“Billie Jean is not my Cardiologist”: How to manage the heart failure patient

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SBHPP 2024

agenda

What is heart failure?

Stages of heart failure

Cardiomyopathies

Interventions

Management

Definitions

- SGLT2i
- ARNi
- ACEi
- ARB
- MRA
- BB
- GDMT
- AHA
- ACC
- HFSA
- NPV

HFrEF (HF with reduced EF)	LVEF ≤40%
HFimpEF (HF with improved EF)	Previous LVEF ≤40% and a follow-up measurement of LVEF >40%
HFmrEF (HF with mildly reduced EF)	LVEF 41%–49% Evidence of spontaneous or provokable increased LV filling pressures (eg, elevated natriuretic peptide, noninvasive and invasive hemodynamic measurement)
HFpEF (HF with preserved EF)	LVEF ≥50% Evidence of spontaneous or provokable increased LV filling pressures (eg, elevated natriuretic peptide, noninvasive and invasive hemodynamic measurement)

ARNi

- Entresto (sacubitril/valsartan)
  - ARB and neprilysin inhibitor
  - Neprilysin = enzyme that breaks down “natriuretic peptides, bradykinin, adrenomedullin, and other vasoactive peptides”
- PARADIGM-HF
  - Prospective Comparison of ARNi with ACEi to Determine Impact on Global Mortality and Morbidity in Heart Failure
  - ARNi vs. enalapril
  - Symptomatic HFrEF patients
  - Reduced CV death or HF hospitalization by 20% (vs enalapril)
- Doses: 24/26 mg, 49/51 mg, and 97/103 mg (BID)

https://www.entresto.com/starting-entresto

SGLT2i

- DAPA-HF and EMPEROR-Reduced trials,
- SGLT2i (dapagliflozin/Farxiga) vs placebo
- Decreased CV death or HF hospitalization by ~ 25%
- Benefit regardless of +/-diabetes
- eGFR decline slower in patients with SGLT2i
- Watch for dehydration, infection

FARXIGA is a prescription medicine used:

- along with diet and exercise to improve blood sugar (glucose) control in adults with type 2 diabetes
- to reduce the risk of hospitalization for heart failure in adults with type 2 diabetes who also have known cardiovascular disease or multiple cardiovascular risk factors
- to reduce the risk of cardiovascular death, hospitalization for heart failure in adult patients with heart failure, when the heart is weak and cannot pump enough blood to the rest of your body
- to reduce the risk of further worsening of your kidney disease, end-stage kidney disease (ESKD), death due to cardiovascular disease, and hospitalization for heart failure in adults with chronic kidney disease.

https://www.farxiga.com

Classes of Recommendations nd Level of Evidence

Applying Class of Recommendations and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care (Updated May 2019)*

CLASS (STRENGTH) OF RECOMMENDATION

CLASS 1 (STRONG) — Benefit >>> Risk

Suggested phrases for writing recommendations:

- Is recommended
- Is indicated/useful/effective/beneficial
- Should be performed/administered/other
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is recommended/indicated in preference to treatment B
  - Treatment A should be chosen over treatment B

CLASS 2a (MODERATE) — Benefit >> Risk

Suggested phrases for writing recommendations:

- Is reasonable
- Can be useful/effective/beneficial
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is probably recommended/indicated in preference to treatment B
  - It is reasonable to choose treatment A over treatment B

CLASS 2b (WEAK) — Benefit > Risk

Suggested phrases for writing recommendations:

- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well established

CLASS 3: No Benefit (WEAK) — Benefit = Risk

Suggested phrases for writing recommendations:

- Is not recommended
- Is not indicated/useful/effective/beneficial
- Should not be performed/administered/other

CLASS III: Harm (STRONG) — Risk > Benefit

Suggested phrases for writing recommendations:

- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

LEVEL (QUALITY) OF EVIDENCE

LEVEL A

- High-quality evidence‡ from more than 1 RCT
- Meta-analyses of high-quality RCTs
- One or more RCTs corroborated by high-quality registry studies

LEVEL B-R (Randomized)

- Moderate-quality evidence‡ from 1 or more RCTs
- Meta-analyses of moderate-quality RCTs

LEVEL B-NR (Nonrandomized)

- Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
- Meta-analyses of such studies

LEVEL C-LD (Limited Data)

- Randomized or nonrandomized observational or registry studies with limitations of design or execution
- Meta-analyses of such studies
- Physiological or mechanistic studies in human subjects

LEVEL C-EO (Expert Opinion)

- Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

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

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR I and 2a; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

https://cpr.heart.org/en/resuscitation-science/cpr-and-ecc-guidelines/tables/applying-class-of-recommendation-and-level-of-evidence

Causes of Heart Failure

- Ischemic heart disease
  - Myocardial infarction (MI)
- Nonischemic causes
  - Hypertension
  - Valvular heart disease
  - Others (other cardiomyopathies, amyloid/sarcoid, cancer, substances, arrythmias, infection, autoimmune, hematologic, endocrine/metabolic, and more)

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Cardiomyopathy

- **Ischemic**
- **Dilated**
- **Hypertrophic**
- **Restrictive**
- Postpartum
- Takotsubo
- Others…

Clinical Assessment/History

- Congestion
- JVP
- BP
- Edema
- Orthopnea
- Family History (consider genetic testing)
- History of MI, PE , infection, etc.
- Don’t forget lifestyle factors, behavioral factors , and social determinants of health

Initial evaluation

COR	LOE	Recommendations
1	B-NR	1. For patients presenting with HF, the specific cause of HF should be explored using additional laboratory testing for appropriate management.[1–8]
1	C-EO	2. For patients who are diagnosed with HF, laboratory evaluation should include complete blood count, urinalysis, serum electrolytes, blood urea nitrogen, serum creatinine, glucose, lipid profile, liver function tests, iron studies, and thyroid-stimulating hormone to optimize management.
1	C-EO	3. For all patients presenting with HF, a 12-lead ECG should be performed at the initial encounter to optimize management.

COR	LOE	Recommendations
1	A	1. In patients presenting with dyspnea, measurement of B-type natriuretic peptide (BNP) or N-terminal prohormone of B-type natriuretic peptide (NT-proBNP) is useful to support a diagnosis or exclusion of HF.[1–12]
1	A	2. In patients with chronic HF, measurements of BNP or NT-proBNP levels are recommended for risk stratification.[11,13–29]
1	A	3. In patients hospitalized for HF, measurement of BNP or NT-proBNP levels at admission is recommended to establish prognosis.[11,13–19]
2a	B-R	4. In patients at risk of developing HF, BNP or NT-proBNP–based screening followed by team-based care, including a cardiovascular specialist, can be useful to prevent the development of LV dysfunction or new-onset HF.[30,31]
2a	B-NR	5. In patients hospitalized for HF, a predischarge BNP or NT-proBNP level can be useful to inform the trajectory of the patient and establish a postdischarge prognosis.[14,17,20–29]

COR	LOE	Recommendations
1	C-LD	1. In patients with suspected or new-onset HF, or those presenting with acute decompensated HF, chest x-ray should be performed to assess heart size and pulmonary congestion and to detect alternative cardiac, pulmonary, and other diseases that may cause or contribute to the patient's symptoms.[1,2]
1	C-LD	2. In patients with suspected or newly diagnosed HF, transthoracic echocardiography (TTE) should be performed during initial evaluation to assess cardiac structure and function.[3]
1	C-LD	3. In patients with HF who have had a significant clinical change, or who have received GDMT and are being considered for invasive procedures or device therapy, repeat measurement of EF, degree of structural remodeling, and valvular function are useful to inform therapeutic interventions.[4–7]
1	C-LD	4. In patients for whom echocardiography is inadequate, alternative imaging (eg, cardiac magnetic resonance [CMR], cardiac computed tomography [CT], radionuclide imaging) is recommended for assessment of LVEF.[8–15]
2a	B-NR	5. In patients with HF or cardiomyopathy, CMR can be useful for diagnosis or management.[16–23]
2a	B-NR	6. In patients with HF, an evaluation for possible ischemic heart disease can be useful to identify the cause and guide management.[24–27]
2b	B-NR	7. In patients with HF and coronary artery disease (CAD) who are candidates for coronary revascularization, noninvasive stress imaging (stress echocardiography, single-photon emission CT [SPECT], CMR, or positron emission tomography [PET]) may be considered for detection of myocardial ischemia to help guide coronary revascularization.[28–32]
3: No Benefit	C-EO	8. In patients with HF in the absence of: 1) clinical status change, 2) treatment interventions that might have had a significant effect on cardiac function, or 3) candidacy for invasive procedures or device therapy, routine repeat assessment of LV function is not indicated.

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Why BNP/NT-proBNP?

- BNP >100 pg/mL = acute HF with 85% accuracy
- BNP has 96% NPV if < 40 pg/mL
- NT-proBNP of 900 pg/mL ~ BNP of 100 pg/mL (age stratified better)
  - ≥450 pg/mL and age <50 years
  - ≥900 pg/mL and age 50-75 years
  - ≥1800 pg/mL and age >75 years
- NT-proBNP:
  - 96% NPV if < 50 pg/mL and age <50
  - 96% NPV if < 75 pg/mL and age 50-75
  - 96% NPV if < 250 pg/mL and age >75
- BNP/NT-proBNP diagnose HF if high and exclude HF if very low

1.Maisel AS, Krishnaswamy P, Nowak RM, et al. Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. *N Engl J Med* 2002;347:161-7
2.Januzzi JL, Jr., Camargo CA, Anwaruddin S, et al. The N-terminal Pro-BNP. Investigation of Dyspnea in the Emergency department (PRIDE) study. *Am J Cardiol* 2005;95:948-54.

Do they need a CardioMEMs?

- Unclear in NYHA III…

COR	LOE	Recommendation
2b	B-R	1. In selected adult patients with NYHA class III HF and history of a HF hospitalization in the past year or elevated natriuretic peptide levels, on maximally tolerated stable doses of GDMT with optimal device therapy, the usefulness of wireless monitoring of PA pressure by an implanted hemodynamic monitor to reduce the risk of subsequent HF hospitalizations is uncertain.[1–4]
Value Statement: Uncertain Value (B-NR)		2. In patients with NYHA class III HF with a HF hospitalization within the previous year, wireless monitoring of the PA pressure by an implanted hemodynamic monitor provides uncertain value.[4–7]

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What about salt and fluid?

- One study showed that sodium restriction improved NYHA class and leg edema in patients with HFrEF, another study showed sodium restriction associated with worse all-cause mortality in patients with HFrEF, and other showed no impact
- More trials are needed

COR	LOE	Recommendation
2a	C-LD	1. For patients with stage C HF, avoiding excessive sodium intake is reasonable to reduce congestive symptoms.[1–6]

COR	LOE	Recommendations
1	B-NR	1. In patients with HF who have fluid retention, diuretics are recommended to relieve congestion, improve symptoms, and prevent worsening HF.[1–5]
1	B-NR	2. For patients with HF and congestive symptoms, addition of a thiazide (eg, metolazone) to treatment with a loop diuretic should be reserved for patients who do not respond to moderate- or high-dose loop diuretics to minimize electrolyte abnormalities.[6]

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Diuretic Guidance

COR	LOE	Recommendations
1	B-NR	1. In patients with HF who have fluid retention, diuretics are recommended to relieve congestion, improve symptoms, and prevent worsening HF.[1–5]
1	B-NR	2. For patients with HF and congestive symptoms, addition of a thiazide (eg, metolazone) to treatment with a loop diuretic should be reserved for patients who do not respond to moderate- or high-dose loop diuretics to minimize electrolyte abnormalities.[6]

Table 12. Commonly Used Oral Diuretics in Treatment of Congestion for Chronic HF

Drug	Initial Daily Dose	Maximum Total Daily Dose	Duration of Action
Loop diuretics			
Bumetanide	0.5–1.0 mg once or twice	10 mg	4–6 h
Furosemide	20–40 mg once or twice	600 mg	6–8 h
Torsemide	10–20 mg once	200 mg	12–16 h
Thiazide diuretics			
Chlorthiazide	250–500 mg once or twice	1000 mg	6–12 h
Chlorthalidone	12.5–25 mg once	100 mg	24–72 h
Hydrochlorothiazide	25 mg once or twice	200 mg	6–12 h
Indapamide	2.5 mg once	5 mg	36 h
Metolazone	2.5 mg once	20 mg	12–24 h

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Is exercise OK?

- Reduces mortality, hospitalizations

COR	LOE	Recommendations
1	A	1. For patients with HF who are able to participate, exercise training (or regular physical activity) is recommended to improve functional status, exercise performance, and QOL.[1–9]
2a	B-NR	2. In patients with HF, a cardiac rehabilitation program can be useful to improve functional capacity, exercise tolerance, and health-related QOL.[1,2,5,6,8]

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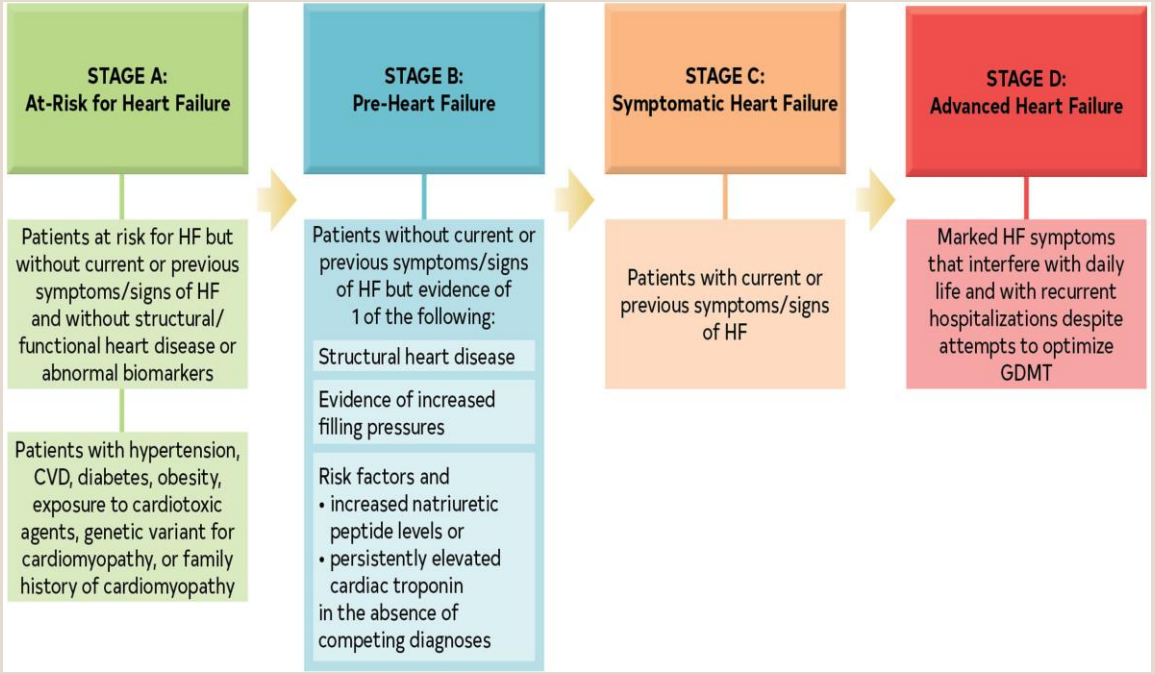
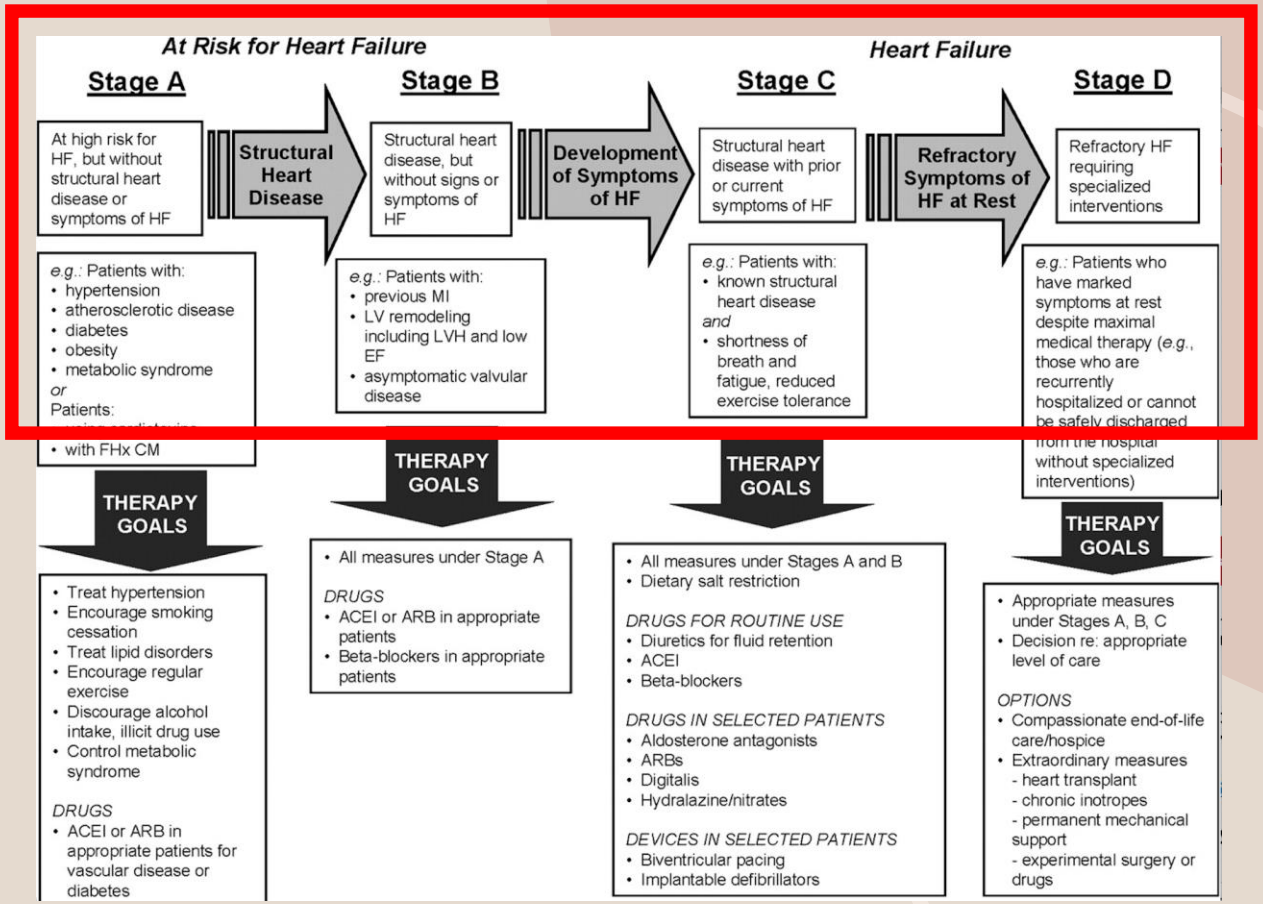
Stages of Heart Failure (2022, 2006)





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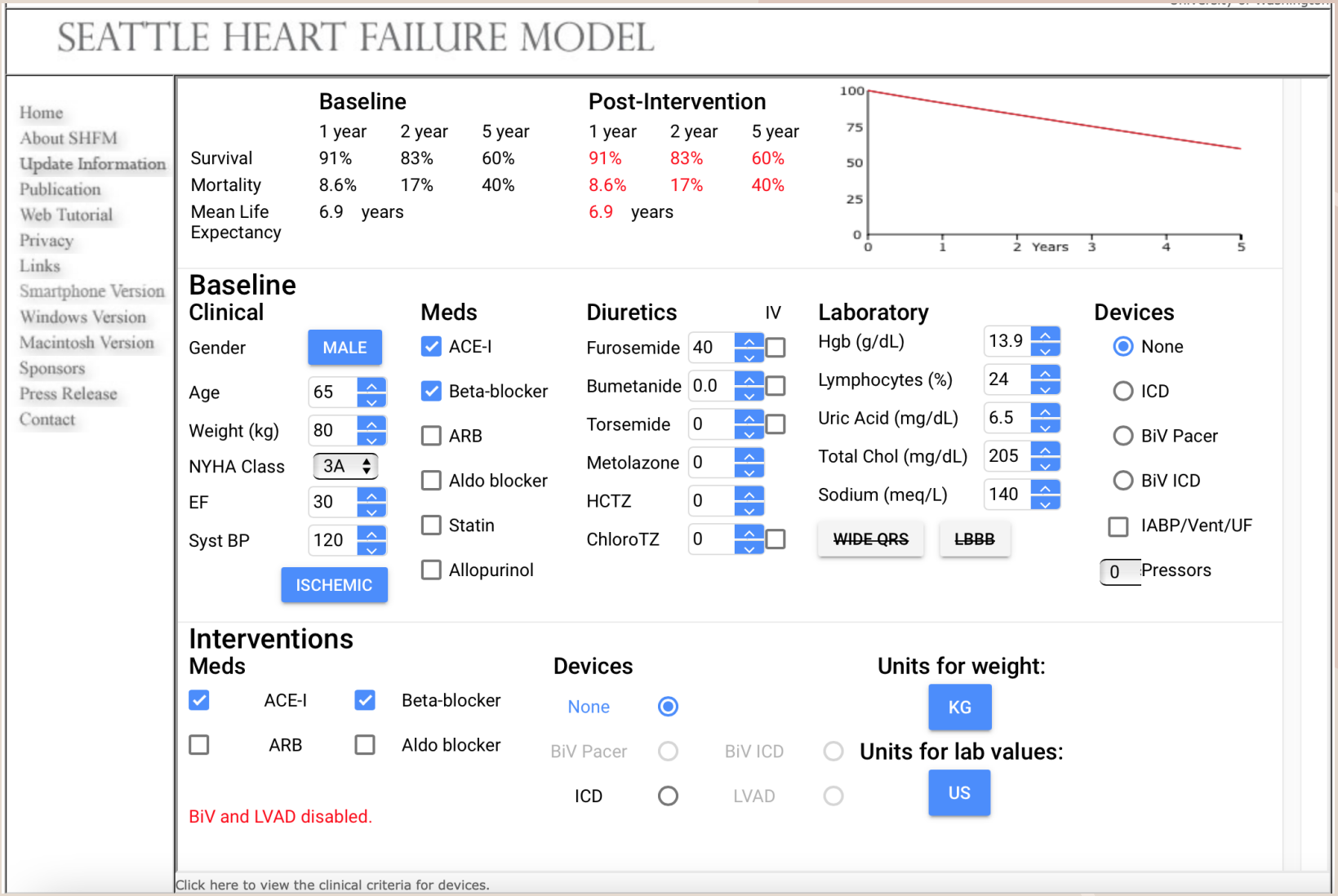
NYHA classes

- I : comfortable at rest, no HF symptoms with ordinary physical activity
- II : comfortable at rest, HF symptoms (dyspnea, fatigue, lightheadedness) with ordinary activity
- III : comfortable at rest, HF symptoms with less than ordinary activity
- IV : symptoms at rest, unable to do physical and have symptoms at rest

Risk Scores

- Consider using for prognostication
- Refer to 2022 AHA/ACC/HFSA guidelines for links
- Example:
  - Seattle Heart Failure Model
  - https://depts.washington.edu/shfm/?width=1440&height=900
  - Be aware of limitations (ex: no option for ARNi, SGLT2i, LVAD, etc.)



2022 AHA/ACC/ HFSA guidelines

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

Paul A. Heidenreich, Biykem Bozkurt, David Aguilar, Larry A. Allen, Joni J. Byun, Monica M. Colvin, Anita Deswal, Mark H. Drazner, Shannon M. Dunlay, Linda R. Evers, James C. Fang, Savitri E. Fedson, Gregg C. Fonarow, Salim S. Hayek, Adrian F. Hernandez, Prateeti Khazanie, Michelle M. Kittleson, Christopher S. Lee, Mark S. Link, Carmelo A. Milano, Lorraine C. Nnacheta, Alexander T. Sandhu, Lynne Warner Stevenson, Orly Vardeny, Amanda R. Vest and **Clyde W. Yancy** **See fewer authors**

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Stage A

Stage A: At Risk for HF	At risk for HF but without symptoms, structural heart disease, or cardiac biomarkers of stretch or injury (eg, patients with hypertension, atherosclerotic CVD, diabetes, metabolic syndrome and obesity, exposure to cardiotoxic agents, genetic variant for cardiomyopathy, or positive family history of cardiomyopathy).
	No symptoms or signs of HF and evidence of 1 of the following:
	*Structural heart disease** Reduced left or right ventricular systolic function Reduced ejection fraction, reduced strain Ventricular hypertrophy Chamber enlargement Wall motion abnormalities Valvular heart disease

COR	LOE	Recommendations
1	A	1. In patients with hypertension, blood pressure should be controlled in accordance with GDMT for hypertension to prevent symptomatic HF.[1–9]
1	A	2. In patients with type 2 diabetes and either established CVD or at high cardiovascular risk, SGLT2i should be used to prevent hospitalizations for HF.[10–12]
1	B-NR	3. In the general population, healthy lifestyle habits such as regular physical activity, maintaining normal weight, healthy dietary patterns, and avoiding smoking are helpful to reduce future risk of HF.[13–21]
2a	B-R	4. For patients at risk of developing HF, natriuretic peptide biomarker–based screening followed by team-based care, including a cardiovascular specialist optimizing GDMT, can be useful to prevent the development of LV dysfunction (systolic or diastolic) or new-onset HF.[22,23]
2a	B-NR	5. In the general population, validated multivariable risk scores can be useful to estimate subsequent risk of incident HF.[24–26]

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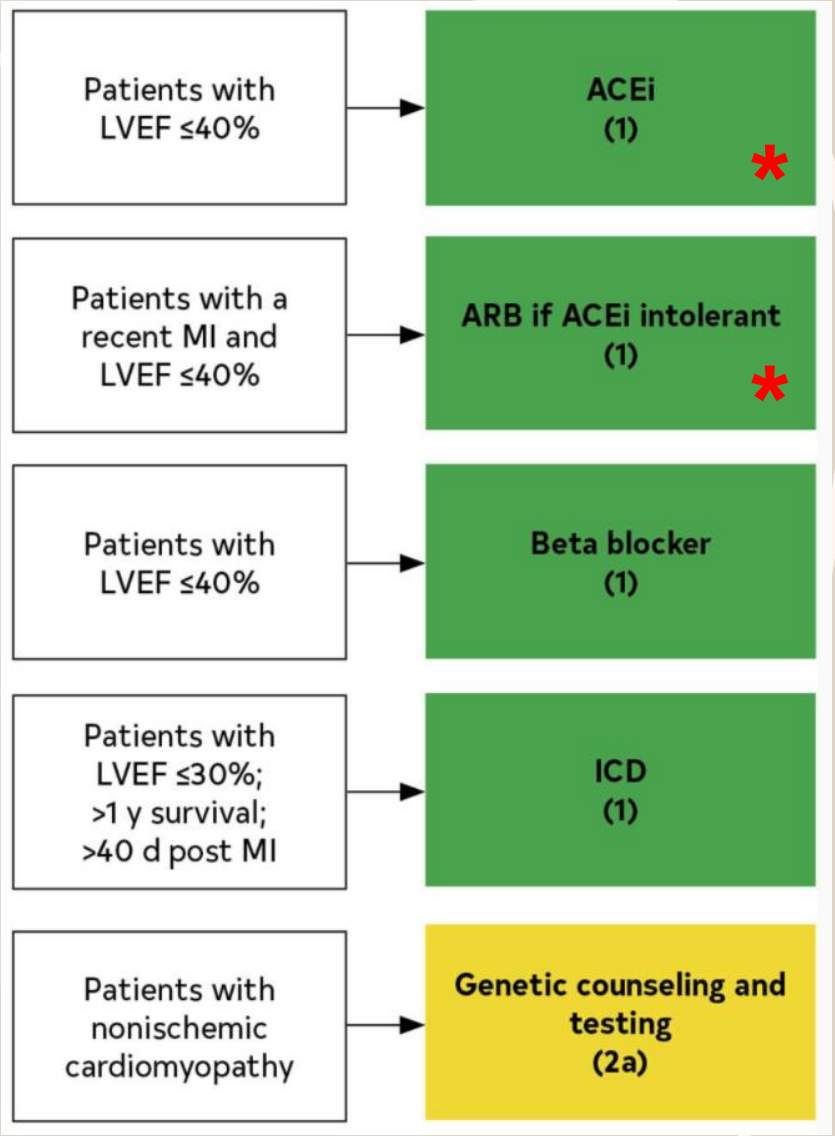
Stage B

*Evidence for increased filling pressures**
By invasive hemodynamic measurements
By noninvasive imaging suggesting elevated filling pressures (eg, Doppler echocardiography)

Patients with risk factors and
*Increased levels of BNPs*or*
Persistently elevated cardiac troponin in the absence of competing diagnoses resulting in such biomarker elevations such as acute coronary syndrome, CKD, pulmonary embolus, or myopericarditis

COR	LOE	Recommendations
1	A	1. In patients with LVEF ≤40%, ACEi should be used to prevent symptomatic HF and reduce mortality.[1–4]
1	A	2. In patients with a recent or remote history of MI or ACS, statins should be used to prevent symptomatic HF and adverse cardiovascular events.[5–9]
1	B-R	3. In patients with a recent MI and LVEF ≤40% who are intolerant to ACEi, ARB should be used to prevent symptomatic HF and reduce mortality.[10]
1	B-R	4. In patients with a recent or remote history of MI or acute coronary syndrome (ACS) and LVEF ≤40%, evidence-based beta blockers should be used to reduce mortality.[11–13]
1	B-R	5. In patients who are at least 40 days post-MI with LVEF ≤30% and NYHA class I symptoms while receiving GDMT and have reasonable expectation of meaningful survival for >1 year, an ICD is recommended for primary prevention of sudden cardiac death (SCD) to reduce total mortality.[14]
1	C-LD	6. In patients with LVEF ≤40%, beta blockers should be used to prevent symptomatic HF.[12,13]
3: Harm	B-R	7. In patients with LVEF <50%, thiazolidinediones should not be used because they increase the risk of HF, including hospitalizations.[15]
3: Harm	C-LD	8. In patients with LVEF <50%, nondihydropyridine calcium channel blockers with negative inotropic effects may be harmful.[16,17]



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When possible, consider ARNi over ACEi/ARB

COR	LOE	Recommendations
1	A	1. In patients with HFrEF and NYHA class II to III symptoms, the use of ARNi is recommended to reduce morbidity and mortality.[1-5]
1	A	2. In patients with previous or current symptoms of chronic HFrEF, the use of ACEi is beneficial to reduce morbidity and mortality when the use of ARNi is not feasible.[6-13]
1	A	3. In patients with previous or current symptoms of chronic HFrEF who are intolerant to ACEi because of cough or angioedema and when the use of ARNi is not feasible, the use of ARB is recommended to reduce morbidity and mortality.[14-18]
Value Statement: High Value (A)		4. In patients with previous or current symptoms of chronic HFrEF, in whom ARNi is not feasible, treatment with an ACEi or ARB provides high economic value.[19-25]
1	B-R	5. In patients with chronic symptomatic HFrEF NYHA class II or III who tolerate an ACEi or ARB, replacement by an ARNi is recommended to further reduce morbidity and mortality.[1-5]
Value Statement: High Value (A)		6. In patients with chronic symptomatic HFrEF, treatment with an ARNi instead of an ACEi provides high economic value.[26-29]
3: Harm	B-R	7. ARNi should not be administered concomitantly with ACEi or within 36 hours of the last dose of an ACEi.[30,31]
3: Harm	C-LD	8. ARNi should not be administered to patients with any history of angioedema.[32-35]
3: Harm	C-LD	9. ACEi should not be administered to patients with any history of angioedema.[36-39]

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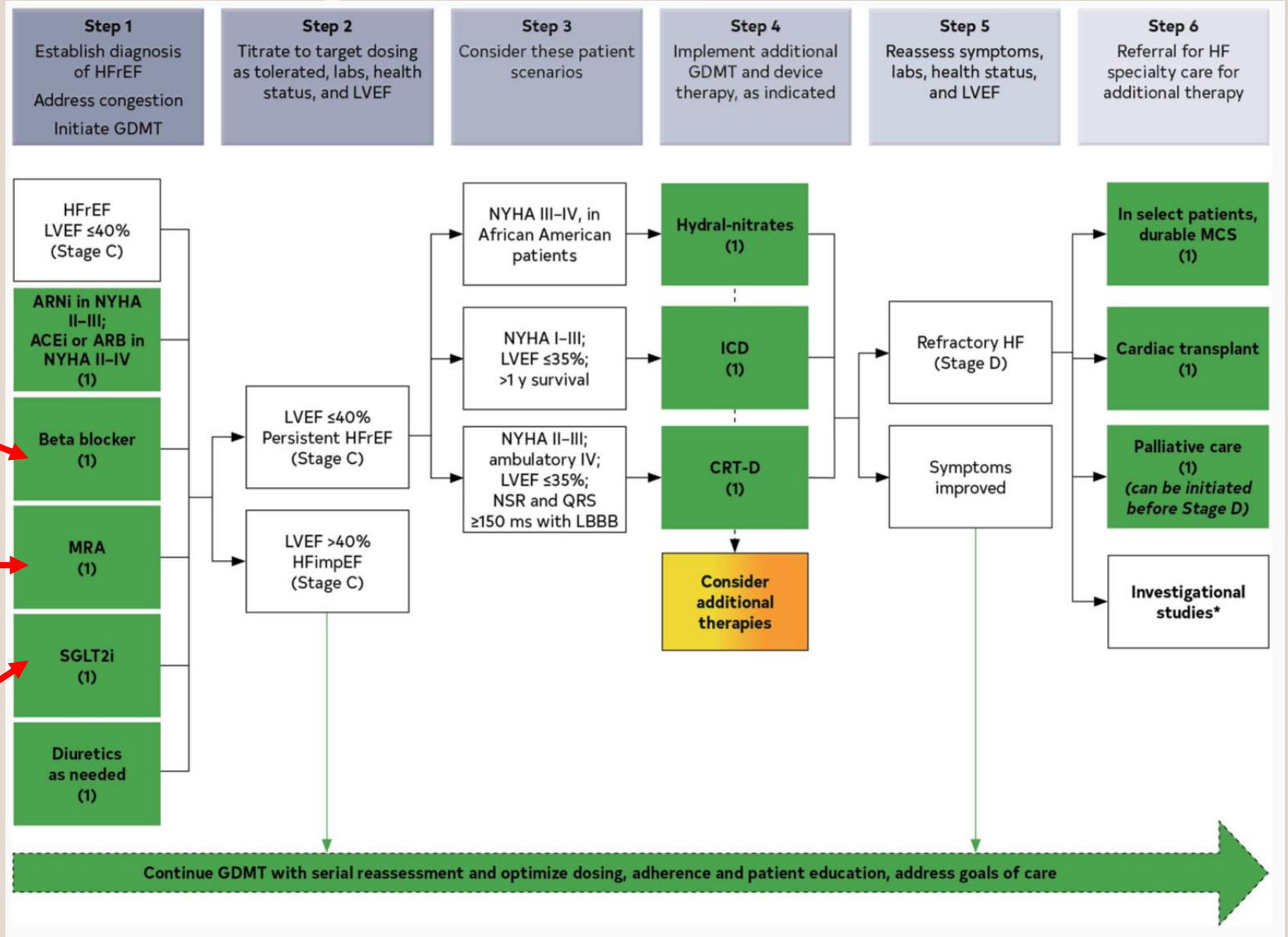
Stage C

Structural heart disease with current or previous symptoms of HF.

In patients with HFrEF, with current or previous symptoms, use of 1 of the 3 beta blockers proven to reduce mortality (eg, bisoprolol, carvedilol, sustained-release metoprolol succinate) is recommended to reduce mortality and hospitalizations.[1-3]

In patients with HFrEF and NYHA class II to IV symptoms, an MRA (spironolactone or eplerenone) is recommended to reduce morbidity and mortality, if eGFR is >30 mL/min/1.73 m² and serum potassium is <5.0 mEq/L. Careful monitoring of potassium, renal function, and diuretic dosing should be performed at initiation and closely monitored thereafter to minimize risk of hyperkalemia and renal insufficiency.[1-3]

In patients with symptomatic chronic HFrEF, SGLT2i are recommended to reduce hospitalization for HF and cardiovascular mortality, irrespective of the presence of type 2 diabetes.[1,2]



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Best Practices

COR	LOE	Recommendations
1	A	1. For patients self-identified as African American with NYHA class III-IV HFrEF who are receiving optimal medical therapy, the combination of hydralazine and isosorbide dinitrate is recommended to improve symptoms and reduce morbidity and mortality.[1,2]
Value Statement: High Value (B-NR)		2. For patients self-identified as African American with NYHA class III to IV HFrEF who are receiving optimal medical therapy with ACEi or ARB, beta blockers, and MRA, the combination of hydralazine and isosorbide dinitrate provides high economic value.[3]
2b	C-LD	3. In patients with current or previous symptomatic HFrEF who cannot be given first-line agents, such as ARNi, ACEi, or ARB, because of drug intolerance or renal insufficiency, a combination of hydralazine and isosorbide dinitrate might be considered to reduce morbidity and mortality.[4,5]

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Stage C HFrEF Drugs

- ACEi
- ARB
- ARNi
- SGLT2i
- BB
- MRA
- Others

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Stage C HFrEF Drug Dosing: ACEi

Drug	Initial Daily Dose(s)	Target Doses(s)	Mean Doses Achieved in Clinical Trials
ACEi			
Captopril	6.25 mg 3 times daily	50 mg 3 times daily	122.7 mg total daily
Enalapril	2.5 mg twice daily	10–20 mg twice daily	16.6 mg total daily
Fosinopril	5–10 mg once daily	40 mg once daily	NA
Lisinopril	2.5–5 mg once daily	20–40 mg once daily	32.5–35.0 mg total daily
Perindopril	2 mg once daily	8–16 mg once daily	NA
Quinapril	5 mg twice daily	20 mg twice daily	NA
Ramipril	1.25–2.5 mg once daily	10 mg once daily	NA
Trandolapril	1 mg once daily	4 mg once daily	NA

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Stage C HFrEF Drug Dosing: ARB

Drug	Initial Daily Dose(s)	Target Doses(s)	Mean Doses Achieved in Clinical Trials
ARB			
Candesartan	4–8 mg once daily	32 mg once daily	24 mg total daily
Losartan	25–50 mg once daily	50–150 mg once daily	129 mg total daily
Valsartan	20–40 mg once daily	160 mg twice daily	254 mg total daily

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Stage C HFrEF Drug Dosing: ARNi, SGLT2i

Drug	Initial Daily Dose(s)	Target Doses(s)	Mean Doses Achieved in Clinical Trials
ARNi			
Sacubitril-valsartan	49 mg sacubitril and 51 mg valsartan twice daily (therapy may be initiated at 24 mg sacubitril and 26 mg valsartan twice daily)	97 mg sacubitril and 103 mg valsartan twice daily	182 mg sacubitril and 193 mg valsartan total daily
SGLT2i			
Dapagliflozin	10 mg once daily	10 mg once daily	9.8 mg total daily
Empagliflozin	10 mg once daily	10 mg once daily	NR

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Stage C HFrEF Drug Dosing: BB

Drug	Initial Daily Dose(s)	Target Doses(s)	Mean Doses Achieved in Clinical Trials
Beta blockers			
Bisoprolol	1.25 mg once daily	10 mg once daily	8.6 mg total daily
Carvedilol	3.125 mg twice daily	25–50 mg twice daily	37 mg total daily
Carvedilol CR	10 mg once daily	80 mg once daily	NA
Metoprolol succinate extended release (metoprolol CR/XL)	12.5–25 mg once daily	200 mg once daily	159 mg total daily

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Stage C HFrEF Drug Dosing: MRA

Drug	Initial Daily Dose(s)	Target Doses(s)	Mean Doses Achieved in Clinical Trials
Mineralocorticoid receptor antagonists			
Spironolactone	12.5–25 mg once daily	25–50 mg once daily	26 mg total daily
Eplerenone	25 mg once daily	50 mg once daily	42.6 mg total daily

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Stage C HFrEF Drug Dosing: Others

Drug	Initial Daily Dose(s)	Target Doses(s)	Mean Doses Achieved in Clinical Trials
Isosorbide dinitrate and hydralazine			
Fixed dose combination	20 mg isosorbide dinitrate and 37.5 mg hydralazine 3 times daily	40 mg isosorbide dinitrate and 75 mg hydralazine 3 times daily	90 mg isosorbide dinitrate and ~175 mg hydralazine total daily
Isosorbide dinitrate and hydralazine	20–30 mg isosorbide dinitrate and 25–50 mg hydralazine 3–4 times daily	120 mg isosorbide dinitrate total daily in divided doses and 300 mg hydralazine total daily in divided doses	NA

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Lab monitoring

- ACEi/ARB/ARNi: metabolic panel 1-2 weeks after initiation, then every 6 months
- SGLT2i- metabolic panel 1-2 weeks after initiation, then every 6 months
- BB- no lab monitoring (NOTE: ensure adequate HR to utilize)
- MRA- metabolic panel should be performed according to clinical status, approximately 1 week, then 4 weeks, then every 6 months
- Isosorbide/Hydralazine – no lab monitoring

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Stage D

Stage D: Advanced HF	Marked HF symptoms that interfere with daily life and with recurrent hospitalizations despite attempts to optimize GDMT.

- Refer to heart failure specialist
- Patients may develop refractory HF, have recurrent HF hospitalizations, and may benefit from advanced therapies
  - LVAD
  - Transplant
  - Inotropes
- Think I NEED HELP

I, Intravenous inotropes

N, New York Heart Association (NYHA) class IIIB to IV or persistently elevated natriuretic peptides

E, End-organ dysfunction

E, EF ≤35%

D, Defibrillator shocks

H, Hospitalizations >1

E, Edema despite escalating diuretics

L, Low systolic BP ≤90, high heart rate

P, Prognostic medication; progressive intolerance or down-titration of GDMT

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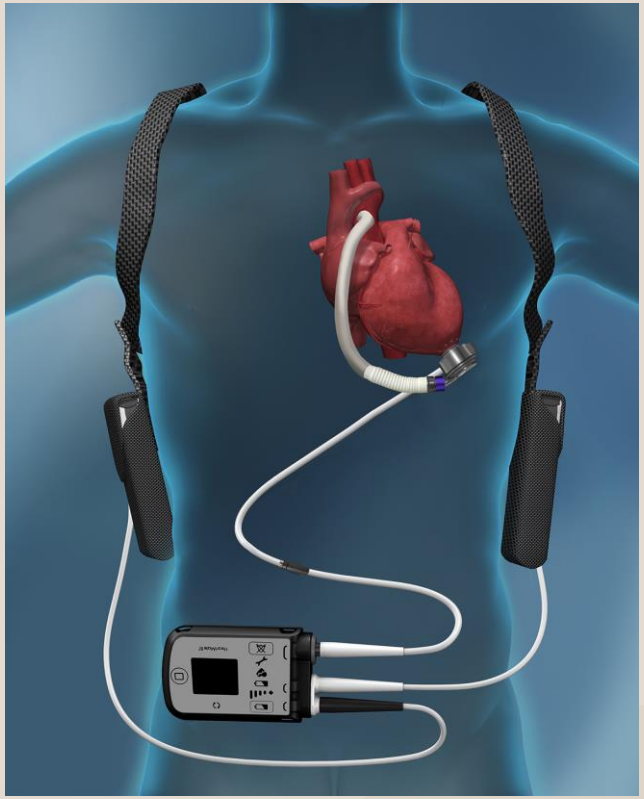
Left Ventricular Assist Device (LVAD)



- https://www.youtube.com/watch?v=T37WrT-lDhQ

What about HFmrEF and HFpEF?

- Recommendations less strong regarding GDMT medications
- They may still help (important to manage BP)
- Diuretics are highly recommended

AHA/ACC/HFSA “Top Take-Home Messages”

- HFrEF: GDMT includes 4 medication classes (now SGLT2i)
- HFrEF with improvement should continue treatment
- HFmrEF: SGLT2i (2a), ARNi, ACEi, ARB, MRA, and BB (2b)
- HFpEF: SGLT2i (2a), MRAs (2b), ARBs and ARNi (2b).
- HFpEF recommendations: treat hypertension (1), treat afib (2a), avoid routine use of nitrates or PDE5i (3: no benefit)
- Primary prevention is important for stage A and B.

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thank you

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