Heart Failure: Guideline-Directed Management and Therapy

Guideline-Directed Management and Therapy (GDMT) was developed by the American College of Cardiology and American Heart Association to define the optimal course of treatment for patients in each stage of heart failure (HF) (Yancy et al., 2013). The recommendations are outlined below.

### Treatment Recommendations by Stage

<table>
<thead>
<tr>
<th>Heart Failure Stage</th>
<th>Treatment Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage A:</strong> At high risk for HF but without structural heart disease or symptoms of HF</td>
<td></td>
</tr>
<tr>
<td><strong>Goals:</strong></td>
<td>Treat elevated blood pressure (BP) in accordance with current guidelines</td>
</tr>
<tr>
<td>• Heart healthy lifestyle</td>
<td>o Diuretic-based antihypertensive therapy</td>
</tr>
<tr>
<td>• Prevent vascular and coronary disease</td>
<td>o Angiotensin converting enzyme inhibitor (ACE inhibitor)</td>
</tr>
<tr>
<td>• Prevent left ventricular (LV) structural abnormalities</td>
<td>o Angiotensin receptor blockers (ARB)</td>
</tr>
<tr>
<td></td>
<td>o Beta-blocker</td>
</tr>
<tr>
<td></td>
<td>• Treat dyslipidemia and vascular risk</td>
</tr>
<tr>
<td></td>
<td>o Aggressive statin therapy as appropriate</td>
</tr>
<tr>
<td></td>
<td>• Recognition and control of risk factors that may lead to HF:</td>
</tr>
<tr>
<td></td>
<td>o Diabetes mellitus (DM)</td>
</tr>
<tr>
<td></td>
<td>o Obesity</td>
</tr>
<tr>
<td></td>
<td>o Obtain 3-generation family history of HF to evaluate genetic risk</td>
</tr>
<tr>
<td></td>
<td>o Atrial fibrillation (AF)</td>
</tr>
<tr>
<td></td>
<td>o Evaluate patients receiving or those who have received cardiotoxic chemotherapy</td>
</tr>
<tr>
<td></td>
<td>o Advise patients to avoid tobacco, heavy alcohol use, cocaine, and amphetamines</td>
</tr>
</tbody>
</table>

| **Stage B:** Structural heart disease but without signs or symptoms of HF | All recommendations for Stage A HF apply to Stage B HF. |
|**Goals:** | In patients with a history of myocardial infarction (MI) or acute coronary syndrome (ACS) and reduced ejection fraction (EF): |
| • Prevent HF symptoms | o ACE inhibitors and beta blockers |
| • Prevent further cardiac remodeling/changes | o ARB use in patients intolerant to ACE inhibitors due to cough or angioedema; may use as first-line therapy alternative to ACE inhibitors or for persistently symptomatic patients. |
| | In patients with MI, use statin therapy. |
| | In select patients: |
| | • Implantable cardioverter-defibrillator (ICD) use in asymptomatic ischemic cardiomyopathy at least 40 days post-MI, left ventricular ejection fraction (LVEF) ≤ 30%, on |
GDMT, and in patients with reasonable functional status and expected survival greater than 1 year. Goal of therapy is primary prevention of sudden cardiac death.
- Revascularization or valvular surgery as appropriate

**AVOID:**
- Non-dihydropyridine calcium channel blockers with negative inotropic effects; may be harmful in asymptomatic patients with low LVEF and no symptoms of HF after MI.

<table>
<thead>
<tr>
<th><strong>Stage C:</strong> Structural heart disease with prior or current symptoms of HF</th>
</tr>
</thead>
<tbody>
<tr>
<td>HF with <strong>PRESERVED</strong> EF (HFpEF): EF ≥ 50%</td>
</tr>
</tbody>
</table>

**Goals:**
- Control blood pressure (BP) – *most important!*
- Patient education
- Manage volume overload
- Improve health-related quality of life (HRQOL)
- Prevent hospitalization
- Prevent mortality

- All recommendations for Stage A and B HF apply to Stage C HF, as appropriate.
- Provide education to facilitate HF self-care including: monitoring symptoms and weight changes, restrict sodium intake, adhere to medication regimen and maintain physical activity
- Diuretics to relieve congestion/volume overload
- Identification and management of comorbidities:
  - Coronary revascularization for coronary artery disease (CAD) if angina or MI is present despite GDMT
  - Atrial fibrillation (AF) managed per clinical practice guidelines
  - Sleep disorders: continuous positive airway pressure (CPAP) may increase LVEF and improve functional status
- Routine use of nutritional supplements is not recommended
- **New:** Consider aldosterone receptor antagonists to decrease hospitalizations in select populations with HFpEF (EF ≥ 45%, elevated BNP levels or HF admission within 1 year, creatinine < 2.5mg/dL, potassium < 5mEq/L) (Yancy et al., 2017).
- **New:** Routine use of nitrates or phosphodiesterase-5 inhibitors are ineffective in increasing activity or quality of life (Yancy et al., 2017).

<table>
<thead>
<tr>
<th><strong>Stage C:</strong> Structural heart disease with prior or current symptoms of HF</th>
</tr>
</thead>
<tbody>
<tr>
<td>HF with <strong>REDUCED</strong> EF (HFrEF): EF ≤ 40%</td>
</tr>
</tbody>
</table>

**Goals:**
- Control symptoms
- Patient education

- All recommendations for Stage A and B HF apply to Stage C HF, as appropriate, including core medications: ACE inhibitors and beta blockers, and ARBs if intolerant to ACE inhibitors.
  - Unless contraindicated, use 1 of 3 beta blockers proven to be effective (bisoprolol, carvedilol, sustained release metoprolol) in all patients with HFrEF.
- Aldosterone receptor antagonists recommended in New York Heart Association (NYHA) class II-IV with LVEF ≤ 35% or
| Prevent hospitalization | following acute MI with LVEF ≤40% with symptoms of HF or DM;  
| Prevent mortality | o Contraindications: serum creatinine > 2.5 mg/dL in men and >2.0 mg/dL in women, or glomerular filtration rate < 30 mL/min/1.73 m, or serum potassium >5 mEq/L.  
| o Avoid routine combined use of ACE inhibitor, ARB, and aldosterone antagonist as this may be harmful for patients with HFrEF (Yancy et al., 2017).  
| o New: Inhibition of the renin-angiotensin system with ACEI or ARB or angiotensin receptor-neprilysin inhibitor (ANRI) in conjunction with:  
| o Betablocker  
| o Aldosterone antagonist (Yancy et al., 2017)  
| o New: Consider replacing ACE inhibitor or ARB with ANRI in chronic symptomatic HFrEF, NYHA Class II or III (Yancy et al., 2017)  
| o New: Do not administer ANRIs within 36 hours of ACEI due to increased risk of angioedema (Yancy et al., 2017).  
| o New: Do not administer ANRIs in patients with history of angioedema (Yancy et al., 2017).  
| o New: Ivabradine to reduce morbidity, mortality and HF hospitalizations in patients with chronic, symptomatic, stable HFrEF (LVEF ≤ 35%) who are receiving GDMT. Use in conjunction with beta-blocker at the maximum tolerated dose in sinus rhythm with HR ≥ 70 at rest. (Yancy et al., 2017)  
| o Digoxin may be added for persistent symptoms when on GDMT. Monitor for toxicity.  
| o For all volume overloaded patients, add loop diuretics.  
| o For persistently symptomatic African American patients with NYHA class III- IV on GDMT, add hydralazine and isosorbide dinitrate.  
| o For NYHA class III-IV, if creatinine > 30 mL/min and K+ < 5 mEq/dL, add aldosterone antagonist.  
| o Chronic HF with permanent/persistent/paroxysmal AF should receive chronic anticoagulant therapy.  
| o Statins are not beneficial unless indicated to treat dyslipidemia.  
| o Omega-3 fatty acid supplementation may be added as adjunctive therapy.  
| o Calcium channel-blockers, NSAIDS, nutritional supplements or hormonal therapies are not recommended.  

Long-term use of positive inotropic drug is not recommended and may be harmful.

Device therapy [refer to clinical practice guidelines for specific recommendations]
  - Implantable Cardioverter-Defibrillator (ICD)
  - Cardiac Resynchronization Therapy (CRT)

**Stage D:** Refractory or Advanced HF – symptoms at rest & recurrent hospitalizations [see detailed definition below]

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

**Acute management of patients hospitalized with HF**

- Fluid restriction (1.5 to 2 L/day) to reduce congestive symptoms
- Intravenous (IV) inotropic support:
  - Temporary use in cardiogenic shock until definite therapy (i.e. coronary revascularization, mechanical circulatory support (MSC), cardiac transplant)
  - Continuous use as “bridge therapy” for patients awaiting cardiac transplant
  - Short-term, continuous use for hospitalized patients with severe systolic dysfunction
  - Long-term use as palliative therapy for symptom control (without specific indication, inotropes may be harmful)
- Temporary or permanent MCS may be beneficial if cardiac recovery anticipated; ventricular assist device (VAD) may be used as “bridge to recovery” or “bridge to decision” for selected patients.
- Cardiac transplantation for carefully selected patients.
- Palliative care and hospice.
- Depending on goals of care, consider ICD deactivation.

- IV loop diuretics: initial dose ≥ chronic total daily oral dose
  - Increase diuretic or add another diuretic if diuresis is inadequate.
  - Monitor serum electrolytes, urea nitrogen and creatinine, fluid intake/output, daily weights, vital signs, and clinical signs and symptoms of fluid overload.
- Continue GDMT except when unstable.
- Low dose dopamine IV may be added with loop diuretics to improve diuresis*
  - *Inotropic therapy with dopamine, dobutamine, or milrinone should only be used in acute decompensated HF patients who are hypotensive with HFREF.
- Initiate beta blocker therapy at low dose after optimization of volume status and discontinuation of IV agents.
- Thrombosis/thromboembolism prophylaxis
Ultrafiltration for volume overload or refractory congestion
• Adjuvant therapies to relieve dyspnea: IV nitroglycerin, nitroprusside or nesiritide
• Vasopressin antagonists in patients with volume overload and severe hyponatremia

Strategies for Achieving Optimal GDMT
• Titrate medications slowly.
• Frequent follow-up visits and lab monitoring during dose titration (elderly & impaired renal function).
• Monitor vital signs, including orthostatic BPs before, during, and after titrations.
• Alternate adjustments of different medication classes.
• Monitor renal function and electrolytes for increasing creatinine and potassium levels.
• Reassure patients that symptoms of fatigue and weakness without instability are transient and usually resolve in a few days.
• Discourage sudden discontinuation of GDMT medications without discussion with prescribing clinicians.
• Carefully review doses of other medications for HF symptom control during up-titration.

Advanced Heart Failure
Some patients with chronic HF will develop severe symptoms despite optimal GDMT. These patients are classified with ACCF/AHA stage D HF (described above) and include “end-stage HF” and “refractory HF”.

European Society of Cardiology Definition
• Severe symptoms of HF with dyspnea and/or fatigue at rest with minimal exertion (NYHA class III or IV)
• Fluid retention (pulmonary and/or systemic congestion, peripheral edema) and/or decreased cardiac output at rest (peripheral hypoperfusion)
• Objective evidence of severe cardiac dysfunction - at least one of the following:
  o LVEF < 30%
  o Pseudonormal or restrictive mitral inflow pattern
  o Mean pulmonary artery wedge pressure (PAWP) > 16 mm Hg and/or right atrial pressure (RAP) > 12 mm Hg by pulmonary artery (PA) catheterization
  o High BNP or NT-proBNP plasma levels in the absence of noncardiac causes
• Severe impairment of functional capacity - one of the following:
  o Inability to exercise
  o 6-Minute walk distance ≤ 300 m
  o Peak VO₂ < 12 to 14 mL/kg/min
• History of ≥ 1 HF hospitalization in prior 6 months
• Presence of all of the previous features despite “attempts to optimize” therapy, including diuretics and GDMT, unless these are poorly tolerated or contraindicated, and CRT when indicated

Clinical Findings of Advanced Heart Failure
• Repeated (≥2) hospitalizations or emergency room visits for HF in the past year
• Progressive deterioration in renal function (i.e. rise in BUN and creatinine)
• Weight loss without other causes (i.e. cardiac cachexia)
• Intolerance of ACE inhibitors due to hypotension and/or worsening renal function
• Intolerance to beta blockers due to worsening HF or hypotension
• Frequent systolic BP < 90 mm Hg
• Persistent dyspnea with dressing or bathing requiring rest
• Inability to walk 1 block on level ground due to dyspnea or fatigue
• Recent need to escalate diuretics to maintain volume status, often reaching daily furosemide equivalent dose over 160 mg/day and/or use of supplemental metolazone therapy
• Progressive decline in serum sodium, usually to < 133 mEq/L
• Frequent ICD shocks

Recommendations for Hospital Discharge
• Implement performance improvement systems in the hospital and early post-discharge outpatient setting to identify HF for GDMT.
• Before hospital discharge, at the first post-discharge visit, and in subsequent follow-up visits, the following should be addressed:
  o Initiation of GDMT if not done and not contraindicated
  o Causes of HF, barriers to care, and limitations in support
  o Assessment of volume status and BP with adjustment of HF therapy
  o Titration and optimization of chronic oral HF therapy
  o Assessment of renal function and electrolytes
  o Management of comorbid conditions
  o HF education, self-care, emergency plans, and adherence
  o Palliative or hospice care
• Arrange multidisciplinary HF disease management for patients at risk for hospital readmission.
• Schedule follow-up visit within 7 to 14 days and a telephone follow-up within 3 days of hospital discharge.
• Use clinical risk-prediction tools and/or biomarkers to identify higher-risk patients.
References:

