Controlling Heart Failure and Improving Clinical Outcome

Heart failure affects more than 4.8 million Americans, with more than 400,000 new cases occurring annually and a resultant 900,000 hospitalizations, which translates into an annual estimated cost of nearly $30 billion dollars. Mortality with this condition is high, approximately 50% at 5 years. Implementation of the advances in management of heart failure have the potential to improve patients’ quality of life, reduce the need for hospitalizations, reduce total medical costs, and prolong survival.

The approach to diagnosis and management of CHF and the goals of therapy are outlined below.

I. Definition

Congestive Heart Failure (CHF) - Inadequate blood supply to maintain normal function. Symptoms may be present at rest and/or only during exercise.

II. Etiology

Common
- Coronary Artery Disease
- Hypertensive Heart Disease
- Idiopathic Dilated Cardiomyopathy
- Valvular Heart Disease
- Drugs - Alcohol, Cocaine, Methamphetamine
- Diastolic Dysfunction

Less Common
- Congenital Heart Disease
- Infiltrative Cardiomyopathy - Amyloid, Sarcoid, Restrictive
- Hemochromatosis
- Thyroid Disease
- Pheochromocytoma
- Chronic Renal Disease
- HIV and Viral Cardiomyopathy

III. History and Physical Evaluation

Evaluate for symptoms/signs of volume excess and/or low cardiac output

- Volume Excess
- Decreased Exercise Tolerance
- SOB, DOE
- PND
- Edema
- Weight Gain
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RUQ tenderness

Rales
Increased JVP
Hepatojugular Reflex/tenderness
Edema
S3

Low Cardiac Output
Decreased Exercise Tolerance
Malaise
Fatigue
Decreased Appetite
Weight Loss

Cachexia
Muscle Loss
Cool Extremities
Tachycardia
S3

IV. Evaluation of CHF

All patients with CHF should have initial assessment of left ventricular ejection fraction

Laboratory
Electrolytes, BUN, Creatinine - exclude renal disease
CBC - exclude anemia
T4, TSH - exclude thyroid disease
Liver Function Tests - evaluate for right heart failure
Cholesterol panel (LDL) - evaluate risk for CAD and need for statin
Urinalysis - exclude nephrotic syndrome
Diagnostic Tests ECG
CXR
Echocardiography - all patients should have assessment of LV function; quantitate LV size, evaluate hemodynamics, exclude diastolic dysfunction, valvular heart disease, CAD, amyloid
Additional Tests If at risk/suspected CAD (angina/MI/risk factors - ETT SestaMIBI PET scan or coronary angiogram) CPX - (Cardiopulmonary exercise test) Quantitate functional capacity, access prognosis, guide exercise prescription Peak VO$_2$ by CPX is the most reliable predictor of prognosis

Hospitalize for initial management or during follow-up for

Hypoxia - O$_2$ < 90%
Pulmonary Edema/Anasarca/Pneumonia
Symptomatic Hypotension (SBP<80 mmHg) with significant volume overload.
Inadequate Social Support in the setting of decompensation CHF refractory to outpatient Rx
Increasing renal dysfunction not due to overdiuresis or hepatic dysfunction.
Suspicion of low cardiac output status with low SBP (cardiac cachexia)

V. Medication for CHF - Systolic Dysfunction

Neurohumoral antagonism is the cornerstone of heart failure management. Because of their beneficial effects on disease progression, functional status, hospitalizations, and mortality risk, ACE inhibitors and beta blockers should be prescribed for all patients with left ventricular systolic dysfunction unless specific well defined contraindications exist.

Antagonism of Neurohumoral Activation

**ACE Inhibitors:** Improve survival (22-37% mortality reduction) in patients with Class I-IV heart failure, asymptomatic LV dysfunction, myocardial infarction, hypertension, coronary artery disease, and diabetes. Additional benefits include reduced hospitalization, myocardial infarction, strokes, renal failure, and new onset diabetes.

Doses of ACE inhibitors should be titrated upward over 2-4 weeks with the goal of reaching the target doses used in the prospective randomized clinical trials to reduce mortality. Benefits are a class effect. Monitor serum K+, BUN, Cr one week after initiation or dose change and periodically thereafter. Contraindications: cardiogenic shock, angioneurotic edema, hyperkalemia. Renal insufficiency is not a contraindication, start at low dose and monitor renal function closely. Use Target (Survival) Doses.

<table>
<thead>
<tr>
<th></th>
<th>Initiation</th>
<th>Target</th>
<th>Maximum</th>
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<tbody>
<tr>
<td>Enalapril</td>
<td>5 mg bid</td>
<td>10 mg bid</td>
<td>20 mg bid</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>10 mg qd</td>
<td>20 mg qd</td>
<td>40 mg qd</td>
</tr>
<tr>
<td>Captopril</td>
<td>25 mg tid</td>
<td>50 mg tid</td>
<td>100 mg qd</td>
</tr>
<tr>
<td>Quinapril</td>
<td>10 mg bid</td>
<td>20 mg bid</td>
<td>40 mg qd</td>
</tr>
<tr>
<td>Benazepril</td>
<td>10 mg qd</td>
<td>40 mg qd</td>
<td>80 mg qd</td>
</tr>
<tr>
<td>Ramipril</td>
<td>5 mg qd</td>
<td>10 mg qd</td>
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**Beta Blockers:** Improve survival (30-65% mortality reduction) in patients with Class I-IV heart failure, asymptomatic LV dysfunction, myocardial infarction, hypertension, coronary artery disease, and diabetes. Additional benefits include reduced hospitalization, myocardial infarction, and sudden death.

Beta blockers should be initiated in patients after adequate diuresis and treatment with ACE inhibitor. Initiate in compensated ambulatory outpatients. Volume overloaded and patients requiring intravenous inotropic agents should have beta blocker therapy deferred until stabilized. Start a low dose and go slow with careful titration. Contraindications: cardiogenic shock, symptomatic bradycardia, 2nd or 3rd degree heart block without pacemaker, severe asthma. Note that diabetes, peripheral vascular disease, asymptomatic bradycardia, and mild to moderated asthma and COPD are not contraindications.

Monitor patients for hypotension or symptomatic bradycardia.

Start at low dose with careful titration. Increase at 2-8 week intervals until target dose.

<table>
<thead>
<tr>
<th></th>
<th>Initiation</th>
<th>Titration</th>
<th>Target</th>
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<tbody>
<tr>
<td>Carvedilol</td>
<td>3.125 mg bid</td>
<td>6.25 mg bid,12.5 mg bid</td>
<td>25 mg bid</td>
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</table>
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Metoprolol 6.25 mg bid 12.5 mg bid, 25 bid, 50 bid 100 mg bid
Metoprolol XL 12.5 mg qd 25 qd, 50qd/100qd, 100qd/200 mg qd
Bisoprolol 1.25 mg qd 2.5 mg qd, 5 mg qd 10 mg qd

The COPERNICUS trial demonstrates survival benefits with carvedilol in patients with class IV heart failure. It is however recommended that treatment be initiated by physicians with extensive heart failure experience, preferably in a heart failure program setting where close monitoring is ensured. For patients who are tenuous or who have failed a prior attempt at beta blocker initiation, ultra low doses may facilitate initiation. One suggested regimen is to initiate 3.125, ½ tab PO qhs (i.e. 1.5625mg). After one week, the dose is given bid, after 3 more weeks, the patient is advanced to 3.125 mg bid, then slowly titrated up from that level at 4-8 week intervals.

Aldosterone Antagonism: Improve survival (30% mortality reduction) in patients with Class III-IV heart failure. Reduction in hospitalizations and sudden death. Benefits in patients with less severe heart failure and asymptomatic dysfunction is likely, but is being further tested in ongoing clinical trials.

Aldosterone antagonist are administered in conjunction with ACE inhibitors and loop diuretics. Since these agents are potassium sparing diuretics, patients will likely require adjustment of potassium supplements, possible alteration in other diuretic dosing, and close monitoring of renal function and serum potassium levels. It is recommended that the dose of potassium supplements be reduced on initiation, check K+, BUN, Cr at 1 week and 4 weeks. After adjustments at 4 weeks, increase dose to target level, rechecking labs at 1 week and 4 weeks.

<table>
<thead>
<tr>
<th>Spironolactone</th>
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<tbody>
<tr>
<td></td>
<td>12.5 mg qd</td>
<td>25 mg qd</td>
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Angiotensin Receptor Antagonists: Hemodynamic and symptomatic benefits demonstrated. Reserved for patients that are ACE inhibitor intolerant or have unacceptable side effects. ELITE II showed a low dose of the ARB losartan was not superior to ACE inhibitor treatment. Survival benefits and dosing has not been established in clinical trials.

<table>
<thead>
<tr>
<th>Losartan</th>
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<tr>
<td></td>
<td>25 mg bid</td>
<td>50 mg bid</td>
<td>100 mg bid</td>
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<tr>
<td>Valsartan</td>
<td>80 mg qd</td>
<td>160 mg qd</td>
<td>320 mg qd</td>
</tr>
<tr>
<td>Candesartan</td>
<td>4 mg qd</td>
<td>16 mg qd</td>
<td>32 mg qd</td>
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Symptomatic Treatments

Vasodilators
Hydralazine up to 100 mg QID If BP remain increased despite Isordil up to 80 mg TID maximum dose of ACEI Doxazosin up to 4-8 mg bid

Inotropes
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Digoxin no benefit, no harm on CHF mortality, decreases need for CHF hospitalizations (keep level 0.5 to 1.1 ng/ml)

Volume Excess
Diuretics Loop diuretics with potassium supplementation
Flexible regimen with doubled dose for 2 lb. weight gain and pm metolazone

Gold standard triple therapy to decrease symptoms, reduce hospitalizations, and improve survival in heart failure is now treatment with ACE inhibitor, Beta Blocker, and Aldosterone Antagonist

The majority of heart failure patients (60-70%) have coronary artery disease. They should receive comprehensive atherosclerosis treatment which includes aspirin, beta blocker, ACE inhibitor and a HMG CoA reductase inhibitor titrated to an LDL $\leq$ 100 mg/dl in conjunction with diet and exercise counseling.

Specific Clinical Scenarios

**Volume Excess**
ACEI (or ARB)
Digoxin
Diuretics/Aldactone
Beta Blocker

**Low Output**
ACEI (or ARB)
Digoxin
Diuretics/Aldactone
Hydralazine/Isordil

**CAD**
ASA
Statin
ACEI
Beta Blocker

**Tachy Arrhythmias**
Atrial fibrillation - Amiodarone
Asymptomatic PVC - Beta Blockers
NSVT and CAD - EPS, if induce, ICD
Syncope, VT, or Sudden Death - ICD

**Tachy Arrhythmias**
Atrial fibrillation - Amiodarone
Asymptomatic PVC - Beta Blockers
NSVT and CAD - EPS, if induce, ICD
Syncope, VT, or Sudden Death - ICD
Brady Arrhythmias
D/C Digoxin/Beta Blockers
Pacemaker - in NSR - DDD
in Afib - VVIR

Indications for anticoagulation: atrial fibrillation, left ventricular thrombus, or prior systemic embolization.
INR 2.0 - 3.0

Medications to Avoid:

Type I Antiarrhythmic Agents
Increase risk of sudden death and mortality 3-4X

Calcium Channel Blockers
Increase risk of CHF admit, progressive ventricular dilation, and mortality

NSAIDS and COX2 inhibit
Increase risk of renal dysfunction/failure

VI. Comprehensive Management

Non Pharmacologic Therapies: Essential Components of Therapy

Diet: 2 gram sodium diet with detailed education of patient and family members
Fluid Restriction: 2 liter (64 oz) daily fluid restriction
Daily Weights: monitor and record daily weights, bring chart to each visit
Flexible Diuretics: Patient centered diuretic dosing, double for 2 lb wt gain, prn metolazone
Daily aerobic exercise: Progressive walking program
Patient Education: detailed patient and family member education with frequent reinforcement
Comprehensive management combining optimization of heart failure medications and patient education can prevent up to 85% of heart failure hospitalizations and reduce total medical costs substantially.

VII. Investigational Agents

Amlodipine: PRAISE 2- Mortality trial in CHF. No benefit in non-ischemic patients.
Anti-tumor necrosis factor alpha antibodies
Endothelial receptor antagonists
Vasopeptidase inhibitors: neutral endopeptidase and ACE inhibitor combination, IMPRESS

VIII. Management of Refractory Patients - Tailored Therapy

Patients with severe decompensated CHF and those that have failed empiric therapy may require cardiology referral and invasive monitoring to appropriately treat CHF. Indications for hemodynamic monitoring include:

Increasing renal or hepatic dysfunction not due to overdiuresis
Hypotension (SBP <80-90 mmHg) with volume excess (increased JVP)
Suspicion of low cardiac output status with low SBP (cardiac cachexia)
Failing to respond to empiric dosing of ACEI inhibitor, digoxin, and diuretic therapy

 Decompensated patients are admitted and right heart catheter is placed. Intravenous nitroprusside and diuretics are titrated. Once optimal hemodynamics are achieved, ACE inhibition is started and the dose advanced while weaning the nitroprusside. Patients have not truly failed ACE inhibitors until they have not tolerated ACE inhibitors under invasive hemodynamic monitoring.

Patients who remain symptomatic despite aggressive medical therapy should be referred to a heart transplantation center for evaluation for orthotopic heart transplantation. Patients with advanced heart failure undergoing orthotopic heart transplantation currently have an expected 85% 1 year and a 70% 5 year survival. Selective patients age 65-70 (with additional risk factors) and those patients age 70 to 74 can be considered for UCLA’s alternative heart transplantation program.

Implantable LV ventricular assist devices (TCI Heart Mate) are available to mechanically bridge patients to cardiac transplantation. Studies are underway to evaluate mechanical LV assist devices as long term CHF treatment without transplantation. Other experimental therapies such as angiogenesis and myocyte transfer are also undergoing further evaluation.

**IX. Prevention of Heart Failure**

**Primary Prevention** (prevent development of left ventricular dysfunction)
Treat Hypertension, especially systolic hypertension (ACEI, ARB, beta blocker)
Treat Hypercholesterolemia (statin)

**Secondary Prevention** (prevent progression from asymptomatic LV dysfunction to clinical CHF)
ACE Inhibitors (ARB)
Beta Blockers
Secondary Prevention after Myocardial Infarction
(Aspirin, Beta Blocker, ACE inhibitor, HMG CoA Reductase Inhibitor, Exercise)

**Tertiary Prevention** (prevent progression of clinical CHF to mortality)
ACE Inhibitors
Beta Blockers
Aldosterone Blockade
Secondary Prevention of Coronary Artery Disease
Exercise

References


