

HHP Care Model and Disease Management Webinar Series

Heart Failure with Reduced Ejection Fraction

Thursday, April 29, 2021

5:30pm – 6:30pm

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Moderator – 04/29/21

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- Specific areas may not pertain directly to your clinical practice area and/or may not be applicable to your practice based on your existing workflows, infrastructure, software (e.g. EHR), and communications processes.

Webinar Information

- You have been automatically muted. You cannot unmute yourself.
- You will be able to submit questions via the Q&A section.
 - Due to time constraints, any unanswered questions will be addressed this week and posted on the HHP website
- A recording of the meeting will be available tomorrow on the HHP website and intranet.

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- You should have completed a brief questionnaire before joining today's live webinar.

2. Step 2: HPH CME team will email you instructions

- Complete and submit evaluation survey that will be emailed to you within one week of the offering.
- Your CE certificate will be immediately available to you upon completion of your evaluation.
- Questions? Email hphcontinuingeduc@hawaiipacifichealth.org

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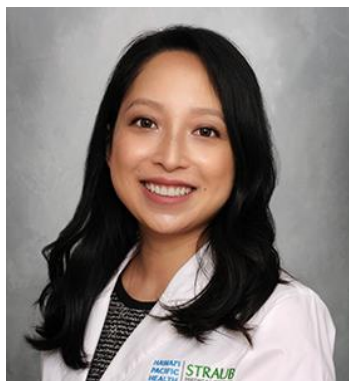


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- Except as noted below, the planners and presenters of this activity report no relationships with companies whose products or services (may) pertain to the subject matter of this meeting, :

Heart Failure with Reduced Ejection Fraction



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Heart Failure with Reduced EF

- Etiology
- Diagnosis
- Treatment

Case

HPI	41 year old male with significant history of methamphetamine and alcohol use who presents with progressive shortness of breath, orthopnea, and abdominal distension
PMH	No significant medical history
FHx	No family history of heart failure and sudden cardiac death
SHx	Drinks 1-2 cases of beer/day for the past 10 years Smokes meth up to 3 times per day for at least 12 years Daily tobacco use, up to 1 pack per day

Case

VS T 97.2, BP 126/86, HR 109, SpO2 84% RA →95% 2L O2

CBC 8.9>14.5/43.3<359

Na 136, K 3.8, BUN 9, Cr 0.97, HbA1c 5.6%

AST/ALT 173/112

Labs Troponin 13, NT-proBNP 1805
Tox positive for methamphetamine
TSH 2.43
Ferritin 281, Iron 52, TIBC 361
HIV non-reactive

EKG Sinus tachycardia

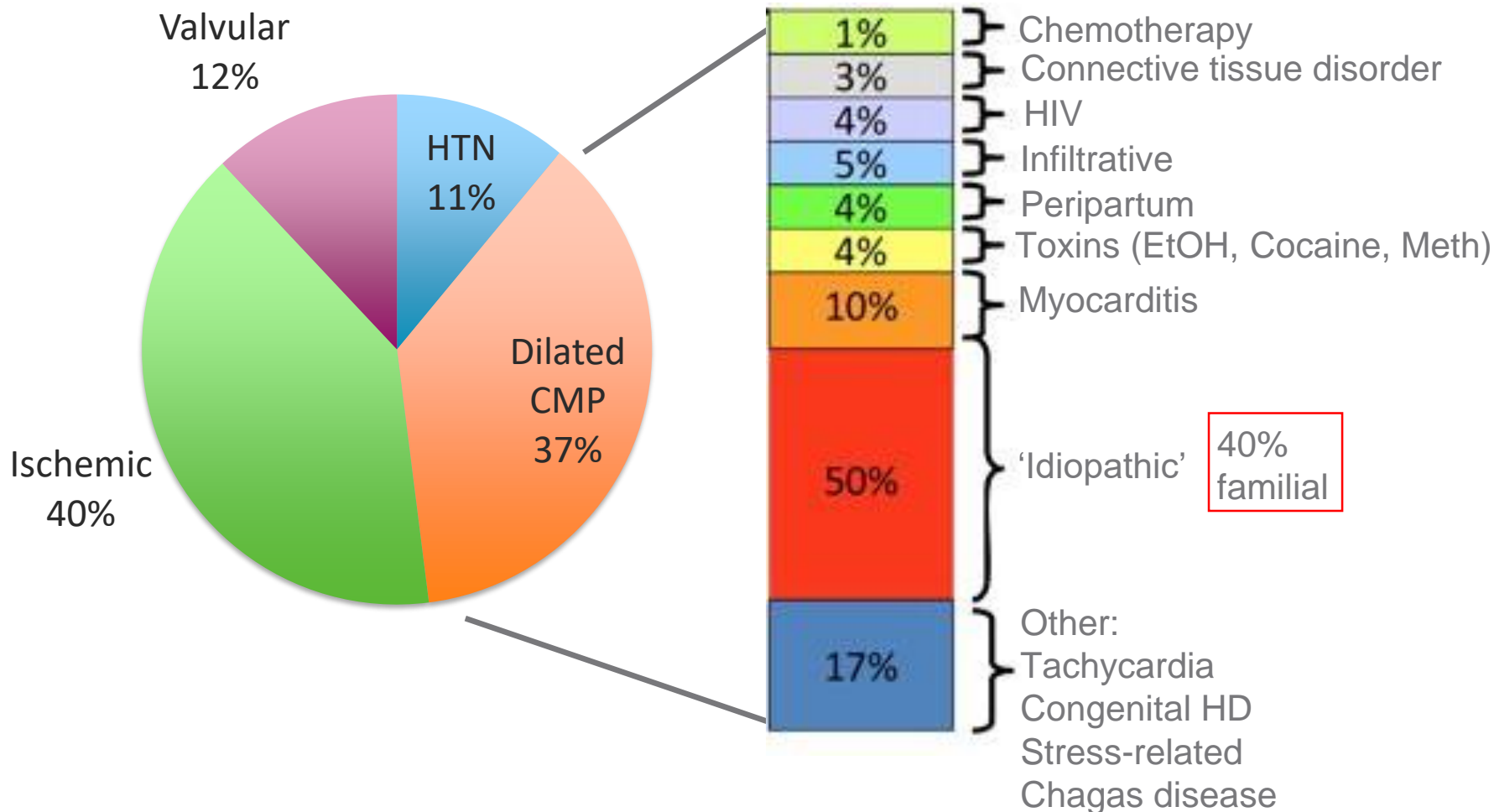
CXR Cardiomegaly

Case



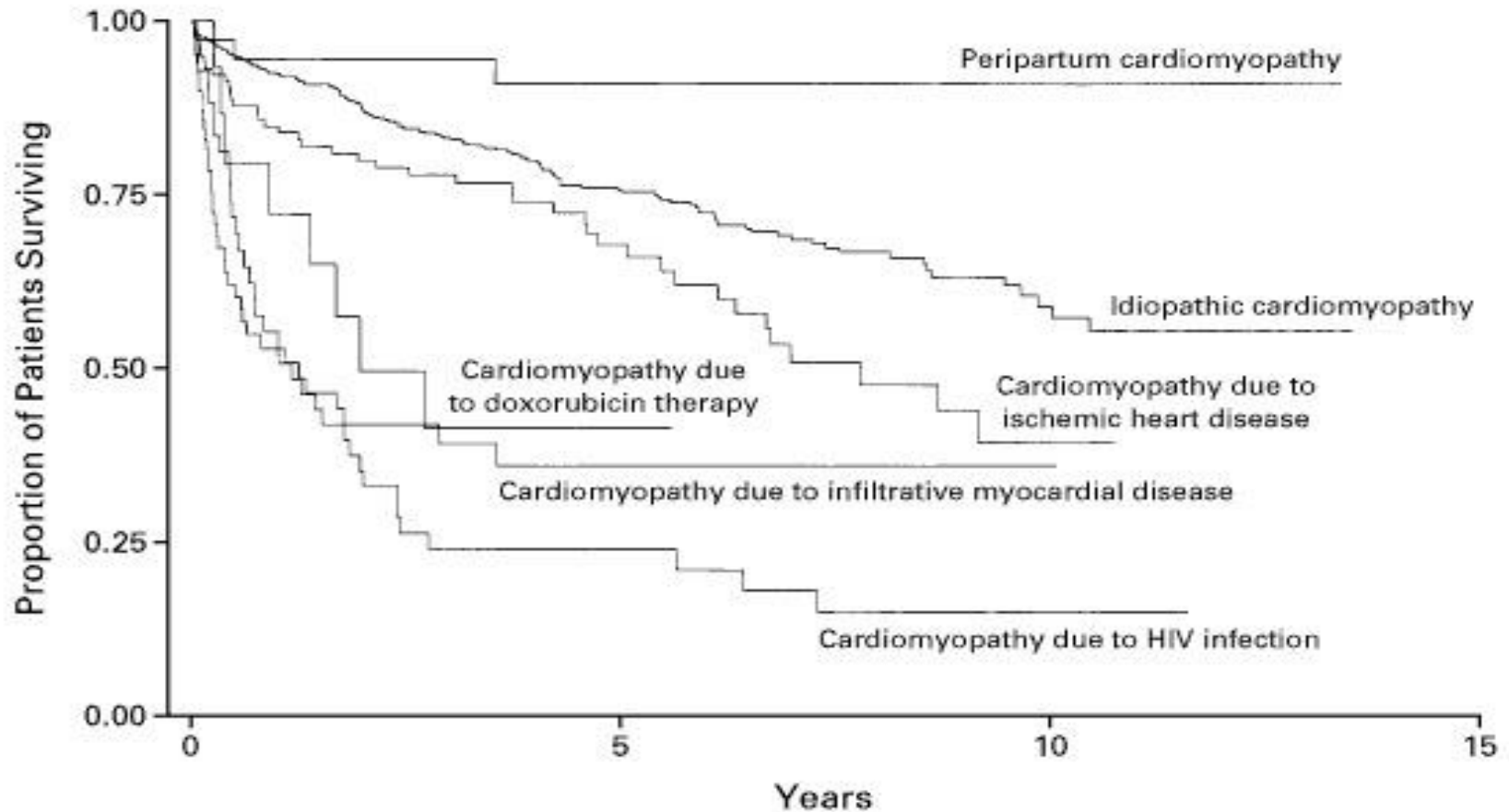
- Severely enlarged LV
- LVEF 10-15%
- Severely increased RV size with decreased function
- Moderate MR
- Severe TR
- Significant pulmonary hypertension, PASP 80mmHg

Etiology



JACC:HF 2015;3(11):906-16

Prognosis According to Etiology



NEJM 2000; 342:1077-1084

Diagnostic Evaluation

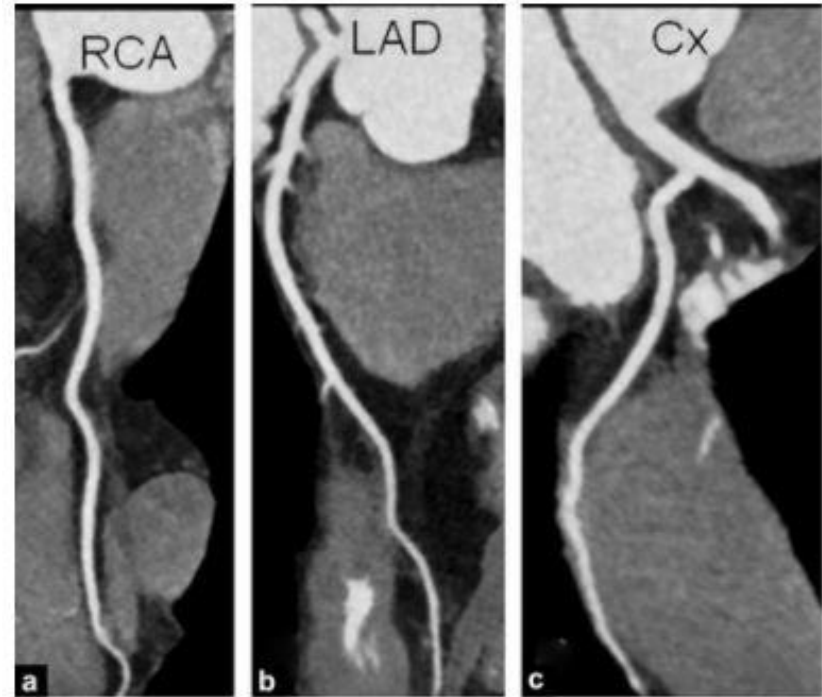
- Laboratory studies:
 - NT-proBNP
 - CBC
 - BMP
 - Liver function tests
 - Iron studies
 - Thyroid function tests
 - HbA1c
 - Lipid panel
- Diagnostic Imaging:
 - CXR
 - Echo
 - Coronary angiography
 - CMR
- Other:
 - ECG
 - RHC
 - EMBx

Coronary Angiography

- Patients with newly diagnosed HF require evaluation of coronary artery disease

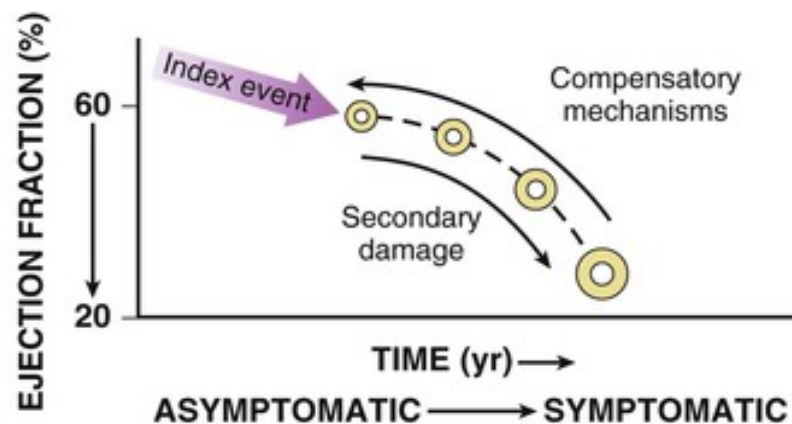
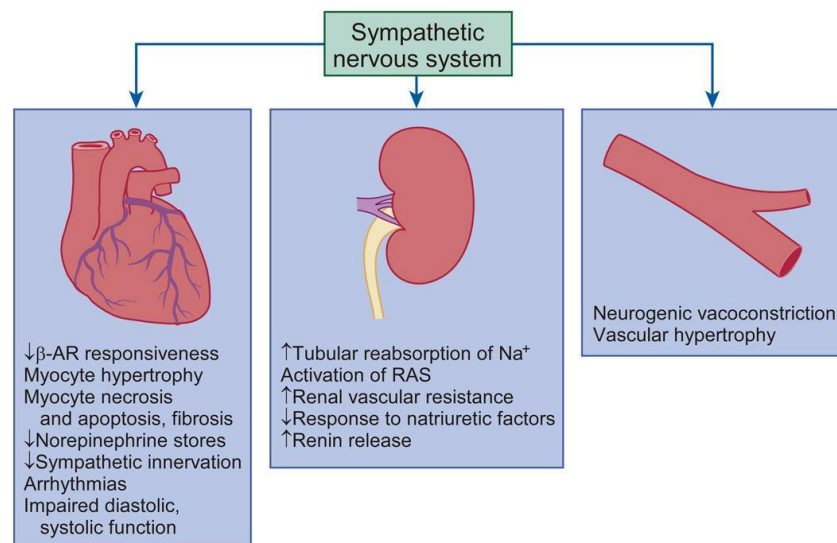
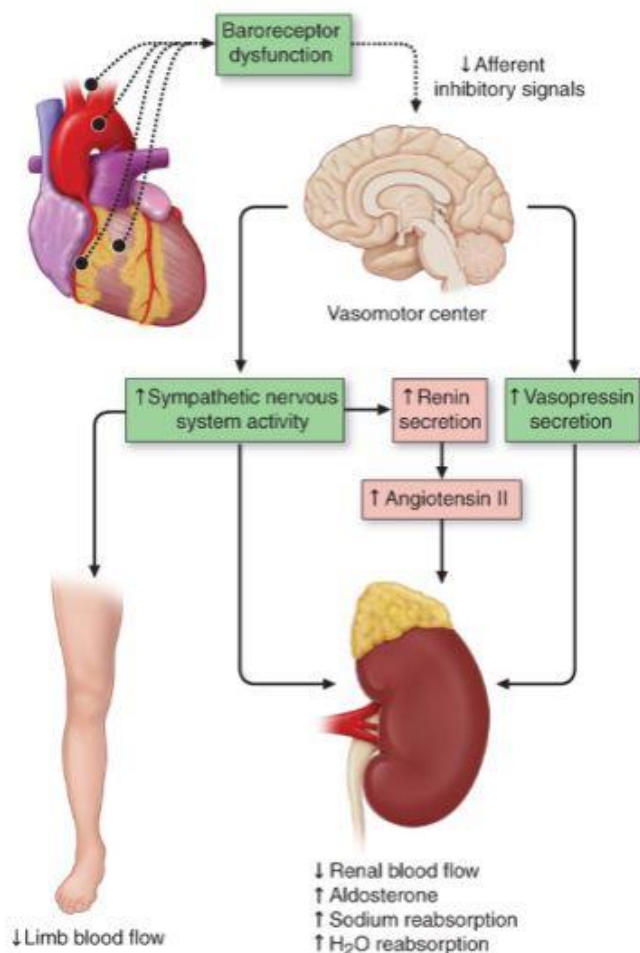


Coronary Angiography



CTA Coronary

Neurohormonal Activation



Nat Rev Cardiol. 2017;14(1); 30-38.

Circ 1999;100:999-1008

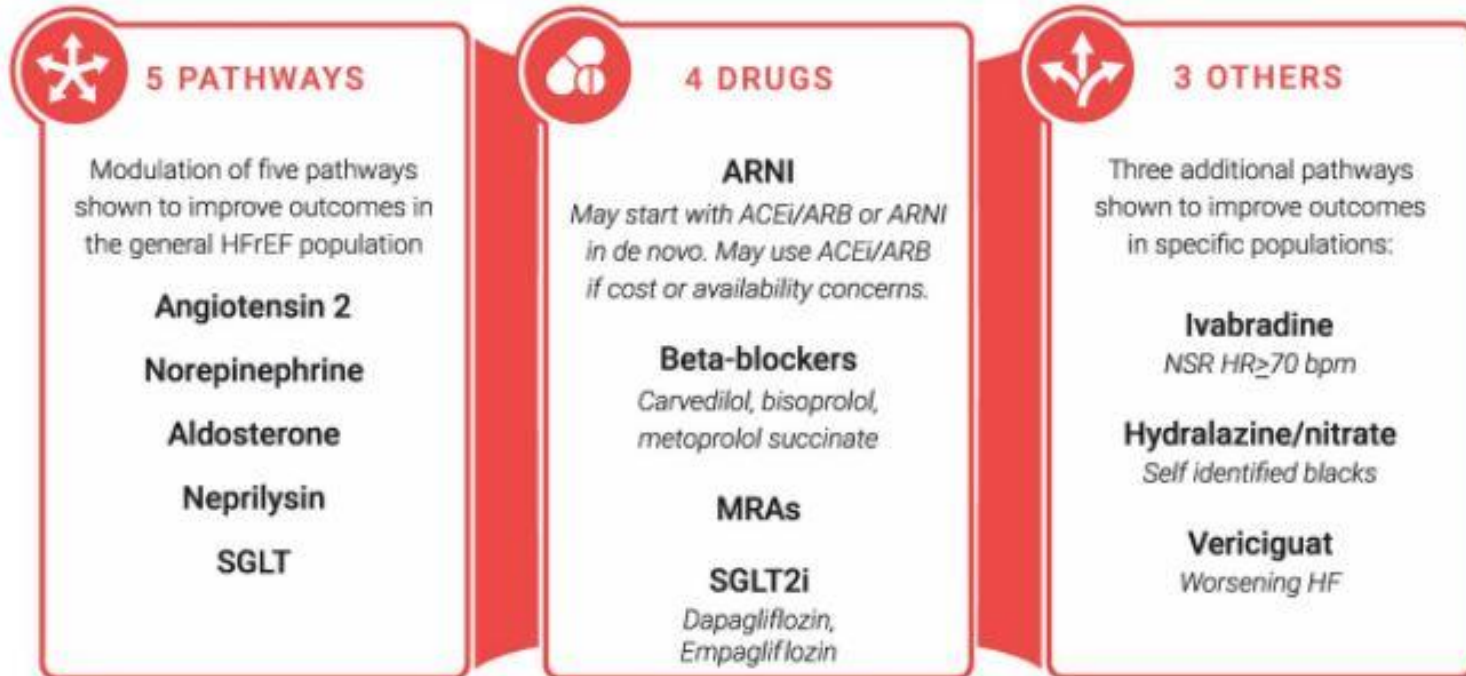
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Guideline Directed Medical Therapy

Principles and Pathophysiologic Targets of HFrEF Pharmacotherapy

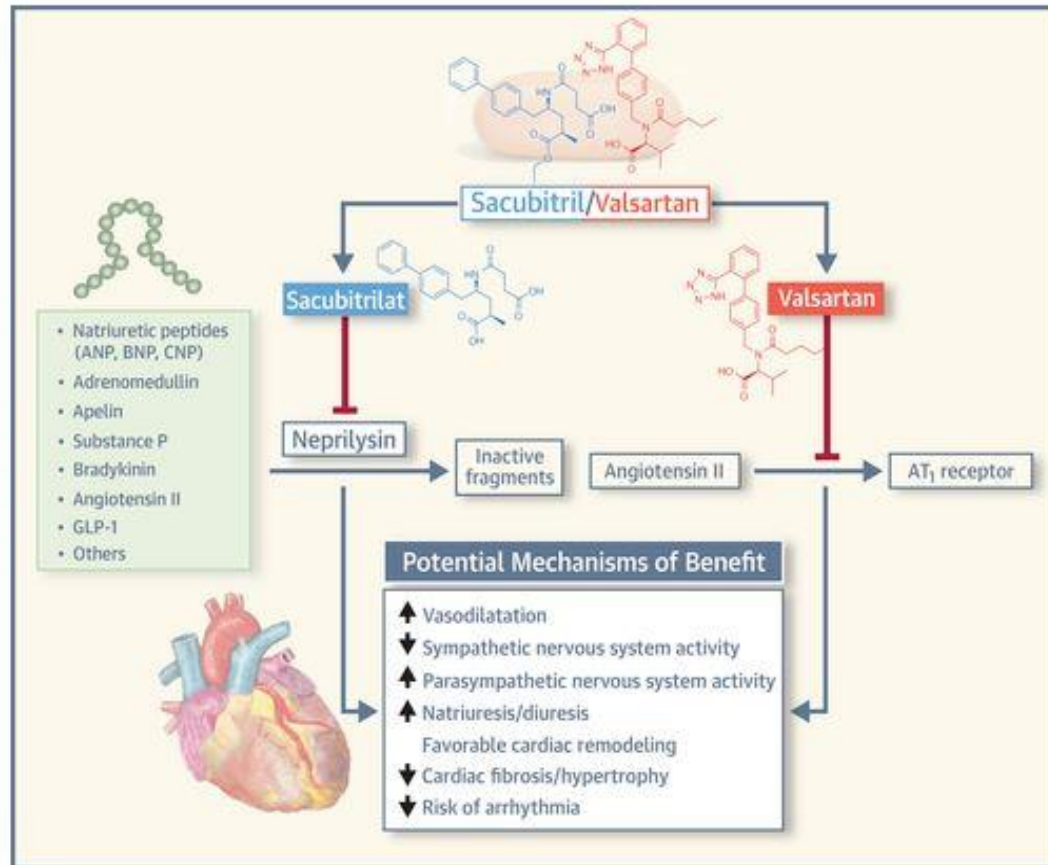


- This 4-drug combination has been suggested to increase survival by >6 years in 55-year olds and almost 1-year in octogenarians
- Patient factors such as tolerability, availability, cost, and patient preference may affect choices, doses, and sequence of therapies

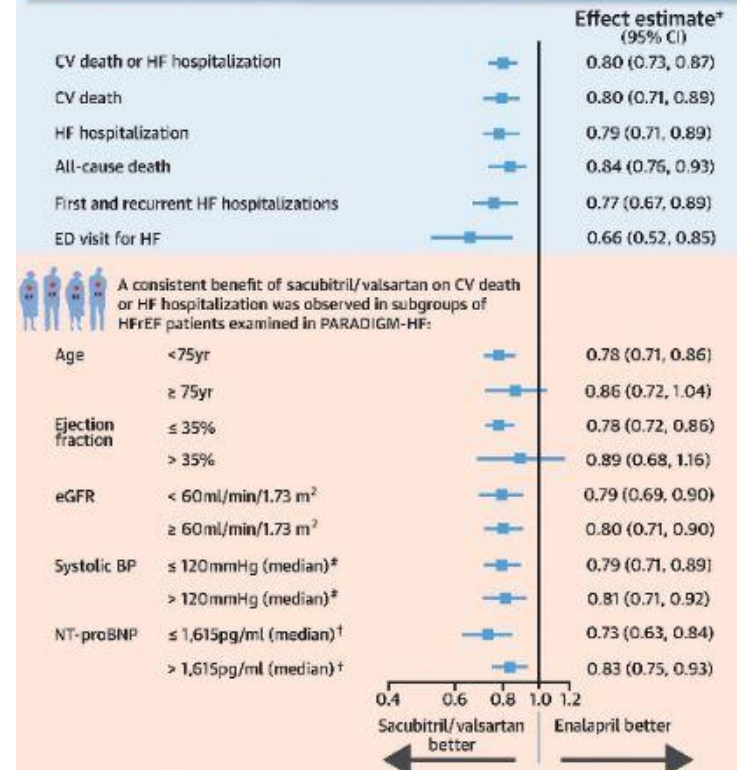
Beta Blockers

- Metoprolol succinate, carvedilol, and bisoprolol
- Choice of beta-blocker depends on blood pressure and co-morbidities
- Initiate and uptitrate when the patient is euvolemic
- Contraindications:
 - Symptomatic bradycardia despite lowest dose
 - Advanced heart failure and low cardiac output
 - Home inotropes (dobutamine)
 - High-grade AV block

Sacubitril/Valsartan



Effect of sacubitril/valsartan compared with enalapril on clinical, mechanistic, and quality-of-life outcomes in patients with heart failure and reduced ejection fraction



JACC:HF. 2020; 8(10): 800-10.

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Initiating Sacubitril/Valsartan

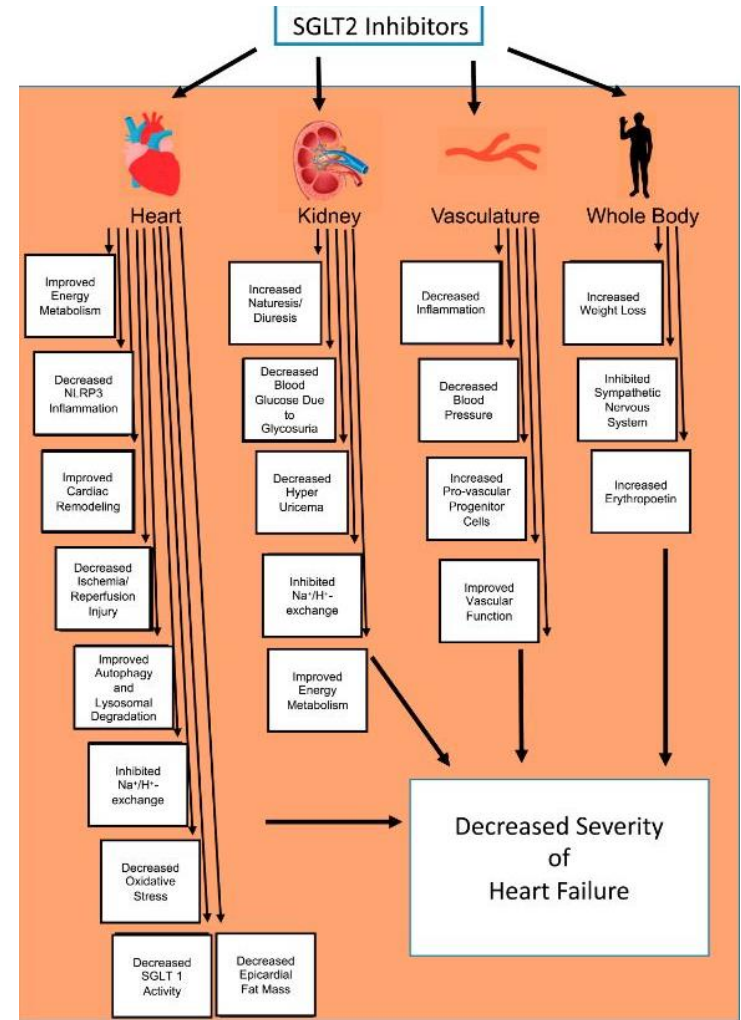
- If not on ACEi/ARB, start 24/26mg BID
- If on a low dose of ACEi/ARB, start 24/26mg BID
- If on a moderate-high dose of ACEi/ARB, start 49/51mg BID
- If $GFR < 30$ or moderate hepatic impairment, start 24/26mg BID
 - If on ACEi, 36-hour wash out period is required to minimize risk of angioedema
- Diuretic dose may need to be reduced or discontinued based on volume status
- Uptitrate every 2-4 weeks
- ARNI increases BNP level. NT-proBNP is not affected.

Mineralocorticoid Receptor Antagonist

- Spironolactone and eplerenone
- Higher incidence of hyperkalemia and renal dysfunction with spironolactone
- Contraindicated in patient with GFR <30 (\sim Cr 2.5) and K >5
- Patients must demonstrate compliance before initiating

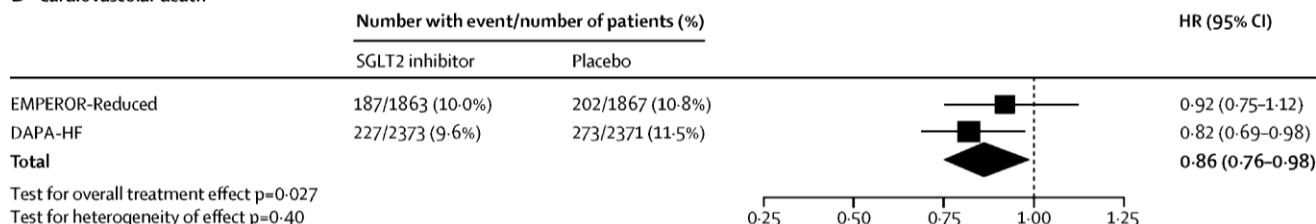
Sodium Glucose Co-Transporter 2 Inhibitors

- Dapagliflozin, empagliflozin, and canagliflozin
- Block renal tubular glucose reabsorption
- Modest improvement in glycemic control
- Osmotic diuresis, weight loss, and blood pressure reduction
- Proposed mechanism: effects on myocardial metabolism, fibrosis, inflammation, vascular function, and ion transport

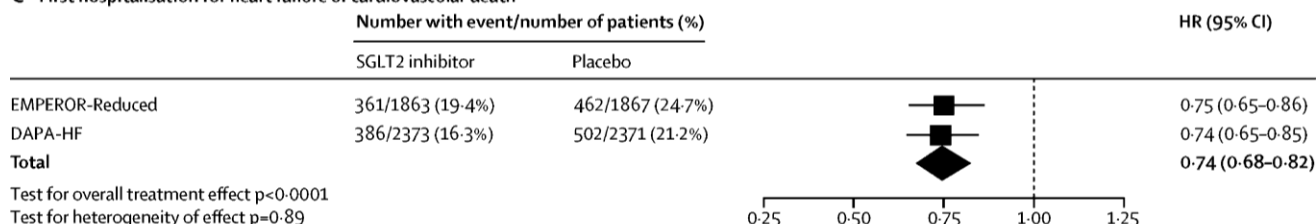


Sodium Glucose Co-Transporter 2 Inhibitors

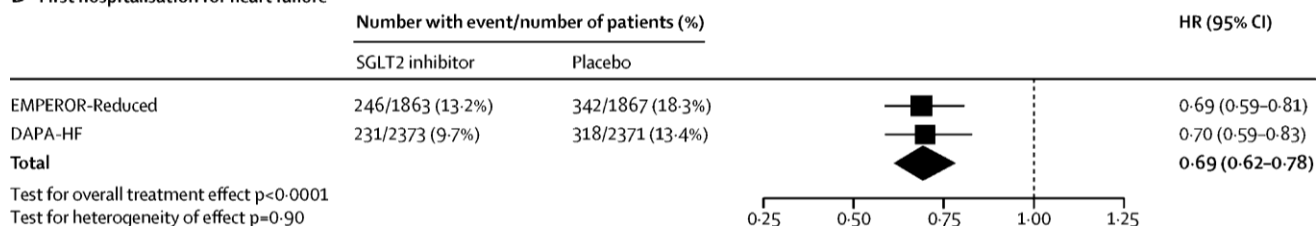
B Cardiovascular death



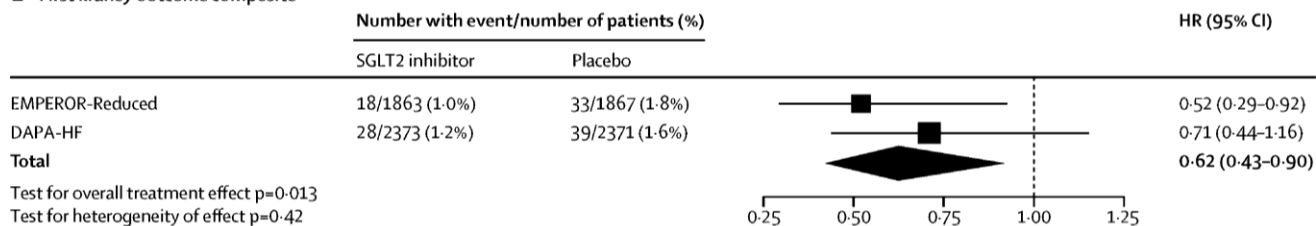
C First hospitalisation for heart failure or cardiovascular death



D First hospitalisation for heart failure



E First kidney outcome composite

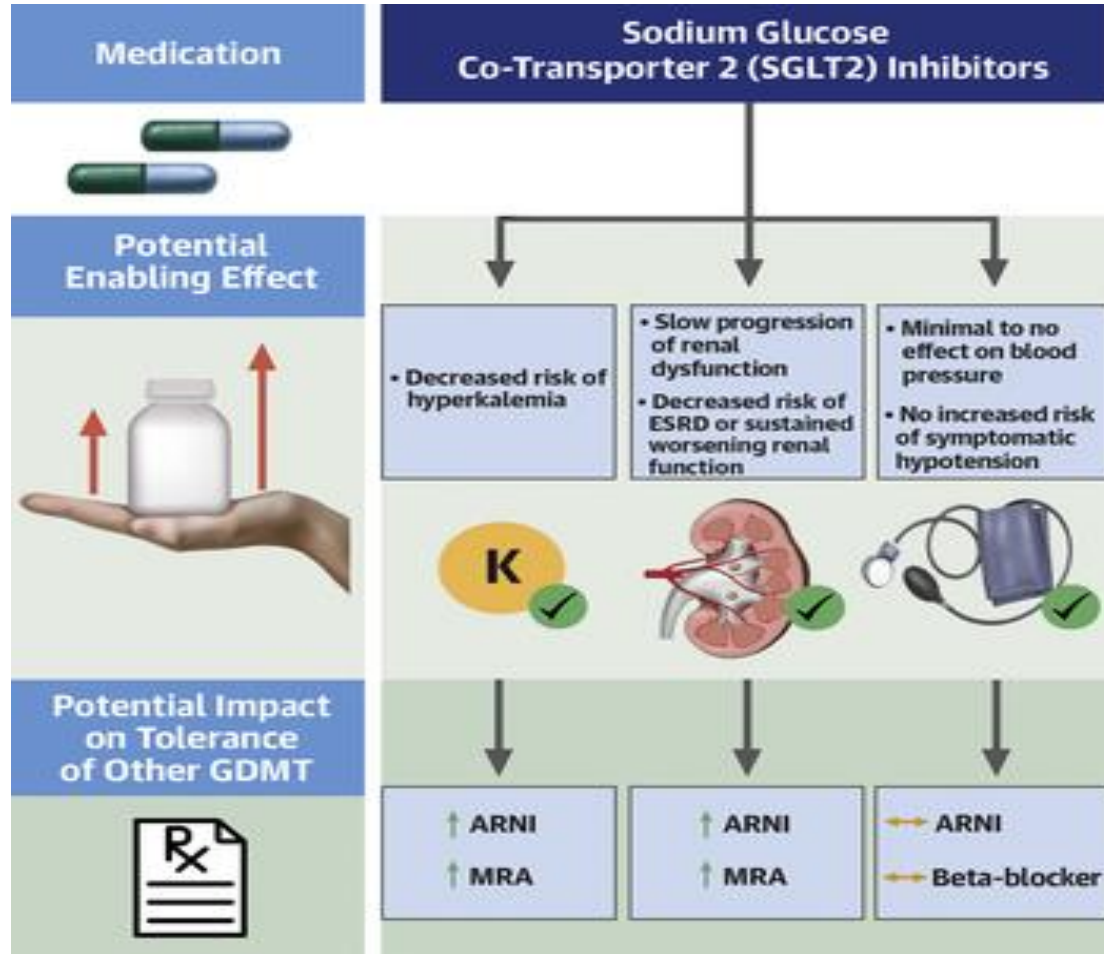


Lancet 2020. 396;819-829

N Eng J Med. 2020;383:1436-1446

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Sodium Glucose Co-Transporter 2 Inhibitors



Stephen J. Greene et al. *J Am Coll Cardiol* 2021; 77:1408-1411.

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Initiation of SGLT2 Inhibitors

SGLT-2 inhibitor	Recommended dose	Dose adjustment	Precautions and warnings
Empagliflozin	10 mg per os OD 25 mg per os OD	Impaired renal function: <ul style="list-style-type: none"> eGFR <30 ml/min/1.73 m²: discontinue 	All SGLT-2 inhibitors <ul style="list-style-type: none"> Diabetic ketoacidosis Hepatic injury Volume depletion Hypotension Critical illness Emergency surgery Recurrent genital mycotic infections Lower limb amputation Electrolyte imbalance
Canagliflozin	100 mg per os OD 300 mg per os OD	Impaired renal function: <ul style="list-style-type: none"> eGFR <30 ml/min/1.73 m²: discontinue 	
Dapagliflozin	10 mg per os OD	Impaired renal function: <ul style="list-style-type: none"> eGFR <30 ml/min/1.73 m²: discontinue Hepatic impairment: <ul style="list-style-type: none"> Starting dose, 5 mg 	

Diuretics

- Most patients will require a diuretic to control fluid retention
- Loop diuretics: furosemide, bumetamide, and torsemide
- Thiazide diuretics, metolazone, for diuretic resistance
- Each + of edema= 5-10 lbs



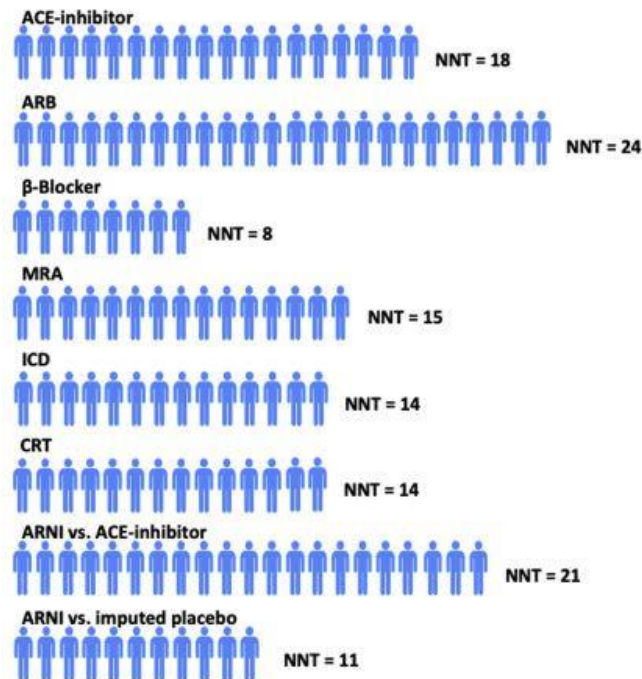
Other Medical Therapy

- Vericiguat, omecamtiv mecarbil, ivabradine, and digoxin have been shown to reduce the combined risk of cardiovascular death and hospitalization for heart failure
- Relative risk has been <10-20%, with no overall benefit on cardiovascular death
- May be considered in selected patients

Impact of GDMT on All-Cause Mortality

	Relative Risk
Beta Blocker	↓35%
ARNI	↓28%
Aldosterone antagonist	↓30%
SGLT2i	↓17%

Estimated 5-year NNT for all-cause mortality



- Cumulative risk reduction in mortality if all evidence-based medical therapies are used:
 - Relative risk reduction 72.9%
 - Absolute risk reduction 25.5%
 - NNT 3.9
- A 55-year old on quadruple therapy is projected to extend life by > 6 years

JACC:HF. 2020; 8(10): 800-10.
Am Heart J. 2011;161(6):1024-1030

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Guideline Directed Medical Therapy

- <25% of patients eligible for all 3 therapies are prescribed triple therapy

A

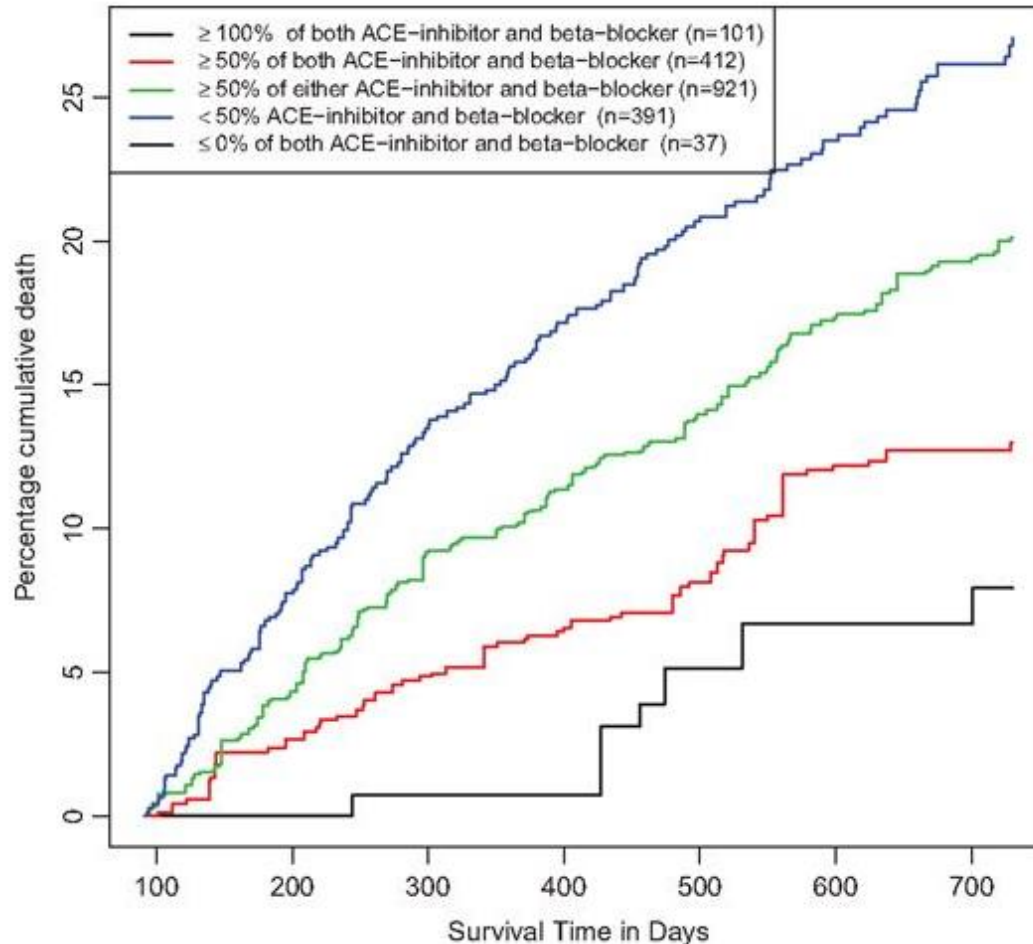


	ACEI/ARB	ARNI	ACEI/ARB/ ARNI	Beta- Blocker	MRA
Without Contraindication and Not Treated	1374	3029	920	1159	2317
Treated	2107	452	2536	2351	1163
With Contraindication	37	37	62	8	38

Lancet 2020; 369:121-128
J Am Coll Cardiol. 2018;72(4):351-366.

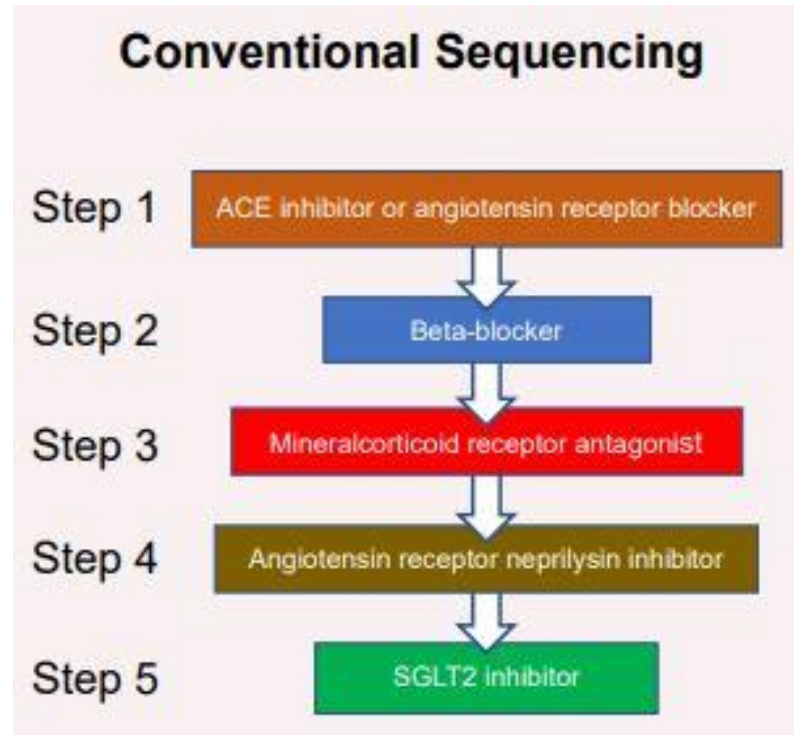
Importance of Target Doses

- Only 1% of eligible patients are prescribed triple therapy at target doses



- E Heart J2017;38:1883-90

Initiation of GDMT



- Uptitration to target doses at each step typically requires 6 months or more

Simultaneous or Rapid Sequence Initiation

	Initiation and optimization of medication dosing				
CDMMT	Day 1	Days 7-14	Days 14-28	Days 21-42	After day 42
ARNI	Initiate at low dose	Continue	Titrate, as tolerated	Titrate, as tolerated	Maintenance or additional titration of the 4 foundational therapies Consideration of EP device therapies or transcatheter mitral valve repair Consideration of add-on medications or advanced therapies, if refractory
β -Blocker	Initiate at low dose	Titrate, as tolerated	Titrate, as tolerated	Titrate, as tolerated	
MRA	Initiate at low dose	Continue	Titrate, as tolerated	Continue	
SGLT2i	Initiate	Continue	Continue	Continue	Manage comorbidities

- Low starting doses should take precedence over uptitration of any individual drug class to target dose
- Goal is to achieve target or maximally tolerated doses by 3-6 months of treatment

Simultaneous or Rapid Sequence Initiation

Benefits with initiating BB+ARNI+MRA+SGLT2i:

- Rapid improvement in health status (within 1-8 weeks).
- Rapid reduction in HF hospitalization (within 2-4 weeks).
- Rapid reduction in HF rehospitalization (within 2-4 weeks).
- Rapid reduction in mortality (within 2-4 weeks).
- Improvement in LVEF (within 12 weeks).
- Improved use, adherence, persistence, and overcoming inertia.

- N Engl J Med. 2014;371:993-1004.
- JAMA. 2019; 322(11):1077-1084
- N Engl J Med. 2019;380:539-548
- Circ 2019;139:2285-2288
- JACC Heart Fail. 2019;7(11):933-941
- E JHF, 2020;3:314

Counseling and Education

- Explain the rationale for guideline directed medical therapy
 - There is substantial opportunity for improvement in symptoms, quality of life, and health outcomes
- Continue regular aerobic exercise to improve functional capacity
- Education regarding sodium and fluid restriction
- Recommend smoking/drug cessation and avoidance of excessive alcohol consumption

Medications to Avoid

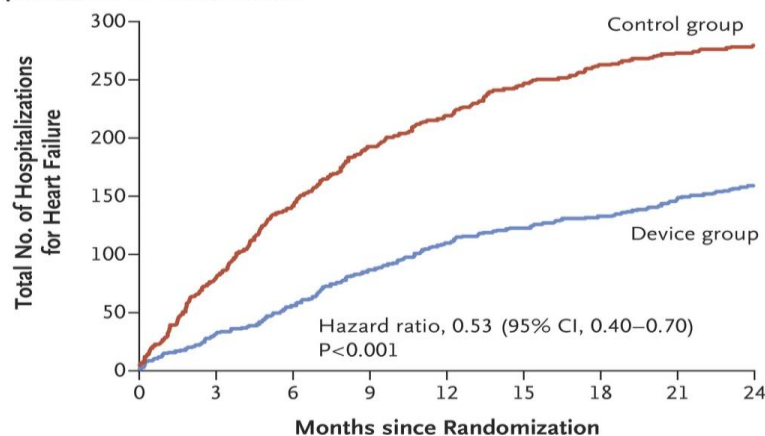
Medication	Adverse Effects
Antiarrhythmics (excluding amiodarone and dofetilide)	Increase risk of death Negative inotrope
Non-dihydropyridine calcium channel blockers (Diltiazem, verapamil)	Negative inotrope
Cilostazol	Increased risk of death
NSAIDs or COX-2 inhibitors	Increased risk of HF-related hospitalization and symptoms. Decreased diuretic response
Thiazolidinediones	Increased risk of HF-related hospitalizations and symptoms

Mitral Regurgitation

- Secondary mitral regurgitation is a common consequence of LV remodeling
- Moderate or severe MR is present in 1/3 of HF patients
- MR is associated with adverse clinical outcomes
- Optimization of GDMT is the first initiate step
 - Attenuate LV dysfunction and remodeling
- Transcatheter edge-to-edge repair should be considered in patients who remain symptomatic despite optimization of GDMT (including CRT when indicated)

COAPT Trial

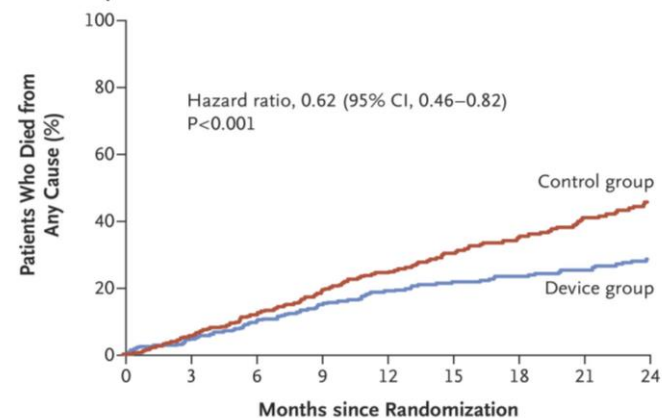
A Hospitalization for Heart Failure



No. at Risk

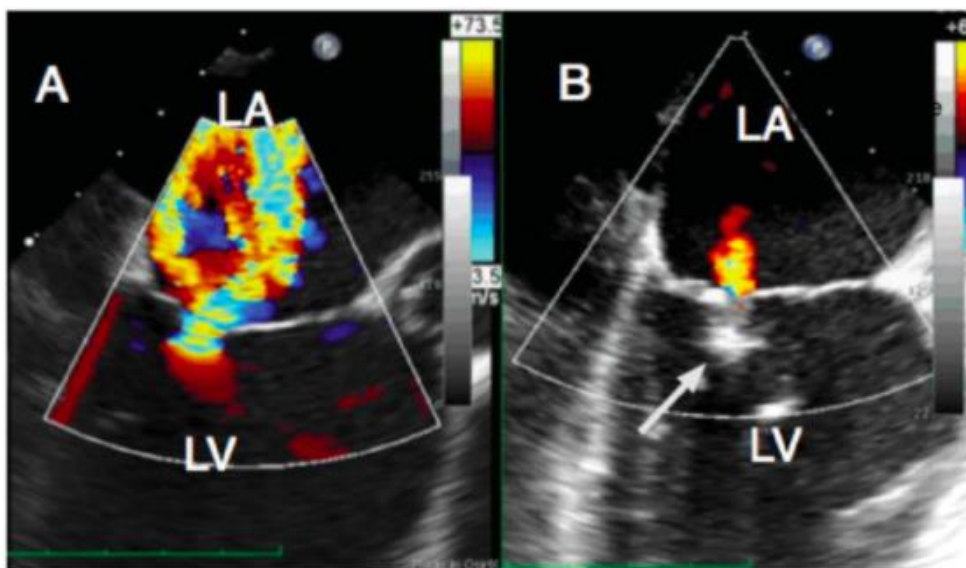
Control group	312	294	271	245	219	176	145	121	88
Device group	302	286	269	253	236	191	178	161	124

C Death from Any Cause



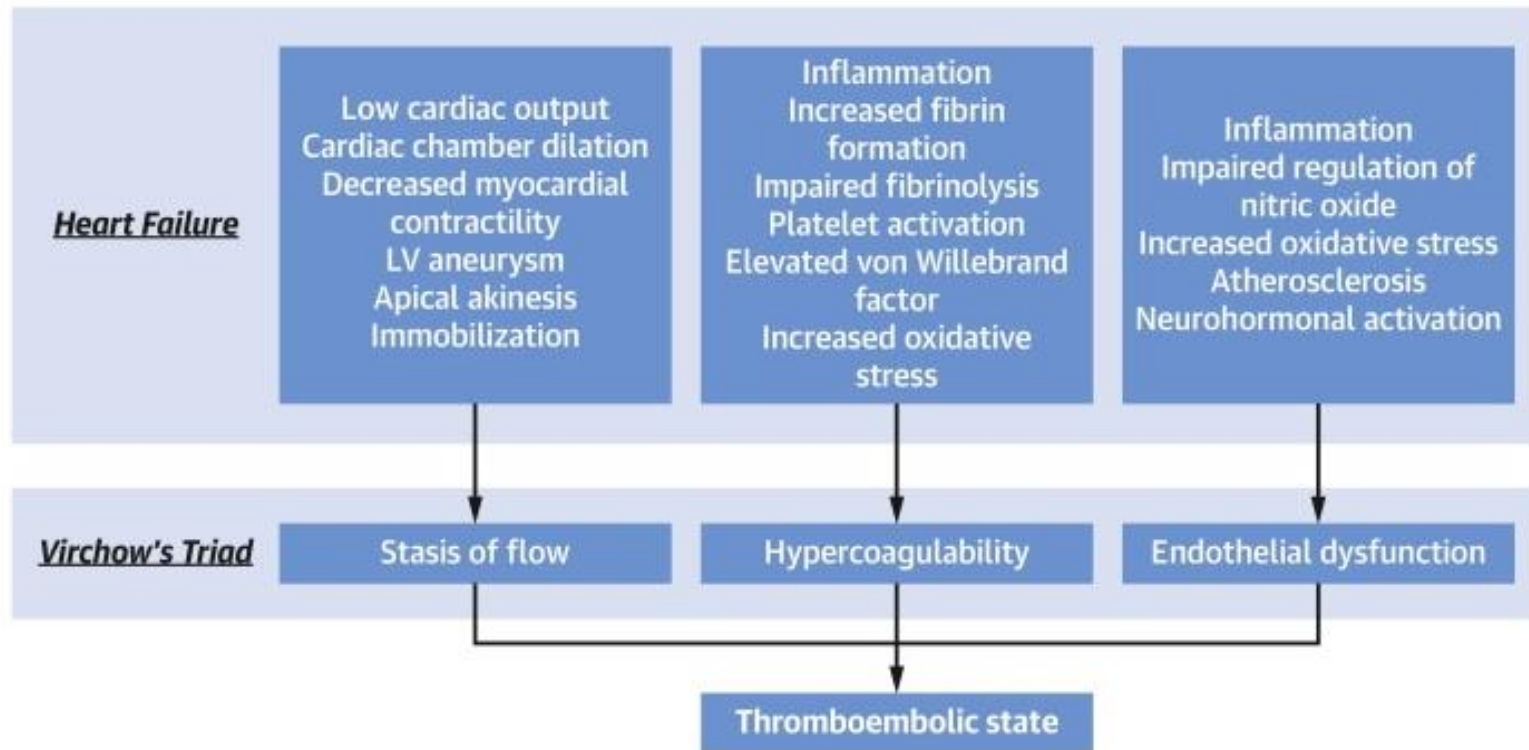
No. at Risk

Control group	312	294	271	245	219	176	145	121	88
Device group	302	286	269	253	236	191	178	161	124



Thromboembolism and Anticoagulation

- Patients with HF are at risk of thromboembolic events, even when in sinus rhythm



Thromboembolism and Anticoagulation

- Earlier studies with warfarin failed to show compelling evidence of clinical benefit
- Recent studies showed decreased stroke risk with low dose NOACs
- Current guidelines do not recommend anticoagulation in patients with HF, without AF, prior thromboembolic event, or cardioembolic source
- Situations in which anticoagulation could be considered:
 - Recent MI
 - Asymptomatic mural thrombus
 - Anterior apical akinesis or dyskinesis

Case

- Patient underwent cardiac catheterization, which was negative for obstructive disease
- Discharged on metoprolol XL, losartan, spironolactone, and furosemide
- Switched to sacubitril/valsartan and dapagliflozin added
- GDMT was uptitrated to maximum doses by 4 months post hospitalization
- Repeat echocardiogram showed LVEF 15-20%. LV diameter decreased, mitral and tricuspid regurgitation now mild
- Symptoms improved from NYHA class IV to class II

Take Home Points

- Every effort should be made to determine the etiology of heart failure
- Ischemic heart disease is the most common etiology and evaluation for coronary artery disease should be obtained
- GDMT with quadruple therapy significantly reduces morbidity and mortality
- Simultaneous or rapid sequence initiation has significant benefits over conventional sequencing, with effects seen in 2-4 weeks
- Target doses matter
- Advanced HF therapies includes device therapy should be considered in patients who remains symptomatic despite maximum tolerated doses of GDMT

Q&A

Next Webinar:

HHP Care Model and Disease Management Webinar

Thursday, May 13, 2021
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Thank you!

- A recording of the meeting will be available afterwards
- Unanswered question?
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