



Same Symptoms, Different Stories

HFrEF and HFpEF Explained

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Disclosures

The planners and speaker have indicated that there are no relevant financial relationships with any ineligible companies to disclose.

Abbreviation Key

- **Afib** = atrial fibrillation
- **ACEi** = angiotensin-converting enzyme inhibitor
- **ADHF** = acute decompensated heart failure
- **ARB** = angiotensin receptor blocker
- **ARNi** = angiotensin receptor-neprilysin inhibitor
- **CVD** = cardiovascular disease
- **DM** = diabetes mellitus
- **EF** = ejection fraction
- **eGFR** = estimated Glomerular Filtration Rate
- **GDMT** = guideline-directed medical therapy
- **HFpEF** = heart failure with preserved ejection fraction
- **HFrEF** = heart failure with reduced ejection fraction
- **HTN** = hypertension
- **LVEF** = left ventricular ejection fraction
- **MRA** = mineralocorticoid receptor antagonist
- **NYHA** = New York Heart Association
- **QD** = once daily
- **SGLT2i** = Sodium-Glucose Transporter 2 inhibitor

Learning Objectives

Compare & contrast the differences in pathophysiology between HFrEF vs HFpEF

Differentiate the current treatment options available for HFrEF and HFpEF

Recall the mechanism of action of drugs used in HFrEF and HFpEF

Outline new clinical trials for HFrEF and HFpEF

Outline

Overview of heart failure

Pathophysiology

Treatment overview

Defining mechanisms of benefit

Literature review

What is Heart Failure?

Heart Failure

The heart cannot pump enough blood to meet the body's needs for blood and oxygen



Compensatory mechanisms

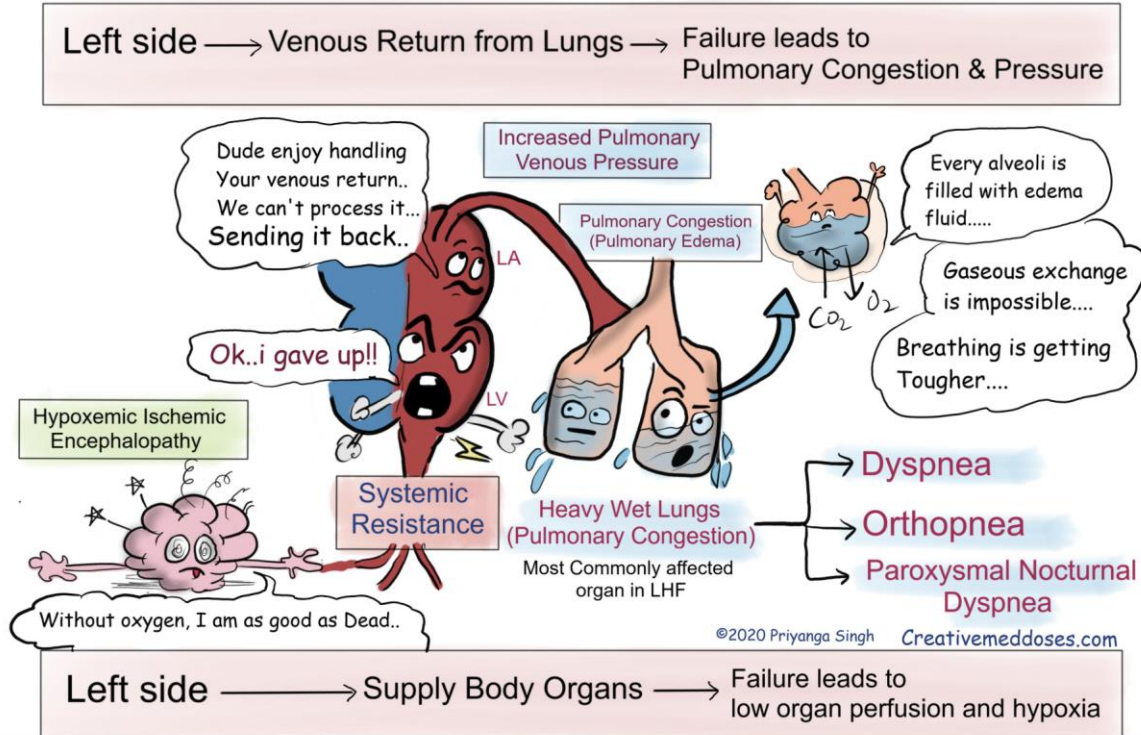
- Heart
- Blood vessels
- Kidney

Ejection Fraction Cut-Offs

Type of HF	Ejection Fraction Cut-offs
Reduced	LVEF \leq 40%
Improved (imp)	Initial LVEF \leq 40% and follow-up LVEF $>$ 40%
Mildly reduced (mr)	LVEF 41 – 49%
Preserved	LVEF \geq 50%

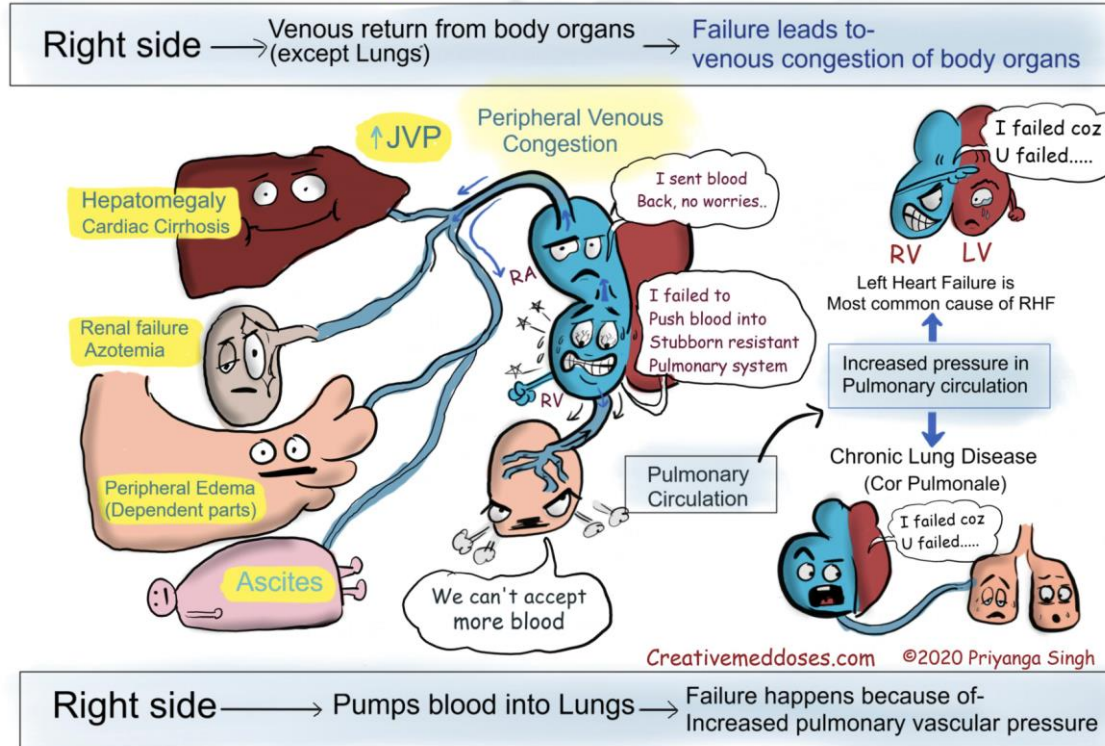
Left vs Right Sided HF

Left-sided Heart Failure



Left vs Right Sided HF Continued

Right-Sided Heart Failure



Signs and Symptoms of Heart Failure

Framingham Heart Failure Diagnostic Criteria

Need 2 major or 1 major and 2 minor criteria

Major Criteria	Minor Criteria
Paroxysmal nocturnal dyspnea or orthopnea	Ankle edema
Neck-vein distension	Night cough
Rales	Dyspnea on exertion
Cardiomegaly	Hepatomegaly
Acute pulmonary edema	Pleural effusion
S3 gallop	Vital capacity decrease 1/3 from max
Increased venous pressure >16cm of water	Tachycardia
Circulation time ≥ 25 sec	**Major or minor criterion: weight loss ≥ 4.5 kg in 5 days in response to treatment**
Hepatojugular reflux	

Symptoms

Abdominal pain

Anorexia
Nausea

Bloating
Constipation

Ascites

Dyspnea on
exertion

Exercise
intolerance

Paroxysmal
nocturnal
dyspnea

Orthopnea

Tachypnea

Cough

Fatigue
Weakness

Nocturia

Confusion

Altered mental
status

Physical Exam Findings

Pitting edema

Jugular venous
distension

Hepatojugular
reflex (HJR)

Hepatomegaly

Weight gain

Bibasilar rales

Pulmonary
edema

S3 gallop

Pleural effusion

Decrease
carotid
upstrokes

Tachycardia

Pallor

Cyanosis of
digits

Displaced point
of maximal
impulse

Staging Heart Failure

Stage A: At-Risk for Heart Failure



At risk for HF but without current or previous symptoms/signs of HF & without structural/functional heart disease or abnormal biomarkers



Patients with HTN, CVD, diabetes, obesity, exposure to cardiotoxic agents, genetic variant for cardiomyopathy, or family history of cardiomyopathy

Stage B: Pre-Heart Failure



Patients without current or previous symptoms/signs of HF but evidence of 1 of the following:



Structural heart disease
Evidence of increased filling pressures
Risk factors and abnormal lab finding

Stage C: Symptomatic Heart Failure



Evidence of structural heart disease



Patients with current or previous symptoms or signs of heart failure

Stage D: Advanced Heart Failure



Marked HF symptoms that interfere with daily life



Recurrent hospitalizations

New York Heart Association Functional Classification

Class	Symptoms
I	<ul style="list-style-type: none"> • No physical activity limitations
II	<ul style="list-style-type: none"> • Slight physical activity limitations • Comfortable at rest
III	<ul style="list-style-type: none"> • Marked physical activity limitations
IV	<ul style="list-style-type: none"> • Symptoms at rest • Any physical activity causes discomfort

Epidemiology

Incidence of Heart Failure


In 2017 estimate that 64.3 million people worldwide had HF



HF prevalence expected to increase 46% between 2012 and 2030



In the United States, more than 6 million people currently have HF



Incidence rate of HF is 20.9 per 1,000 person-years

Risk Factors

Males were more likely to develop HFrEF than HFpEF

Afib and pulmonary hypertension were more strongly associated with the risk of HFpEF

- Afib most influential comorbidity

Cardiomyopathy and myocardial infarction were more strongly associated with risk of HFrEF

- Cardiomyopathy most influential comorbidity

HFrEF vs HFpEF Pathophysiology

HFrEF – Initial Cardiac Insult

Myocardial
infarction

Hypertension

Idiopathic/genetic

Valve
abnormalities

Viral illness

Alcohol

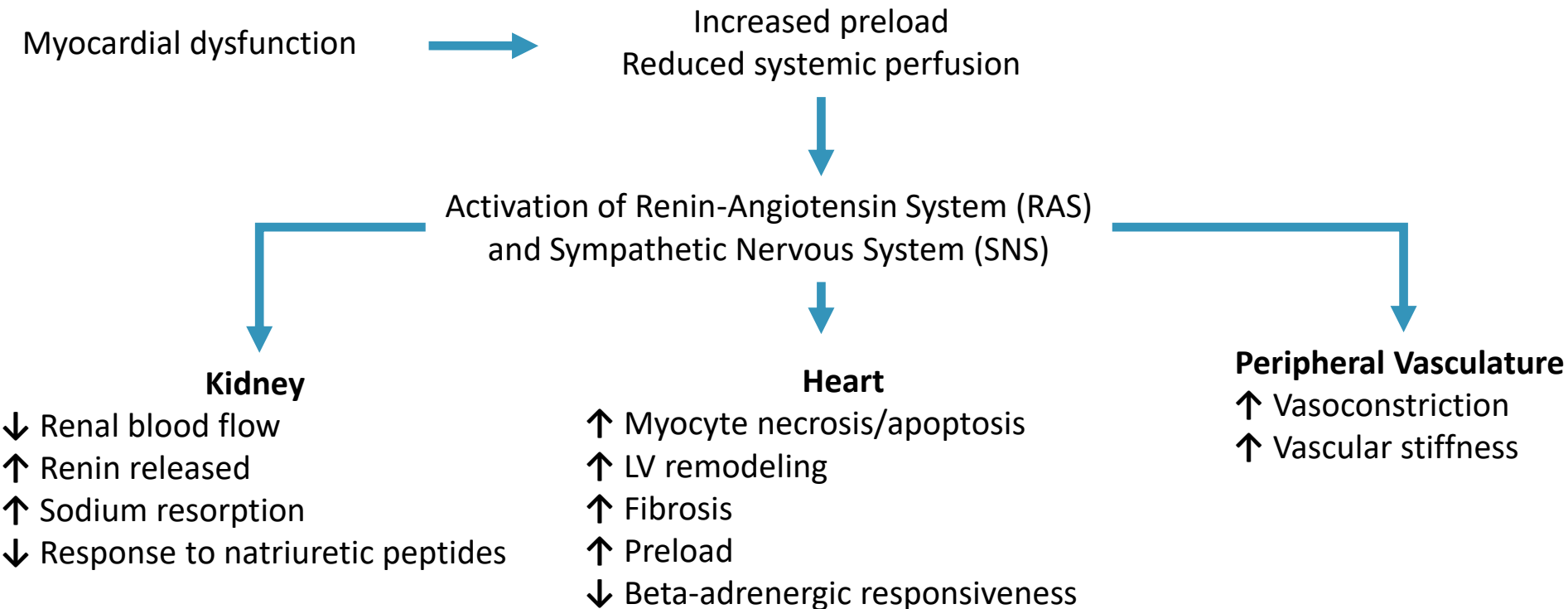
Drugs

Tachycardia

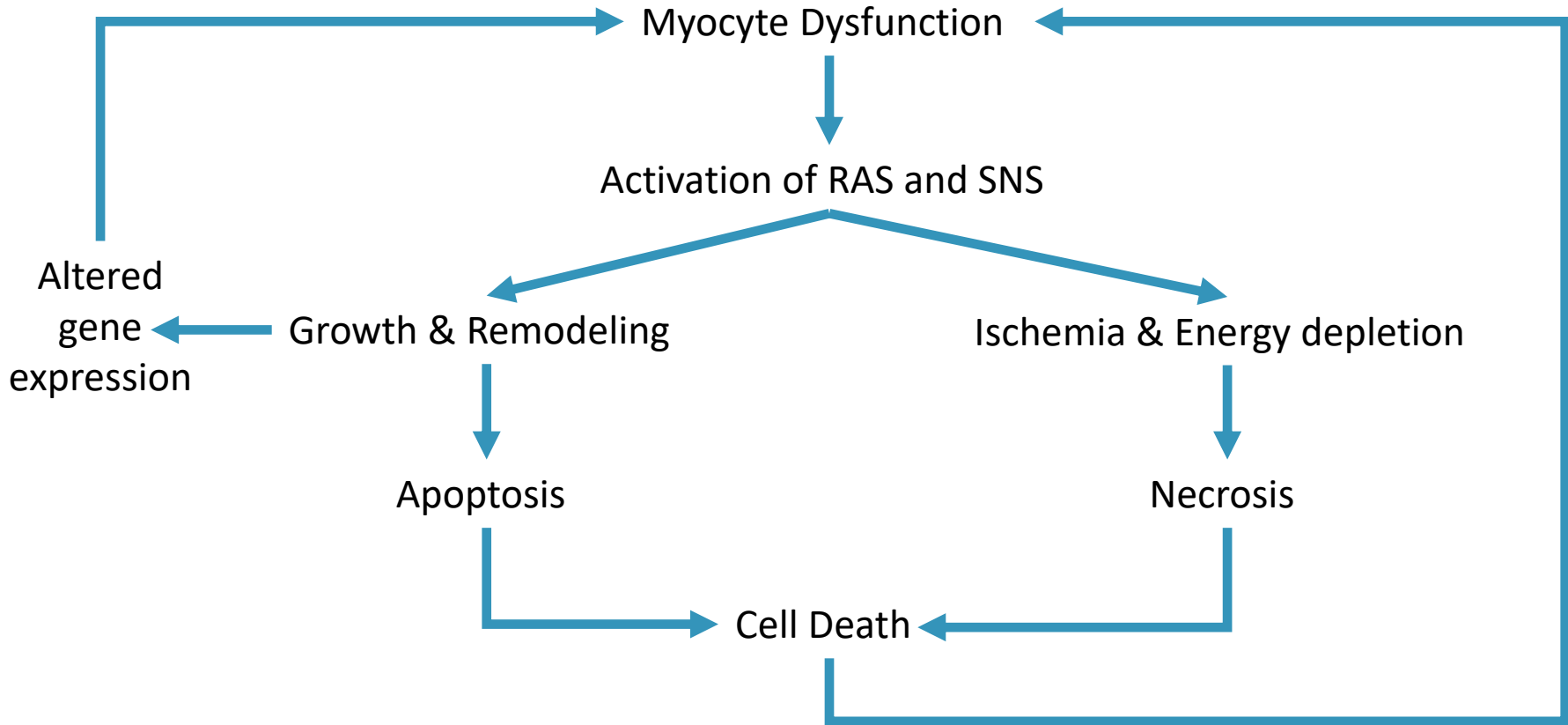
Connective tissue
disease

High output
states

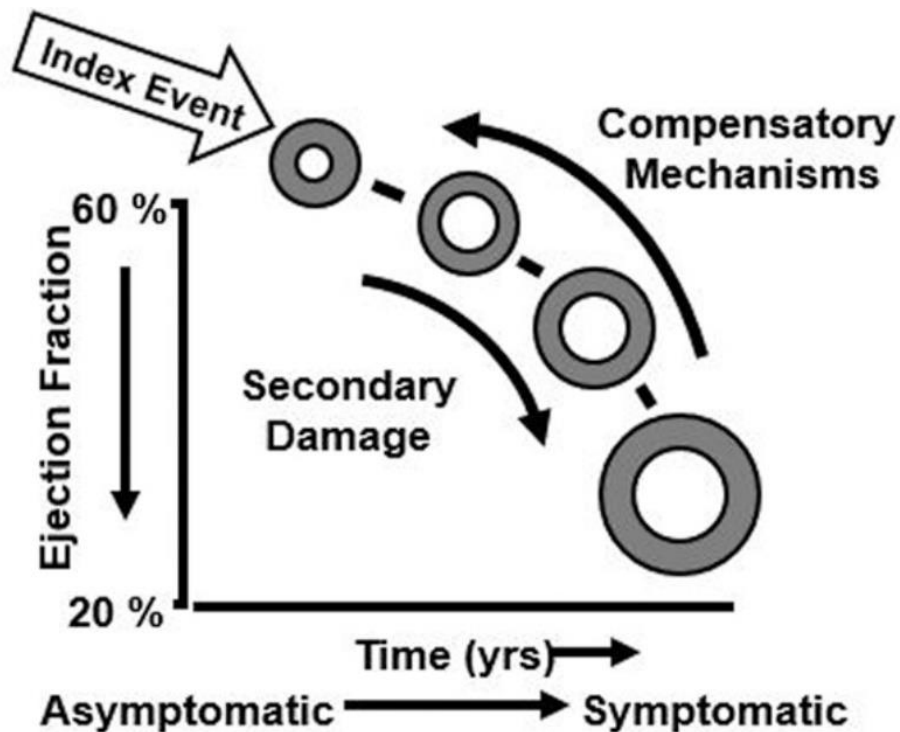
Compensatory Mechanisms



Myocyte Loss



Over Time



HFpEF Pathophysiology

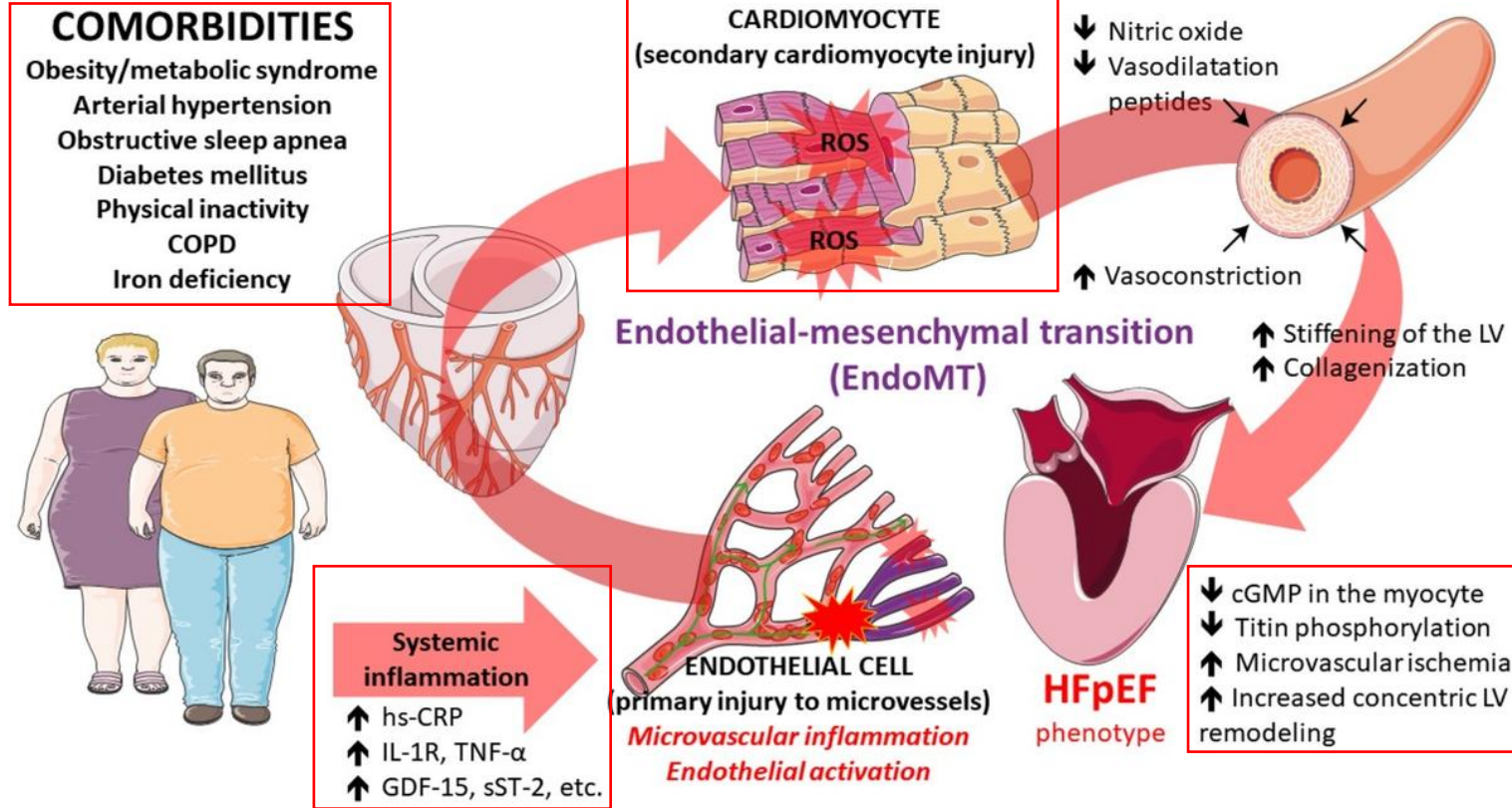
Impaired myocardial relaxation +/- increased diastolic stiffness

Ventricular chamber and ejection fraction are normal

Heterogenous disorder

Left ventricular hypertrophy most common structural abnormality associated with HFpEF

Proposed Hypothesis



Assessment Question #1

Which of the following statement(s) is true regarding the pathophysiology of HFrEF and HFpEF?

- A. In HFrEF, there is an increase in nitric oxide and brain natriuretic peptide
- B. In HFrEF, there is activation of the RAAS and parasympathetic nervous system
- C. In HFpEF, comorbidities such as diabetes and atrial fibrillation lead to a pro-inflammatory state
- D. HFpEF is a homogenous disorder where patients will have the same morphology and functional presentation

HFrEF's Treatment Algorithm

Stage A: At-Risk for Heart Failure

SGLT2i*

Optimize
blood
pressure

Optimize CVD
management

*only in patients with diabetes

1 (Strong)

2a (Moderate)

2b (Weak)



Stage B: Pre-Heart Failure

SGLT2i*

ACEi

ARB

*only in patients with diabetes

Beta Blocker

Optimize
blood
pressure

Optimize CVD
management

1 (Strong)

2a (Moderate)

2b (Weak)

Stage C and D: Symptomatic Heart Failure & Advanced Heart Failure

Diuretics, as needed	ARNI in NYHA Class II-III	ACEi or ARB in NYHA Class II-IV	Beta Blocker
MRA	SGLT2i	Hydralazine + Isosorbide Dinitrate	Ivabradine
	Vericiguat	Digoxin	

1 (Strong)

2a (Moderate)

2b (Weak)

HFpEF's Treatment Algorithm

Standard of Care

Loop diuretic
agents – fluid
retention &
NYHA Class II-IV

SGTL2i

MRA

ARNi

ARB

1 (Strong)

2a (Moderate)

2b (Weak)

Medication Dosing Review

Class	Drug Name	Starting Dose	Target Dose
ACEi	Captopril	6.25-12.5 mg TID	25-50 mg TID
	Enalapril	1.25-2.5 mg BID	10 mg BID
	Lisinopril	2.5-5 mg QD	20-40 mg QD
	Ramipril	1.25-2.5 mg BID	5 mg BID
ARBs	Candesartan	4-8 mg QD	32 mg QD
	Losartan	25-50mg QD	150mg QD
	Valsartan	40 mg BID	160 mg BID
ARNI	Sacubitril/Valsartan	24/26 mg BID	97/103 mg BID

Class	Drug Name	Starting Dose	Target Dose
Beta Blockers	Carvedilol	3.125 mg BID	25 mg BID
	Bisoprolol	1.25 mg QD	10 mg QD
	Metoprolol CR/XL	12.5-25 mg QD	200 mg QD
MRAs	Spironolactone	12.5-25 mg QD	25-50 mg QD
	Eplerenone	25 mg QD	50 mg QD
SGLT2i	Empagliflozin	10 mg QD	25 mg if DM
	Dapagliflozin	5 mg QD	10 mg QD

Assessment Question #2

OG is a 65-year-old male with normal renal function and a PMH of diabetes, CHF with a LVEF 39%, and atrial fibrillation who presents to the clinic with increased lower extremity edema and increased shortness of breath with normal daily activities. The patient is currently on metoprolol succinate 50mg once daily, metformin 1,000mg BID, and empagliflozin 25mg once daily.

Which of the following agents could be recommended to add to this patient based on the 2022 AHA guidelines? Select all that apply.

- A. Valsartan/sacubitril
- B. Furosemide
- C. Carvedilol
- D. Spironolactone

Defining Mechanisms of Benefit

HFrEF – SGLT2i



Stimulation of natriuresis and osmotic diuresis

Decreases tubuloglomerular feedback

Inhibition of cardiac fibrosis

Decreases central nervous system sympathetic nervous activity

Shifts to ketone based myocardial metabolism

HFrEF – Beta Blocker



Blocks adrenergic receptors

Heart rate reduction

Reduce myocardial oxygen consumption

Strongly modulate LV remodeling

HFrEF – MRAs



A vertical line on the left side of the slide has four circles attached to it. Each circle is connected to a horizontal teal bar that contains text. The circles are white with a thin blue outline. The teal bars are a medium blue color. The text is white and centered within each bar.

Inhibit effects of aldosterone

Decrease preload and vascular congestion

Improve endothelial function

Block effects of norepinephrine from sympathetic nerve terminals

HFrEF – ACEi/ARB

ACEi – angiotensin converting enzyme inhibitor

- Inhibits conversion of angiotensin I to angiotensin II

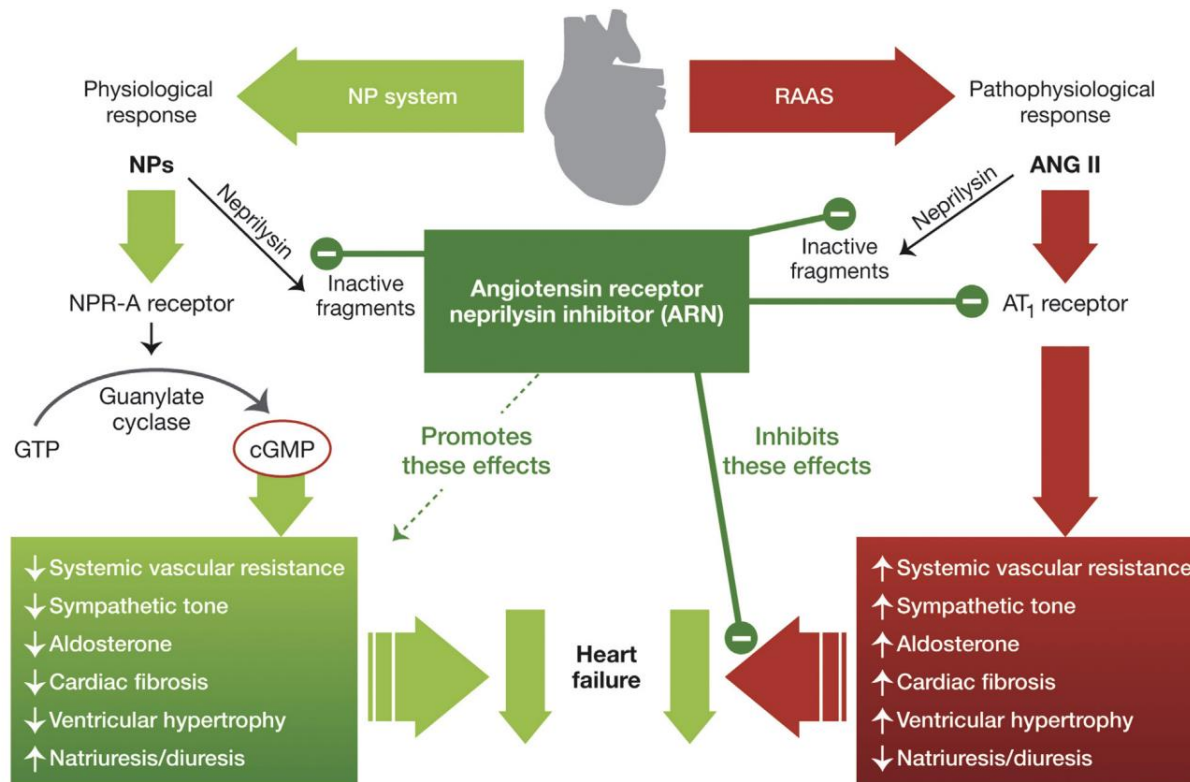
ARB – angiotensin receptor blocker

- Block angiotensin I receptor

Both agents:

- Decrease preload and vascular congestion
- Stop vasoconstriction
- Attenuate cardiac remodeling

HFrEF - ARNi



HFpEF – SGLT2i

HFpEF and diastolic dysfunction

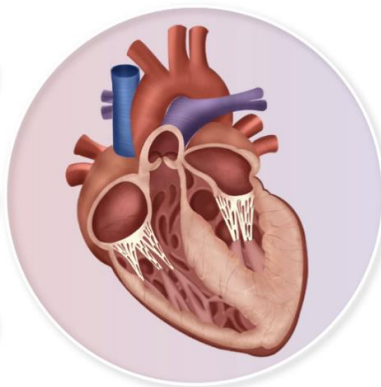
Oxidative stress, inflammation, fibrosis

Cardiac remodelling and hypertrophy

Myofilament stiffness

Impaired energetics

Ionic imbalances



Mechanisms of SGLT2 inhibitors in HFpEF

Improved NO-sGC-cGMP-PKG signaling

Improved metabolism and energetics

Reduced renal deterioration

Increased autophagic flux

Improved diastolic function

Reduced oxidative stress and inflammation

HFpEF – MRAs



Reduce excessive fibrosis

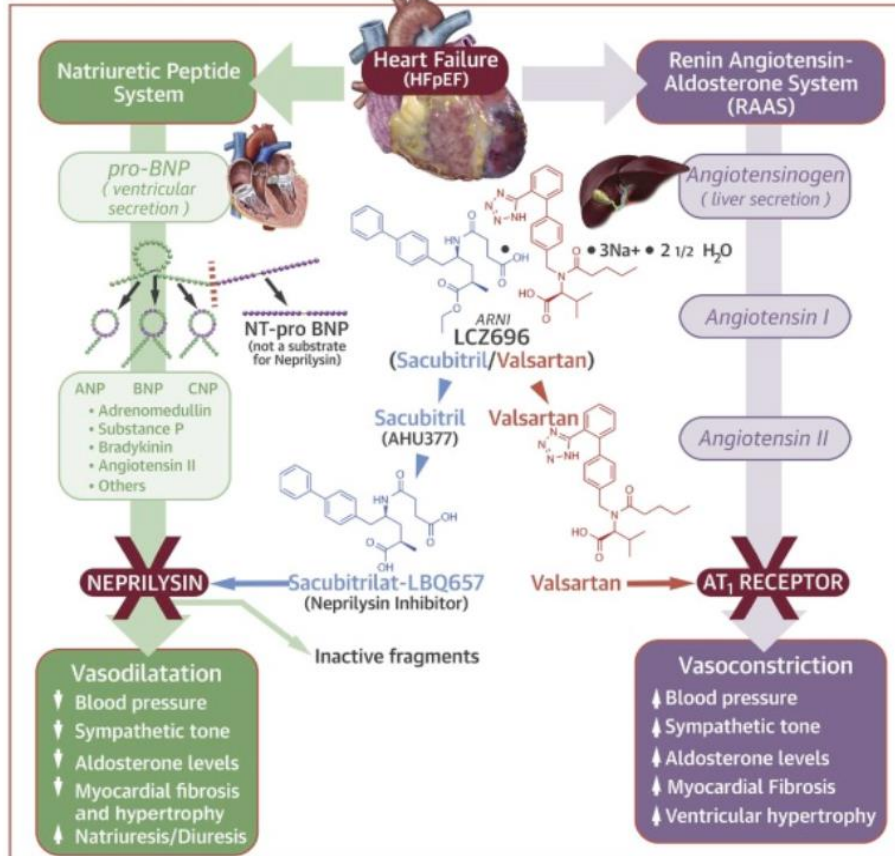
Decrease proinflammatory pathways

Prevention of cardiac remodeling

Decrease blood pressure

HFpEF – ARBs and ARNi

MECHANISM OF ACTION



Solomon SD, et al. Angiotensin Receptor Neprilysin Inhibition in Heart Failure With Preserved Ejection Fraction: Rationale and Design of the PARAGON-HF Trial. *JACC Heart Fail.* 2017

Assessment Question #3

Of the statements below, please select the true statements.

- I. SGLT2i have no beneficial mechanism of action in HFrEF nor HFpEF
- II. MRAs can decrease cardiac remodeling via reduction in fibrosis in HFrEF & HFpEF
- III. ACEi/ARB/ARNi are all able to decrease preload, prevent vasoconstriction, and attenuate cardiac remodeling
- IV. Beta blockers bind to cholinergic receptors which enhances cardiac myocyte function

A. I only

C. I and IV

B. II and III

D. II, III, and IV

Medication Use Challenges

Cracks in the System

Possibilities for most common reasons for failing to initiate or optimize treatment include

Providers simply forgetting to do so

Lack of specialized education and training

Resources and time

Belief that it is someone else's responsibility

Clinical Pharmacists Role

2018 study completed at Advocate Trinity Hospital
examined hospitalizations before and after
implementation of a clinical pharmacist

- Found a 50% decrease in heart failure hospitalizations in patients regularly scheduled with a clinical pharmacist within the first 10 months
- 2% of high-risk patients had 30-day readmission for HF when regularly seen by clinical pharmacists

Clinical Pharmacists Role Continued

Inpatient and outpatient clinical pharmacists have varying types of contributions, however, there are some aspects that are consistently performed in both settings

- Medication reconciliation
- Patient education
- Providing pharmacotherapeutic recommendation and monitoring
- Improving medication adherence
- Access to medications and transitions of care

HFrEF Literature Review

- QUAD Score
- DIGIT-HF

QUAD Score

Retrospective, observational study

Primary Outcome

- Composite of 1st unplanned hospitalization for HF (HHF) or all-cause mortality at 1 year

Secondary Outcomes

- Components of primary outcome
- Time taken to final therapy titration

Useability of QUAD Score

QUAD Score

QUAD Score HFrEF Therapeutic Score

Medication Class	Score
ACEi, AIIIRB, ARNI	<input type="text"/>
BB	<input type="text"/>
MRA	<input type="text"/>
SGLT2i	<input type="text"/>
Weight	<input type="text"/>
QUAD Score	<input type="text"/>

Legend	
Dose	Score
<50%	1
≥50%	4
Weight	8

EXAMPLES

Excellent (15-24)

1. 4 medication classes at ≥50% dose $(4+4+4+4)+8 = 24$
(Sacubitril Valsartan 200mg, Bisoprolol 10mg, Eplerenone 50mg, Dapagliflozin 10mg)
2. 1 medication class at ≥50% and 3 at <50% dose $(4+1+1+1)+8 = 15$
(Dapagliflozin 10mg, Sacubitril Valsartan 50mg, Bisoprolol 2.5mg, Eplerenone 12.5mg)

Good (8-14)

1. 3 medication classes at ≥ 50% dose $(4+4+4)= 12$
(Sacubitril Valsartan 100mg, Bisoprolol 5mg, Eplerenone 25mg)
2. 2 medication classes at 50% dose $(4+4) = 8$

Poor (<8)

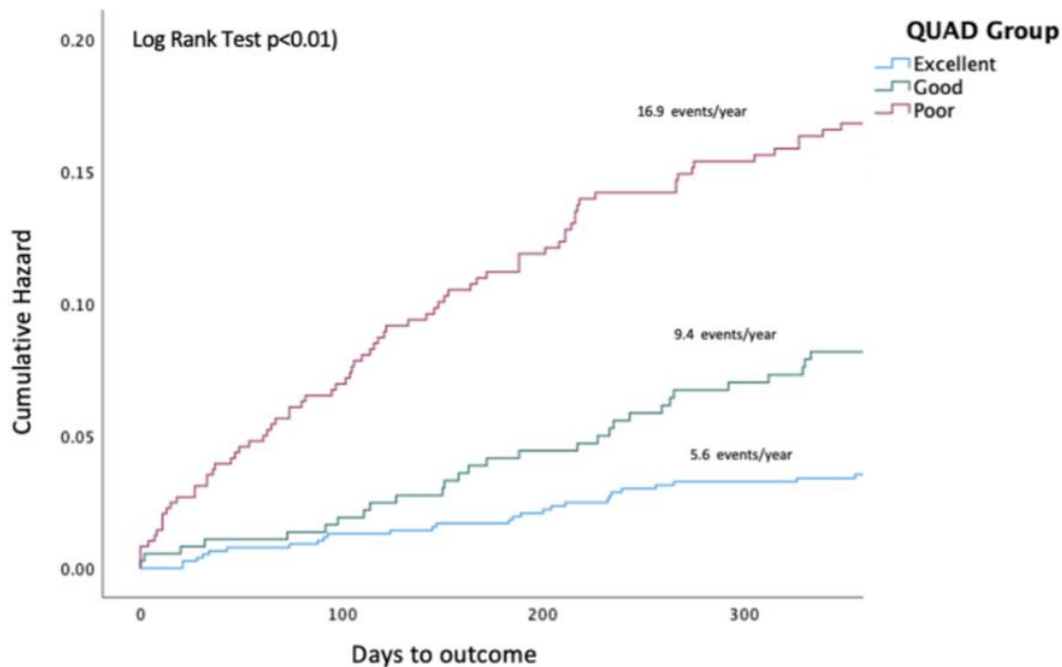
1. 3 medication classes at <50% dose $(1+1+1) = 3$
(Sacubitril Valsartan 50mg, Bisoprolol 1.25mg, Eplerenone 12.5mg)
2. 1 medication class at ≥50% dose = 4
(Dapagliflozin 10mg)

An 'e' is added to the score to mark an exemption or variance in medication class use. For example, If a patient is on >50% doses of 3 medication classes but have a clinical reason they are exempt from an MRA, they would be scored a 12e, with appropriate documentation in the clinical notes.

Results

(A)

Composite of Mortality or Hospitalization for Heart Failure at 1 year



Results

Primary Outcome Components			Time taken to final optimization
QUAD Score	HHF	Mortality	Median (IQR) days
Excellent	3.2%	2.4%	174 (99– 290)
Good	3.9%	6.5%	133 (80 – 232)
Poor	7.7%	13.1%	108 (57 – 193)

Conclusion

Simple tool



```
graph TD; A[Simple tool] --> B[Incentivize and audit GDMT]; B --> C[Excellent scores associated with better outcome];
```

Incentivize and audit GDMT

Excellent scores associated with better outcome

DIGIT-HF

Evaluate efficacy and safety of digitoxin at lower concentrations

Digitoxin starting dose = 0.07mg QD

- Decreased to 0.05 mg QD or increased to 0.1 mg QD

Noninferiority defined by hazard ratio of no more than 1.303

Lower participants than anticipated participated in the trial

Outcomes

Primary

- Composite of death from any cause or hospital admission for worsening heart failure

Secondary

- Death from any cause
- Composite of death from any cause and any hospitalization due to HF
- Death from HF
- Composite of death from cardiovascular causes or first hospitalization for HF

Safety

- Digitoxin concentrations, adverse events

Results

Primary outcome and components	Digitoxin N = 613	Placebo N = 599	Hazard/Rate Ratio (95% CI)
Death from any cause or first hospitalization for HF	242 (39.5%)	264 (44.1%)	0.82 (0.69 to 0.98)
Death from any cause	167 (27.2%)	177 (29.5%)	0.86 (0.69 to 1.07)
First hospitalization for HF	172 (28.1%)	182 (30.4%)	0.85 (0.69 to 1.05)

Key secondary outcome	Digitoxin N = 613	Placebo N = 599	Hazard/Rate Ratio (95% CI)
Death from any cause and hospitalization for HF	537 25.1 events/100 pt yr	531 26.6 events/100 pt yr	0.85 (0.67 to 1.09)

Safety Outcomes

Mean serum concentration at

- 6 weeks: 17 ± 5.9 ng/mL
- 12 months: 13.5 ± 5.1 ng/mL

Serious adverse event

- Occurred in 4.7% in digitoxin group and 2.8% in the placebo group

Discontinuation

- Occurred in 9.1% in digitoxin group and 10.2% in the placebo group

Conclusion

Patients with HFrEF on GDMT benefited from digitoxin



Lower combined risk of death from any cause or hospital admission for worsening heart failure than placebo

HFpEF Literature Review

- FINEARTS-HF
- STEP-HFpEF and STEP-HFpEF DM
- SUMMIT

FINEARTS-HF

Assess efficacy of finerenone in patients with HFmrEF or HFpEF

Randomized, placebo-controlled, event-driven Phase 3 trial

- Starting dose: finerenone 10mg or 20mg
- Dose adjusted based on eGFR
- Titration occurred after 4 weeks

Outcomes

Primary

- Composite of total worsening HF events and death from cardiovascular causes

Secondary

- Total worsening HF events
- Death from cardiovascular causes
- Changes in the Kansas City Cardiomyopathy Questionnaire (KCCQ)
- Improvement in NYHA Functional Class
- Kidney composite outcomes
- Composite of sustained decrease in eGFR $\geq 50\%$, decline in eGFR <15 , or initiation of long-term dialysis or kidney transplant
- Death from any cause

Results

Primary Outcome	Finerenone N = 3003	Placebo N = 2998	Rate Ratio (95% CI) P value
Total worsening HF event and death from CV causes - # of events (%)	1083 (36.06%)	1283 (42.8%)	0.84 (0.74 – 0.95) P = 0.007
Total worsening HF events - # of events (%)	842 (28.04%)	1024 (34.16%)	0.82 (0.71 – 0.94) P = 0.006
Death from CV causes - # of pts (%)	242 (8.1%)	260 (8.7%)	Hazard ratio 0.93 (0.78 – 1.11)

Secondary outcomes	Finerenone	Placebo	Difference (95% CI) P value
Change from baseline in KCCQ	8.0 ± 0.3	6.4 ± 0.3	1.6 (0.8 – 2.3) P < 0.001

Conclusion

Significant reduction in rates of composite worsening HF events and death from CV causes



Significant reduction rates of worsening HF events alone



No difference in rate of death from CV causes alone

STEP-HFpEF and STEP-HFpEF DM

	STEP-HFpEF	STEP-HFpEF DM
Objective	Evaluate if semaglutide can lead to reductions in symptoms, physical limitations, and weight loss compared to placebo	Evaluate the efficacy and safety of semaglutide in patients with obesity, HFpEF, and DM
Design	Randomized, double-blind placebo-controlled trial	
Dose	Starting dose: semaglutide 0.25mg SC once weekly Max dose: semaglutide 2.4mg SC once weekly	

Outcomes

	STEP-HFpEF	STEP-HFpEF DM
Primary	Change in KCCQ Percent change in body weight	
Secondary	Change in 6-minute walk distance Hierarchical composite reported as win ratio Change in C-reactive protein level	

Results

	STEP-HFpEF			STEP-HFpEF DM		
Outcome	Semaglutide N = 263	Placebo N = 266	Estimated Difference or Ratio (95% CI) P-value	Semaglutide N = 310	Placebo N = 306	Estimated Difference or Ratio (95% CI) P-value
Change in KCCQ -points	16.6	8.7	7.8 (4.8 – 10.9) P < 0.001	13.7	6.4	7.3 (4.1 – 10.4) P < 0.001
Percent change in body weight	-13.3	-2.6	-10.7 (-11.9 to -9.4) P < 0.001	-9.8	-3.4	-6.4 (-7.6 to -5.2) P < 0.001
Change in 6- minute walk distance – m	21.5	1.2	20.3 (8.6 – 32.1) P < 0.001	12.7	-1.6	14.3 (3.7 – 24.9) P = 0.008

Conclusions

STEP-HFpEF	STEP-HFpEF DM
Semaglutide had a larger reductions in symptoms, physical limitations, improved exercise function, and had greater weight loss than placebo	Semaglutide had a larger reduction in HF symptoms, physical limitations, and had greater weight loss than placebo.

SUMMIT

Evaluate tirzepatide for patients with HFpEF and obesity

Double-blind, randomized, placebo-controlled Phase 3 trial

- Starting dose of tirzepatide: 2.5mg SC once weekly
- Max dose of tirzepatide: 15mg SC once weekly
- Titration occurred every 4 weeks

Outcomes

Primary

- Composite of adjudicated death from cardiovascular causes or worsening HF events
- Change from baseline to 52 weeks in KCCQ total symptom score

Secondary outcomes

- Change at 52 weeks in 6-minute walk distance
- Percent change at 52 weeks in body weight
- Percent change at 52 weeks in high-sensitivity C-reactive protein level

Results

Primary Outcomes	Tirzepatide N = 364	Placebo N = 367	Hazard Ratio or Difference (95% CI); P – value
Composite adjudicated death from CV causes or worsening HF event -no. (%)	36 (9.9%)	56 (15.3%)	0.62 (0.41 – 0.95) P = 0.026
Adjudicated death from CV causes -no. (%)	8 (2.2%)	5 (1.4%)	1.58 (0.52 – 4.83)
Adjudicated worsening HF events -no. (%)	29 (8%)	52 (14.2%)	0.54 (0.34 – 0.85)
Change at 52 weeks in KCCQ	19.5 ± 1.2	12.7 ± 1.3	6.9 (3.3 – 10.6) P < 0.001

Conclusion

Significant reduction in rates of composite death from CV causes or worsening HF events



Significant reduction in worsening HF events alone



No difference in rate of death from CV causes alone

Assessment Question #4

Which of the following statements are **NOT** true? Select all that apply.

- A. There was no significant difference between finerenone and placebo in the composite primary endpoint
- B. There was a significant difference between finerenone and placebo in the composite primary endpoint
- C. There was no significant difference between finerenone and placebo for worsening HF events alone
- D. There was no significant difference between finerenone and placebo for death from CV causes alone

Take Away Points

HF is a diverse disease state with many different treatment algorithms available

Emphasis should be placed on counseling patients and medication reconciliations

Emerging roles for pharmacists to handle drug titration

New literature is still coming out regarding HF

New and promising therapeutic options are emerging

Resources

1. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, Abate D, Abate KH. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018;392:1789–858.
2. Virani SS, Alonso A, Aparicio HJ, et al. Heart disease and stroke statistics—2021 update. *Circulation* 2021;143:e254–743.
3. Lee MP, Glynn RJ, Schneeweiss S, et al. Risk factors for heart failure with preserved or reduced ejection fraction among Medicare beneficiaries: application of competing risks analysis and gradient boosted model. *Clin Epidemiol* 2020;12:607–16.
4. Al-Tamimi MA, Gillani SW, Abd Alhakam ME, Sam KG. Factors Associated With Hospital Readmission of Heart Failure Patients. *Front Pharmacol*. 2021;12:732760. Published 2021 Oct 11. doi:10.3389/fphar.2021.732760
5. Pierce JB, Ikeaba U, Peters AE, DeVore AD, Chiswell K, Allen LA, et al. Quality care and outcomes among patients hospitalized for heart failure in rural vs urban US hospitals. *JAMA Cardiol* 2023 April; 8:376. Doi: 10.1001/jamacardio.2023.0241
6. Ouwerkerk W, Voors AA, Anker SD, et al. Determinants and clinical outcome of uptitration of ACE-inhibitors and beta-blockers in patients with heart failure: a prospective European study. *Eur Heart J*. 2017;38(24):1883-1890. doi:10.1093/eurheartj/ehx026
7. Jarjour M, Henri C, de Denus S, et al. Care Gaps in Adherence to Heart Failure Guidelines: Clinical Inertia or Physiological Limitations?. *JACC Heart Fail*. 2020;8(9):725-738. doi:10.1016/j.jchf.2020.04.019
8. Schumacher C, Moaddab G, Colbert M, Kliethermes MA. The Effect of Clinical Pharmacists on Readmission Rates of Heart Failure Patients in the Accountable Care Environment. *J Manag Care Spec Pharm*. 2018;24(8):795-799. doi:10.18553/jmcp.2018.24.8.795
9. Cheng JW. Current perspectives on the role of the pharmacist in heart failure management. *Integr Pharm Res Pract*. 2018;7:1-11. Published 2018 Mar 9. doi:10.2147/IPRP.S137882
10. McKee PA, Castelli WP, McNamara PM, Kannel WB. The natural history of congestive heart failure: the Framingham study. *N Engl J Med*. 1971;285(26):1441-1446. doi:10.1056/NEJM197112232852601
11. Heart Failure. In: Schwinghammer TL, DiPiro JT, Ellingrod VL, DiPiro CV. eds. *DiPiro's Pharmacotherapy Handbook*, 12e. McGraw Hill; 2023. Accessed December 06, 2025. <https://accesspharmacy-mhmedical-com.proxy.cc.uic.edu/content.aspx?bookid=3324§ionid=276995779>
12. Mann DL, Felker GM. Mechanisms and Models in Heart Failure: A Translational Approach. *Circ Res*. 2021;128(10):1435-1450. doi:10.1161/CIRCRESAHA.121.318158

Resources

13. Eichhorn EJ, Bristow MR. Medical therapy can improve the biological properties of the chronically failing heart. A new era in the treatment of heart failure. *Circulation*. 1996;94(9):2285-2296. doi:10.1161/01.cir.94.9.2285
14. Mancini GB, Howlett JG, Borer J, et al. Pharmacologic Options for the Management of Systolic Heart Failure: Examining Underlying Mechanisms. *Can J Cardiol*. 2015;31(10):1282-1292. doi:10.1016/j.cjca.2015.02.013
15. Narayan SI, Terre GV, Amin R, et al. The Pathophysiology and New Advancements in the Pharmacologic and Exercise-Based Management of Heart Failure With Reduced Ejection Fraction: A Narrative Review. *Cureus*. 2023;15(9):e45719. Published 2023 Sep 21. doi:10.7759/cureus.45719
16. Heidenreich PA, Bozkurt B, Aguilar D, et al. 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. *Circulation*. 2022;145(18):e895-e1032. doi:10.1161/CIR.0000000000001063
17. American Heart Association. Classes and Stages of Heart Failure. [www.heart.org](https://www.heart.org/en/health-topics/heart-failure/what-is-heart-failure/classes-of-heart-failure). May 21, 2025. Accessed December 6, 2025. <https://www.heart.org/en/health-topics/heart-failure/what-is-heart-failure/classes-of-heart-failure>.
18. Heinzel FR, Hohendanner F, Jin G, Sedej S, Edelmann F. Myocardial hypertrophy and its role in heart failure with preserved ejection fraction. *J Appl Physiol* (1985). 2015;119(10):1233-1242. doi:10.1152/jappphysiol.00374.2015
19. Kittleson MM, Panjra GS, Amancherla K, Davis LL, Deswal A, Dixon DL, Januzzi JL Jr, Yancy CW. 2023 ACC Expert Consensus Decision Pathway on Management of Heart Failure With Preserved Ejection Fraction: A Report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol*. 2023 May 9;81(18):1835-1878. doi: 10.1016/j.jacc.2023.03.393. Epub 2023 Apr 19. PMID: 37137593.
20. D'Amario D, Migliaro S, Borovac JA, et al. Microvascular Dysfunction in Heart Failure With Preserved Ejection Fraction. *Front Physiol*. 2019;10:1347. Published 2019 Nov 5. doi:10.3389/fphys.2019.01347
21. Davis BR, Kostis JB, Simpson LM, et al. Heart failure with preserved and reduced left ventricular ejection fraction in the antihypertensive and lipid-lowering treatment to prevent heart attack trial. *Circulation*. 2008;118(22):2259-2267. doi:10.1161/CIRCULATIONAHA.107.762229
22. IQWiG. Heart failure: Learn More – Types of Heart Failure. [InformedHealth.org \[Internet\]](https://www.ncbi.nlm.nih.gov/books/NBK481485/). November 28, 2023. Accessed December 16, 2025. <https://www.ncbi.nlm.nih.gov/books/NBK481485/>.
23. Singh P. Heart failure: Left Sided vs Right Sided. *Creative Med Doses*. May 6, 2020. Accessed December 16, 2025. <https://creativemeddoses.com/topics-list/heart-failure-left-sided-vs-right-sided/>.
24. Mann DL, Felker GM. Mechanisms and Models in Heart Failure: A Translational Approach. *Circ Res*. 2021;128(10):1435-1450. doi:10.1161/CIRCRESAHA.121.318158

Resources

25. Pandey AK, Bhatt DL, Pandey A, et al. Mechanisms of benefits of sodium-glucose cotransporter 2 inhibitors in heart failure with preserved ejection fraction. *Eur Heart J*. 2023;44(37):3640-3651. doi:10.1093/eurheartj/ehad389
26. Ferreira JP, Pitt B, Zannad F. Mineralocorticoid Receptor Antagonists in Heart Failure: An Update. *Circ Heart Fail*. 2024;17(12):e011629. doi:10.1161/CIRCHEARTFAILURE.124.011629
27. Solomon SD, Rizkala AR, Gong J, et al. Angiotensin Receptor Neprilysin Inhibition in Heart Failure With Preserved Ejection Fraction: Rationale and Design of the PARAGON-HF Trial. *JACC Heart Fail*. 2017;5(7):471-482. doi:10.1016/j.jchf.2017.04.013
28. Bavendiek U, Großhennig A, Schwab J, et al. Digitoxin in Patients with Heart Failure and Reduced Ejection Fraction. *N Engl J Med*. 2025;393(12):1155-1165. doi:10.1056/NEJMoa2415471
29. Savage HO, Dungu JN, Dimarco A, et al. A novel treatment score (QUAD score) to promote treatment optimization in heart failure with a reduced ejection fraction. *ESC Heart Fail*. Published online September 8, 2025. doi:10.1002/ehf2.15407
30. Solomon SD, McMurray JJV, Vaduganathan M, et al. Finerenone in Heart Failure with Mildly Reduced or Preserved Ejection Fraction. *N Engl J Med*. 2024;391(16):1475-1485. doi:10.1056/NEJMoa2407107
31. Kosiborod MN, Abildstrøm SZ, Borlaug BA, et al. Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity. *N Engl J Med*. 2023;389(12):1069-1084. doi:10.1056/NEJMoa2306963
32. Kosiborod MN, Petrie MC, Borlaug BA, et al. Semaglutide in Patients with Obesity-Related Heart Failure and Type 2 Diabetes. *N Engl J Med*. 2024;390(15):1394-1407. doi:10.1056/NEJMoa2313917
33. Packer M, Zile MR, Kramer CM, et al. Tirzepatide for Heart Failure with Preserved Ejection Fraction and Obesity. *N Engl J Med*. 2025;392(5):427-437. doi:10.1056/NEJMoa2410027

Questions?

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