Heart Failure-Stop Failing

AAPA 2023

Nashville, Tennessee

Presented by: Jaan Kelly, DMS, MSPAS, PA-C

Objectives

1. Recognize the financial and societal burdens of heart failure
2. Discuss the multi-system pathophysiology associated with congestive heart failure
3. Apply current cardiac nomenclature to clinical practice and an interactive case study
4. Discuss the 2022 ACC/AHA/HFSA guidelines for management of heart failure
5. Identify new FDA approved interventions for the treatment of heart failure
6. Integrate the 2022 ACC/AHA/HFSA guidelines for management of heart failure in a case study

Heart Failure Nomenclature

Type of HF According to LVEF	Criteria
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)

Case 1: HFrEF

- 37-year-old woman with 6-year hx DCM LVEF 30% presents for yearly ov.
- PMHx: DM (HbA1C 7.4), HTN, obesity, tobacco abuse remote, ICD
- Current Rx: Carvedilol 6.25 mg po BID, Spironolactone 25 mg po daily, Entresto 24/26 mg po BID, Metformin 500 mg po BID
- Diagnostics: Cath 2021 no CAD, echo 2/22 LVEF 30%, est RVSP 22mg, mild valvular disease; GFR > 90
- ROS: NYHA class II
- Physical Exam: BP 128/78, HR 72, warm/dry

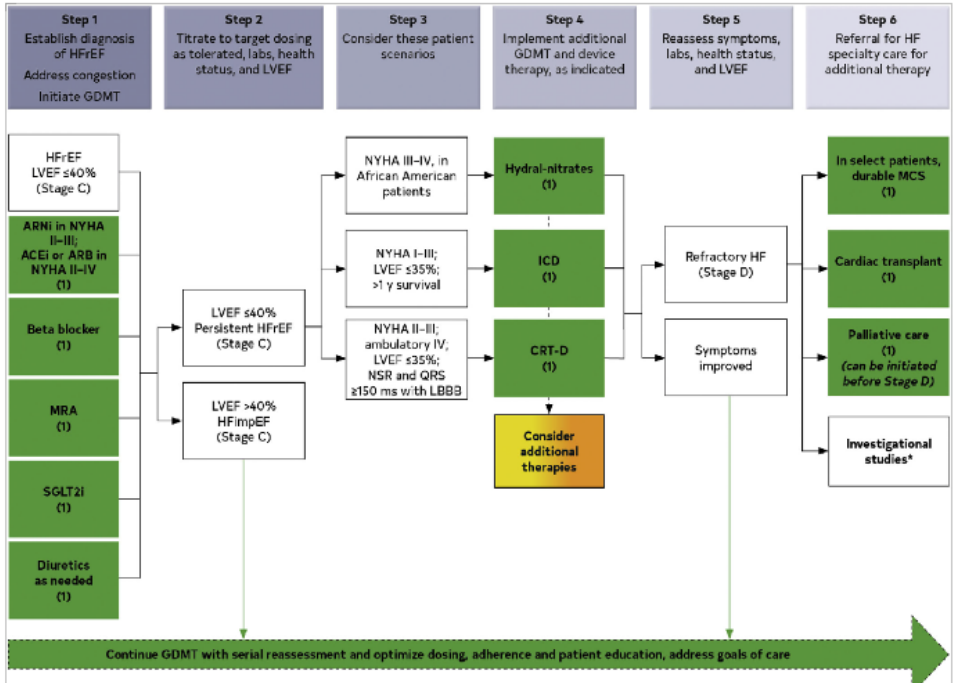
1. GDMT for **HFrEF**(LVEF <40) includes 4 medication classes

SGLT2i: Dapagliflozin, Empagliflozin

RAAS: ARNI/ACE-I/ARB

Beta-blocker: Carvedilol, Metoprolol ER, Bisoprolol

MRA: Spironolactone



COR	LOE	Recommendations
1	A	In patients with HFrEF and NYHA class II to III symptoms, the use of **ARNi** is recommended to reduce morbidity and mortality
1	A	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
1	B - R	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	A	In patients with HFrEF, with current or previous symptoms, use of 1 of the 3 **beta blockers** proven to reduce mortality is recommended to reduce mortality and hospitalizations
1	A	In patients with HFrEF and NYHA class II to IV symptoms, an **MRA** is recommended to reduce morbidity and mortality, if eGFR >30 mL/min/ 1.73 m2 and serum potassium is <5.0 mEq/L
1	A	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

2022 ACC/AHA/HFSA Guideline for the Management of Heart Failure - DOI: 10.1016/j.cardfail.2022.02.010

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Benefit of Evidence-Based Therapies HFrEF

Evidence-Based Therapy	Relative Risk Reduction in All-Cause Mortality in Pivotal RCTs, %	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†	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
CRT	36	12 over 24 mo	24	8
ICD	23	14 over 60 mo	70	23

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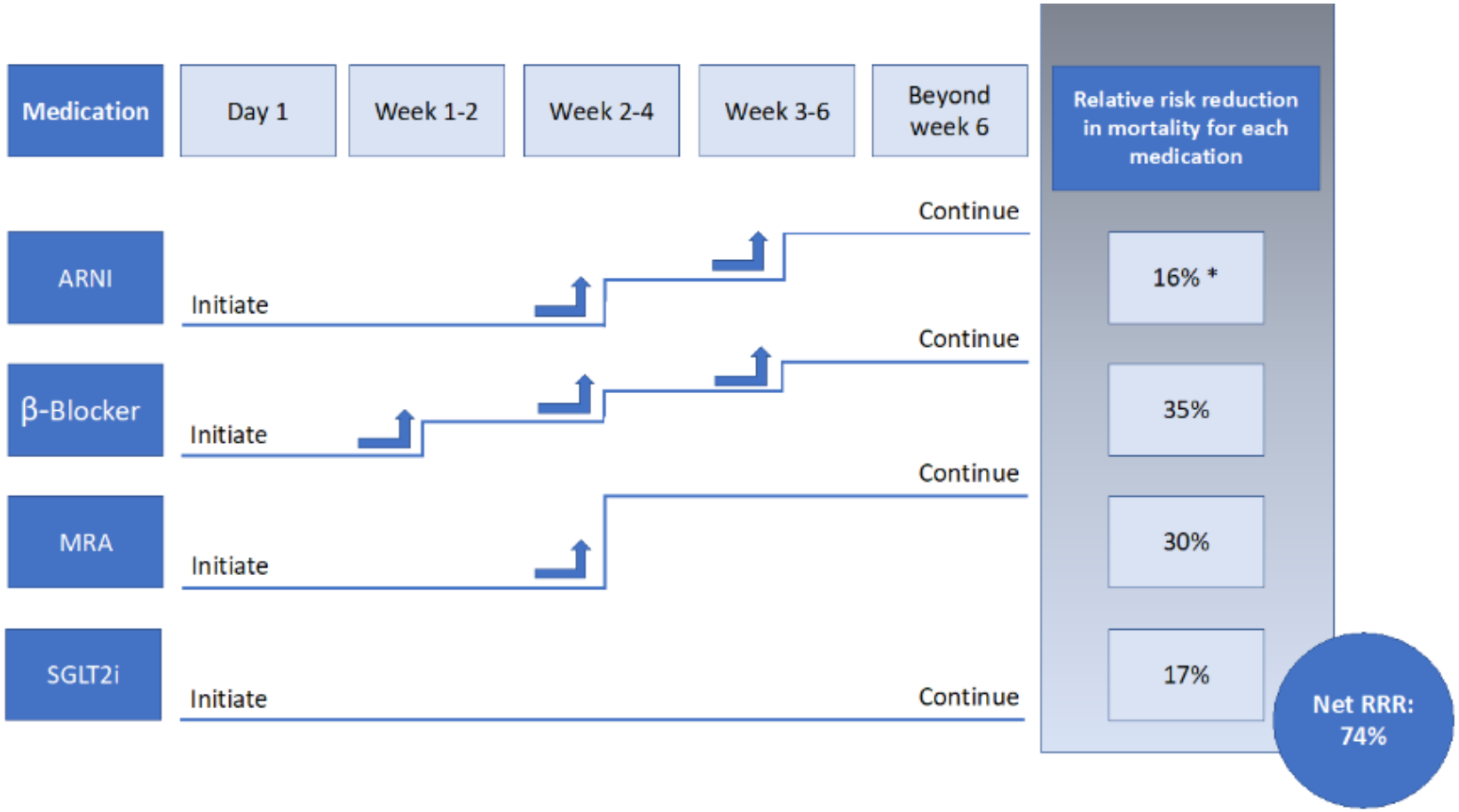
Recommendations for Renin-Angiotensin System Inhibition: ACEi or ARB or ARNi?

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]

Simultaneous Initiation and Rapid Titration

COR	LOE	Recommendations
1	A	1. In patients with HFrEF, titration of guideline-directed medication dosing to achieve target doses showed to be efficacious in RCTs is recommended, to reduce cardiovascular mortality and HF hospitalizations, unless not well tolerated.[1–10]
2a	C-EO	2. In patients with HFrEF, titration and optimization of guideline-directed medications as frequently as every 1 to 2 weeks depending on the patient's symptoms, vital signs, and laboratory findings can be useful to optimize management.



American College of Cardiology

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- <u>Recommendations per Current Guidelines</u>

Titrate

Carvedilol 25 mg po BID (Ia)

Entresto 97/103 mg (Ia)

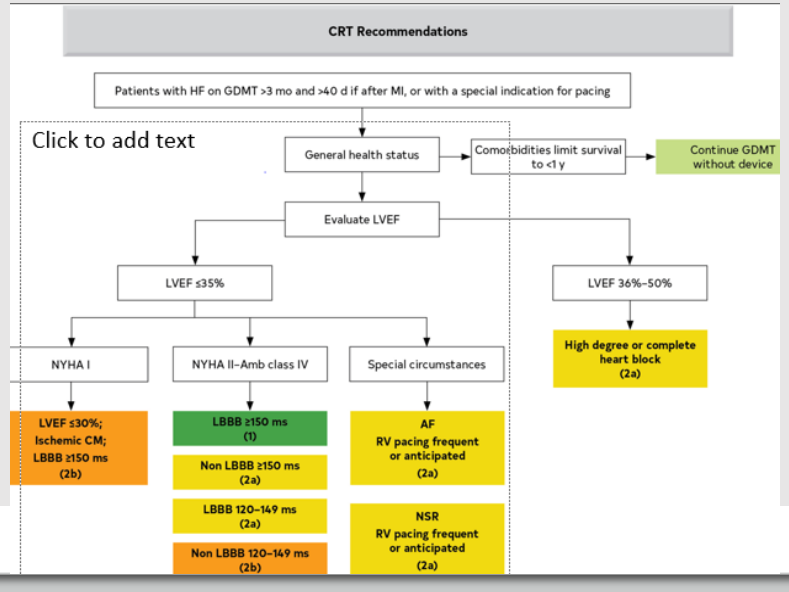
Start

SGLT2i (Ia)

***reduce CV death/HF hosp**

Other considerations

Does she qualify for Bi-V? (QRS > 150ms)



Case 2: HFmrEF

- 57-year-old man with DOE
- PMHx: CAD hx PCI 2019, HTN, obesity, CKD stage II, LVEF 45%
- Current Rx: Asa 81 mg daily, Atorvastatin 40mg @ hs, Lisinopril 10 mg po BID
- Diagnostics: Echo EF 45%, mild valvular disease, est. RVSP 28mmHg; GFR 65, HbA1c 6.0
- ROS: NYHA class III
- Physical Exam: BP 110/78, HR 88, warm/dry

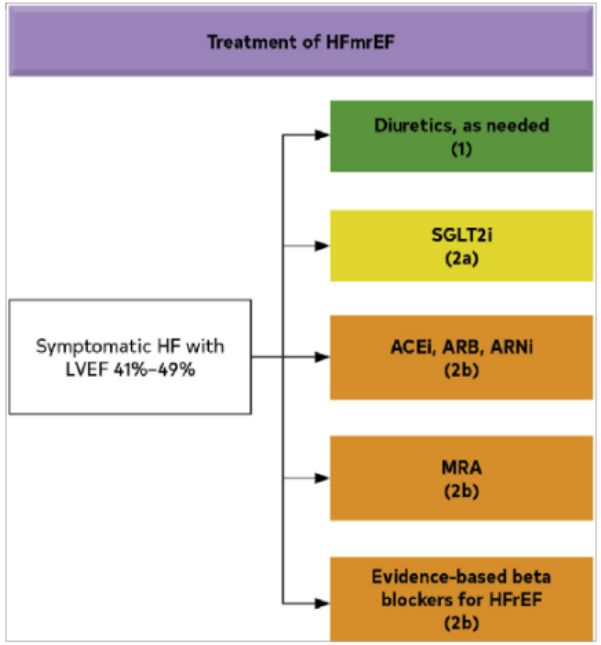
2. Guideline-directed medical therapy for **HFmrEF** (LVEF 41-49%) now includes:

SGLT2i: Dapagliflozin, Empagliflozin

RAAS: ARNI/ACE-I/ARB

Beta-blocker: Carvedilol, Metoprolol ER, Bisoprolol

MRA: Spironolactone



COR	LOE	Recommendations
2a	B - R	In patients with HFmrEF, **SGLT2i** can be beneficial in decreasing HF hospitalizations and cardiovascular mortality
2b	B - NR	Among patients with current or previous symptomatic HFmrEF, use of evidence-based beta blockers for HFrEF, **ARNi, ACEi, or ARB, and MRAs** may be considered, to reduce the risk of HF hospitalization and cardiovascular mortality, particularly among patients with LVEF on the lower end of this spectrum

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Case 2: HFmrEF

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<u>Recommendations per Current guidelines</u>

Stop Lisinopril and start ARNI (IIb)

Start SGLT2i (IIa)

Start MRA (IIb)

Start Carvedilol (IIb)

- Heart Failure patient goals:
  - Maintain/restore NSR (IIa)
  - BMI < 27.0 (daily exercise > 35 minutes, Mediterranean, DASH)
  - Blood pressure < 120
  - Treat underlying sleep disorder
  - Average heart rate < 70 bpm

Case 3: HFpEF

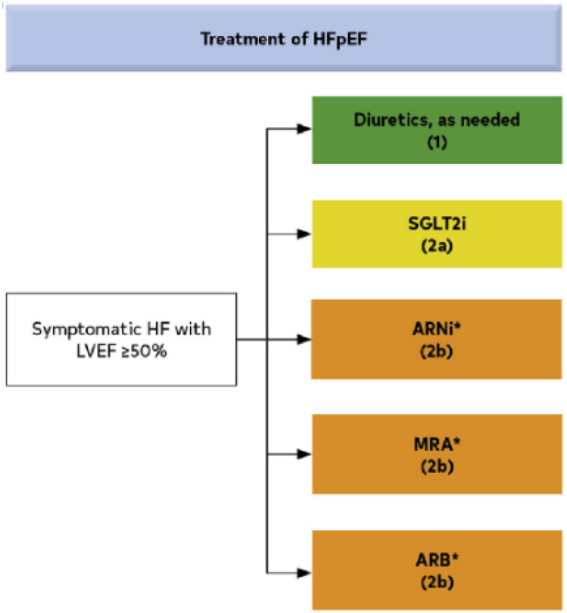
- 64-year-old man follow-up post-hospitalization for Acute HF
- PMHx: DM (HbA1C 6.9),CKD stage II, HTN, CAD hx CABG 2020
- Current Rx: Asa 81 mg daily, Atorvastatin 40mg @ hs, valsartan 80 mg daily
- Diagnostics: Echo LVEF 50%, mild valvular disease; GFR 65, HbA1c 6.9
- ROS: NYHA class II
- Physical Exam: BP 140/88, HR 88, warm/dry

3. Guideline-directed medical therapy for **HFpEF** (LVEF > 50)now includes:

SGLT2i: Dapagliflozin, Empagliflozin

RAAS: ARNI/ACE-I/ARB

MRA: Spironolactone



COR	LOE	Recommendations
2a	B - R	In patients with HFpEF, **SGLT2i** can be beneficial in decreasing HF hospitalizations and cardiovascular mortality
2b	B - R	In selected patients with HFpEF, **MRAs** may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum
2b	B - R	In selected patients with HFpEF, **ARNi** may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum

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- Diagnostics: Echo EF 50%, mild valvular disease; GFR 65, HbA1c 6.9
- ROS: NYHA class II
- Physical Exam: BP 140/88, HR 88, warm/dry

<u>Recommendations per Current Guidelines</u>

Stop Valsartan and start Entresto (IIb)

Start SGLT2i (IIa)

Start MRA (IIb)

Case 4: HFimpEF

Patient presents previous DCM 35% now on maximally tolerated GDMT presents with preclinic echo LVEF now 46%

Current Rx:

- Carvedilol 12.5 mg po BID
- Entresto 97/103 mg po BID
- Dapagliflozin 10 mg po daily
- Spironolactone 25 mg po daily

“If my heart muscle is healed and stronger, do I still have to take all of these medications?”

4. **HFimpEF** refers to HFrEF where LVEF is now > 40%; these patients should continue HFrEF

COR	LOE	Recommendations
1	B - R	In patients with HFimpEF after treatment, GDMT should be continued to prevent relapse of HF and left ventricular dysfunction, even in patients who may become asymptomatic

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5. Value Statements for Recommendations

- HF causes more hospitalizations than all forms of cancer combined; it is the most common cause of hospitalization in people > 65 years
- Average cost of hospitalization for HF: $ 17,830*
- Average cost of ED evaluation for HF: $3,526*
- Average cost of GDMT HF Rx in 2023: $ 1,166 a year (Medicare patient)**
- Estimated that HF hospitalization in USA costs $18 billion a year*

Level	Statements
High	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
High	In patients with chronic symptomatic HFrEF, treatment with an **ARNi** instead of an ACEi provides high economic value
High	In patients with HFrEF, with current or previous symptoms, **beta-blocker** therapy provides high economic value
High	In patients with HFrEF and NYHA class II to IV symptoms, **MRA** therapy provides high economic value
High	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
High	A **transvenous ICD** provides high economic value in the primary prevention of sudden cardiac death particularly when the patient's risk of death caused by ventricular arrythmia is deemed high and the risk of nonarrhythmic death is deemed low based on the patient's burden of comorbidities and functional status
High	For patients who have LVEF ≤35%, sinus rhythm, LBBB with a QRS duration of ≥150 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT, **CRT implantation** provides high economic value

Level	Statements
Intermediate	In patients with symptomatic chronic HFrEF, **SGLT2i** therapy provides intermediate economic value
Intermediate	In patients with stage D (advanced) HF despite GDMT, **cardiac transplantation** provides intermediate economic value
Low	At 2020 list prices, **tafamidis** provides low economic value (>$180,000 per QALY gained) in patients with HF with wild-type or variant transthyretin cardiac amyloidosis
Uncertain	In patients with advanced HFrEF who have NYHA class IV symptoms despite GDMT, **durable mechanical circulatory support devices** provide low to intermediate economic value based on current costs and outcomes
Uncertain	In patients with NYHA class III HF with a HF hospitalization within the previous year, wireless monitoring of the pulmonary artery pressure by an **implanted hemodynamic monitor** provides uncertain value

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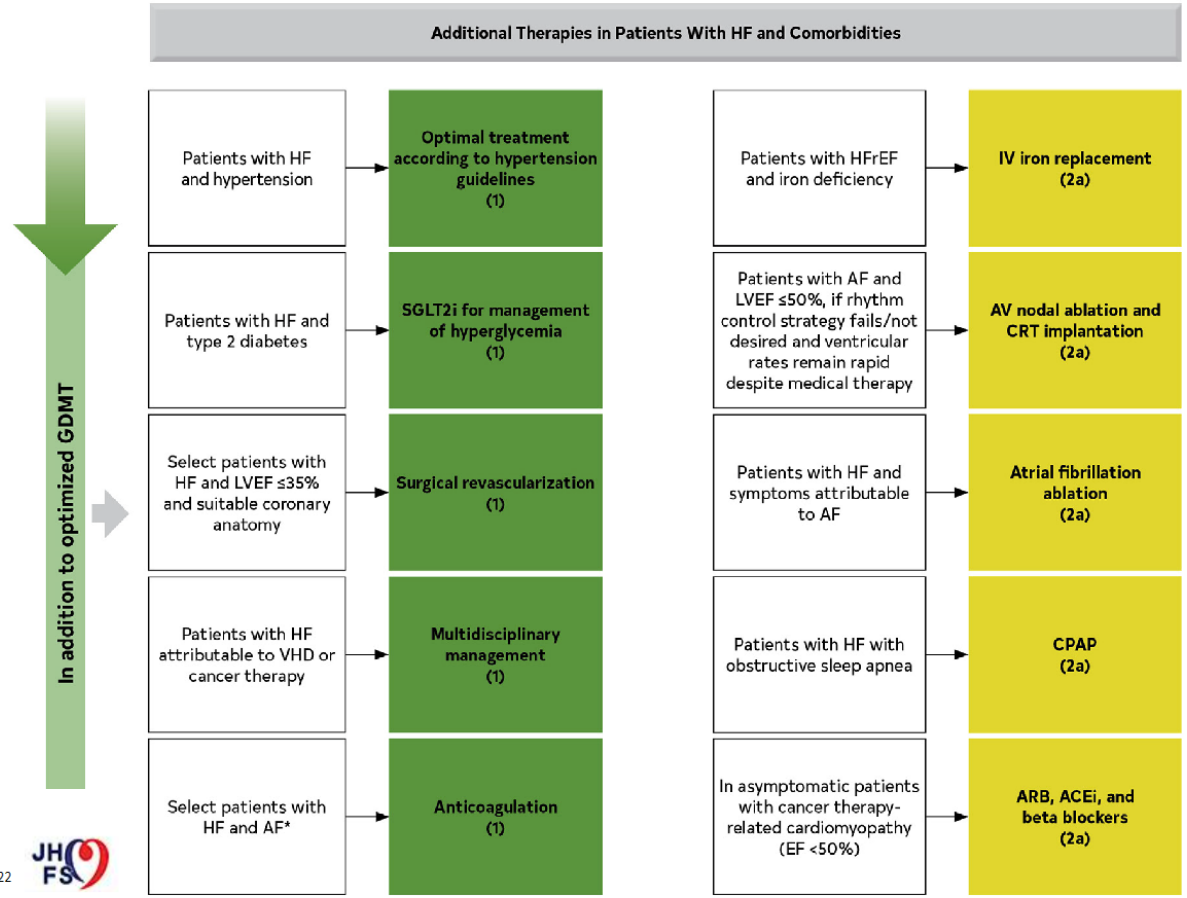
6. Current HF guidelines include recommendations for HF patients with iron deficiency, anemia, hypertension, sleep disorders, atrial fibrillation, coronary artery disease, and malignancy



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7. Patients with advanced HF who wish to prolong survival should be referred to a team specializing in HF including palliative care consistent with the patient's goals of care

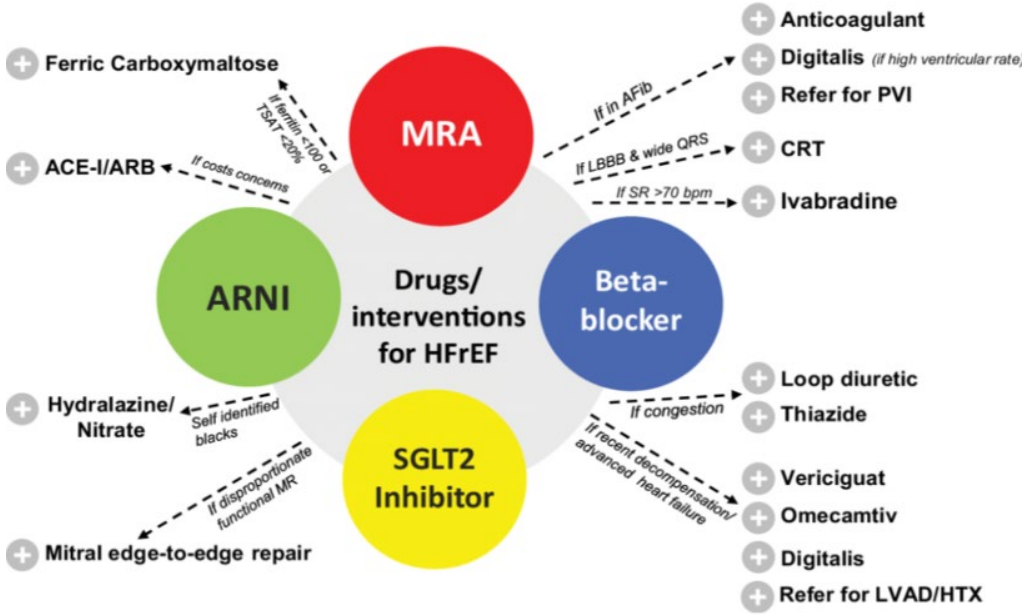
COR	LOE	Recommendations
1	C – LD	In patients with advanced HF, when consistent with the patient's goals of care, timely **referral for HF specialty** care is recommended to review HF management and assess suitability for advanced HF therapies (e.g., left ventricular assist devices, cardiac transplantation, palliative care, and palliative inotropes)

- After a single hospitalization, mortality risk at 1 year of 34%
- "advanced HF" diagnosis 50-80% mortality in 1 year

AHA Statistical Update 2014

Improved survival in patients with chronic mild/moderate systolic heart failure followed up in a Heart Failure clinic

Fragasso, Gabriele; Marinosci, Giovanni; Calori, Giliola; Spoladore, Roberto; Arioli, Francesco; Bassanelli, Giorgio; Salerno, Anna; Cuko, Amarild; Puccetti, Patrizia; Silipigni, Carmela; Palloshi, Altin; Margonato, Alberto



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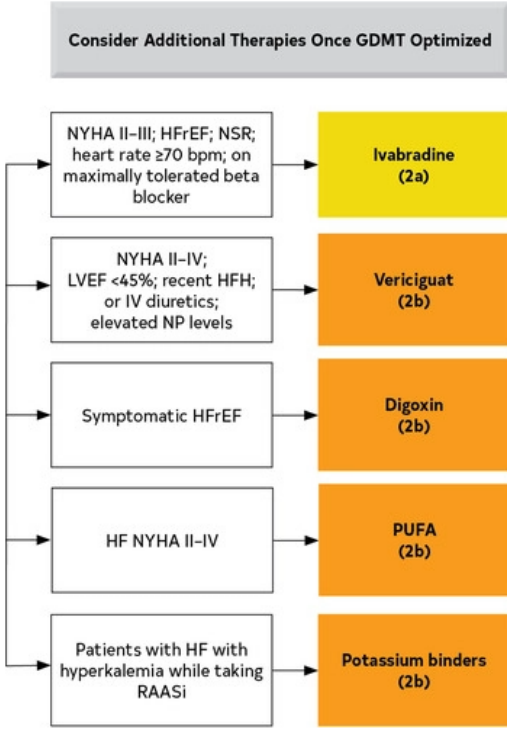
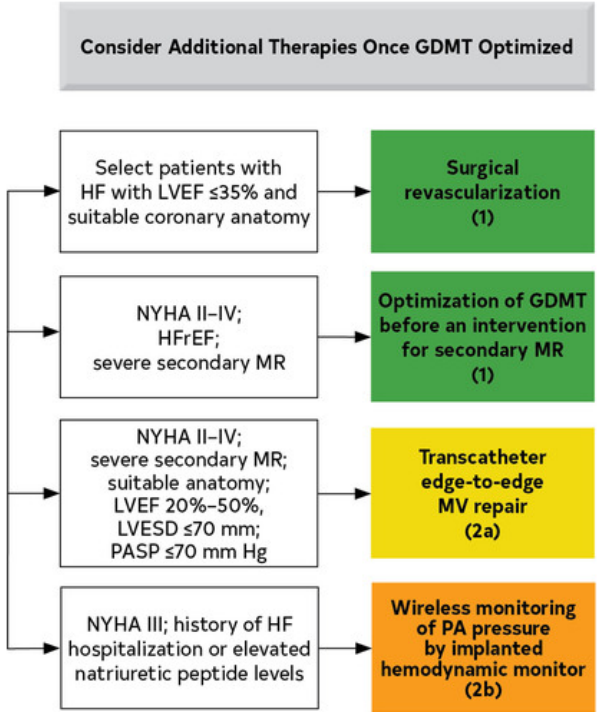
This is a lot of stuff!

- Rx
- ICD/CRT
- PA monitoring device
- Secondary MR (Mitral valve repair/ Mitra clip), TAVR
- Inotropes
- Mechanical Circulatory Support: LVAD, RVAD
- Transplant: bridge to recovery or bridge to decision





COR	LOE	Recommendations
1	A	1. In select patients with advanced HFrEF with NYHA class IV symptoms who are deemed to be dependent on continuous intravenous inotropes or temporary MCS, durable LVAD implantation is effective to improve functional status, QOL, and survival.[1–18]
2a	B-R	2. In select patients with advanced HFrEF who have NYHA class IV symptoms despite GDMT, durable MCS can be beneficial to improve symptoms, improve functional class, and reduce mortality.[2,4,7,10,12–17,19]
Value Statement: Uncertain Value (B-NR)		3. In patients with advanced HFrEF who have NYHA class IV symptoms despite GDMT, durable MCS devices provide low to intermediate economic value based on current costs and outcomes.[20–24]
2a	B-NR	4. In patients with advanced HFrEF and hemodynamic compromise and shock, temporary MCS, including percutaneous and extracorporeal ventricular assist devices, are reasonable as a "bridge to recovery" or "bridge to decision."[25–29]

COR	LOE	Recommendations
2a	B-NR	1. In patients with advanced (stage D) HF refractory to GDMT and device therapy who are eligible for and awaiting MCS or cardiac transplantation, continuous intravenous inotropic support is reasonable as "bridge therapy."[1–4]
2b	B-NR	2. In select patients with stage D HF, despite optimal GDMT and device therapy who are ineligible for either MCS or cardiac transplantation, continuous intravenous inotropic support may be considered as palliative therapy for symptom control and improvement in functional status.[5–7]
3: Harm	B-R	3. In patients with HF, long-term use of either continuous or intermittent intravenous inotropic agents, for reasons other than palliative care or as a bridge to advanced therapies, is potentially harmful.[5,6,8–11]

Stop Failing!

CHAMP-HF Registry 5/2019

Contemporary Utilization of HF Drugs in the US

- **Only 13% of eligible pts were receiving aldosterone blockade at baseline**
- **Over 12 months, only 22% of eligible patients were simultaneously treated with any dose of all 3 drug classes (ACE-I/ARB/ARNI, beta blocker, MRA)**
- **Other than a modest bump in ARNI use, there was essentially no drug up-titration within any class over the observation period**
- **Target dose utilization rates did not exceed 25% for any drug class**
- **Over 12 months, <1% of pts simultaneously received target doses of all 3 drug classes**

JACC Journals › JACC: Heart Failure › Archives › Vol. 11 No. 1

Heart Failure Drug Treatment—Inertia, Titration, and Discontinuation: A Multinational Observational Study (EVOLUTION HF)

OPEN ACCESS

Clinical Research

Gianluigi Savarese, Takuya Kishi, Orly Vardeny, Samuel Adamsson Eryd, Johan Bodegård, Lars H. Lund, Marcus Thuresson, and Biykem Bozkurt

Perspectives

COMPETENCY IN MEDICAL KNOWLEDGE: HF guidelines recommend early and rapid initiation of the 4 pillars of GDMT that reduce morbidity and mortality in patients with HFrEF.

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: Despite substantial clinical benefits achieved with optimal implementation of GDMT, EVOLUTION HF demonstrates that there is still delayed initiation of novel GDMTs (dapagliflozin and sacubitril/valsartan). An SGLT2 inhibitor, namely dapagliflozin 10 mg once daily in this study, showed the lowest discontinuation rates compared with other the GDMT classes, which often also require lengthy titrations.

TOP Take-Aways

1. Guideline-directed medical therapy for **HFrEF** includes 4 medication classes

- RAAS: ARNI/ACE-I/ARB (Ia)
- Beta-blocker: Carvedilol, Metoprolol ER (Ia)
- MRA: Spironolactone (Ia)
- SGLT2i: Dapagliflozin, Empagliflozin (Ia)

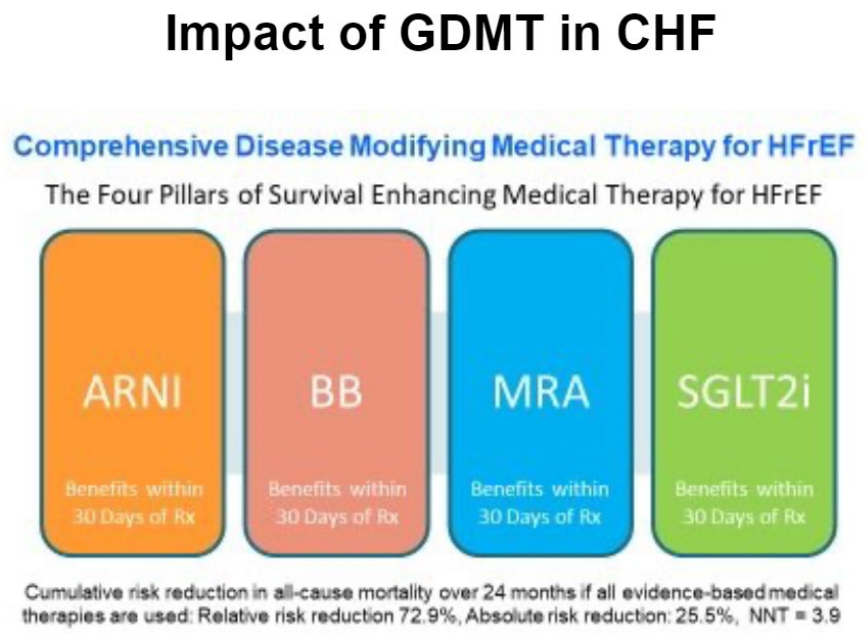
2. Guideline-directed medical therapy for **HFmrEF** now includes

- RAAS: ARNI/ACE-I/ARB (IIb)
- MRA: Spironolactone (IIb)
- SGLT2i: Dapagliflozin, Empagliflozin (IIa)
- Beta-blocker: Carvedilol, Metoprolol ER (IIb)

3. Guideline-directed medical therapy for **HFpEF** now includes

- SGLT2i (IIa)
- MRA (IIb)
- ARNI (IIb)

4. **HFimpEF** refers to HFrEF where LVEF is now > 40%; these patients should continue HFrEF



TOP Take-Aways

5. Value statements for recommendations where high-quality, cost-effectiveness studies have been published

6. Current HF guidelines include recommendations for HF patients with iron deficiency, anemia, hypertension, sleep disorders, atrial fibrillation, coronary artery disease, and malignancy

7. Patients with advanced HF who wish to prolong survival should be referred to a team specializing in HF including palliative care consistent with the patient's goals of care

References

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