Practical Outpatient Management of Heart Failure in the Office

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Disclosure/Conflict of Interests

• Nothing to disclose.
1. Definition, Statistics, Epidemiology
2. Classification of HF
3. Risk Factors, Causes/Etiology
4. Diagnosis and Evaluation
5. Pathophysiology and Management
Definition of Heart Failure

A clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood.

The heart is unable to maintain an adequate forward blood volume or Cardiac Output to meet the physiologic demands of the circulatory system.
Heart Failure Statistics and Epidemiology

- **Prevalence**: 5.8 million in USA; 2.6% worldwide.
- **Incidence**: 650,000 (USA)
- **Risk of mortality from diagnosis**:
  - 20% at 1 year
  - 40% at 5 years
  - *Class III-IV*: ≥ 50% 1 year
Heart Failure Prevalence Increases with Age

Most common Hospital Diagnosis (DRG) > 65 years old

Cost of Heart Failure Treatment in the USA

Distribution of Direct Costs ($39 Billion)

- Hospital care (60%)
- Home health care (9%)
- Medication (9%)
- Physicians (7%)
- Nursing home (13%)

ICDs: $893 million (29% of the total growth in cost).

Hospitalizations: Major cost driver

20.9$ Billion

Classification of HF
Classification of HF

1*. Symptoms and Disease Progression
   - NYHA Functional Class
   - ACC/AHA Stage

2*. Ejection Fraction
   - Reduced EF
   - Preserved EF

3. Acute or Chronic

4. Cardiac Output (Low or High)

5. Left or Right Ventricular Failure
The fundamentals for diagnosis and classification of HF: Based in History-Symptoms* and Physical Exam

Principal manifestations:
1. Fatigue*: Due to low Stroke Volume/Cardiac output.

2. Dyspnea*: due elevated ventricular filling pressure due to volume overload → pulmonary congestion.
1. Classification of Heart failure by Symptoms

Functional Classification: New York Heart Association *

*Designed in 1918 to quantify the degree of functional limitation imposed by HF

<table>
<thead>
<tr>
<th>Class</th>
<th>Symptoms: Dyspnea or fatigue</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>No Symptoms with ordinary activity.</td>
</tr>
<tr>
<td>II</td>
<td>Symptoms with ordinary activity.</td>
</tr>
<tr>
<td>III</td>
<td>Symptoms with less than ordinary activity.</td>
</tr>
<tr>
<td>IV</td>
<td>Symptoms at rest.</td>
</tr>
</tbody>
</table>
2. Classification and Evaluation of Heart failure by Stage:
ACC/AHA Stages

<table>
<thead>
<tr>
<th>ACC/AHA Stages of HF*</th>
<th>NYHA CLASS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage A: At Risk</strong></td>
<td>None</td>
</tr>
<tr>
<td>No structural abnormalities.</td>
<td></td>
</tr>
<tr>
<td><strong>Stage B: Asymptomatic</strong></td>
<td>I</td>
</tr>
<tr>
<td>Structural abnormality.</td>
<td></td>
</tr>
<tr>
<td><strong>Stage C: Symptomatic</strong></td>
<td>I, II, III, IV</td>
</tr>
<tr>
<td>Structural abnormality.</td>
<td></td>
</tr>
<tr>
<td><strong>Stage D: Symptomatic</strong></td>
<td>IV</td>
</tr>
<tr>
<td>Structural abnormality.</td>
<td></td>
</tr>
</tbody>
</table>
### 3. Classification of Heart Failure

#### Ejection Fraction

<table>
<thead>
<tr>
<th>Classification</th>
<th>EF (%)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HF with reduced Ejection Fraction (HFrEF)</td>
<td>&lt; 40%</td>
<td>Referred to as Systolic HF.</td>
</tr>
<tr>
<td>HF with preserved Ejection Fraction (HFpEF)</td>
<td>&gt;50 %</td>
<td>Referred to as Diastolic HF.</td>
</tr>
<tr>
<td>a. HFpEF, borderline</td>
<td>41-49%</td>
<td>HFmrREF (ESC) These patients are treated (GDMT) similar to patients with HFrEF.</td>
</tr>
<tr>
<td>b. HFrEF, with improved EF</td>
<td>&gt;40 %</td>
<td></td>
</tr>
</tbody>
</table>
4. Classification of Heart failure: High Output Heart Failure

- Inappropriately high CO/CI: > 8 L/min or 4 L/min/m2
- Causes/Mechanisms: ↓ Peripheral vascular resistance, A-V communication
  - A-V fistulae and A-V malformations
  - Anemia
  - Hyperthyroidism
  - Beriberi (thiamine)
  - Paget’s disease
Evaluation HF
1. Clinical Diagnosis*

- There is no single diagnostic test for HF.

- The clinical diagnosis is based on history and physical examination: **Framingham Criteria**.

- Complementary Information:
  - Biomarkers of HF: BNP or NT-pro BNP.
  - Imaging the Heart for LVEF Determination:
    - Echocardiogram, Catheterization, MUGA, MRI
### 1. Framingham Criteria (1971) Today-On line Application*


<table>
<thead>
<tr>
<th>Major criteria (Symptoms/Signs* of congestion)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- <em>Paroxysmal nocturnal dyspnea (PND)</em> or <em>Orthopnea</em></td>
</tr>
<tr>
<td>- <em>Neck-vein distension (JVD)</em></td>
</tr>
<tr>
<td>- Rales*</td>
</tr>
<tr>
<td>- <em>Cardiomegaly</em></td>
</tr>
<tr>
<td>- <em>Acute pulmonary edema</em></td>
</tr>
<tr>
<td>- <em>S₃ gallop</em></td>
</tr>
<tr>
<td>- Hepatojugular reflux*</td>
</tr>
<tr>
<td>- Bentopnea</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Minor criteria:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Ankle edema</td>
</tr>
<tr>
<td>- Night cough</td>
</tr>
<tr>
<td>- <em>Dyspnea on exertion</em></td>
</tr>
<tr>
<td>- Hepatomegaly</td>
</tr>
<tr>
<td>- Pleural effusion</td>
</tr>
<tr>
<td>- Tachycardia : rate of ≥120/min (Major or minor criterion)</td>
</tr>
<tr>
<td>- Weight loss ≥4-5 kg in 5 days in response to treatment</td>
</tr>
<tr>
<td>- Bentopnea</td>
</tr>
</tbody>
</table>
1. Framingham Criteria

**Interpretation** Heart Failure diagnosis requires:
1. At least 1 major and 2 minor criteria.
2. 2 major criteria.

**Efficacy in HF Diagnosis:** Sensitive but not specific.
1. Sensitivity: 97%
2. Specificity: 79%
3. Best for ruling out particularly HFrEF. High Negative Predictive Value.

The absence of the Framingham criteria rules out the diagnosis of heart failure, particularly systolic heart failure. The presence of criteria do not necessarily confirm the diagnosis, which may need in additional information.
3. Initial Evaluation of HF- Investigate Etiology*

1. **Important Risk Factors for HF:**

1. Hypertension: The single most important risk factor for HF.

2. Diabetes Mellitus: 2-3 times risk of heart failure.

3. Metabolic Syndrome.

4. Atherosclerosis: CAD
Causes of HF: Cardiac Structural Abnormalities

- Dilated Cardiomyopathies*: A large group of heterogeneous myocardial diseases.

- Note- In clinical practice and multicenter HF studies:
  - Etiology of HF-Categorized into Ischemic or Nonischemic CMP.
  - But the term “Nonischemic CMP” may include CMP due to any volume or pressure overload, not conventionally accepted as IDC.

Idiopathic Dilated CMP*: Refers to Dilated Cardiomyopathy without ischemic heart disease/ CAD, pressure or volume overload, or other obvious etiology.
Initial Evaluation- Investigate Etiology:

History: Review of Systems and Family History*

Potential Clues/Information regarding Etiology:

Common Causes:

1*. CAD (MI, CABG, PCI, Angina)
2*. Hypertension
3*. Idiopathic Dilated CM (30% Familial CM)* (2 members afflicted, 3 generation pedigree, Screening- Clinical and Genetic)
- Valvular an Congenital Heart Disease
- Tachycardia Induced CM: Hx. Palpitations Syncope. (SVT, VT, PM, >10% PVCs burden)
- Alcohol*, Illicit Drugs (90 grs Eth-OH, 4-18% Asymptomatic cocaine users have ALVD)
- Cancer-Chemotherapy/Radiation (Genetic damage)
Initial Evaluation of HF - Investigate Etiology:

2. History: Review of Systems-Continuation:

Less Common Causes:

- Pericarditis and Myocarditis
- HIV: (12% of asymptomatic HIV+ patients with asymptomatic LVD)
- Post Partum Cardiomyopathy (HF during last trimester)
- HCM
- Amyloid (Low EKG voltage < 5mm, Thick LV, RV increased thickness, LAE)
- Endocrine Diseases: DM, Thyroid Disease, Pheo., Acromegally
- Collagen Disease: SLE, RA, Scleroderma
- Hemocrohrmatosis
- Sarcoid
Initial Evaluation of HF: Basic Studies
4. Initial Evaluation of HF: Basic Studies

Diagnostic Evaluation Tests:

1. Electrocardiogram* (Class I)
   - Rate, rhythm, QRS duration, ischemia

2. Chest radiography* (Class I):
   - Cardiomegaly, pulmonary edema/congestion, other causes of dyspnea
4. Initial Evaluation of HF

Basic Routine Laboratory Tests (Class I):

- CBC, UA
- Renal Function and Electrolytes (Na, K, Mg)
- Liver Function Tests
- TSH, Lipids
- BNP* or NT-proBNP*
Initial Diagnostic Evaluation of HF
Natriuretic Peptide Concentrations*

**BNP**
- < 100 pg/mL - HF unlikely
- >400 pg/mL - HF likely
- 100-400 pg/mL - Use clinical judgment

**NT-proBNP: Age adjudgments**
- < 450 pg/mL - HF unlikely
- Age < 50 years >450 pg/mL - HF likely
- Age 50-75 years >900 pg/mL - HF likely
- Age >75 years >1800 pg/mL - HF likely
Other factors may affect BNP levels

Lower levels:
- In obese patients

Higher levels:
- Women
- Anemia
- Age: Older patients
- Concomitant pulmonary disease
  - Chronic obstructive disease
  - Pulmonary hypertension
  - Pulmonary embolus
- Renal dysfunction
- Atrial fibrillation.
Initial Diagnostic Evaluation of HF

Transthoracic Echocardiogram (Class I)

Most Important initial Imaging modality*
(Availability, and low cost)

1. Assessment of ventricular function to categorize HFrEF** or HFpEF*
2. Assessment of chambers size, wall thickness, wall motion, valve function.

HFrEF: LVEF < 40%, Eccentric Remodeling

HFpEF: EF>50%, Concentric Remodeling
Diagnostic Criteria: HFrEF and HFpEF

HFrEF** [Systolic HF]
1. Symptoms and Signs of HF
2. LVEF < 40%
3. ↑BNP.

HFpEF* [Diastolic HF]
1. Symptoms and Signs of HF
2. LVEF >50%
4. ↑BNP*.

The prevalence of HF is evenly divided between HFrEF-(Systolic) and HFpEF-(Diastolic).

The Gold Standard to determine Diastolic Dysfunction is Cardiac Catheterization:
-LVEDP= >12 mmHg or PCWP= >16mmHg
Evaluation of HF

Repeat assessment of ventricular function (LVEF):

- Repeat EF after a major change in clinical status or after optimizing medical Rx - typically 3-6 months (Class IIa)

- Implications for electrical device therapy – AICD and or CTR

- Routine repeat measurement of LV function assessment in the absence of clinical status change or treatment intervention should not be performed (Is not useful - Class III)
Initial Evaluation of HF

Other Evaluation Laboratory Tests: Class IIa

- Screening for other diagnosis in selected patients:
  - Hemochromatosis (Iron studies)
  - HIV
  - Rheumatologic diseases (Autoimmune serology, Inflammatory markers)
    - Amyloidosis (Protein Electrophoresis)
    - Endocrine/Metabolic (Ex. Pheochromocytoma).
Initial Evaluation of HF
Other Evaluation Tests: Class IIa

- Cardiac MRI:
  - Iron Overload-Hemochromatosis, Sarcoidosis Myocarditis, Viability in CAD, Pericardial Disease.
- PET Scan: If concern of Sarcoidosis- Active disease.
- Cardiopulmonary Exercise Test:
  1. Determine cardiac versus non cardiac cause of symptoms.
  2. Quantify severity of physical limitation to consider advanced therapies (<14 ml O2/Kg/Min).
- Overnight oximetry: If OSA is suspected.
Initial Evaluation of HF Assessment for CAD

 ♥ Coronary angiography*:
  ▪ Class I: If angina or known ischemia.
  ▪ Class IIa: When ischemia may be contributing to HF.
    ▪ Ex: If atypical chest pain, known or suspected CAD

 ♥ Non Invasive Studies*: Stress Testing and/or imaging:
  ▪ Class IIa: if known CAD but no angina.
  ▪ Class IIb: To define likelihood of CAD.
Initial Evaluation of HF
Endomyocardial Biopsy

⚠️ Only useful in particular situations if results will influence therapy
1. Rapidly worsening ventricular dysfunction despite medical therapy.
   ▪ Giant cell myocarditis
2. Sarcoidosis
3. Infiltrative cardiomyopathies
   ▪ Amyloidosis
   ▪ Hemochromatosis

⚠️ Usually not indicated in systolic heart failure:
   ▪ Should not be performed in the routine evaluation of systolic HF: Class III-Harm.
Pathophysiology

Heart Failure with reduced Ejection Fraction
Pathophysiology of Chronic Systolic Heart Failure

Neuroendocrine Model

Myocardial Insult

→ ↓ LV Function

↓ Peripheral Vascular Resistance

Sodium and Water Retention

Progression of Heart Failure and Symptoms

↓ Stroke Volume

↓ Cardiac Output

↓ Blood Pressure

BP = CO x SVR

Neurohormone Activation:
Catecholamines
RAA System

Catecholamines
- Vasoconstriction
- Tachycardia

Angiotensin II
- Vasoconstriction
- Vasopressin secretion
- Sodium reabsorption
- Catecholamine release
- Growth stimulation
- Left ventricular remodeling
- Aldosterone Secretion

Figure 1. Pathophysiology of heart failure in the 1980s.
Goal of therapies in HF with Reduced Ejection fraction

- Improves QOL
- Improves Morbidity
- Improves Survival

Adverse Remodeling in HFrEF

Not Dilated
Normal Elliptical Shape
- Improves QOL
- Improves Morbidity
- Improves Survival

Dilated
Wall thinning
Heavier
Spherical

Reversing Adverse Remodeling
Management of HF

1. Heart Failure with reduced Ejection Fraction*
   - Well established Evidence based therapy
   - Improved survival, QOL, and reversed remodeling
2. Heart Failure with preserved Ejection Fraction
Treatment of HF with Reduced Ejection Fraction: Stage A

**ACC/AHA Stages of Heart Failure**

- **At Risk**
  - Stage A
  - Address Risk Factors*
    - Hypertension
    - CAD
    - Diabetes
  - Control of risk factors reduce the risk of HF by 50%.

- **Asymptomatic**
  - Stage B

- **Symptomatic Heart Failure**
  - Stage C
  - Stage D
  - Advanced Therapies
Treatment of HF with Reduced Ejection Fraction: Stage B

- ACEi or ARB (Class I)
- Beta Blocker (Class I)
Treatment of HF with Reduced Ejection Fraction

Stage B: ACE or ARB (Class I)

1. Class effect, but preferred agents proved in clinical trials.
2. * Improves mortality: RRR=17%.
3. * Improves morbidity-hospitalizations: RRR=31%
4. Start with ACEi.
5. ARB when ACEi contraindicated.
6. **Routine** combination of ACEi/ARB is contraindicated (Class III)

SOLVD Studies*
<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
<th>Initial Daily Dose</th>
<th>Target Dose</th>
<th>Mean Dose in Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Captopril</td>
<td>Capoten</td>
<td>6.25 mg tid</td>
<td>50 mg tid</td>
<td>128 mg</td>
</tr>
<tr>
<td>Enalapril*</td>
<td>Vasotec</td>
<td>2.5 mg bid</td>
<td>10 mg bid</td>
<td>17 mg</td>
</tr>
<tr>
<td>Lisinopril*</td>
<td>Zestril, Prinivil</td>
<td>2.5-5 mg qd</td>
<td>20 mg qd</td>
<td>35 mg</td>
</tr>
<tr>
<td>Fosinopril</td>
<td>Monopril</td>
<td>5-10 mg qd</td>
<td>80 mg qd</td>
<td>N/A</td>
</tr>
<tr>
<td>Quinapril</td>
<td>Accupril</td>
<td>5 mg bid</td>
<td>80 mg qd</td>
<td>N/A</td>
</tr>
<tr>
<td>Ramipril</td>
<td>Altace</td>
<td>1.25-2.5 mg qd</td>
<td>10 mg qd</td>
<td>N/A</td>
</tr>
<tr>
<td>Trandolapril</td>
<td>Mavik</td>
<td>1 mg qd</td>
<td>4 mg qd</td>
<td>N/A</td>
</tr>
</tbody>
</table>
# Angiotensin Receptor Blockers Used in Clinical Trials

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
<th>Initial Daily Dose</th>
<th>Target Dose</th>
<th>Mean Dose in Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candesartan</td>
<td>Atacand</td>
<td>4-8 mg qd</td>
<td>32 mg qd</td>
<td>24 mg/day</td>
</tr>
<tr>
<td>Losartan</td>
<td>Cozaar</td>
<td>12.5-25 mg qd</td>
<td>150 mg qd</td>
<td>129 mg/day</td>
</tr>
<tr>
<td>Valsartan</td>
<td>Diovan</td>
<td>40 mg bid</td>
<td>160 mg bid</td>
<td>254 mg/day</td>
</tr>
<tr>
<td>Irbesartan</td>
<td>Avapro</td>
<td>75 mgs qd</td>
<td>300 mg qd</td>
<td>N/A</td>
</tr>
</tbody>
</table>
Treatment of HF with Reduced Ejection Fraction

Stage B: Beta Blockers (Class I)

1. No Class effect.
2. Improves cardiovascular mortality: RRR=34*.
3. Improves morbidity-hospitalizations: RRR=41%
4. Approved Agents:
   - Carvedilol* (Capricorn Trial)
   - Metoprolol Succinate
   - Bisoprolol
## Beta Blockers Used in Clinical Trials

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
<th>Initial Daily Dose</th>
<th>Target Dose</th>
<th>Mean Dose in Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carvedilol*</td>
<td>Coreg</td>
<td>3.125 mg bid</td>
<td>25 mg bid</td>
<td>37 mg/day</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>Coreg CR</td>
<td>10 mg qd</td>
<td>80 mg qd</td>
<td>N/A</td>
</tr>
<tr>
<td>Metoprolol* succinate</td>
<td>Toprol XL</td>
<td>12.5-25 mg qd</td>
<td>200 mg qd</td>
<td>159 mg/day</td>
</tr>
<tr>
<td>Bisoprolol*</td>
<td>Zebeta</td>
<td>1.25 mg qd</td>
<td>10 mg</td>
<td>8.6 mg</td>
</tr>
</tbody>
</table>
## Treatment of HF with Reduced Ejection Fraction
### Carvedilol vs. Metoprolol Succinate

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Carvedilol</th>
<th>Metoprolol Succinate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosing (Mgs)</strong></td>
<td>3.125→6.25→12.5→25</td>
<td>25→50→100→200</td>
</tr>
<tr>
<td></td>
<td>- Low dose response (6.25 Mgs)</td>
<td>Once daily dose</td>
</tr>
<tr>
<td></td>
<td>- Goal: 25 Mgs BID</td>
<td>Goal: 200 Mgs</td>
</tr>
<tr>
<td><strong>Blood Pressure Effect</strong></td>
<td>Greater BP actions</td>
<td>Less BP ↓ action</td>
</tr>
<tr>
<td></td>
<td>Use in setting of concomitant hypertension</td>
<td>May facilitate up titration of other medications</td>
</tr>
<tr>
<td></td>
<td>Preferred agent when BP is not a limitation.</td>
<td></td>
</tr>
<tr>
<td><strong>Specific Populations</strong></td>
<td>DM: Less insulin resistance</td>
<td>BA/COPD: Less bronchospasm</td>
</tr>
<tr>
<td></td>
<td>Bisoprolol: Similar to Metoprolol Succinate</td>
<td></td>
</tr>
</tbody>
</table>
**Treatment of HF with Reduced Ejection Fraction: Stage C**

- **ACEi or ARB (class I)**
- **Beta Blocker (class I)**
- **Aldosterone Antagonists (class I)**
- **ARNI (class I)**
- **Hydralazine / Nitrates**
- **Digoxin**
- **Ivabradine**

*If Volume Overloaded:*
- **Diuretic(s)**

**Routine combination of ACEi + ARB + Aldosterone antagonist is contraindicated** (Class III)
1. Aldosterone Antagonists

1. NYHA Class II-IV and LVEF < 40%. (Rec. Class I).
2. Follow potassium (K) closely:
   ▪ Do not initiate if > 5 Meq/L.
   ▪ Recheck in 3 days, each week x4 w, each month x3 months.
   ▪ Avoid if Creatinine > 2.5 in men and 2.0 in women.
3. Start with spironolactone.
4. Change to eplerenone if gynecomastia with spironolactone.
## Treatment of HF with Reduced Ejection Fraction Stage C

### 2. Loop Diuretics for congestion

<table>
<thead>
<tr>
<th>Agent</th>
<th>Initial Dose</th>
<th>Maximal Dose</th>
<th>Bioavailability</th>
<th>Action Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Furosemide</td>
<td>20-40 Mgs QD or BID</td>
<td>600 Mgs</td>
<td>10-100%</td>
<td>4- 6 Hours</td>
</tr>
<tr>
<td>Bumetanide</td>
<td>0.5-1 Mgs QD or BID</td>
<td>10 Mgs</td>
<td>80-100%</td>
<td>6-8 hours</td>
</tr>
<tr>
<td>Torsemide</td>
<td>10-20 Mgs QD</td>
<td>200 Mgs</td>
<td>80-100%</td>
<td>12-16 Hours</td>
</tr>
<tr>
<td>Ethacrynic Acid</td>
<td>25-50 Mgs QD or BID</td>
<td>200 Mgs</td>
<td>90-100%</td>
<td>6 Hours</td>
</tr>
</tbody>
</table>

Consider Torsemide or Bumetanide in Right Sided HF due to better bioavailability.

Ethacrynic Acid: 1. Caution with sulfa allergy. 2. Very expensive (Particularly IV.)
Treatment of HF with Reduced Ejection Fraction Stage C

2. Thiazide Diuretics

I. Use in combination with loop diuretics.

II. Watch/Caution for electrolytes disturbances:
   1. Hypokalemia.
      ▪ Consider K supplement /or K sparing diuretic
   2. Hypomagnesemia.
   3. Hyponatremia.

III. Azotemia.

IV. Avoid daily dosing. (Ex. Start metolazone qod)
2. Intensifying Diuresis as an Outpatient

1. Verify compliance, assess for precipitants of fluid overload
2. Double Tipple loop diuretic dose.
3*. Change to an alternative loop diuretic
   ▪ Torsemide
   ▪ Bumetanide
4*. Add a thiazide diuretic (Metolazone)
Treatment of HF with Reduced Ejection Fraction: Stage C

3. Hydralazine/Nitrates Class I

1. For persistently symptomatic African-Americans.
   - Despite ACE/ARB and Beta Blocker therapy.

2. Class IIa for patients intolerant to ACE/ARB:
   - Due to renal dysfunction or hyperkalemia.
Treatment of HF with Reduced Ejection Fraction: Stage C

4. Digoxin Class IIa

1. Consider if LVEF < 40%.
   ▪ Decreases HF hospitalizations, not mortality.
2. Consider in AF with suboptimal heart rate control despite or intolerant to beta blocker
3. Goal blood level 0.5-0.9 ng/ml²
Treatment of HF with Reduced Ejection Fraction: Stage C

2016 and 2017 ACC/AHA HF Guideline Update

- Sacubitril/Valsartan (ARNI)* : COR I
- Ivabradine* : COR IIa
*More BNP available.

- ↑ BNP levels.

*Neprilsyn also inhibits Bradykinin degradation.
Treatment of HF with Reduced Ejection Fraction: Stage C

**PARADIGM-HF**

- Sacubitril / valsartan versus enalapril
- LVEF < 40%; NYHA II-IV; tolerated ACEi

<table>
<thead>
<tr>
<th></th>
<th>LCZ696 (n=4187)</th>
<th>Enalapril (n=4212)</th>
<th>Hazard ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary endpoint</td>
<td>914 (21.8%)</td>
<td>1117 (26.5%)</td>
<td>0.80 (0.73-0.87)</td>
<td>0.0000002</td>
</tr>
<tr>
<td>Cardiovascular death</td>
<td>558 (13.3%)</td>
<td>693 (16.5%)</td>
<td>0.80 (0.71-0.89)</td>
<td>0.00004</td>
</tr>
<tr>
<td>Hospitalization for heart failure</td>
<td>537 (12.8%)</td>
<td>658 (15.6%)</td>
<td>0.79 (0.71-0.89)</td>
<td>0.00004</td>
</tr>
</tbody>
</table>

*Improved hospitalizations vs. ACEi: 20% RRR. Improves mortality vs. ACEi: 19% RRR.*
5. Sacubitril/Valsartan

- Paradigm HF Trial: Published 2014
- FDA approved: 2015
- ACC/AHA HF Guidelines Update: 2016 and 2017
- Class I indication HFrEF NYHA Class II-IV:
  1) In patients previously tolerated ACEi or ARB: EF< 40%.
  2) Contraindicated in history of angioedema.
  3) Contraindicated concomitant ACEi or ARB.
  4) Hold ACEi or ARB for 48 hours before starting.
  5) *NT-pro BNP: Biomarker in patients using Sacubitril/Valsartan.
Ivabradine Class IIa

- Inhibits the If current in the sinoatrial node, reduces heart rate
- SHIFT trial (published 2010): reduced HF admissions among EF < 35%, NYHA II-IV, sinus rhythm, HR > 70; no mortality benefit
- FDA approved in 2015
- Ila recommendations in the 2016 ACC / AHA HF guideline update
- Ensure goal beta blocker dose before starting
TIPS Treatment of HF with Reduced Ejection Fraction

1. Go slowly with doses:
   - Start lowest dose, and Increase (2x dose) every 2 weeks.
2. Tolerate “asymptomatic hypotension”.
3. Diuretic requirements may decrease with positive remodeling.
4. Treat the patient not the creatinine.
5. Repeat TTE 3-6 months after medical optimization
Drugs to Avoid in HFrEF

- NSAIDs
- Calcium channel blockers (Except amlodipine- neutral in mortality)
- Most antiarrhythmic drugs (Except amiodarone and dofetilide)
- Thiazolidinedione (Glitazones: rosiglitazone, pioglitazone)
Treatment of HF with Reduced Ejection Fraction

Lifestyle and Non-Medical Interventions

- Sodium restriction: < 2 grams per day.
- Fluid restriction: < 2 liters per day.
- Exercise: 30 minutes, 5 days per week.
- Alcohol intake: Ideally abstinence, otherwise < 2 drinks per week.
Device Therapy HF-rEF (Systolic HF)

<table>
<thead>
<tr>
<th>AICD: Class I Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. NYHA Class II-III.</td>
</tr>
<tr>
<td>2. LVEF ≤ 35%.</td>
</tr>
<tr>
<td>3. Caveats:</td>
</tr>
<tr>
<td>• Survival &gt; 40 days post MI.</td>
</tr>
<tr>
<td>• Survival expectancy &gt; 1 year</td>
</tr>
<tr>
<td>4. Decreases mortality.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CRT or AICD/CRTAICD: Class I Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. NYHA Class II-IV.</td>
</tr>
<tr>
<td>2. LVEF ≤ 35%.</td>
</tr>
<tr>
<td>3. EKG</td>
</tr>
<tr>
<td>• NSR.</td>
</tr>
<tr>
<td>• QRS ≥ 150 Ms, with LBBB.</td>
</tr>
<tr>
<td>4. Decreases mortality, hospitalization, and reverse remodeling.</td>
</tr>
</tbody>
</table>
Therapeutic Interventions that Improve Mortality and morbidity and reverse Remodeling

**Improve Mortality**

- ACE I
- ARBs
- ARNI
- Aldosterone antagonists
- Beta Blockers
- CRT
- AICD

**Improve Mortality, Morbidity and Remodeling:**

- ACE I
- ARBs
- ARNI
- Aldosterone antagonists
- Beta Blockers
- CRT
- LVADs in Stage D
- Digoxin and Ivabradine*: Only hospitalizations.
H F Preserved Ejection Fraction
Diastolic Heart Failure
DIASTOLIC HEART FAILURE
Causes HFNEF with LV diastolic dysfunction

1. Hypertension
2. Infiltrative cardiomyopathy
   - Amyloidosis
   - Hemochromatosis
3. Hypertrophic cardiomyopathy
4. Restrictive cardiomyopathy
5. Diabetes
6. Obesity
7. Advanced age
Treatment of HF with Preserved Ejection Fraction

Not well established evidence base therapeutic recommendations as in HFrEF.

Therapeutic recommendations: Generalizations.

Guidelines for Treatment of HFpEF...

- 2005 similar to 2001
- 2009 similar to 2005
- 2013 similar to 2009
- HFpEF not addressed in 2016 update
## Treatment of HF with Preserved Ejection Fraction

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>B</td>
<td>Control of Systolic and diastolic blood pressure* in accordance with clinical practice guidelines.</td>
<td>Same 2013 Guidelines</td>
</tr>
<tr>
<td>I</td>
<td>C</td>
<td>Diuretics for relief volume overload.</td>
<td>Same 2013 Guidelines</td>
</tr>
<tr>
<td>Ila</td>
<td>C</td>
<td>Coronary revascularization: with CAD in with symptoms (angina) or that demonstrable ischemia is having an adverse effect on HFpEF despite GDMT.</td>
<td>Same 2013 Guidelines</td>
</tr>
</tbody>
</table>
### Treatment of HF with Preserved Ejection Fraction

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIa</td>
<td>C</td>
<td><strong>Hypertension:</strong> Beta-blocking agents, ACE inhibitors, and ARBs first line therapy. ARBs may reduce hospitalizations. Goal of blood pressure: &lt; 130/80 mm Hg.</td>
<td>Same 2013 And new HTN Guideline</td>
</tr>
<tr>
<td>IIa</td>
<td>C</td>
<td><strong>Atrial Fibrillation:</strong> Management according to published guidelines. Goal: rhythm control.</td>
<td>Same 2013 HF, Guideline</td>
</tr>
<tr>
<td>IIb</td>
<td>B-R</td>
<td><strong>Aldosterone receptor antagonists:</strong> Selected patients with EF &gt;45%, elevated BNP levels or HF admission within 1 year, GFR &gt;30 mL/min, Cr. &lt;2.5 mg/dL, K &lt;5.0 mEq/L, to decrease hospitalizations</td>
<td>NEW</td>
</tr>
</tbody>
</table>
Treatment of HF with Preserved Ejection Fraction

**Clinical Pearls:**

- Focus on aggressive treatment of hypertension.
  - Beta-blocking agents, ACE inhibitors, and ARBs preferred.
- Diuretics for volume overload.
- Goal in atrial fibrillation: Rhythm control.
- Exercise program.
- Consider aldosterone antagonist.
Thank You!
hector.banchs3@upr.edu