



Managing Heart Failure in Primary Care

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Key takeaways

1

Identify and treat risk factors for heart failure such as hypertension, diabetes, and atrial fibrillation to prevent or delay the development of heart failure.

2

To improve mortality and morbidity in patients with HFrEF, initiate and titrate angiotensin receptor blockers (ARNI/ACEI/ARB), beta blockers, SGLT-2 inhibitors, and mineralocorticoid receptor antagonists to target doses, or maximally tolerated dose.

3

In patients unable to tolerate dose titration due to hypotensive symptoms, utilize lowest tolerated doses of GDMT to improve morbidity and mortality.

4

For patients with HFpEF, manage contributing comorbidities, use diuretics to control fluids, initiate an SGLT-2 inhibitor, and consider an ARNI or MRA in selected patients.

5

Avoid using non-dihydropyridine calcium channel blockers, nifedipine, cilostazol, NSAIDs, and thiazolidinediones (e.g., rosiglitazone, pioglitazone) in HFrEF patients to prevent exacerbation of HF symptoms and hospitalizations.

6

Engage patients in appropriate care coordination, including RPM-HT, referring to cardiology specialists and post-hospitalization follow-up.

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These materials were developed by:

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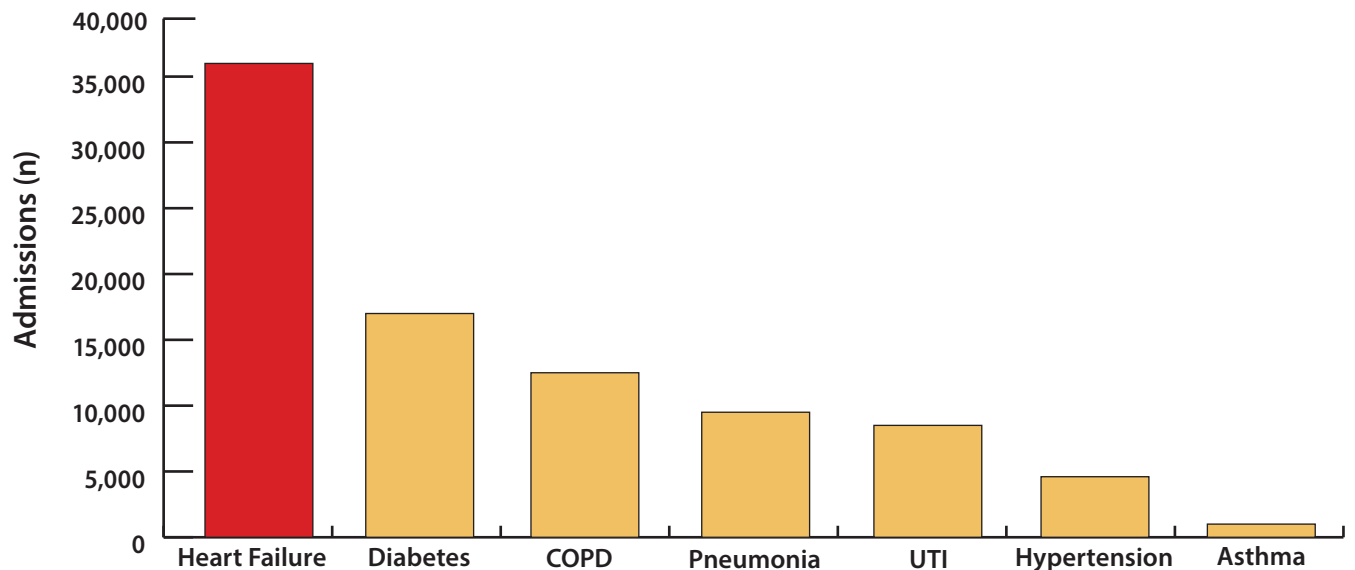
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Heart failure epidemiology

Heart failure (HF) affects about 6 million people in the U.S.—a number expected to increase to more than 8 million by 2030.¹ HF is one of the most common reasons for hospitalizations and is the most expensive Medicare diagnosis.² It is also one of the leading causes of hospital admissions in VA.

Figure 1. Heart failure is a leading cause of hospitalization in veterans



Data obtained from the Ambulatory Care Sensitive Conditions (ACSC) Dashboard on the Veterans Health Administration Support Service Center (VCSS) Capital Assets Databases from December 2020 to November 2021. Hospitalizations due to ACSC such as hypertension, heart failure, and pneumonia can be largely avoided and prevented if ambulatory care is provided in a timely and effective manner. COPD = chronic obstructive pulmonary disease; UTI = urinary tract infections.

Although survival after HF diagnosis has improved over the past several decades, around 42% of patients will die within five years of diagnosis.¹

Morbidity and mortality associated with HF are high, but using appropriate evidence-based treatments allows Veterans to live longer and have a better quality of life.² This module reviews evidence-based practices for the evaluation and management of HF in primary care settings.

Preventing heart failure

Traditional heart failure risk factors:²⁻⁴

- Coronary heart disease
- Diabetes
- Hypertension
- Obesity
- Smoking
- Valvular disease
- Substance abuse (e.g., alcohol, cannabis, cocaine)

Obesity and insulin resistance are important factors for the development of HF.² For every 1% rise in hemoglobin (Hgb) A1c above 7%, the risk for developing heart failure increases by 12%.¹²

Many factors are associated with an increased risk of developing HF. Identification and treatment of these conditions has been proven to reduce the development of HF.²

For example:

- Optimized blood pressure leads to decreased risk of cardiovascular death and incidence of HF.^{5,6}
- The treatment of hyperlipidemia with statins reduces risk in at-risk patients.^{7,8}
- Use of sodium-glucose co-transporter-2 (SGLT-2) inhibitors reduces the incidence of HF in patients with diabetes and atherosclerotic cardiovascular disease (ASCVD).⁹⁻¹¹

Figure 2. Treating hypertension (HTN) reduces incidence of HF⁵

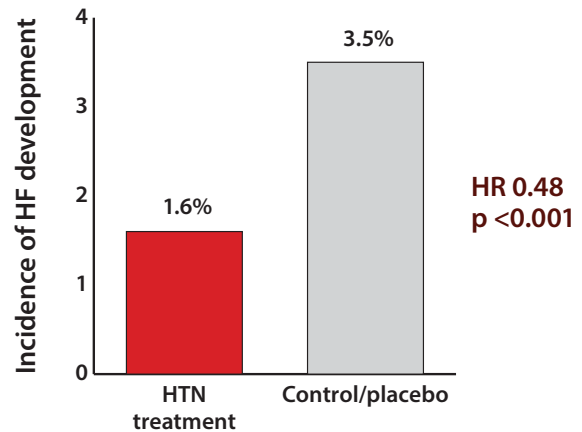
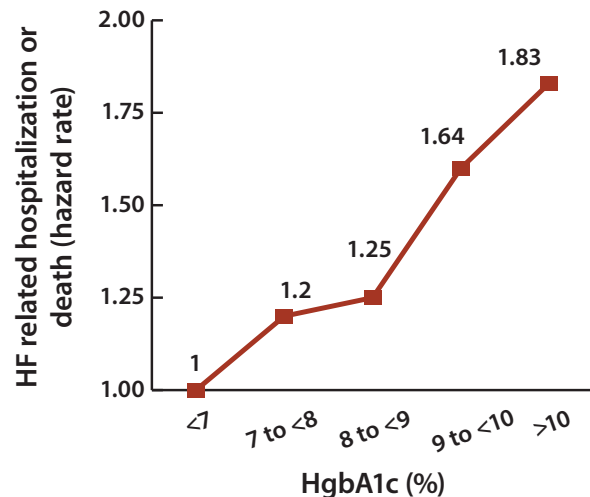


Figure 3. Poor HbA1c control associated with an increased risk of HF¹²



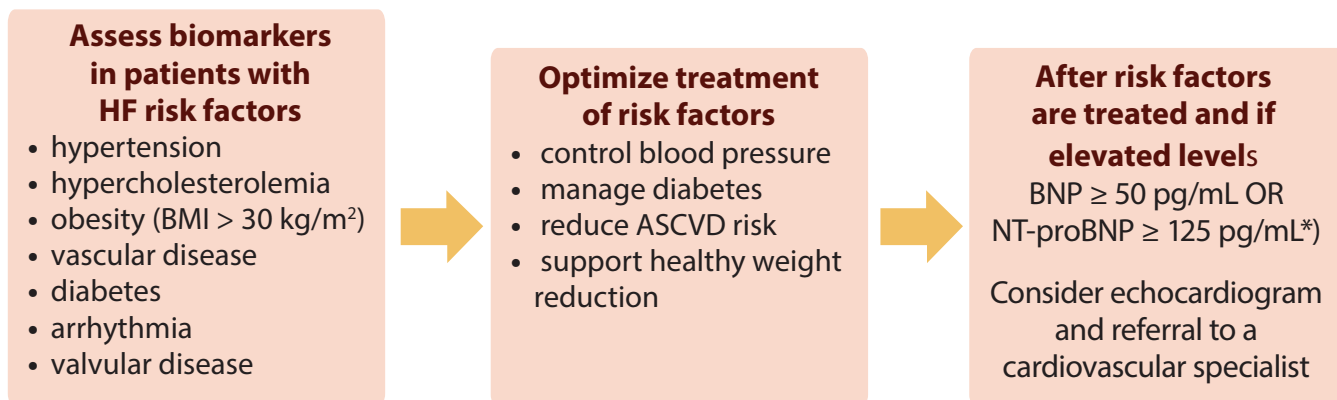
Identify and treat risk factors to prevent or delay the development of HF.

Identifying heart failure in those at risk

Early detection of elevated biomarkers, B-type natriuretic peptide (BNP), or N-terminal pro-B-type natriuretic peptide (NT-proBNP) can assist in identifying patients at risk for developing left ventricular dysfunction and subsequent HF.

BNP and NT-proBNP may be falsely low in patients with obesity. A high value is predictive, but a low value in an obese patient does not exclude HF.

Figure 4. Using biomarkers to reduce HF risk¹³⁻¹⁶



*Anemia may lead to elevated levels. BMI = body mass index; ASCVD = atherosclerotic cardiovascular disease

Optimize management of risk factors and pharmacologic, and non-pharmacologic therapies in patients at risk for HF.²

Diagnosing and classifying heart failure

Diagnosis of heart failure requires structural or functional changes to the heart and clinical signs and symptoms (e.g., shortness of breath, fatigue, exercise intolerance, coughing, **volume overload** such as ascites, lower extremity swelling, and weight gain).






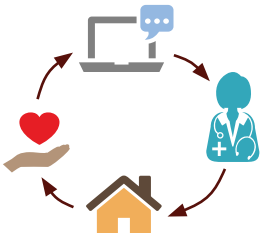
Table 1. Classifications for heart failure¹⁶

Acronym	Classification	Ejection fraction	Description
HFrEF	HF with reduced EF	≤ 40%	Previously referred to as “systolic HF.” Guideline-directed medical therapy (GDMT) should be initiated and optimized as tolerated.
HFpEF	HF with preserved EF	≥ 50%*	Previously referred to as “diastolic HF.” Diagnosis of exclusion. Evidence-based therapies are limited.
HFmrEF	HF with mildly reduced EF	41-49%*	Trend toward treating like HFrEF. No major clinical trials in this population; it is unclear whether characteristics and outcomes are more like HFpEF.
HFimpEF	HF with improved EF	Previously ≤ 40% and a subsequent measurement > 40%	Continue GDMT for HFrEF, if tolerating. Further data needed to determine best management strategy.

*With evidence of spontaneous or provokable increased left ventricular filling pressures (e.g., elevated natriuretic peptide, noninvasive and invasive hemodynamic measurement); EF = ejection fraction

Components of heart failure management

Table 2. Principles of HF management¹⁶⁻²⁰

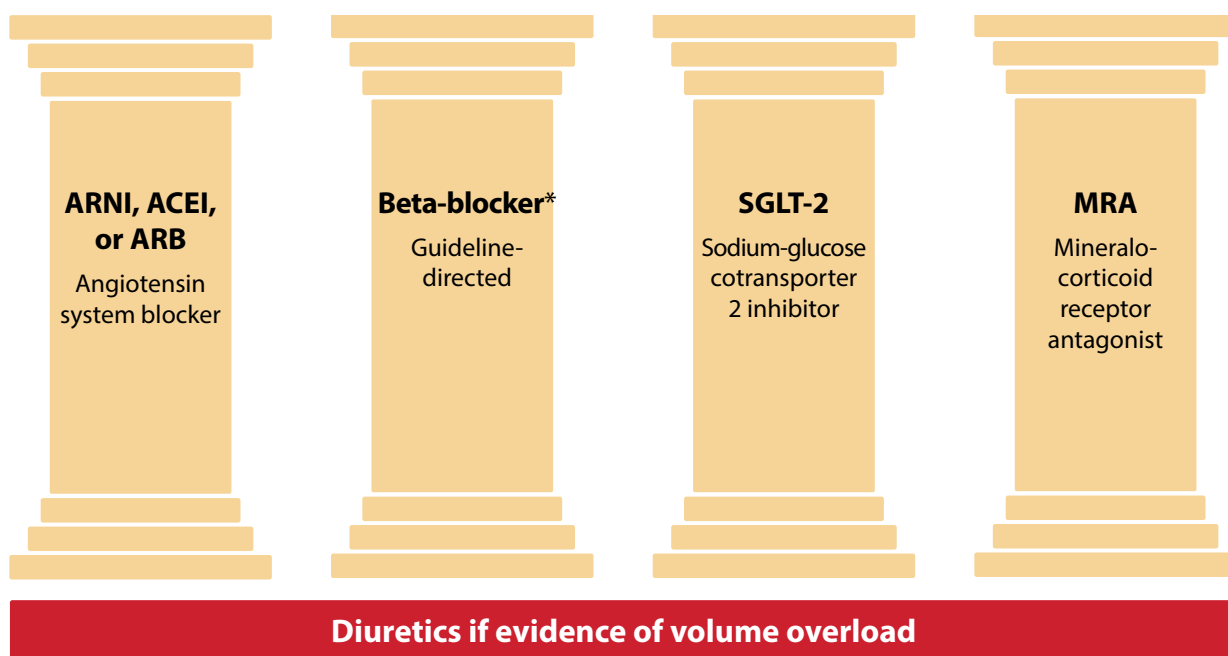
	<p>Optimize medications</p> <ul style="list-style-type: none"> • Initiate GDMT and titrate where appropriate. • Avoid medications that may worsen HF (e.g., NSAIDs). See page 14 for additional medications.
	<p>Assess volume status</p> <ul style="list-style-type: none"> • Evaluate symptoms of fluid overload. • Initiate and adjust diuretic to lowest effective dose. • Consider fluid restriction in selected patients.
	<p>Review dietary patterns</p> <ul style="list-style-type: none"> • Recommend sodium reduction. Reduce intake to < 2,300 mg/day for general CV health promotion (optimal goal in HF unknown). • Refer to nutrition.
	<p>Engage patient in self-care*</p> <ul style="list-style-type: none"> • Take and record daily weight. • Monitor and record blood pressure and heart rate. • Self-monitor HF symptoms.
	<p>Encourage physical activity</p> <ul style="list-style-type: none"> • Increase regular physical activity in patients who are able to participate. • Consider referral to cardiac rehabilitation for symptomatic (NYHA Class II-III) HF patients with EF ≤ 35% despite GDMT.
	<p>Utilize care coordination</p> <ul style="list-style-type: none"> • Utilize Remote Patient Monitoring–Home Telehealth (RPM-HT). • Refer to cardiology when appropriate. • Refer to other team members (e.g., PACT pharmacist or nurse, physical therapist, social worker, psychologist, dietician, whole health team). • Follow-up with Veteran, generally within seven days of hospital discharge. • Assess for sleep-disordered breathing and treat as appropriate. • Discuss/refer to palliative care.

*Confirm that the patient has a reliable scale and blood pressure cuff. NSAID = nonsteroidal anti-inflammatory drug; GDMT = guideline directed medical therapy; PACT = patient aligned care team; CV = cardiovascular; NYHA = New York Heart Association

Medications for HFrEF

GDMT for patients with HFrEF focuses on four main medication classes to reduce mortality and morbidity. Veterans should be prescribed a medication from each pillar and have doses titrated to target doses to optimize benefit.¹⁷ **Achievement of optimal doses of initial medication(s) not required prior to adding the next medication** and **no specific order for initiation** has been established or recommended.

Figure 5. Foundational GDMT for patients with HFrEF¹⁷



*Guideline-directed beta-blockers include bisoprolol, carvedilol, or metoprolol succinate.

The following recommendations are for patients with HF with *reduced* EF. For medication review for patients with HF with *preserved* EF see page 15.

Tips for monitoring medications for heart failure:

- **Laboratory monitoring**
 - Electrolytes (especially serum potassium)
 - Renal function
- **Blood pressure**
 - Many of the medications used to treat HFrEF can have an impact on BP. Start low and monitor BP when initiating these medications in patients with already low BP. Ensure timely follow-up in the clinic or utilizing telehealth.
 - Do not stop GDMT in patients with low BP unless symptomatic. See the Quick Reference Guide (QRG) for guidance on managing symptomatic low BP.
 - Amend prescription indication to 'for the heart' to prevent discontinuation due to incorrect indication (i.e., blood pressure).
- **Heart rate**

Angiotensin system blockers

Angiotensin system blockers include angiotensin converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), and angiotensin receptor/neprilysin inhibitors (ARNI).

Sacubitril/valsartan is preferred over an ACEI or ARB in patients with NYHA II-III symptoms in combination with other GDMT.^{17,21}

Figure 6. Sacubitril/valsartan reduced composite outcome of CV death and HF hospitalization more than enalapril

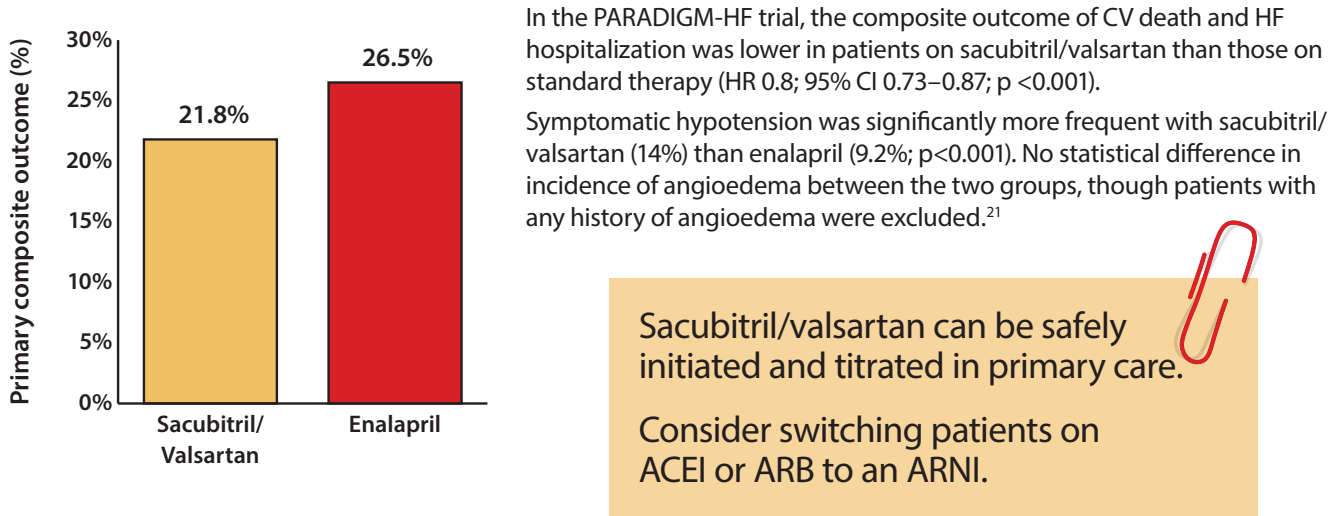


Table 3. Prescribing sacubitril/valsartan

1. Select starting dose			
Is patient switching from an ACEI/ARB?	Yes*	Ensure STRICT washout period for ACEI: Start sacubitril/valsartan 36 hours after the last dose of ACEI. Washout period is not required for ARBs. ACEI, ARB, and ARNI should not be taken concurrently.	
		LOW dose ACEI/ARB (daily dose ≤ 10 mg enalapril, ≤ 160 mg valsartan, ≤ 10 mg lisinopril, ≤ 100 mg losartan or equivalent)	24/26 mg twice daily
		High dose ACEI/ARB (daily dose > enalapril 10 mg, valsartan 160 mg, lisinopril 10 mg, or equivalent)	49/51 mg twice daily
Metabolic dose adjustments	No	No current ACEI or ARB therapy	24/26 mg twice daily
	Renal	eGFR <30 mL/min/1.73m ²	24/26 mg twice daily
	Hepatic	Child-Pugh Class B	24/26 mg twice daily
Child-Pugh Class C		Not recommended	
2. Monitor within 2-4 weeks of initiation and each dose titration:			
<ul style="list-style-type: none"> • blood pressure • electrolytes • renal function 			
3. Double dose every 2-4 weeks as tolerated to target 97/103 mg twice daily			

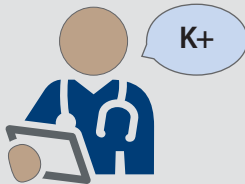
*Recommendations for stable and acceptable blood pressure. For patients who have symptomatic hypotension, start with a lower dose of ARNI.

Reminders for safe use of sacubitril/valsartan:

- Do not use in patients with any history of angioedema, not only to an ACEI or ARB.¹⁷
- Do not use with potassium > 5.5 mEq/L.
- Do not use within 36 hours of an ACEI or concomitantly with an ARB.¹⁷
- Caution in patients with NYHA class IV, as it is not as well tolerated and failed to show benefit in the LIFE trial.²²

Clinical pearls: managing common situations with ACEI, ARB, or ARNI therapy

My patient has mild hyperkalemia (< 6 mEq/dL) after starting treatment



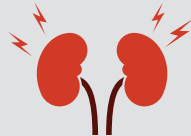
- Evaluate for symptoms of hyperkalemia such as muscle weakness, paresthesias, muscular fasciculations, or cardiac arrhythmias and take appropriate action if present.
- Review other medications that may increase potassium.
- Reduce or discontinue potassium supplements.
- Counsel on low K⁺ diet, consider referral for nutrition education.
- Reduce dose of sacubitril/valsartan to highest tolerated dose.
- Consider K⁺ binder, if appropriate.
- Repeat serum potassium measurement as clinically indicated.

My patient has symptomatic hypotension



- Consider reducing or temporarily holding diuretic dose*, if appropriate.
- Consider reducing or discontinuing other blood pressure medications not indicated for heart failure.
- If unable to decrease diuretic or antihypertensive medications, consider reducing the dose of sacubitril/valsartan.

When is worsening renal function of concern?



- > 30% decrease in eGFR or development of hyperkalemia.
- If hypovolemic, reduce diuretic dose.*
- If euvoletic, consider reducing sacubitril/valsartan dose or reducing/holding MRA.
- Rule out additional causes.

*Reducing diuretic dose can increase K⁺ levels.

- If an ARNI is not tolerated or appropriate, an ACEI or ARB may reduce mortality and HF hospitalization by 26% compared to placebo.^{17,23-25}
- Titrating an ARNI, ACEI, or ARB to target dose decreases HF-related hospitalization and composite of all-cause death.^{24,26}



Angioedema



Did you know? An ARB may be considered in patients with a history of ACEI-induced angioedema.

Initial considerations	<ul style="list-style-type: none">• Consider the risk vs. benefit of ARB therapy in patient with a history of angioedema on an individual basis (e.g., severity of angioedema, patient's ability to recognize recurrence).• ARNIs should not be considered in patients with a history of ACEI-induced angioedema.
Educate patients	<ul style="list-style-type: none">• Educate patients on the rare risk of recurrent angioedema with an ARB.• Look for signs of lip swelling, difficulty breathing or swallowing, or muffled voice.
Plan for recurrent angioedema	<ul style="list-style-type: none">• Instruct patients to alert provider as soon as possible and seek emergency care.• Understand the risk of recurrence is between 2-17%.

.....

Start an angiotensin system blocker, such as an ARNI (generally preferred), ACEI, or ARB and titrate to target dose in Veterans with HFrEF to reduce mortality and HF-related hospitalizations.

.....

Beta blockers (BB)

Choice of BB is important as benefit is not a class-effect. The preferred beta blockers for the treatment of HF are:¹⁷

- Bisoprolol
- Metoprolol succinate
- Carvedilol

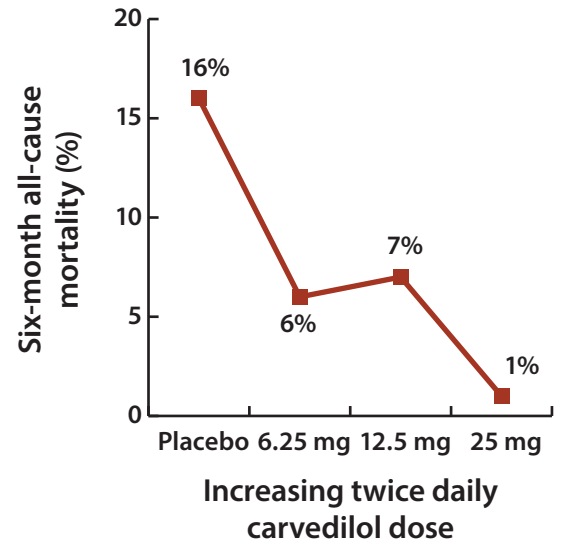
Initiation or titration of beta blockers may exacerbate fluid retention.

Start low, go slow, and be very cautious in hypervolemic patients. Diuretics may need to be increased temporarily.

Beta blockers in pulmonary disease

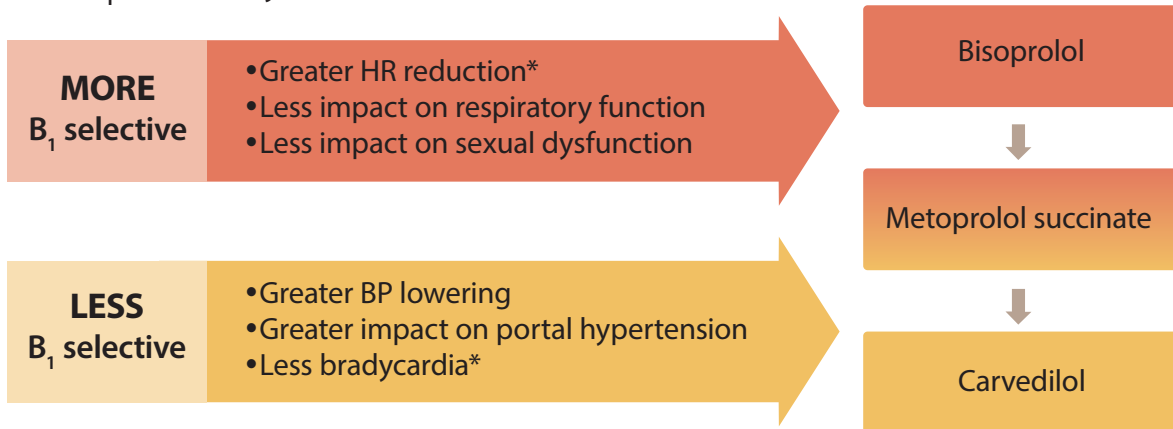
- If a BB is to be used in a patient with reversible airway disease, a cardioselective (B_1) agent like metoprolol succinate or bisoprolol may be preferred, taking into consideration the risk vs. benefit.^{28,29}
- There is a lack of conclusive data demonstrating any clinical harm associated with the use of BB in patients with COPD.^{30,31}

Figure 7. Mortality rate decreases as beta blockers are titrated to target dose¹⁹



In the MOCHA Trial, patients with HFrEF receiving 25 mg BID of carvedilol had a significantly decreased mortality rate compared to lower dosages at six months.

Figure 8. B_1 selectivity of BB used in HFrEF³²



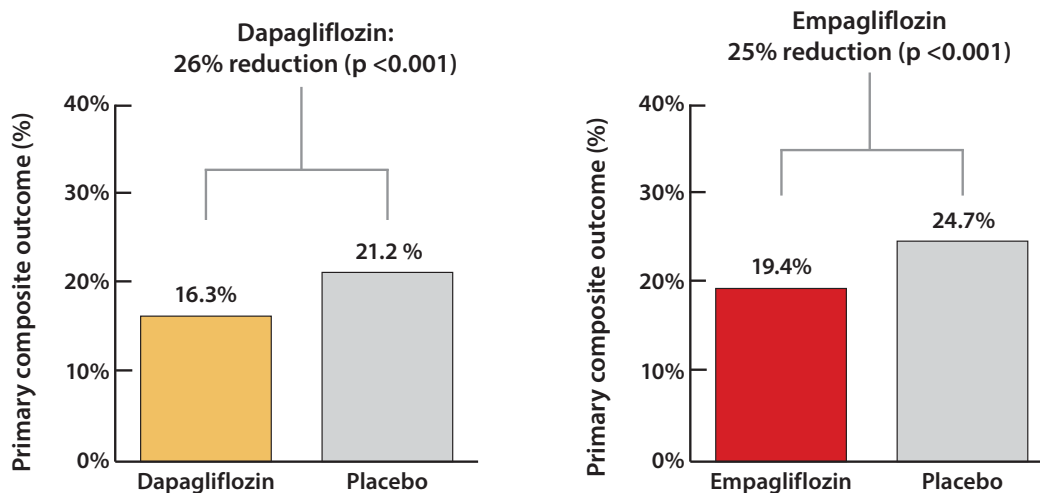
*Based on theoretical comparisons using relative receptor activity

Initiate beta blockers and titrate to target doses or maximally tolerated dose in Veterans with HFrEF.

Sodium-glucose co-transporter 2 (SGLT-2) inhibitors

SGLT-2 inhibitors (i.e., empagliflozin and dapagliflozin) have been shown to reduce the composite outcomes of CV death or worsening heart failure over placebo regardless of whether a patient has diabetes or not.^{33,34}

Figure 9. SGLT-2 inhibitors decreased CV mortality or slowed HF from worsening^{33,34}



Primary composite outcome: worsening HF or death from CVD causes.

The DAPA-HF and EMPEROR-Reduced trials evaluated dapagliflozin and empagliflozin, respectively, in patients with HFrEF in NYHA class II-IV patients on background ARNI/ACEI/ARB therapy. In the DAPA-HF trial there were ~11% of patients on ARNI, while in EMPEROR-Reduced there were ~18%. In both trials there was ~71% mineralocorticoid receptor antagonist use.

Special considerations when starting SGLT-2 inhibitors for patients with HF:³⁵⁻³⁷

SGLT-2 inhibitor clinical pearls for fluid balance and renal function	
Renal	Loop diuretics
<p>Ensure adequate kidney function prior to use:</p> <ul style="list-style-type: none"> Dapagliflozin eGFR ≥ 25 mL/min/1.73 m² Empagliflozin eGFR ≥ 20 mL/min/1.73 m² <p>Initial decline in eGFR expected.</p> <ul style="list-style-type: none"> 20-30% decline, consider adjustment of other medications (e.g., ACEI, diuretics) and assess for other causes. > 30% decline, discontinue and evaluate <p>Patients with chronic kidney disease may experience improved renal outcomes.</p>	<p>If patient is not hypervolemic consider dose reduction of loop diuretic, if concerned about hypovolemia.</p> <p>Educate on managing fluid, how and when to restart diuretic, and when to call the clinic.</p>

Other considerations for SGLT-2 inhibitor use (e.g., blood pressure, genital infections) are detailed in the QRG.

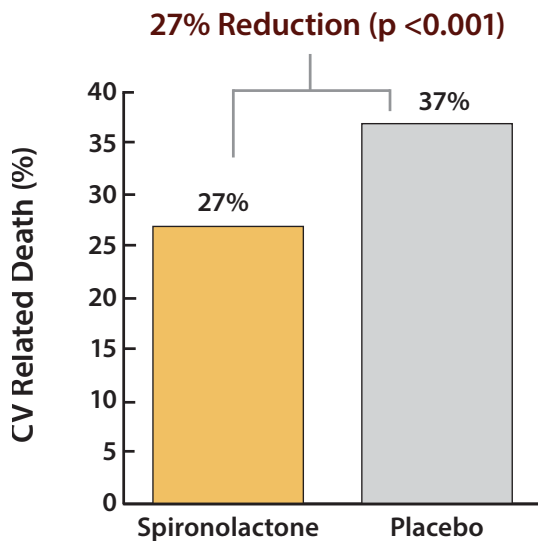
Initiate an SGLT-2 inhibitor in Veterans with HFrEF.

Mineralocorticoid receptor antagonists (MRA)

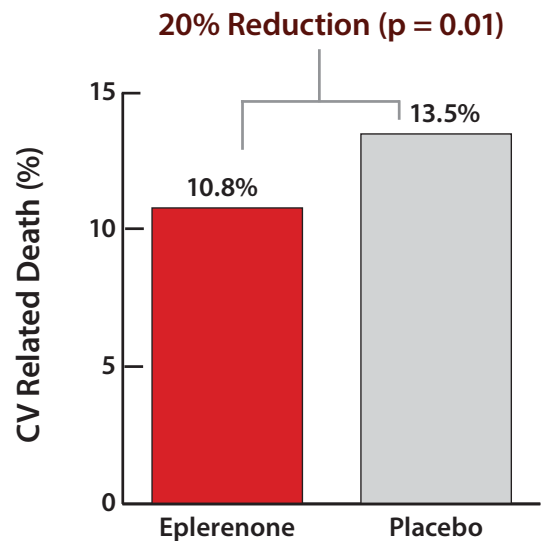
MRAs (e.g., spironolactone or eplerenone), previously called aldosterone antagonists (AA), should be considered in HFrEF when the Veteran has an EF $\leq 40\%$, NYHA class II-IV, $K^+ \leq 5\text{mEq/L}$, and $\text{eGFR} \geq 30 \text{ mL/min/1.73m}^2$.

A basic metabolic panel (BMP) is recommended within one week of initiating or titrating MRA to monitor for the presence of hyperkalemia.¹⁶

Figure 10. MRAs decreased cardiovascular (CV) mortality in HFrEF^{38,39}



The RALES trial evaluated CV-related death in patients with HFrEF in New York Heart Association (NYHA) class III and IV at the time of enrollment. This study was conducted before beta blockers were widely used for HF; only ~10% of patients were on beta blockers.



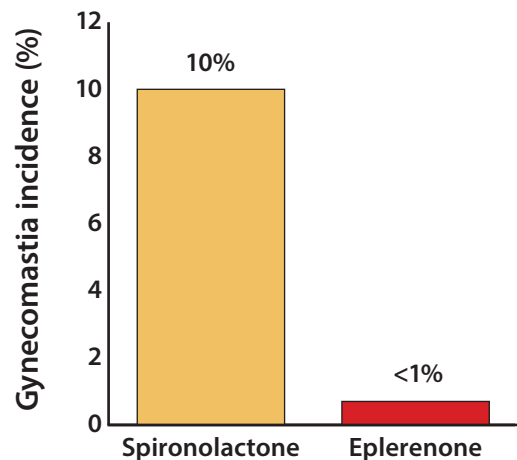
The EMPHASIS-HF trials evaluated CV-related death in patients with HFrEF in NYHA class II. In this study, 87% of patients were on beta blockers. This trial expanded utilization of mineralocorticoid receptor antagonists to include HF NYHA class II—IV.

Gynecomastia^{38,39}

The incidence of gynecomastia is higher with spironolactone than eplerenone. If a patient experiences gynecomastia on spironolactone, eplerenone should be considered as an alternative.

Add a mineralocorticoid receptor antagonist in patients with HFrEF to reduce mortality.

Figure 11. Gynecomastia incidence^{38,39}

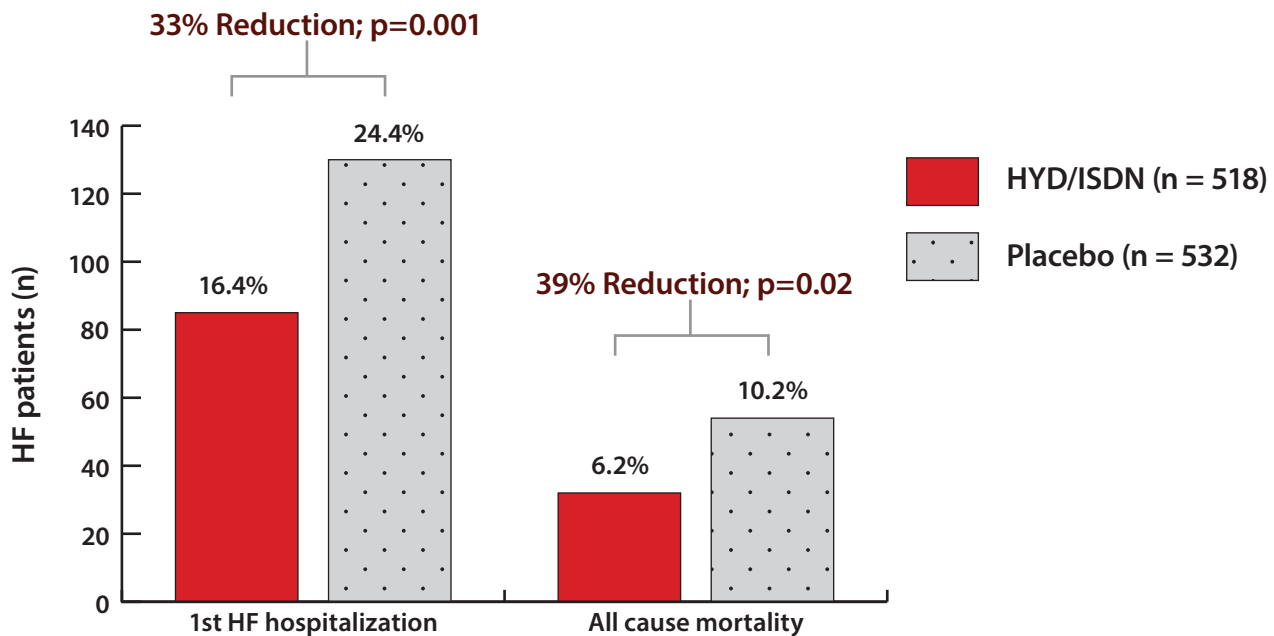


Hydralazine and isosorbide dinitrate

- In Black patients with NYHA class III-IV, the addition of hydralazine and isosorbide dinitrate to standard therapy is recommended to improve survival and decreases hospitalization.^{16,40}
- Hydralazine and isosorbide dinitrate may play a role in patients who do not tolerate either an ACEI or an ARB due to renal dysfunction, hyperkalemia, or angioedema.¹⁷

Side effects, drug interactions, and unappealing dosing schedule may impede the utilization of these medications. Starting at a lower dose and utilizing a slower titration to enhance the tolerability of these medications is recommended.¹⁷

Figure 12. Hydralazine and isosorbide dinitrate reduced hospitalizations and improved all-cause mortality in Black patients with heart failure⁴⁰



Black patients with NYHA class III or IV HF on standard therapy for heart failure; Study terminated early, secondary to the higher mortality rate in the placebo group. HYD = hydralazine; ISDN = isosorbide dinitrate

Consider adding hydralazine and isosorbide dinitrate in Black patients with HFrEF who remain symptomatic despite concomitant use of ARNI/ACEI/ARB, beta blocker, SGLT-2 inhibitor, and MRA.

Other medications used in selected patients with HFrEF

Table 4. Medications with a supplemental role in managing HFrEF^{2,17,41-44}

Medication	When to consider	Important notes
Ivabradine	Consider addition in patients with : <ul style="list-style-type: none"> • NYHA Class II-III HF, AND • EF ≤ 35%, AND • in normal sinus rhythm with a resting HR > 70 BPM despite optimal use of GDMT, or • if the patient is unable to tolerate BB or has contraindications to BB¹⁷ 	Initiate and titrate BB to maximally tolerated dose BEFORE assessing resting HR for ivabradine consideration.
Vericiguat	Consider addition in patients with: <ul style="list-style-type: none"> • recent HF hospitalization or outpatient IV diuretic use • no current use of long-acting nitrates (e.g., isosorbide dinitrate) • other mortality-reducing HF medications optimized 	Vericiguat reduced composite CV death and HF hospitalization by 10%, but the benefit is largely driven by a reduction in HF hospitalizations.
Digoxin	Consider use in HFrEF patients with: <ul style="list-style-type: none"> • persistent symptoms despite GDMT 	Target concentration < 1 ng/ml (ideally 0.5 to 0.9 ng/ml). Patients with elevated trough levels, especially > 2 ng/mL, and those with hypokalemia, hypomagnesemia, hypercalcemia, and hypothyroidism are at increased risk of digoxin toxicity. See the QRG for other risk factors.
Omega-3 polyunsaturated fatty acids (PUFA)	Consider use in patients with NYHA class II-IV symptoms despite GDMT.	Benefit was seen after three years in patients with EF < 40%. HF dose is 1,000 mg EPA/DHA daily, much lower than for lowering triglycerides. EPA/DHA are a portion of fatty acids in fish oil and product contents vary widely. Can increase LDL and the risk of bleeding
Intravenous iron therapy	Consider use in HFrEF patients with: <ul style="list-style-type: none"> • NYHA stage II and III, despite maximally tolerated GDMT for a least 4 weeks prior to infusion • EF < 45% or EF < 50% if recently hospitalized for HF • Ferritin <100 mg/dL or 100-299 mg/dL if transferrin saturation is < 20% 	Treating iron deficiency with intravenous iron infusions may alleviate HF symptoms, improve exercise capacity, and quality of life and reduces HF re-hospitalizations in symptomatic patients with EF < 50%. ^{15,43,44} Oral iron is not effective. Work with hematology to develop a treatment plan.

Medications for heart failure with preserved EF

The medications used for managing patients with HFrEF have not all been found to provide the same benefit for patients with HFpEF (EF \geq 50%). Most studies did not find a benefit in co-primary outcomes of CV death or HF hospitalization. Some studies suggest a decrease in HF hospitalization.

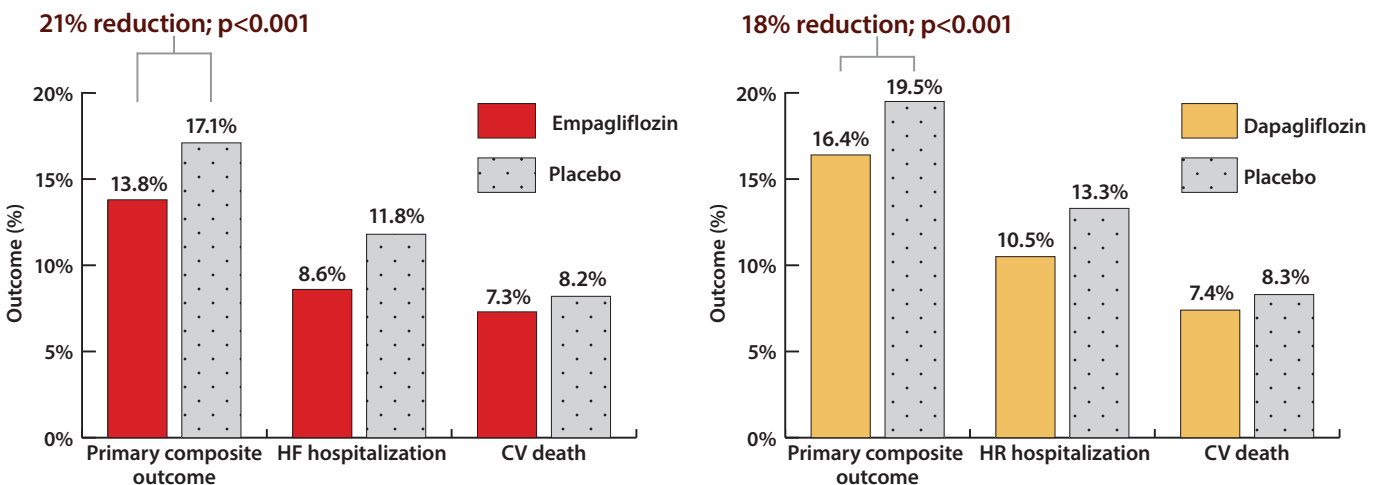
Table 5. Summary of studies in patients with HFpEF^{2,15,47-51}

Medication	Mortality decrease	HF hospitalization decrease
SGLT-2 inhibitor	?*	✓
ARNI (vs. ARB)	X	✓ (sub-group analysis)**
MRA	X	✓ (sub-group analysis)#
ARB	X	Possible benefit - conflicting data

X = no benefit; ✓ = benefit; For characteristics of patients most likely to benefit, see QRG.

*The primary outcome in the EMPEROR-preserved and DELIVER trials consisted of composites of CV death or heart failure hospitalization (HFH) or CV death or worsening heart failure (HFH or urgent visit for HF) respectively and did show a significant improvement. However, this effect was mainly related to a lower risk of HFH and the impact on mortality is not clear. **The PARAGON-HF did not show a difference in the primary composite endpoint of cardiovascular death or total HF hospitalization. However, in prespecified subgroup analyses a benefit was seen in those with an LVEF below 57% and in women. # The TOPCAT trial did not show a difference in the primary composite outcome of CV death, aborted cardiac arrest, or HFH. However, when looked at as a component of the primary outcome there was a significant decrease in HFH.

Figure 13. SGLT-2 Inhibitors reduce CV mortality and HF events in patients with HFpEF^{50,51}



The EMPEROR-Preserved and DELIVER trials enrolled 5,899 and 6,263 patients with NYHA class II-IV with LVEF > 40% to 10 mg of empagliflozin or 10 mg of dapagliflozin respectively. The benefit in each trial was driven by a reduction in HF hospitalization (HR 0.79; 95% CI: 0.60-0.83 and HR 0.77; 95% 0.67-0.89 respectively).

Assessing heart failure symptoms and fluid management

Fluid retention (hypervolemia) in patients with HF can be the stimulus for acute decompensated HF that requires hospitalization.⁵²

It is important that patients with HF are educated on:

- Weighing themselves daily and maintaining their dry weight
- Taking their medications as prescribed
- Monitoring how they feel
- Understanding the symptoms of HF and the best responses to stay in balance



Table 6. Sample HF assessment questions⁵³

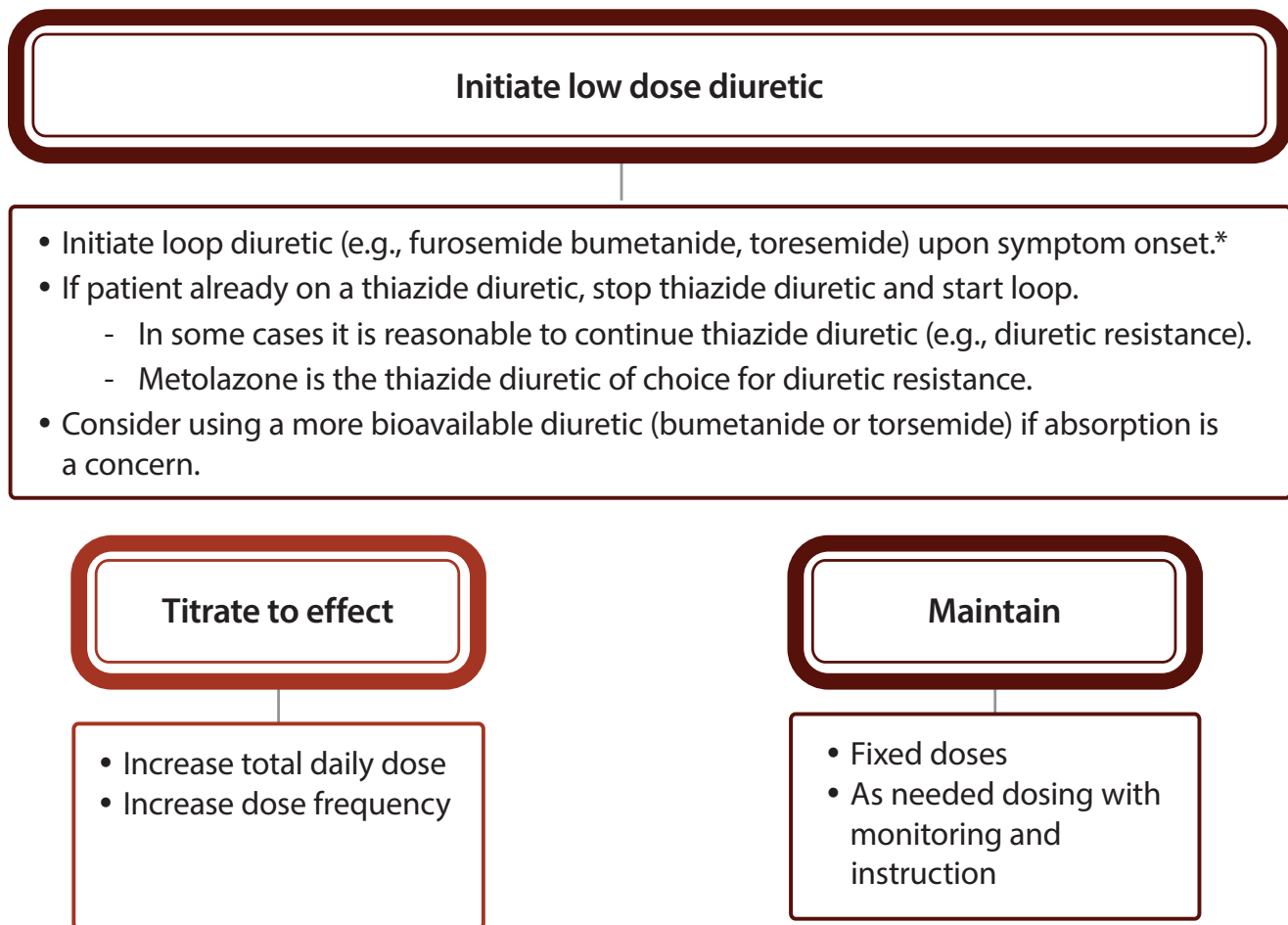
Breathing	Swelling	Neurologic changes
<ul style="list-style-type: none"> • What types of activities make you short of breath (SOB) or more SOB? • Are you experiencing SOB while sitting still? • Are you able to sleep lying down? With how many pillows, or do you need to sleep in a chair? 	<ul style="list-style-type: none"> • Are you having any swelling in your feet, ankles, legs, or stomach? • Is this new or worse than before? • Have you gained unusual or unexplained weight? • Have you gained more than three pounds in one day or five pounds in one week? 	<ul style="list-style-type: none"> • Are you having any dizziness? New or worse than before? • Are you having any confusion? New or worse than before? <div style="text-align: center; margin-top: 20px;"> </div>

Assess patients for symptoms of HF at each visit including physically assessing for edema. Remind patients of the importance of daily monitoring and acting on worsening symptoms.

Diuretics

Diuretics are often needed to help many patients with symptomatic HF remain euvolemic. In patients with HFrEF they should be combined with ARNI/ACE/ARB, BB, MRA, and SGLT-2 inhibitors in most patients with evidence of, or a prior history of, fluid retention.² In addition, moderate dietary sodium restriction can be used in conjunction with oral diuretics.⁴⁰

Figure 14. Starting a diuretic^{2,54}



*Avoid if hypersensitivity to furosemide, bumetanide, or toseamide. Use ethacrynic acid in these patients.

Risks of diuretics:^{2,54}

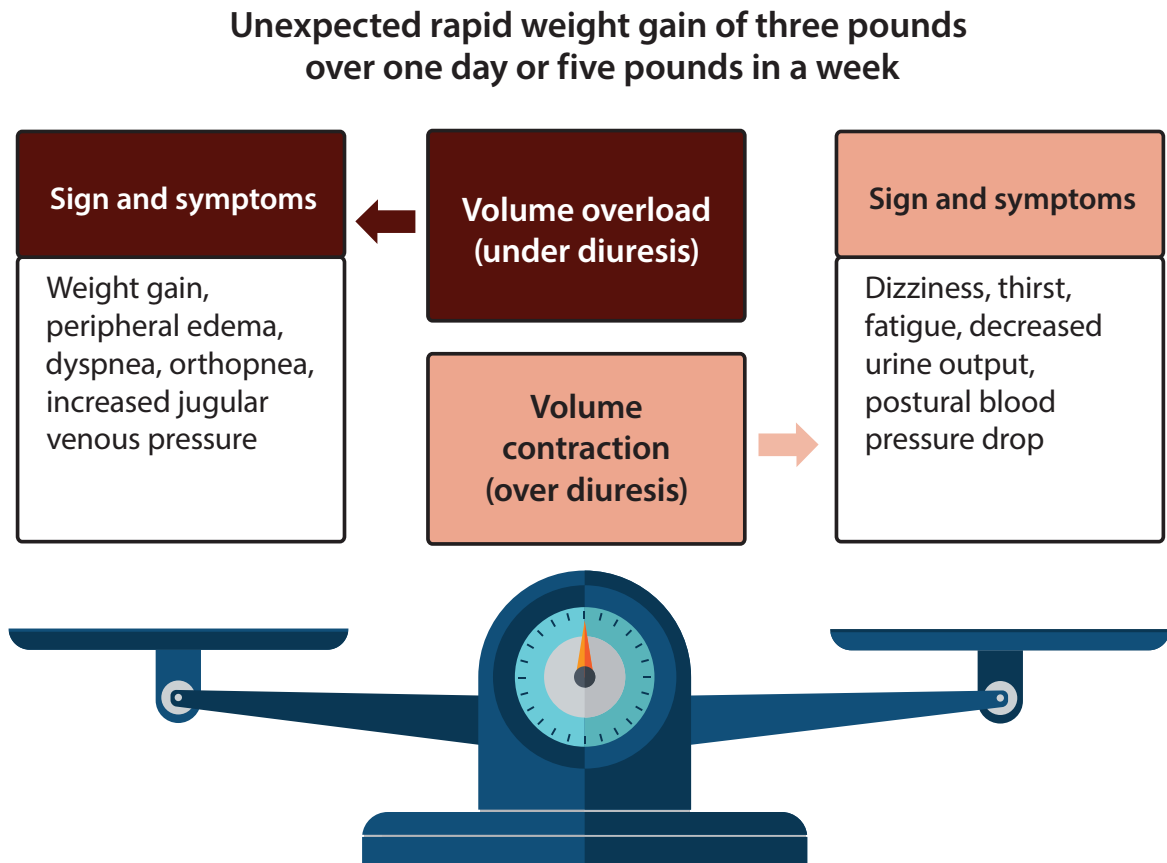
- Hypokalemia, hypomagnesemia, hyponatremia, electrocardiogram (ECG) changes, hypotension, acute kidney injury
- Combining diuretics increases risk of adverse events.

.....

Add diuretics to guideline-directed medical therapy for relief of symptoms due to volume overload in patients with HF.

.....

Figure 15. The great balancing act^{2,16,52,55}



1. Check adherence to medications, diet, and fluid restrictions.*
2. Review biochemistry and previous diuretic response.
3. Adjust loop diuretic dose (increase if fluid overloaded or decrease if dehydrated).
 - a. Volume overload:
 - i. An effective dose of a diuretic will elicit a urinary response within 30 to 60 minutes and results in increased urinary frequency for at least two hours.
 - ii. If urinary response is not noted within 60 minutes, consider increasing the dose by 50% to 100% to elicit diuresis.
 - iii. If urinary response is noted but the patient remains fluid overloaded and is not losing one to two pounds/day or showing improvement in fluid retention/congestion, consider increasing dosing frequency or switching diuretic or adding thiazide diuretic.
 - b. Volume contraction:
 - i. Trial diuretic reduction until minimal dose is achieved to maintain baseline weight.
4. Monitor renal function, potassium, magnesium, and response to therapy.

*Although fluid restriction is a common recommendation, it has no effect on clinical outcomes and has minimal evidence to support the practice.¹⁶

Treatment of heart failure in patients with chronic kidney disease (CKD)

Heart failure treatment recommendations for patients with concomitant renal dysfunction in general are not different from those for patients with preserved renal function.⁵⁶⁻⁵⁸ There is often concern that medications like ACEI, ARB, and ARNI will lead to deterioration of renal function and subsequently lead to worsening of HF. Despite the increase in serum creatinine with these medications, usually < 20% in the first month of treatment, there is often improvement seen in hospitalization and survival.⁵⁷

SGLT-2 inhibitors slow progression of kidney disease in addition to benefits to managing heart failure. While useful for renal protection, initiation in low eGFR or hypovolemia are not recommended.⁶⁰

Patients with CKD are more likely to develop hyperkalemia. Closer monitoring of renal function and electrolytes (potassium) is important to assist in guiding treatment decisions.⁵⁷ Treatment with SGLT-2 inhibitors may help lower serum potassium.⁶¹

ACEI and ARB can be continued when:^{56,59}

- eGFR decline at two months is less than 30%
- Serum Potassium is ≤ 5.5

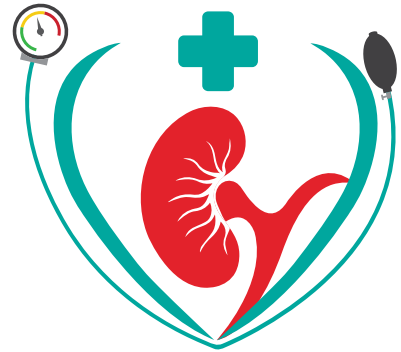
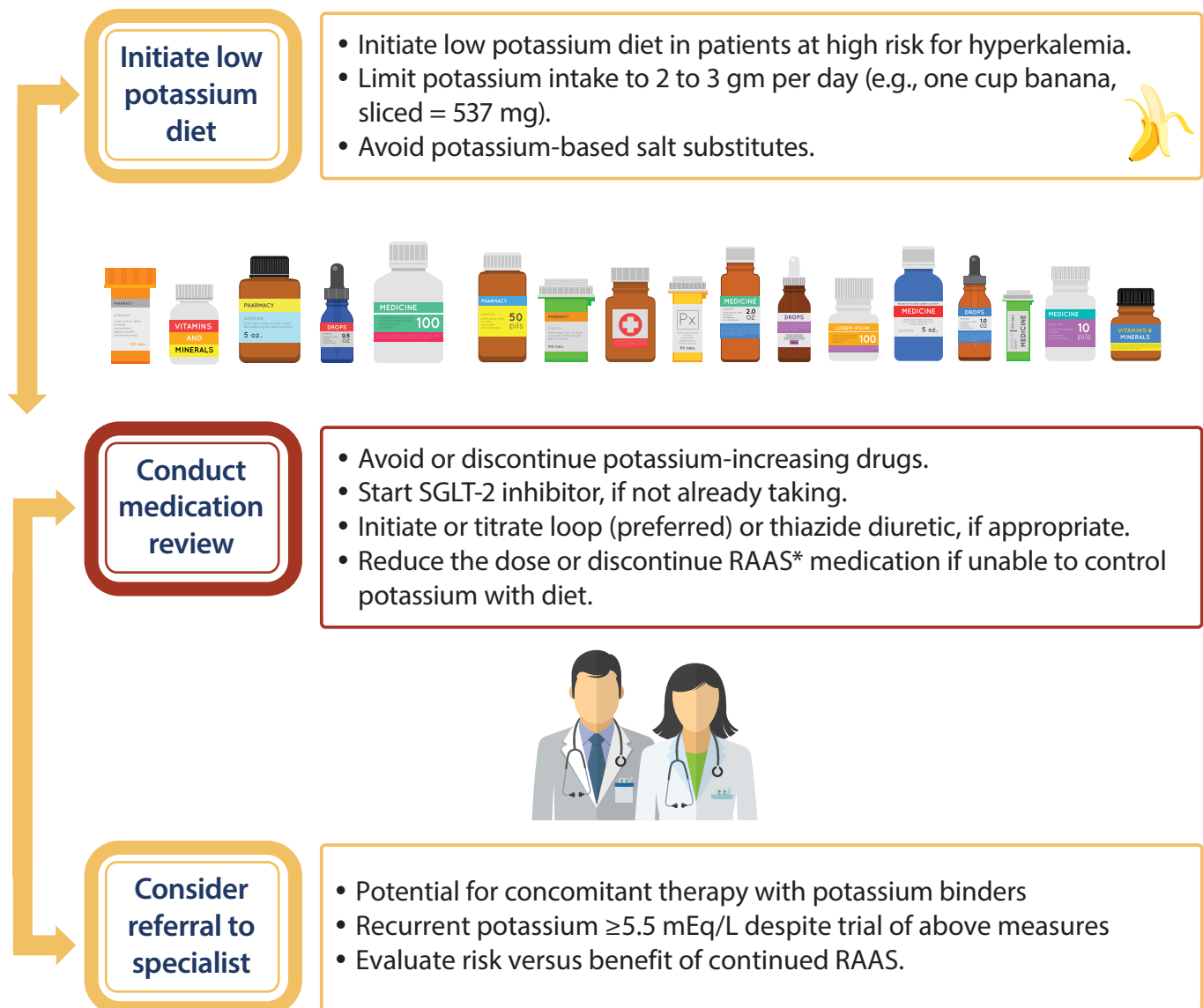




Figure 16. Measures to prevent and manage hyperkalemia⁶¹⁻⁶⁴



Medications to avoid or use with caution in heart failure

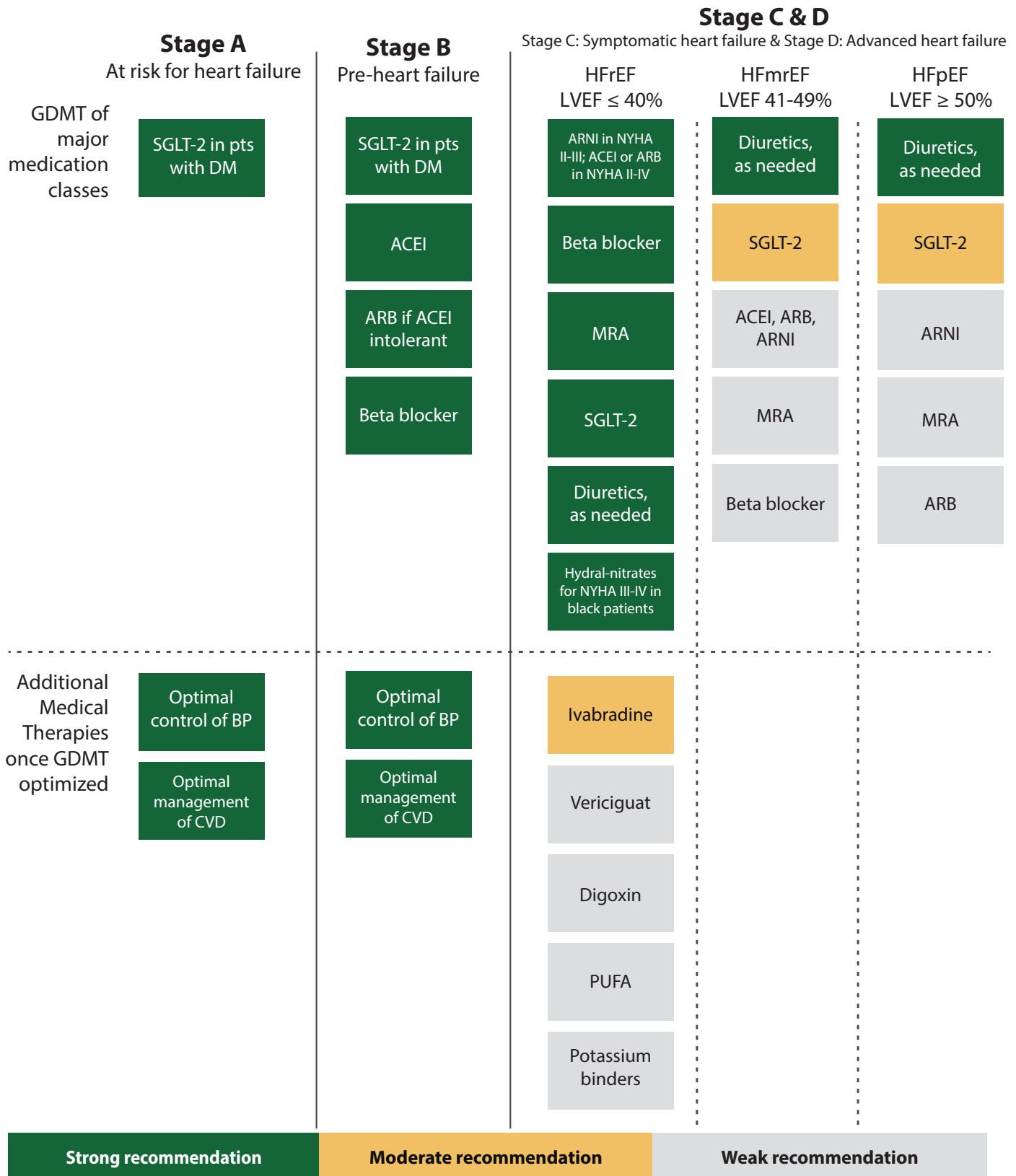
Table 7. Medications to avoid or use cautiously in HF^{16,65-70}

Medication	Issue
DISCONTINUE 	
Systemic nonsteroidal anti-inflammatory drugs (NSAIDs) (both COX-selective and non-selective inhibitors)	<ul style="list-style-type: none"> • May cause sodium and water retention, peripheral vasoconstriction, worsen heart failure, and decrease renal function • Acute renal failure may be more likely when these agents are used in combination with an ACEI, ARB, ARNI, or diuretic
Intermittent claudication agents (e.g., cilostazol)	Several drugs with the same pharmacologic effect as cilostazol have caused decreased survival compared to placebo in patients with NYHA class III-IV heart failure. Effects may be seen within one month of starting cilostazol. Cilostazol is contraindicated in patients with heart failure of any severity.
Nifedipine	<ul style="list-style-type: none"> • Negative inotropic effects • Increased risk of hospitalization for HF exacerbation in patients with HFrEF • Use amlodipine or felodipine if a dihydropyridine calcium channel blocker is needed in a patient with HFrEF
Non-dihydropyridine calcium channel blockers (e.g., verapamil and diltiazem)	<ul style="list-style-type: none"> • Negative inotropic effects • May be useful in HFpEF when slowing HR could increase filling time • Contraindicated in HFrEF
Thiazolidinediones (e.g., rosiglitazone, pioglitazone)	<ul style="list-style-type: none"> • May cause or exacerbate heart failure through increased fluid retention and blood pressure • Consider conversion to an anti-diabetic drug with HF benefits such as an SGLT-2 inhibitor
Some antiarrhythmics (e.g., flecainide, propafenone, dronedarone)	<ul style="list-style-type: none"> • Increased risk of hospitalization for HF exacerbation • Increased risk of mortality • Preference is for heart failure-specific beta blocker, amiodarone, or dofetilide
Dipeptidyl peptidase-4 (DPP4) inhibitors	<ul style="list-style-type: none"> • Increased risk of developing HF in patient with pre-existing heart and/or kidney disease; Avoid saxagliptin and alogliptin, use sitagliptin if alternative therapies (i.e., SGLT-2 inhibitors, GLP-1 receptor agonists) with cardiovascular benefit are not an option.

Medication	Issue
THINK 	
Corticosteroids	<ul style="list-style-type: none"> • Increased fluid and sodium retention and blood pressure
Anticoagulant	<ul style="list-style-type: none"> • Warfarin or direct oral anticoagulants do not improve thrombotic outcomes but increase bleeding risk in patients with chronic HF without an indication (e.g., atrial fibrillation, venous thromboembolism, prior thrombotic event, or cardioembolic source).
Miscellaneous	<ul style="list-style-type: none"> • Clozapine may cause cardiomyopathy and myocarditis. • Tricyclic antidepressants or cyclobenzaprine may prolong QT interval and contribute to hypotension. • Avoid or use caution with medications that increase fluid retention (e.g., gabapentin) and contribute to peripheral edema. • Doxazosin may worsen underlying myocardial dysfunction. • Tumor necrosis factor (TNF) inhibitors (e.g., infliximab, adalimumab, etanercept) may exacerbate HF.

Medication treatment algorithm for heart failure

Figure 17. Guideline-directed medical therapy across heart failure stages¹⁶

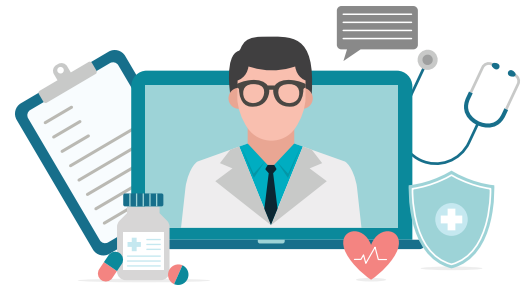


See the ACC/AHA/SFSA Guideline for Management of Heart Failure for specific patient population criteria.¹⁶

Care coordination

Remote patient monitoring-home telehealth (RPM-HT)⁷¹

- RPM-HT clinics may reduce all-cause mortality and the incidence of hospitalizations related to HF compared to patients receiving usual care alone.
- Enroll patients with HFrEF in RPM-HT to reduce mortality and HF hospitalizations.⁷¹



Referrals

- Appropriate and timely referral to an HF specialist is essential in selected patients to optimize therapies (e.g., device therapy) and evaluate advanced HF care options.
- Depression and anxiety are frequently associated with cardiovascular disease and increase mortality.⁷² Screen patients frequently for these disorders and consider treatment and/or referral to mental health if appropriate.

Presence of any of these high-risk features would support clinical consideration for referral to an advanced heart failure specialist.

A team-based approach

- Every patient with a diagnosis of HF should be assigned to a PACT Team.
- A principal HF manager should be identified for all patients (cardiology or PCP).
- If managed by primary care, ongoing reassessment of needs recommended.

Use "**I NEED HELP**" to identify candidates for referral to a HF specialist¹⁷

I: IV inotropes

N: NYHA Class IIIB/IV HF or persistently elevated natriuretic peptides

E: End-organ dysfunction

E: Ejection fraction < 35%

D: Defibrillator shocks

H: Hospitalizations > 1

E: Edema, despite escalating diuretics

L: Low blood pressure, high heart rate

P: Prognostic medication: progressive intolerance or down-titration of guideline-directed medical therapy

Timely post-hospitalization follow-up

- Timely follow-up after discharge from a HF hospitalization can reduce the risk of readmission.⁷³ Visits should occur within 7 days of discharge.^{16,19}
- At post-discharge visits, providers should evaluate and address precipitants of HF exacerbation, barriers to care (including self-care), volume status as well as renal function and electrolytes, medication regimen and adherence, patient education, and opportunities to initiate and/or titrate GDMT.¹⁶

Engage patients in appropriate care coordination, including RPM-HT, referring to cardiology specialists, and post-hospitalization follow-up.

Summary

- 1 Identify and treat risk factors for heart failure such as hypertension, diabetes, and atrial fibrillation to prevent or delay the development of heart failure.
- 2 To improve mortality and morbidity in patients with HFrEF, initiate and titrate angiotensin receptor blockers (ARNI/ACEI/ARB), beta blockers, SGLT-2 inhibitors, and mineralocorticoid receptor antagonists to target doses, or maximally tolerated dose.
- 3 In patients unable to tolerate dose titration due to hypotensive symptoms, utilize lowest tolerated doses of GDMT to improve morbidity and mortality.
- 4 For patients with HFpEF, manage contributing comorbidities, use diuretics to control fluids, initiate an SGLT-2 inhibitor, and consider an ARNI or MRA in selected patients.
- 5 Avoid using non-dihydropyridine calcium channel blockers, nifedipine, cilostazol, NSAIDs, and thiazolidinediones (e.g., rosiglitazone, pioglitazone) in HFrEF patients to prevent exacerbation of HF symptoms and hospitalizations.
- 6 Engage patients in appropriate care coordination, including RPM-HT, referring to cardiology specialists and post-hospitalization follow-up.

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VA



U.S. Department of Veterans Affairs

Veterans Health Administration
PBM Academic Detailing Services

This reference guide was created to be used as a tool for VA providers and is available from the Academic Detailing SharePoint.

These are general recommendations only; specific clinical decisions should be made by the treating provider based on an individual patient's clinical condition.

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