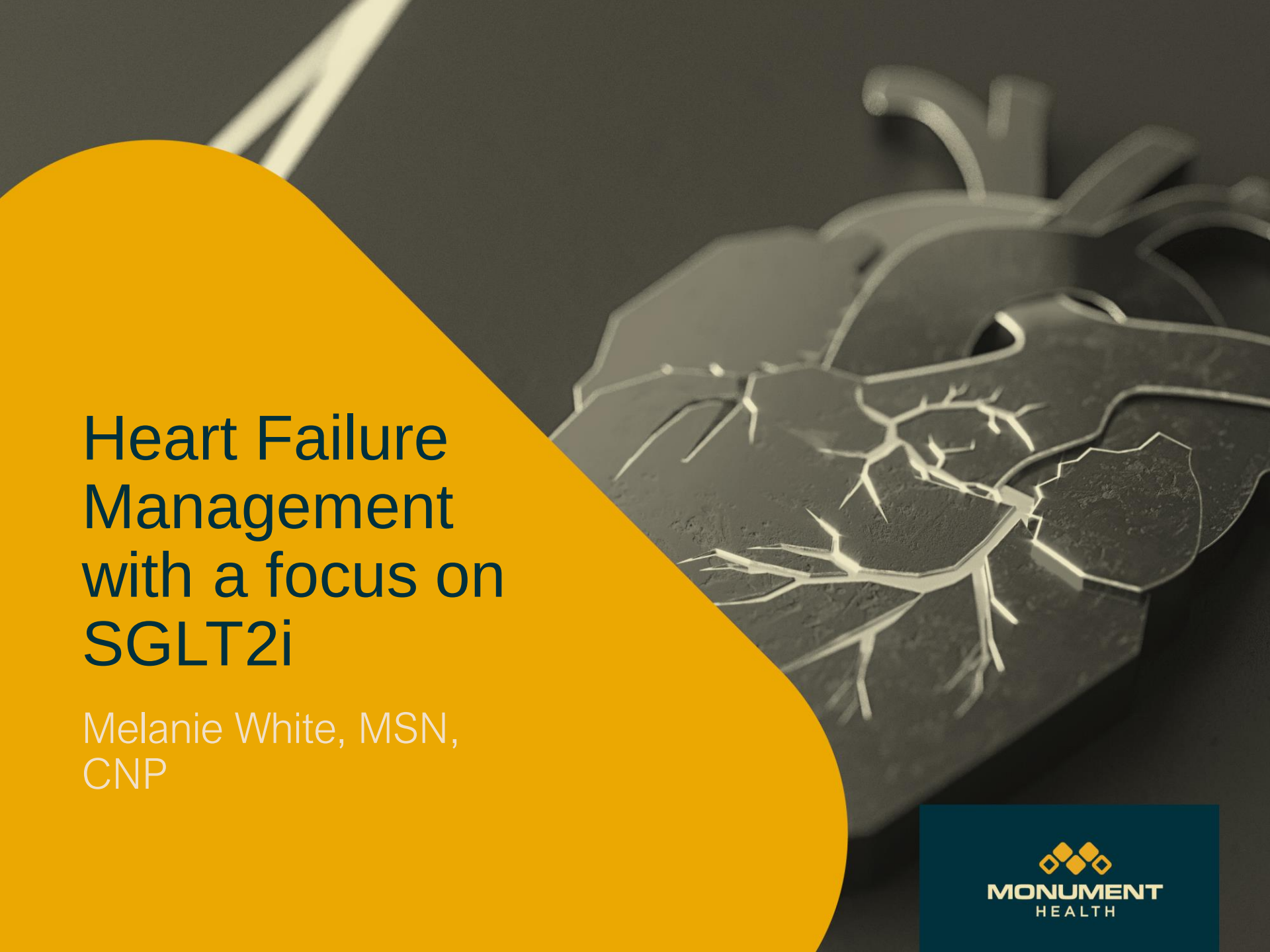


# Heart Failure Management with a focus on SGLT2i

Melanie White, MSN, CNP

MONUMENT HEALTH

Conflict of Interest

- None

Financial Disclosure

- None

# Objectives

- Describe the updated definition of heart failure and the updated terminology when describing stages of heart failure.
- Describe the 2022 ACC/AHA updated guideline recommendations for pharmacological management heart failure
- Explain the pharmacology, summarize the clinical trials and discuss the role of SGLT2i in management of HF.

# Mr. Ed Deehma

**Patient History**

62 year old male, Hx of HTN, PAD, CKD

- Hospitalized with new diagnosis of HF
- NKDA

**Social History**

- Former smoker, quit 20 yrs ago, 20 yr pack Hx
- Social ETOH, 1-2 glasses wine per week
- CPA with good health insurance

**Presentation**

- NYHA class III

# Clinical Course

- Hospitalized and diuresed with IV loop diuretics- signs and symptoms improved.
- TTE – LVEF 30% with mod MR
- Labs: K+ 4.4, GFR 46, Creat 1.71, NT-Pro BNP 2400
- Coronary angiogram – non-obstructive CAD

# Physical Exam at discharge

- HR 78 bpm
- BP 98/58
- Euvolemic
- JVP mildly elevated, regular heart sounds, clear lungs, 0 LE edema
- Discharged on Carvedilol 6.25 mg BID, Lisinopril 5 mg QD, Spironolactone 12.5 mg, Lasix 40 mg QD.

# Follow up appointment 2 weeks later

**Vitals and Labs**

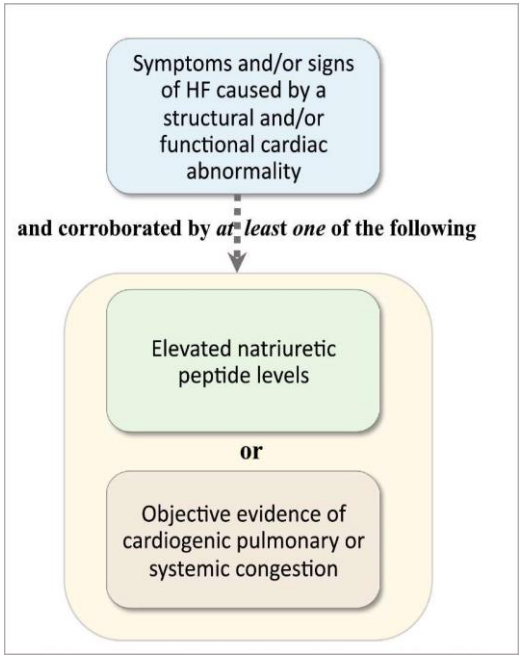
- BP 100/60
- HR 77
- K 4.3, eGFR 46
- Euvolemic on exam

**Options**

- Uptitrate current GDMT
- Change Lisinopril to Entresto
- Start SGLT2i

**Considerations**: Blood pressure, volume status, renal function, cost

# Universal HF Definition




HF is a clinical syndrome with current or prior symptoms and/or signs caused by a structural and/or functional cardiac abnormality and corroborated by at least one of the following:

•Elevated natriuretic peptide levels

| | Ambulatory | Hospitalized/Decompensated |
|---|---|---|
| BNP pg/ml | ≥35 | ≥100 |
| NT-proBNP pg/ml | ≥125 | ≥300 |

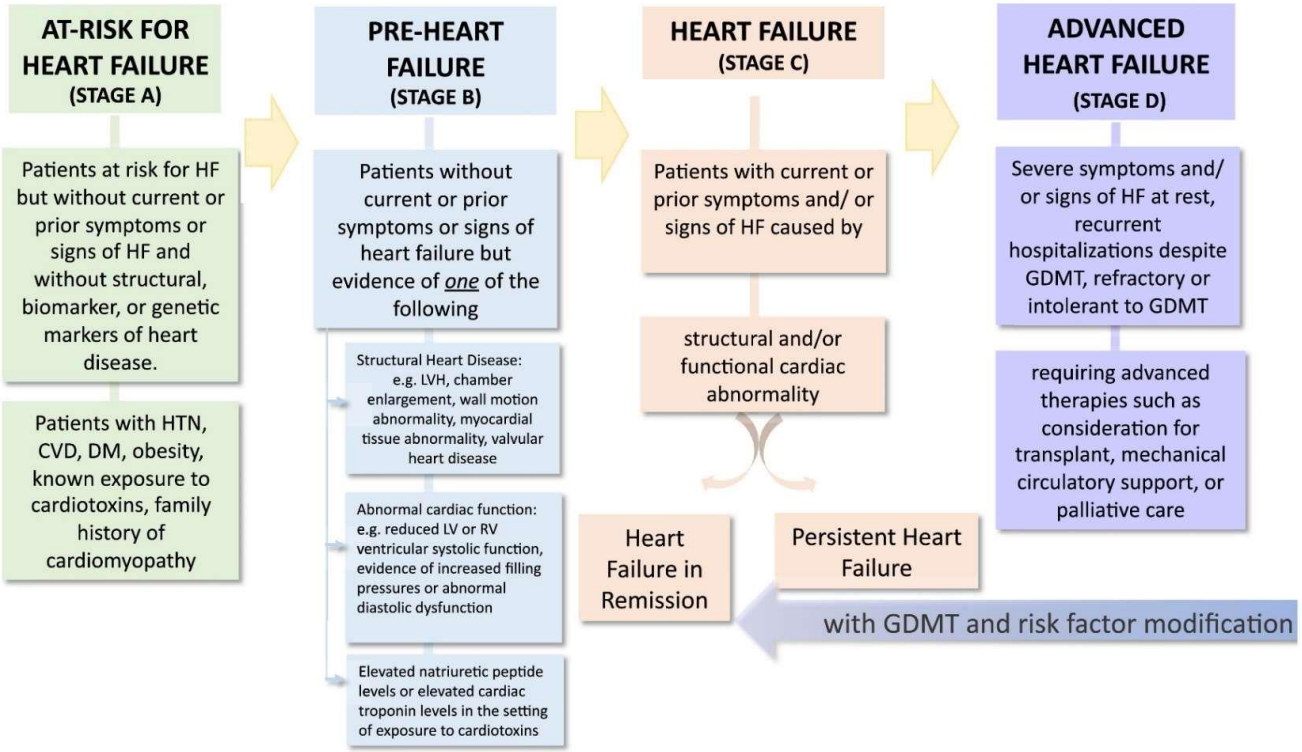
•Objective evidence of cardiogenic pulmonary or systemic congestion by diagnostic modalities, such as imaging (chest radiograph) elevated filling pressures on echocardiography, hemodynamic measurement (eg, right heart catheterization, pulmonary artery catheter) at rest or with during exercise.

Bozkurt, B., Coats, A. J., Tsutsui, H., Abdelhamid, M., Adamopoulos, S., Albert, N., ... & Zieroth, S. (2021). Universal definition and classification of heart failure: a report of the heart failure society of America, heart failure association of the European society of cardiology, Japanese heart failure society and writing committee of the universal definition of heart failure. Journal of cardiac failure, 27(4), 387-413.

# 2022 HF Guidelines

- In May 2022 a joint committee that included AHA/ACC/HFSA published new Guidelines for the Management of Heart Failure.
- Replaced the 2013 ACC/AHA Guidelines and the 2017 ACC/AHA/HFSA and the Focused Update of the 2013 ACC/AHA Guidelines.
- More patient-centric recommendations for clinicians to prevent, diagnose, and manage patients with heart failure.
- Important changes in the way we manage heart failure based on new clinical trial data.

# Stages of Heart Failure

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# New Revised Classification of HF According to EF

| Classification | Ejection Fraction | Previous Terminology |
|---|---|---|
| **HF with reduced EF (HFrEF)** | **LVEF ≤ 40%** | Systolic HF |
| **HF with mildly reduced EF (HFmrEF)** | **LVEF 41-49%** | Borderline |
| **HF with preserved EF (HFpEF)** | **LVEF ≥ 50%** | Diastolic HF |
| **HF with improved EF (HFimpEF )** | **Baseline LVEF ≤ 40%, ≥ 10 point increase from baseline, second LVEF >40%** | Borderline, recovered-sometimes referred to as HFrecEF. Not always linear-can improve and deteriorate. |

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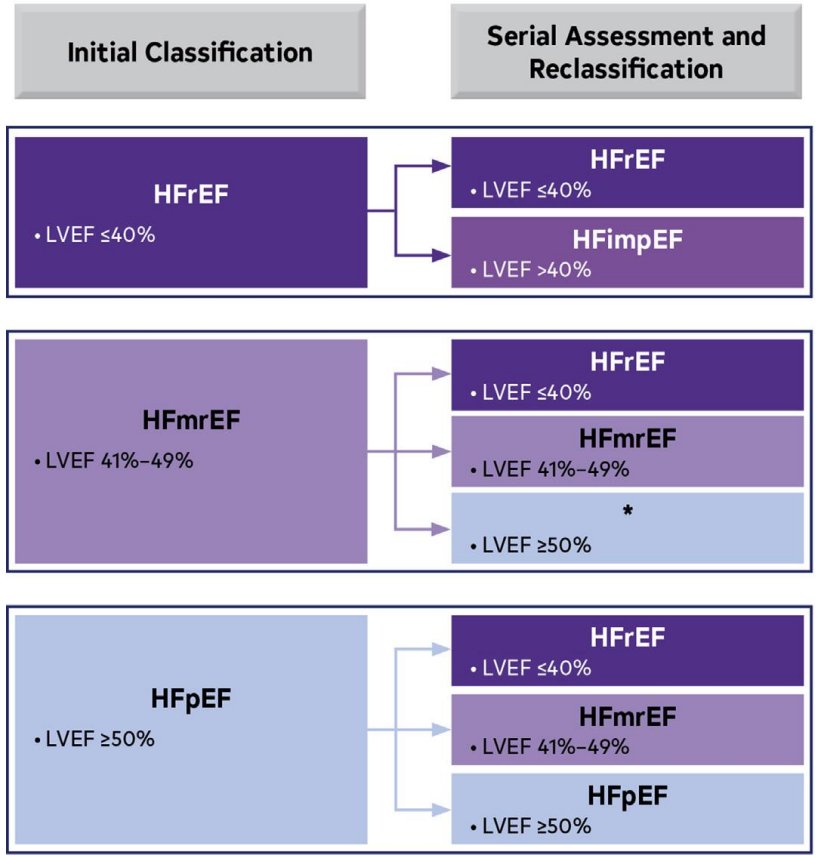
# Classification and Trajectories of HF Based on LVEF

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# NYHA Class

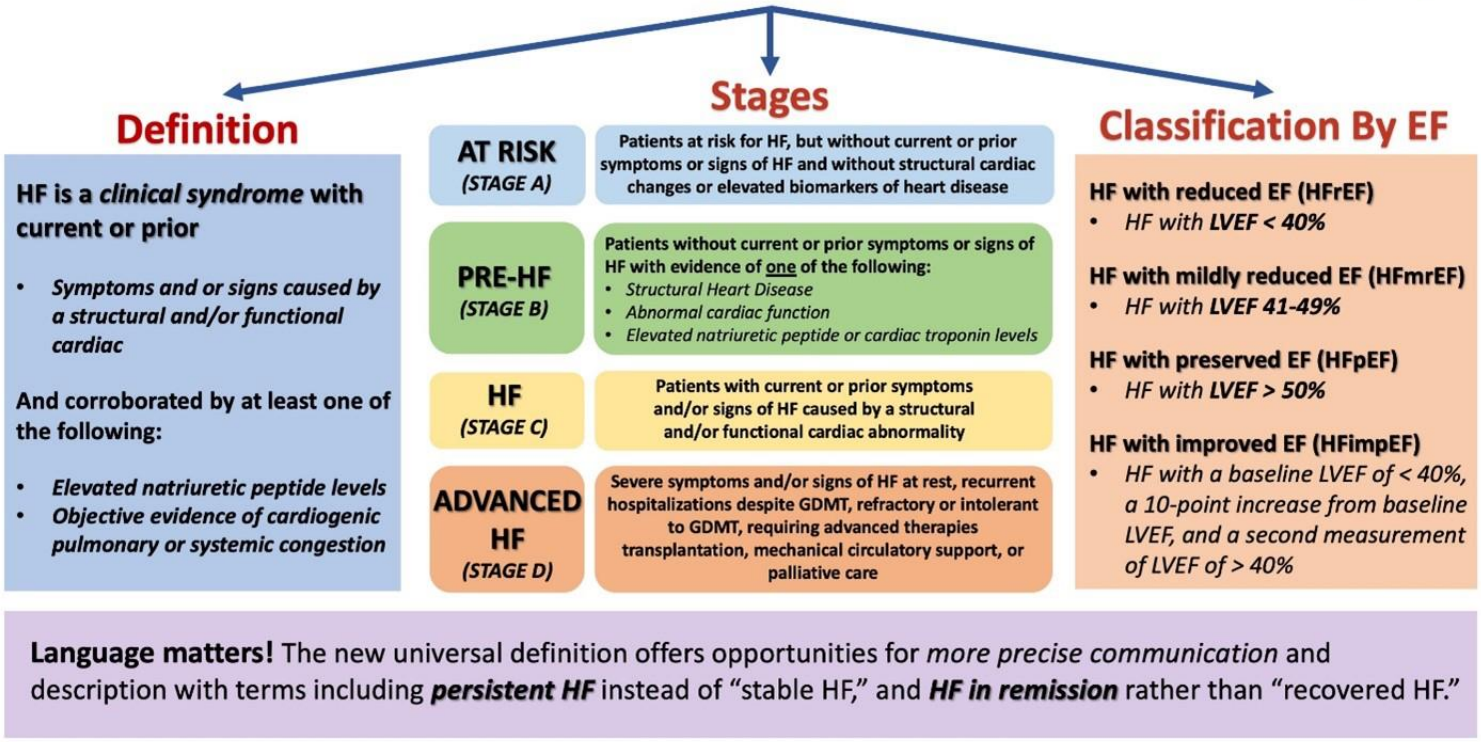
| HYHA Class | |
|---|---|
| I | No limitation of Physical Activity |
| II | Slight limitation of physical activity |
| III | Marked limitation of physical activity |
| IV | Symptoms at rest |

# Trajectory of Stage C HF

| New Onset/De Novo HF: | Resolution of Symptoms: | Persistent HF: | Worsening HF: |
|---|---|---|---|
| • Newly diagnosed HF<br>• No previous history of HF | • Resolution of symptoms/ signs of HF<br>Stage C with previous symptoms of HF with persistent LV dysfunction \| HF in remission with resolution of previous structural and/or functional heart disease* | • Persistent HF with ongoing symptoms/signs and/or limited functional capacity | • Worsening symptoms/ signs/functional capacity |

Heidenreich, P. A., Bozkurt, B., Aguilar, D., Allen, L. A., Byun, J. J., Colvin, M. M., ... & Yancy, C. W. (2022). 2022 AHA/ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Journal of the American College of Cardiology, 79(17), e263-e421.

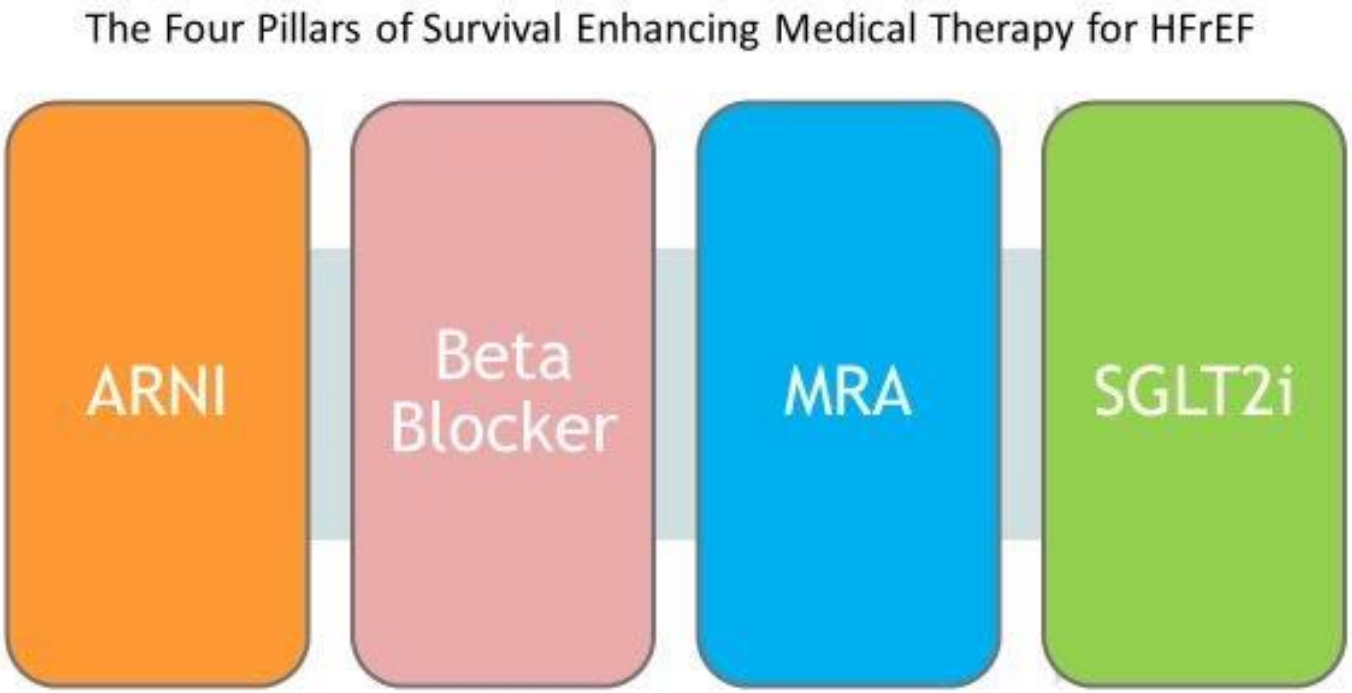
# Universal Definition and Classification of Heart Failure (HF)




**Language matters!** The new universal definition offers opportunities for *more precise communication* and description with terms including ***persistent HF*** instead of "stable HF," and ***HF in remission*** rather than "recovered HF."

https://www.acc.org/latest-in-cardiology/articles/2021/07/12/12/31/universal-definition-and-classification-of-heart-failure

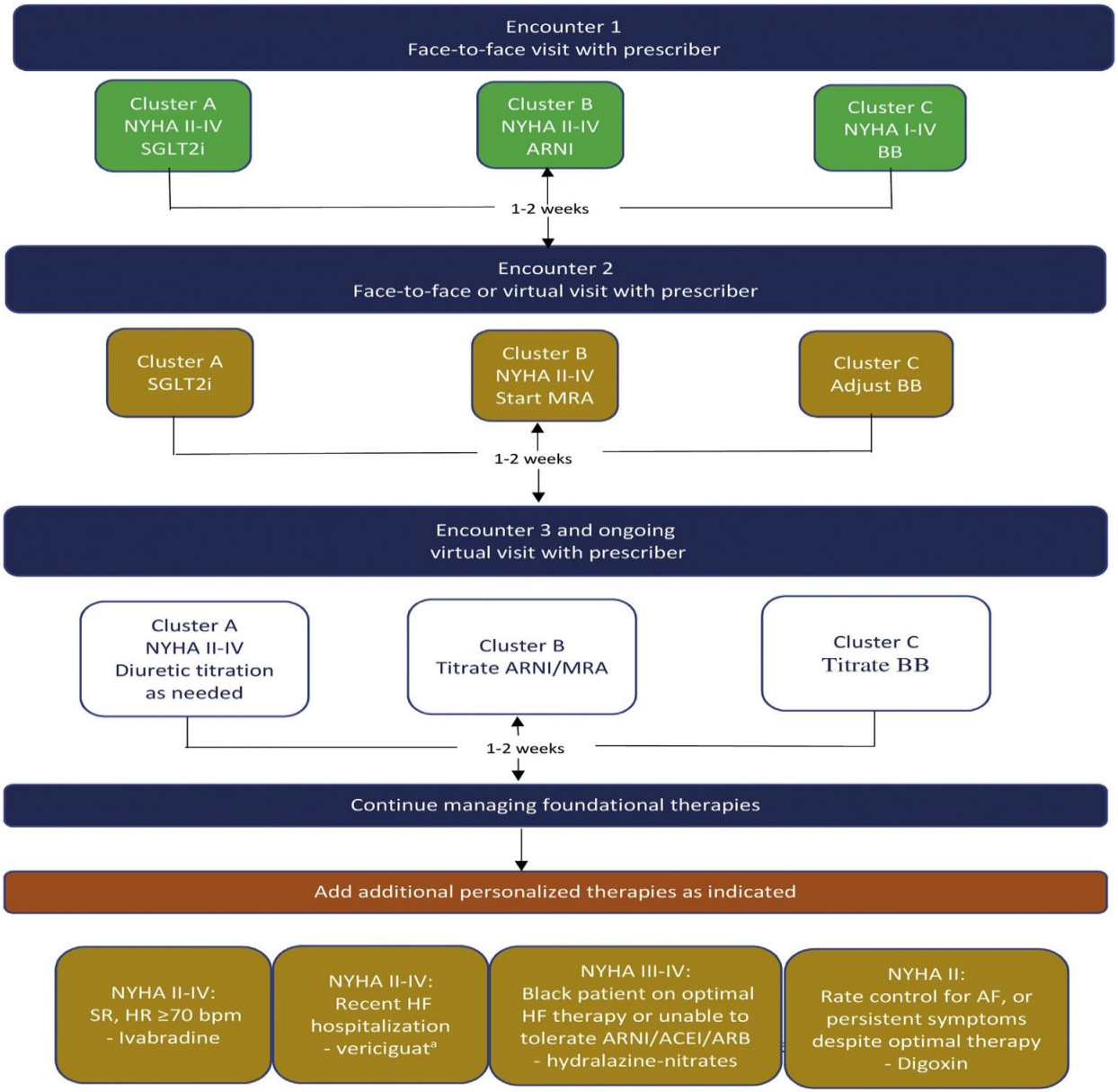
# Pillars of Guideline Directed Medical Therapy in HFrEF




Updated from Fonarow GC, et al. Am Heart J 2011;161:1024-1030 and Lancet 2008;372:1195-1196; Bassi NS et al JAMA Cardiol 2020, May 6, e200898

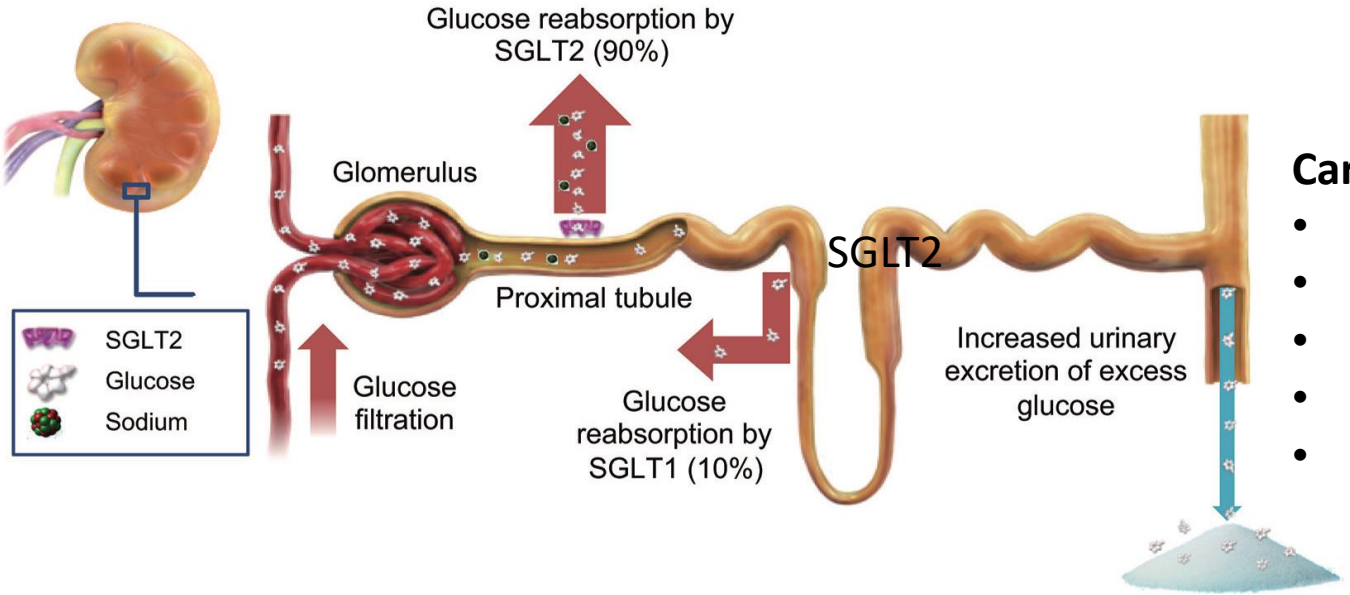
# Cluster Approach to HFrEF Therapy

- Cluster A - SGLT2i and Loop diuretics
- Cluster B - ARNI/ACEI/ARBs and  MRAs
- Cluster C - Beta blockers
- Uptitrate every 1-2 weeks.
- Patients with SBP > 110, HR >70, eGFR >40, K 5 - 3 drug class changes per visit with a low risk of adverse events.
- Weaker patients – change 1 drug class every two weeks.
- Don’t add any additional therapies until all 4 drug classes are optimized.




El Hussein, M. T., & Negash, S. (2022). Cluster Scheme Approach to Foundational Heart Failure With Reduced Ejection Fraction Therapy. The Journal for Nurse Practitioners, 18(6), 628-635.

# SGLT2i (Sodium–Glucose coTransporter–2 inhibitor)

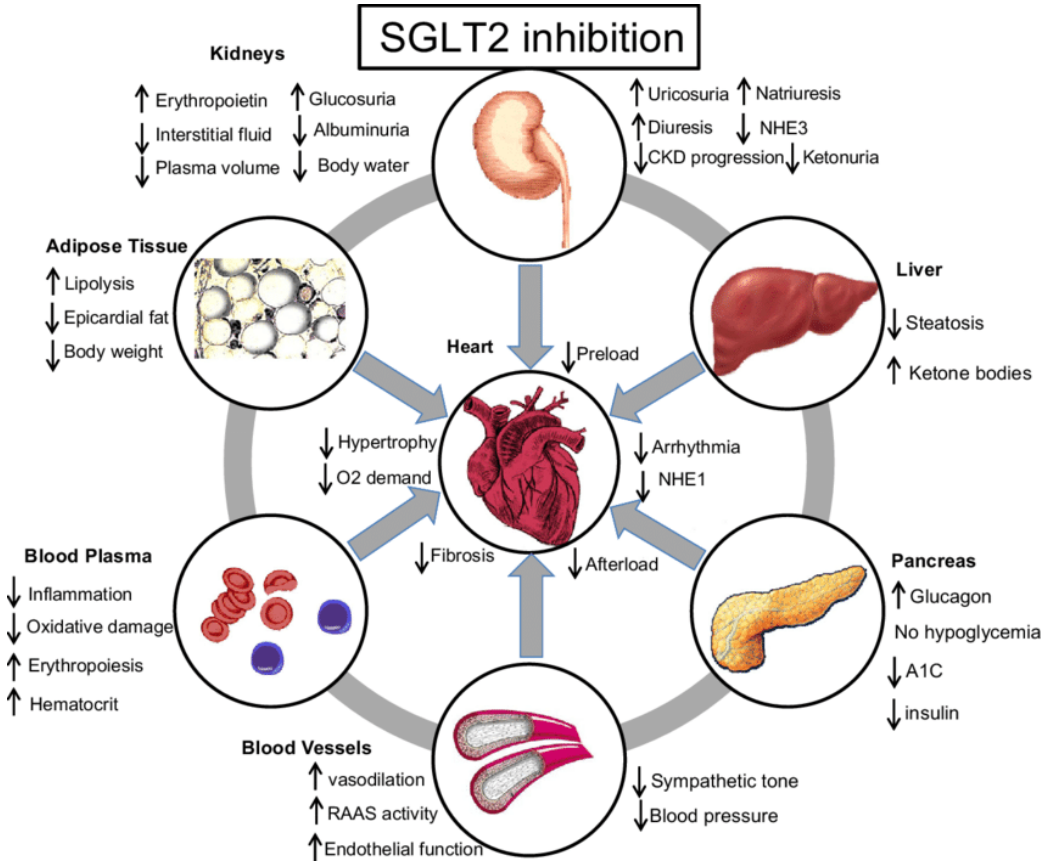



**Cardiovascular Benefits**

- Diuresis
- Natriuresis
- A1C reduction
- Weight loss
- BP reduction

# Cardiovascular Benefit

- Improving glucose control
- Weight loss
- Minimal reduction in SBP, no increase in HR.
- Reduces arterial stiffness and vascular resistance
- Increases HDL
- Reduces albuminuria
- Improved renal function
- Decreases visceral adiposity
- Osmotic diuresis/Natriuresis
- Improving cardiac energy metabolism
- Preventing inflammation
- Inhibiting the sympathetic nervous system
- Preventing adverse cardiac remodeling


SGLT2 inhibition
Kidneys
↑ Erythropoietin
↓ Interstitial fluid
↓ Plasma volume
↑ Glucosuria
↓ Albuminuria
↓ Body water
↑ Uricosuria
↑ Natriuresis
↑ Diuresis
↓ NHE3
↓ CKD progression
↓ Ketonuria
Adipose Tissue
↑ Lipolysis
↓ Epicardial fat
↓ Body weight
Liver
↓ Steatosis
↑ Ketone bodies
Heart
↓ Preload
↓ Hypertrophy
↓ O2 demand
↓ Arrhythmia
↓ NHE1
↓ Fibrosis
↓ Afterload
Blood Plasma
↓ Inflammation
↓ Oxidative damage
↑ Erythropoiesis
↑ Hematocrit
Pancreas
↑ Glucagon
No hypoglycemia
↓ A1C
↓ insulin
Blood Vessels
↑ vasodilation
↑ RAAS activity
↑ Endothelial function
↓ Sympathetic tone
↓ Blood pressure

# Summary of Clinical Trials for SGLT2i

| | Dapagliflozin (Farxiga) | Empagliflozin (Jardiance) |
|---|---|---|
| **HFrEF** | DAPA-HF | EMPEROR-Reduced |
| **HFpEF** | PRESERVED_HF<br>DELIVER | EMPEROR-Preserved |
| **Acute HF** | DAPA ACT HF-TIMI 68 | EMPULSE |
| **Acute MI** | DAPA-MI | EMPACT-MI |

# HFrEF

| | DAPA-HF | EMPEROR-Reduced |
|---|---|---|
| **Intervention** | Farxiga 10mg and GDMT versus placebo and GDMT (1:1) | Jardiance 10mg versus placebo |
| **Inclusion Criteria** | ≥ 18 years old<br>NYHA class II-IV (LVEF ≤ 40%<br>eGFR≥ 30<br>55% without Type II DM | Age ≥18<br>NYHA class II-IV (LVEF ≤ 40%)<br>eGFR ≥20<br>50% without DM |
| **Sample Size** | 4744 patients | 3730 patients |
| **Primary outcome** | Composite of worsening HF (hospitalization or UC visit requiring IV therapy) or CV death | Composite of worsening HF (hospitalization or UC visit requiring IV therapy) or CV death |
| **Duration** | 18 months | 16 months |

# Conclusions

- DAPA-HF trial concluded that individuals with HFrEF who received Dapagliflozin (Farxiga) had a reduced risk of worsening HF or CV death compared with placebo. The risk of having the first incident worsening HF, hospitalization for HF/Urgent HF visits and the risk of CV mortality was reduced.
- EMPEROR-reduced–HF trial establish low CV mortality and HF hospitalization rates regardless of DM status in patients who are given Empagliflozin (Jardiance).
- All cause deaths and CV deaths were also lower in both landmark trials.
- Empagliflozin resulted in the 20% to 40% improvement in NYHA functional class.
- Dapagliflozin reduced the decline in EGFR and renal outcomes.

# HFpEF

| | DELIVER | EMPEROR-Preserved |
|---|---|---|
| **Intervention** | Dapagliflozin 10 mg daily versus placebo (1: 1) | Empagliflozin 10 mg daily versus placebo (1: 1) |
| **Inclusion Criteria** | Age ≥ 40 y. o. with symptomatic NYHA class II-IV HF; LVEF > 40% and evidence of structural heart disease; eGFR ≥ 25 mL/min; off IV HF therapies for > 24 hours | age ≥ 18 years old with NYHA class II-IV heart failure and stable p.o. diuretic dose; left ventricular ejection fraction > 40% and evidence of structural heart disease; GFR ≥ 20 mL/min; no episodes of AD HF within 1 week |
| **Sample Size** | 6263 patient's | 5988 patient's |
| **Primary outcome** | time to first occurrence of any component of the Compass cardiovascular death or heart failure events in patients with left ventricular ejection fraction less than 60% | Time to first occurrence of any component of the Compass of cardiovascular death or heart failure hospitalized |
| **Duration** | 39 months | 38 months |

# Conclusions

## EMPEROR-preserved

Empagliflozin reduced the combined risk of CV death or hospitalization for HF in patients with HFpEF regardless of the presence or absence of diabetes.

## DELIVER Trial

Dapagliflozin reduced cardiovascular death or HF events across the spectrum of age, with a consistent safety profile, including among the traditionally under-treated older segment of patients >= 75 years of age.

# Acute HF Trials

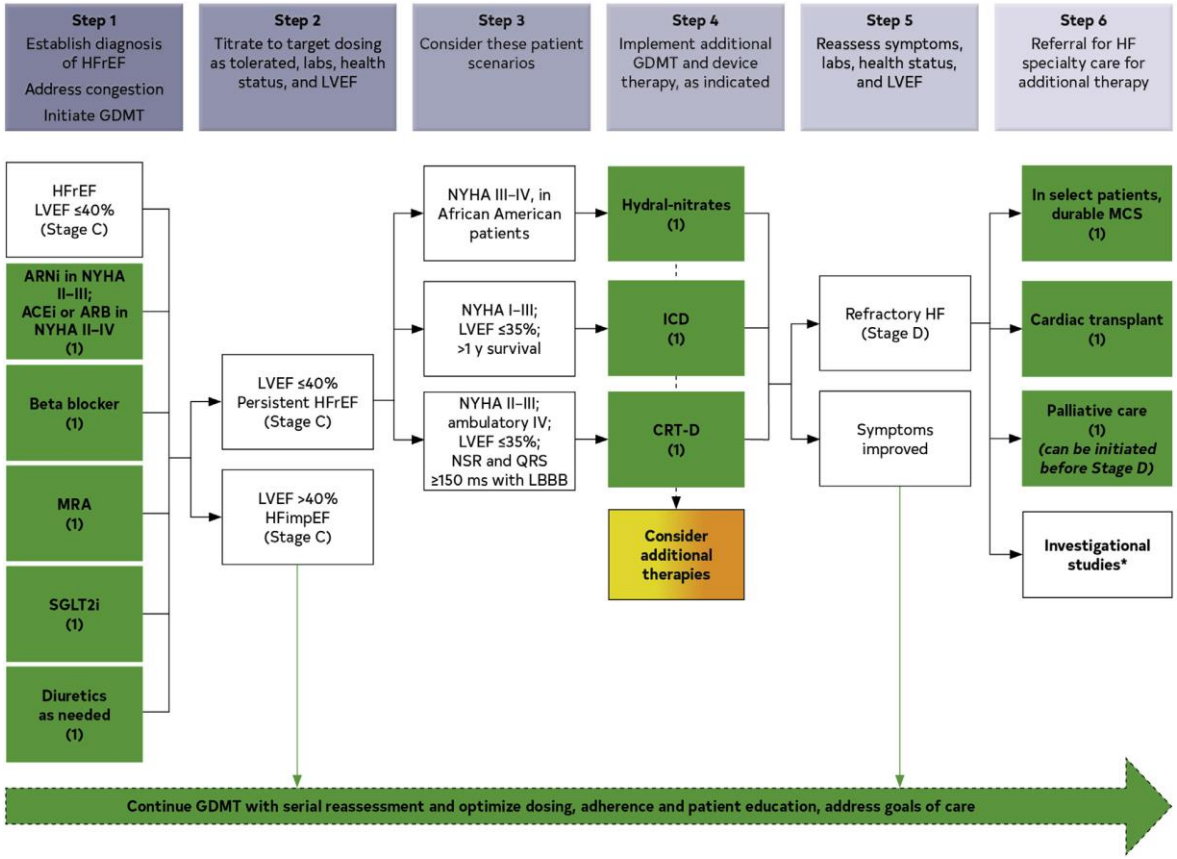
| | Data ACT HF–TIMI 68 | EMPULSE |
|---|---|---|
| **Interventions** | Dapagliflozin 10 mg daily versus placebo (1: 1) | Empagliflozin 10 mg daily versus placebo (1:1) |
| **Treatment timing** | from greater than or equal to 24 hours to day 7 of admission until 60 days | from within 24 hours to day 5 of admission until 90 days |
| **Patient population** | Age ≥18 years old; currently hospitalized for AHF and stabilized; LVEF less than or equal to 40% within last 12 months; eGFR ≥ to 30 mL/min | Age ≥18 years old; hospitalized for CHF (any LVEF) and stabilized; dyspnea with/≥ 2 Sxof heart failure; ≥ 40 mg IV furosemide's or equivalent; EGFR ≥ to 20 mls/minute |
| **Sample size:** | 2400 patients (estimated) | 530 patient's (actual) |
| **Primary outcome** | Time to first occurrence of cardiovascular death or worsening heart failure | Clinical benefit at 90 days (come for set of time to all because day, #of heart failure events, time to first heart failure event and increase in KCCQ score) |
| **Completion** | quarter 1 of 2023 (estimated) | |

# Conclusions

## EMPULSE

- Initiation of empagliflozin during hospitalization for acute HF provided clinical benefit regardless of the degree of symptomatic impairment at baseline, and improved symptoms, physical limitations, and quality of life, with benefits seen as early as 15 days and maintained through 90 days.
- Dapagliflozin is currently being tested in the DAPA ACT HF-TIMI 68 trial in patients hospitalized with acute HF.

# Treatment of HFrEF Stages C and D

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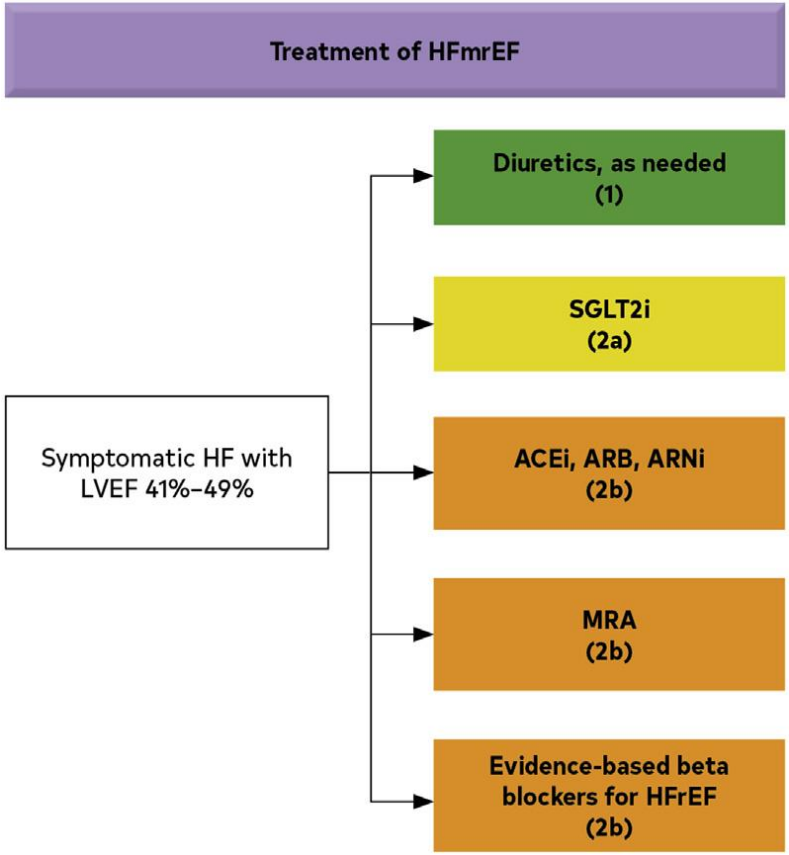
# Recommendations for Patients With Mildly Reduced LVEF (41%–49%)

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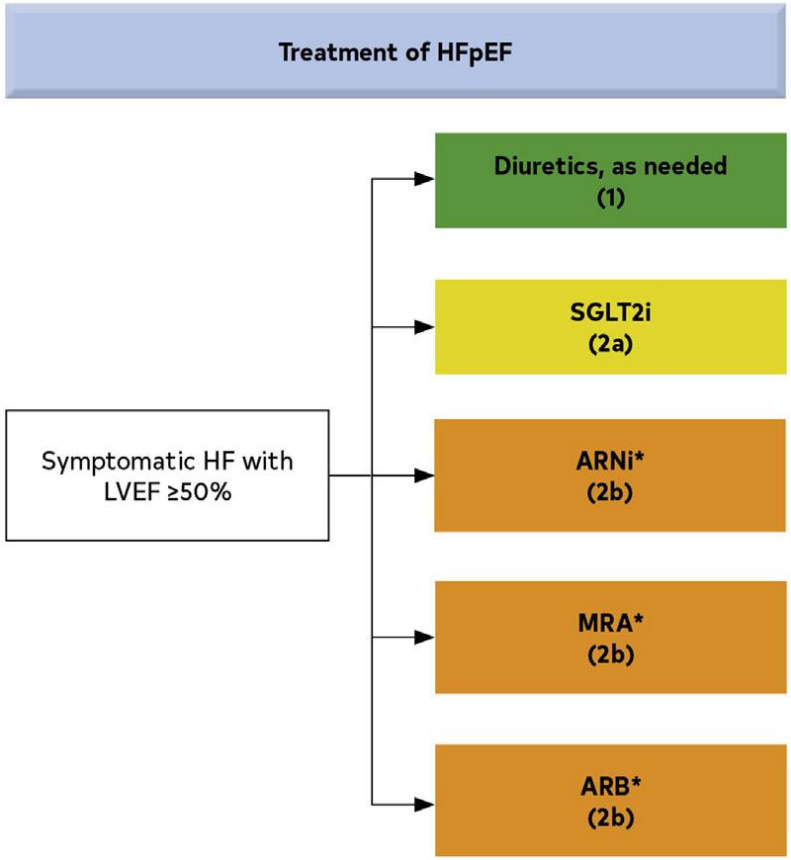
# Recommendations for Patients With Preserved LVEF (≥ 50%)

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# SGLT2i FDA approved for HF

- **Dapagliflozin (Farxiga) 10mg QD**
  - Caution if eGRF is < 25 ml/min
  - FDA Approved for **HFrEF**
  - Also FDA approved for CKD and Type II DM
- **Empagliflozin (Jardiance) 10mg QD**
  - Caution if eGFR< 20 ml/min
  - FDA Approved for both **HFrEF** and **HFpEF**
  - Also FDA approved for Type II DM

**1 dose per day with no need to up titrate.**

# Prescribing Considerations

- Cost
- eGFR
- NYHA class II-IV
- Diuretics
- Diabetes medications

# Contraindications

- Hemodialysis
- Pregnancy/breast feeding (no data)
- Type I DM (increased risk of DKA)

**Caution**

- History of ketoacidosis in Type II DM patients
- Volume depletion- always know volume status before initiation. Correct before prescribing
- Hx of UTIs or pyelonephritis
- Hx of AKI

# Adverse effects

- Hypotension
- Polyuria- Dehydration -Acute kidney injury
- UTI/ pyelonephritis
- Genital mycotic infections

**Rare**

- Ketoacidosis (Euglycemic DKA)
- Necrotizing fasciitis of the perineum (Fournier's Gangrene)

# Monitoring

- A1C and blood glucose levels in diabetics
  - May need to adjust insulin or sulfonylureas
- Renal Function
- Volume status
  - Monitor for hypovolemia, adjust diuretics if needed.
- Blood pressure
- Euvolemic Ketoacidosis

# Other Benefits

- Reduced risk of hyperkalemia
- Minimal effect on blood pressure
- Slow progression of renal failure
- Reduced risk of ESRD

# Mr. Ed Deehma

**Patient History**

62 year old male, Hx of HTN, PAD, CKD

- Hospitalized with new diagnosis of HF
- NKDA

**Social History**

- Former smoker, quit 20 yrs ago, 20 yr pack Hx
- Social ETOH, 1-2 glasses wine per week
- CPA with good health insurance

**Presentation**

- NYHA class III

# Clinical Course

- Hospitalized and diuresed with IV loop diuretics- signs and symptoms improved.
- TTE – LVEF 30% with mod MR
- Labs: K+ 4.4, GFR 46, Creat 1.71, NT-Pro BNP 2400
- Coronary angiogram – non-obstructive CAD

# Physical Exam at discharge

- HR 78 bpm
- BP 98/58
- Euvolemic
- JVP mildly elevated, regular heart sounds, clear lungs, 0 LE edema
- Discharged on Carvedilol 6.25 mg BID, Lisinopril 5 mg QD, Spironolactone 12.5 mg, Lasix 40 mg QD.

# Follow up appointment 2 weeks later

**Vitals and Labs**

- BP 100/60
- HR 77
- K 4.3, eGFR 46
- Euvolemic on exam

**Options**

- Uptitrate current GDMT
- Change Lisinopril to Entresto
- Start SGLT2i

**Considerations**: Blood pressure, volume status, renal function, cost

# Plan

- Change Carvedilol to Metoprolol succinate 25 mg QD to reduce the effect on blood pressure
- Reduce the dose of Lasix by 25% to avoid dehydration
- Start Dapafliglozin 10mg QD
- Continue Lisinopril and Spironolactone.
- Monitor blood pressures and volume status at home. Daily weights in case need to increase diuretic.
- Check urinalysis for ketones at 1 week and 1 month. Check BMP in 1 month.
- Follow up in 2 weeks with plan to change Lisinopril to Entresto if blood pressure allows.

# Questions?

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