Managing Heart Failure in Primary Care

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PBM Academic Detailing Service

Managing Heart Failure in Primary Care

A VA Clinician's Guide

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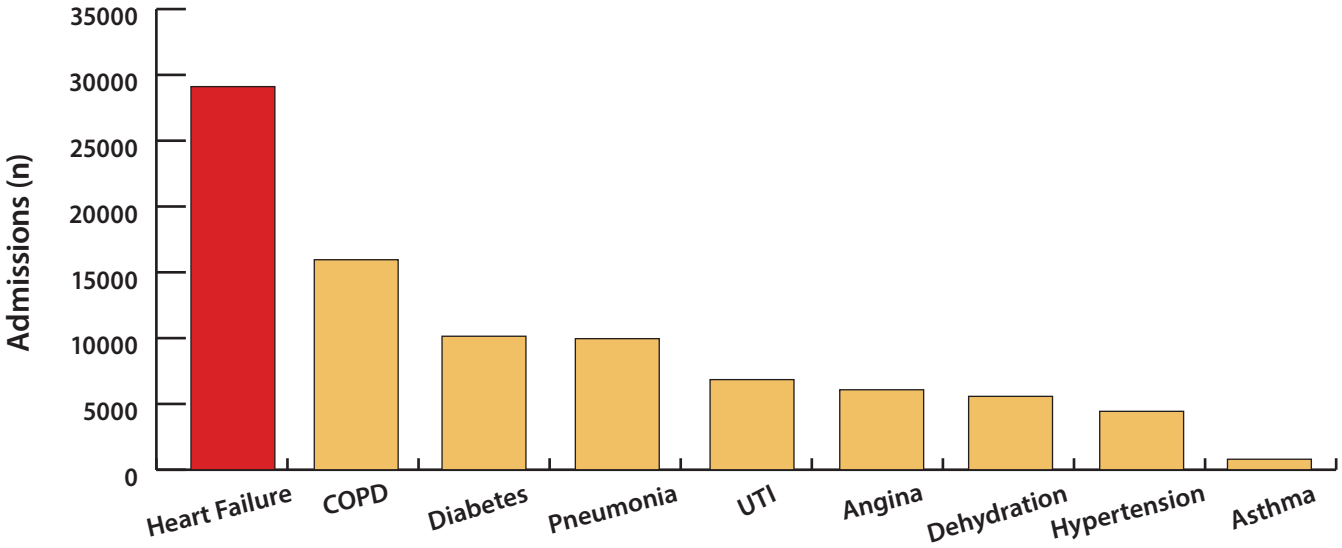
Heart Failure Epidemiology

Heart failure (HF) affects 6.5 million people in the U.S.—a number expected to increase to more than eight 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 the VA.

Figure 1. Heart Failure was the Leading Cause of Admissions Among Ambulatory Care Sensitive Conditions from May 2017 to April 2018



Data obtained from the Ambulatory Care Sensitive Conditions (ACSC) Dashboard on the Veterans Health Administration Support Service Center (VSSC) Capital Assets Databases. 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 50% of patients will die within five years of diagnosis.[3]

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.

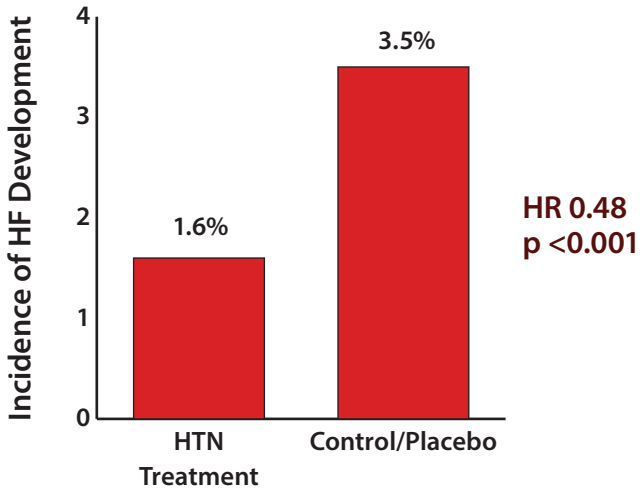
Preventing Heart Failure

Traditional Heart Failure Risk Factors:[3,4]

- Coronary Heart Disease
- Diabetes
- Hypertension
- Obesity
- Smoking
- Valvular Disease

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]

Figure 2. Treating Hypertension (HTN) Reduces Incidence of Heart Failure[5]



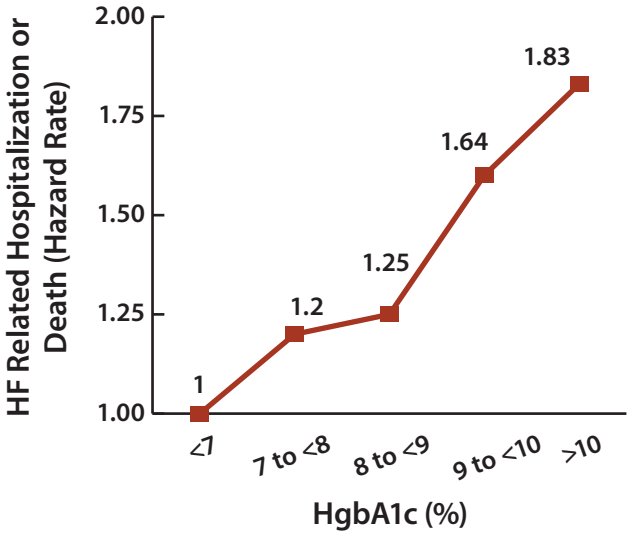
For example:

- 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.[8,9]

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

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

Figure 3. Poor Glycemic Control Associated with an Increased Risk of Heart Failure.[7]



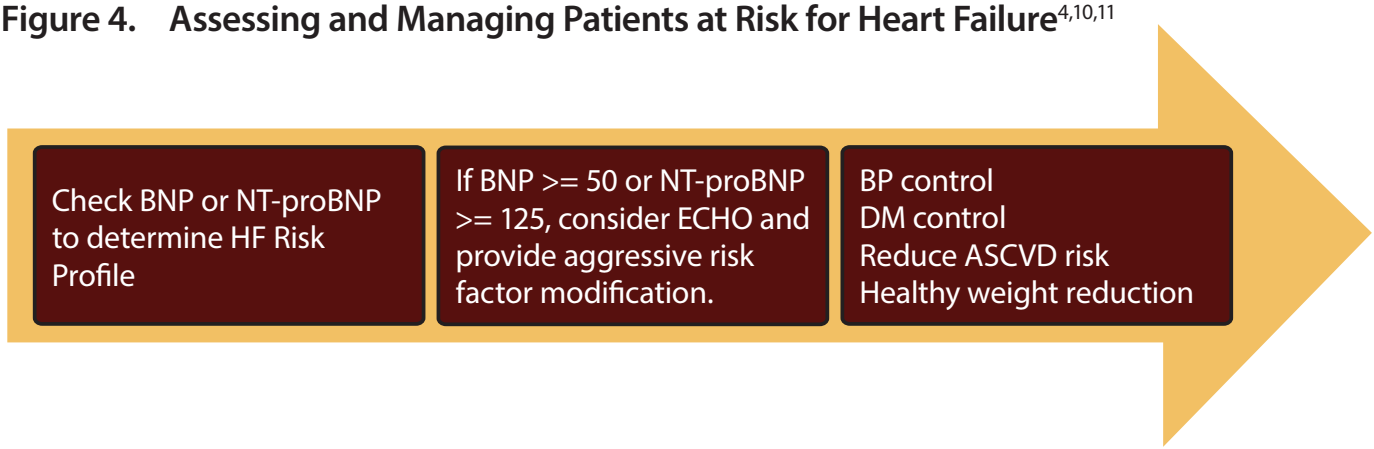
Model adjusted for age and gender.
HF = heart failure; Hgb = hemoglobin

Identifying Heart Failure in Those at Risk

New evidence suggests that early detection of elevated B-type natriuretic peptide (BNP) or N-terminal pro-B-type natriuretic peptide (NT-proBNP), in addition to collaborative care and optimization of guideline-directed medical therapy (GDMT), may decrease the risk of symptomatic HF and left ventricular dysfunction.[4] Consider checking BNP or NT-proBNP to determine risk in patients with hypertension, diabetes, or vascular disease.

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. Assessing and Managing Patients at Risk for Heart Failure[4,10,11]



ASCVD = atherosclerotic cardiovascular disease; BNP = B-type natriuretic peptide; BP = blood pressure; DM = diabetes mellitus; HF = heart failure; NT-proBNP = N-terminal pro-B-type natriuretic peptide

Optimize management of risk factors, pharmacologic, and non-pharmacologic therapies in patients at risk for HF.[4]

Diagnosing and Classifying Heart Failure[2]

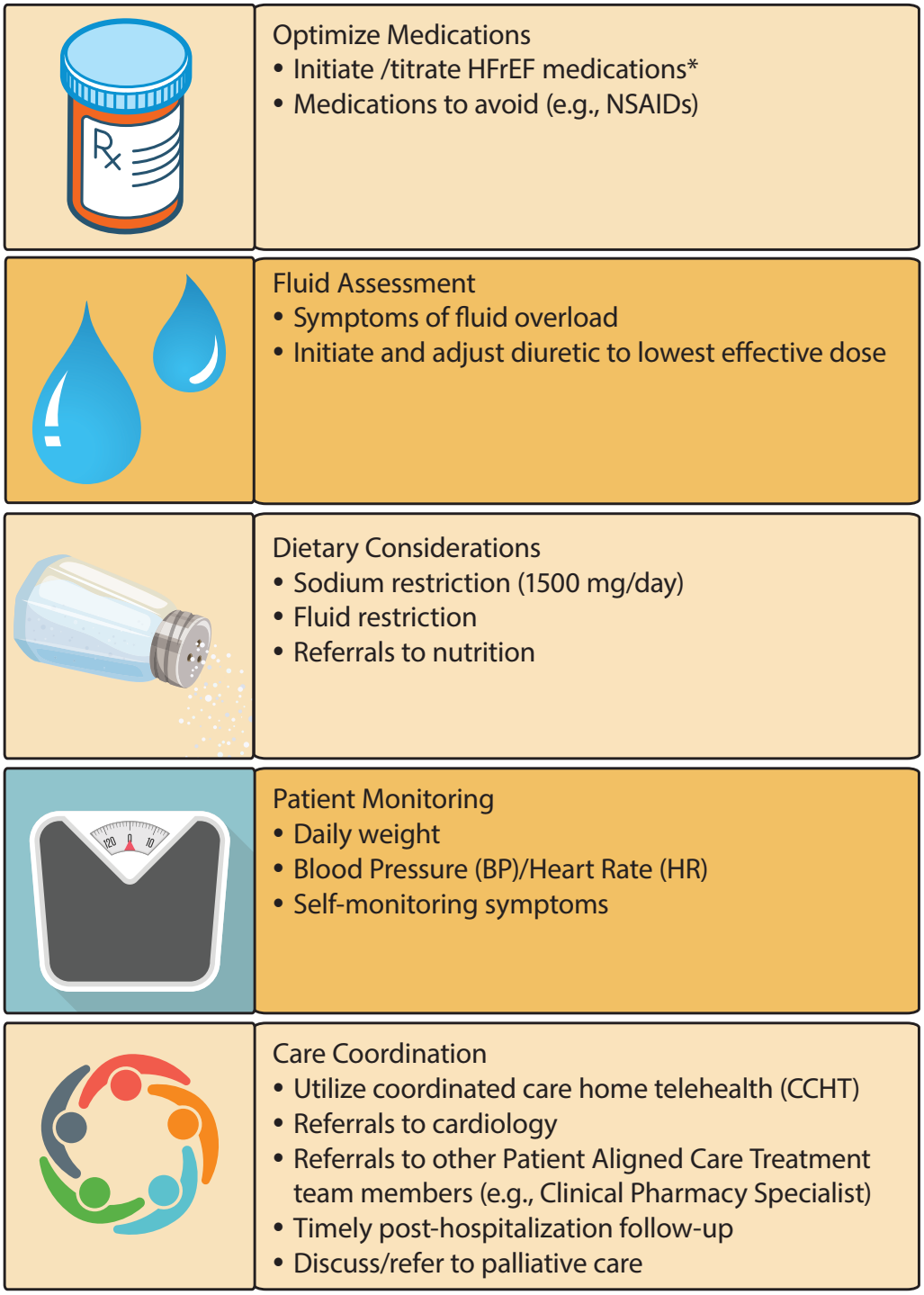
Diagnosis of heart failure requires structural changes to the heart and clinical symptoms.

Table 1. Two Primary Classifications for Heart Failure

Heart Failure with Reduced Ejection Fraction (HFrEF; EF ≤40%)	Heart Failure with Preserved Ejection Fraction (HFpEF; EF ≥50%)
REDUCED 	 PRESERVED
• Pharmacologic treatment should follow guideline directed medical therapies (GDMT).	• GDMT do not show the same morbidity and mortality benefits.
• GDMT improve survival and/or reduce hospitalization.	• Treatments focus on management of comorbidities and symptoms.

Principles of Heart Failure Management

Figure 5. Principles of HF Management



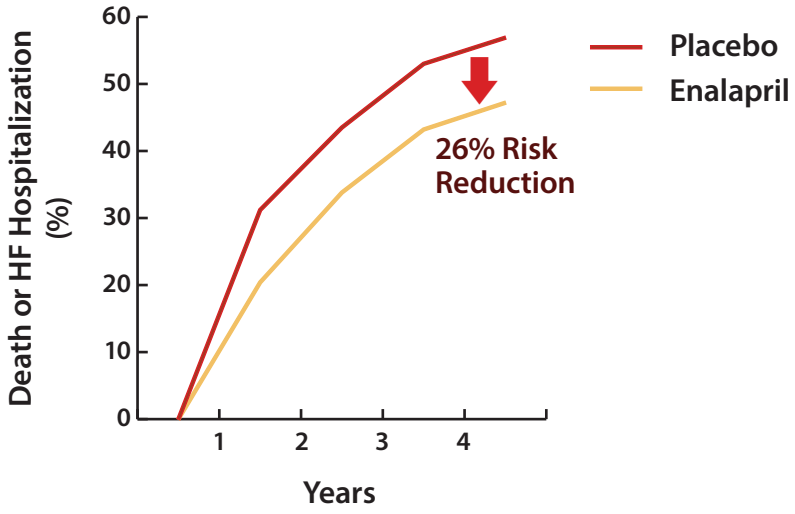
*Evidence evaluating any specific pharmacotherapy intervention is weak or neutral for reducing hospitalizations or mortality with HFpEF. NSAID = nonsteroidal anti-inflammatory drug

Angiotensin-Converting Enzyme Inhibitors (ACEI) or Angiotensin Receptor Blockers (ARB)

ACEI are the **first-line treatment** (in combination with beta blockers (BB)) for patients with HFrEF.[2] ARBs can be used as alternatives in Veterans intolerant to ACEI.[2]

- ✓ Treatment with an ACEI or ARB reduce combined mortality and hospitalizations.[2,12,13,14]
- ✓ Titrating ACEI or ARB to target dose decreases HF-related hospitalization and composite of all-cause death or HF admission.[13,15]

Figure 6. Addition of an ACEI Decreased Death and Hospitalizations in Patients with Heart Failure with Reduced Ejection Fraction (HFrEF)[12]

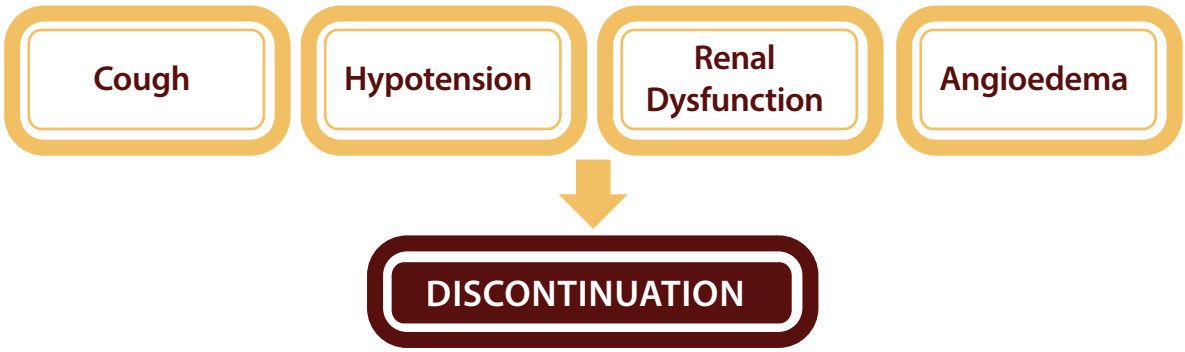


In the SOLVD study, patients with HFrEF who received enalapril had significantly lower rates of death and hospitalizations compared to patients receiving placebo.

When to Consider an ARB

When an ACEI is not tolerated due to cough or angioedema, consider switching the Veteran to an ARB.

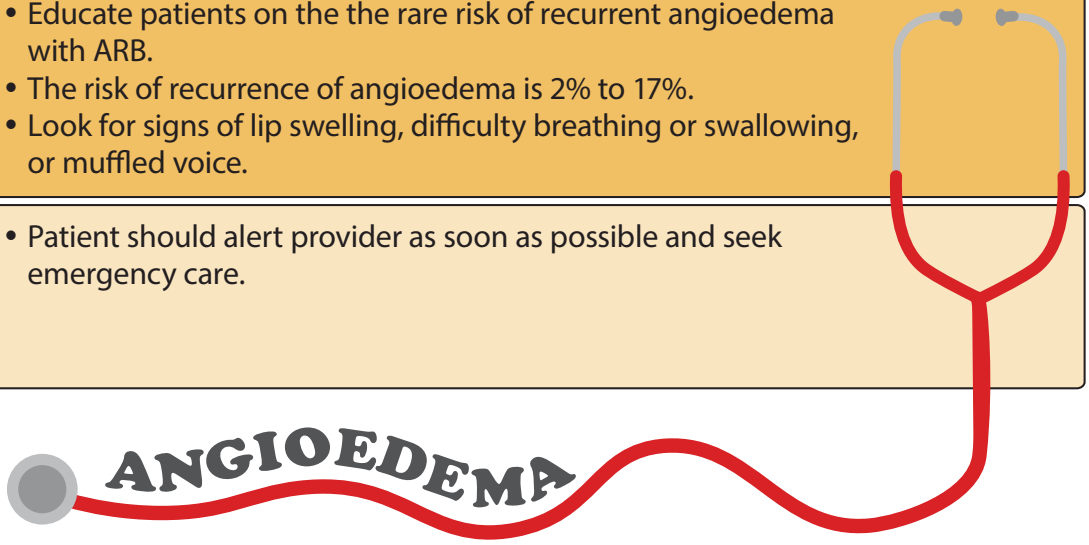
Figure 7. Common Causes of ACEI Intolerance Leading to Discontinuation[16]



- Hypotension and/or renal dysfunction can occur with an ACEI or ARB.
- Dose reduction or retrial later with slower titration are appropriate for most patients.

Figure 8. An ARB May be Considered in Patients with a History of ACEI-Induced Angioedema

History of ACEI-induced angioedema	• Weigh risk versus benefit of starting ARB (e.g., severity of angioedema, patient's ability to recognize recurrence). • Guidelines recommend substituting with ARB for HFrEF.
Use ARB as alternative	• Educate patients on the the rare risk of recurrent angioedema with ARB. • The risk of recurrence of angioedema is 2% to 17%. • Look for signs of lip swelling, difficulty breathing or swallowing, or muffled voice.
Plan for recurrent angioedema	• Patient should alert provider as soon as possible and seek emergency care.

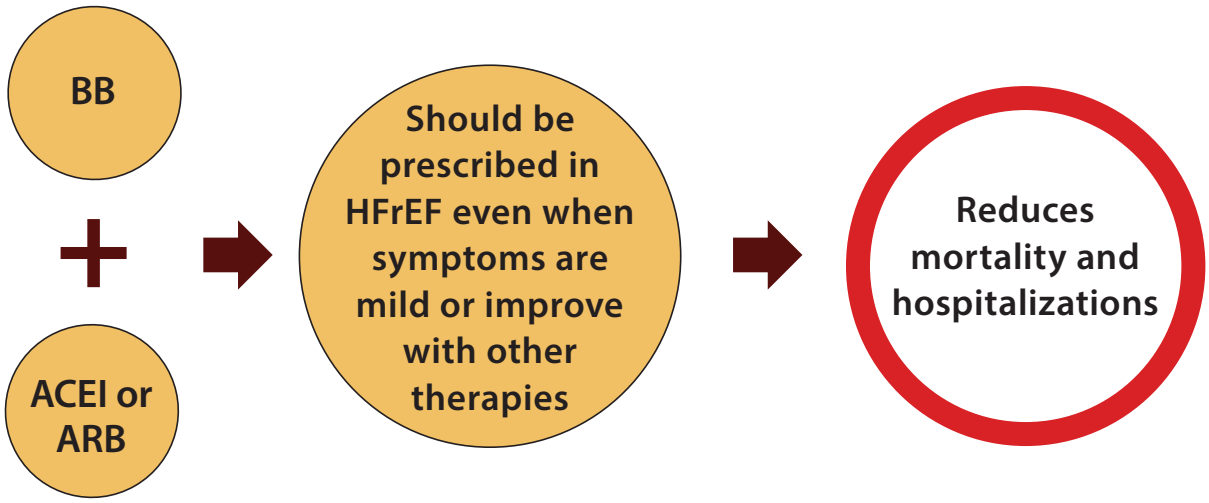


The risk vs. benefit of ARB therapy in patients with a history of ACEI-induced angioedema should be considered on an individual basis.[18]

Start an ACEI or ARB (if ACEI is not tolerated) and titrate to target dose in Veterans with HFrEF to reduce mortality and HF-related hospitalizations.

Beta Blockers (BB)

Figure 9. First-Line Treatment for All Patients with HFrEF[2]



Choice of BB is important as benefit is not a class-effect. The preferred beta blockers for the treatment of HF are:[1]

- Bisoprolol
- Metoprolol succinate
- Carvedilol

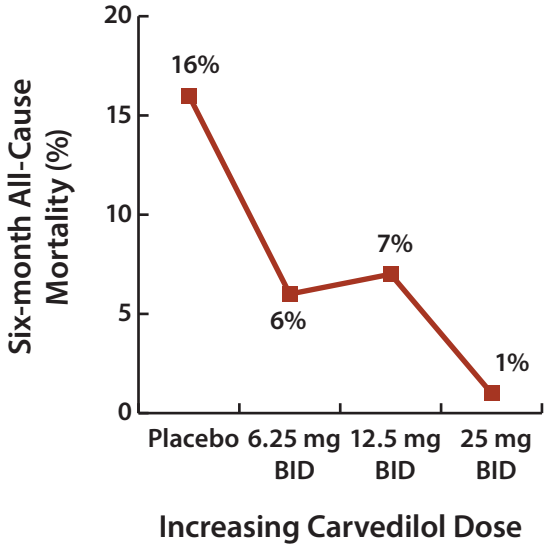
Initiation or titration of beta blockers may exacerbate fluid retention.

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

Beta Blockers in Pulmonary Disease

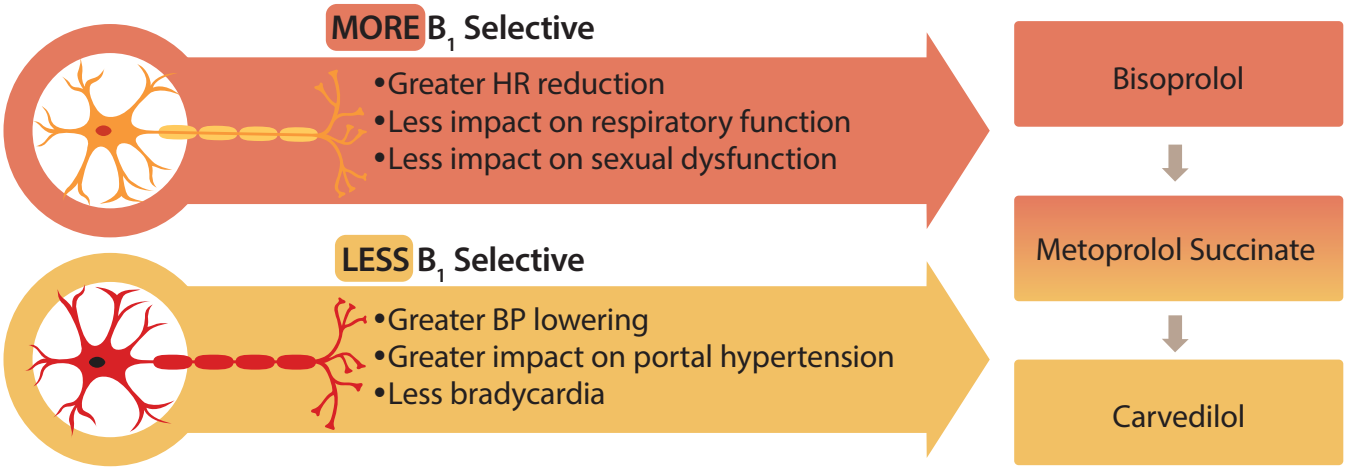
- If a BB is to be used in a patient with asthma, a cardioselective (B1) agent may be preferred, taking into consideration the risk vs. benefit.[20,21]
- There is a lack of conclusive data demonstrating any clinical harm associated with the use of BB in patients with COPD.[22,23]

Figure 10. Mortality Rate Decreases as Beta Blockers are Titrated to Target Dose[19]



MOCHA study evaluated the dose-related effect of carvedilol in patients with HFrEF over six months. Patients receiving target dose of carvedilol (25 mg BID) had a significantly decreased rate of mortality compared to patients receiving only a low to moderate dose (6.25 mg–12.5 mg BID). BID = twice a day

Figure 11: B_1 Selectivity of BB Used in HFrEF[24]



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

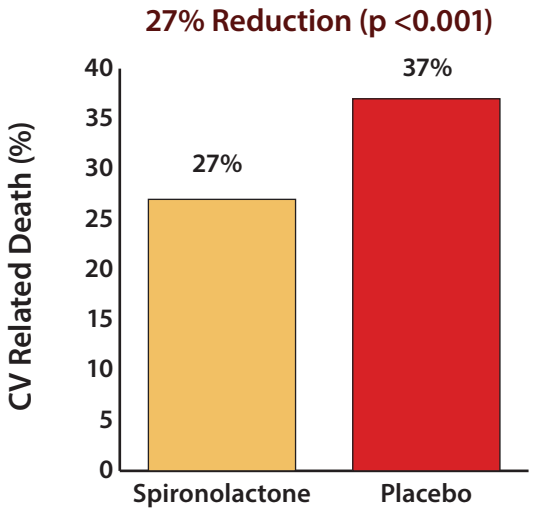
Aldosterone Antagonists (AA)

Aldosterone Antagonists (AA), e.g., spironolactone or eplerenone, should be considered in HFrEF when the Veteran:[2]

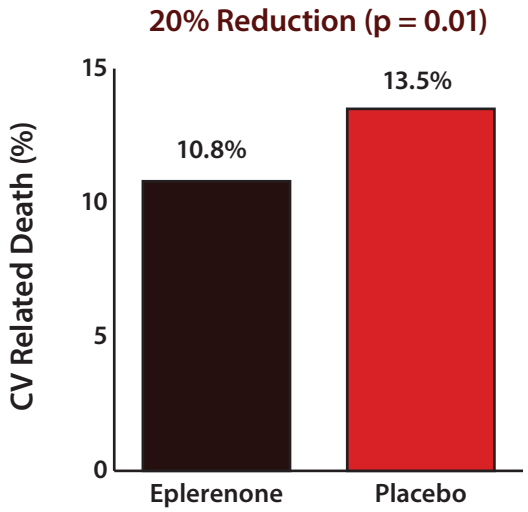
- Remains symptomatic on ACEI (or ARB) and a BB
- AND has an EF ≤35%.

A basic metabolic panel (BMP) is recommended within one week of initiating or titrating AA to monitor for the presence of hyperkalemia.[2]

Figure 12. Aldosterone Antagonists Decreased Cardiovascular (CV) Mortality in HFrEF[25,26]



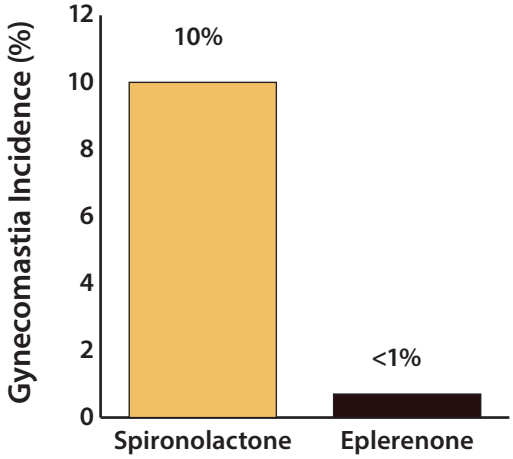
The RALES trial evaluated CV-related death in patients with HFrEF in New York Heart Association (NYHA) class III and IV at the time of enrollment. This study was conducted before beta blockers were widely used for HF; only ~10% of patients were on beta blockers.



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 aldosterone antagonists to include HF NYHA class II—IV.

Add an aldosterone antagonist in patients with HFrEF (NYHA class II-IV) with an EF ≤35% to reduce mortality.

Figure 13. AA Gynecomastia Incidence[27,28]



Gynecomastia[27,28]

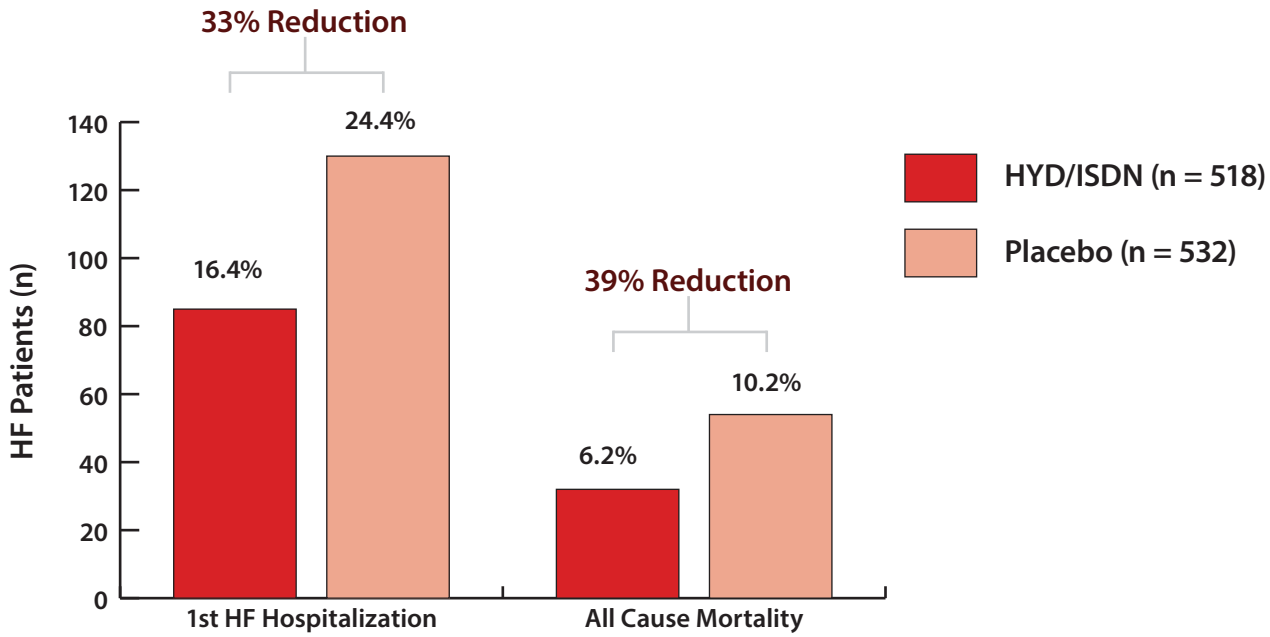
The incidence of gynecomastia is higher with spironolactone than eplerenone. If a patient experiences gynecomastia on spironolactone, eplerenone should be considered as an alternative.

Hydralazine and Isosorbide Dinitrate

- In African Americans, the addition of hydralazine and isosorbide dinitrate to standard therapy improves survival and decreases hospitalization.[29,30]
- 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.[2]

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.[2]

Figure 14. Effects of Hydralazine and Isosorbide Dinitrate on Heart Failure in African Americans[29]



African American 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 African American patients with HFrEF who remain symptomatic despite concomitant use of ACEI or ARB, beta blockers, and aldosterone antagonists.

Sacubitril/valsartan

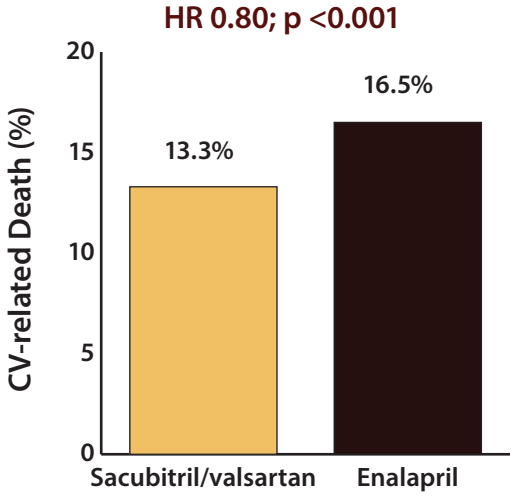
Sacubitril/valsartan is an angiotensin receptor/neprilysin inhibitor (ARNI) that has been shown to reduce cardiovascular (CV)-related death and hospitalizations.[4,31]

- Replace ACEI or ARB with ARNI in selected patients with symptomatic (NYHA Class II-III) HFrEF despite optimal use of a BB, ACEI or ARB, and AA.[4]
- Patients should tolerate a moderate dose of an ACEI or ARB before attempting a trial on sacubitril/valsartan.

Don'ts

- Do not use ARNI in patients with a history of angioedema.[4]
- Do not use ARNI within 36 hours of the last dose of an ACEI.[4]

Figure 15. Sacubitril/valsartan Reduced CV Death and HF[31]



In the PARADIGM-HF trial, the benefit of sacubitril/valsartan was shown in patients with reduced EF, elevated BNP, and mild to severe HF symptoms on standard therapy (HR 0.8; 95% CI 0.73–0.87; p <0.001). Sacubitril/valsartan reduced the relative risk of all-cause mortality by 16% (p<0.001). The incidence of symptomatic hypotension and angioedema was higher with sacubitril/valsartan vs. enalapril.

Omega-3 Polyunsaturated Fatty Acids (PUFA)

Omega-3 Polyunsaturated Fatty Acids (PUFA) may be used as adjunctive therapy in patients with heart failure and NYHA class II–IV symptoms to reduce all-cause mortality and cardiovascular related hospitalizations.[2,32]

Table 2. PUFA Dosing

Dosing	1,000 mg EPA/DHA (eicosapentaenoic acid/docosahexaenoic acid) Daily
• Dose studied in heart failure is much lower than doses studied for lowering triglycerides. • Only a portion of the fatty acids contained in fish oil are EPA/DHA, and their content varies widely between products. • It is important to dose fish oil for heart failure to achieve a dose of 1,000 mg DHA/EPA daily.	

Medications that Reduce HF-Related Hospitalization but NOT Mortality: Ivabradine and Digoxin

Table 3. Medications that Reduce HF-related Hospitalization but not Mortality[2,4,33,34]

Medication	Ivabradine	Digoxin
When to Consider 	Consider addition in patients with NYHA Class II-III HF, EF <35% in normal sinus rhythm with a resting HR >70 BPM despite optimal use of a BB, ACEI or ARB, and AA, or if the patient is unable to tolerate BB or has contraindications to BB.[4]	Consider use in HFrEF patients with persistent symptoms despite guideline-directed medical therapy.
Important Notes 	Initiate and titrate BB BEFORE assessing resting HR for ivabradine consideration.	Patients with elevated trough levels, especially >2 ng/mL, and those with hypokalemia, hypomagnesemia, hypercalcemia, and hypothyroidism are at increased risk of digoxin toxicity.

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.[35]

It is important that patients with HF are educated on:

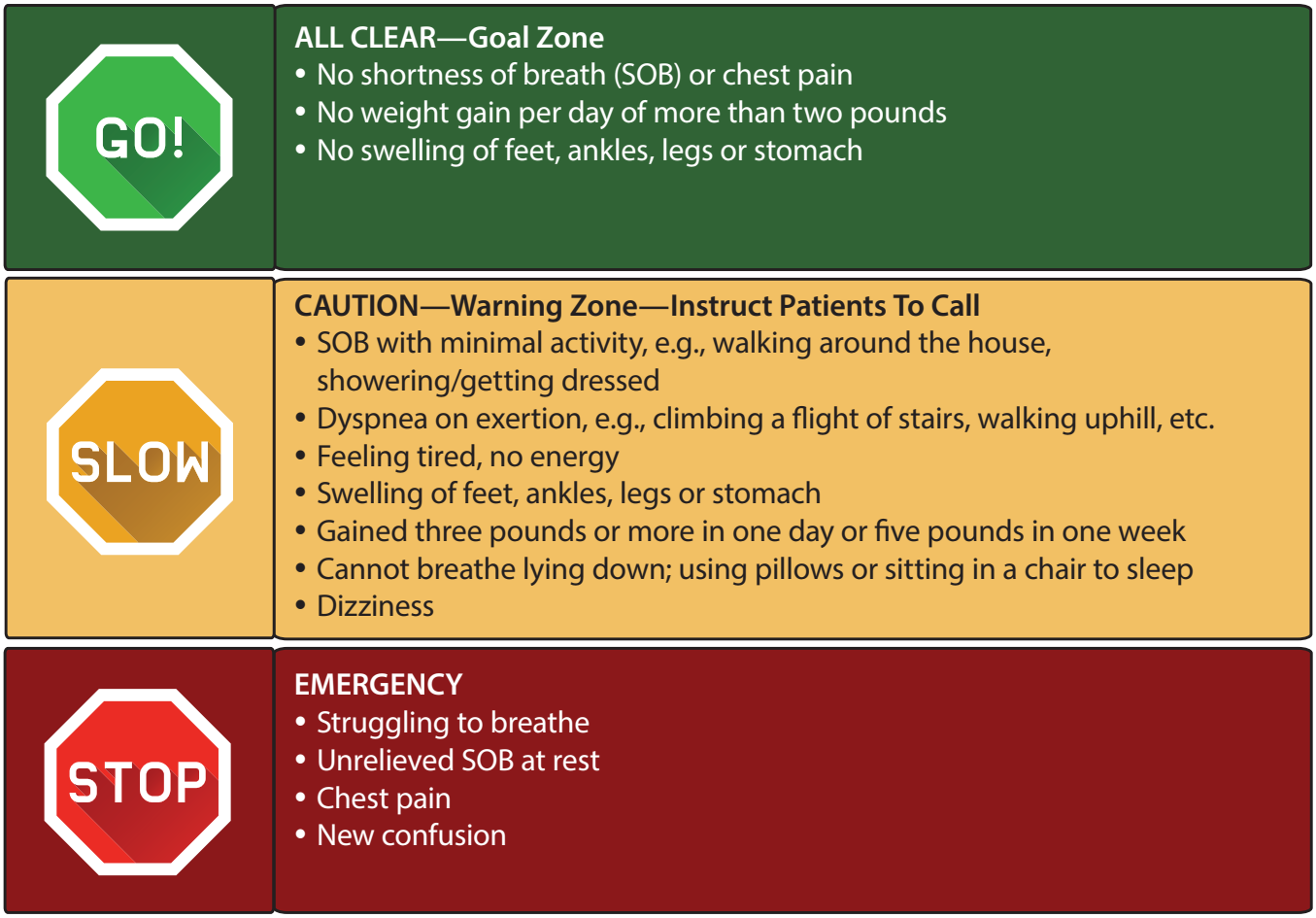
- Weighing themselves daily and maintenance of their dry weight
- Taking their medications as prescribed
- Monitoring how they feel
- Understanding the symptoms of HF and the best responses to stay in balance.

Table 4. Sample HF Assessment Questions[36]

Breathing	Swelling	Neurologic Changes
• Are you able to carry out your ordinary activities without experiencing shortness of breath (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?	• Are you having any swelling in your feet, ankles, legs or stomach? • Is this new or worse than before? • Have you gained more than three pounds in one day or five pounds in one week?	• Are you having any dizziness? New or worse than before? • Are you having any confusion? New or worse than before? 

Assess patients for symptoms of HF at each visit and remind them of the importance of monitoring for and acting on worsening symptoms daily.

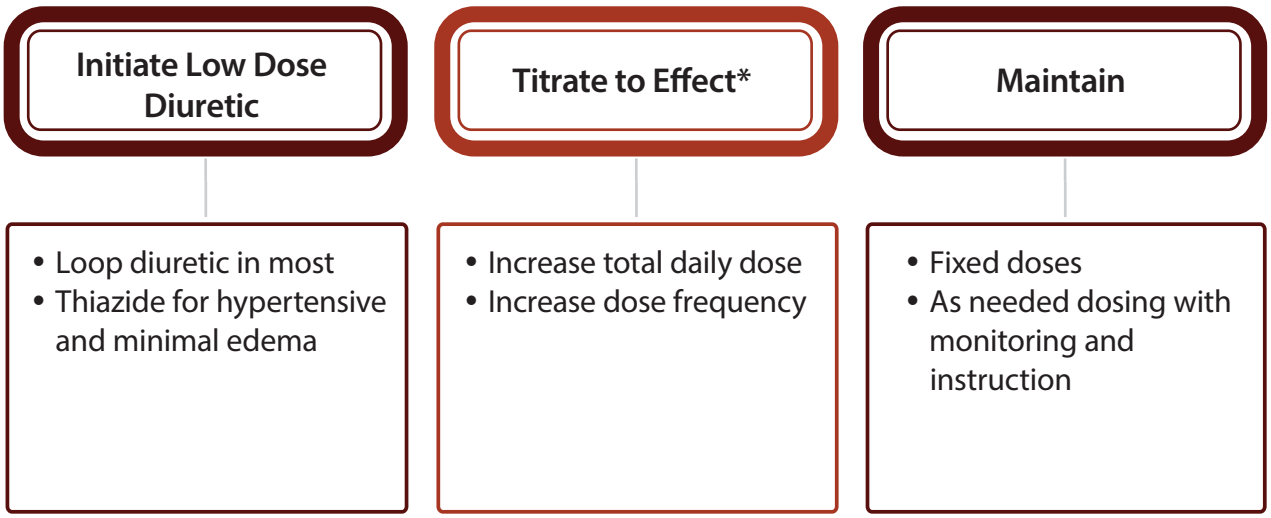
Figure 16. Heart Failure Zones[36–38]



Diuretics

Diuretics are often needed to help HF patients maintain their target weight. They should be combined with the ACEI or ARB, BB, and AA 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.[29]

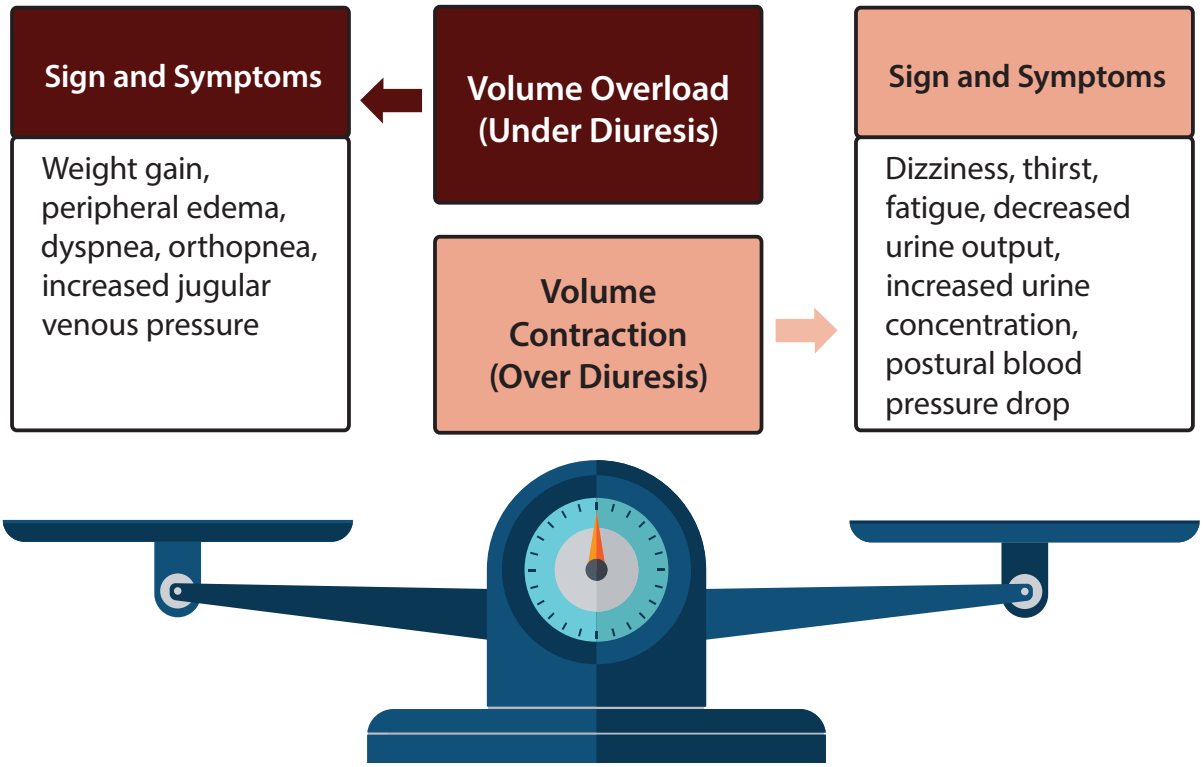
Figure 17. Starting a Diuretic[2,39]



*Consider using a more bioavailable diuretic (bumetanide or torsemide) if diuretic resistance is suspected.

Figure 18. The Great Balancing Act[2,35,40]

Unexpected rapid weight gain of three lbs or more over two days or longer



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, consider increasing dosing frequency or switching 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.

*Evidence supports fluid restriction of 1.5–2 L/day for management of stage D HF. This may also be prudent in patients with difficult to control volume status or while actively diuresing.

Loop Diuretics

Consider using bumetanide or torsemide in patients with an inadequate response to furosemide.[2,39] Consider ethacrynic acid in patients with severe sulfonamide or sulfa drug allergies where risk outweighs trial of other loop diuretics.

Risks of Diuretics:[2,39]

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

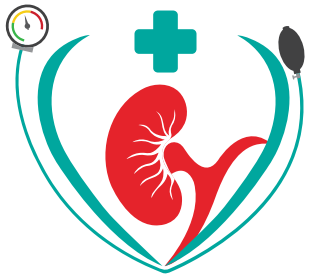
Add diuretics to guideline-directed medical therapy for relief of symptoms due to volume overload in patients with HF.

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.[41,43,44] There is often concern that medications like ACEI and ARB will lead to deterioration of renal function and subsequently lead to worsening of HF. Despite the increase in serum creatinine with these medications, there is often improvement seen in hospitalization and survival.[43]

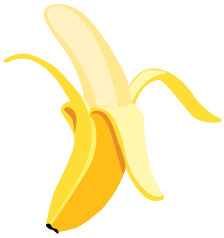
ACEI and ARB can be continued when:[41,42]

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



Patients with Chronic Kidney Disease (CKD) are more likely to develop hyperkalemia. Closer monitoring of renal function and electrolytes (potassium) is important to assist in guiding treatment decisions.[43]

Figure 19. Measures to Prevent and Manage Hyperkalemia[45–49]



Initiate Low Potassium Diet

- Initiate low potassium diet in patients at high risk for hyperkalemia.
- Limit potassium intake to 2 to 3 gm per day (e.g., one cup banana, sliced = 537 mg).
- Avoid potassium-based salt substitutes.

Conduct Medication Review

- Avoid or discontinue potassium-increasing drugs.
- Initiate or titrate loop or thiazide diuretic, if appropriate.
- Reduce the dose or discontinue RAAS* medication.

Consider Referral to Specialist

- Potential for concomitant therapy with cation exchangers
- Recurrent potassium ≥5.5 mEq/L despite trial of above measures
- Evaluate risk versus benefit of continued RAAS.

*RAAS = renin–angiotensin–aldosterone system medications (e.g., ACEI, ARB, AA)

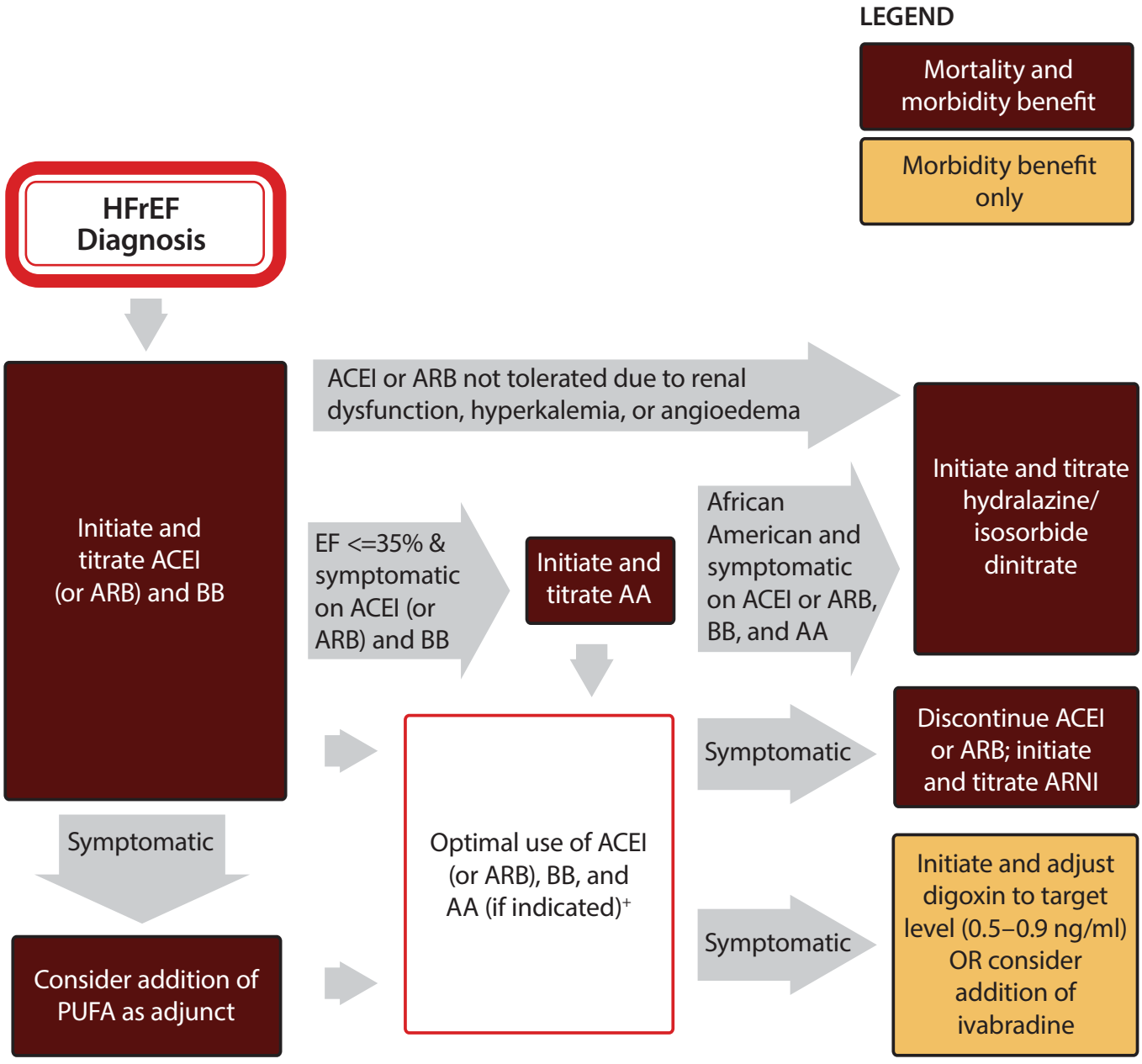
Medications to Avoid or Use with Caution in Heart Failure

Table 5. Relative Contraindicated Medications in HF[50–57]

Medication	Issue
DISCONTINUE 	
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. Cilostazol is contraindicated in patients with heart failure of any severity.
Non-dihydropyridine calcium channel blockers (e.g., verapamil and diltiazem)	• Negative inotropic effects • May be useful in HFpEF when slowing HR could increase filling time.
Systemic nonsteroidal anti-inflammatory drugs (NSAIDs) (both COX-selective and non-selective inhibitors)	• 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.
Thiazolidinediones (e.g., rosiglitazone, pioglitazone)	• May cause or exacerbate heart failure through increased fluid retention and blood pressure.
Some anti-arrhythmics (e.g., flecainide and propafenone)	• Increased risk of hospitalization for HF exacerbation • Increased risk of mortality • Preference is for heart failure-specific beta blocker or amiodarone.
THINK 	
Corticosteroids	• Increased fluid and sodium retention and blood pressure
Dipeptidyl peptidase-4 (DPP4) inhibitors	• Increased risk of developing HF in patient with pre-existing heart and/or kidney disease
Miscellaneous	• Clozapine may cause cardiomyopathy and myocarditis. • Tricyclic antidepressants may prolong QT interval, contribute to hypotension. • Medications that increase fluid retention (e.g., gabapentin) and contribute to peripheral edema

Medication Treatment Algorithm for Heart Failure with Reduced Ejection Fraction (HFrEF)

Figure 20. Medication Treatment Algorithm*[2–4]



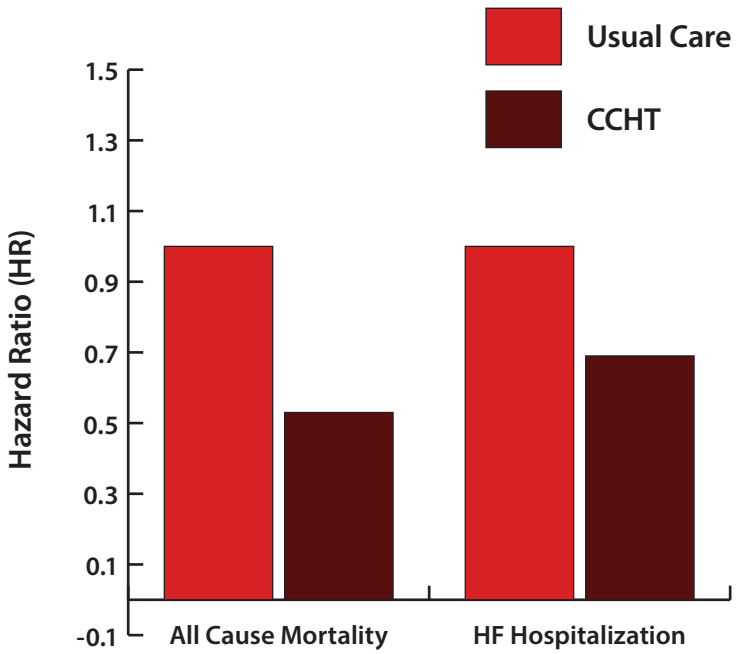
*See appropriate section for clinical considerations. +It is reasonable to combine hydralazine/isosorbide dinitrate with an ARNI as well as either digoxin or ivabradine in patients who remain symptomatic despite optimization of other therapies. AA = aldosterone antagonist; ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor/neprilysin inhibitor; PUFA = omega-3 polyunsaturated fatty acids

Care Coordination for Management of Heart Failure

Coordinated Care Home Telehealth (CCHT)[58]

- CCHT clinics can significantly reduce all-cause mortality and the incidence of hospitalizations related to HF compared to patients receiving usual care alone.
- Enroll patients with HFrEF in CCHT to reduce mortality and HF hospitalizations.[58]

Figure 21. CCHT Reduces Mortality and HF Hospitalizations[58]



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.[60] Screen patients frequently for these disorders and consider referral to mental health for treatment.

Use "**I NEED HELP**" to Identify Candidates for Referral to a HF Specialist[59]

- **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

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

Timely Post-hospitalization Follow-up

- Timely follow-up after discharge from a HF hospitalization can reduce the risk of readmission.[61]

- In 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, and patient education.[2]

Engage patients in appropriate care coordination, including CCHT, 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. Titrate ACEI (or ARB) and beta blockers to target doses, or maximally tolerated dose, to improve morbidity and mortality.
3. In patients unable to tolerate dose titration, utilize low doses of ACEI (or ARB) and beta blockers to improve morbidity and mortality.
4. Add an aldosterone antagonist to reduce mortality in patients with reduced EF (≤35%, NYHA class II-IV HF) on maximum doses of a BB and ACEI or ARB. Also consider adding an AA to reduce hospitalizations in patients with HF with preserved ejection fraction.
5. The addition of isosorbide dinitrate and hydralazine is beneficial in symptomatic African American patients with NYHA Class III or IV HF optimized on ACEI or ARB and beta blocker.
6. Replace ACEI or ARB with sacubitril/valsartan in patients with NYHA Class II-III symptomatic HF with reduced EF despite optimal use of a ACEI or ARB, BB, and aldosterone antagonist.
7. Avoid using non-dihydropyridine calcium channel blockers, cilostazol, NSAIDs, thiazolidinediones (e.g., rosiglitazone, pioglitazone) in HFrEF patients to prevent exacerbation of HF symptoms and hospitalizations.
8. Engage patients in appropriate care coordination, including CCHT, referring to cardiology specialists, and post-hospitalization follow-up.

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