Review of the 2013 Heart Failure Guidelines: What You Need to Know (Part 1)

09/27/2013
Presenter: Clyde Yancy
Thank you for Joining the Webinar Today.

The Presentation will Begin Shortly.
Clyde Yancy
*M.D., MSc, FACC, FAHA, MACP*
2013 ACCF/AHA Guideline for the Management of Heart Failure

Developed in Collaboration With the American Academy of Family Physicians, American College of Chest Physicians, Heart Rhythm Society, and International Society for Heart and Lung Transplantation

Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation

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From Risk Factors to Heart Failure: The Cardiovascular Continuum

Risk factors
- Hyperlipidemia
- Hypertension
- Diabetes
- Insulin resistance

Atherosclerosis
- CAD
- LVH

Myocardial ischemia
- Coronary thrombosis

Myocardial infarction
- Arrhythmia
- Loss of muscle
- Sudden death
- Ventricular dilation
  - Remodeling (due to neurohormonal activation)
  - Heart failure
  - Death

Remodeling (due to neurohormonal activation)

Death

Adapted from Dzau and Braunwald. Am Heart J. 1991;131:1244-1263.
Stages, Phenotypes and Treatment of HF

**At Risk for Heart Failure**

**STAGE A**
At high risk for HF but without structural heart disease or symptoms of HF
- Patients with:
  - HTN
  - Atherosclerotic disease
  - DM
  - Obesity
  - Metabolic syndrome
  - Using cardiotonics
  - With family history of cardiomyopathy

**THERAPY**
Goals:
- Heart healthy lifestyle
- Prevent vascular, coronary disease
- Prevent LV structural abnormalities

Drugs:
- ACEI or ARB in appropriate patients for vascular disease or DM
- Statins as appropriate

**STAGE B**
Structural heart disease but without signs or symptoms of HF
- Patients with:
  - Previous MI
  - LV remodeling including LVH and low EF
  - Asymptomatic valvular disease

**THERAPY**
Goals:
- Prevent HF symptoms
- Prevent further cardiac remodeling

Drugs:
- ACEI or ARB as appropriate
- Beta blockers as appropriate

In selected patients:
- ICD
- Revascularization or valvular surgery as appropriate

**STAGE C**
Structural heart disease with prior or current symptoms of HF
- Patients with:
  - Known structural heart disease and HF signs and symptoms

**THERAPY**
Goals:
- Control symptoms
- Improve HRQOL
- Prevent hospitalization
- Prevent mortality

Drugs for routine use:
- Diuretics for fluid retention
- ACEI or ARB
- Beta blockers
- Aldosterone antagonists

Drugs for use in selected patients:
- Hydralazine/nifedipine dinitrate
- ACEI and ARB
- Digoxin

In selected patients:
- CRT
- ICD
- Revascularization or valvular surgery as appropriate

**Heart Failure**

**STAGE D**
Refractory HF
- Patients with:
  - Marked HF symptoms at rest
  - Recurrent hospitalizations despite GDMT

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

Options:
- Advanced care measures
- Heart transplant
- Chronic inotropes
- Temporary or permanent MCS
- Experimental surgery or drugs
- Palliative care and hospice
- ICD deactivation
**Classification of Recommendations and Levels of Evidence**

| Level A | Multiple populations evaluated*  
|---------|---------------------------------  
| Data derived from multiple randomized clinical trials or meta-analyses |  
| - Recommendation that procedure or treatment is useful/effective  
| - Sufficient evidence from multiple randomized trials or meta-analyses |  
| CLASS I | Benefit >> Risk  
| Procedure/Treatment SHOULD be performed/administered |  

| Level B | Limited populations evaluated*  
|---------|---------------------------------  
| Data derived from a single randomized trial or nonrandomized studies |  
| - Recommendation that procedure or treatment is useful/effective  
| - Evidence from single randomized trial or nonrandomized studies |  

| LEVEL C | Very limited populations evaluated*  
|---------|---------------------------------  
| Only consensus opinion of experts, case studies, or standard of care |  
| - Recommendation that procedure or treatment is useful/effective  
| - Only expert opinion, case studies, or standard of care |  

- Suggested phrases for writing recommendations:
  - should be recommended
  - is indicated
  - is useful/effective/beneficial
  - is reasonable
  - may/might be considered
  - may/might be reasonable
  - usefulness/effectiveness is unknown/undefinite/cannot be evaluated

**Comparative effectiveness phrases**

- treatment A is recommended/indicated in prefer to treatment B
- treatment A should be chosen over treatment B
- treatment A is probably recommended/indicated in preference to treatment B
- it is reasonable to choose treatment A over treatment B

- COR III: No Benefit
- COR III: Harm
- COR III: Potentially Harmful
- COR III: Excess mortality

---

A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Although randomized trials are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as sex, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use.

†For comparative effectiveness recommendations (Class I and IIa; Level of Evidence A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.
Do the HF clinical practice guidelines actually work?
The baseline process measure conformity was significantly lower among patients who died compared with those who survived for 5 of 7 individual measures.
Each 10% improvement in guideline recommended composite care was associated with a 13% lower odds of 24-month mortality (adjusted OR 0.87; 95% CI, 0.84 to 0.90; \( P<0.0001 \)).

The adjusted odds for mortality risk for patients with conformity to each measure for which they were eligible was 38% lower than for those whose care did not conform for 1 or more measures for which they were eligible (adjusted OR 0.62; 95% CI, 0.52 to 0.75; \( P<0.0001 \)).
Incremental Benefit with HF Therapies
(Cumulative % Reduction in Odds of Death at 24 Months Associated with Sequential Treatments)

- ACEI/ARB: -38% (+20% to -68%, P=0.1566)
- ACEI/ARB + BB: -77% (-43% to -91%, P<0.0001)
- ACEI/ARB + BB + CRT + ICD: -90% (-70% to -96%, P<0.0001)

Results: Mortality Reduction Based on Number of Guideline-Recommended Therapies at Baseline

Number of Therapies (vs 0 or 1 therapy)  |  Odds Ratio (95% confidence interval)
---|---
2 therapies  | 0.63 (0.47-0.85) (p=0.0026)
3 therapies  | 0.38 (0.29-0.51) (p<0.0001)
4 therapies  | 0.30 (0.23-0.41) (p<0.0001)
5, 6, or 7 therapies  | 0.31 (0.23-0.42) (p<0.0001)
Stages, Phenotypes and Treatment of HF

**At Risk for Heart Failure**

**STAGE A**
At high risk for HF but without structural heart disease or symptoms of HF

- **E.g.:** Patients with:
  - HTN
  - Atherosclerotic disease
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- **E.g.:** Patients with:
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  - LV remodeling including LVH and low EF
  - Asymptomatic valvular disease

**THERAPY**
- **Goals:**
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  - Prevent further cardiac remodeling

- **Drugs:**
  - ACEI or ARB as appropriate
  - Beta blockers as appropriate

- **In selected patients**
  - ICD
  - Revascularization or valvular surgery as appropriate

**STAGE C**
Structural heart disease with prior or current symptoms of HF

- **E.g.:** Patients with:
  - Known structural heart disease and HF signs and symptoms

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  - Hydralazine/isosorbide dinitrate
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  - Digoxin

- **In selected patients**
  - CRT
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**Heart Failure**

**STAGE D**
Refractory HF

- **E.g.:** Patients with:
  - Marked HF symptoms at rest
  - Recurrent hospitalizations despite GDMT

**THERAPY**
- **Goals:**
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  - Heart transplant
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  - Temporary or permanent MCS
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  - Palliative care and hospice
  - ICD deactivation

**Helping Cardiovascular Professionals**
**Learn. Advance. Heal.**
Clinical Evaluation
## Definition of Heart Failure

<table>
<thead>
<tr>
<th>Classification</th>
<th>Ejection Fraction</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Heart Failure with Reduced Ejection Fraction (HF(r)EF)</td>
<td>≤40%</td>
<td>Also referred to as systolic HF. Randomized clinical trials have mainly enrolled patients with HF(r)EF and it is only in these patients that efficacious therapies have been demonstrated to date.</td>
</tr>
<tr>
<td>II. Heart Failure with Preserved Ejection Fraction (HF(p)EF)</td>
<td>≥50%</td>
<td>Also referred to as diastolic HF. Several different criteria have been used to further define HF(p)EF. The diagnosis of HF(p)EF is challenging because it is largely one of excluding other potential noncardiac causes of symptoms suggestive of HF. To date, efficacious therapies have not been identified.</td>
</tr>
<tr>
<td>a. HF(p)EF, Borderline</td>
<td>41% to 49%</td>
<td>These patients fall into a borderline or intermediate group. Their characteristics, treatment patterns, and outcomes appear similar to those of patient with HF(p)EF.</td>
</tr>
<tr>
<td>b. HF(p)EF, Improved</td>
<td>&gt;40%</td>
<td>It has been recognized that a subset of patients with HF(p)EF previously had HF(r)EF. These patients with improvement or recovery in EF may be clinically distinct from those with persistently preserved or reduced EF. Further research is needed to better characterize these patients.</td>
</tr>
</tbody>
</table>
## Classification of Heart Failure

<table>
<thead>
<tr>
<th>ACCF/AHA Stages of HF</th>
<th>NYHA Functional Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>A At high risk for HF but without structural heart disease or symptoms of HF.</td>
<td>None</td>
</tr>
<tr>
<td>B Structural heart disease but without signs or symptoms of HF.</td>
<td>I No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.</td>
</tr>
<tr>
<td>C Structural heart disease with prior or current symptoms of HF.</td>
<td>I No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.</td>
</tr>
<tr>
<td></td>
<td>II Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in symptoms of HF.</td>
</tr>
<tr>
<td></td>
<td>III Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes symptoms of HF.</td>
</tr>
<tr>
<td>D Refractory HF requiring specialized interventions.</td>
<td>IV Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest.</td>
</tr>
</tbody>
</table>
Initial and Serial Evaluation of the HF Patient
Initial and Serial Evaluation of the HF Patient

History and Physical Examination
A thorough history and physical examination should be obtained/perform ed in patients presenting with HF to identify cardiac and noncardiac disorders or behaviors that might cause or accelerate the development or progression of HF.

In patients with idiopathic DCM, a 3-generational family history should be obtained to aid in establishing the diagnosis of familial DCM.

Volume status and vital signs should be assessed at each patient encounter. This includes serial assessment of weight, as well as estimates of jugular venous pressure and the presence of peripheral edema or orthopne a.
Risk Scoring
Validated multivariable risk scores can be useful to estimate subsequent risk of mortality in ambulatory or hospitalized patients with HF.
## Risk Scores to Predict Outcomes in HF

<table>
<thead>
<tr>
<th>Risk Score</th>
<th>Reference (from full-text guideline)/Link</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chronic HF</strong></td>
<td></td>
</tr>
<tr>
<td><em>All patients with chronic HF</em></td>
<td></td>
</tr>
<tr>
<td>Seattle Heart Failure Model</td>
<td>(204) / <a href="http://SeattleHeartFailureModel.org">http://SeattleHeartFailureModel.org</a></td>
</tr>
<tr>
<td>Heart Failure Survival Score</td>
<td>(200) / <a href="http://handheld.softpedia.com/get/Health/Calculator/HFSS-Calc-37354.shtml">http://handheld.softpedia.com/get/Health/Calculator/HFSS-Calc-37354.shtml</a></td>
</tr>
<tr>
<td>CHARM Risk Score</td>
<td>(207)</td>
</tr>
<tr>
<td>CORONA Risk Score</td>
<td>(208)</td>
</tr>
<tr>
<td><strong>Specific to chronic HFpEF</strong></td>
<td></td>
</tr>
<tr>
<td>I-PRESERVE Score</td>
<td>(202)</td>
</tr>
<tr>
<td><strong>Acutely Decompensated HF</strong></td>
<td></td>
</tr>
<tr>
<td>ADHERE Classification and Regression Tree (CART) Model</td>
<td>(201)</td>
</tr>
<tr>
<td>EFFECT Risk Score</td>
<td>(203) / <a href="http://www.ccort.ca/Research/CHFRiskModel.aspx">http://www.ccort.ca/Research/CHFRiskModel.aspx</a></td>
</tr>
<tr>
<td>ESCAPE Risk Model and Discharge Score</td>
<td>(215)</td>
</tr>
<tr>
<td>OPTIMIZE HF Risk-Prediction Nomogram</td>
<td>(216)</td>
</tr>
</tbody>
</table>
Diagnostic Tests
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 HIV 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.
Initial and Serial Evaluation of the HF Patient

Biomarkers
Ambulatory/Outpatient
Ambulatory/Outpatient

In ambulatory patients with dyspnea, measurement of BNP or N-terminal pro-B-type natriuretic peptide (NT-proBNP) is useful to support clinical decision making regarding the diagnosis of HF, especially in the setting of clinical uncertainty.

Measurement of BNP or NT-proBNP is useful for establishing prognosis or disease severity in chronic HF.
BNP- or NT-proBNP guided HF therapy can be useful to achieve optimal dosing of GDMT in select clinically euvolemic patients followed in a well-structured HF disease management program.

The usefulness of serial measurement of BNP or NT-proBNP to reduce hospitalization or mortality in patients with 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 chronic HF.
Initial and Serial Evaluation of the HF Patient

Biomarkers
Hospitalized/Acute
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.
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.
# Recommendations for Biomarkers in HF

<table>
<thead>
<tr>
<th>Biomarker, Application</th>
<th>Setting</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Natriuretic peptides</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis or exclusion of HF</td>
<td>Ambulatory, Acute</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Prognosis of HF</td>
<td>Ambulatory, Acute</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Achieve GDMT</td>
<td>Ambulatory</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Guidance of acutely decompensated HF therapy</td>
<td>Acute</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td><strong>Biomarkers of myocardial injury</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Additive risk stratification</td>
<td>Acute, Ambulatory</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td><strong>Biomarkers of myocardial fibrosis</strong></td>
<td></td>
<td></td>
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<td>Additive risk stratification</td>
<td>Ambulatory</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>Acute</td>
<td>IIb</td>
<td>A</td>
</tr>
</tbody>
</table>

**Helping Cardiovascular Professionals**

Causes for Elevated Natriuretic Peptide Levels

<table>
<thead>
<tr>
<th>Cardiac</th>
<th>Noncardiac</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Heart failure, including RV syndromes</td>
<td>• Advancing age</td>
</tr>
<tr>
<td>• Acute coronary syndrome</td>
<td>• Anemia</td>
</tr>
<tr>
<td>• Heart muscle disease, including LVH</td>
<td>• Renal failure</td>
</tr>
<tr>
<td>• Valvular heart disease</td>
<td>• Pulmonary causes: obstructive sleep apnea, severe pneumonia, pulmonary hypertension</td>
</tr>
<tr>
<td>• Pericardial disease</td>
<td>• Critical illness</td>
</tr>
<tr>
<td>• Atrial fibrillation</td>
<td>• Bacterial sepsis</td>
</tr>
<tr>
<td>• Myocarditis</td>
<td>• Severe burns</td>
</tr>
<tr>
<td>• Cardiac surgery</td>
<td>• Toxic-metabolic insults, including cancer chemotherapy and envenomation</td>
</tr>
</tbody>
</table>
Noninvasive Cardiac Imaging
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 patients’ 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.
Magnetic resonance imaging is reasonable when assessing myocardial infiltrative processes or scar burden.

Routine repeat measurement of LV function assessment in the absence of clinical status change or treatment interventions should not be performed.
## 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</td>
<td>C</td>
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<td>A 2-dimensional echocardiogram with Doppler should be performed for initial evaluation of HF</td>
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<td>C</td>
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<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>I</td>
<td>C</td>
</tr>
<tr>
<td>Noninvasive imaging to detect myocardial ischemia and viability is reasonable in HF and CAD</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Viability assessment is reasonable before revascularization in HF patients with CAD</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Radionuclide ventriculography or MRI can be useful to assess LVEF and volume</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>MRI is reasonable when assessing myocardial infiltration or scar</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Routine repeat measurement of LV function assessment should not be performed</td>
<td>III: No Benefit</td>
<td>B</td>
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</table>
Initial and Serial Evaluation of the HF Patient

Invasive Evaluation
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 intracardiac 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.
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 decompensated HF and congestion with symptomatic response to diuretics and vasodilators.

Endomyocardial biopsy should not be performed in the routine evaluation of patients with HF.
# Recommendations for Invasive Evaluation

<table>
<thead>
<tr>
<th>Recommendation</th>
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<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</td>
<td>C</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</td>
<td>C</td>
</tr>
<tr>
<td>When coronary ischemia may be contributing to HF, coronary arteriography is reasonable</td>
<td>IIa</td>
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<td>IIa</td>
<td>C</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>
Guideline for HF

Treatment of Stages A to D
Stage A
Hypertension and lipid disorders should be controlled in accordance with contemporary guidelines to lower the risk of HF.

Other conditions that may lead to or contribute to HF, such as obesity, diabetes mellitus, tobacco use, and known cardiotoxic agents, should be controlled or avoided.
Stage B
In all patients with a recent or remote history of MI or ACS and reduced EF, ACE inhibitors should be used to prevent symptomatic HF and reduce mortality. In patients intolerant of ACE inhibitors, ARBs are appropriate unless contraindicated.

In all patients with a recent or remote history of MI or ACS and reduced EF, evidence-based beta blockers should be used to reduce mortality.

In all patients with a recent or remote history of MI or ACS, statins should be used to prevent symptomatic HF and cardiovascular events.
In patients with structural cardiac abnormalities, including LV hypertrophy, in the absence of a history of MI or ACS, blood pressure should be controlled in accordance with clinical practice guidelines for hypertension to prevent symptomatic HF.

ACE inhibitors should be used in all patients with a reduced EF to prevent symptomatic HF, even if they do not have a history of MI.

Beta blockers should be used in all patients with a reduced EF to prevent symptomatic HF, even if they do not have a history of MI.
Stage B (cont.)

To prevent sudden death, placement of an ICD is reasonable in patients with asymptomatic ischemic cardiomyopathy who are at least 40 days post-MI, have an LVEF of 30% or less, are on appropriate medical therapy and have reasonable expectation of survival with a good functional status for more than 1 year.

Nondihydropyridine calcium channel blockers with negative inotropic effects may be harmful in asymptomatic patients with low LVEF and no symptoms of HF after MI.
# Recommendations for Treatment of Stage B HF

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>In patients with a history of MI and reduced EF, ACE inhibitors or ARBs should be used to prevent HF</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>In patients with MI and reduced EF, evidence-based beta blockers should be used to prevent HF</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>In patients with MI, statins should be used to prevent HF</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Blood pressure should be controlled to prevent symptomatic HF</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>ACE inhibitors should be used in all patients with a reduced EF to prevent HF</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Beta blockers should be used in all patients with a reduced EF to prevent HF</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>An ICD is reasonable in patients with asymptomatic ischemic cardiomyopathy who are at least 40 d post-MI, have an LVEF ≤30%, and on GDMT</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Nondihydropyridine calcium channel blockers may be harmful in patients with low LVEF</td>
<td>III: Harm</td>
<td>C</td>
</tr>
</tbody>
</table>
Stage C
Nonpharmacological Interventions
Stage C: Nonpharmacological Interventions

**B**

Patients with HF should receive specific education to facilitate HF self-care.

**A**

Exercise training (or regular physical activity) is recommended as safe and effective for patients with HF who are able to participate to improve functional status.

**C**

Sodium restriction is reasonable for patients with symptomatic HF to reduce congestive symptoms.
Stage C: Nonpharmacological Interventions (cont.)

Continuous positive airway pressure (CPAP) can be beneficial to increase LVEF and improve functional status in patients with HF and sleep apnea.

Cardiac rehabilitation can be useful in clinically stable patients with HF to improve functional capacity, exercise duration, HRQOL, and mortality.
Pharmacological Treatment for Stage C HF/ÆEF
Pharmacological Treatment for Stage C HF rEF

Measures listed as Class I recommendations for patients in stages A and B are recommended where appropriate for patients in stage C. (Levels of Evidence: A, B, and C as appropriate)

GDMT as depicted in Figure 1 should be the mainstay of pharmacological therapy for HF rEF.
Pharmacologic Treatment for Stage C HFrEF

HFrEF Stage C
NYHA Class I – IV

Treatment:

Class I, LOE A
ACEI or ARB AND Beta Blocker

For all volume overload, NYHA class II-IV patients
Add
Class I, LOE C
Loop Diuretics

For persistently symptomatic African Americans, NYHA class III-IV
Add
Class I, LOE A
Hydral-Nitrates

For NYHA class II-IV patients. Provided estimated creatinine >30 mL/min and K+ <5.0 mEq/dL
Add
Class I, LOE A
Aldosterone Antagonist
Diuretics are recommended in patients with HFrEF who have evidence of fluid retention, unless contraindicated, to improve symptoms.

ACE inhibitors are recommended in patients with HFrEF and current or prior symptoms, unless contraindicated, to reduce morbidity and mortality.

ARBs are recommended in patients with HFrEF with current or prior symptoms who are ACE inhibitor-intolerant, unless contraindicated, to reduce morbidity and mortality.
# Drugs Commonly Used for HFrEF (Stage C HF)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial Daily Dose(s)</th>
<th>Maximum Doses(s)</th>
<th>Mean Doses Achieved in Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACE Inhibitors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Captopril</td>
<td>6.25 mg 3 times</td>
<td>50 mg 3 times</td>
<td>122.7 mg/d (421)</td>
</tr>
<tr>
<td>Enalapril</td>
<td>2.5 mg twice</td>
<td>10 to 20 mg twice</td>
<td>16.6 mg/d (412)</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>32.5 to 35.0 mg/d (444)</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</td>
<td>20 mg twice</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>
<tr>
<td><strong>ARBs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Candesartan</td>
<td>4 to 8 mg once</td>
<td>32 mg once</td>
<td>24 mg/d (419)</td>
</tr>
<tr>
<td>Losartan</td>
<td>25 to 50 mg once</td>
<td>50 to 150 mg once</td>
<td>129 mg/d (420)</td>
</tr>
<tr>
<td>Valsartan</td>
<td>20 to 40 mg twice</td>
<td>160 mg twice</td>
<td>254 mg/d (109)</td>
</tr>
<tr>
<td><strong>Aldosterone Antagonists</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spironolactone</td>
<td>12.5 to 25 mg once</td>
<td>25 mg once or twice</td>
<td>26 mg/d (424)</td>
</tr>
<tr>
<td>Eplerenone</td>
<td>25 mg once</td>
<td>50 mg once</td>
<td>42.6 mg/d (445)</td>
</tr>
<tr>
<td>Drug</td>
<td>Initial Daily Dose(s)</td>
<td>Maximum Doses(s)</td>
<td>Mean Doses Achieved in Clinical Trials</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>--------------------------------------</td>
<td>-----------------------------------</td>
<td>----------------------------------------</td>
</tr>
<tr>
<td><strong>Beta Blockers</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bisoprolol</td>
<td>1.25 mg once</td>
<td>10 mg once</td>
<td>8.6 mg/d (118)</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>3.125 mg twice</td>
<td>50 mg twice</td>
<td>37 mg/d (446)</td>
</tr>
<tr>
<td>Carvedilol CR</td>
<td>10 mg once</td>
<td>80 mg once</td>
<td>---------</td>
</tr>
<tr>
<td>Metoprolol succinate extended release (metoprolol CR/XL)</td>
<td>12.5 to 25 mg once</td>
<td>200 mg once</td>
<td>159 mg/d (447)</td>
</tr>
<tr>
<td><strong>Hydralazine &amp; Isosorbide Dinitrate</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fixed dose combination (423)</td>
<td>37.5 mg hydralazine/20 mg isosorbide dinitrate 3 times daily</td>
<td>75 mg hydralazine/40 mg isosorbide dinitrate 3 times daily</td>
<td>~175 mg hydralazine/90 mg isosorbide dinitrate daily</td>
</tr>
<tr>
<td>Hydralazine and isosorbide dinitrate (448)</td>
<td>Hydralazine: 25 to 50 mg, 3 or 4 times daily and isosorbide dinitrate: 20 to 30 mg 3 or 4 times daily</td>
<td>Hydralazine: 300 mg daily in divided doses and isosorbide dinitrate 120 mg daily in divided doses</td>
<td>---------</td>
</tr>
</tbody>
</table>
Pharmacological Treatment for Stage C HFrEF (cont.)

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, unless contraindicated.

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.
Pharmacological Treatment for Stage C HFrEF (cont.)

Routine *combined* use of an ACE inhibitor, ARB, and aldosterone antagonist is potentially harmful for patients with HFrEF.

Use of 1 of the 3 beta blockers proven to reduce mortality (i.e., bisoprolol, carvedilol, and sustained-release metoprolol succinate) is recommended for all patients with current or prior symptoms of HFrEF, unless contraindicated, to reduce morbidity and mortality.
Aldosterone receptor antagonists [or mineralocorticoid receptor antagonists (MRA)] are recommended in patients with NYHA class II-IV and who have LVEF of 35% or less, unless contraindicated, to reduce morbidity and mortality. 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 or less in women (or estimated glomerular filtration rate >30 mL/min/1.73m²) and potassium should be less than 5.0 mEq/L. Careful monitoring of potassium, renal function, and diuretic dosing should be performed at initiation and closely followed thereafter to minimize risk of hyperkalemia and renal insufficiency.
Aldosterone receptor antagonists are recommended to reduce morbidity and mortality following an acute MI in patients who have LVEF of 40% or less who develop symptoms of HF or who have a history of diabetes mellitus, unless contraindicated.

Inappropriate use of aldosterone receptor antagonists is potentially harmful because of life-threatening hyperkalemia or renal insufficiency when serum creatinine greater than 2.5 mg/dL in men or greater than 2.0 mg/dL in women (or estimated glomerular filtration rate <30 mL/min/1.73m2), and/or potassium above 5.0 mEq/L.
The combination of hydralazine and isosorbide dinitrate is recommended to reduce morbidity and mortality for patients self-described as African Americans with NYHA class III–IV HF\textsubscript{rEF} receiving optimal therapy with ACE inhibitors and beta blockers, unless contraindicated.

A combination of hydralazine and isosorbide dinitrate can be useful to reduce morbidity or mortality in patients with current or prior symptomatic HF\textsubscript{rEF} who cannot be given an ACE inhibitor or ARB because of drug intolerance, hypotension, or renal insufficiency, unless contraindicated.
Digoxin can be beneficial in patients with HFrEF, unless contraindicated, to decrease hospitalizations for HF.

Patients with chronic HF with permanent/persistent/paroxysmal AF and an additional risk factor for cardioembolic stroke (history of hypertension, diabetes mellitus, previous stroke or transient ischemic attack, or ≥75 years of age) should receive chronic anticoagulant therapy (in the absence of contraindications to anticoagulation).
The selection of an anticoagulant agent (warfarin, dabigatran, apixaban, or rivaroxaban) for permanent/persistent/paroxysmal AF should be individualized on the basis of risk factors, cost, tolerability, patient preference, potential for drug interactions, and other clinical characteristics, including time in the international normalized rate therapeutic ration if the patient has been taking warfarin.

Chronic anticoagulation is reasonable for patients with chronic HF who have permanent/persistent/paroxysmal AF but are without an additional risk factor for cardioembolic stroke (in the absence of contraindications to anticoagulation).
Anticoagulation is **not recommended** in patients with chronic HFrEF without AF, a prior thromboembolic event, or a cardioembolic source.

Statins are not beneficial as adjunctive therapy when prescribed solely for the diagnosis of HF in the absence of other indications for their use.

Omega-3 polyunsaturated fatty acid (PUFA) supplementation is reasonable to use as adjunctive therapy in patients with NYHA class II-IV symptoms and HFrEF or HFrPEF, unless contraindicated, to reduce mortality and cardiovascular hospitalizations.
Nutritional supplements as treatment for HF are not recommended in patients with current or prior symptoms of HFrEF.

Hormonal therapies other than to correct deficiencies are not recommended for patients with current or prior symptoms of HFrEF.

Drugs known to adversely affect the clinical status of patients with current or prior symptoms of HFrEF are potentially harmful and should be avoided or withdrawn whenever possible (e.g., most antiarrhythmic drugs, most calcium channel blocking drugs (except amlodipine), NSAIDs, or TZDs).
Long-term use of infused positive inotropic drugs is potentially harmful for patients with HFrEF, except as palliation for patients with end-stage disease who cannot be stabilized with standard medical treatment (see recommendations for stage D).

Calcium channel blocking drugs are not recommended as routine treatment for patients with HFrEF.
## Pharmacological Therapy for Management of Stage C HFrEF

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diuretics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diuretics are recommended in patients with HFrEF with fluid retention</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td><strong>ACE Inhibitors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE inhibitors are recommended for all patients with HFrEF</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td><strong>ARBs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ARBs are recommended in patients with HFrEF who are ACE inhibitor intolerant</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>ARBs are reasonable as alternatives to ACE inhibitor as first line therapy in HFrEF</td>
<td>IIa</td>
<td>A</td>
</tr>
<tr>
<td>The addition of an ARB may be considered in persistently symptomatic patients with HFrEF on GDMT</td>
<td>IIb</td>
<td>A</td>
</tr>
<tr>
<td>Routine <em>combined</em> use of an ACE inhibitor, ARB, and aldosterone antagonist is potentially harmful</td>
<td>III: Harm</td>
<td>C</td>
</tr>
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</table>
Pharmacological Therapy for Management of Stage C HFrEF (cont.)

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beta Blockers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of 1 of the 3 beta blockers proven to reduce mortality is recommended for all stable patients</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td><strong>Aldosterone Antagonists</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aldosterone receptor antagonists are recommended in patients with NYHA class II-IV HF who have LVEF ≤35%</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Aldosterone receptor antagonists are recommended in patients following an acute MI who have LVEF ≤40% with symptoms of HF or DM</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Inappropriate use of aldosterone receptor antagonists may be harmful</td>
<td>III: Harm</td>
<td>B</td>
</tr>
<tr>
<td><strong>Hydralazine and Isosorbide Dinitrate</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>The combination of hydralazine and isosorbide dinitrate is recommended for African-Americans, with NYHA class III–IV HFrEF on GDMT</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>A combination of hydralazine and isosorbide dinitrate can be useful in patients with HFrEF who cannot be given ACE inhibitors or ARBs</td>
<td>IIa</td>
<td>B</td>
</tr>
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</table>
Pharmacologic Therapy for Management of Stage C HFrEF (cont.)

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Digoxin</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digoxin can be beneficial in patients with HFrEF</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td><strong>Anticoagulation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with chronic HF with permanent/persistent/paroxysmal AF and an additional risk factor for cardioembolic stroke should receive chronic anticoagulant therapy*</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>The selection of an anticoagulant agent should be individualized</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Chronic anticoagulation is reasonable for patients with chronic HF who have permanent/persistent/paroxysmal AF but without an additional risk factor for cardioembolic stroke*</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Anticoagulation is not recommended in patients with chronic HFrEF without AF, prior thromboembolic event, or a cardioembolic source</td>
<td>III: No Benefit</td>
<td>B</td>
</tr>
<tr>
<td><strong>Statins</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statins are not beneficial as adjunctive therapy when prescribed solely for HF</td>
<td>III: No Benefit</td>
<td>A</td>
</tr>
<tr>
<td><strong>Omega-3 Fatty Acids</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omega-3 PUFA supplementation is reasonable to use as adjunctive therapy in HFrEF or HFpEF patients</td>
<td>IIa</td>
<td>B</td>
</tr>
</tbody>
</table>
**Pharmacological Therapy for Management of Stage C HF (cont.)**

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Other Drugs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nutritional supplements as treatment for HF are not recommended in HFrEF</td>
<td>III: No Benefit</td>
<td>B</td>
</tr>
<tr>
<td>Hormonal therapies other than to replete deficiencies are not recommended in HFrEF</td>
<td>III: No Benefit</td>
<td>C</td>
</tr>
<tr>
<td>Drugs known to adversely affect the clinical status of patients with HFrEF are potentially harmful and should be avoided or withdrawn</td>
<td>III: Harm</td>
<td></td>
</tr>
<tr>
<td>Long-term use of an infusion of a positive inotropic drug is not recommended and may be harmful except as palliation</td>
<td>III: Harm</td>
<td></td>
</tr>
<tr>
<td><strong>Calcium Channel Blockers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium channel blocking drugs are not recommended as routine in HFrEF</td>
<td>III: No Benefit</td>
<td>A</td>
</tr>
</tbody>
</table>
### Medical Therapy for Stage C HF r EF: Magnitude of Benefit Demonstrated in RCTs

<table>
<thead>
<tr>
<th>GDMT</th>
<th>RR Reduction in Mortality</th>
<th>NNT for Mortality Reduction (Standardized to 36 mo)</th>
<th>RR Reduction in HF Hospitalizations</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitor or ARB</td>
<td>17%</td>
<td>26</td>
<td>31%</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>34%</td>
<td>9</td>
<td>41%</td>
</tr>
<tr>
<td>Aldosterone antagonist</td>
<td>30%</td>
<td>6</td>
<td>35%</td>
</tr>
<tr>
<td>Hydralazine/nitrate</td>
<td>43%</td>
<td>7</td>
<td>33%</td>
</tr>
</tbody>
</table>
Thank You!

- For more information and to register for Target: HF®, go to www.heart.org/targethf.
  - In order to claim your continuing education credits for attending this Target: Heart Failure webinar please download the document entitled “Instructions for Claiming CME/CE Credits”
  - Please follow the instructions listed in this document.
  - Remember to visit learn.heart.org
  - This is also a great site that the American Heart Association provides where you can Learn at Heart with the latest Cardiovascular and Stroke CME/CE activities