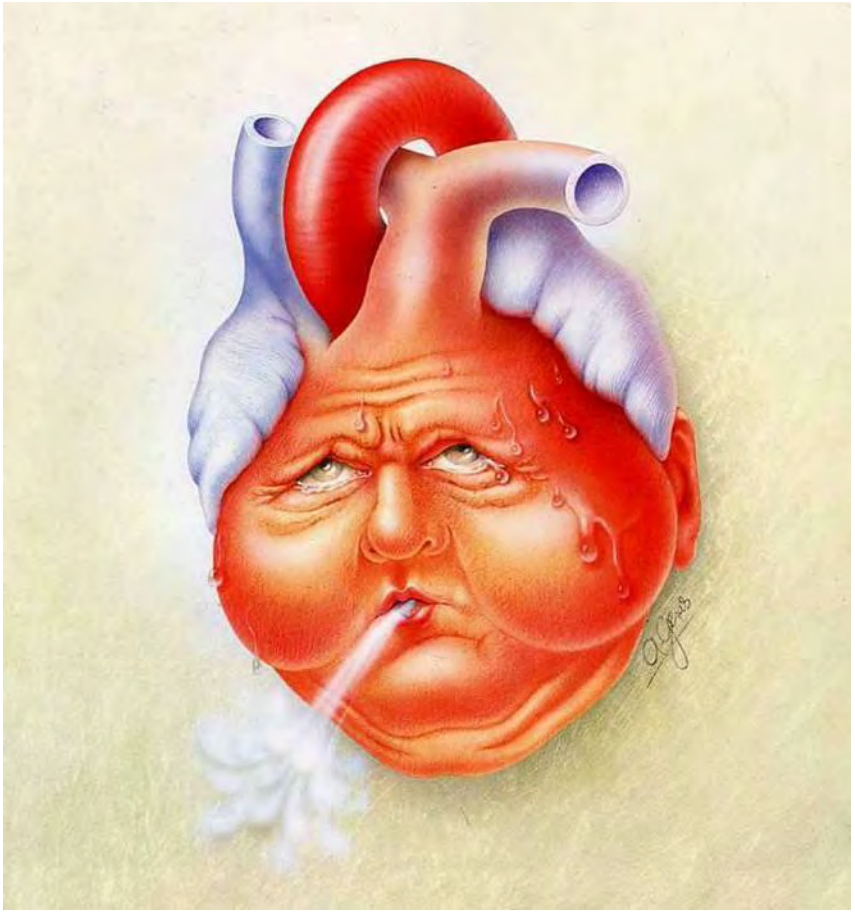
Definition of Heart Failure

Classifications	Ejection Fraction	Description
Heart Failure with Reduced Ejection Fraction (HFrEF)	≤ 40%	• Systolic HF • Reduced Left Ventricle contractility • Diminished ejection fraction
Heart Failure with Preserved Ejection Fraction (HFpEF)	≥ 50%	• Diastolic HF • Stiffing of the ventricle • Problem with ventricular filling or relaxation
HFpEF Borderline	41 to 49%	• Borderline or intermediate group
HFpEF Improved	≥ 40%	• Previously had HFrEF

HFrEF

40-50% of HF population

- Decreased EF ≤ 40%
  - Impaired wall motion and ejection
  - Dilated left ventricle
- Coronary artery disease is cause in 2/3^{rds} of the patients

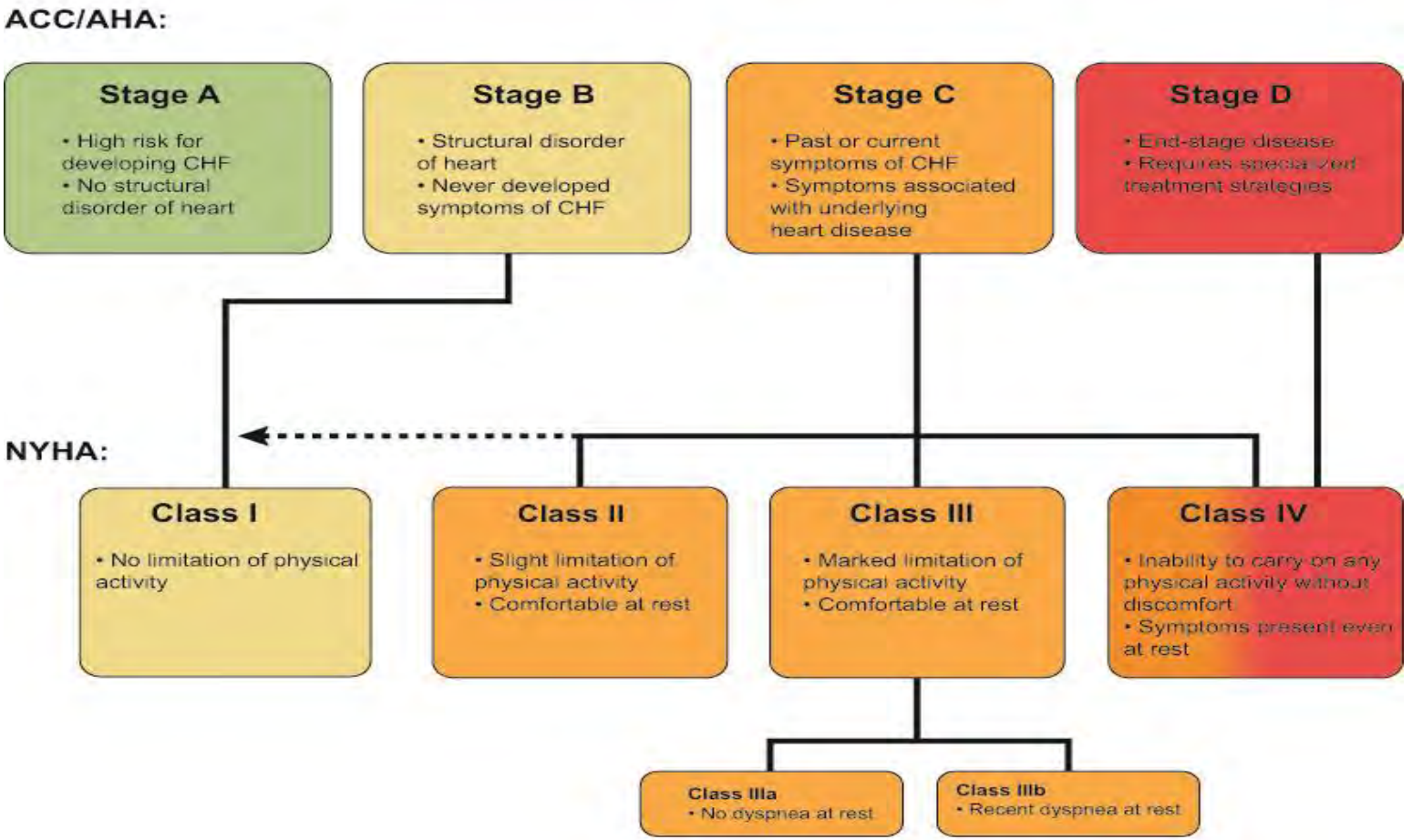


HFpEF

50% of HF population

- Filling impairment
  - Normal or increased LVEF
- Caused by or related to
  - Hypertension
  - Obesity
  - Sleep apnea
  - Atrial fibrillation
  - Anemia
  - Diabetes

NYHA Class vs. ACC/AHA Stages



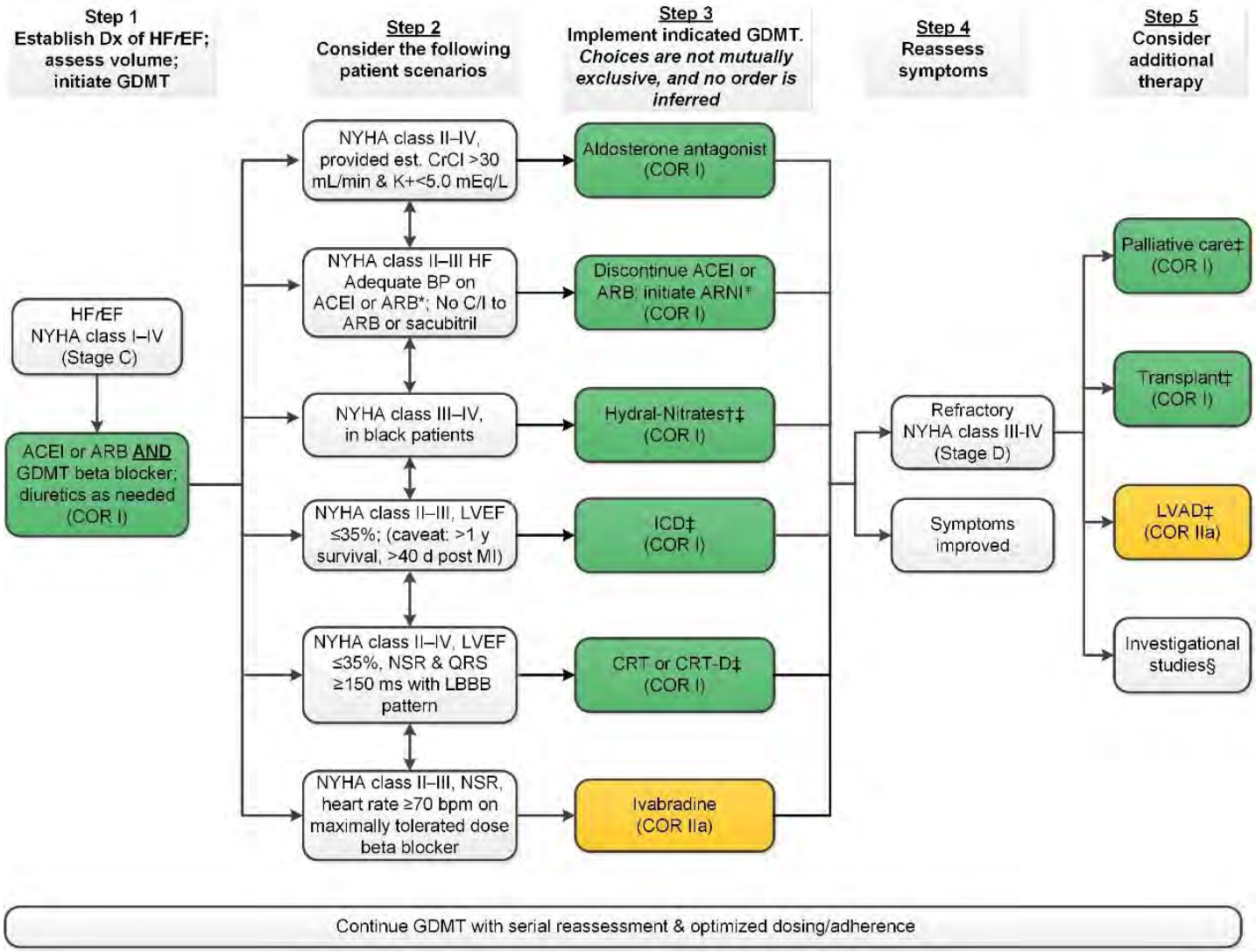
Goals & Treatment Strategies

Stage	Goal	Treatments	Mortality Benefit
A	• Heart healthy lifestyle • Prevent vascular, coronary disease • Prevent LV structural abnormalities	• HTN screening, management • ACE-I or ARB in appropriate patients with vascular disease or diabetes • Statins per recommendations • Rick factor modification	Benefit!!
B	• Structural heart disease without s/s of HF	• Medications to prevent ventricular remodeling • ICD • Revascularization • Valvular surgery	Benefit!

Goals & Treatment Strategies

Stage	Goals	Treatments	Mortality Benefit
C	• Control symptoms • Patient education • Prevent hospitalization • Prevent mortality	• Guideline directed medication management • CRT- ICD • Revascularization or valvular surgery • Address co-morbidities • Palliative care partnering	Hope to reduce mortality, hospitalizations
D	• Control symptoms • Improve quality of life • Prevent hospitalization	• Advanced care measures • Palliative care and hospice • ICD deactivation	Quality of life

2017 update for Stages C & D



Evaluation for HF

Thorough history and physical

- Serial assessment of weight, jugular venous pressure, peripheral edema, orthopnea
- 3-generational family history

12 Lead ECG

2D echo with doppler

Chest x-ray

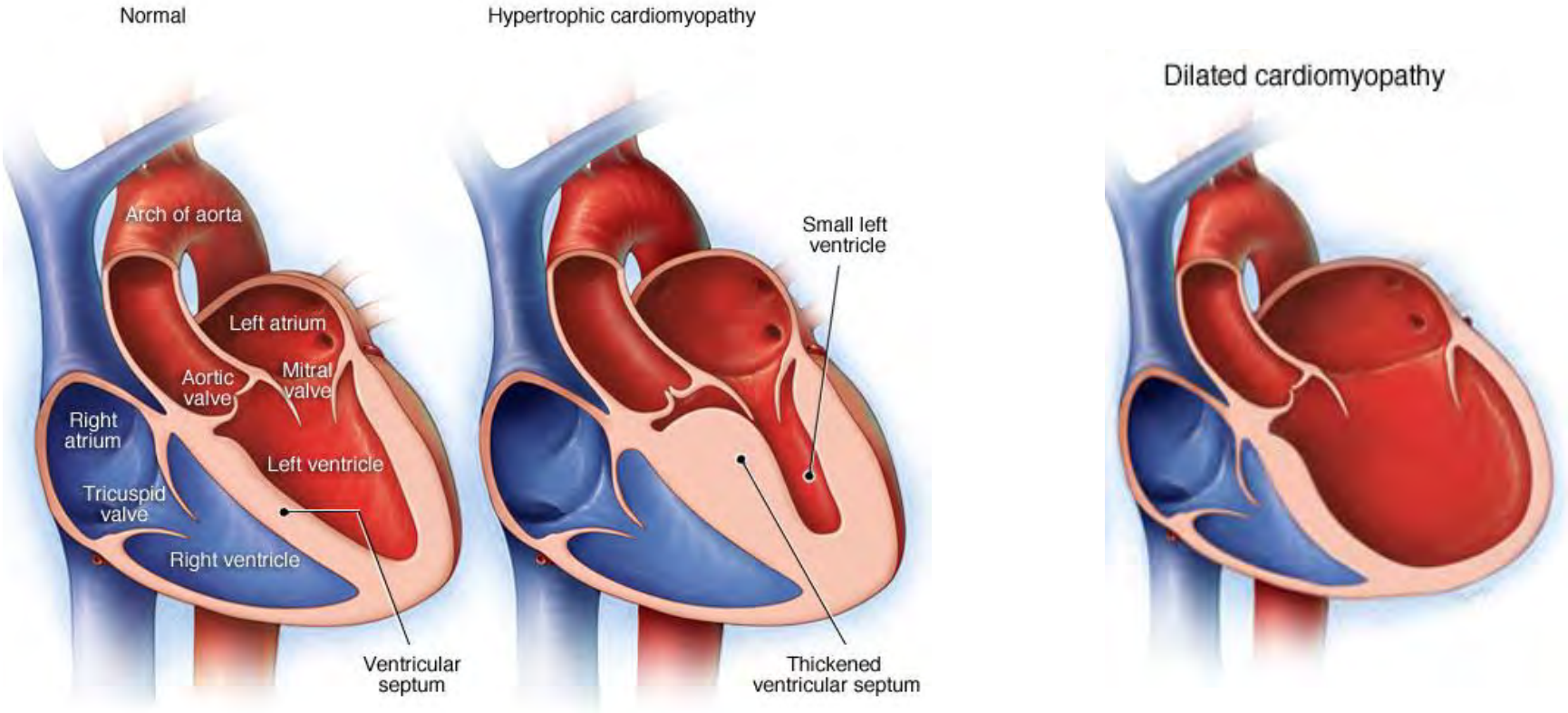
Laboratory

- CBC, UA, electrolytes, calcium and magnesium, BUN, creatinine, glucose, lipid profile, liver function, TSH
- BNP

Later in selected patients

- Cardiac viability, right heart cath, left heart cath, endomyocardial biopsy

Cardiomyopathy



Dilated Cardiomyopathy

DCM is characterized by ventricular dilation and decreased myocardial contractility

- Ischemic
- Non-ischemia
  - Volume or pressure overload
    - Hypertension
    - Valvular heart disease

Idiopathic familial DCM

Endocrine and Metabolic CM

- Obesity
- Diabetic CM
- Thyroid Disease
- Acromegaly and Growth Hormone Deficiency

DCM

Toxic DCM
- Alcohol, Cocaine, Cardiotoxicity r/t cancer therapies

Anabolic steroids
- Other athletic performance enhancements

Ephedra

Thiamine deficiency

L-carnitine deficiency

Peri-partum CM

Inflammation
- Myocarditis, HIV-assoc

Non-infectious
- Hypersensitivity myocarditis
- Systemic Lupus

Takotsubo CM

Hypertrophic Cardiomyopathy

Previously known as

- Hypertrophic obstructive cardiomyopathy – HCOM
- Idiopathic hypertrophic subaortic stenosis – IHSS

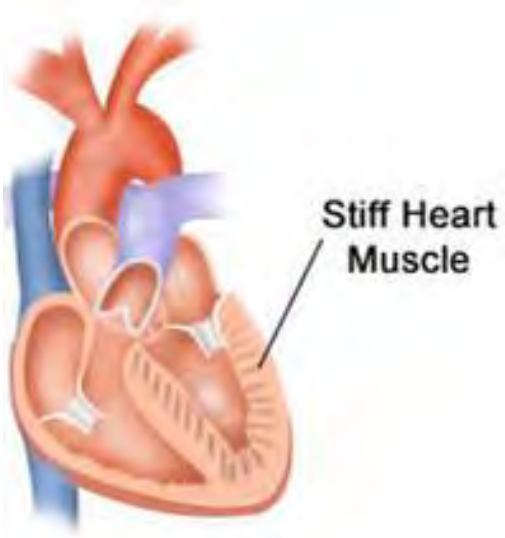
Number one cause of sudden cardiac death in young athletes (1-2%).

Inheritance is primarily autosomal dominant.

ECG changes

- Left ventricular hypertrophy pattern
  - Tall R waves
  - Large precordial voltages

Restrictive Cardiomyopathy



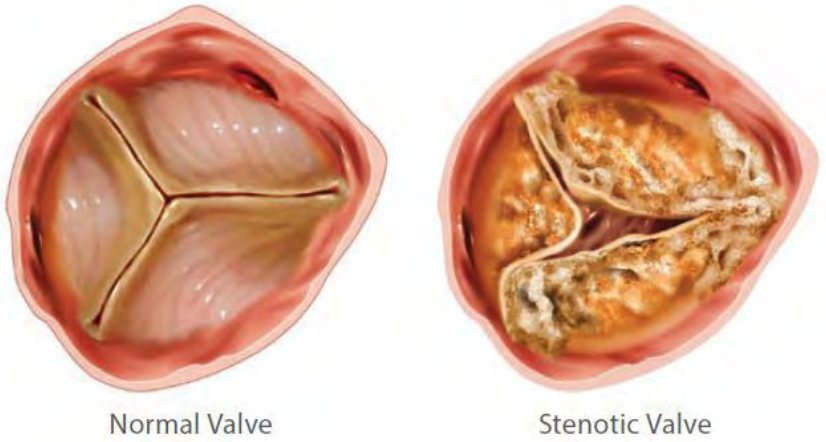
Heart does not relax normally

Causes

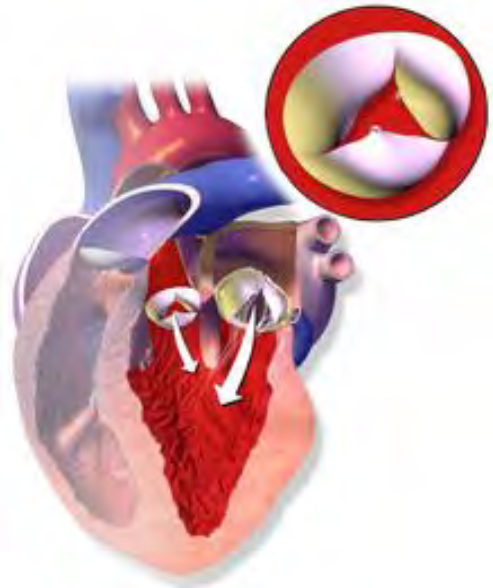
- Scarring after radiation and chemotherapy
- Amyloidosis
- Sarcoidosis
- Scleroderma
- Iron overload

Valvular Disease

- Aortic stenosis
- Aortic insufficiency/ regurgitation
- Mitral regurgitation



Mitral valve with degenerative mitral regurgitation



BNP – B type Natriuretic Peptide

Released by the cardiomyocytes with myocardial stretch.

Release modulated by calcium ions.

Poor prognosis if BNP stays chronically elevated.

- Serial assessment to guide GDMT is not recommended

Causes for elevated BNP levels

Cardiac

- Heart Failure, including right ventricle syndromes
- Acute coronary syndrome
- Heart muscle disease, including left ventricular hypertrophy
- Valvular heart disease
- Pericardial disease
- Atrial fibrillation
- Myocarditis
- Cardiac surgery
- Cardioversion

Non-cardiac

- Advancing age
- Anemia
- Renal dysfunction or failure
- Pulmonary causes; obstructive sleep apnea, severe pneumonia, pulmonary HTN
- Critical illness
- Bacterial sepsis
- Severe burns
- Toxic-metabolic insults

BNP or NT-pro BNP

Both affected by renal insufficiency

Ability to diagnose decompensated heart failure is the same

Differences are dwarfed by similarities

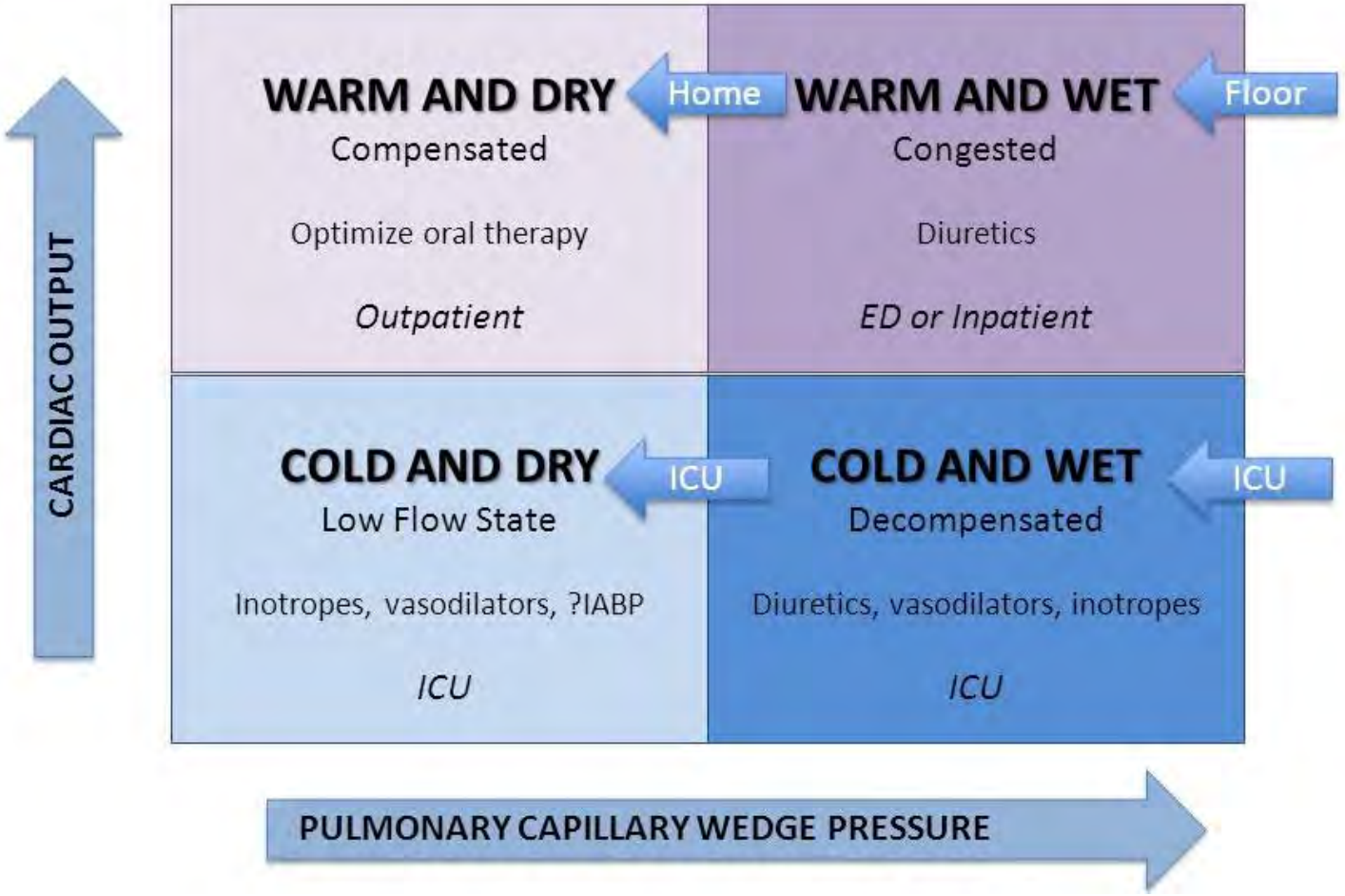
BNP

- B-natriuretic or brain natriuretic peptide
- Substrate for neprilysin
  - ARNI increases BNP levels

NT-proBNP

- N-terminal prohormone of BNP with a 76 amino acid N-terminal inactive protein

Warm-Cold, Wet-Dry



Recommendations

1. Treat and reduce risk factors
   a. Follow clinical practice guidelines for AMI, ACS, hypertension
2. Re-vascularize ischemic myocardium
3. Improve structural function
4. Optimize GDMT – guideline directed medical therapy

Re-vascularize and Functional Options

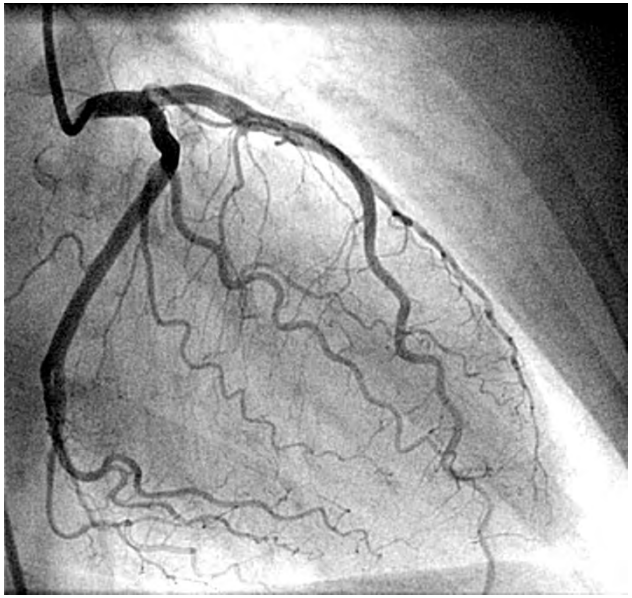
- Percutaneous Coronary Intervention
- Coronary revascularization (CABG)

- Transcatheter aortic valve replacement (TAVR)
- Mitral valve repair or replacement
  - Repair any valvular disease
- Transcatheter mitral valve implantation

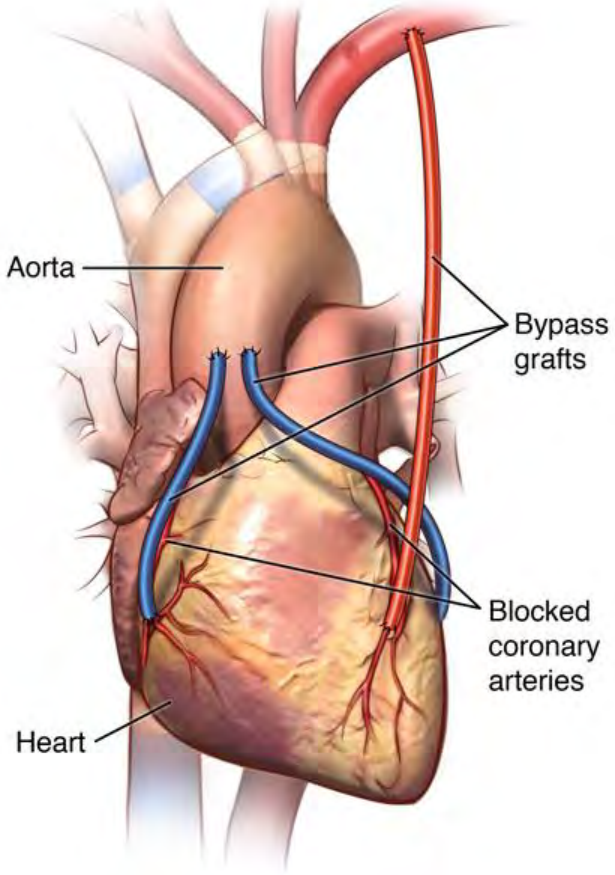
Percutaneous Coronary Intervention - PCI

Left heart catheterization with

- Angioplasty
- Atherectomy
- Coronary stenting
  - Bare metal (BMS)
  - Drug eluting (DES)

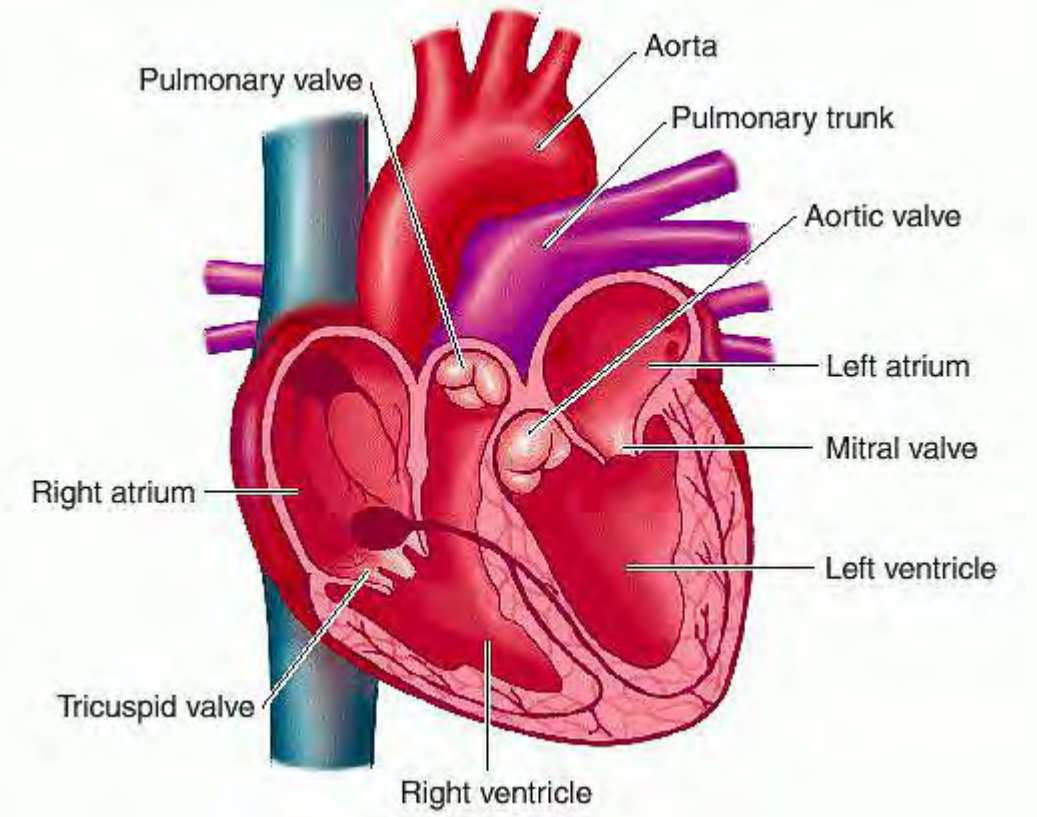


Coronary Artery Bypass Grafting



- Internal (thoracic) mammary artery
  - LIMA or RIMA
- Saphenous vein graft
  - Anastomosis aortic root, distal to obstruction
    - Open harvest technique
    - Endoscopic vessel harvest technique
- Radial artery – rare
  - From non-dominant hand

Valve Disease Options



Surgical repair or replacement

Structural cardiology procedures

Prosthetic Heart Valves

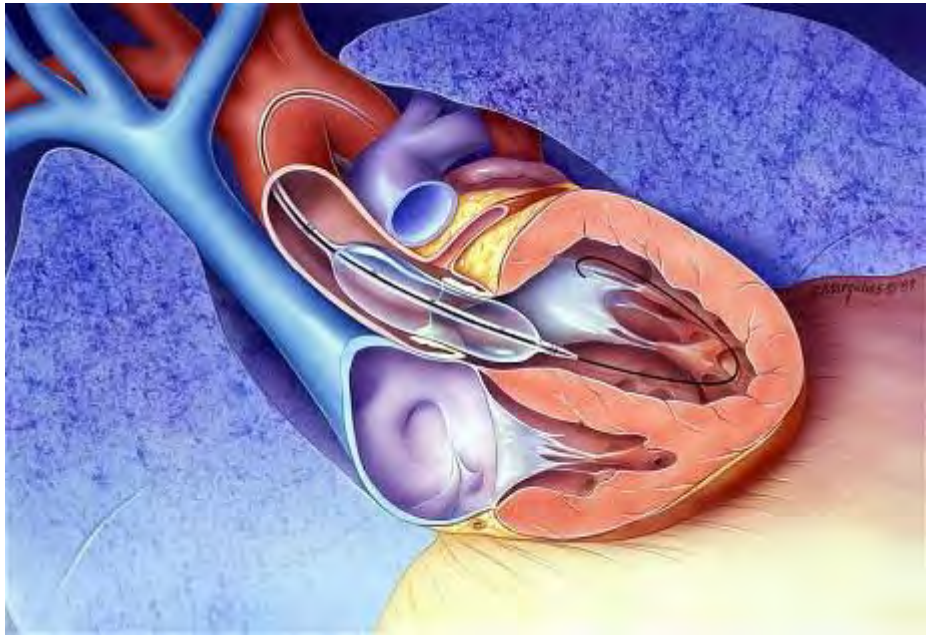
Biologic

- Lasts 8-10 years
- No anticoagulation
- No Click

Mechanical

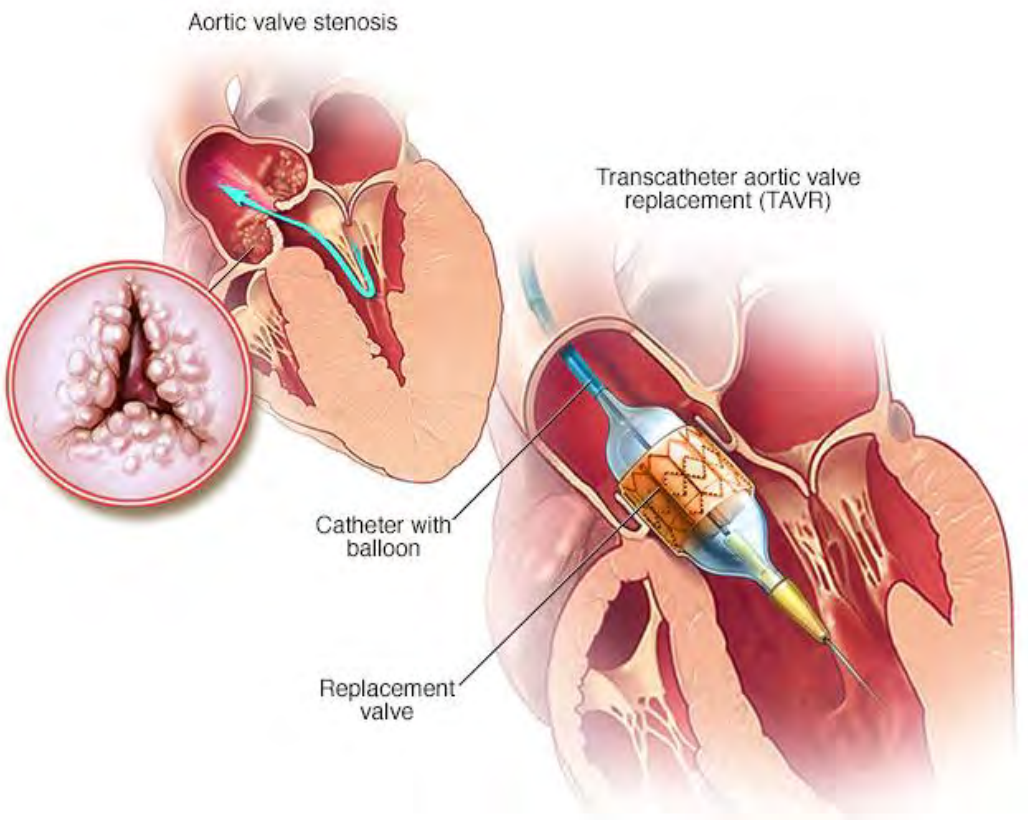
- Lasts > 20 years
- Lifelong anticoagulation
- Click

Balloon Aortic Valvuloplasty



- Performed in HCL or Surgery
  - Wire across the stenotic valve
  - Rapid pace to decrease stroke volume
  - Balloon stenotic valve
  - Alone or with TAVR

Transcatheter Aortic Valve Replacement - TAVR



Performed in Hybrid OR

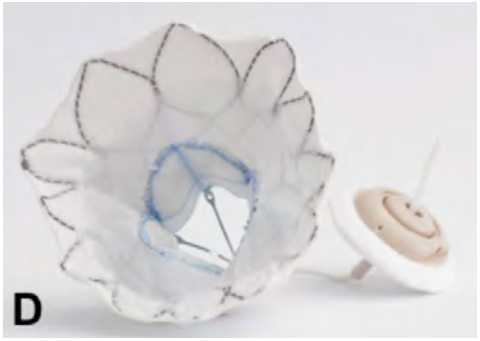
- Balloon valvuloplasty
- Percutaneous deployed artificial valve

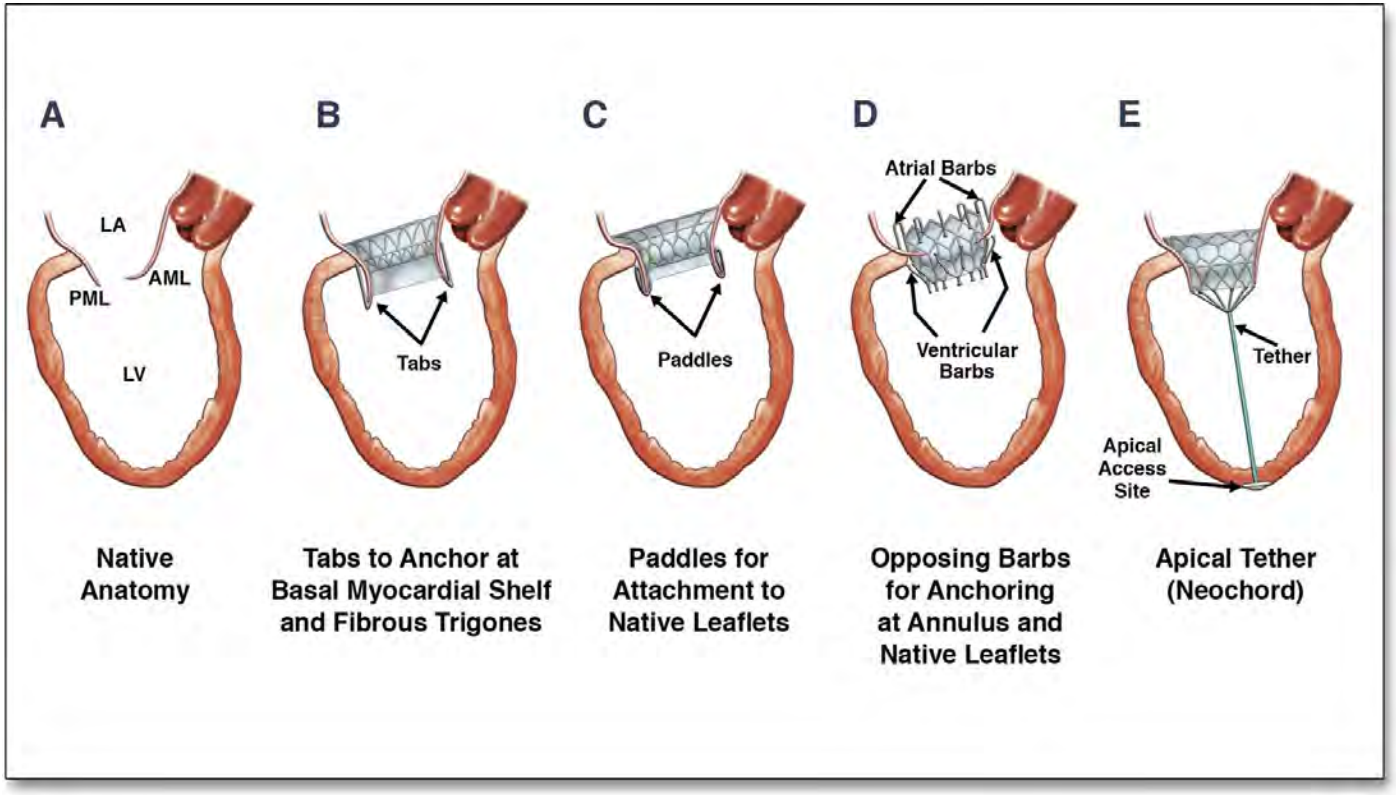
MitraClip

Minimally invasive procedure to reduce severe mitral valve regurgitation in high risk patients.

Transcatheter Mitral Valve Implantation - TMVI

Tendyne by Abbott

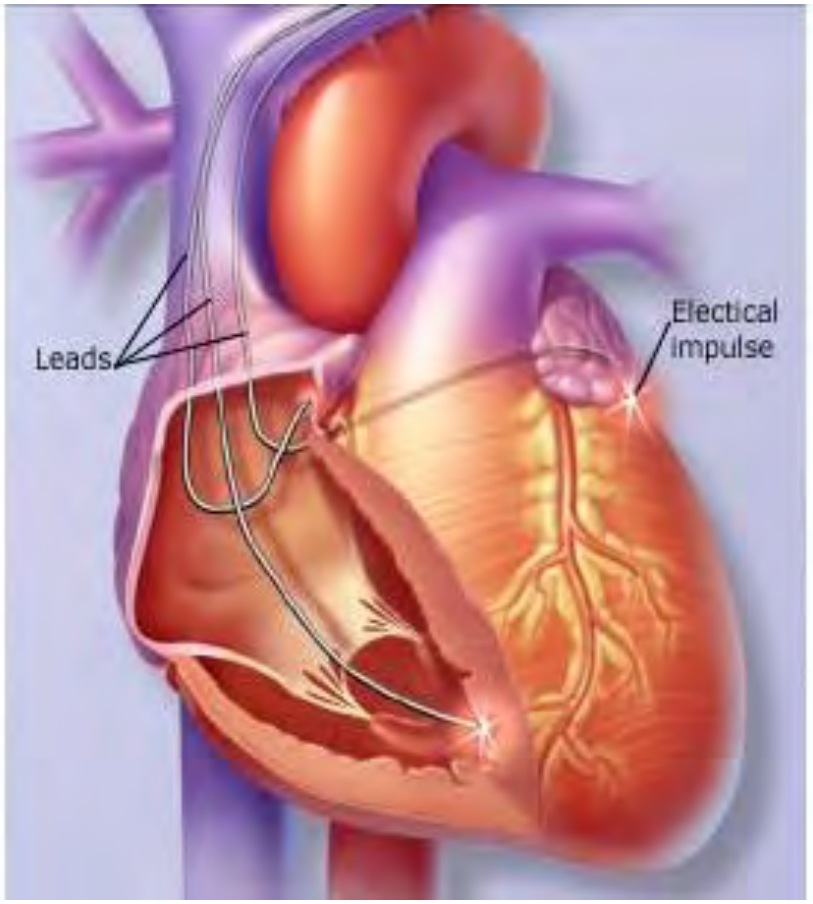




CRT- BiVentricular Pacing

Cardiac Synchronization Therapy

- Biventricular pacing
- 3 leads – right atrium, right ventricle, left ventricle
- Combo CRT-D
  - Pacemaker with ICD
  - Right ventricular lead paces and defibrillates



Life Vest & Cardiac Devices

- Life Vest
  - Often prelude to an implantable device
  - Non-invasive and continuous monitor
  - 98% first shock success rate

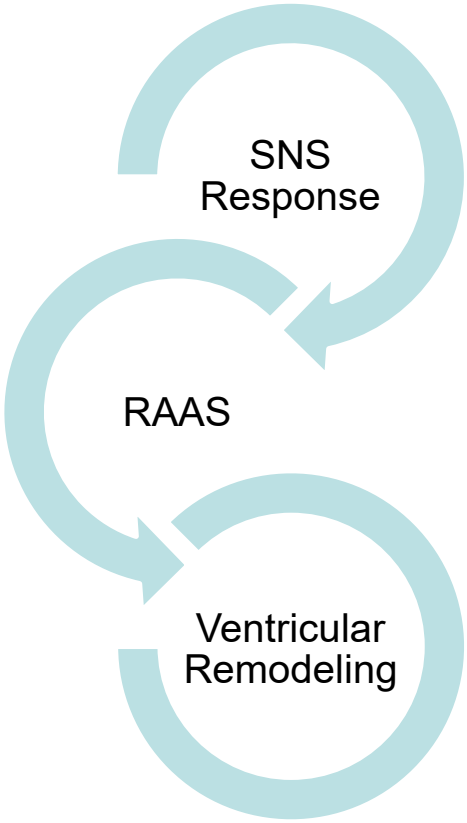
- Implantable Cardioverter Defibrillator
  - CABG or PCI must wait 3 months
  - AMI must wait 40 days
  - EF ≤ 35%, wide QRS

Heart Failure Clinical Practice Guidelines

Medical management more complex.

- Ejection Fraction (EF%) must be documented.
  - New or documentation of known, or when will be performed
- Discharged on
  - Specific Beta Blocker
  - ACE-I or ARB therapy for HFrEF, EF (ejection fraction) ≤ 40%, left ventricular systolic dysfunction
- Educated on
  - Daily weights
  - Fluid limitations
  - Diet
  - Signs and symptoms
  - Follow up appointment

Neurohormonal Response



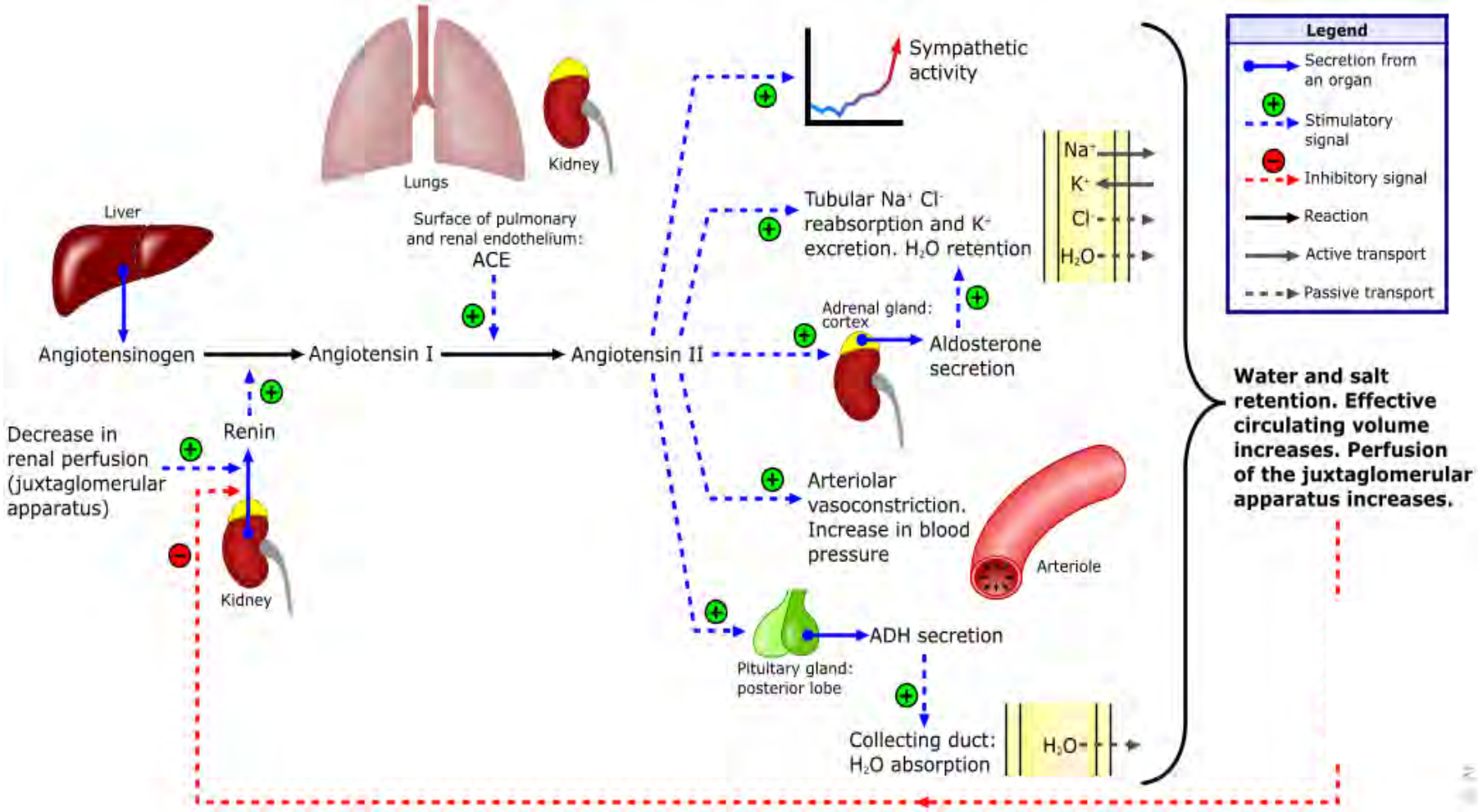
First responder good.

Over time, not so good.

Sympathetic Nervous System

- Increase in circulating catecholamines

Renin-Angiotensin-Aldosterone System



ACE-I & ARBs

ACE-I

Lisinopril – Prinivil, Zestril
Benazepril – Lotensin
Captopril – Capoten
Ramipril - Altace
Enalapril – Vasotec
Fosinopril – Monopril

Adverse effect – cough, angioedema, hyperkalemia
Watch renal function.

ARB

Losartan – Cozaar
Valsartan – Diovan
Candesartan- Atacand
Irbesartan – Avapro

Tend not to have as many adverse effects. Cough rarely seen.

ACE-Is and ARBs

ACE Inhibitors

Drug	Initial Daily Dose	Maximum Dose
Captopril	6.25 mg TID	50 mg TID
Enalapril	2.5 mg BID	10-20 BID
Fosinopril	5-10 mg daily	40 mg daily
Lisinopril	2.5-5 mg daily	20-40 mg daily
Ramipril	1.25-2.5 daily	10 mg daily

ARBs

Drug	Initial Daily Dose	Maximum Dose
Losartan	25-50 mg daily	50-150 mg daily
Valsartan	20-40 mg BID	160 mg BID
Candesartan	4-8 mg daily	32 mg daily

Angioedema

Types

Histamine-mediated

Bradykinin-mediated

- Idiopathic angioedema
- Allergic angioedema
- Food, insects
- Hereditary angioedema
- Acquired angioedema – C1 inhibitor deficiency or dysfunction
- ACE-I induced

ACE-I block the degradation of bradykinin by the angiotensin-converting enzyme

- Increased levels of bradykinin and other kinins
- Leads to vasodilation and more tissue permeability

Treatment for angioedema

- Corticosteroids
- Antihistamines
- Epinephrine

- Kallikrein receptor blocker- ecallantide
- Bradykinin receptor antagonist - icatibant

1. Airway management
2. Discontinue offending agent
3. Medications to counter
4. Fresh frozen plasma- contains kininase II which is similar to ACE. Catalyzes to decrease excessive bradykinin

Beta Blockers for HFrEF

- Reduce sympathetic activity (catecholamine release)
- Inhibit the release of renin by the kidneys
- Reduce myocardial workload and oxygen demand
- Reduce supraventricular and malignant ventricular arrhythmias

Metoprolol succinate – Toprol XL, metoprolol succinate CR

Carvedilol – Coreg

Bisoprolol - Zebeta

Only three BBs have been shown in studies to help in heart failure.

Adverse Effects for BB

- Bradycardia and heart blocks
- Hypotension
- Erectile dysfunction
- Fatigue

The issue of fatigue.

- Education initial response
- Address other factors
  - Over diuresis
  - Sleep apnea
  - Depression

Beta Blockers for HF

Drug	Initial Daily Dose	Maximum Dose
Carvedilol	3.125 mg BID	50 mg BID
Carvedilol CR	10 mg daily	80 mg daily
Metoprolol succinate extended release	12.5-25 mg daily	200 mg daily
Bisoprolol	1.25 mg daily	10 mg daily

Tip

OK to initiate either, yet sometimes easier to work with ACE-I first.

Then as blood pressure is ok, add in beta blocker.

More Medications

- Diuresis
  - Challenge is finding the perfect balance
  - Patient to call if up > 2 pounds over night or > 5 pounds in one week – from baseline
- Aldosterone antagonist
  - Spironolactone
- Digoxin mixed reviews
- Avoid NSAIDs
- Hydralazine/nitrate
  - Hydralazine and isosorbide dinitrate
  - Alternative for ACE-I / ARBs in some patients
- Chronic anticoagulation for permanent or persistent atrial fibrillation
- Calcium Channel Blockers are not recommended in HFrEF

Diuretics

Start with loop diuretic

- Thiazide diuretic may be added later

Diuretic resistance

- High sodium levels, NSAIDS, severe renal impairment, renal hypoperfusion

Strategies

- Change the loop diuretic
- IV instead of PO

Equivalents

- Bumetanide (Bumex) 1 mg
  - Max 10 mg / day
- Torsemide (Demadex) 20 mg
  - Max 200 mg / day
- Furosemide (Lasix) 40 mg
  - Max 600 mg / day
  - BID dosing when GFR is low

Diuretics and NSAIDs

Don’t take together.

NSAIDs

- Inhibit renal prostaglandins – I_2 and E_2
- Increase sodium and water retention
- Blunt the response to diuretics
- Lose nitric oxide vasodilation

Thiazide Diuretics

Inhibits reabsorption of sodium and chloride in distal convoluted tubule

- More sodium loss than with loop diuretic
- More potent antihypertensive than loop

Give 30 minutes before the loop diuretic

Adverse Effects

- Hyponatremia
- Hypokalemia
- Hypomagnesemia
- Hypercalcemia
- Impaired glucose tolerance, hyperglycemia
- Increase cholesterol and triglycerides
- Gout, hyperuricemia
- Impotence

Tip

Don’t over diurese.

- Causes dizziness
  - Orthostatic changes, falls
- Hypotension
- Renal insufficiency

Aldosterone antagonist

For mortality reduction, not just diuresis

- Aldosterone hormone is produced in the cortex of the adrenal glands
- Sends signal to increase the amount of sodium into the bloodstream or potassium in the urine
  - Inhibited by potassium depletion and inhibitors of the RASS system, dopamine and atrial natriuretic factor

Aldosterone antagonists

Stop potassium sparing medications

- Consider potassium based salt substitutes

Potassium and renal monitoring

- Potassium < 5.o mEq/L
- Creatinine ≤ 2.5 mg/dL for men and ≤ 2.0 mg/dL for women

Monitor for hyponatremia.

Aldosterone antagonists

Drug	Initial Daily Dose	Maximum Dose
spironolactone (Aldactone)	12.5 – 25 mg daily	25mg daily or BID
eplerenone (Inspra)	25 mg daily	50 mg daily

Digoxin and Na-K-ATPase pump

Increased sodium (resulting from Na-K-AtPase inhibition by digoxin) > reduces sodium-calcium exchange >leading to intracellular calcium concentration

- Improved myocyte contractile performance

Digoxin

Benefit may be improved symptoms and exercise tolerance*

No effect on mortality.

Negative chronotrope

Positive inotrope

- Don’t take with grapefruit juice, green leafy vegetables, natural black licorice, tyramine containing foods (strong or aged cheeses, cured or smoked meats and fish), salt substitutes

Digoxin

- Low dose, don't load
  - Keep dig levels < 1 (0.05 to 0.9) ng/mL

Watch for toxicity

- Confusion
- Irregular pulse
- Loss of appetite
- Nausea, vomiting, diarrhea
- Fast heartbeat
- Vision changes (unusual), including blind spots, blurred vision, changes in how colors look, or seeing spots

Multiple medication interactions

- Amiodarone increases serum digoxin

Hypokalemia increases risk of toxicity

Hypocalcemia decreases sensitivity to digoxin

Isosorbide dinitrate and hydralazine

For those

- Cannot tolerate ACE-I or ARB due to intolerance, hypotension, or renal insufficiency.
- African Americans not responding to ACE-I or ARB

Slow titration to enhance tolerance.

Isosorbide dinitrate and hydralazine

Drug	Initial Daily Dose	Maximum Dose
Fixed-dose combination	20 mg isosorbide dinitrate / 37.5 mg hydralazine TID	40 mg isosorbide dinitrate / 75 mg hydralazine TID
Isosorbide dinitrate and hydralazine	20-30 mg isosorbide dinitrate / 25-50 mg hydralazine TID or daily	40 mg isosorbide dinitrate / 100 mg hydralazine TID

2016 Pharmacological & 2017 Heart Failure Update

ARNI – angiotensin receptor-neprilysin inhibitor

Sinoatrial node modulator

- Both Level B-R recommendation

Entresto (sacubitril / valsartan)

Neprilysin inhibitor results in an increased concentration of natriuretic peptides and inhibit RAAS.

- Promotes natriuretic and vasodilatory properties.

- Film-coated tablets (sacubitril/valsartan): 24/26 mg; 49/51 mg; 97/103 mg BID
  - Valsartan in Entresto is more bioavailable than valsartan alone
  - Intended to be substitute for ACE-I or ARB

PARADIGM-HF Trial

Multinational, randomized, double-blind

Comparing Entresto with enalapril

N= 8,442 adults with chronic HF (NYHA class II-IV) and systolic dysfunction (EF ≤ 40%)

Results:

- 20% reduction in rate of death or hospitalization for HF
- 16% reduction in rate of all-cause death compared to enalapril, at 3.5 years of follow-up

Entresto

- Do not administer concomitantly with ACE-I or within 36 hours of last ACE-I dose
  - Washout period not necessary if on ARB
- Adverse effects: Hypotension, hyperkalemia, renal impairment
  - Do not administer with a history of angioedema

Monitor kidney function, blood pressure, and potassium levels.

- BNP levels are not accurate, but pro-BNP levels may be used.

Heart rate matters

Heart rate is an independent predictor of outcomes in HFrEF.

- BB trials have shown lowering directly relates to improved outcomes

Optimize BB dose before adding another heart rate slowing agent.

Corlanor (ivabradine)

Funny current works on pacemaker (SA node) activity and modulations

- Patients did better with a decreased heart rate ~70.
- Do keep heart rate above 70 sinus rhythm.
- Not for patients in atrial fibrillation, 100% paced, or unstable.

Adverse effects: Bradycardia, sinus node disease, cardiac conduction defects, prolonged QT interval, visual disturbances (enhanced brightness)

- More about funny channel blockers @ http://circres.ahajournals.org/content/106/3/434.full

New HF medications

ARNI

Drug	Initial Daily Dose	Maximum Dose
Sacubitril/valsartan (Entresto)	24/26 mg - 49/51 mg BID	97/103 mg BID

I_f channel inhibitor

Drug	Initial Daily Dose	Maximum Dose
Ivabradine (Corlanor)	5 mg BID (2.5 mg BID)	7.5 mg BID

2017 Pathway for Optimization of Heart Failure Treatment

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EXPERT CONSENSUS DECISION PATHWAY

2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment: Answers to 10 Pivotal Issues About Heart Failure With Reduced Ejection Fraction

A Report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways

Initiation tips

It is safe to initiate either a BB or ACE-I first in HF.

ACE-I is better tolerated when the patient is wet

- RAAS activation is less during volume overload.

Aldosterone antagonist if indicated can be added before reaching target of other medications.

Titration tips

Titrate every 2 weeks based on tolerance.

BB have priority in getting to target dose.

Optimal therapy within 3 to 6 months of diagnosis is goal.

Nonpharmacological Interventions

Nutritional supplements

- For HFrEF patients

Exercise training or regular physical activity

Sodium restriction is reasonable

- 2000-3000 mg daily, avoid potassium-based salt substitutes

Daily weight monitoring

Daily fluid limitation

- 2 liters per day

New 2017 Additions

Anemia

- NYHA II and III HF with iron deficiency
  - IV iron replacement might be reasonable (IIb)
  - Erythropoietin-stimulating agent not beneficial

Sleep Disorders

- Formal sleep assessment is reasonable (IIa)
  - Distinguish obstructive vs. central sleep apnea

HF Achievement Measures

1. ACE-I / ARB at discharge
2. Evidence-based specific beta blockers
3. Measure LV function
4. Post-discharge appointment for heart failure patients

American Heart Association®

GET WITH THE GUIDELINES®
HEART FAILURE

HF Quality Measures

- Aldosterone antagonist at discharge
- Anticoagulation for atrial fibrillation or atrial flutter
- Angiotensin Receptor – Neprilysin Inhibitor at discharge
- Hydralazine/nitrate at discharge
- DVT prophylaxis (by hospital day 2)
- CRT-D or CRT-P placed or prescribed at discharge
- ICD counseling or ICD placed or prescribed at discharge
- Influenza vaccine during flu season
- Pneumococcal vaccination
- Follow-up visit within 7 days or less

HF Reporting Measures

- Advanced care plan
  - Advance directive executed
- Follow-up visit or contact with 48 hours of discharge scheduled
  - 72 hours
- QRS duration documented
- Beta blocker at discharge
  - % on BB at discharge
  - Histogram all patients grouped by specific BB
  - Histogram of eligible patient grouped by specific BB
- Ivabradine (Corlanor) at discharge, % eligible

HF Reporting Measures

- Blood pressure control at discharge
  - Care transition record transmitted
- Lipid-lowering medications at discharge
  - Omega-3 fatty acid supplement use at discharge
- Discharge disposition
- Education
  - 60 minutes by qualified HF educator
  - Activity level instruction
  - Diabetes teaching
    - % on treatment
  - Diet instruction
  - Medication instruction
  - Smoking cessation
  - Weight instruction

HF Reporting Measures

- Discharge instructions
  - Symptoms worsening instruction
- Length of stay
- In-hospital mortality
- Heart failure disease management program referral
- Referral to HF Interactive workbook
- Outpatient cardiac rehab program referral

30 Day Follow-Up Measures

- ACE-I / ARB or ARNI
- Aldosterone antagonist
- Beta blocker for LVSD
- Hydralazine Nitrate for LVSD
- Lipid lowering medication
- Diabetic treatment
- Re-hospitalization
- Mortality post (hospital) discharge
- Mortality (in-hospital)

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“ I’m not telling you it is going to be easy. I’m telling you it is going to be worth it.”

Art Williams

Heart Failure- Managing a Complex Clinical Syndrome

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- Thank you for your participation

Clinical Professional Development

CPD Consultant

Disclaimer: The overview is not all inclusive and I recommend reviewing the ACC/AHA guidelines.

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