2013 Updated ACC/AHA Guidelines for the Management of Systolic Heart Failure

> Darrin Majors, Pharm. D. PGY1 Pharmacy Resident Memorial Health Care System Chattanooga, TN

Objectives

- Review the possible causes and pathophysiology of heart failure syndrome
- Explain the rationale for the treatment of heart failure syndrome
- Review current pharmacologic recommendations
- Identify monitoring parameters for patients with heart failure

Definitions

- Ejection Fraction the percent of blood in the left ventricle after diastole that is ejected in systole
- Cardiac Output = Heart Rate x Stroke Volume
- Mean Arterial Pressure = Cardiac Output x Systemic Vascular Resistance
- Stroke volume
 - Preload, Afterload

Defining Heart Failure

- Clinical Syndrome
- Cardinal Manifestations
 - Dyspnea
 - Fatigue
 - Fluid retention
- Causes
 - Variety of disorders
 - Pericardium, myocardium, endocardium, heart valves, or great vessels
 - Impaired left ventricular (LV) myocardial dysfunction is most common
- No single diagnostic test

Defining Heart Failure

- Heart Failure with Reduced Ejection Fraction
 - Ejection Fraction < 40%
 - Inability of the heart to contract effectively
 - Most clinical trials about heart failure have utilized only patients with reduced EF
- Heart Failure with Preserved Ejection Fraction
 - Ejection Fraction > 50%
 - Impaired filling or relaxation
 - Efficacious therapies have not been identified

Common Heart Failure Risk Factors

- Age
- Hypertension
- Diabetes Mellitus
- Metabolic Syndrome
- Atherosclerotic Disease

Initial Evaluation and Diagnosis

- History and Physical Examination
- Diagnostic Tests
 - CBC, UA, Electrolytes, BUN, SCr, Glucose, FLP, LFTs, TSH
 - 12 Lead ECG
 - Chest X-Ray, 2D-Echocardiogram (TTE)
- Cardiac Biomarkers
 - BNP or NT-proBNP, Troponin

Heart Failure Staging

• NYHA

- **—** |
 - No limitation of physical activity
- II
 - Slight limitation of physical activity
- III
 - Marked limitation of physical activity
- -IV
 - Unable to carry on physical activity without symptoms of HF, or symptoms of HF at rest

• ACC/AHA

- A
 - At high risk for HF but without structural heart disease or symptoms of HF
- B
 - Structural heart disease but without signs or symptoms of HF
- C
 - Structural heart disease with prior or current symptoms of HF

— D

 Refractory HF requiring specialized interventions

Heart Failure Etiologies

- Systolic Dysfunction
 - Dilated
 Cardiomyopathies
 - Ventricular Hypertrophy
 - Infarction

- Diastolic Dysfunction
 - Increased ventricular stiffness
 - Valvular heart disease
 - Pericardial disease

Atria Aorta Left Ventricle Figure 2 Systolic Heart Failure

Left

Left Left Atrium Aorta Atrium Aorta Left LV Ventricle Figure 3 Figure 4 **Diastolic Heart Failure** Normal Heart



http://www.medCirculation 2001; 104; e89-e91.uc.edu/kranias/heart_failure.htm

Medication Therapy for Heart Failure

- Beta Blockers
- Angiotensin Converting Enzyme Inhibitors/ Angiotensin Receptor Binders
- Diuretics
- Aldosterone Antagonists
- Hydralazine/Isosorbide Dinitrate
- Digoxin

Beta Blockers

- Change the progression of the disease
 - Decrease hospitalizations
 - Decrease need for heart transplant
 - Decrease mortality
- Improves survival
- Provides symptomatic and hemodynamic improvement
- Carvedilol, Metoprolol Succinate, Bisoprolol
 Studied and indicated for use in heart failure

Beta Blockers in Clinical Trials

Trial	Drug	Initial Dose	Maximum Dose
CIBIS-II	Bisoprolol	1.25 mg daily	10 mg daily
COMET	Carvedilol	3.125 mg BID	50 mg BID
COMPARE	Carvedilol-CR	10 mg daily	40-80 mg daily
MERIT-HF	Metoprolol Succ.	12.5-25 mg daily	200 mg daily

Angiotensin Converting Enzyme Inhibitors

- Antagonizes the activation of the RAAS system
- Benefits
 - Improve survival, reduce HF progression, decrease hospitalizations, improve exercise tolerance and reduce dyspnea
- Indicated in ALL patients with heart failure due to left ventricular systolic dysfunction

 Unless contraindicated

ACEI in Clinical Trials

Trial	Drug	Starting Dose	Maximum Dose
Controlled Trial of Captopril in HF	Captopril	6.25 mg TID	50 mg TID
CONSENSUS	Enalapril	2.5-5 mg BID	10-20 mg BID
ATLAS	Lisinopril	2.5-5 mg daily	20-40 mg daily
FEST	Fosinopril	10 mg daily	40 mg daily
TRACE	Trandolapril	1 mg daily	4 mg daily
Quinapril Heart Failure	Quinapril	5 mg BID	20 mg bid
AIRE	Ramipril	1.25-2.5 mg daily	10 mg daily
PEP-CHF	Perindopril	2 mg daily	8-16 mg daily

Angiotensin Receptor Blockers

- Block angiotensin II effects at the AT₁ Receptor
 Do not affect bradykinin
- Patients intolerant to ACEI
- Valsartan and Candesartan are FDA approved for use in heart failure
- Adverse Effects
 - Hypotension
 - Renal insufficiency
 - Hyperkalemia
- Contraindications
 - Pregnancy, bilateral renal artery stenosis and hyperkalemia

ARB in Clinical Trials

Trial	Drug	Initial Dose	Maximum Dose
CHARM-ALT	Candesartan	4 mg daily	32 mg daily
VALIANT	Valsartan	20 mg BID	160 mg BID

Diuretics

- Primary target: symptomatic relief
- Thiazides vs. Loops
- Adverse Effects
 - Electrolyte depletion (K, Mg)
 - Cardiac arrhythmias
 - Hypotension
 - Azotemia
- Monitoring
 - Jugular venous pressure, edema, renal function, electrolytes, daily weights

Aldosterone Antagonists

- Block the effects of aldosterone, which is released by angiotensin II stimulation
- Use in patients on optimal heart failure therapy (diuretics, ACEI, beta blockers)
 - Provides mortality benefits
- Recommended for patients with moderately-severe to severe symptoms of HF with reduced LVEF and in certain mild to moderate heart failure (NYHA Class II) patients
- Adverse Effects
 - Hyperkalemia
 - Gynecomastia (spirinolactone)

Aldosterone Antagonists in Clinical Trials

Trial	Drug	Starting Dose	Maximum Dose
RALES	Spironolactone	12.5-25 mg daily	25 mg daily or BID
EPHESUS	Eplerenone	25 mg daily	50 mg daily

Hydralazine/Isosorbide

- Use in patients with symptoms and reduced LVEF that cannot take an ACEI or ARB
- African American > Caucasian patients
 - Considered add-on therapy to standard treatment of heart failure in African Americans
- Adverse Effects
 - Headache
 - Dizziness
 - Nausea
 - Systemic lupus erythematous

Hydralazine/Isosorbide in Clinical Trials

Trial	Drug	Starting Dose	Maximum Dose
V-HeFT	Hydralazine/ Isosorbide Dinitrate	37.5/20 mg TID	75/40 mg TID
A-HeFT	Hydralazine/ Isosorbide Dinitrate	37.5/20 mg TID	225/120 mg TID

Digoxin

- Benefits
 - Improved symptoms of heart failure
 - Improved exercise tolerance
 - Improved quality of life
 - Decreased number of hospitalizations
- No effect on mortality
- Adverse Effects
 - CNS (visual disturbance, photophobia, impaired color vision)
 - GI (anorexia, N/V)
 - Arrhythmia (especially with hypoK+ or hypoMg+)

Digoxin in Clinical Trials

Trial	Drug	Median Dose	Outcome
Digitalis Study Group	Digoxin	0.25 mg daily	Decreased hospitalizations; no effect on mortality



Yancy C et al. Circulation 2013;128:e240-e327



Additional Recommendations in Stage C Heart Failure

- ARB + ACEI + BB
 - Persistently symptomatic patients with reduced EF in whom an aldosterone antagonist is not indicated/tolerated
- ACEI + ARB + Aldosterone Antagonist
 - Potentially harmful
- Omega-3 Fatty Acids
 - Adjunctive therapy in patients with NYHA class II-IV symptoms and reduced or preserved EF

Additional Recommendations in Stage C Heart Failure

- Nutritional supplements
 - Not recommended with current or prior symptoms of HF with reduced EF
- Hormonal therapies
 - Not recommended except to correct deficiencies

At-Home Monitoring Parameters/Counseling Points

- Daily Weights
 - Assess for volume overload
- Sodium Intake
 - Prevent retaining consumed water
- Water/Fluid Intake
 - Prevent congestive symptoms
- Other medications
 - Certain classes of medications should be avoided because they can worsen your heart failure (Example: NSAIDs)
- Medication compliance
 - Prevent disease progression and exacerbation



References

- UpToDate. Overview of the therapy of heart failure due to systolic dysfunction
- Yancy C et al. 2013 ACCF/AHA Guideline for the Management of Heart Failure. Circulation 2013;128:e240-e327