



# An Introduction to Heart Failure

Tushak Heart Failure



# Disclosures

- Paid advisory board member for Pfizer
- Paid advisory board member and speaker for Alnylam
- Paid advisory board and speaker for AstraZeneca
- Paid speaker for BridgeBio



# Agenda

- What is heart failure
- What are the signs and symptoms
- What are the types of heart failure
- Diagnostic tools
- Treatment Modalities
- Advanced heart failure and when to refer



# What is Heart Failure?

- Most basic terms: the heart is not pumping blood like it should



# What is Heart Failure?

- Causes:
  - Ischemia
  - Chemotherapy and other cardiotoxic medications
  - Rheumatologic or autoimmune conditions
  - Endocrine/metabolic (thyroid, pheo, DM, obesity, acromegaly)
  - Familial/inherited/genetic heart disease
  - Arrhythmia
  - Hypertension
  - Infiltrative (amyloid, sarcoid, hemochromatosis)
  - Myocarditis (infectious, toxin, or medication, immunologic, hypersensitivity)
  - Peripartum
  - Stress cardiomyopathy (Takotsubo)
  - Illicit substance use (alcohol, cocaine, methamphetamine)



# Signs and Symptoms of Heart Failure

- Decreased exercise capacity/easy fatiguability
- Edema
- Abdominal bloating and/or lack of appetite
- Orthopnea
- PND
- Tachycardia and hypotension



# Types of Heart Failure: terms

- Systolic/reduced ejection fraction
- Midrange ejection fraction
- Diastolic/preserved ejection fraction
- Restrictive cardiomyopathy



# Types of Heart Failure

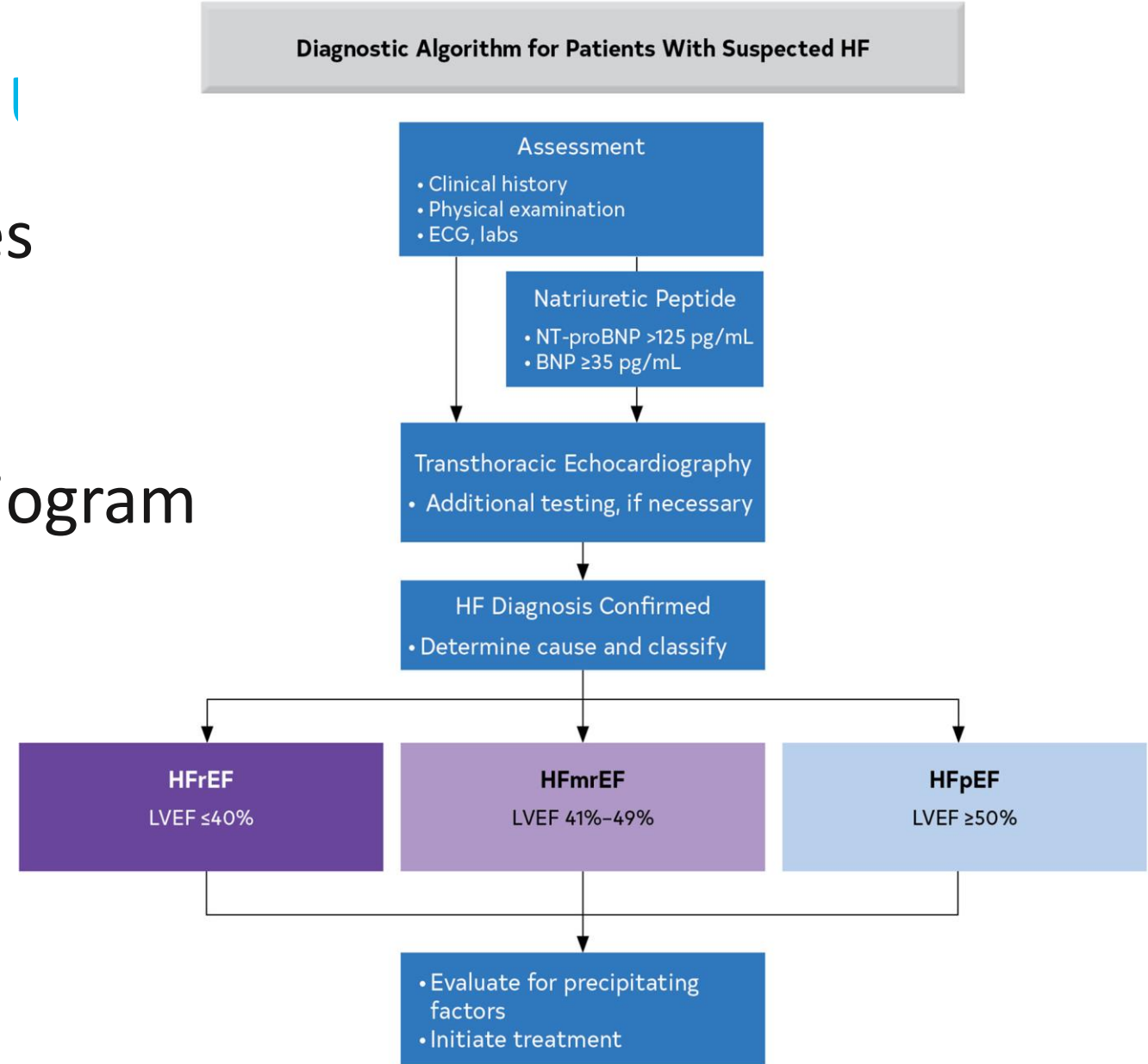
| Type   | Finding  |
|--------|--|
| HFrEF  | LVEF $\leq$ 40%  |
| HFmrEF | LVEF 41-49%  |
| HFpEF  | LVEF $\geq$ 50% but evidence of increased LV filling pressures |





# Types of Heart Failure

- Initial diagnostic modalities
  - EKG
  - Lab testing
  - Transthoracic echocardiogram



# Types of Heart Failure

- Additional initial testing

| 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. <sup>1-8</sup>   |
| 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.   |



# Reduced/midrange Heart Failure



# Reduced/midrange Heart Failure

| Type   | Finding         |
|--------|-----------------|
| HFrEF  | LVEF $\leq$ 40% |
| HFmrEF | LVEF 41-49%     |



# Reduced/midrange Heart Failure

- Causes: ischemic vs. nonischemic



# Reduced/midrange Heart Failure

- Ischemic evaluation
  - Noninvasive
    - Stress testing
    - Coronary CTA
  - Invasive
    - Left heart catheterization and diagnostic angiography



# Reduced/midrange Heart Failure

- Additional testing
  - CMR
  - Cardiac monitor
  - Other specific testing
  - Genetic testing



# Reduced/midrange Heart Failure

- Treatment





# Reduced/midrange Heart Failure

- Treatment
  - NYHA class
  - AHA class



# Reduced/midrange Heart Failure

- NYHA class
  - I: no limitations in active
  - II: dyspnea with ordinary activity
  - III: dyspnea with less than ordinary activity
  - IV: dyspnea at rest



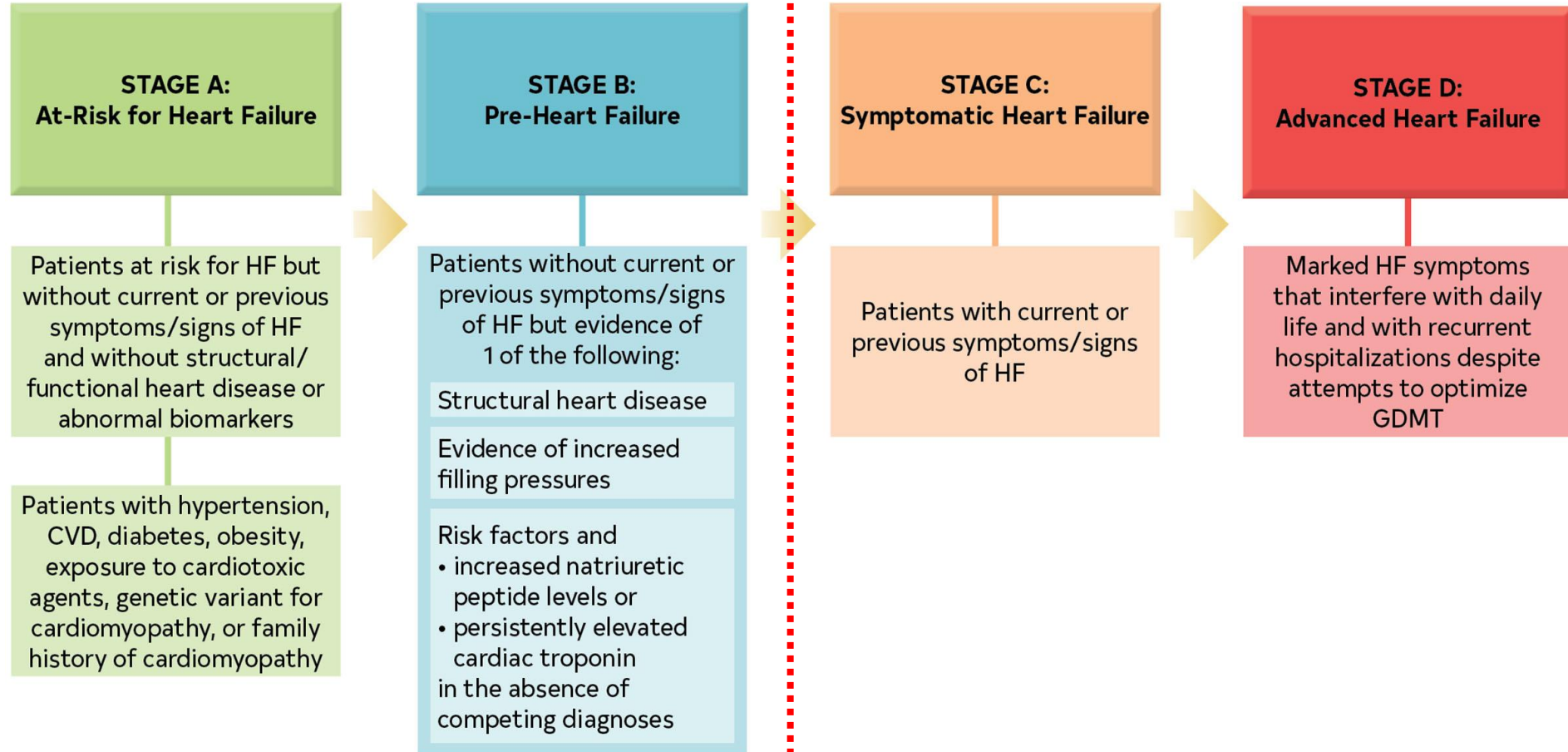
# Reduced/midrange Heart Failure

- AHA class
  - A
  - B
  - C
  - D



# Reduced/midrange Heart Failure

- AHA class

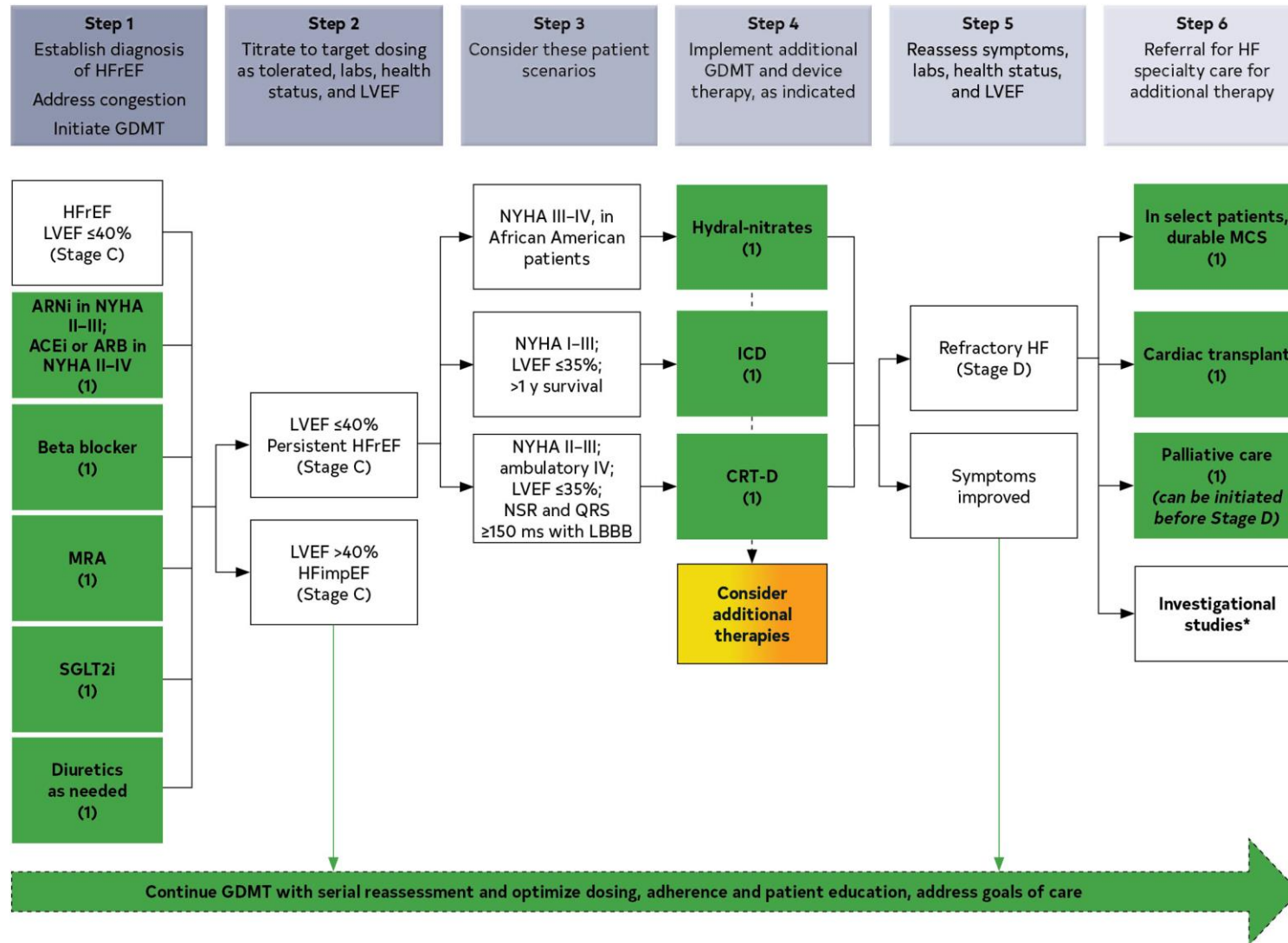


# Reduced Heart Failure

- Treatment



# Reduced Heart Failure



# Reduced Heart Failure

- Medications
  - Goal directed medical therapy: mortality benefit
    - 1<sup>st</sup> tier: Beta blockers, RAAS blockade, mineralocorticoid antagonists, SGLT2 inhibitors
    - 2<sup>nd</sup> tier: Hydralazine and nitrate combination
  - Supportive care: symptom management without mortality benefit



# Reduced Heart Failure

- Beta blockade
  - Selective: Bisoprolol, Toprol XL
  - Nonselective: Coreg
  - Indicated for AHA B or greater
  - Target HR goal 70-80 BPM
  - Coreg preferred over others in DM
  - Depression: possibly avoid Coreg

| COR                                | LOE | Recommendation  |
|------------------------------------|-----|---|
| 1                                  | A   | 1. 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. <sup>1-3</sup> |
| Value Statement:<br>High Value (A) |     | 2. In patients with HFrEF, with current or previous symptoms, beta-blocker therapy provides high economic value. <sup>4-8</sup>   |





# Reduced Heart Failure

- RAAS blockade
  - ACEi, ARBs, ARNIs
  - Indicated for AHA B or greater
  - Avoid if eGFR  $\leq 30$  mL/min/1.73 m<sup>2</sup>

| 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. <sup>1-5</sup>   |
| 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. <sup>6-13</sup>  |
| 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. <sup>14-18</sup> |
| Value Statement:<br>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. <sup>19-25</sup>   |



# Reduced Heart Failure

- RAAS blockade
  - ARNI: PARADIGM-HF significantly reduced the composite endpoint of cardiovascular death or HF hospitalization by 20% relative to enalapril.

|                                    |     |   |
|------------------------------------|-----|---|
| 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. <sup>1-5</sup> |
| Value Statement:<br>High Value (A) |     | 6. In patients with chronic symptomatic HFrEF, treatment with an ARNi instead of an ACEi provides high economic value. <sup>26-29</sup>   |



# Reduced Heart Failure

- RAAS blockade
  - Converting ACEi to ARNI
  - History of angioedema
  - Wary if  $\geq 30\%$  acute increase in serum creatinine
  - Hyperkalemia  $\geq 5.6$  mEq/L

|         |      |   |
|---------|------|---|
| 3: Harm | B-R  | 7. ARNi should not be administered concomitantly with ACEi or within 36 hours of the last dose of an ACEi. <sup>30,31</sup> |
| 3: Harm | C-LD | 8. ARNi should not be administered to patients with any history of angioedema. <sup>32-35</sup>                             |
| 3: Harm | C-LD | 9. ACEi should not be administered to patients with any history of angioedema. <sup>36-39</sup>                             |



# Reduced Heart Failure

- Mineralocorticoid antagonists
  - Spironolactone and Eplerenone
  - Indication for AHA C NYHA II-IV
  - Close monitoring if renal dysfunction or hyperkalemia.
  - Avoid if  $\text{eGFR} \leq 30 \text{ mL/min/1.73 m}^2$  or serum potassium  $\geq 5.0 \text{ mEq/L}$
  - Stop if potassium  $> 5.5 \text{ mEq/L}$

| COR                                | LOE  | Recommendations   |
|------------------------------------|------|---|
| 1                                  | A    | 1. 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 $>30 \text{ mL/min/1.73 m}^2$ and serum potassium is $<5.0 \text{ mEq/L}$ . 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. <sup>1-3</sup> |
| Value Statement:<br>High Value (A) |      | 2. In patients with HFrEF and NYHA class II to IV symptoms, MRA therapy provides high economic value. <sup>4-7</sup>  |
| 3: Harm                            | B-NR | 3. In patients taking MRA whose serum potassium cannot be maintained at $<5.5 \text{ mEq/L}$ , MRA should be discontinued to avoid life-threatening hyperkalemia. <sup>8,9</sup>  |



# Reduced Heart Failure

- SGLT2 inhibitors
  - Dapagliflozin, Empagliflozin, ~~Canagliflozin~~
  - Avoid if eGFR  $\leq 30$  mL/min/1.73 m<sup>2</sup>
    - 20? 15? mL/min/1.73

| COR   | LOE | Recommendation   |
|---|-----|--|
| 1   | A   | 1. 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. <sup>1,2</sup> |
| Value Statement:<br>Intermediate Value<br>(A) |     | 2. In patients with symptomatic chronic HFrEF, SGLT2i therapy provides intermediate economic value. <sup>3,4</sup>   |



# Reduced Heart Failure

- Hydralazine and nitrate
- Indication
  - AHA C NYHA III-IV in addition to optimal GDMT
    - Primary benefit is in African-Americans
  - Intolerant of RAAS blockade

| 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. <sup>1,2</sup>                                    |
| Value Statement:<br>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. <sup>3</sup>                                   |
| 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. <sup>4,5</sup> |



# Reduced Heart Failure

- Why treat?



# Reduced Heart Failure

- Why treat?

| Evidence-Based Therapy                | Relative Risk Reduction in All-Cause Mortality, % | NNT to Prevent All-Cause Mortality Over Time* | NNT for All-Cause Mortality (Standardized to 12 mo) | NNT for All- Cause Mortality (Standardized to 36 mo) |
|---------------------------------------|---|---|---|--|
| ACEi or ARB                           | 17  | 22 over 42 mo                                 | 77  | 26   |
| ARNi <sup>†</sup>                     | 16  | 36 over 27 mo                                 | 80  | 27   |
| Beta blocker                          | 34  | 28 over 12 mo                                 | 28  | 9  |
| Mineralocorticoid receptor antagonist | 30  | 9 over 24 mo                                  | 18  | 6  |
| SGLT2i                                | 17  | 43 over 18 mo                                 | 63  | 22   |
| Hydralazine or nitrate‡               | 43  | 25 over 10 mo                                 | 21  | 7  |





# Reduced Heart Failure

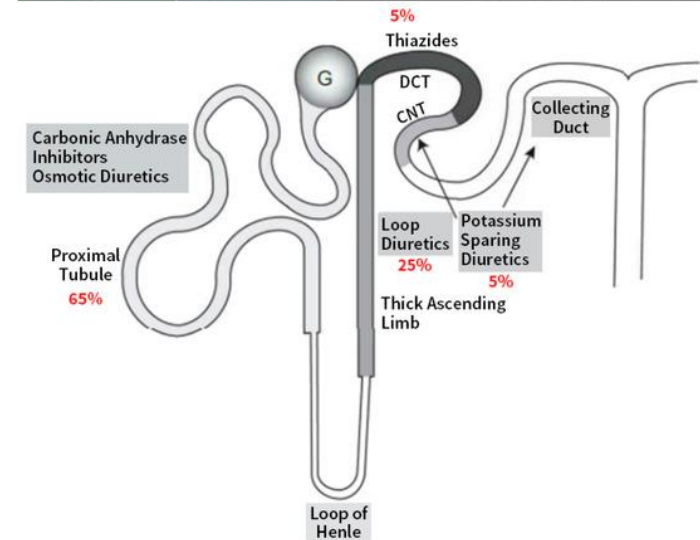
- Other supportive care:
  - Diuretics
  - Ivabradine
  - Vericiguat
  - Digoxin



# Reduced Heart Failure

- Diuretics
  - Loop diuretics: Lasix, Bumex, Torsemide
  - Thiazide diuretics: Metolazone, Chlorothiazide, HCTZ, Chlorthalidone
  - Daily weights in the AM. If the weight increases by more than 3 lbs from baseline dry weight, take an extra dose of diuretic.

| 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. <sup>1-5</sup>   |
| 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. <sup>6</sup> |



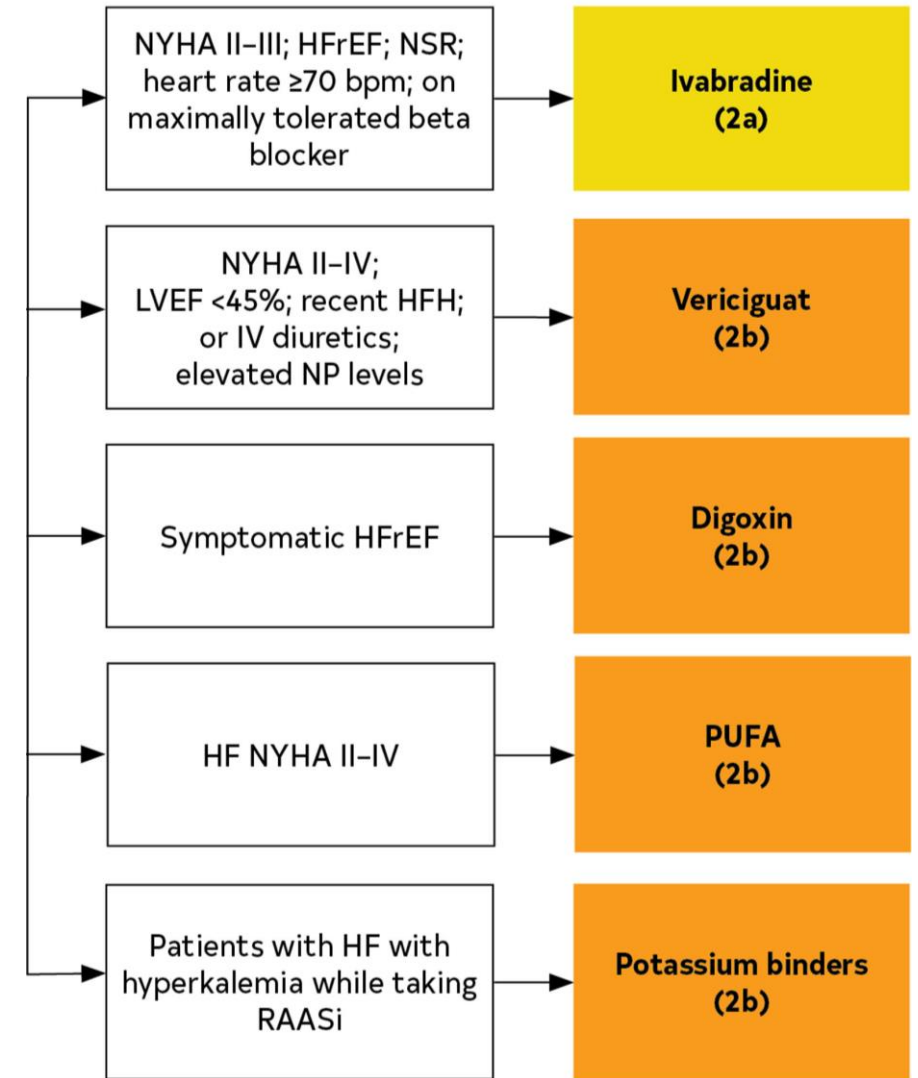
# Reduced Heart Failure

| Drug                      | Initial Daily Dose | Max. Daily Dose | Duration of Action |
|---------------------------|--------------------|-----------------|--------------------|
| <b>Loop diuretics</b>     |                    |                 |                    |
| Bumetanide                | 0.5–1.0 mg 1-2x/d  | 10 mg           | 4–6 h              |
| Furosemide                | 20–40 mg 1-2x/d    | 600 mg          | 6–8 h              |
| Torsemide                 | 10–20 mg 1x/d      | 200 mg          | 12–16 h            |
| <b>Thiazide diuretics</b> |                    |                 |                    |
| Chlorthiazide             | 250–500 mg 1-2x/d  | 1000 mg         | 6–12 h             |
| Chlorthalidone            | 12.5–25 mg 1x/d    | 100 mg          | 24–72 h            |
| Hydrochlorothiazide       | 25 mg 1-2x/d       | 200 mg          | 6–12 h             |
| Indapamide                | 2.5 mg once        | 5 mg            | 36 h               |
| Metolazone                | 2.5 mg once        | 20 mg           | 12–24 h            |



# Reduced Heart Failure

- Other supportive care:
  - Ivabradine
  - Vericiguat
  - Digoxin



# Reduced Heart Failure

- Other supportive care:
  - Ivabradine
    - Indication AHA C NYHA II-III  
LVEF <35% in sinus rhythm  
with a HR 70+ BPM

| COR | LOE | Recommendation   |
|-----|-----|--|
| 2a  | B-R | 1. For patients with symptomatic (NYHA class II to III) stable chronic HFrEF (LVEF $\leq$ 35%) who are receiving GDMT, including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of $\geq$ 70 bpm at rest, ivabradine can be beneficial to reduce HF hospitalizations and cardiovascular death. <sup>1,2</sup> |



# Reduced Heart Failure

- Other supportive care:
  - Vericiguat
    - Indication LVEF <45% and recent exacerbation

| COR | LOE | Recommendation   |
|-----|-----|--|
| 2b  | B-R | 1. In selected high-risk patients with HFrEF and recent worsening of HF already on GDMT, an oral soluble guanylate cyclase stimulator (vericiguat) may be considered to reduce HF hospitalization and cardiovascular death. <sup>1</sup> |



# Reduced Heart Failure

- Other supportive care:
  - Digoxin

| COR | LOE | Recommendation   |
|-----|-----|--|
| 2b  | B-R | 1. In patients with symptomatic HFrEF despite GDMT (or who are unable to tolerate GDMT), digoxin might be considered to decrease hospitalizations for HF. <sup>1,2</sup> |



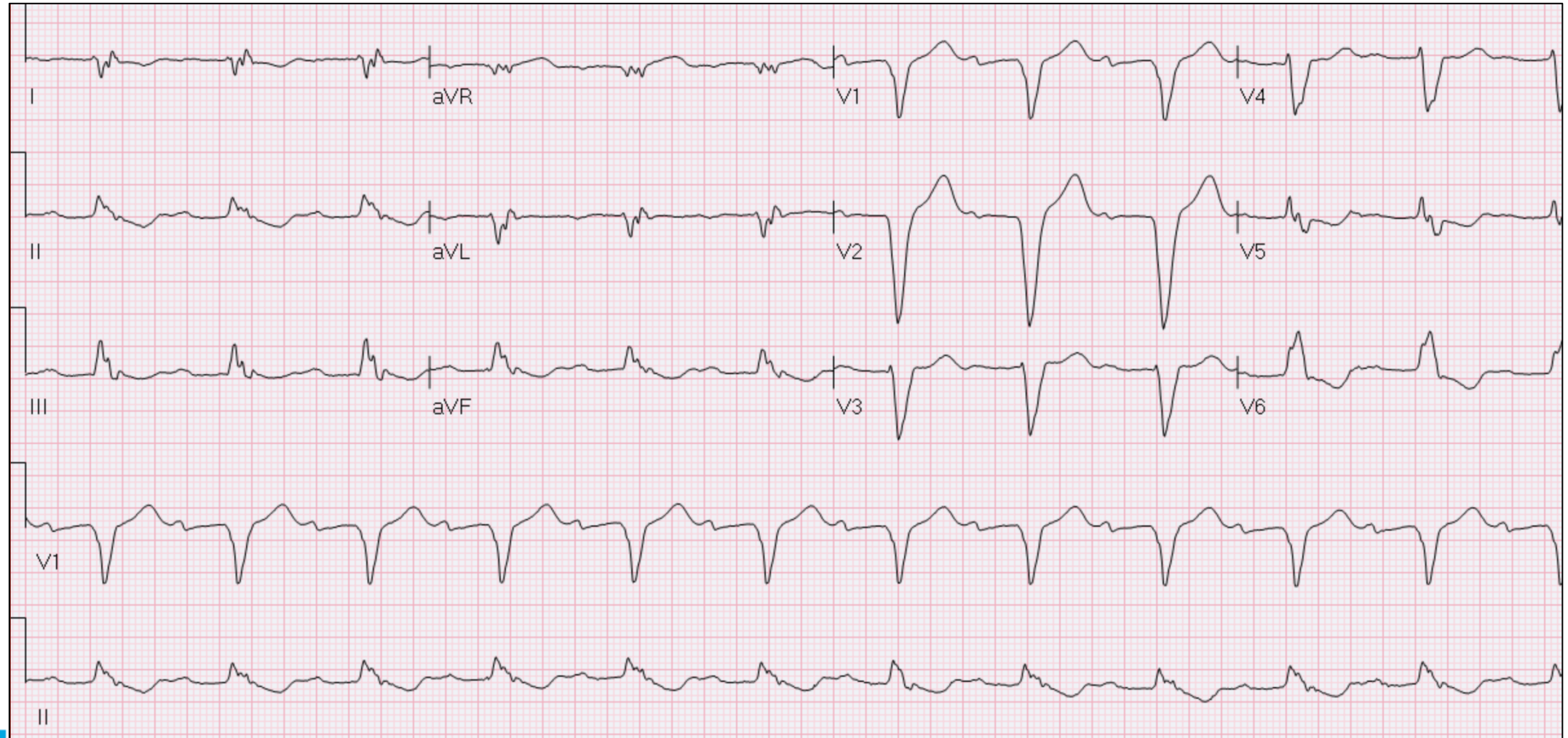
# Reduced Heart Failure

- Other treatment modalities

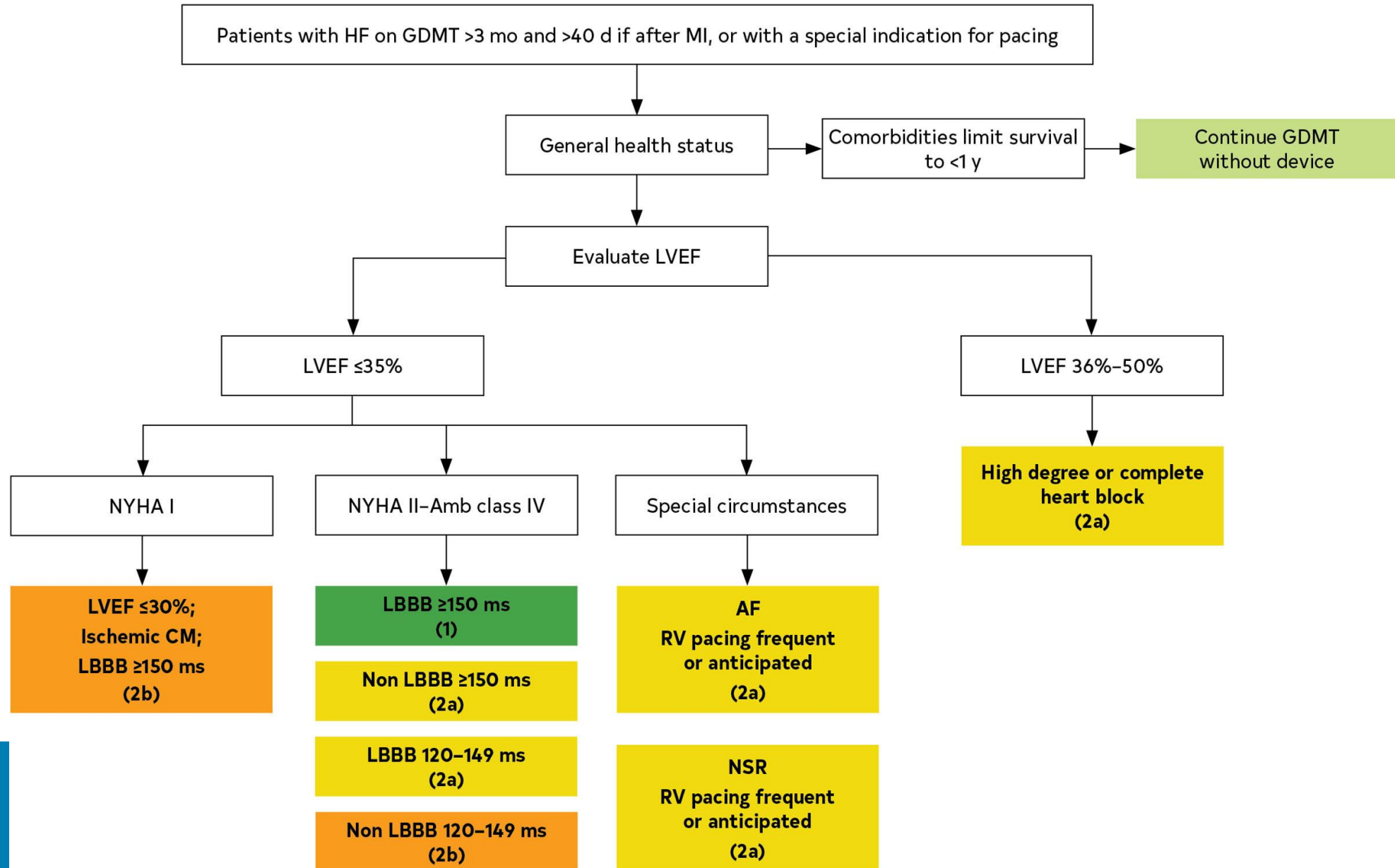




# Reduced Heart Failure



# Reduced Heart Failure



# Reduced Heart Failure

- CRT
  - LBBB
    - (1) 150 ms
    - (2a) 120-149 ms
  - Non-LBBB
    - (2a) 150 ms
    - (2b) 120-149 ms

**LBBB  $\geq 150$  ms  
(1)**

**Non LBBB  $\geq 150$  ms  
(2a)**

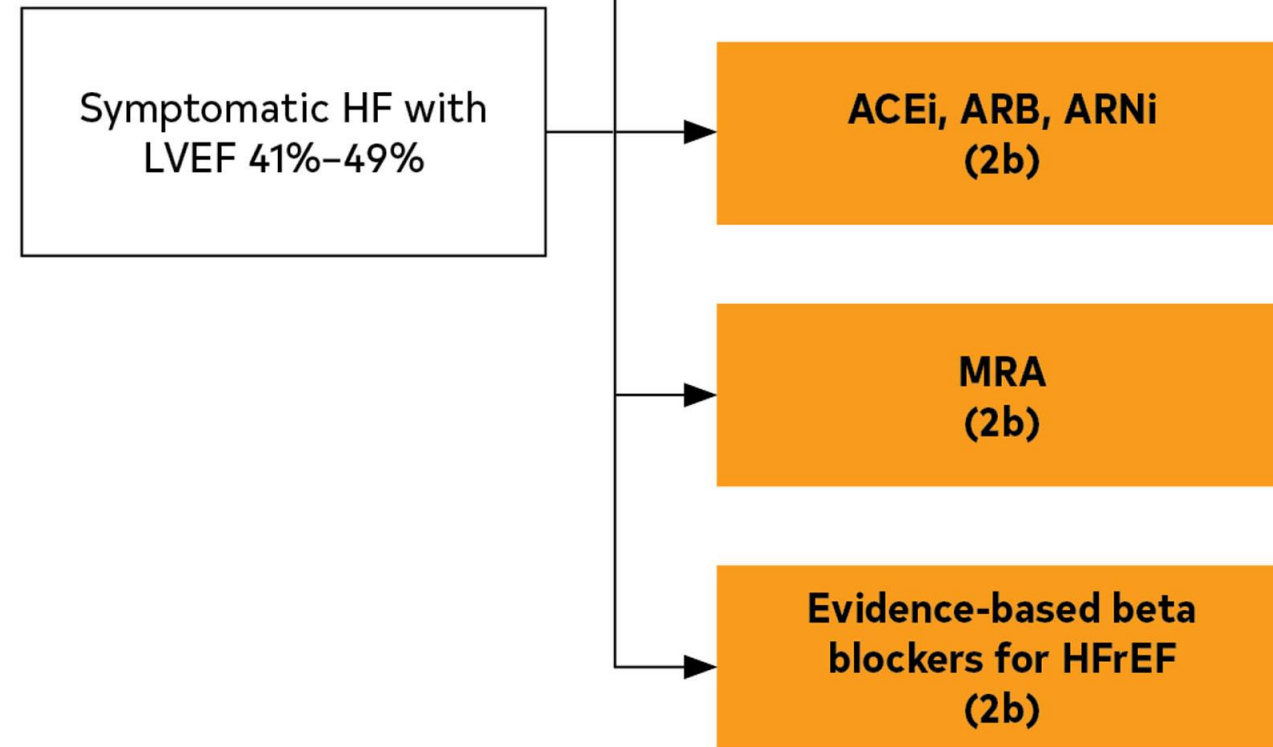
**LBBB 120–149 ms  
(2a)**

**Non LBBB 120–149 ms  
(2b)**



# Midrange Heart Failure

- Diuretic as needed
- SGLT2i (2a)
  - RAAS (2b)
  - MRA (2b)
  - Beta blocker (2b)



# Other Considerations

- Iron deficiency anemia
  - IV repletion of iron showed:
    - Improved NYHA class, 6MWT, QOL (FAIR HF trial)
    - Reduce hospitalizations (AFFIRM trial)



# Other Considerations

- OSA
  - Avoid adaptive servo-ventilation: this can worsen heart failure



# Improved Heart Failure

“I feel so good now, do I really need all these medicines?”

## Rx List

Toprol XL 200 mg PO daily

Entresto 49-51 mg PO BID

Farxiga 10 mg PO daily

Eplerenone 25 mg PO daily



# Improved Heart Failure

“I feel so good now, do I really need all these medicines?”

- a. Toprol XL
- b. Entresto
- c. Farxiga
- d. Eplerenone
- e. None

## Rx List

Toprol XL 200 mg PO daily

Entresto 49-51 mg PO BID

Farxiga 10 mg PO daily

Eplerenone 25 mg PO daily





# Improved Heart Failure

“I feel so good now, do I really need all these medicines?”

a. Toprol XL

Rx List

Toprol XL 200 mg PO daily

| COR | LOE | Recommendation  |
|-----|-----|---|
| 1   | B-R | 1. In patients with HFimpEF after treatment, GDMT should be continued to prevent relapse of HF and LV dysfunction, even in patients who may become asymptomatic. <sup>1</sup> |



# Improved Heart Failure

- Always treat these patients like HFrEF even if LVEF normalizes
  - Avoid nondihydropyridine calcium channel blockers



# Preserved Heart Failure



# Preserved Heart Failure

- Causes
  - Hypertensive heart disease
  - Metabolic disorders
  - Valvular heart disease
  - Constriction or restriction
  - Infiltrative cardiomyopathies: amyloidosis, hemochromatosis
  - Hypertrophic cardiomyopathy



# Preserved Heart Failure

- H<sub>2</sub>FPEF Score

**Prior to completion, confirm patient has exertional dyspnea and LVEF > 40%.**  
Enter the points in the fields to the right for all conditions that apply to the patient. ↘

|  |                                     |  |           |                      |
|--|-------------------------------------|--|-----------|----------------------|
| <b>H<sub>2</sub></b>                   | <b>H</b> Heavy                      | Body mass index > 30 kg/m <sup>2</sup> | <b>+2</b> | <input type="text"/> |
|  | <b>H</b> Hypertensive               | On > 2 anti-hypertensives              | <b>+1</b> | <input type="text"/> |
| <b>F</b>                               | <b>A</b> trial <b>F</b> ibrillation | Paroxysmal or Persistent AF            | <b>+3</b> | <input type="text"/> |
| <b>P</b>                               | <b>P</b> ulmonary Hypertension      | RVSP > 35 mmHg                         | <b>+1</b> | <input type="text"/> |
| <b>E</b>                               | <b>E</b> lder                       | Age > 60 years                         | <b>+1</b> | <input type="text"/> |
| <b>F</b>                               | <b>F</b> illing Pressure            | E/e' > 9                               | <b>+1</b> | <input type="text"/> |
| <b>Score</b><br>(Sum of above numbers) |                                     |  |           | <input type="text"/> |

Consider sending high probability HFpEF patients for further evaluation

| A score of                       | 3    | 4    | 5    | 6+   |
|----------------------------------|------|------|------|------|
| Indicates a HFpEF probability of | >50% | >70% | >80% | >90% |



# Preserved Heart Failure

- Additional testing
  - Labs
  - Stress echo
  - CPET
  - CMR
  - Nuclear scintigraphy scan (PYP scan)
  - Genetic testing



# Preserved Heart Failure

- Additional testing
  - Labs
    - NT proBNP <450 pg/ml or BNP <150 pg/ml is diagnostic



# Preserved Heart Failure

- Additional testing
  - Stress echo and CPET
    - Shows dynamic changes in diastolic function





# Preserved Heart Failure

- Additional testing
  - CMR: useful for looking for underlying pathophysiology such as infiltrative processes, constriction, previous infarcts or ischemic events.
    - If hemochromatosis is suspect must order with T2 star mapping.



# Preserved Heart Failure

- Additional testing
  - Nuclear scintigraphy scan (PYP scan): used to diagnose ATTR-CM
  - May need a tissue sample



# Preserved Heart Failure

- Medications



# Preserved Heart Failure

| COR                  | LOE         | Recommendations   |
|----------------------|-------------|---|
| <b>1</b>             | <b>C-LD</b> | 1. Patients with HFpEF and hypertension should have medication titrated to attain blood pressure targets in accordance with published clinical practice guidelines to prevent morbidity. <sup>1-3</sup> |
| <b>2a</b>            | <b>B-R</b>  | 2. In patients with HFpEF, SGLT2i can be beneficial in decreasing HF hospitalizations and cardiovascular mortality. <sup>4</sup>  |
| <b>2a</b>            | <b>C-EO</b> | 3. In patients with HFpEF, management of AF can be useful to improve symptoms.  |
| <b>2b</b>            | <b>B-R</b>  | 4. In selected patients with HFpEF, MRAs may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum. <sup>5-7</sup>                        |
| <b>2b</b>            | <b>B-R</b>  | 5. In selected patients with HFpEF, the use of ARB may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum. <sup>8,9</sup>              |
| <b>2b</b>            | <b>B-R</b>  | 6. In selected patients with HFpEF, ARNi may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum. <sup>10,11</sup>                      |
| <b>3: No-Benefit</b> | <b>B-R</b>  | 7. In patients with HFpEF, routine use of nitrates or phosphodiesterase-5 inhibitors to increase activity or QOL is ineffective. <sup>12,13</sup>   |



# Preserved Heart Failure

- Medications
  - SGLT2 inhibitors
  - Mineralocorticoid receptor antagonist
  - RAAS blockade: Entresto?
  - Beta blockade?

Symptomatic HF with  
LVEF  $\geq 50\%$

Diuretics, as needed  
(1)

SGLT2i  
(2a)

ARNi\*  
(2b)

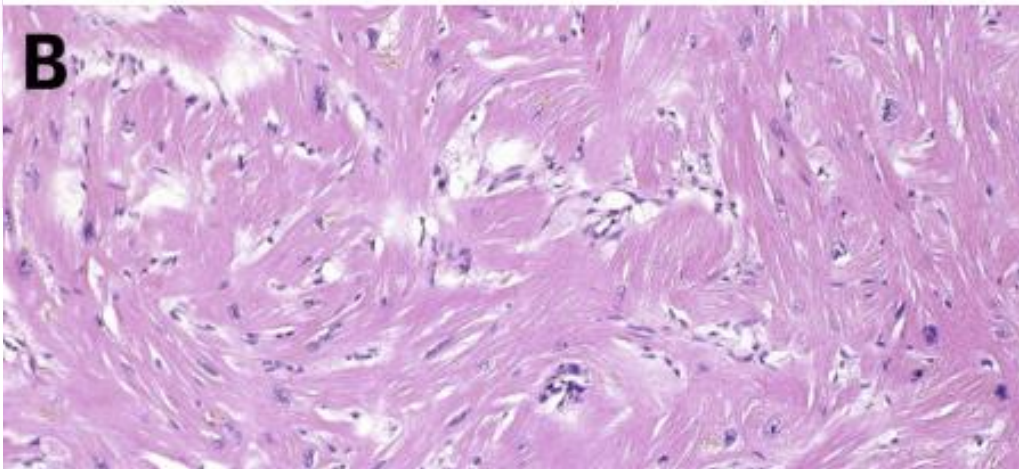
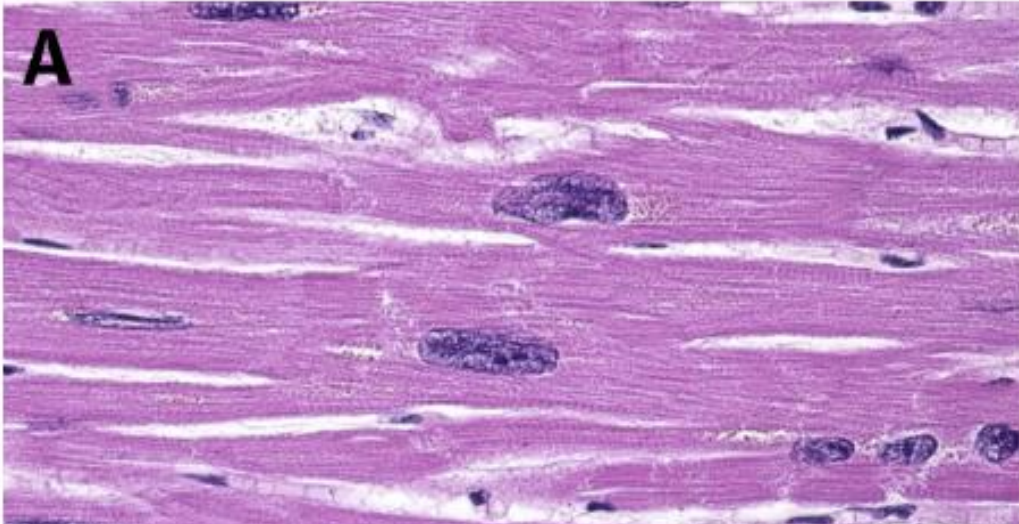
MRA\*  
(2b)

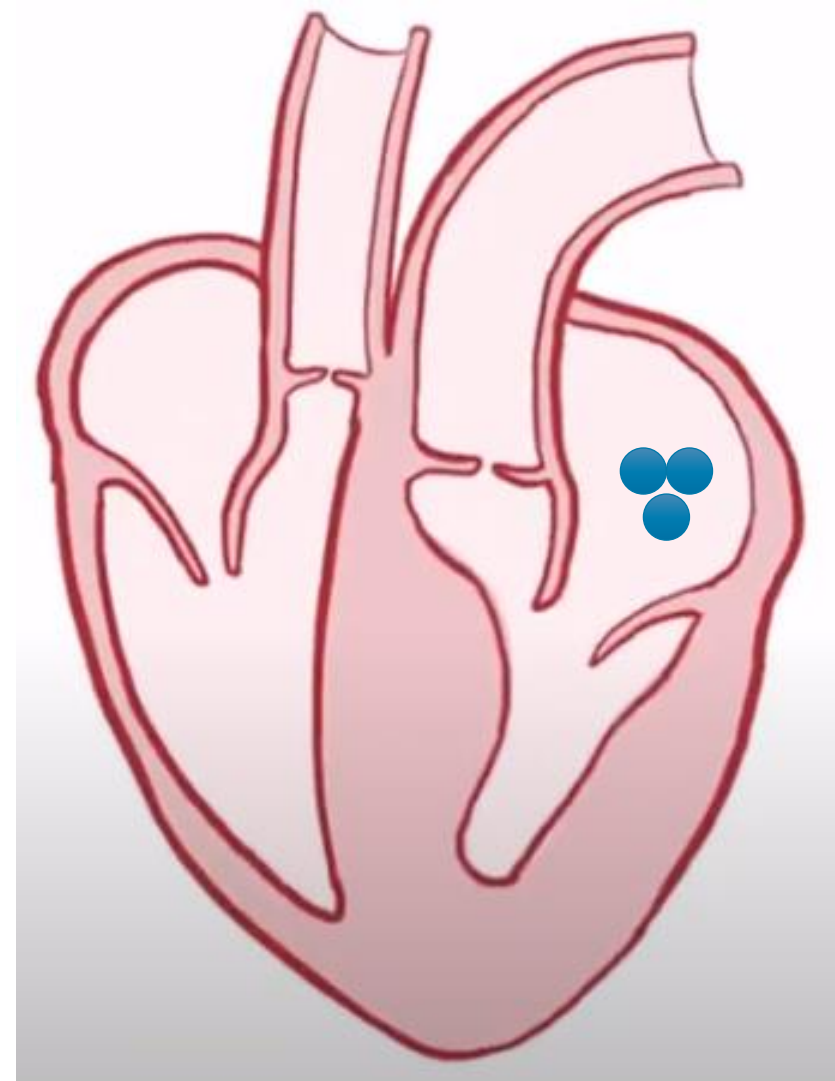
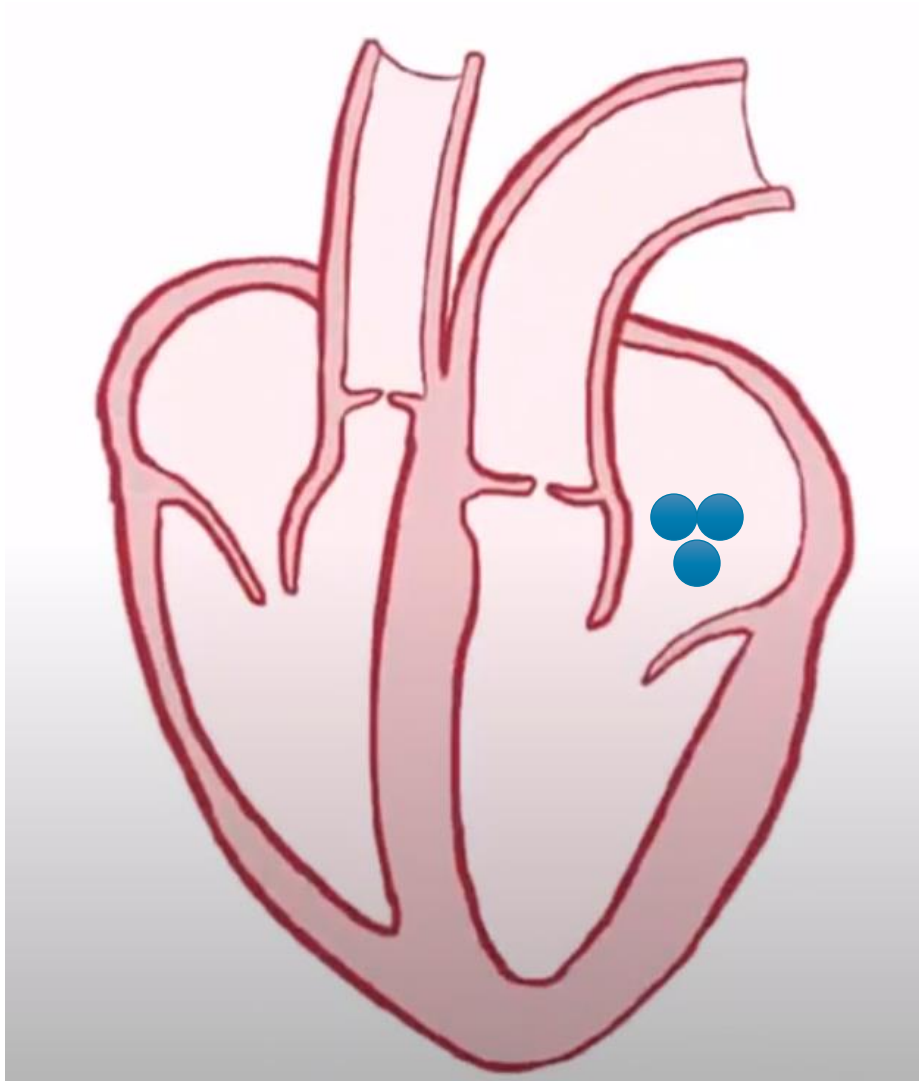
ARB\*  
(2b)





# Hypertrophic Cardiomyopathy





Tushak Heart Failure





# HCM

- Benefit from BB and/or CCB to reduce diastolic filling time and negative inotropy
- Are often intolerant of afterload reducing medications
- May need consideration of disease modifying therapies like myosin inhibitor therapy, alcohol septal ablation, or myectomy.
- Are at increased risk of atrial and ventricular arrhythmias and sudden cardiac death
- Needs familial screening





# Amyloidosis

- Systemic disease caused by the deposition of an insoluble protein
- Most common cardiac variants: AL and TTR



# Amyloidosis: TTR

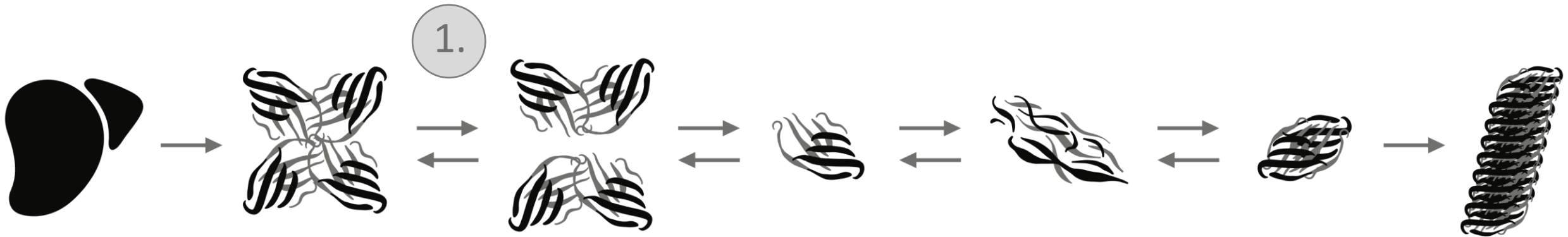
## TTR TransThyRetin

- Tetramer synthesized by the liver to bind and transport the hormone thyroxine and retinol-binding protein within the systemic circulation



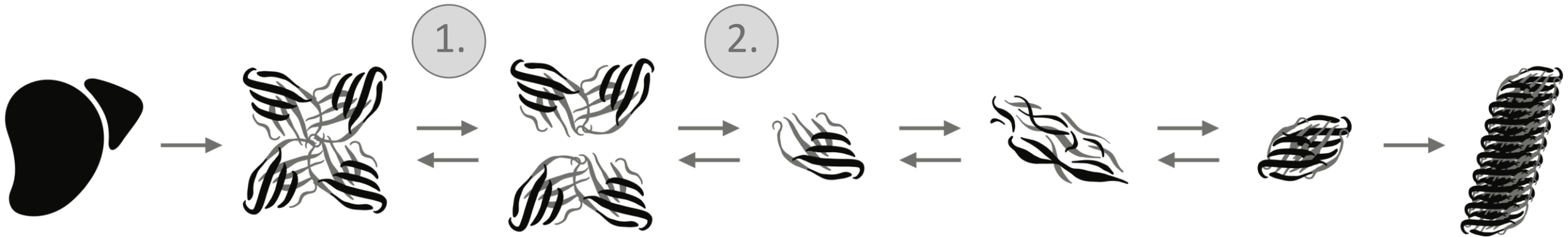
# Amyloidosis: TTR

The TTR amyloidosis is a systemic disease caused by (1) destabilization of the tetramer into (2) unstable monomers that are then (3) misfolded and then (4) aggregate as insoluble amyloid fibrils which then (5) deposit within tissue.



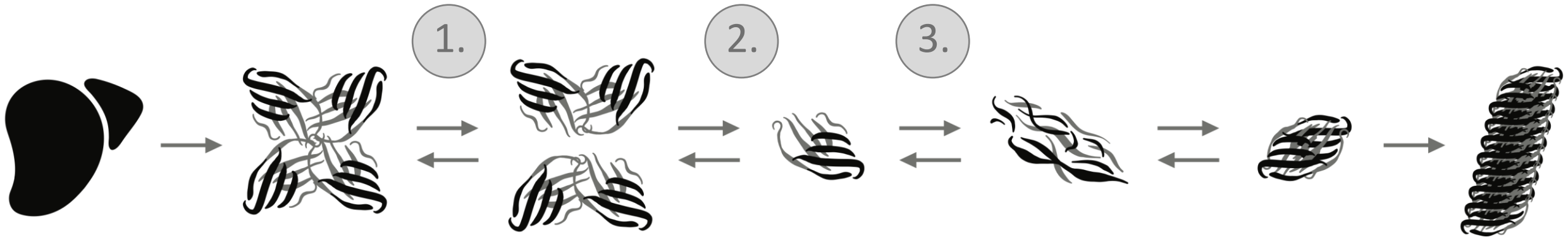
# Amyloidosis: TTR

The TTR amyloidosis is a systemic disease caused by (1) destabilization of the tetramer into (2) unstable monomers that are then (3) misfolded and then (4) aggregate as insoluble amyloid fibrils which then (5) deposit within tissue.



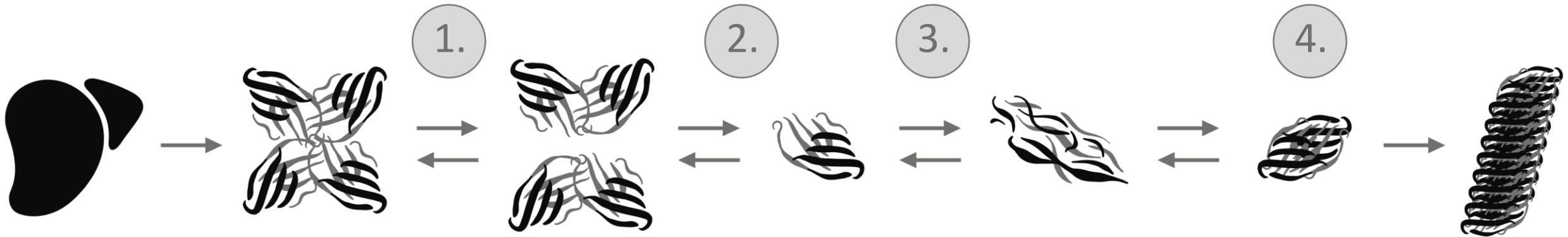
# Amyloidosis: TTR

The TTR amyloidosis is a systemic disease caused by (1) destabilization of the tetramer into (2) unstable monomers that are then (3) misfolded and then (4) aggregate as insoluble amyloid fibrils which then (5) deposit within tissue.



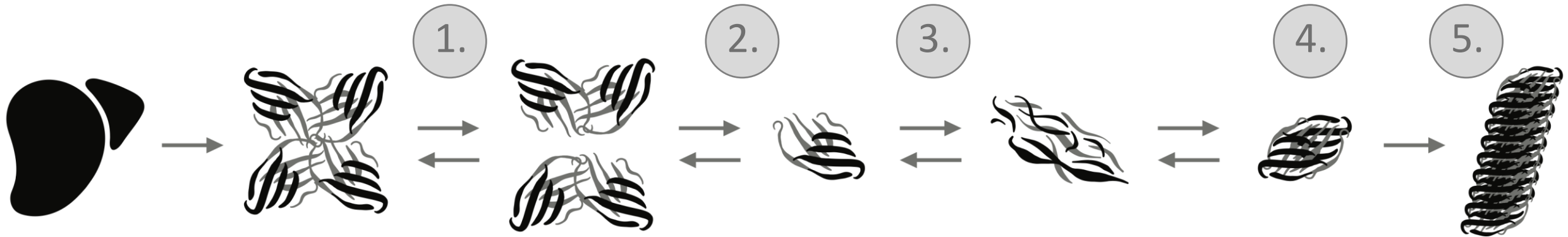
# Amyloidosis: TTR

The TTR amyloidosis is a systemic disease caused by (1) destabilization of the tetramer into (2) unstable monomers that are then (3) misfolded and then (4) aggregate as insoluble amyloid fibrils which then (5) deposit within tissue.



# Amyloidosis: TTR

The TTR amyloidosis is a systemic disease caused by (1) destabilization of the tetramer into (2) unstable monomers that are then (3) misfolded and then (4) aggregate as insoluble amyloid fibrils which then (5) deposit within tissue.



# Amyloidosis: TTR

## Systemic manifestations:

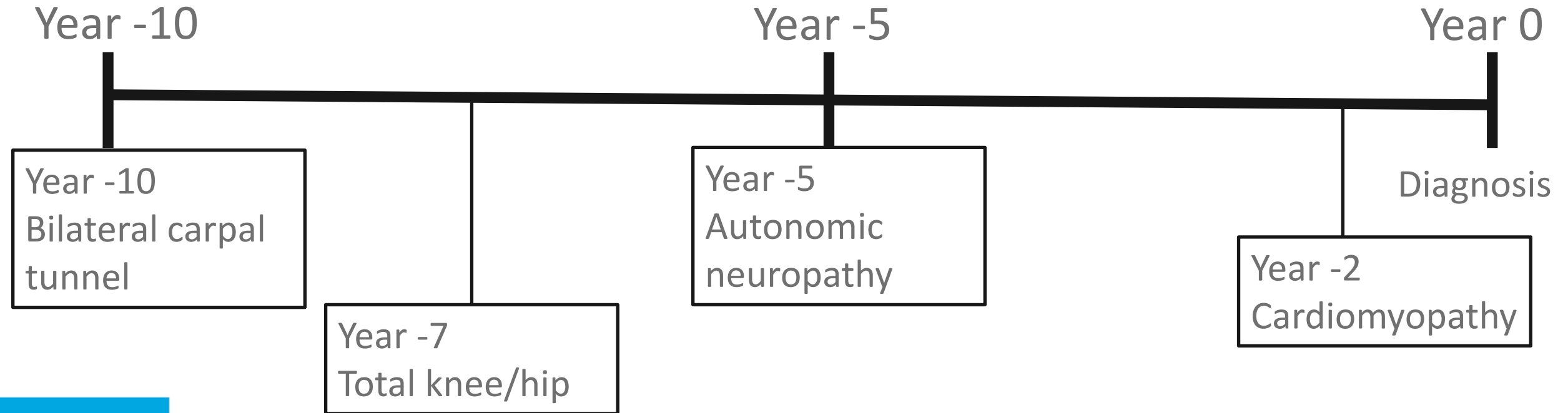
- Cardiac: Heart failure, restrictive physiology, arrhythmias, valvular heart disease (AS).
- Neuropathic: bilateral carpal tunnel, sensory neuropathies, orthostatic hypotension, diarrhea/constipation, gastroparesis, urinary retention, erectile dysfunction, sciatica.
- MSK: bicep tendon rupture, early hip/knee arthroplasties



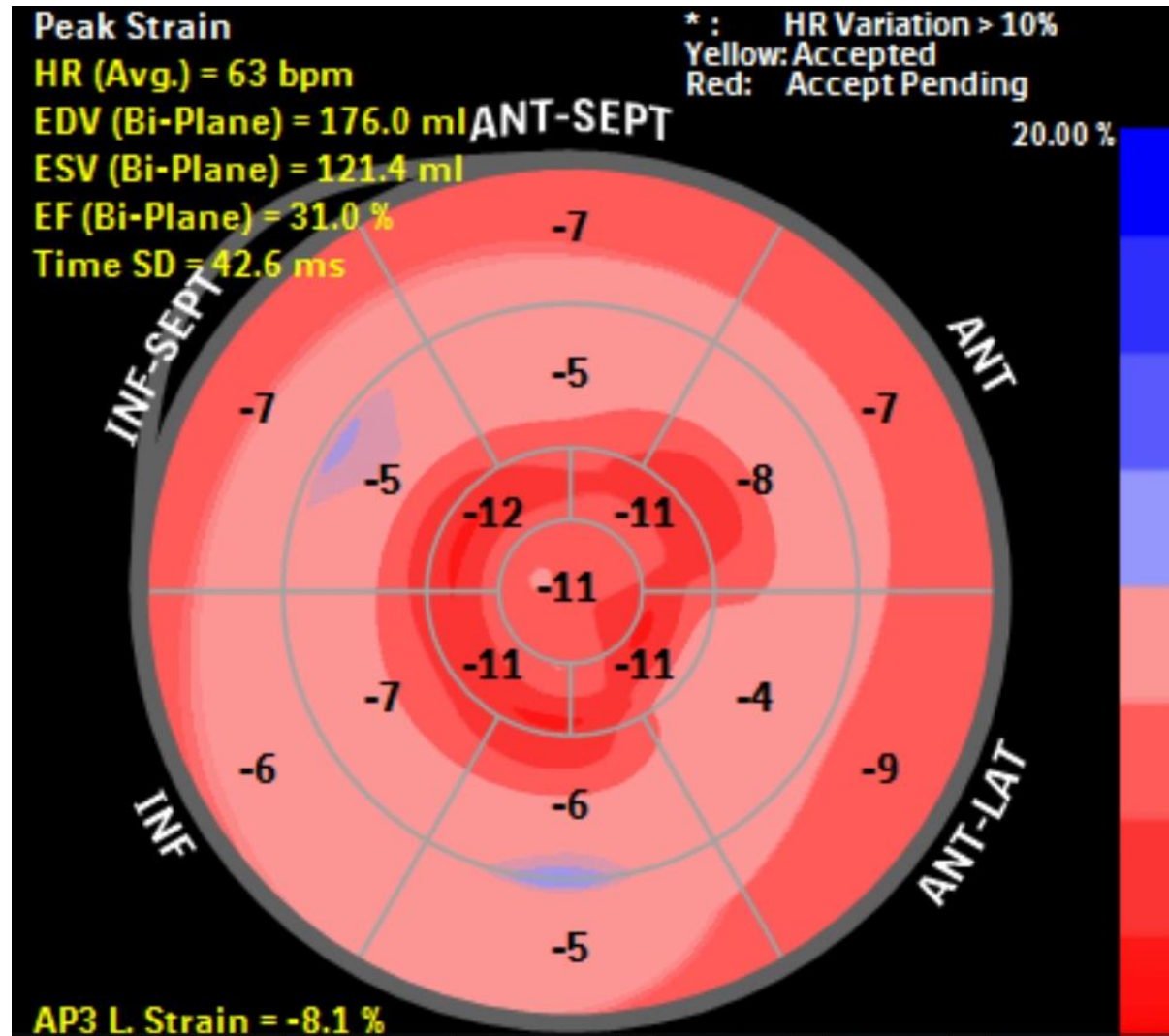


# Amyloidosis: TTR

Red flag symptoms may precede diagnosis by years...



# Amyloidosis: TTR



# Amyloidosis: TTR

- Often see multiple providers and go years before diagnosis.
- Are often intolerant of blood pressure medications and rate control medicines like beta blockers.
- Always require disease modifying therapies to prevent progression to reduce mortality and morbidity.
- Genetic testing is important to differentiate regardless of age.



# Other Considerations

- Sleep apnea and NIV
  - CPAP associated with better quality of sleep and nocturnal oxygenation
  - Less heart failure symptoms and arrhythmias
  - Meta-analyses showed positive airway pressure therapy had a moderate reduction in BNP and improvement in blood pressure and LVEF
  - Adaptive servo-ventilation was associated with increased mortality in patients with HFrEF and central sleep apnea



# Advanced Heart Failure

Repeated hospitalizations or emergency department visits for HF in the past 12 mo.

Need for intravenous inotropic therapy.

Persistent NYHA functional class III to IV symptoms despite therapy.

Severely reduced exercise capacity on CPET, 6MWT <300 m, inability to walk 1 block

Intolerance of GDMT

Recent need to escalate diuretics to maintain volume status or refractor congestion

Progressive deterioration in renal or hepatic function.

Worsening right HF or secondary pulmonary hypertension.

Frequent SBP  $\leq 90$  mm Hg.

Cardiac cachexia.

Persistent hyponatremia (serum sodium, <134 mEq/L).

Refractory or recurrent ventricular arrhythmias; frequent ICD shocks.



# Advanced Heart Failure

- Reasons to refer:
- LVEF <40% with NYHA III+ symptoms with
  - 2+ hospitalizations in 1 year for HF
  - Dilated left ventricle with a left ventricular end diastolic diameter (LVEDD) of greater than 6 cm
  - Intolerance of even low dose GDMT due to hypotension
  - Low cardiac index on right heart catheterization with or without the use of home inotropes
  - Evidence of worsening end-organ perfusion (renal or hepatic) not related to other factors



# Advanced Heart Failure

- Reasons to refer:
  - If the LVEF <30% and the LVESD is 6 cm+ the patient is less likely to recover



# Advanced Heart Failure

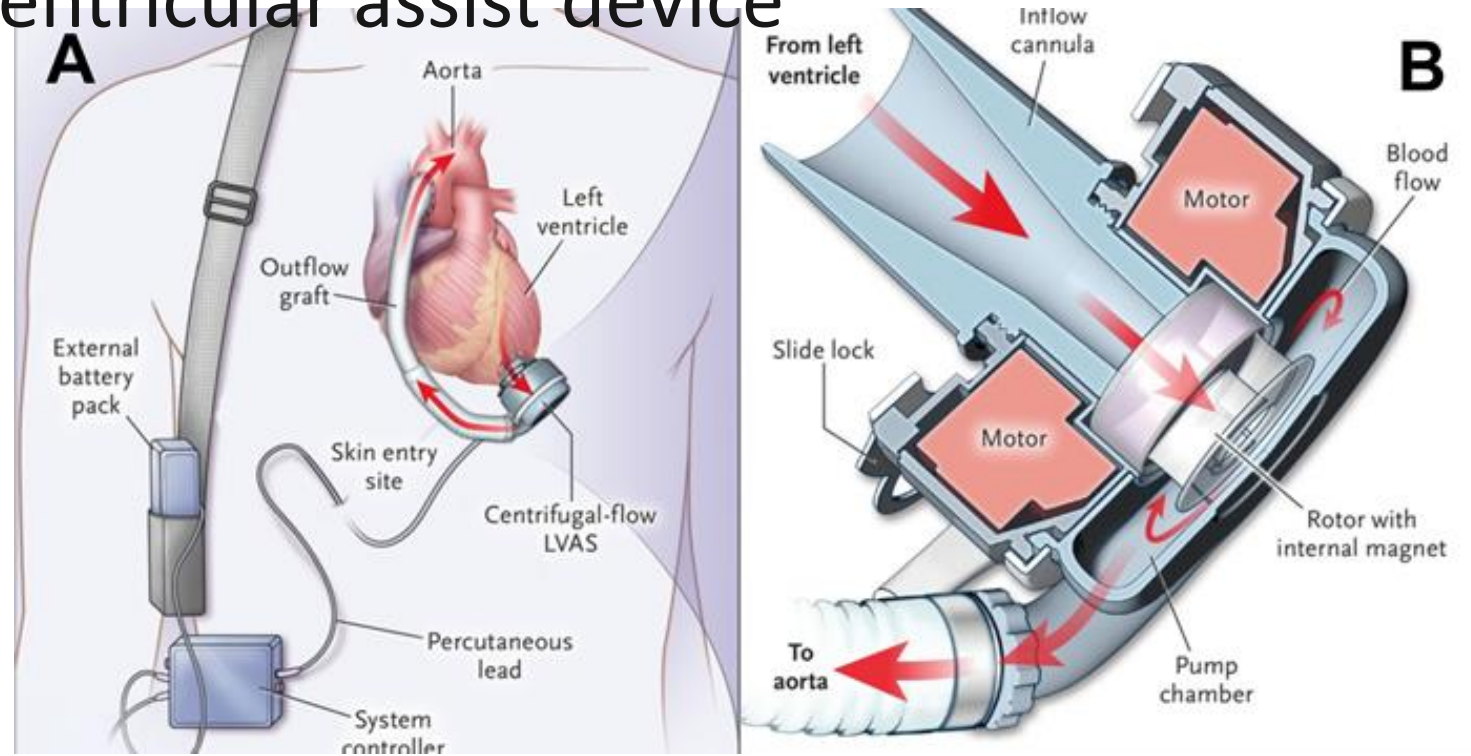
- Reasons to refer:
- Any LVEF
  - Cardiac amyloidosis
  - Hypertrophic cardiomyopathy
  - Fabry's
  - Hemochromatosis
  - Sarcoidosis





# Advanced Heart Failure

- ASO
  - Heart transplant
  - Implantable left ventricular assist device



# Advanced Heart Failure

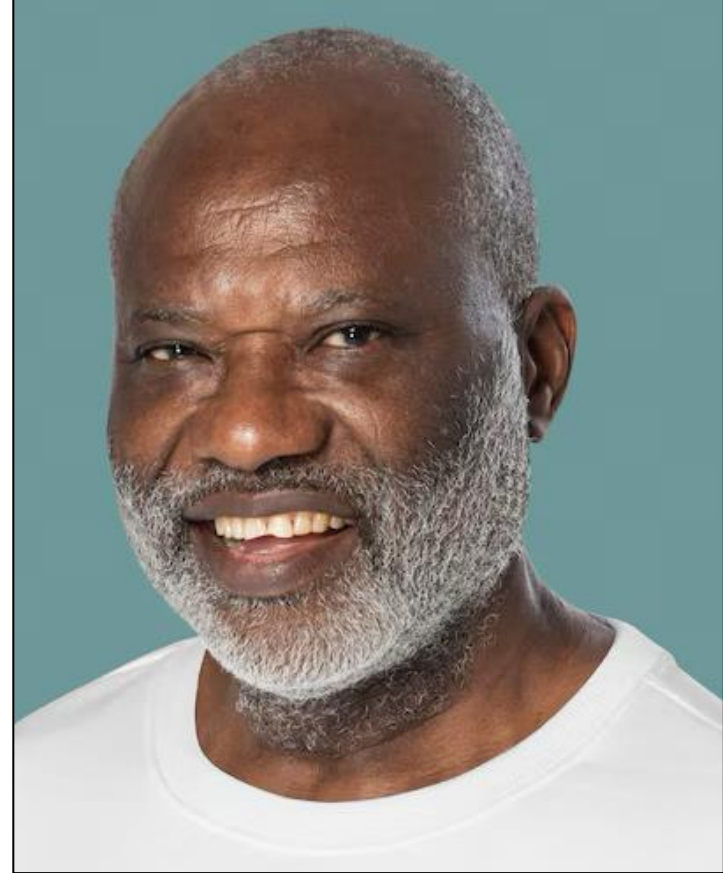
- ASO

| Indication                                    | Absolute Contraindications        | Relative Contraindications                        |                                |
|---|-----------------------------------|---|--------------------------------|
| Frequent HF hospitalizations                  | Irreversible renal or hepatic d/s | Age >80 y/o                                       | Impaired cognitive function    |
| NYHA IIIb-IV symptoms                         | Irreversible neurologic d/s       | Obesity or malnutrition                           | Unmanaged psychiatric disorder |
| Intolerance to GDMT                           | Medical nonadherence              | Inability to rehab                                | Lack of social support         |
| Inotropic dependence                          | Severe psychosocial limitations   | Active systemic infection or prolonged intubation | Active substance use           |
| Low peak VO2 <14-16                           |                                   | Untreated malignancy                              |                                |
| Evidence of low CO with end-organ dysfunction |                                   | Severe PVD  |                                |



# Case 1

- Mr. Jones is a 56-year-old male with a PMHx of HTN, bilateral carpal tunnel syndrome, IBS, who saw you with complaints of shortness of breath. He recently saw you with complaints of dizziness when he stood up so you took him off his blood pressure medications.
- Family history: heart failure, carpal tunnel



# Case 1

- Diagnosis?
  - A. Hypertensive heart disease
  - B. Cardiac amyloidosis
  - C. Hypertrophic cardiomyopathy



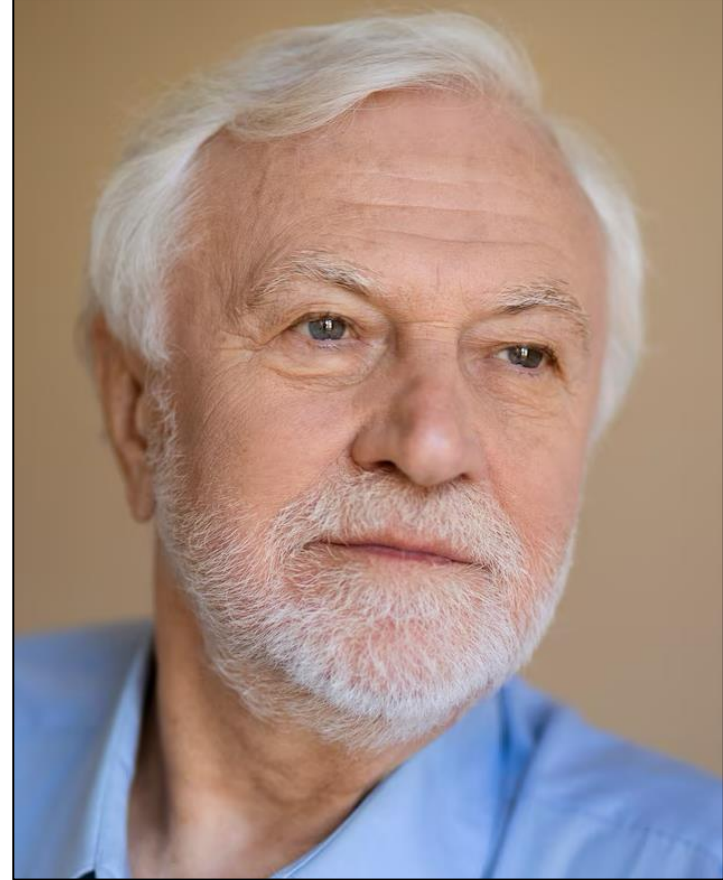
# Case 1

- Diagnosis?
  - A. Hypertensive heart disease
  - B. Cardiac amyloidosis – highly suspicious for h-ATTR**
  - C. Hypertrophic cardiomyopathy



## Case 2

- Mr. Smith is a 82-year-old male with a PMHx of HTN, HFpEF, aortic stenosis s/p TAVR, sick sinus syndrome s/p pacemaker who saw you with complaints of shortness of breath, swelling, and fatigue.
- Family history: HTN, DM



## Case 2

- Diagnosis?
  - A. Hypertensive heart disease
  - B. Cardiac amyloidosis
  - C. Hypertrophic cardiomyopathy



## Case 2

- Diagnosis?
  - A. Hypertensive heart disease
  - B. Cardiac amyloidosis – highly suspicious for wt-ATTR**
  - C. Hypertrophic cardiomyopathy





## Case 3

- Ms. Miller is a 42-year-old female with a PMHx of passing out in her teens when running track who presented for shortness of breath. She was told she had a murmur when she was a child.
- Family history: her uncle died as a teen playing basketball of unknown cause, her grandfather died sudden while at work



# Case 3

- Diagnosis?
  - A. Hypertensive heart disease
  - B. Cardiac amyloidosis
  - C. Hypertrophic cardiomyopathy



# Case 3

- Diagnosis?
  - A. Hypertensive heart disease
  - B. Cardiac amyloidosis
  - C. Hypertrophic cardiomyopathy**



# Questions?

Zackary Tushak, DO FACC

[zjtusha2@Sentara.com](mailto:zjtusha2@Sentara.com)

Advanced Heart Failure and Transplant Cardiology

Director Cardiac Amyloidosis Program

Director Hypertrophic Cardiomyopathy Program

Director Cardio-Oncology Program

