HEART FAILURE

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EMMA

DEFINITION

- Condition in which heart is unable to pump sufficient blood for metabolizing tissues or can do so only from an abnormally elevated filling pressure.

OR

- An abnormality of cardiac structure or function that prevents the heart from ejecting or filling, causing dyspnea, fatigue, weakness and circulatory congestion

Forms of HF

- Systolic versus diastolic failure
  - Systolic failure: inability of the ventricle to contract normally, with symptoms resulting from inadequate cardiac output
    - Ejection fraction <40%
  - Diastolic failure: inability of the ventricle to relax and fill normally, with symptoms from elevated filling pressures
    - Ejection fraction >50%
  - Systolic and diastolic failure coexist in most patients with HF.

- Low-output versus high-output HF
  - Low-output HF: cardiac output at rest <2.2 L/min per m^2 (lower limit of normal) and fails to increase normally with exertion
    - Seen after myocardial infarction (MI), hypertension, dilated cardiomyopathy, and valvular or pericardial disease
    - Often accompanied by vasodilation and warm extremities
  - High-output HF: cardiac output >3.5 L/min per m^2 or upper limit of normal (before development of HF)
    - Seen in hyperthyroidism, anemia, pregnancy, arteriovenous fistulas, beriberi, and Paget's disease, usually with underlying heart disease
- Left-sided versus right-sided HF
  - Left-sided HF: left ventricle is hemodynamically overloaded and/or weakened, resulting in pulmonary congestion (dyspnea, orthopnea).
  - Right-sided HF: abnormality primarily affecting right ventricle, resulting in edema, congestive hepatomegaly and systemic venous distention

Risk Factors

- Hypertension
- Coronary artery disease
- Diabetes mellitus
- Dilated or hypertrophic cardiomyopathy
- Valvular heart disease
- Cardiotoxins

ETIOLOGIES OF HF

Depressed Ejection Fraction (<40%)	
Coronary artery disease	Nonischemic dilated cardiomyopathy
Myocardial infarction[a]	Familial/genetic disorders
Myocardial ischemia[a]	Infiltrative disorders[a]
Chronic pressure overload	Toxic/drug-induced damage
Hypertension[a]	Metabolic disorder[a]
Obstructive valvular disease[a]	Viral
Chronic volume overload	Chagas' disease
Regurgitant valvular disease	Disorders of rate and rhythm
Intracardiac (left-to-right) shunting	Chronic bradyarrhythmias
Extracardiac shunting	Chronic tachyarrhythmias
Chronic lung disease	
Cor pulmonale	
Pulmonary vascular disorders	

Preserved Ejection Fraction (>40–50%)

- Pathologic hypertrophy
  - Primary (hypertrophic cardiomyopathies)
  - Secondary (hypertension)
- Aging
- Restrictive cardiomyopathy
  - Infiltrative disorders (amyloidosis, sarcoidosis)
  - Storage diseases (hemochromatosis)
  - Fibrosis
  - Endomyocardial disorders

High-Output States

Metabolic disorders	Excessive blood flow requirements
Thyrotoxicosis	Systemic arteriovenous shunting
Nutritional disorders (beriberi)	Chronic anemia

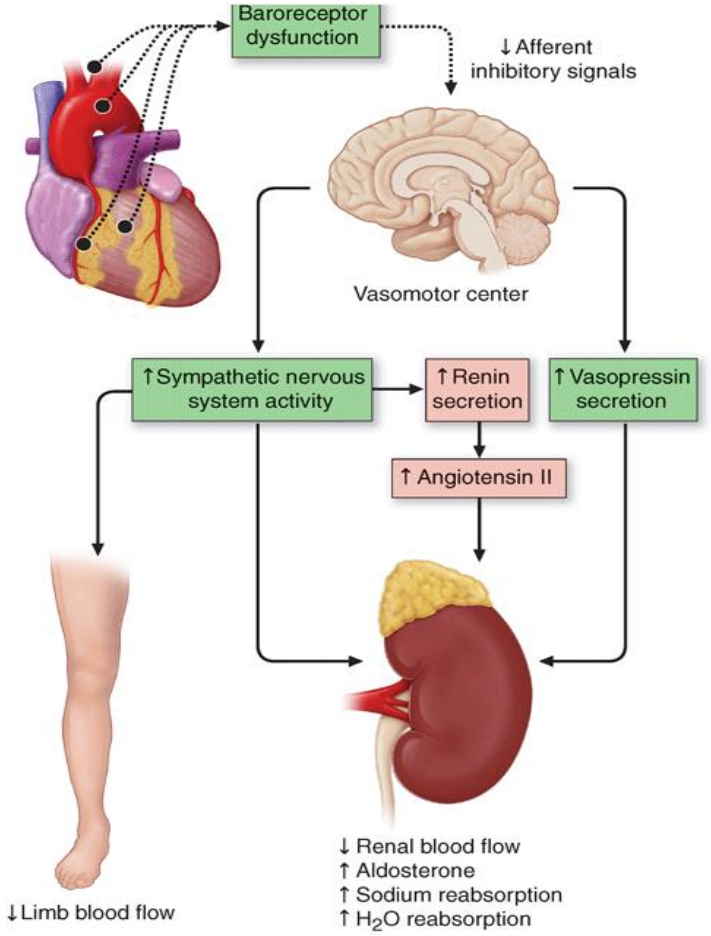
PATHOGENESIS OF HFrEF

- Index event >> initial decline in the heart's pumping capacity.
- **Variety of compensatory mechanisms are activated**:

1. Adrenergic nervous system
2. RAAS
3. Cytokine system.

- Activation of a family of countervailing vasodilatory molecules, i.e ANP and BNP, PGE2 and PGI2, and NO, that offsets the excessive peripheral vasoconstriction.
- Sustained activation of these systems >> worsening LV remodeling and subsequent cardiac decompensation.

Activation of neuro-hormonal systems in HF



Pathophysiology

Etiology

- Ventricles respond to chronic hemodynamic overload with development of hypertrophy.
- Chronic pressure overload leads to development of concentric ventricular hypertrophy.
  - Ratio between wall thickness and ventricular cavity size increases.
- When elevated stroke volume is required for prolonged periods (e.g., valvular regurgitation, high-output states), the ventricle dilates and develops eccentric hypertrophy
  - Ratio between wall thickness and ventricular cavity diameter remains relatively constant
- In both eccentric hypertrophy and concentric hypertrophy, wall tension is initially maintained.
  - Cardiac function may remain stable for years; initially, progression of HF is usually slow, then accelerates.
  - Ultimate deterioration of myocardial function (or new insult, such as MI) leads to HF.
    - The ventricle dilates, and the ratio between wall thickness and cavity size decreases, increasing stress on the myocardium.
    - The ventricle undergoes remodeling to more spherical shape, further increasing stresses on the wall and sometimes causing mitral regurgitation, which may initiate a vicious circle.
    - Endogenous neurohormonal systems are activated, and cytokines appears to be involved.

TABLE 279-2 NEW YORK HEART ASSOCIATION CLASSIFICATION

Functional Capacity	Objective Assessment
Class I	Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitations, dyspnea, or anginal pain.
Class II	Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.
Class III	Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.
Class IV	Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

Classification

- Stage A
  - At high risk for HF, but no evident structural heart disease or symptoms of HF
  - Examples
    - Hypertension
    - Coronary artery disease
    - Diabetes mellitus
- Stage B
  - Structural heart disease without symptoms of HF
  - Examples
    - Previous MI
    - Left ventricular systolic dysfunction, as in longstanding hypertension
    - Asymptomatic valvular disease
    - Dilated, hypertrophic, or restrictive cardiomyopathy
- Stage C
  - Structural heart disease with prior or current symptoms of HF
    - Shortness of breath
    - Fatigue
    - Reduced exercise tolerance

- Stage D
  - Refractory HF requiring specialized interventions
    - Marked symptoms at rest despite maximal medical therapy (e.g., recurrent hospitalizations or unable to be safely discharged from hospital without specialized interventions)

ACUTE PRECIPITATING FACTORS

- Include;
- (1) increased Na intake**,**
- (2) noncompliance with anti-CHF medications,
- (3) acute MI (may be silent),
- (4) exacerbation of hypertension,
- (5) acute arrhythmias,
- (6) infections
- (7) pulmonary embolism,
- (8) anemia,
- (9) thyrotoxicosis,
- (10) pregnancy,
- (11) acute myocarditis or infective endocarditis.

Symptoms & Signs

Symptoms

- Dyspnea with exertion (early) or at rest (late)
- Orthopnea
    - Dyspnea when recumbent; relief with sitting upright or use of several pillows

- Paroxysmal nocturnal dyspnea
  - Attacks of severe shortness of breath and coughing at night; usually awakens patient
  - Coughing and wheezing often persist even with sitting upright.
  - Cardiac asthma: nocturnal dyspnea, wheezing and cough due to bronchospasm
- Fatigue and weakness
- Abdominal symptoms
  - Anorexia
  - Nausea
  - Abdominal pain and fullness
- Cerebral symptoms
  - Altered mental status due to reduced cerebral perfusion
    - Confusion
    - Difficulty concentrating
    - Impaired memory
    - Headache
    - Insomnia
    - Anxiety
- Nocturia

Physical findings

- Pulmonary rales with or without expiratory wheeze
- Lower-extremity edema
- Hydrothorax (pleural effusion)
- Ascites
    - Most common in constrictive pericarditis and tricuspid valve disease
- Congestive hepatomegaly
    - Positive abdominojugular reflux
- Jugular venous distention
- Third and fourth heart sounds: often present but not specific
- Elevated diastolic arterial pressure
- Depression
- Sexual dysfunction

- Findings in late/severe HF
  - Pulsus alternans
    - Regular rhythm with alternation in strength of peripheral pulses
    - Most common in cardiomyopathy, hypertensive, and ischemic heart disease
  - Diminished pulse pressure
  - Jaundice
  - Decreased urine output
  - Cardiac cachexia

Differential Diagnosis

- Pulmonary disease with dyspnea
  - Obstructive airway disease
  - Diffuse parenchymal lung disease
  - Pulmonary vascular occlusive disease
  - Disease of chest wall and respiratory muscles
  - Cardiac asthma: wheezing secondary to bronchospasm occurring at night

- Other conditions leading to peripheral edema
  - Varicose veins, cyclic edema, or gravitational effects: no jugular venous hypertension
  - Renal disease: abnormal renal function tests, urinalysis
  - Elevation of venous pressure is uncommon.
- Hepatic cirrhosis
  - Enlargement of liver
  - Ascites
  - Normal jugular venous pressure
  - Negative abdominojugular reflux

Diagnostic Approach

- Approach to patient
  - Detailed clinical examination
  - Two-dimensional echocardiography with Doppler flow studies
  - Electrocardiography (ECG)
  - Chest radiography
  - Brain natriuretic peptide (BNP) measurement
- Framingham criteria for diagnosis of congestive heart failure (CHF)
  - To establish a clinical diagnosis of CHF by these criteria, at least 1 major and 2 minor criteria are required.
  - Major criteria
    - Paroxysmal nocturnal dyspnea
    - Neck vein distention
    - Rales
    - Cardiomegaly
    - Acute pulmonary edema
    - S_3 gallop
    - Increased venous pressure
    - Positive hepatojugular reflux

- Minor criteria
  - Extremity edema
  - Night cough
  - Dyspnea on exertion
  - Hepatomegaly
  - Pleural effusion
  - Vital capacity reduced by one-third from normal
  - Tachycardia (≥120 beats/min)
- Major or minor criterion
  - Weight loss ≥4.5 kg over 5 days of treatment

Laboratory Tests

- ECG
  - Aids in determining etiology; e.g. abnormal Q waves in old MI, left ventricular hypertrophy in hypertension
- BNP measurement
  - >200 pg/mL supports diagnosis
  - <40 pg/mL rarely seen in HF
  - Useful in diagnosis, prognosis, and monitoring therapy
  - Helps in differentiating between cardiac and pulmonary causes of dyspnea

- Urinalysis
  - Albuminuria
  - High specific gravity
  - Low sodium level
- Renal function
  - Prerenal azotemia
- Electrolytes
  - Hypokalemia from thiazide diuretics
  - Hyperkalemia from potassium-retaining diuretics
  - Dilutional hyponatremia in late HF
- Liver function testing
  - Hepatic enzymes; frequently elevated
  - Elevated direct and indirect bilirubin level (late finding)

Imaging

- 2-dimensional echocardiography with Doppler flow
  - To determine underlying causes
  - To assess severity of ventricular systolic and/or diastolic dysfunction, valvular dysfunction
  - Question diagnosis if all cardiac chambers normal in volume, shortening and wall thickness
- Chest radiography
  - To detect cardiomegaly and pulmonary congestion

Treatment Approach

- Recommended therapy, by disease stage
  - Stage A
    - Treat hypertension.
    - Prescribe angiotensin-converting enzyme (ACE) inhibition, especially in hypertension
    - Encourage smoking cessation.
    - Treat lipid disorders.
    - Encourage regular exercise.
    - Discourage alcohol intake and illicit drug use.
  - Stage B
    - All measures under Stage A
    - Add beta-blocker.
  - Stage C
    - All measures under stages A and B
    - Add diuretic.
    - Add digitalis in systolic HF.
    - Add spironalactone.
    - Restrict dietary salt to <2 g/d (eliminate salt-rich foods and added salt in cooking or at table)

- Stage D
  - All measures under Stages A, B, and C
  - Dietary salt restriction to <1 g/d
  - Mechanical assist devices
  - Heart transplantation
  - Continuous intravenous inotropic infusions for palliation (does not prolong life)
  - Hospice care

Specific Treatments

General measures

- Treat hypertension.
- Treat lipid disorders.
- Encourage smoking cessation.
- Discourage alcohol intake and illicit drug use.
- Recommend influenza and pneumococcal vaccines.
- Achieve optimal weight.
- Activity
    - Regular isotonic exercise in compensated HF
    - In moderately severe chronic HF: additional rest on weekend, scheduled naps or rest periods, avoidance of strenuous exertion
    - Avoid temperature extremes and tiring trips.

Diet

- Reduce sodium intake (normal diet contains 6–10 g of sodium daily)
  - Intake can be halved by excluding salt-rich foods and eliminating table salt.
  - Can be reduced to one-quarter with the above measures and omitting salt from cooking
  - In severe HF: limit to 1 g/d
  - Late in course: often, both sodium and water intake must be restricted.

Loop diuretics

- Indications for loop diuretics
  - All forms of HF, particularly in patients with severe or refractory HF and pulmonary edema
- Side effects
  - Metabolic alkalosis
  - Hypokalemia
  - Hyperuricemia
  - Hyperglycemia
  - Weakness
  - Nausea
  - Dizziness
- Specific agents
  - Furosemide
    - IV: initial dose, 20 mg (maximum, 80 mg)
    - PO: initial dosage, 20–40 mg 1–2 times daily (maximum, 400 mg/d)

- Bumetanide
  - IV: initial dose, 0.5 mg (maximum, 2 mg)
  - PO: initial dosage, 0.5–1.0 mg 1–2 times daily (maximum, 10 mg/d)
- Torsemide
  - IV: initial dose, 5 mg (maximum, 20 mg)
  - PO: initial dosage, 10 mg 1–2 times daily (maximum, 200 mg/d)

Other diuretics

- Metolazone
  - Dosage: 2.5 mg 1–2 times daily (maximum, 10 mg/d)
  - Actions and indications similar to thiazides
- Spironolactone
  - Dose: 12.5 to 25 mg/d; max: 25 mg twice daily
  - Use with loop diuretic
  - Weak diuretic, but has been shown to prolong life in Stage C HF
  - Side effects:
    - Hyperkalemia
    - Nausea
    - Epigastric distress
    - Mental confusion
    - Drowsiness
    - Gynecomastia
    - Erythematous eruptions
  - Contraindications to potassium-sparing diuretics
    - Potassium level >5 mmol/L
      - Monitor potassium level.
    - Renal failure
    - Hyponatremia

ACE inhibitors

- ACE inhibitors have a central role in prevention and treatment of HF at all stages.
- Contraindications
  - Do not use in hypotensive, pregnant, or possibly pregnant patients
- Side effects
  - Cough
  - Angioneurotic edema
  - Leukopenia
  - Teratogenic effects in first trimester
- Specific agents
  - Enalapril maleate
    - Initial dosage: 2.5 mg bid (maximum, 10–20 mg bid)
  - Fosinopril sodium
    - Initial dosage: 5–10 mg/d (maximum, 40 mg/d)
  - Lisinopril
    - Initial dosage: 2.5–5.0 mg/d (maximum, 20–40 mg/d)
  - Quinapril hydrochloride
    - Initial dosage: 10 mg bid (maximum, 40 mg bid)
  - Ramipril
    - Initial dosage: 1.25–2.5 mg/d (maximum, 10 mg/d)

Angiotensin receptor blockers

- Indications for angiotensin receptor blockers
  - Intolerance to ACE inhibitors
- Specific agents
  - Losartan
    - Initial dosage, 25 mg qd; target dosage, 50 mg bid
  - Valsartan
    - Initial dosage, 40 mg bid; target dose, 160 mg bid
  - Candesartan
    - Initial dosage, 4 mg qd, target dose, 32 mg qd

Beta blockers

- Indications for beta blockers: patients in Stage C HF
  - Stabilize first with ACE inhibitor, diuretics, and possibly digoxin.
  - Begin with low doses.
    - Titrate slowly.
    - Observe closely for hypotension, bradycardia, and worsening HF.
- Contraindications
  - Unstable HF
  - Hypotension
  - Severe fluid overload
  - Recent receipt of intravenous inotropic agents
  - Sinus bradycardia
  - Atrioventricular block
  - Bronchospastic disorders
- 15% of patients cannot tolerate beta blockade.
- 15% cannot tolerate target doses.
  - Low-dose beta blockade is preferable to no therapy.
- Specific agents
  - Bisoprolol
    - Initial dosage, 1.25 mg/d (maximum, 10 mg/d)
  - Carvedilol
    - Initial dosage, 3.125 mg bid (maximum, 25–50 mg bid)
  - Metoprolol CR/XL
    - Initial dosage, 12.5–25 mg/d (maximum, 200 mg/d)

Digoxin

- Indications for digoxin
  - Systolic HF complicated by atrial flutter and fibrillation and rapid ventricular rate
    - Especially useful in this setting
  - Systolic HF and sinus rhythm
    - Reduces symptoms of HF and need for hospitalization
    - Does not improve survival
- Little or no value in HF with sinus rhythm and the following conditions
  - Any form of diastolic HF
  - Hypertrophic cardiomyopathy
  - Myocarditis
  - Mitral stenosis
  - Chronic constrictive pericarditis

- Oral dosage: 0.50 mg/d for 2–3 days, then 0.125 mg every other day to 0.25 mg/d (maximum, 0.50 mg/d to avoid toxic effects)
- Complications: digitalis intoxication
  - Serious and potentially fatal
  - Risk factors
    - Advanced age
    - Hypokalemia
    - Hypomagnesemia
    - Hypoxemia
    - Renal insufficiency
    - Hypercalcemia
    - Acute MI
    - Quinidine, verapamil, amiodarone, and propafenone therapy
      - Reduce digoxin dose by half when patient is receiving these dru
  - Signs and symptoms
    - Anorexia
    - Nausea and vomiting
    - Exacerbations of HF
    - Weight loss
    - Cachexia
    - Neuralgias
    - Gynecomastia
    - Yellow vision
    - Delirium
- Most frequent disturbances of cardiac rhythm
  - Nonparoxysmal atrial tachycardia and/or variable atrioventricular block
  - Ventricular premature beats, bigeminy
  - Ventricular tachycardia or rarely ventricular fibrillation
- Treatment
  - Discontinue digoxin therapy.
  - β-adrenoceptor blocker or lidocaine
  - Oral potassium replacement (if hypokalemic)
  - Fab fragments of purified, intact digitalis antibodies (if life threatening)

Other vasodilators

- Indications
  - Chronic HF with systemic vasoconstriction despite ACE inhibitor therapy
- Specific agents
  - Isosorbide dinitrate
    - Initial dosage, 10 mg tid daily (maximum, 80 mg tid)
  - Sublingual isosorbide
    - Dosage: 2.5 mg as needed or before exercise to decrease dyspnea
  - Hydralazine
    - Initial dosage, 25 mg tid (maximum, 150 mg qid)

Ventricular resynchronization (biventricular pacing)

- Indications: chronic HF with impaired intraventricular conduction (QRS interval > 120 msec)
  - Increases ejection fraction
  - Increases distance walked in 6 minutes
  - Improved New York Heart Association class

- Improved quality of life and survival
- Need for hospitalization and/or intravenous medication for worsening HF halved

Management of arrhythmias

- Premature ventricular contractions and asymptomatic ventricular tachycardia (VT) are common in advanced HF.
- Sudden death due to ventricular fibrillation causes half of all deaths in advanced HF.
- Treatment of arrhythmias
    - Correction of electrolyte and acid–base disturbances (especially hypokalemia and digitalis intoxication)
    - Amiodarone (class III antiarrhythmic): drug of choice in HF with atrial fibrillation but not for preventing sudden death
    - Class I antiarrhythmics (quinidine, procainamide, flecainide) are contraindicated in HF.
    - Automatic implantable cardioverter-defibrillator (ICD) has been shown to prolong life.
        - After resuscitation from sudden death
        - Syncope or presyncope due to ventricular arrhythmia
        - Asymptomatic VT
        - VT can be induced during electrophysiologic testing.
        - Systolic HF with ejection fraction <35%
        - ICD is often combined in a single device with ventricular resynchronization.

Anticoagulants

- Warfarin
  - May be indicated in severe HF
- Heparin followed by warfarin
  - HF and
    - Atrial fibrillation
    - Previous venous thrombosis
    - Pulmonary or systemic emboli

Refractory HF

- Therapeutic options
  - Combination diuretics
  - Left ventricular or biventricular pacing
  - Additional vasodilators
  - Intravenous nitroglycerin or nesiritide
  - Mechanical circulatory support
  - Cardiac transplantation
  - Novel cardiac surgery, often accompanies multivessel coronary artery bypass grafting
    - Ventricular remodeling surgery
    - Mitral valve repair
  - Mechanical removal of extracellular fluid (rare; done in severe HF)
    - Thoracentesis
    - Paracentesis
- Exhaustion of all therapeutic options
  - Comfort care; possible hospice

- Continuous infusions of inotropic agents
  - Relieve symptoms, may stabilize patient awaiting transplantation but may shorten life (see Acute Heart Failure for dosing)
  - Dopamine if hypotension is present
  - Dobutamine in normotensive patients
- Consider continued infusions of inotropic agents, diuretics, anxiolytics, and analgesics.

Monitoring

- Serial BNP measurements
- Daily measurement of weight to aid in adjustment of diuretic dosage
- Education of patient and family about condition and critical importance of close attention to compliance
- Supervision of outpatient care by specially trained nurse or physician assistant

Complications

- Arrhythmias
- Sudden death, most due to ventricular fibrillation
  - Responsible for ~50% of all deaths
  - Can be prevented by ICD
- Pulmonary emboli secondary to venous thrombosis and systemic emboli secondary to intracardiac thrombi
  - Patients with HF and atrial fibrillation, previous venous thrombosis, and pulmonary or systemic emboli are at especially high risk and require anticoagulation.

Prognosis

- Poor prognosis is associated with:
  - Severely depressed ejection fraction (<15%)
  - Reduced maximal oxygen uptake (<12 mL/kg per min)
  - Inability to walk on a level and at a normal pace for more than 3 minutes
  - Reduced serum sodium concentration (<133 mEq/L)
  - Reduced serum potassium concentration (<3 mEq/L)
  - Markedly elevated BNP level (>500 pg/mL)
  - Frequent ventricular extrasystoles
- Natural history of HF: progressive but not predictable
  - Annual mortality rate
    - Asymptomatic patients: <5%
    - Mild disease: 10%
    - Moderate disease: 20–30%
    - Severe disease: 30–80%
  - Mechanism of death
    - Sudden death: 50%
    - Worsening HF (pump failure): 40%
    - Other: 10%
  - Survival rate of up to 80% at 2 years for patients rendered free of congestion
  - Survival rate may be as low as 50% at 6 months in patients with refractory symptoms.

Prevention

- For persons at risk for HF:
  - Treat hypertension.
  - Prescribe ACE inhibitors.
  - Encourage smoking cessation.
  - Treat lipid disorders.
  - Encourage regular exercise.
  - Discourage alcohol intake and illicit drug use.

In partnership with...