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) (Heidenreich, et al., 2022).

**Please also refer to the Pocket Card: Assessment and Diagnosis of Heart Failure.*

Treatment Recommendations by Stage

Treatment Recommendations by Stage	
Stage A	
Definition	• At high risk for HF but without structural heart disease or symptoms of HF
Goals	• Primary prevention of cardiovascular disease (CVD) • Heart healthy lifestyle • Prevent symptomatic heart failure

Recommendations	• Treat hypertension in accordance with current guidelines.
	  ○ Treatment goal is blood pressure (BP) < 130/80 for patient with CVD risk of ≥ 10%.
	  ○ Medications include diuretic-based antihypertensive therapy, angiotensin converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), or beta-blockers.
	• In patients with type 2 diabetes mellitus (DM) and established CVD or a high cardiovascular risk, a sodium glucose cotransporter 2 inhibitor (SGLT2i) is recommended.
	• Encourage a heart healthy lifestyle: regular physical activity, healthy body weight, healthy diet, and avoidance of tobacco.
	• Advise patients to avoid tobacco, heavy alcohol use, cocaine, and amphetamines.
	• Optimize management of CVD.
	• Evaluate and manage patients with exposure to cardiotoxic agents using a multidisciplinary approach.
	• Refer first-degree relatives of patients with genetic or inherited cardiomyopathies for genetic screening and counseling.
	• Use validated multivariable risk score tools to estimate risk of HF.
	• Consider natriuretic peptide biomarker screening.
	• Recognize and control risk factors that may lead to HF, such as DM, obesity, and atrial fibrillation (AF).

	• Evaluate patients receiving or who have received cardiotoxic chemotherapy.
Stage B	
Definition	• Pre-HF • Clinically asymptomatic • Structural and functional cardiac abnormalities present
Goals	• Prevent the syndrome of clinical HF (stage C/D) • Prevent further cardiac remodeling/changes

Recommendations	• Continue strategies implemented in Stage A.
	• If left ventricular ejection fraction (LVEF) is ≤ 40%, begin an ACEi, or angiotensin receptor blocker (ARB), if ACEi intolerant, and evidence- based beta blocker, regardless of etiology.
	• In patients with stage B and with a recent or remote history of myocardial infarction (MI) or acute coronary syndrome (ACS), GDMT is as follows:
	  ○ Statin therapy
	  ○ If LVEF ≤ 40%, initiate evidence-based beta blockers and ACEi, or ARB if ACEi intolerant.
	  ○ In patients who are at least 40 days post-MI and have LVEF ≤ 30% with NYHA class I symptoms, while on GDMT, consider referral for implantable cardioverter-defibrillator (ICD) for primary prevention of sudden cardiac death (SCD), if meaningful life expectancy is > 1 year.
	• Avoid thiazolidinediones as they can lead to fluid retention and increased rates of symptomatic HF.
	• Avoid non-dihydropyridine calcium channel blockers because they have negative inotropic effects and are myocardial depressants.

Stage C	
Definition	• Structural heart disease with prior or current symptoms of HF
Goals	• Patient education • Manage volume overload • Improve health-related quality of life (HRQOL) • Prevent hospitalization • Prevent mortality
Recommendations	• Continue recommendations for Stage A and B, as

	appropriate.
	• Non-pharmacological interventions
	  ○ Use a multidisciplinary team approach to care to address potential barriers to care, reduce rehospitalization rate for HF, and improve survival.
	  ○ Provide HF education to facilitate HF self-care, including monitoring symptoms and weight changes, restricting sodium intake by adhering to Dietary Approaches to Stop Hypertension (DASH) diet, adhering to medication regimen and maintaining physical activity.
	  ○ Encourage regular physical activity to improve functional status, exercise performance and quality of life. Consider referral and prescription to cardiac rehabilitation for stable HF patients on GDMT for exercise training with medical evaluation, education, and psychosocial support.
	  ○ Screen for depression, frailty, and low health literacy.
	• Vaccinate against respiratory illnesses, as appropriate.
	• Diuretics help relieve congestion and improve symptoms.
	  ○ Loop diuretics (e.g., furosemide, bumetanide, and torsemide) are preferred.
	  ○ Thiazide diuretics (e.g., chlorthalidone and hydrochlorothiazide) can be used in patients with mild HF symptoms and a history of hypertension.
	  ○ Consider adding thiazide diuretic (e.g., metolazone) in patients with refractory fluid retention unresponsive to loop diuretics alone.
	• Pharmacological treatment for HFrEF with NYHA class II-III symptoms
	  ○ ARNi, ACEi, or ARB are first-line therapy to inhibit the renin-angiotensin system.
	  • Start with angiotensin receptor-neprilysin inhibitor (ARNi), if feasible.
	  • Use ACEi if ARNi is not feasible.
	  • Use ARB if intolerant to ACEi, and if ARNi is not feasible.
	  • *Note: ARNi should not be administered concomitantly with ACEi or within 36 hours from last dose of an ACEi.*
	  • *Note: ARNi and ACEi should not be administered to patients with any history of angioedema.*
	  ○ Beta blocker therapy reduces risk of hospitalization and death.
	  • Initiate therapy at time of diagnosis with or

	without history of CAD. • Three evidence-based agents: carvedilol, metoprolol succinate, and bisoprolol ○ Mineralocorticoid receptor antagonists (MRAs), spironolactone or eplerenone, are recommended in HFrEF class II-IV symptoms, if eGFR > 30 mL/min/1.73m^2 and serum potassium is < 5 mEq/L. • Closely monitor potassium, renal function, and diuretic dosing at initiation and at regular intervals. ○ Initiate SGLT2i *irrespective* of presence of type 2 diabetes to reduce HF hospitalizations. ○ African American patients with HFrEF class III-IV who are receiving optimal GDMT, add combination of hydralazine and isosorbide dinitrate to improve symptoms and reduce morbidity and mortality. • Consider this combination as first-line therapy in patients who have intolerance or contraindications to preferred first-line agents (ARNi, ACEi, ARB). ○ Once GDMT is initiated, the goal shifts to achieving optimized target doses, by titration every 1-2 weeks, depending on patient's symptoms, vital signs, and laboratory data. ○ Additional therapies to consider when GDMT is optimized include ivabradine (a sinoatrial node modulator), omega-3 polyunsaturated fatty acid (PUFA), potassium binders, digoxin, and oral soluble guanylyl cyclase stimulator. • Device and interventional therapies for HFrEF ○ ICD therapy is recommended for primary prevention of sudden cardiac death (SCD) in the following patients: • Nonischemic dilated cardiomyopathy or ischemic at least 40 days post-MI with EF ≤35% with NYHA class II-III symptoms on GDMT who have reasonable meaningful life expectancy greater than 1 year. • At least 40 days post-MI with EF ≤30% with NYHA class I symptoms on GDMT. ○ Cardiac resynchronization therapy (CRT) is indicated to reduce mortality and hospitalizations and improve quality of life in the following patients: • EF ≤35%, in sinus rhythm, with QRS ≥150 ms (with or without a left bundle branch block) and NYHA class II-III or ambulatory class IV symptoms on GDMT.

	○ Revascularization for CAD • In appropriate patients with HF and EF ≤35% with suitable coronary anatomy, surgical revascularization (coronary artery bypass grafting [CABG]) plus GDMT improves symptoms, reduces hospitalizations and mortality. CABG is beneficial over percutaneous coronary intervention in patients with diabetes, CAD, and LV dysfunction and with left main CAD and moderate to severe LV dysfunction. • Valvular disease ○ Ensure a multidisciplinary team approach in accordance with valvular heart disease clinical practice guidelines. ○ In patient with severe chronic secondary mitral valve regurgitation and HFrEF, optimize GDMT prior to any intervention. • HF with mildly reduced EF (HFmrEF) ○ SGLT2i may help decrease hospitalizations and CV mortality. ○ Use of beta blockers, ARNi, ACEi, or ARB, and MRAs may reduce risk of hospitalization and CV mortality. • HF with improved EF (HFimpEF) ○ Continue GDMT to prevent relapse of HF and LV dysfunction. • HF with preserved EF (HFpEF) ○ In patients with hypertension, titrate medications to achieve BP targets. ○ SGLT2i may help decrease hospitalizations and CV mortality. ○ Manage AF to help improve symptoms. ○ Consider MRAs, ARB, and ARNi to help decrease hospitalizations and CV mortality. ○ Routine use of nitrates or phosphodiesterase-5 inhibitors is ineffective. • Cardiac amyloidosis ○ If cardiac amyloidosis is suspected, screen for serum and urine monoclonal light chains; if no evidence, perform bone scintigraphy to confirm presence of transthyretin cardiac amyloidosis. ○ If diagnosis is made, genetic testing is recommended. ○ Treatment is managed by hematology/oncology specialists. • Use tafamidis (transthyretin tetramer stabilizer) for patients with variant or wild-

	type cardiac amyloidosis with NYHA class II-III symptoms. • If patient also has atrial fibrillation, consider anticoagulation. • GDMT typically used for patients with EF ≤40% may not be well tolerated due to hypotension and worsening of HF symptoms. • The role of ICD/CRT devices in this patient population has not been well studied.
Stage D	
Definition	• Advanced, refractory, or end-stage HF
Goals	• Control symptoms • Improve HRQOL • Reduce hospital readmissions • Establish patient's end-of-life goals
Recommendations	• Refer to HF specialty care to review HF management and assess suitability for advanced HF therapies (left ventricular assist device, cardiac transplantation, palliative care, and palliative inotropes). • Assess for clinical indicators for advance HF and need of referral. ○ Repeated HF hospitalizations over the past 12 months ○ Intravenous inotropic therapy ○ Persistent NYHA class III-IV despite maximally tolerated doses of GDMT ○ Severely reduced exercise capacity ○ Intolerance to Renin-Angiotensin-Aldosterone-System inhibitors (RAASi) due to hypotension or worsening renal function ○ Intolerance to beta blockers due to hypotension or worsening HF ○ Escalating diuretic dosing reaching furosemide equivalent dose > 160 mg/day or use of supplemental metolazone ○ Refractory clinical congestion ○ Deterioration of renal or hepatic function; worsening right HF or secondary pulmonary hypertension ○ Frequent systolic blood pressure ≤ 90 mm Hg ○ Cardiac cachexia ○ Persistent hyponatremia ○ Refractory or recurrent ventricular arrythmias; frequent ICD shocks

	• Nonpharmacological management
	  ○ Fluid restriction to help with congestion and hyponatremia (benefits are uncertain as data on this recommendation is low quality)
	• Consider inotropic support.
	  ○ "Bridge to therapy" while waiting for mechanical circulatory support (MSC) or cardiac transplantation
	  ○ Palliative therapy for symptom control and functional status improvement for patients who are ineligible for either MCS or cardiac transplantation.
	  ○ Hospitalized patients with documented severe systolic dysfunction with hypotension and low cardiac index to maintain perfusion to organs and provide hemodynamic support/stabilization (however not shown to improve survival)
	• Consider MCS to prolong life and improve functional capacity.
	  ○ Durable MCS is indicated for HF stage D with NYHA class IV symptoms who are dependent on continuous intravenous inotropes or temporary MCS or stage D with NYHA class IV symptoms on GDMT
	  ○ Temporary MCS is indicated for HF stage D with hemodynamic compromise and shock as "bridge to therapy or recovery"
	• Cardiac transplantation is an option for eligible patients with stage D HF refractory to GDMT, device, and surgical optimization to improve survival and quality of life.

Acute Management of Hospitalized Patients

Goals

- Address reversible factors.
- Establish optimal volume status.
- Advance GDMT toward optimization of dosing.

Recommendations

- Triage severity of congestion and adequacy of perfusion to dictate initial therapy.
- Identify precipitating factors:
  - Acute coronary syndrome
  - Uncontrolled hypertension
  - Arrhythmias (e.g., atrial fibrillation)
  - Other cardiac diseases (e.g., endocarditis)

  - Infections
  - Noncompliance with medications and/or diet
  - Anemia
  - Hyperthyroidism or hypothyroidism
  - Use of medications that should be avoided (e.g., medications that increase sodium retention and medications with negative inotropic effects)
- Initiate GDMT during hospitalizations as soon as patient is clinically stable.
- Continue established GDMT throughout hospitalization, unless contraindicated.
- If temporary discontinuation of pre-existing GDMT is necessary, reinstitute it as soon as possible.
- IV loop diuretics provide the most rapid and effective treatment for decongestion therapy.
  - Start at a dose at least two times the chronic daily home oral dose and administer by bolus or infusion.
  - 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.
  - In patients admitted with decompensated HF, without systemic hypotension, IV nitroglycerin or nitroprusside may be used with diuretics to relieve dyspnea.
  - The discharge regimen should include a plan for diuretic dose adjustment to reduce rehospitalizations.
- Manage cardiogenic shock.
  - Use a multidisciplinary team approach of clinicians experienced in shock management and palliative care.
  - Use IV inotropic support to increase cardiac output and improve hemodynamics, maintain systemic perfusion, and avoid end-organ damage.
  - Consider temporary mechanical circulatory support (MCS) when pharmacological strategies are not sufficient to maintain end-organ perfusion.
  - Consider placement of a pulmonary artery catheter to guide therapy when MCS is being used or in setting of hemodynamic uncertainly.
  - Seek transfer to higher level of centers when needed. Triage and initiate transfer early to help mitigate a trajectory of worsening end-organ malperfusion.
- Ensure thrombosis/thromboembolism prophylaxis. In patients with adequate renal function, use enoxaparin 40 mg subcutaneously once daily, unfractionated heparin 5000 units subcutaneously every 8 hours, or rivaroxaban 10 mg orally once daily.

Considerations for Patients with Comorbidities

- Iron deficiency with or without anemia: IV iron therapy is reasonable to improve functional status and quality of life.
- Sleep disorders: conduct formal sleep assessment to confirm diagnosis and treat with continuous positive airway pressure as needed.
- Hypertension: treat according to current clinical guidelines.
- Type 2 DM: use SGLT2i.

- Atrial fibrillation and LVEF ≤50%: if rhythm control strategies fail, consider AV nodal ablation and CRT implantation.

Recommendations for Hospital Discharge

- Transition from inpatient to outpatient care is a vulnerable time when patients are at highest risk for decompensation and rehospitalization.
- Use clinical risk-prediction tools and/or biomarkers to identify higher-risk patients.
- Refer to multidisciplinary HF disease team management to reduce risk of rehospitalization.
- Provide clearly written discharge instructions to patient, family members or caregivers including medications, activity level, diet, follow-up appointments, weight monitoring, cardiac rehab, and action plan for what to do if symptoms worsen.
- Arrange for early outpatient follow-up care to minimize gaps in education, care, and monitoring of symptoms and disease progression.
- Transmit details of hospital course and transition of care plan as soon as possible to all clinicians who will be participating in follow-up care.
- Before hospital discharge, at the first post-discharge visit, and in subsequent follow-up visits, the following should be addressed:
    - Initiation of GDMT if not done and not contraindicated
    - Causes of HF, barriers to care, and limitations in support
    - Assessment of volume status and BP with adjustment of HF therapy
    - Titration and optimization of chronic oral HF therapy
    - Assessment of renal function and electrolytes
    - Management of comorbid conditions
    - HF education, self-care, emergency plans, and adherence
    - Palliative or hospice care
- Schedule follow-up visit within 7 to 14 days and a telephone follow-up within 3 days of hospital discharge.

Strategies for Achieving Optimal GDMT

- Titrate medications slowly. Aim for dose titration every 1-2 weeks, as tolerated.
- 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 prescriber.
- 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 and include "end-stage HF" and "refractory HF."

European Society of Cardiology Definition of Advanced HF

- 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:
    - LVEF ≤ 30%
    - Isolated right ventricular failure
    - Nonoperable severe valve disease or congenital heart disease
    - EF ≥ 40% with elevated natriuretic peptide levels and evidence of significant diastolic dysfunction
- Severe impairment of functional capacity - one of the following:
    - Inability to exercise
    - 6-minute walk distance ≤ 300 m
    - Peak VO_2 < 12 to 14 mL/kg/min
- History of 1 or more hospitalizations in prior 6 months for the management of:
    - Congestion requiring high-dose intravenous diuretics
    - Low cardiac output requiring inotropes or vasoactive medications
    - Malignant arrhythmias

Clinical Performance and Quality Measures

In response to the AHA/ACC/AHFSA Guideline update in 2022, the AHA updated the performance and quality measures for the care of patients with heart failure.

Three performance measures were added. Performance measures are selected from the strongest recommendations (Class 1 or Class 3) provided in the 2022 guideline update and include:

- Start GDMT at discharge from a HF hospitalization (measures the percentage of patients 18 years of age or older with a diagnosis of HF and an LVEF ≤ 40% who are prescribed GDMT at discharge)
- BP control in HFpEF with hypertension (measure the percentage of patients 18 years of age or older with a diagnosis of HF and an LVEF ≥ 50% who have optimal BP control for hypertension (defined as a SBP < 130 mm Hg and a DBP < 80 mm Hg).
- SGLT2 inhibitor therapy for HFrEF (measures the percentage of patients 18 years of age or older with a diagnosis of Stage C HF with an LVEF ≤ 40% who were prescribed an SGLT inhibitor within a 12 month period in the outpatient setting or at hospital discharge).

Six quality measures were added. Quality measures may be useful for local quality improvement. These include:

- SGLT2 inhibitor therapy for HFMrEF or HFpEF (measures the percentage of patients 18 years of age or older with a diagnosis of HF with an LVEF ≥ 40% who were prescribed an SGLT inhibitor within a 12-month period in the outpatient setting or at hospital discharge).
- Screening and documented action for social determinants of health in HF patients (measures the percentage of patients 18 years of age or older with a diagnosis of HF who are screened for social determinants of health with a documented action to close the identified gap).
- Counseling regarding pregnancy and cardiovascular risk (measures the percentage of individuals 14 – 55 years of age who are of childbearing potential and have a diagnosis of HF or cardiomyopathy who received counseling regarding cardiovascular risks of pregnancy and contraception).
- Continuation of GDMP in patients with HFimpEF (measures the percentage of patients 18 years of age or older with a diagnosis of HFrEF (LVEF < 40) and a follow-up measurement of an improved LVEF > 40% (HFimpEF) with continued prescriptions of GDMP in the outpatient setting).
- Optimizing GDMT prior to transcatheter edge-to-edge repair (TEER) for secondary mitral regurgitation (MR) (measures the percentage of patients 18 years of age or older with a diagnosis of HFrEF who have symptomatic chronic severe MR secondary to LV dysfunction who are documented as receiving optimal GDMT prior to TEER).
- Monoclonal protein screen in patients who have undergone bone scintigraphy for suspected cardiac amyloidosis (measure the percentage of patients 18 years of age or older with suspected cardiac amyloidosis who undergo serum and urine monoclonal protein screen and have undergone bone scintigraphy).

Reference:

Heidenreich, P. A., Bozkurt, B., Aguilar, D., Allen, L. A., Byun, J. J., Colvin, M. M., Deswal, A., Drazner, M. H., Dunlay, S. M., Evers, L. R., Fang, J. C., Fedson, S. E., Fonarow, G. C., Hayek, S. S., Hernandez, A. F., Khazanie, P., Kittleson, M. M., Lee, C. S., Link, M. S., Milano, C. A., … Yancy, C. W. (2022). 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*, *145*(18), e895–e1032. https://doi.org/10.1161/CIR.0000000000001063

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