Heart Failure - Managing a Complex Clinical Syndrome

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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

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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

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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 2/3rds of patients

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HFpEF

50% of HF population

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

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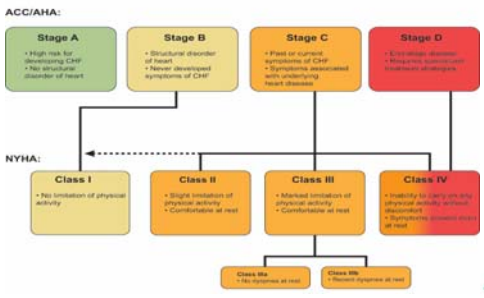
NYHA Class vs. ACC/AHA Stages



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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!

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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

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

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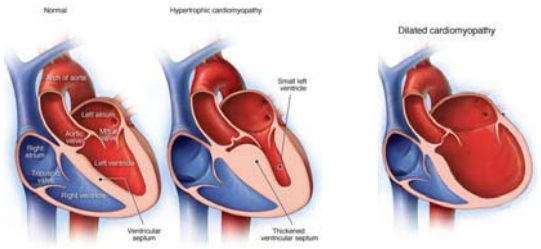
Cardiomyopathy



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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

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DCM

Toxic DCM

- Alcoholic, 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

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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

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Restrictive Cardiomyopathy

Heart does not relax normally

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

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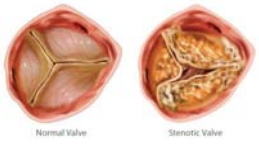
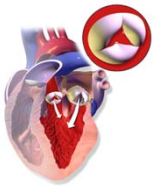
Valvular Disease

Aortic stenosis

Aortic insufficiency/ regurgitation

Mitral regurgitation





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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

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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 failure
- Pulmonary causes; obstructive sleep apnea, severe pneumonia, pulmonary HTN
- Critical illness
- Bacterial sepsis
- Severe burns
- Toxic-metabolic insults

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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

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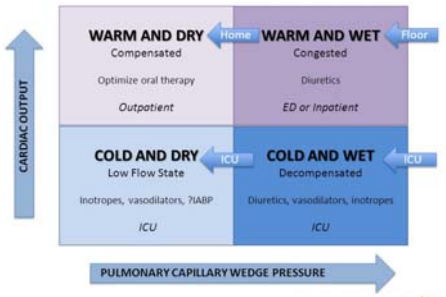
Warm-Cold, Wet-Dry



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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

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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

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Percutaneous Coronary Intervention - PCI

Left heart catheterization with

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

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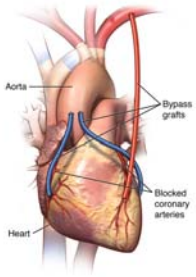
Coronary Artery Bypass Grafting



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

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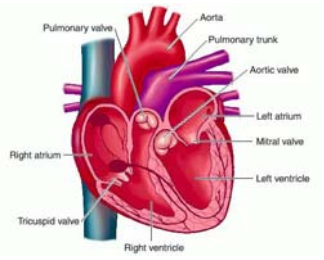
Valve Disease Options



Surgical repair or replacement

Structural cardiology procedures

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Prosthetic Heart Valves

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

Mechanical
- Lasts > 20 years
- Lifelong anticoagulation
- Click

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Balloon Aortic Valvuloplasty

Performed in HCL
- Wire across the stenotic valve
- Rapid pace to decrease stroke volume
- Balloon stenotic valve

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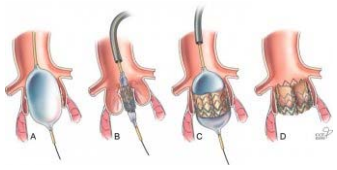
Transcatheter Aortic Valve Replacement - TAVR



Performed in Hybrid OR
- Balloon valvuloplasty
- Percutaneous deployed artificial valve

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TAVR valves

Edwards Sapien 3

Abbott Portico

Medtronic CoreValve

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MitraClip

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

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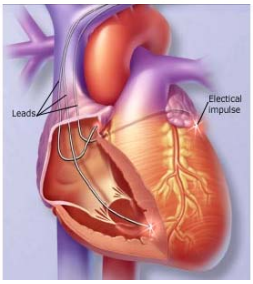
CRT- BiVentricular Pacing

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



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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

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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

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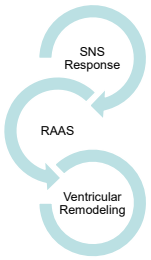
Neurohormonal Response



First responder good.

Over time, not so good.

Sympathetic Nervous System

- Increase in circulating catecholamines

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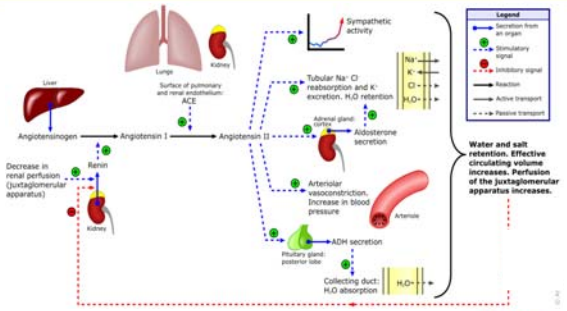
Renin-Angiotensin-Aldosterone System



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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 not really seen.

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Common Heart Failure Medications

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

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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

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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

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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.

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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

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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

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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
- Avoid NSAIDs
- Digoxin mixed reviews
- 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

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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

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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

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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

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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

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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.

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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

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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

2016 Pharmacological & 2017 Heart Failure Update

ARNI – angiotensin receptor-neprilysin inhibitor

Sinoatrial node modulator

- Both Level B-R recommendation

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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

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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 $\leq$ 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

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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.

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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.

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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

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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

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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

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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

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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

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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

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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

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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

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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

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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

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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

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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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Heart Failure- Managing a Complex Clinical Syndrome

"I'm not telling you it is going to be easy. I'm telling you it is going to be worth it."

Art Williams

Dawn.gosnell@ascension.org

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

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