HEART FAILURE: MANAGEMENT IN THE ACUTE CARE SETTING

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NORTON HEART SPECIALISTS
HEART RHYTHM CENTER

Speaker Disclosures
None

AGENDA FOR THE DAY...

• 1. Overview of Heart Failure
• 2. Epidemiology
• 3. Classification
  • Signs and Symptoms
  • Pathophysiology
• 4. Management: Acute Care Setting
  • Evaluation and workup
  • Drug classes- Ace-I, Beta Blockers, Diuretics, Aldosterone Antagonists, Neprilisyin inhibitors, Corlanor
  • ICD’s and biventricular pacing
  • Cardiac Transplant, LVAD, etc.

Definition of Heart Failure

“Heart failure is a clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood”

Heart failure is on the rise

5.7 MILLION
2009-2012
6.5 MILLION
2011-2014
About 6.5 million adults in the United States have heart failure.

One in 9 deaths in 2009 included heart failure as a contributing cause.

About half of people who develop heart failure die within 5 years of diagnosis.

Heart failure costs the nation an estimated $30.7 billion each year. This total includes the cost of health care services, medications to treat heart failure, and missed days of work.

**EPIDEMIOLOGY OF HF**

<table>
<thead>
<tr>
<th>ADHERE (n=110,800)</th>
<th>Euro-HF (n=11,300)</th>
<th>OPTIMIZE-HF (n=48,612)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age, y</td>
<td>75</td>
<td>71</td>
</tr>
<tr>
<td>Women (%)</td>
<td>52</td>
<td>47</td>
</tr>
<tr>
<td>Known heart failure (%)</td>
<td>75</td>
<td>65</td>
</tr>
<tr>
<td>Preserved EF (%)</td>
<td>40</td>
<td>54</td>
</tr>
<tr>
<td><strong>Medical history (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHD</td>
<td>57</td>
<td>68</td>
</tr>
<tr>
<td>Hypertension</td>
<td>72</td>
<td>53</td>
</tr>
<tr>
<td>Diabetes</td>
<td>44</td>
<td>27</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>31</td>
<td>43</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>30</td>
<td>17</td>
</tr>
<tr>
<td>COPD</td>
<td>31</td>
<td></td>
</tr>
</tbody>
</table>

**Heart Failure is Progressive**

- Normal heart
- Chronic heart failure
  - CHF: 3 M in US, 7 M in Europe
  - ACHF: 1 My in US, 1.7 My in Europe

**Morbidity and mortality in Heart failure**

- Heart failure is associated with significant mortality.
  - Hospital: 30 days
  - 1 year
  - 5 years
  - Mortality: 4.7%, 10%, 20%, 50%

**Heart Failure Death Rates, 2014-2016**

- Adults, Ages 35+, by County
Burden of Heart Failure

- Lifetime risk > 20% for Americans >40 years of age
- 870,000 new cases diagnosed annually
- Prevalence in US: 5.7 million

ACC/AHA Guidelines 2013


HF groups: ACC/AHA Guidelines

The current definition of HF based on left ventricular ejection fraction (EF):
- HF with reduced EF (HFrEF, EF ≤40%)
- HF failure with preserved EF (HFpEF, EF ≥50%)
- HFpEF, borderline (EF 41-49%)
- HFpEF, improved (EF >40%)

NYHA Class and Mortality

<table>
<thead>
<tr>
<th>NYHA Class</th>
<th>1-Yr Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>5-10%</td>
</tr>
<tr>
<td>II</td>
<td>5-10%</td>
</tr>
<tr>
<td>III</td>
<td>10-25%</td>
</tr>
<tr>
<td>IV</td>
<td>25-60%</td>
</tr>
</tbody>
</table>

PROGNOSIS IN ADVANCED HEART FAILURE

UNCHANGED IN 20 YEARS

<table>
<thead>
<tr>
<th>Stages, NYHA Class</th>
<th>50% Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage D, NYHA Class IV</td>
<td>Imminent</td>
</tr>
<tr>
<td>Acute cardiogenic shock</td>
<td>1 month</td>
</tr>
<tr>
<td>End organ dysfunction</td>
<td>3-6 months</td>
</tr>
<tr>
<td>Inotrope-dependent</td>
<td>6 months</td>
</tr>
<tr>
<td>ACE-inhibitor intolerant</td>
<td>6-12 months</td>
</tr>
<tr>
<td>Cachexia, hyponatremia, CKD</td>
<td>&gt; 24 months</td>
</tr>
<tr>
<td>Tolerating oral therapies</td>
<td>± 12 months</td>
</tr>
<tr>
<td>Stabilized to NYHA Class III</td>
<td>&gt; 24 months</td>
</tr>
</tbody>
</table>
HEART FAILURE IN CONTEXT
ONE YEAR MORTALITY

1 Year Mortality (%)

AIDS  Leukemia  Lung Cancer  Pancreatic Cancer  End-stage HF with Optimal Medical Management


SYMPTOMS

CLINICAL PRESENTATION GENERALLY DIVIDED INTO TWO TYPES

Clinical: Symptoms of HF
- Left Heart Failure:
  - Dyspnea on exertion
  - Dyspnea at rest
  - Orthopnea
  - Paroxysmal nocturnal dyspnea (PND)
  - Fatigue, inability to exercise
- Right Heart Failure:
  - Swelling of feet, hands
  - Abdominal distention/fullness
  - Right upper quadrant pain
  - Early satiety
  - Weight loss (cardiac cachexia)

Clinical: Signs of HF
- Left Heart Failure:
  - Rales/Crackles
  - Pleural effusions
  - CM: Displaced apical impulse
  - Tachycardia, LVSD, murmur of M
  - Narrow pulse pressure
- Right Heart Failure:
  - Edema of lower extremities
  - Elevated JVP/+ HJR
  - RVSD, murmur of TR
  - Hepatomegaly, RUQ tenderness
  - Ascles
  - Pleural effusions

PATHOPHYSIOLOGY

Congestive Heart Failure

CLINICAL PRESENTATION GENERALLY DIVIDED INTO TWO TYPES

Clinical: Symptoms of HF
- Left Heart Failure:
  - Dyspnea on exertion
  - Dyspnea at rest
  - Orthopnea
  - Paroxysmal nocturnal dyspnea (PND)
  - Fatigue, inability to exercise
- Right Heart Failure:
  - Swelling of feet, hands
  - Abdominal distention/fullness
  - Right upper quadrant pain
  - Early satiety
  - Weight loss (cardiac cachexia)
**Pathologic Progression of CV Disease**

- Coronary artery disease
- Hypertension
- Diabetes
- Cardiomyopathy
- Valvular disease

**Compensatory Mechanisms: Renin-Angiotensin-Aldosterone System (Neurohormonal Mechanism)**

- Beta Stimulation
- Renin + Angiotensinogen

- Angiotensin I
- Angiotensin II

- Aldosterone Secretion
- Kaliuresis

- ACE

- Peripheral Vasoconstriction
- Salt & Water Retention

- Cardiac Output
- Plasma Volume

- Heart Failure
- Cardiac Workload

**Neurohormonal Mechanism**

- **Renin**
  - Converts angiotensinogen to angiotensin I

- **Angiotensin I**
  - Vasoconstriction, cardiomyocyte hypertrophy, aldosterone and vasopressin release, thirst

- **Angiotensin II**
  - ACE
  - Vasoconstriction, cardiomyocyte hypertrophy, aldosterone and vasopressin release, thirst

- **Aldosterone**
  - Sodium retention, cardiac fibrosis

- **Norepinephrine**
  - Chronotropy, inotropy, vasoconstriction, renin secretion

**Terms have been used to characterize AHF in the literature, including:**

- *“acute heart failure syndromes” (AHFS),*
- *“acutely” decompensated heart failure” (ADHF),*
- *“acute decompensation of chronic heart failure” (ADCHF),*
- *“hospitalization for heart failure” (HHF).*

**Acute Decompensated Heart Failure**

- **Signs and Symptoms**
  - “WET”
  - Dyspnea, orthopnea, PND, morning cough, peripheral edema, rales, ankle, hepatic congestion, jugular venous distention

- **“D”**
  - Decline in mental status, anorexia, nausea, reduced cardiac output, renal pulse pressure

- **Pulmonary Capillary Wedge Pressure**

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INPATIENT TRIAGE
DECOMPENSADED HEART FAILURE

<table>
<thead>
<tr>
<th>WARM AND DRY</th>
<th>WARM AND WET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compensated</td>
<td>Decompensated</td>
</tr>
<tr>
<td>Optimize oral therapy</td>
<td>Diuretics</td>
</tr>
<tr>
<td>Outpatient</td>
<td>ED or Inpatient</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LOW FLOW STATE</th>
<th>COLD AND WET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inotropes, vasodilators, Support</td>
<td>Diuretics, vasodilators, Inotropes</td>
</tr>
<tr>
<td>ICU</td>
<td>ICU</td>
</tr>
</tbody>
</table>

PULMONARY CAPILLARY WEDGE PRESSURE

WHO’S COLD?
PROPORTIONAL PULSE PRESSURE

Pulse Pressure
Systolic BP- Diastolic BP

Proportional Pulse Pressure
Pulse Pressure
Systolic BP

Proportional Pulse Pressure ≤ 25% predicts Cardiac Index ≤ 2.2
Sensitivity 85%
Specificity 83%

WHO’S WET?

<table>
<thead>
<tr>
<th>Finding</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>JVP &gt; 11cm</td>
<td>67%</td>
<td>74%</td>
</tr>
<tr>
<td>Edema &gt; trace</td>
<td>48%</td>
<td>69%</td>
</tr>
<tr>
<td>Increased apical P2</td>
<td>37%</td>
<td>75%</td>
</tr>
<tr>
<td>Rales</td>
<td>15%</td>
<td>85%</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>15%</td>
<td>92%</td>
</tr>
<tr>
<td>S3 gallop</td>
<td>63%</td>
<td>40%</td>
</tr>
<tr>
<td>Valsalva square root sign</td>
<td>13%</td>
<td>96%</td>
</tr>
</tbody>
</table>

PRELOAD AND AFTERLOAD

Preload
Volume of blood in ventricles at end of diastole (and diastolic pressure)
Increased in:
Hypertension

Afterload
Resistence left ventricle must overcome to circulate blood
Increased in:
Acute Heart Failure Treatment According To Hemodynamics

High Preload
Diuretics
Lasix, Bumex

High Afterload
Vasodilators
Nitroprusside, milrinone

Poor Contractility
Inotropes
Dopamine, Dobutamine

Acute decompenesated heart failure
MANAGEMENT OF HEART FAILURE

- 1. Diagnostic Testing
- 2. Biomarkers in the hospitalized/acute setting
- 3. Non-invasive cardiac imaging
- 4. Invasive evaluation
- 5. Treatment

### Applying Classification of Recommendations and Level of Evidence

<table>
<thead>
<tr>
<th>Level A</th>
<th>Class I</th>
<th>Class Ia</th>
<th>Class Ib</th>
<th>Class II</th>
<th>Class IIa</th>
<th>Class IIb</th>
<th>Class III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple (2-5) pop. risk &amp; strata evaluated</td>
<td>Recommendation that procedure or treatment is useful/effective</td>
<td>Recommendation that procedure or treatment is useful/effective</td>
<td>Recommendation that procedure or treatment is useful/effective</td>
<td>Some conflicting evidence from single randomized trials or meta-analyses</td>
<td>Greater conflicting evidence from multiple randomized trials or meta-analyses</td>
<td>Sufficient evidence from randomized trials or meta-analyses</td>
<td>No additional studies needed; may be harmful</td>
</tr>
<tr>
<td>Class I</td>
<td>Recommendation that procedure or treatment is useful/effective</td>
<td>Recommendation that procedure or treatment is useful/effective</td>
<td>Recommendation that procedure or treatment is useful/effective</td>
<td>Greater conflicting evidence from multiple randomized trials or meta-analyses</td>
<td>Class IIa</td>
<td>Class IIb</td>
<td>Class III</td>
</tr>
<tr>
<td>Class II</td>
<td>Class IIa</td>
<td>Class IIb</td>
<td>Class III</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Diagnostic Tests

- Initial laboratory evaluation of patients presenting with HF should include complete blood count, urinalysis, serum electrolytes (including calcium and magnesium), blood urea nitrogen, serum creatinine, glucose, fasting lipid profile, liver function tests, and thyroid-stimulating hormone.

- Serial monitoring, when indicated, should include serum electrolytes and renal function.
A 12-lead ECG should be performed initially on all patients presenting with HF.

Screening for hemochromatosis or HSV is reasonable in selected patients who present with HF.

Diagnostic tests for rheumatologic diseases, amyloidosis, or pheochromocytoma are reasonable in patients presenting with HF in whom there is a clinical suspicion of these diseases.

Measurement of natriuretic peptides (B-type natriuretic peptide (BNP) or N-terminal pro-B-type natriuretic peptide (NT-proBNP) can be useful in the evaluation of patients presenting in the urgent care setting in whom the clinical diagnosis of HF is uncertain. Measurement of natriuretic peptides (BNP and NT-proBNP) can be helpful in risk stratification.

The value of serial measurements of BNP to guide therapy for patients with HF is not well established.

**BNP (NT-proBNP) in HF**

- BNP or B-type natriuretic peptide is produced mostly by cardiac ventricles in response to stress/strain/stretch on the myocardium
- BNP has beneficial effects in heart failure: promotes vasodilation, diuresis and natriuresis
- Levels increased in patients with HF; levels correlate with wedge pressures and prognosis
- BNP < 100 pg/ml usually will rule out significant HF in acute dyspnea

**BNP IS INCREASED WITH HEART FAILURE IRRESPECTIVE OF EJECTION FRACTION**

**HOSPITALIZED/ACUTE**

Measurement of BNP or NT-proBNP is useful to support clinical judgment for the diagnosis of acutely decompensated HF, especially in the setting of uncertainty for the diagnosis.

Measurement of BNP or NT-proBNP and/or cardiac troponin is useful for establishing prognosis or disease severity in acutely decompensated HF.

**BNP LEVELS HAVE PROGNOSTIC VALUE**

DIRECT CORRELATION WITH MORTALITY AND READMISSION RATE
HOSPITALIZED/ACUTE (CONT.)

The usefulness of BNP- or NT-proBNP guided therapy for acutely decompensated HF is not well-established.

Measurement of other clinically available tests such as biomarkers of myocardial injury or fibrosis may be considered for additive risk stratification in patients with acutely decompensated HF.

CAUSES FOR ELEVATED NATRIURETIC PEPTIDE LEVELS

Cardiac
- Heart failure, including RV syndromes
- Acute coronary syndrome
- Heart muscle disease, including LVH
- Valvular heart disease
- Pericardial disease
- Atrial fibrillation
- Myocarditis
- Cardiac surgery
- Cardiorenal

Noncardiac
- Advancing age
- Anemia
- Renal failure
- Pulmonary causes: obstructive sleep apnea, severe pneumonia, pulmonary hypertension
- Critical illness
- Bacterial sepsis
- Severe burns
- Toxic-metabolic insults, including cancer chemotherapy and envenomation

NONINVASIVE CARDIAC IMAGING

Patients with suspected or new-onset HF or those presenting with acute decompensated HF should undergo a chest x-ray to assess heart size and pulmonary congestion, and to detect alternative cardiac, pulmonary, and other diseases that may cause or contribute to the patient's symptoms.

A 2-dimensional echocardiogram with Doppler should be performed during initial evaluation of patients presenting with HF to assess ventricular function, size, wall thickness, wall motion, and valve function.

Repeat measurement of EF and measurement of the severity of structural remodeling are useful to provide information in patients with HF who have had a significant change in clinical status; who have experienced or recovered from a clinical event; or who have received treatment, including GDMT, that might have had a significant effect on cardiac function; or who may be candidates for device therapy.

NONINVASIVE CARDIAC IMAGING (CONT.)

Noninvasive imaging to detect myocardial ischemia and viability is reasonable in patients presenting with de novo HF who have known CAD and no angina unless the patient is not eligible for revascularization of any kind.

Viability assessment is reasonable in select situations when planning revascularization in HF patients with CAD.

Radionuclide ventriculography or magnetic resonance imaging can be useful to assess LVEF and volume when echocardiography is inadequate.

Caveats: BNP (NT-proBNP) in HF

• Patients discharged with BNP > 400-500 pg/ml at discharge are at a higher risk for HF readmissions and mortality

• However, patients with low LVEF can have normal levels if diuresed well (20-25% chronic HF)

• Levels ↑ with age, especially in older women, and with renal dysfunction

• ↑ in HFrEF & HFpEF (overall higher in HFrEF)

• ↓ ↓ in obesity

• Elevated BNP also seen with RV dysfunction, PE

• Although prognostic no definitive data to recommend titrating diuretics or meds to BNP levels outside of structured HF programs.
SUMMARY RECOMMENDATIONS FOR NONINVASIVE IMAGING

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with suspected, acute, or new-onset HF should undergo a chest x-ray.</td>
<td>I C</td>
<td></td>
</tr>
<tr>
<td>3-dimensional echocardiography with Doppler should be performed for initial evaluation of HF.</td>
<td>IIa C</td>
<td></td>
</tr>
<tr>
<td>Repeat measurement of EF is useful in patients with HF who have had a significant change in clinical status or received treatment that might affect cardiac function, or for consideration of device therapy.</td>
<td>IIa C</td>
<td></td>
</tr>
<tr>
<td>Noninvasive imaging to detect myocardial ischemia and viability is reasonable in HF and CAD.</td>
<td>IIa C</td>
<td></td>
</tr>
<tr>
<td>Viability assessment is reasonable before revascularization in HF patients with CAD.</td>
<td>IIa B</td>
<td></td>
</tr>
<tr>
<td>Radionuclide ventriculography or MRI can be useful to assess LVEF and volume.</td>
<td>IIa C</td>
<td></td>
</tr>
<tr>
<td>MRI is reasonable when assessing myocardial infiltration or scar.</td>
<td>IIa B</td>
<td></td>
</tr>
<tr>
<td>Routine repeat measurement of LV function assessment should not be performed.</td>
<td>III: No Benefit</td>
<td>B</td>
</tr>
</tbody>
</table>

INVASIVE EVALUATION

Invasive hemodynamic monitoring with a pulmonary artery catheter should be performed to guide therapy in patients who have respiratory distress or clinical evidence of impaired perfusion in whom the adequacy or excess of filling pressures cannot be determined from clinical assessment.

Invasive hemodynamic monitoring can be useful for carefully selected patients with acute HF who have persistent symptoms despite empiric adjustment of standard therapies and:

- a. whose fluid status, perfusion, or systemic or pulmonary vascular resistance is uncertain;
- b. whose systolic pressure remains low, or is associated with symptoms, despite initial therapy;
- c. whose renal function is worsening with therapy;
- d. who require parenteral vasoactive agents; or
- e. who may need consideration for MCS or transplantation.

INVASIVE EVALUATION (CONT.)

When ischemia may be contributing to HF, coronary arteriography is reasonable for patients eligible for revascularization.

Endomyocardial biopsy can be useful in patients presenting with HF when a specific diagnosis is suspected that would influence therapy.

Routine use of invasive hemodynamic monitoring is not recommended in normotensive patients with acute decompenated HF and congestion with symptomatic response to diuretics and vasoactive agents.

Endomyocardial biopsy should not be performed in the routine evaluation of patients with HF.

RECOMMENDATIONS FOR INVASIVE EVALUATION

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monitoring with a pulmonary artery catheter should be performed in patients with respiratory distress or impaired systemic perfusion when clinical assessment is inadequate.</td>
<td>I C</td>
<td></td>
</tr>
<tr>
<td>Invasive hemodynamic monitoring can be useful for carefully selected patients with acute HF with persistent symptoms and/or when hemodynamics are uncertain.</td>
<td>IIa C</td>
<td></td>
</tr>
<tr>
<td>When coronary ischemia may be contributing to HF, coronary arteriography is reasonable.</td>
<td>IIa C</td>
<td></td>
</tr>
<tr>
<td>Endomyocardial biopsy can be useful in patients with HF when a specific diagnosis is suspected that would influence therapy.</td>
<td>IIa B</td>
<td></td>
</tr>
<tr>
<td>Routine use of invasive hemodynamic monitoring is not recommended in normotensive patients with acute HF.</td>
<td>III: No Benefit</td>
<td>B</td>
</tr>
<tr>
<td>Endomyocardial biopsy should not be performed in the routine evaluation of HF.</td>
<td>III: Harm</td>
<td>C</td>
</tr>
</tbody>
</table>
NON INVASIVE CVP ASSESSMENT

- Patient is lying at 45°
- Internal jugular vein
- Top of jugular venous pulsation
- Measure the vertical height in centimeters


Management of Acute Heart Failure


THE GUIDELINES
OUTPATIENT MANAGEMENT

Stage A: Severe symptoms
Stage B: Structural heart disease, no symptoms
Stage C: Structural heart disease, progressive no symptoms
Stage D: End-stage disease, requiring palliative care

Enlarged heart, reduced ejection fraction
Coronary, multivessel bypass
Embolization, initial valve surgery
Cardiac transplantation of heart/lung

Diuretics, mineralocorticoid receptor blockers, angiotensin-converting enzyme inhibitors
ACE inhibitors or ARBs in patients with history of coronary artery disease
ACE inhibitors or ARBs in patients with diabetes mellitus

ACE inhibitors with ARBs in patients with diabetes mellitus
Angiotensin receptor blockers in patients with diabetes mellitus
Diuretics, mineralocorticoid receptor blockers, angiotensin-converting enzyme inhibitors
ACE inhibitors with ARBs in patients with diabetes mellitus
Angiotensin receptor blockers in patients with diabetes mellitus

**PHARMACOLOGICAL THERAPY FOR MANAGEMENT OF STAGE C HFREF**

### Key Drugs

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Corm</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta Blockers</td>
<td>I A</td>
<td></td>
</tr>
<tr>
<td>Aldosterone Antagonists</td>
<td>I A</td>
<td></td>
</tr>
<tr>
<td>Digoxin</td>
<td>IIa B</td>
<td></td>
</tr>
<tr>
<td>Anticoagulation</td>
<td>I A</td>
<td></td>
</tr>
</tbody>
</table>

### ACE-Inhibitors

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enalapril (Vasotec)</td>
<td>10 mg bid</td>
</tr>
<tr>
<td>Captopril (Capoten)</td>
<td>50 mg tid</td>
</tr>
<tr>
<td>Ramipril (Altace)</td>
<td>20 mg qd</td>
</tr>
<tr>
<td>Lisinopril (Prinivil, Zestril)</td>
<td>40 mg qd</td>
</tr>
<tr>
<td>Quinapril (Accupril)</td>
<td>20-40 mg bid</td>
</tr>
</tbody>
</table>

### β-Blockers

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carvedilol (Coreg)</td>
<td>25-50 mg bid</td>
</tr>
<tr>
<td>Metoprolol (Toprol XL)</td>
<td>200 mg qd</td>
</tr>
<tr>
<td>Bisoprolol (Zebeta)</td>
<td>10 mg qd</td>
</tr>
</tbody>
</table>

### Aldosterone Antagonists

- Recommended in patients with NYHA class II-IV HF who have LVEF ≤35%
- Recommended in patients following an acute MI who have LVEF ≤40% with symptoms of HF or DM

### Digoxin

- Use of digoxin is recommended for all stable patients
- Digoxin can be beneficial in patients with HFrEF

### Anticoagulation

- Patients with chronic HF who have permanent/persistent paroxysmal AF and an additional risk factor for thromboembolic events should receive chronic anticoagulant therapy

### Omega-3 Fatty Acids

- Omega-3 PUFA supplementation is reasonable to use as adjunctive therapy in HFrEF or HFpEF patients

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**Note:** The text and diagrams are from a medical document focusing on heart failure management, specifically detailing pharmacological therapies and their recommendations for different stages of heart failure.

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**OPTIMAL MEDICAL MANAGEMENT**

**THE NEUROHORMONAL COMPONENT**

- **ACE-inhibitors**
  - Enalapril (Vasotec)
  - Captopril (Capoten)
  - Ramipril (Altace)
  - Lisinopril (Prinivil, Zestril)
  - Quinapril (Accupril)

- **β-Blockers**
  - Carvedilol (Coreg)
  - Metoprolol (Toprol XL)
  - Bisoprolol (Zebeta)

- **Diuretics**

- **ACE Inhibitors**

- **ARBs**

- **Digoxin**

- **Anticoagulation**

- **Statins**

- **Omega-3 Fatty Acids**

---

**Hypertension:**

- **Diuretics**

- **ACE Inhibitors**

- **ARBs**

- **β-Blockers**

- **Aldosterone Antagonists**

**Diabetes:**

- **ACE Inhibitors**

- **β-Blockers**

- **Aldosterone Antagonists**

---

**3/4/2019**
Use of Beta Blockers in HFrEF

- Indicated for symptomatic or asymptomatic EF ≤40%.
- Use agents and target doses used in clinical trials.
- Initiate when relatively euvolemic, off IV vasoactive agents and prior to hospital discharge.
- Titrte upward every 2 to 4 weeks as long as tolerable.
- Most trials held titration for HR <60 or SBP <90.
- Adjust other agents if dyspnea, BP, or weight gain occur in order to titrate to target doses.

Which Beta Blocker; How Much?

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial Daily Dose(s)</th>
<th>Maximum Dose(s)</th>
<th>Mean Dose Achieved in Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisoprolol</td>
<td>1.25 mg qd</td>
<td>10 mg qd</td>
<td>8.6 mg/d</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>3.125 mg bid</td>
<td>50 mg bid</td>
<td>37 mg/d</td>
</tr>
<tr>
<td>Carvedilol CR</td>
<td>10 mg qd</td>
<td>80 mg qd</td>
<td></td>
</tr>
<tr>
<td>Metoprolol succinate extended release (metoprolol CR/XL)</td>
<td>12.5 - 25 mg qd</td>
<td>200 mg qd</td>
<td>159 mg/d</td>
</tr>
</tbody>
</table>

Which ACE I; How Much?

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial Daily Dose(s)</th>
<th>Maximum Dose(s)</th>
<th>Mean Dose Achieved in Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Captopril</td>
<td>25 mg 3 times/week</td>
<td>50 mg 3 times/week</td>
<td>122.7 mg/d</td>
</tr>
<tr>
<td>Enalapril</td>
<td>2.5 mg twice/week</td>
<td>10 to 20 mg twice/week</td>
<td>16.6 mg/d</td>
</tr>
<tr>
<td>Fosinopril</td>
<td>5 to 10 mg once</td>
<td>40 mg once</td>
<td></td>
</tr>
<tr>
<td>Lisinopril</td>
<td>2.5 to 5 mg once</td>
<td>20 to 40 mg once</td>
<td></td>
</tr>
<tr>
<td>Perindopril</td>
<td>2 mg once</td>
<td>8 to 16 mg once</td>
<td></td>
</tr>
<tr>
<td>Quinapril</td>
<td>5 mg twice/week</td>
<td>20 mg twice/week</td>
<td></td>
</tr>
<tr>
<td>Ramipril</td>
<td>1.25 to 2.5 mg once</td>
<td>10 mg once</td>
<td></td>
</tr>
<tr>
<td>Trandolapril</td>
<td>1 mg once</td>
<td>4 mg once</td>
<td></td>
</tr>
</tbody>
</table>
**ACE I or ARB or Both?**

- ARBs are recommended in patients with HFrEF who are ACE inhibitor-intolerant (cough +/- angioedema), unless contraindicated, to reduce morbidity and mortality.

- ARBs are reasonable to reduce morbidity and mortality as alternatives to ACE inhibitors as first-line therapy for patients with HFrEF, especially for patients already taking ARBs for other indications.

- Addition of an ARB may be considered in persistently symptomatic patients with HFrEF who are already being treated with an ACE inhibitor and a beta blocker in whom an aldosterone antagonist is not indicated or tolerated.

**ALDO**

1° Outcome (CV Death, HF Hosp, or Resuscitated Cardiac Arrest)

**Which ARB; How Much?**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial Daily Dose(s)</th>
<th>Maximum Dose(s)</th>
<th>Mean Doses Achieved in Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARBs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Candesartan</td>
<td>4-8 mg qd</td>
<td>32 mg qd</td>
<td>24 mg/d</td>
</tr>
<tr>
<td>Losartan</td>
<td>25-50 mg qd</td>
<td>50 to 100 mg qd</td>
<td>129 mg/d</td>
</tr>
<tr>
<td>Valsartan</td>
<td>20-40 mg BID</td>
<td>160 mg BID</td>
<td>254 mg/d</td>
</tr>
</tbody>
</table>

**Aldosterone Antagonists**

- Aldosterone receptor antagonists (or mineralocorticoid receptor antagonists [MRA]) are recommended in patients with NYHA class II-IV and who have LVEF of ≤ 35%.

- Patients with NYHA class II should have a history of prior cardiovascular hospitalization or elevated plasma natriuretic peptide levels to be considered for aldosterone receptor antagonists.

- Creatinine should be ≤ 2.5 mg/dL or less in men or ≤ 2.0 mg/dL in women (or eGFR >30 mL/min/1.73m²) and potassium < 5.0 mEq/L.

- Careful monitoring of potassium, renal function, and diuretic dosing should be performed at initiation, within 7-10 days after initiation and followed thereafter to minimize risk of hyperkalemia and renal insufficiency.

**Aldosterone Antagonists**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial Daily Dose(s)</th>
<th>Maximum Dose(s)</th>
<th>Mean Doses Achieved in Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aldosterone Antagonists</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spironolactone</td>
<td>12.5 to 25 mg qd</td>
<td>25 mg qd</td>
<td>26 mg/d</td>
</tr>
<tr>
<td>Eplerenone</td>
<td>25 mg qd</td>
<td>50 mg qd</td>
<td>42.6 mg/d</td>
</tr>
</tbody>
</table>

- Eplerenone is a more specific aldosterone receptor antagonist; it can be used if spironolactone causes gynecomastia or breast pain.

- It causes the same effects on potassium and renal function as spironolactone.
Nitrate/Hydralazine (ISDN/HDZ)

- HDZ/ISDN combination is recommended for African Americans with NYHA class III–IV HFrEF receiving optimal therapy with ACE inhibitors and beta blockers.
- HDZ/ISDN can be useful to reduce morbidity or mortality in patients with current or prior symptomatic HFrEF who cannot be given an ACE inhibitor or ARB because of drug intolerance, hypotension, or renal insufficiency, unless contraindicated.

Digoxin

- Digoxin can be beneficial in patients with HFrEF and sinus rhythm to decrease hospitalizations for HF: consider adding if on other therapy and still symptomatic.
- Digoxin can be used in HF patients with atrial fibrillation to help rate control.
- **Dose:** 0.125 -0.25 mg qd depending on renal function (levels not for dosing but for toxicity)
- **Interaction with amiodarone, which ↑ Digoxin levels**

New Agent: Neprilysin as a Therapeutic Target

- Neprilysin breaks down endogenous vasoactive peptides, including the natriuretic peptides.
- Inhibition of neprilysin potentiates the action of these peptides.
- Because angiotensin II is also a substrate for neprilysin, neprilysin inhibitors must be co-administered with a RAAS blocker.
- The combination of a neprilysin inhibitor and an ACE inhibitor is associated with unacceptably high rates of angioedema.

Sacubitril/Valsartan (Entresto): Angiotensin Receptor–Neprilysin Inhibitor (ARNI)

- Sacubitril: Prodrug that inhibits neprilysin leading to increased levels of natriuretic peptides
- Valsartan: Angiotensin II receptor blocker

ARNI

Entresto (Combination of Sacubitril and Valsartan)

- Sacubitril: Prodrug that inhibits neprilysin leading to increased levels of natriuretic peptides
- Valsartan: Angiotensin II receptor blocker

Side Effects

Angioedema, hypotension, impaired renal function, and hyperkalemia.
- Should not be administered concomitantly with ACE inhibitors or within 36 hours of the last dose of an ACEI.

PARADIGM-HF: CV Death or HF Hospitalization (Primary Endpoint)
NEW DRUG: IVABRADINE (CORLANOR)

• Hyperpolarization-activated cyclic nucleotide-gated (HCN) channel blocker.
• Reduces diastolic depolarization slope in the SA node, thereby decreasing heart rate via direct sinus node inhibition without direct effects on myocardial contractility and intracardiac conduction
• Indicated to reduce the risk of HF hospitalization in patients with stable, symptomatic chronic HF with LVEF ≤35%, who are in sinus rhythm with resting heart rate ≥70 bpm and either are on maximally tolerated doses of beta-blockers or have a contraindication to beta-blocker use

SHIFT Trial Primary Composite Endpoint: CV Death or Hospitalization for Worsening HF

Medications & Devices
Effects on Mortality

<table>
<thead>
<tr>
<th>Medication</th>
<th>Symptoms</th>
<th>Hospitalizations</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretics</td>
<td>√</td>
<td>√ (? )</td>
<td>?</td>
</tr>
<tr>
<td>ACE I / ARBs</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>Beta-Blockers</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>Aldosterone Antagonists</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>Digitalis</td>
<td>√</td>
<td>√</td>
<td>X</td>
</tr>
<tr>
<td>Nitrates/Hydralazine</td>
<td>√</td>
<td>√</td>
<td>X</td>
</tr>
<tr>
<td>Neprilysin Inhibitor</td>
<td>√</td>
<td>√</td>
<td>?</td>
</tr>
<tr>
<td>Ivabradine</td>
<td>√</td>
<td>√</td>
<td>X</td>
</tr>
<tr>
<td>ICD (Defibrillators)</td>
<td>X</td>
<td>X</td>
<td>?</td>
</tr>
<tr>
<td>CRT (BiV pacemakers)</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
</tbody>
</table>

Medical Therapy for Stage C HFrEF: Magnitude of Benefit in RCTs

<table>
<thead>
<tr>
<th>Medication</th>
<th>RR to ↓ Mortality</th>
<th>NNT to ↓ mortality (standardized 36 months)</th>
<th>RR ↓ HF Hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE I / ARBs</td>
<td>17%</td>
<td>26</td>
<td>31%</td>
</tr>
<tr>
<td>Beta-Blockers</td>
<td>34%</td>
<td>9</td>
<td>41%</td>
</tr>
<tr>
<td>Aldosterone Antagonists</td>
<td>30%</td>
<td>6</td>
<td>35%</td>
</tr>
<tr>
<td>Nitrates/Hydralazine</td>
<td>43%</td>
<td>7</td>
<td>33%</td>
</tr>
</tbody>
</table>

A NOTE ABOUT HEART FAILURE WITH PRESERVED EF: SYSTOLIC VS DIASTOLIC

Systolic vs. diastolic

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>HTN</td>
<td>Cardiac hypertrophy, stiff heart, chronic renal failure, medication, age</td>
</tr>
<tr>
<td>DM</td>
<td>Cardiac hypertrophy, stiff heart, chronic renal failure, medication, age</td>
</tr>
<tr>
<td>Preserved EF or Diast HF</td>
<td>Cardiac hypertrophy, stiff heart, chronic renal failure, medication, age</td>
</tr>
</tbody>
</table>

Systolic vs Diastolic HF: Different Diseases with the Same Prognosis?
**HFpEF CLINICAL TRIALS**

- Trials have not shown significant mortality or morbidity benefit with use of ACEI/ARB specifically in HFpEF.
- No trials showing definite benefit of Beta blockers, sildenafil.

**TOPCAT trial**
- Randomized-double blind trial of spironolactone (15-45 mg) vs. placebo in HFpEF patients with:
  - Prior HF hospitalization or
  - BNP > 100 pg/ml

---

**TREATMENT OF HFpEF**

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic and diastolic blood pressure should be controlled according to published clinical practice guidelines</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Diuretics should be used for relief of symptoms due to sodium overload</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>A coronary comorbidity by Framingham, CAD, or a demonstrable myocardial ischemia in present despite GDMT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Management of HF according to published clinical practice guidelines for HFpEF to improve symptoms</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Use of beta-blocking agents, ACE inhibitors, and ARBs for hypertension in HFpEF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ARBs might be considered to decrease hospitalizations in HFpEF</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Nutritional supplementation is not recommended in HFpEF</td>
<td>II</td>
<td>No Benefit</td>
</tr>
</tbody>
</table>

---

**The Hospitalized Patient**

**Maintenance of GDMT During Hospitalization**

- **Goals**
  - Control symptoms
  - Improve HRQOL
  - Reduce hospital readmissions
  - Establish patient’s end-of-life goals

- **Options**
  - Advanced care measures
  - Heart transplant
  - Chronic home care
  - Temporary or permanent MCS
  - Experimental surgery or drugs
  - Palliative care and hospice
  - ICD deactivation

- **Stage D Refractory HF**
  - Marked HF symptoms at rest
  - Recurrent hospitalizations despite GDMT

---

**HFpEF**

<table>
<thead>
<tr>
<th>Goals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control symptoms</td>
</tr>
<tr>
<td>Improve HRQOL</td>
</tr>
<tr>
<td>Prevent hospitalization</td>
</tr>
<tr>
<td>Prevent mortality</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification of comorbidities</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease to relieve symptoms of congestion</td>
</tr>
<tr>
<td>Follow guideline-driven indications for comorbidities, e.g., HTN, AF, CAD, DM</td>
</tr>
<tr>
<td>Revascularization or valve surgery as appropriate</td>
</tr>
</tbody>
</table>

**HFpEF THERAPY**

- TIA (97)
- HFpEF (98)
- Treatment of HFpEF (99)
- The Hospitalized Patient (100)
- Maintenance of GDMT During Hospitalization (101)
- HFpEF THERAPY (102)
MAINTENANCE OF GDMT DURING HOSPITALIZATION

In patients with HF requiring hospitalization during chronic maintenance treatment with GDMT, it is recommended that GDMT be continued in the absence of hemodynamic instability or contraindications.

Initiation of beta-blocker therapy is recommended after optimization of volume status and successful discontinuation of intravenous diuretics, vasodilators, and inotropic agents. Beta-blocker therapy should be initiated at a low dose and only in stable patients. Caution should be used when initiating beta blockers in patients who have required inotropes during their hospital course.

DIURETICS IN HOSPITALIZED PATIENTS

Patients with HF admitted with evidence of significant fluid overload should be promptly treated with intravenous loop diuretics to reduce morbidity.

If patients are already receiving loop diuretic therapy, the initial intravenous dose should equal or exceed their chronic oral daily dose and should be given as either intermittent boluses or continuous infusion. Urine output and signs and symptoms of congestion should be serially assessed, and the diuretic dose should be adjusted accordingly to relieve symptoms, reduce volume excess, and avoid hypotension.

When diuresis is inadequate to relieve symptoms, it is reasonable to intensify the diuretic regimen using either:

a. higher doses of intravenous loop diuretics.

b. addition of a second (e.g., thiazide) diuretic.

Low-dose dopamine infusion may be considered in addition to loop diuretic therapy to improve diuresis and better preserve renal function and renal blood flow.
Commonly Used Diuretics

<table>
<thead>
<tr>
<th>Diuretic</th>
<th>Initiating Daily Dose (mg)</th>
<th>Maximum Daily Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCTZ</td>
<td>25</td>
<td>50</td>
</tr>
<tr>
<td>Loop Diuretics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Furosemide</td>
<td>20-40</td>
<td>480</td>
</tr>
<tr>
<td>Bumetanide</td>
<td>0.5-2</td>
<td>10</td>
</tr>
<tr>
<td>Torsemide</td>
<td>10-20</td>
<td>200</td>
</tr>
<tr>
<td>Metolazone</td>
<td>2.5</td>
<td>10</td>
</tr>
</tbody>
</table>

CEILING DOSES OF LOOP DIURETICS

<table>
<thead>
<tr>
<th></th>
<th>Furosemide</th>
<th>Bumetanide</th>
<th>Torsemide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal Insufficiency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>moderate</td>
<td>80</td>
<td>2-3</td>
<td>2-3</td>
</tr>
<tr>
<td>severe</td>
<td>240</td>
<td>8-10</td>
<td>8-10</td>
</tr>
<tr>
<td>Cirrhosis (normal GFR)</td>
<td>40-80</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>CHF (normal GFR)</td>
<td>40-80</td>
<td>200</td>
<td>20-50</td>
</tr>
</tbody>
</table>

WHAT TO DO WHEN THE CREATININE RISES

HINT: IT'S ALWAYS "PRE-RENAL"

- Check volume status
- Orthostatics, skin turgor, mucous membranes
- Check blood pressure (especially at peak onset of vasodilators)
- Restrict sodium intake (and water if hyponatremic)
- Check for intrinsic renal problems
- U/A with sediment
- Consider vasodilators or inotropes
- Consider ultrafiltration

The Hospitalized Patient

Parenteral Therapy in Hospitalized HF

Parenteral Therapy in Hospitalized HF

If symptomatic hypotension is absent, intravenous nitroglycerin, nitroprusside or nesiritide may be considered an adjuvant to diuretic therapy for relief of dyspnea in patients admitted with acutely decompensated HF.
Renal Replacement Therapy

Ultrafiltration may be considered for patients with obvious volume overload to alleviate congestive symptoms and fluid weight.

Ultrafiltration may be considered for patients with refractory congestion not responding to medical therapy.

In patients with evidence of severely symptomatic fluid overload in the absence of systemic hypotension, vasodilators such as intravenous nitroglycerin, nitroprusside or neseritide can be beneficial when added to diuretics and/or in those who do not respond to diuretics alone.

Inotropes

Dobutamine +++ ++ +/- +/-
Milrinone +++ + (SVT)
Dopamine* + ++ ++ ++

*assuming moderate dose (2 – 5 mcg/kg/min)
INFUSION OF POSITIVE INOTROPIC DRUGS

Routine intermittent infusions of vasoactive and positive inotropic agents are not recommended for patients with refractory end-stage HF.

Use of parenteral inotropes in normotensive patients with acute decompensated HF without evidence of decreased organ perfusion is not recommended.

INOTROPS IN ADVANCED HF

- Milrinone and Dobutamine are two commonly used inotropes approved for HF use in the US.
- Both increase cardiac output by increasing the intracellular level of cyclic adenosine monophosphate (cAMP).
- Dobutamine increases cAMP indirectly through adrenergic agonism.
- Milrinone, a phosphodiesterase inhibitor, directly blocks cAMP breakdown.

DOBUTAMINE

- Sympathomimetic amine, which acts on beta-1, beta-2, and alpha-1 adrenergic receptors.
- Strong inotropic effect and relatively weak chronotropic effect.
- No significant change in BP due to its alpha-1 agonist activity causing vasoconstriction, that balances the beta-2 vasodilatory effect.
- The use is problematic in patients who take beta blockers due to its adrenergic properties.
MILRINONE

- Milrinone inhibits phosphodiesterase 3 (PDE3), which prevents the degradation of cAMP and ultimately leads to an increase in protein kinase A (PKA).
- It is an inodilator, both increasing cardiac contractility and reducing afterload with a consequent reduction in left ventricular filling pressures.
- PKA increases contractility of the left ventricle and cardiac output through cAMP dependent-PKA.

SIMILARITIES

- Most of the hemodynamic effects of dobutamine and milrinone are similar.
- Increase cardiac output
- Cause peripheral vasodilation
- Decrease pulmonary capillary wedge pressure

DIFFERENCES

<table>
<thead>
<tr>
<th>Dobutamine</th>
<th>Milrinone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greater increase in heart rate</td>
<td>More hypotension</td>
</tr>
<tr>
<td>Greater increase in myocardial oxygen consumption</td>
<td>Greater reduction in left and right heart filling pressures</td>
</tr>
<tr>
<td>Greater proarrhythmic effect, including ventricular tachycardia</td>
<td>Greater reduction in MAP and IAP</td>
</tr>
<tr>
<td>Effects are attenuated in patients who receive beta blockers</td>
<td>Greater hemodynamic effects in general when the patient is on beta-blockers</td>
</tr>
<tr>
<td>Oxygen duration of action after discontinuation, especially in the presence of renal dysfunction</td>
<td></td>
</tr>
</tbody>
</table>

MORTALITY ON INOTROPIC SUPPORT

If symptomatic hypotension is absent, intravenous nitroglycerin, nitroprusside or nesiritide may be considered an adjuvant to diuretic therapy for relief of dyspnea in patients admitted with acutely decompensated HF.
ADVANCED HEART FAILURE
• Limited treatment options
  - Heart transplantation
  - Mechanical circulatory support (MCS)
  - Long-term inotropic therapy
  - Palliative care

ADVANCED HF THERAPIES
• Mechanical Circulatory support
  - ECMO
  - IABP

VENTRICULAR ASSIST DEVICES
Consideration of a left ventricular assist device as permanent or "destination" therapy is reasonable in highly selected patients with refractory end-stage HF and an estimated 1-year mortality over 50% with medical therapy.

CARDIAC TRANSPLANTATION
• Ideal treatment for advanced HF
• Provides increased longevity and symptomatic relief
• Approximately 3,000 people are on waiting list at any given time
• In 2015, there was only 2804 donors in US

LISTING CRITERIA FOR HEART TRANSPLANTATION
• Cardiopulmonary exercise testing: VO2 max <14ml/kg/min or if patients intolerant to BB, <12ml/kg/min in the presence T BB, or <50% of predicted VO2 in young patients (50yrs) and women.
• Acceptable pulmonary artery pressure
• Age <70
• Diabetes well controlled
• Absence on neoplasm
• Psychosocial support
CONTRAINDICATION

- Noncompliance with medical regimen
- Active substance abuse
- Severe symptomatic cerebrovascular disease
- Severe organ dysfunction (lung, kidney, liver, coagulopathy)
- Active infection
- Active mental illness
- Inadequate social support
- Fixed, severe pulmonary hypertension
- Morbid obesity (BMI > 35 kg/m²)
- Age > 70 years
- Recent or uncured malignancy

Implantable Cardiac Defibrillators (ICD)

- Sustained ventricular tachycardia is associated with sudden cardiac death in HF.
- About one-third of mortality in HF is due to sudden cardiac death.
- ICDs for primary prevention have been shown to improve survival in selected patients with HF.

ICD Therapy and Heart Failure

ICD Therapy is recommended for secondary prevention of SCD in patients who survived VT or hemodynamically unstable VF or VT who do not improve with medical therapy, and who have an LVEF less than or equal to 40%, and who are receiving chronic optimal medical therapy, and who have a reasonable expectation of survival with a good functional status for more than 1 year.

ICD Therapy is recommended for primary prevention to reduce total mortality or a reduction in SCD in patients with LV dysfunction due to prior MI who are at least 45 days post-MI, have an LVEF less than or equal to 30%, to 40%, are NYHA functional class II or III receiving chronic optimal medical therapy, and who have a reasonable expectation of survival with a good functional status for more than 1 year.

Primary Prevention Trials

- Multicenter Automatic Defibrillator Implantation Trial (MADIT) 2002
- Sudden Cardiac Death in Heart Failure; NEJM 2003

Indications for ICD Therapy

- ICD therapy is recommended for primary prevention of SCD in selected patients with HFrEF at least 40 days post-MI with LVEF ≤30%, and NYHA class II or III symptoms on chronic GDMT, who are expected to live ≥1 year.
- ICD therapy is recommended for primary prevention of SCD in selected patients with HFrEF at least 40 days post-MI with LVEF ≤30%, and NYHA class I symptoms while receiving GDMT, who are expected to live ≥1 year.
- ICDs do not improve symptoms; most patients should be on GDMT; should have an expected life-expectancy of at least 1 year.

Cardiac Resynchronization Pacing: Consequences of a Prolonged QRS

- Delayed Ventricular Activation
- Delayed lateral wall contraction
- Disorganized ventricular contraction
- Decreased pumping efficiency
- Reduction in diastolic filling times
- Prolongation of the duration of mitral regurgitation
Mechanism: Ventricular Resynchronization

- Intraventricular Activation
- Organized ventricular activation sequence
- Coordinated septal and free-wall contraction
- Improved pumping efficiency

Cardiac Resynchronization Rx (CRT)

- LVEF < 35%
- Greatest benefit in patients with systolic HF with LBBB + QRS > 150 msec already on GDMT and in sinus rhythm
- Can consider in patients with symptomatic HF with LBBB and QRS 120-149 msec
- Can consider in symptomatic HF with non-LBBB and QRS ≥ 150 msec
- Can be considered in atrial fibrillation if ventricular pacing is needed and rate control will allow nearly 100% ventricular pacing with CRT

2013 ACCF/AHA Guideline for the Management of Heart Failure

The Hospitalized Patient
Inpatient and Transitions of Care

Throughout the hospitalization as appropriate, before hospital discharge, at the first postdischarge visit, and in subsequent follow-up visits, the following should be addressed:

1. Initiation of GDMT if not previously established and not contraindicated.
2. Precipitant causes of HF, barriers to optimal care transitions, and limitations in postdischarge support.
3. Assessment of volume status and supine/upright hypotension with adjustment of HF therapy, as appropriate.
4. Titration and optimization of chronic oral HF therapy.
5. Assessment of renal function and electrolytes, where appropriate.
6. Assessment and management of co-morbid conditions.
7. Reinforcement of HF education, self-care, emergency plans, and need for adherence.
8. Consideration for palliative care or hospice care in selected patients.

INPATIENT AND TRANSITIONS OF CARE

The use of performance improvement systems and/or evidence-based systems of care is recommended in the hospital and early postdischarge outpatient setting to identify appropriate HF patients for GDMT, provide clinicians with useful reminders to advance GDMT, and to assess the clinical response.

Multidisciplinary HF disease-management programs are recommended for patients at high risk for hospital readmission, to facilitate the implementation of GDMT, to address different barriers to behavioral change, and to reduce the risk of subsequent rehospitalization for HF.

Scheduling an early follow-up visit (within 7 to 14 days) and early telephone follow-up (within 3 days) of hospital discharge is reasonable.

Use of clinical risk prediction tools and/or biomarkers to identify patients at higher risk for postdischarge clinical events is reasonable.
### THERAPIES IN THE HOSPITALIZED HF PATIENT

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>HF patients hospitalized with fluid overload should be treated with intravenous diuretics</td>
<td>I B</td>
<td></td>
</tr>
<tr>
<td>HF patients receiving loop diuretic therapy, should receive an initial parenteral dose greater than or equal to their chronic oral daily dose, then should be serially adjusted</td>
<td>I B</td>
<td></td>
</tr>
<tr>
<td>HFrEF patients requiring HF hospitalization on GDMT should continue GDMT unless hemodynamic instability or contraindications</td>
<td>I B</td>
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<tr>
<td>Initiation of beta-blocker therapy at a low dose is recommended after optimization of volume status and discontinuation of intravenous agents</td>
<td>I B</td>
<td></td>
</tr>
<tr>
<td>Thrombosis/thromboembolism prophylaxis is recommended for patients hospitalized with HF</td>
<td>I B</td>
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</tbody>
</table>

### THERAPIES IN THE HOSPITALIZED HF PATIENT (CONT.)

<table>
<thead>
<tr>
<th>Recommendation</th>
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<tbody>
<tr>
<td>When diuresis is inadequate, it is reasonable to</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>a) Give higher doses of intravenous loop diuretics; or</td>
<td></td>
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<tr>
<td>b) Add a second diuretic (e.g., thiazide)</td>
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<tr>
<td>Low-dose dopamine infusion may be considered with loop diuretics to improve diuresis</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>Ultrafiltration may be considered for patients with obvious volume overload</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>Ultrafiltration may be considered for patients with refractory congestion</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>Intravenous nitroglycerin, nitroprusside or nesiritide may be considered an adjunct to diuretic therapy for stable patients with HF</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>In patients hospitalized with volume overload and severe hyponatremia, vasopressin antagonists may be considered</td>
<td>IIb</td>
<td>C</td>
</tr>
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### HOSPITAL DISCHARGE

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<tr>
<td>Performance improvement systems in the hospital and early postdischarge support ensuring adherence to GDMT are recommended</td>
<td>I B</td>
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<tr>
<td>Before hospital discharge, at the first postdischarge visit, and in subsequent follow-up visits, the following should be addressed:</td>
<td>I B</td>
<td></td>
</tr>
<tr>
<td>a) Initiation of GDMT if not done or contraindicated;</td>
<td></td>
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</tr>
<tr>
<td>b) Causes of HF, barriers to care, and limitations in support;</td>
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</tr>
<tr>
<td>c) Assessment of volume status and blood pressure with adjustment of HF therapy;</td>
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<tr>
<td>d) Optimization of chronic HF therapy;</td>
<td></td>
<td></td>
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<tr>
<td>e) Clinical, functional, and dietary considerations;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>f) Management of concomitant conditions;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>g) Palliation, self-care, emergency plans, and adherence;</td>
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<tr>
<td>h) Palliative or hospice care</td>
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</table>

### SURGICAL/PERCUTANEOUS/TRANSCATHETER INTERVENTIONAL TREATMENTS OF HF

**Coronary artery revascularization via CABG or percutaneous intervention is indicated for patients (HFrEF and HFrEF) on GDMT with angina and suitable coronary anatomy, especially for a left main stenosis (>50%) or left main equivalent disease.**

**CABG to improve survival is reasonable in patients with mild to moderate LV systolic dysfunction (EF 35% to 50%) and significant (≥70% diameter stenosis) multivessel CAD or proximal LAD coronary artery stenosis when viable myocardium is present in the region of intended revascularization.**

**Surgical aortic valve replacement is reasonable for patients with critical aortic stenosis and a predicted surgical mortality of no greater than 10%.**

**Transcatheter aortic valve replacement after careful candidate consideration is reasonable for patients with critical aortic stenosis who are deemed inoperable.**

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**Guideline for HF**

**Surgical/Percutaneous/Transcatheter Interventional Treatments of HF**

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**SURGICAL/PERCUTANEOUS/TRANSCATHETER INTERVENTIONAL TREATMENT OF HF (CONT.)**

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<td>CABG or medical therapy is reasonable to improve morbidity and cardiovascular mortality for patients with severe LV dysfunction (EF &lt;35%), HF, and significant CAD.</td>
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SURGICAL/PERCUTANEOUS/TRANSCATHETER INTERVENTIONAL TREATMENT OF HF (CONT.)

CABG may be considered with the intent of improving survival in patients with ischemic heart disease with severe LV systolic dysfunction (EF <35%), and operable coronary anatomy whether or not viable myocardium is present.

Transcatheter mitral valve repair or mitral valve surgery for functional mitral insufficiency is of uncertain benefit and should only be considered after careful candidate selection and with a background of GDMT.

Surgical reverse remodeling or LV aneurysmectomy may be considered in carefully selected patients with HF for specific indications including intractable HF and ventricular arrhythmias.

COORDINATING CARE FOR PATIENTS WITH CHRONIC HF

Effective systems of care coordination with special attention to care transitions should be deployed for every patient with chronic HF that facilitate and ensure effective care that is designed to achieve GDMT and prevent hospitalization.

Every patient with HF should have a clear, detailed and evidence-based plan of care that ensures the achievement of GDMT goals, effective management of comorbid conditions, timely follow-up with the healthcare team, adequate dietary and physical activities, and compliance with Secondary Prevention Guidelines for cardiovascular disease. This plan of care should be updated regularly and made readily available to all members of each patient’s healthcare team.

Palliative and supportive care is effective for patients with symptomatic advanced HF to improve quality of life.

RECONCILING AND ADJUSTING MEDICATIONS

OPTIMIZE-HF AND B-CONVINCED: DON’T STOP THE β-BLOCKERS

In patients with reduced ejection fraction experiencing a symptomatic exacerbation of HF requiring hospitalization during chronic maintenance treatment with β-blocker therapy, it is recommended that these therapies be continued in most patients in the absence of hemodynamic instability or contraindications.

CAN WE WAIT TO START THE β-BLOCKERS?

OPTIMIZE-HF substudy: Fonarow GC et al. JACC 2008; 52(3) 190-199

WITHDRAWN

NOT TREATED

CONTINUED

NEWLY STARTED
ACE-INHIBITOR OR BETA-BLOCKER FIRST?
CIBIS-III

Referral for cardiac transplantation in potentially eligible patients is recommended for patients with refractory end-stage HF.

Referral of patients with refractory end-stage HF to an HF program with expertise in the management of refractory HF is useful.

Q QUALITY METRICS/PERFORMANCE MEASURES

Performance measures based on professionally developed clinical practice guidelines should be used with the goal of improving quality of care for HF.

Participation in quality improvement programs and patient registries based on nationally endorsed, clinical practice guideline-based quality and performance measures may be beneficial in improving quality of HF care.

ACCF/AHA/AMA-PCPI 2011 HF PERFORMANCE MEASUREMENT SET

Quality Metrics/Performance Measures

Guideline for HF
ACCF/AHA/AMA-PCPI 2011 HF PERFORMANCE MEASUREMENT SET (CONT.)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Measure Description*</th>
<th>Care Setting</th>
<th>Level of Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>4. Symptom management†</td>
<td>Percentage of patient visits for those patients aged ≥18 y with a diagnosis of HF and with quantitative results of an evaluation of both level of activity and clinical symptoms documented in which patient symptoms have improved or remained consistent with treatment goals since last assessment OR patient symptoms have deteriorated clinically, important deterioration since last assessment with a documented plan of care</td>
<td>Outpatient Individual practitioner</td>
<td>Individual practitioner</td>
</tr>
<tr>
<td>5. Patient self-care education†‡</td>
<td>Percentage of patients aged ≥18 y with a diagnosis of HF who were provided with self-care education on ≥3 elements of education during ≥1 visits within a 12 mo period</td>
<td>Outpatient Individual practitioner</td>
<td>Individual practitioner</td>
</tr>
<tr>
<td>6. Beta-blocker therapy for LVSD (outpatient and inpatient setting)</td>
<td>Percentage of patients aged ≥18 y with a diagnosis of HF with a current or prior LVEF &lt;40% who were prescribed beta-blocker therapy with bisoprolol, carvedilol, or sustained release metoprolol succinate either within a 12 mo period when seen in the outpatient setting or at hospital discharge</td>
<td>Inpatient and Outpatient Individual practitioner Facility</td>
<td>Individual practitioner Facility</td>
</tr>
</tbody>
</table>

*Please refer to the complete measures for comprehensive information, including measure exception.
†Test measure designated for use in internal quality improvement programs only. These measures are not appropriate for any other purpose, e.g., pay for performance, physician ranking or public reporting programs.
‡New measure.


QUESTIONS?

- Also, feel free to email me questions to
- Robert.Rogers@nortonhealthcare.org