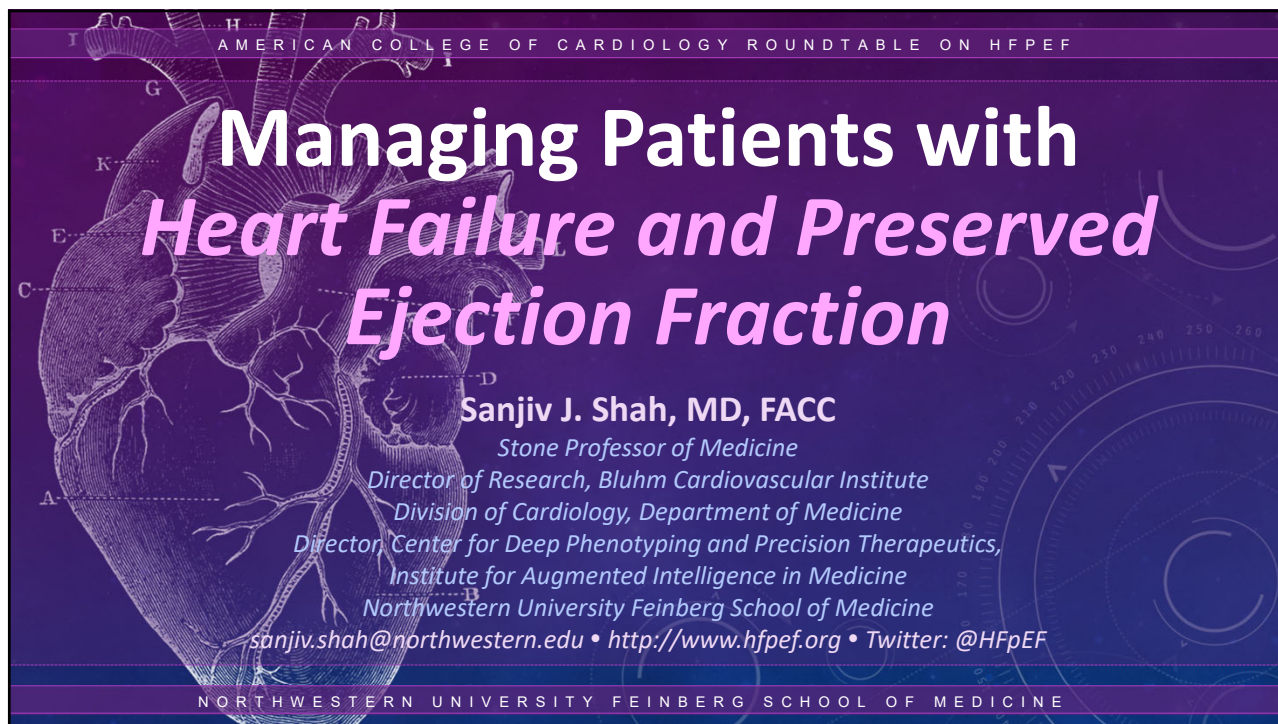




AMERICAN COLLEGE OF CARDIOLOGY ROUNDTABLE ON HFPEF

Managing Patients with *Heart Failure and Preserved Ejection Fraction*

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- **Consulting / advisory board / steering committee:**
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Treatment strategies for *HFpEF in 2022*

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2022 ACC/AHA guidelines: HFpEF

COR	LOE	Recommendation
I	C-LD	Hypertension should be controlled according to guidelines
I	B-NR	Diuretics for relief of symptoms, volume overload
IIa	B-R	SGLT2 inhibitors to reduce HF hospitalizations
IIa	C-EO	Management of AF according to published guidelines
IIb	B-R	Spirolactone to reduce HF hospitalization
IIb	B-R	ARBs to reduce HF hospitalization
IIb	B-R	ARNIs to reduce HF hospitalization
III	B-R	PDE5i and nitrates are ineffective for QOL, physical activity

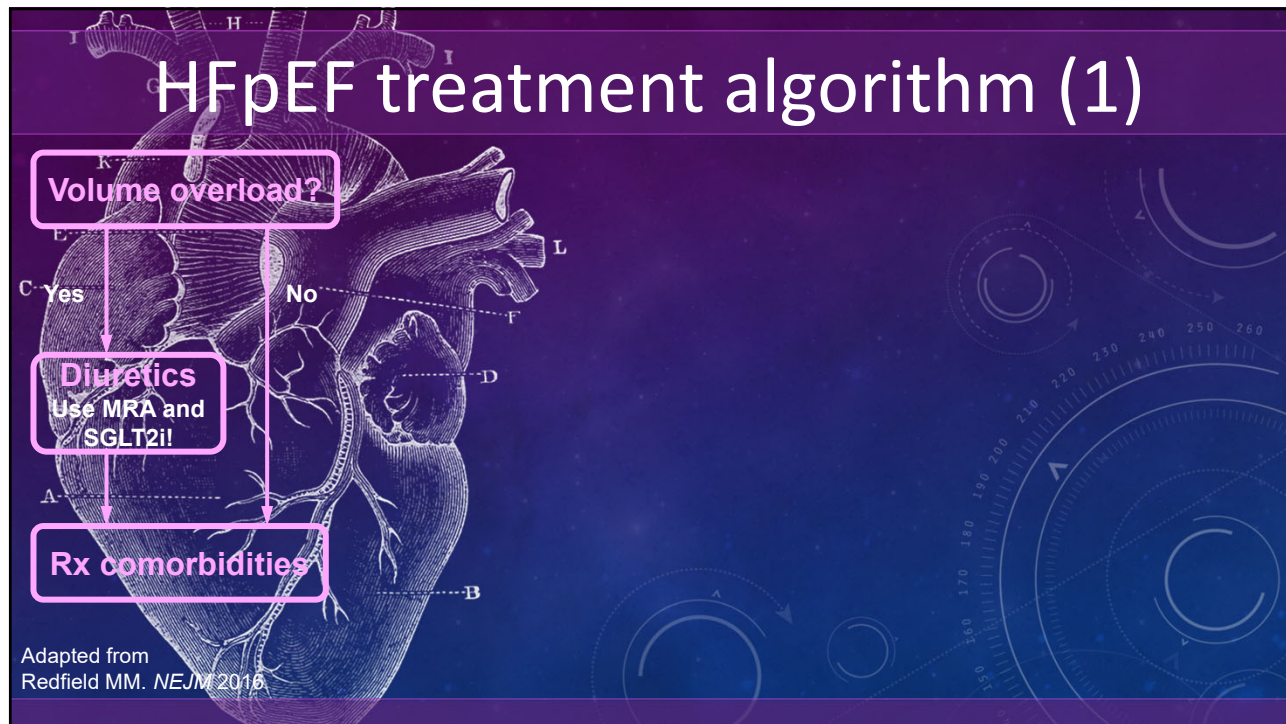
Summary:

- Treat SBP, goal < 130
- Decongest with SGLT2i and use MRA if GFR>30 and K⁺<5.0
- ARNI in LVEF <55-60%
- PDE5 inhibitors and nitrates don't work

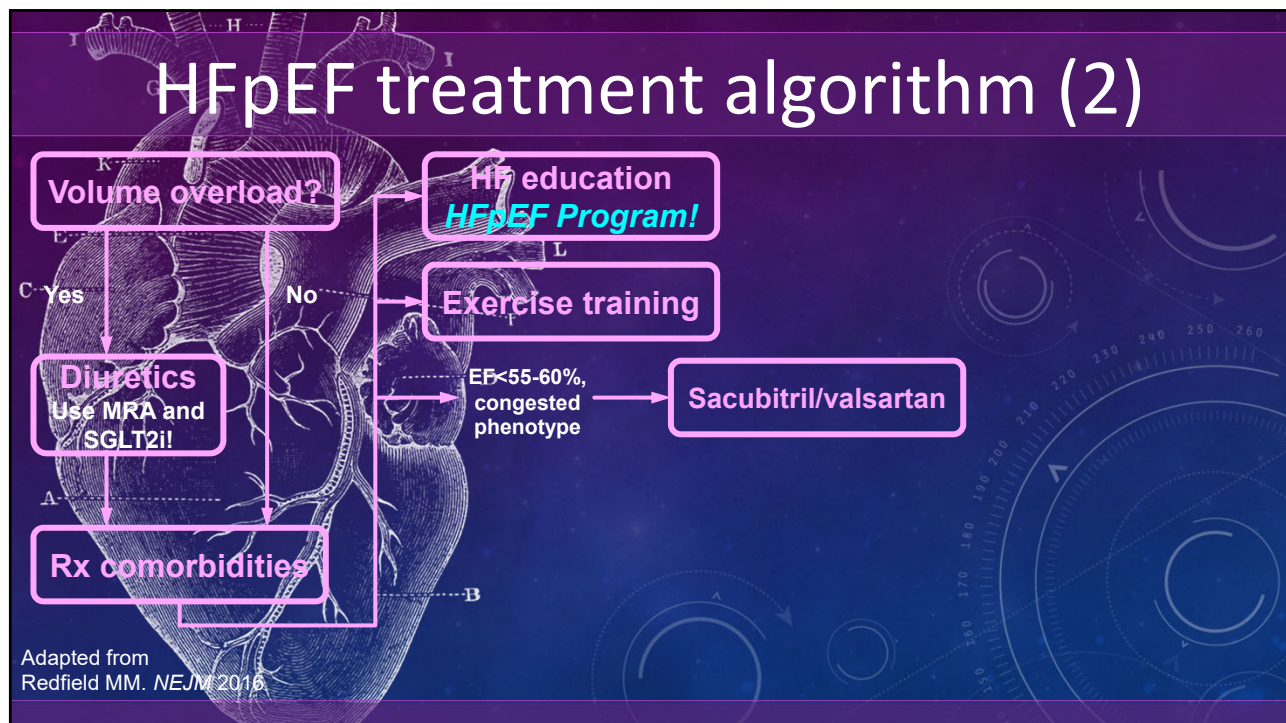
COR = class of recommendation; LOE = level of evidence
LD = limited data; EO = expert opinion; NR = non-randomized trial; R = randomized trial

Heidenreich P, et al. *Circulation* 2022

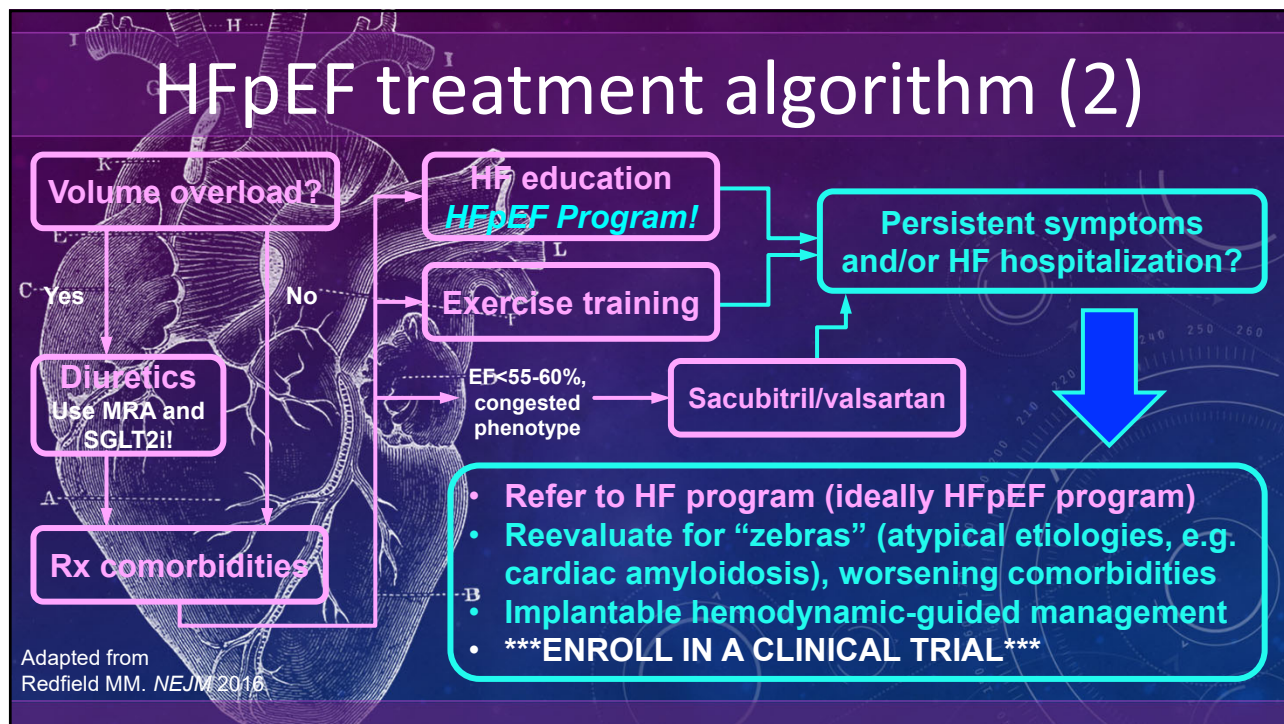
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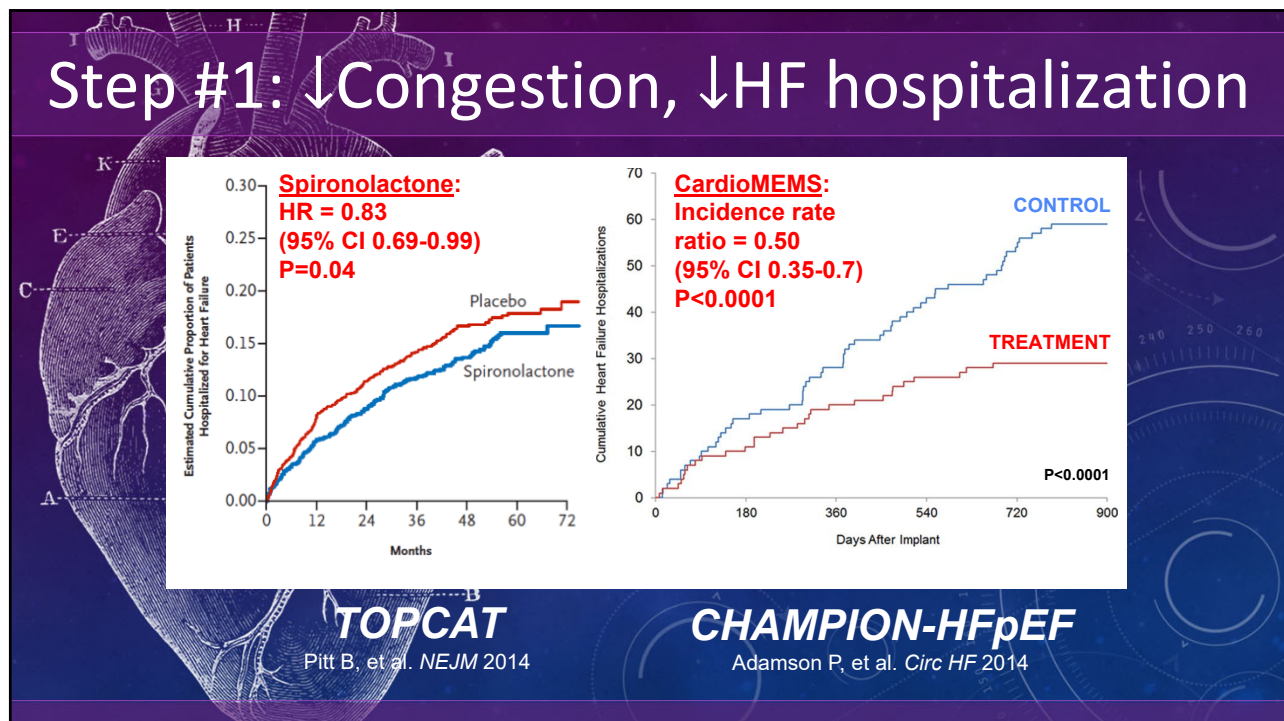
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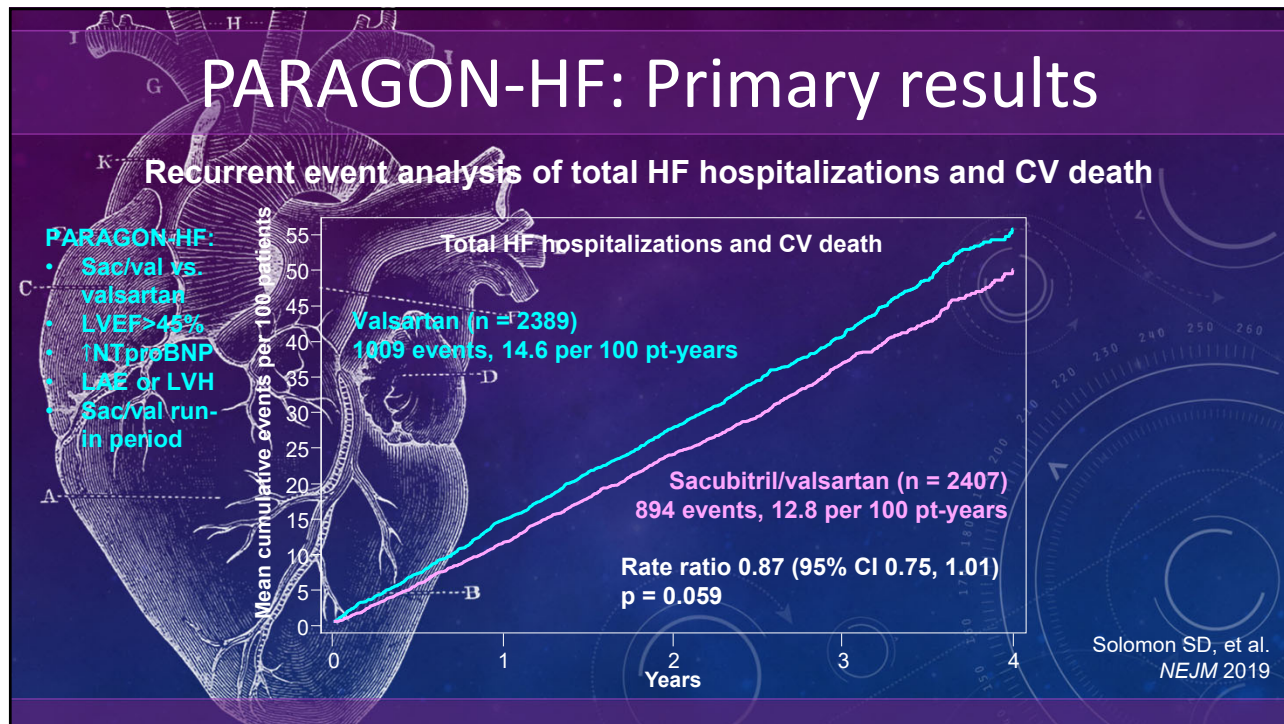
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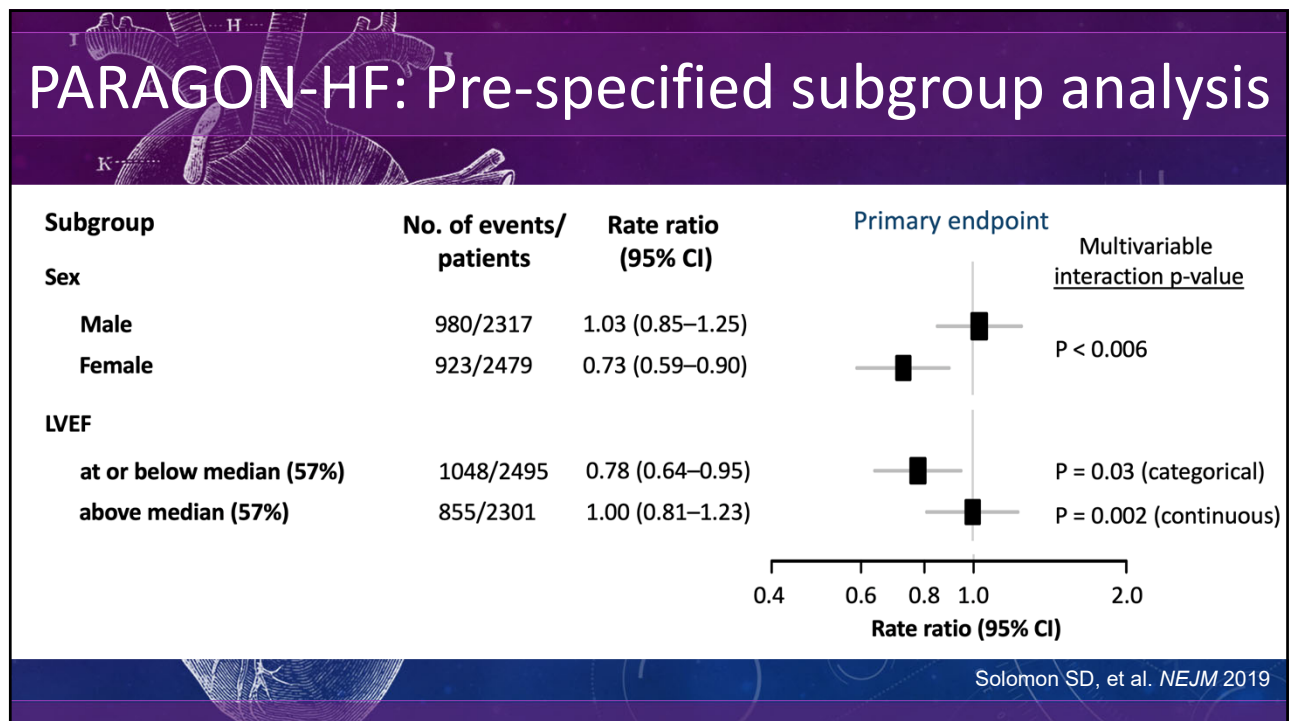
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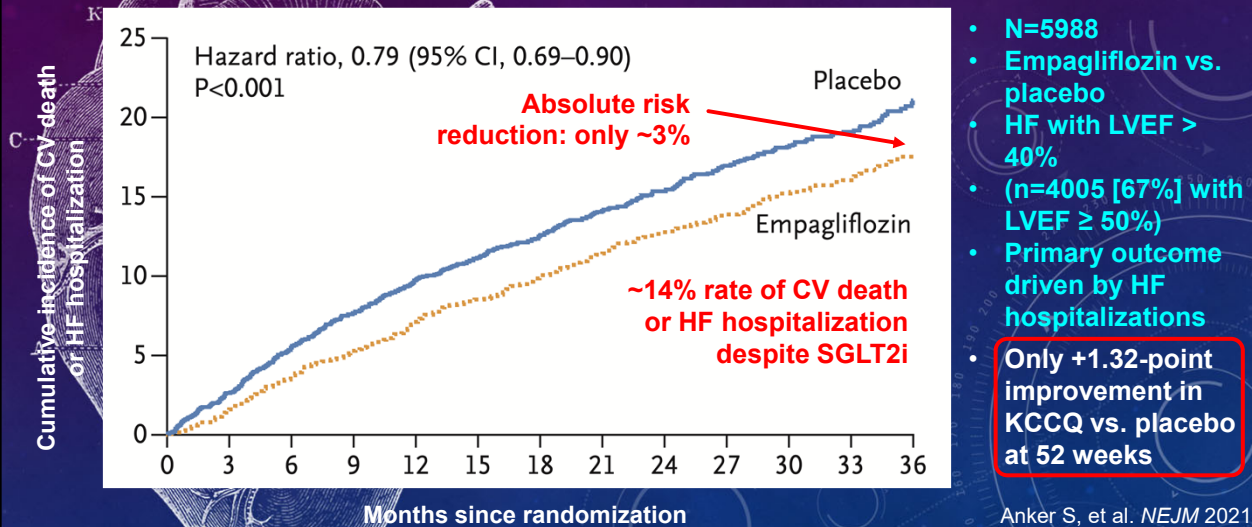


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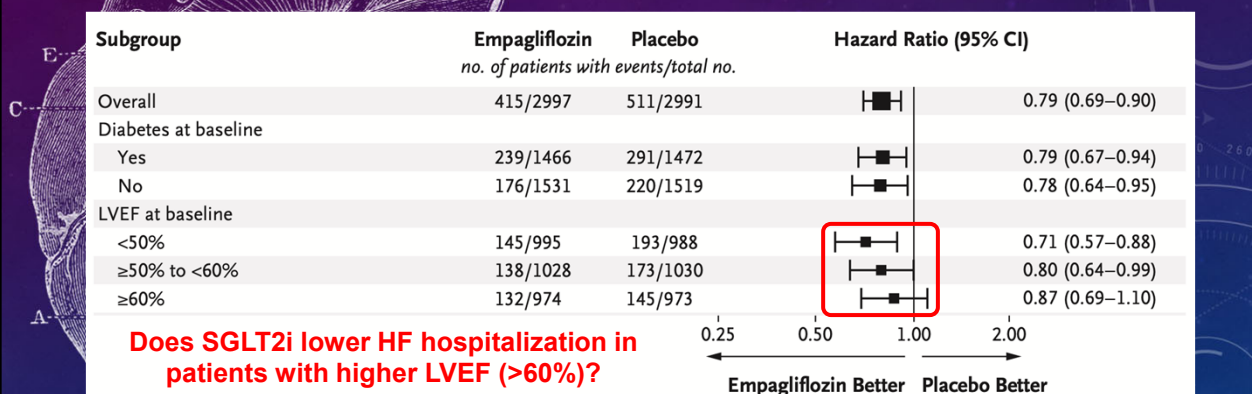
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EMPEROR-Preserved (SGLT2 inhibitor)

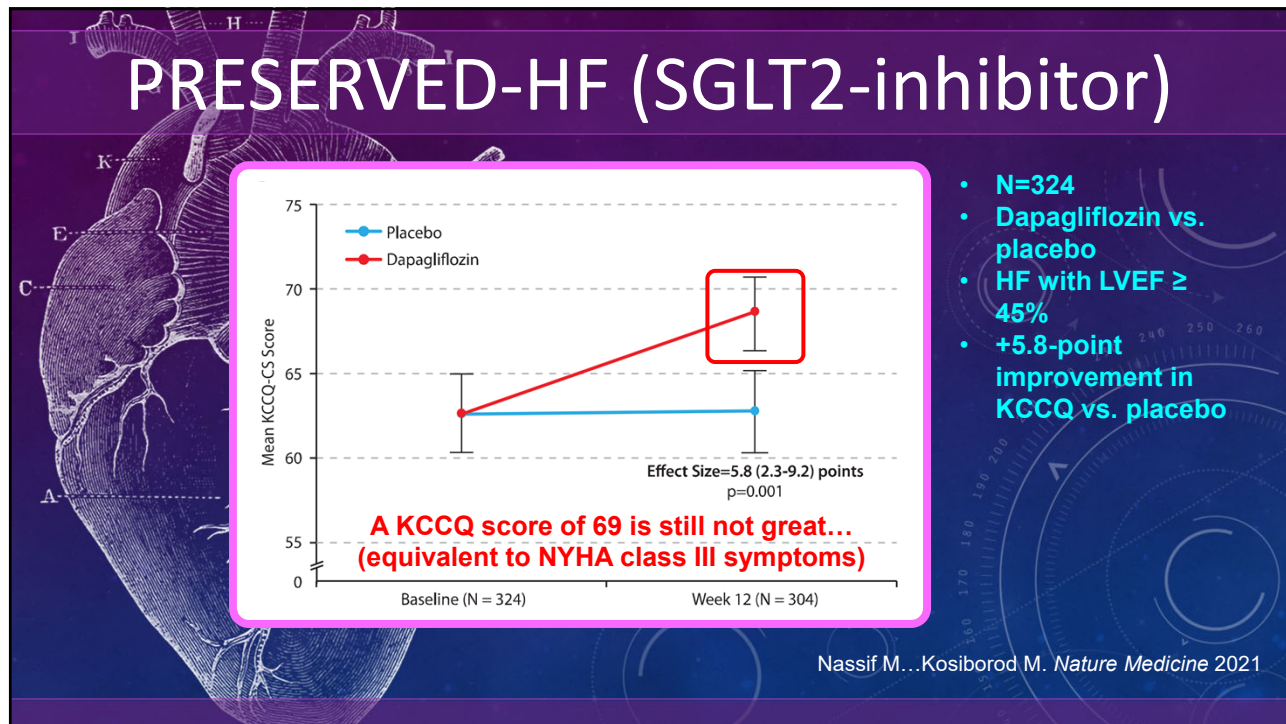


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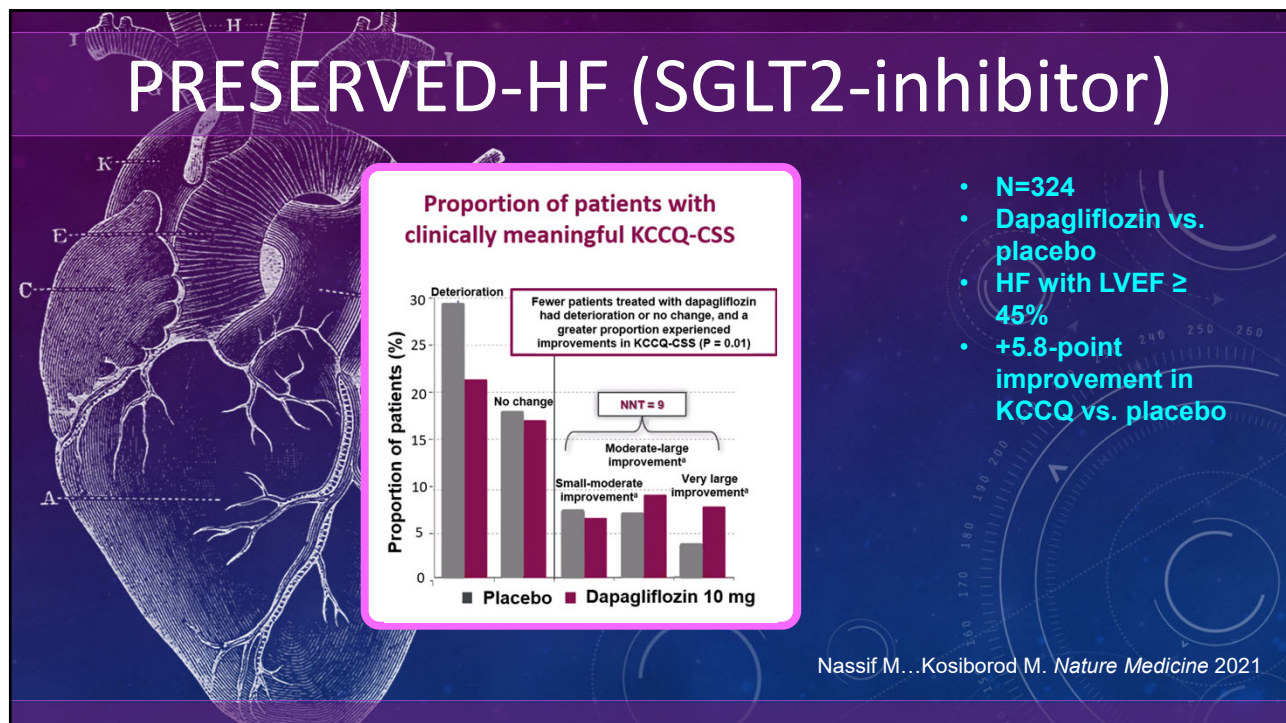
EMPEROR-Preserved (SGLT2 inhibitor)

Anker S, et al. *NEJM* 2021

12

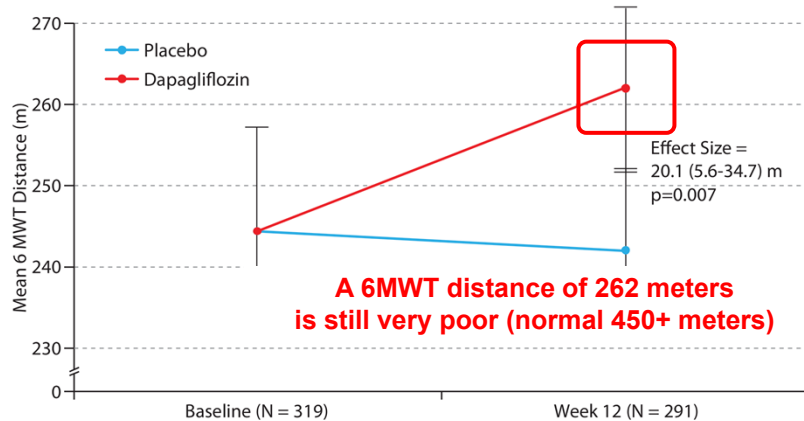


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PRESERVED-HF (SGLT2-inhibitor)

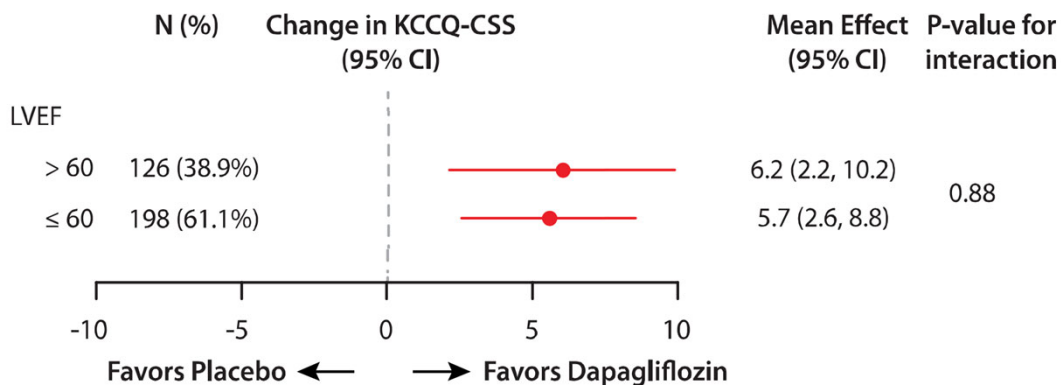


- N=324
- Dapagliflozin vs. placebo
- HF with LVEF $\geq$ 45%
- +5.8-point improvement in KCCQ vs. placebo
- +20.1-meter improvement in 6MWT distance vs. placebo

Nassif M...Kosiborod M. *Nature Medicine* 2021

15

PRESERVED-HF (SGLT2-inhibitor)

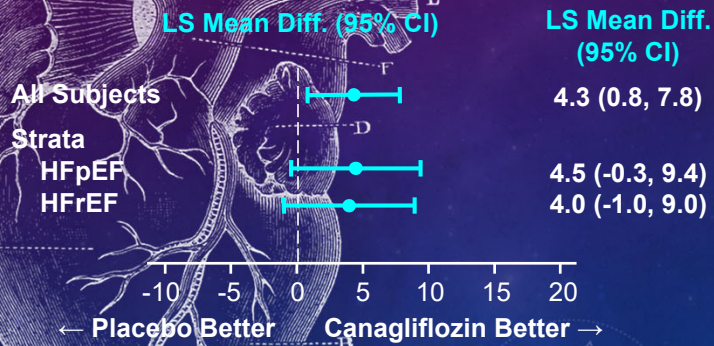


Nassif M...Kosiborod M. *Nature Medicine* 2021

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CHIEF-HF (SGLT2-inhibitor)

Benefit across the spectrum of LVEF

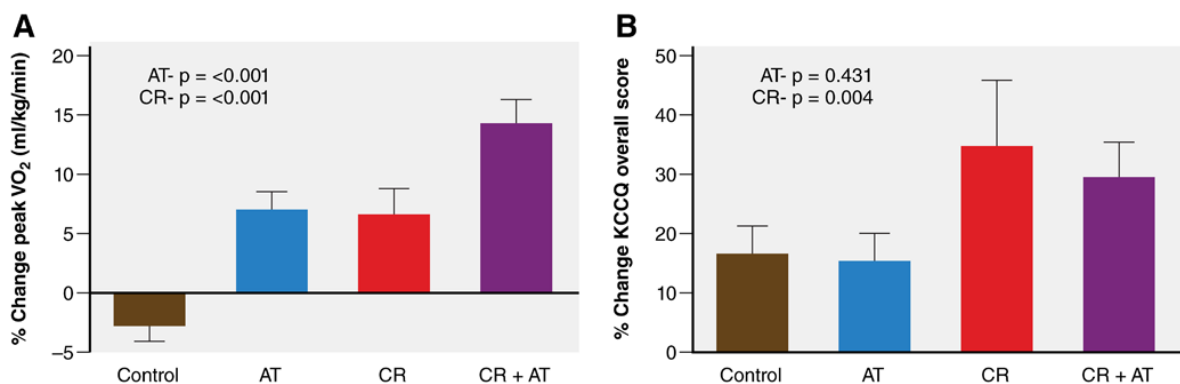


- N=476
- Pragmatic trial, no in-person visits
- Canagliflozin vs. placebo
- HF, any EF
- 59% HFpEF
- Median age = 65
- 14% AAs
- 72% non-diabetic
- **+4.3-point greater improvement in KCCQ vs. placebo at 12 weeks**

Spetrus J, et al. *Nature Medicine* 2022

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Step #2: Diet, exercise training

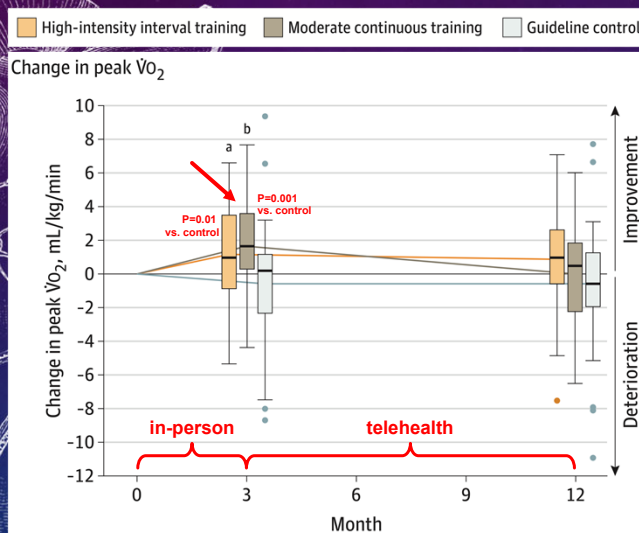


AT = aerobic exercise training, CR = caloric restriction

Kitzman D, et al. *JAMA* 2016

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Step #2: Diet, exercise training



- **SECRET trial**
 - ✓ Kitzman JAMA 2016
 - ✓ N=100
 - ✓ Mean peak $\dot{V}O_2 \sim 14.5$ mL/min/kg
- **OptimEx-Clin trial**
 - ✓ Mueller JAMA 2021
 - ✓ N=180
 - ✓ Mean peak $\dot{V}O_2 \sim 18.8$ mL/min/kg

Mueller S, et al. JAMA 2021

19

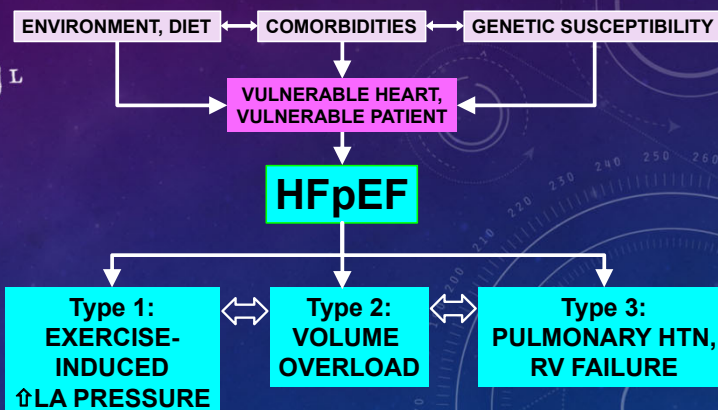
Step #3: Phenotype-guided approach

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EDITORIAL COMMENT

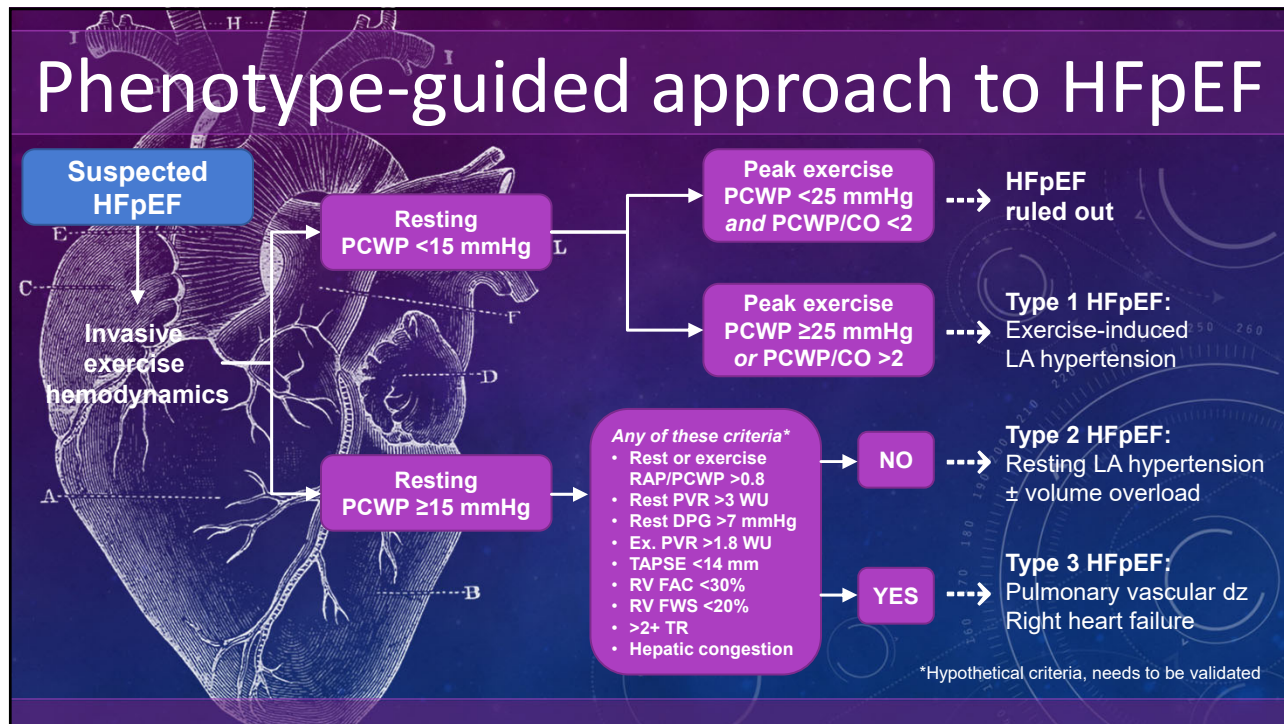
Matchmaking for the Optimization of Clinical Trials of Heart Failure With Preserved Ejection Fraction

Sanjiv J. Shah, MD
Chicago, Illinois



Shah SJ. JACC 2013

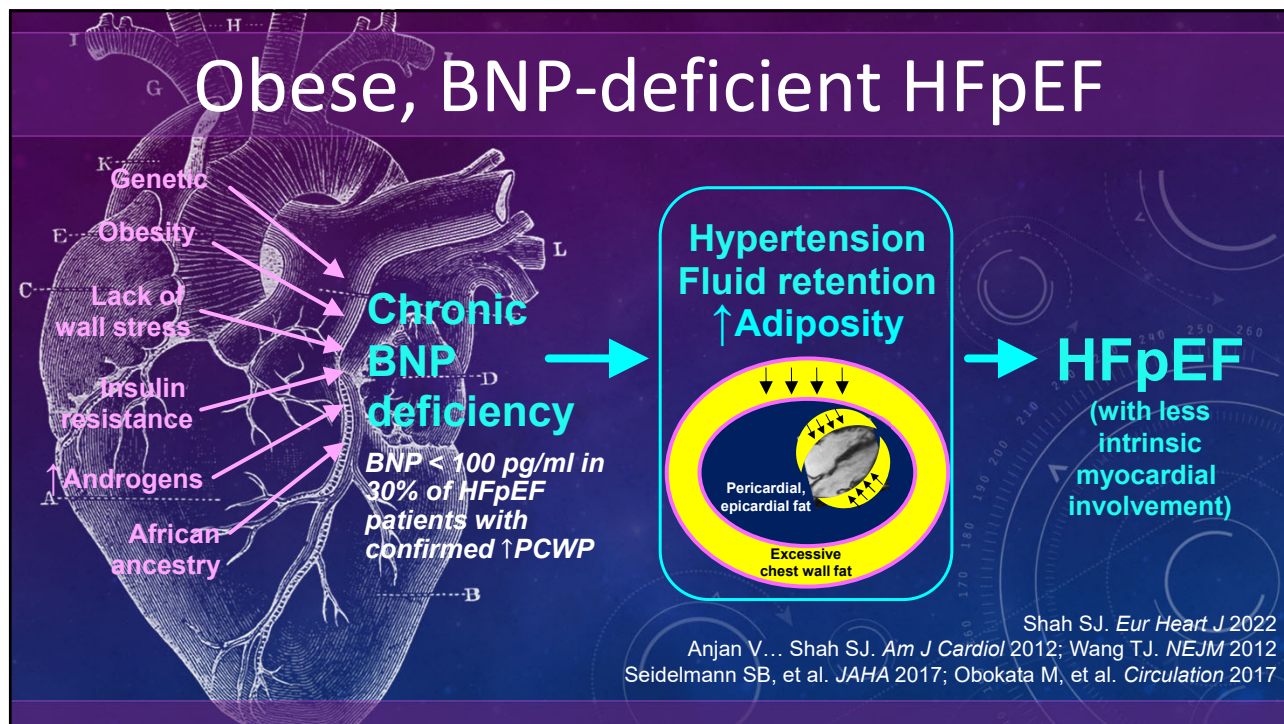
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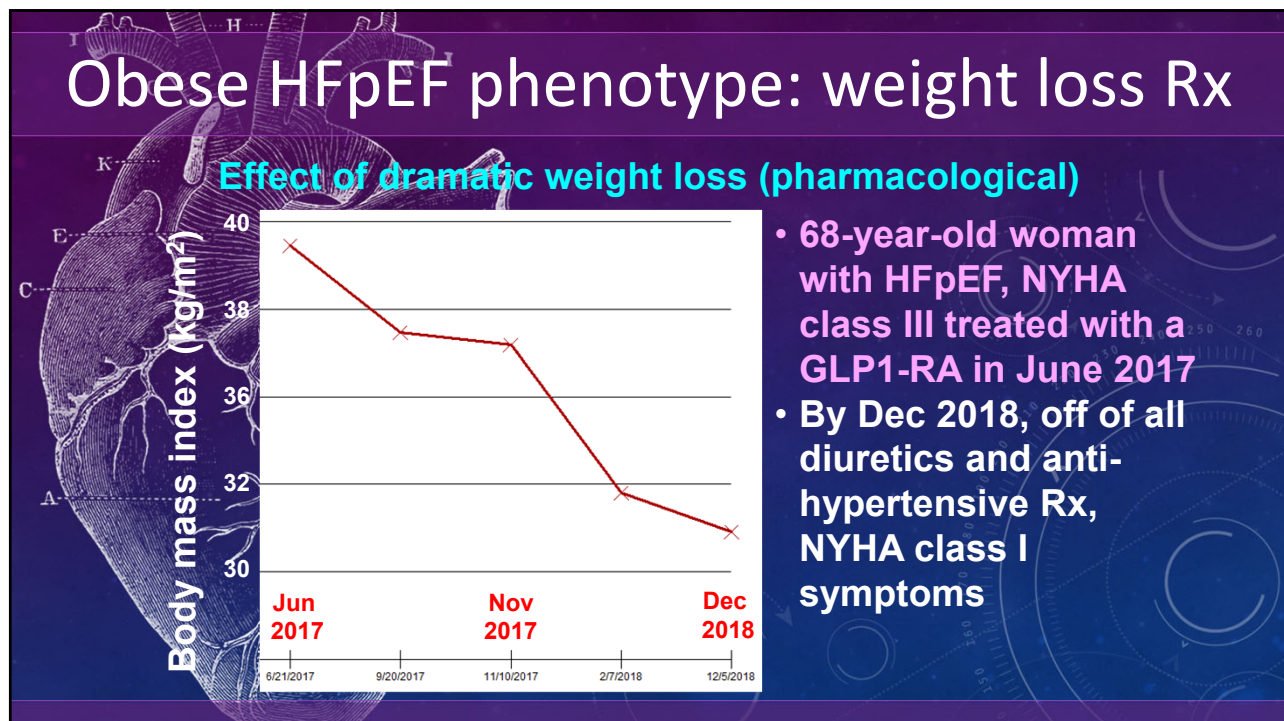
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Precision therapeutics *for HFpEF*

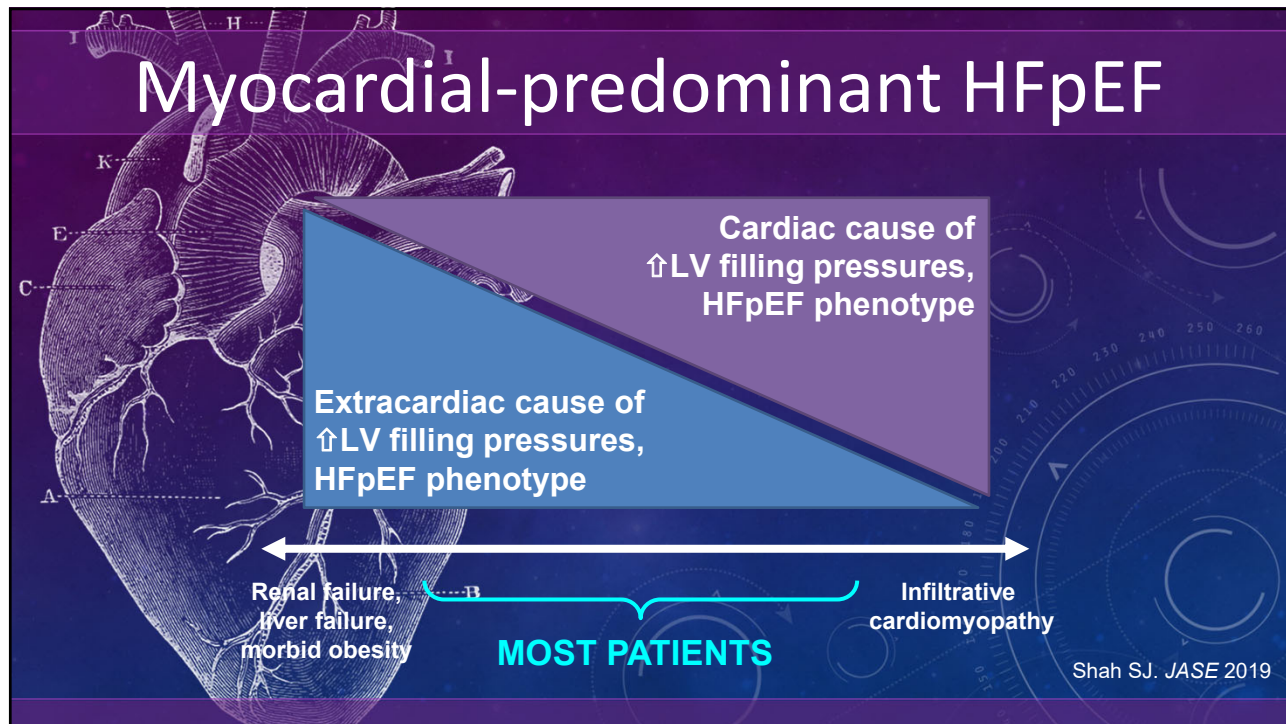
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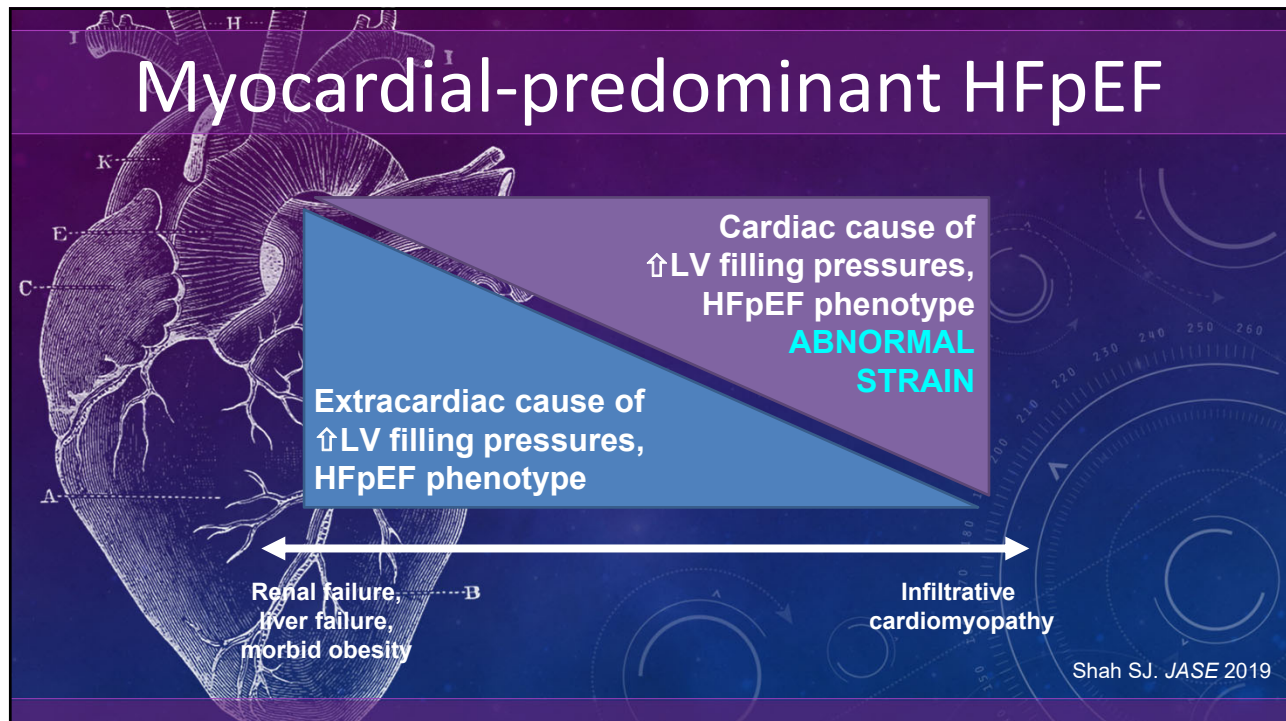
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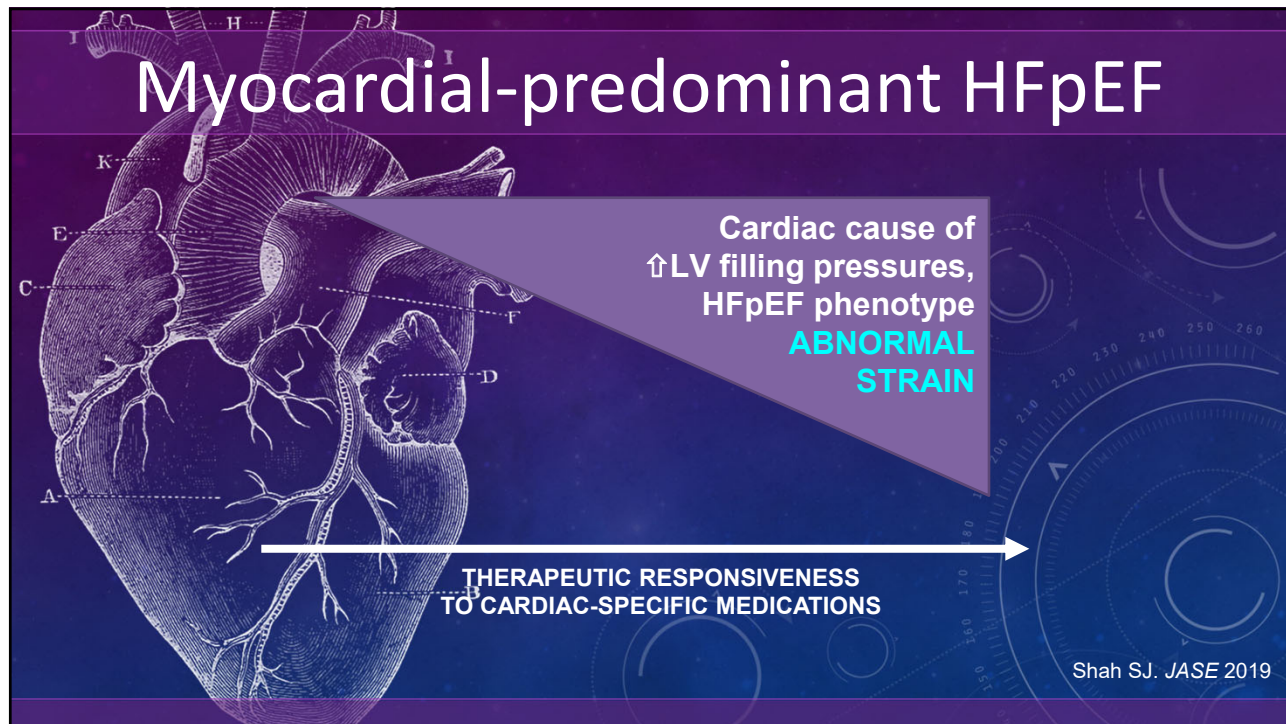
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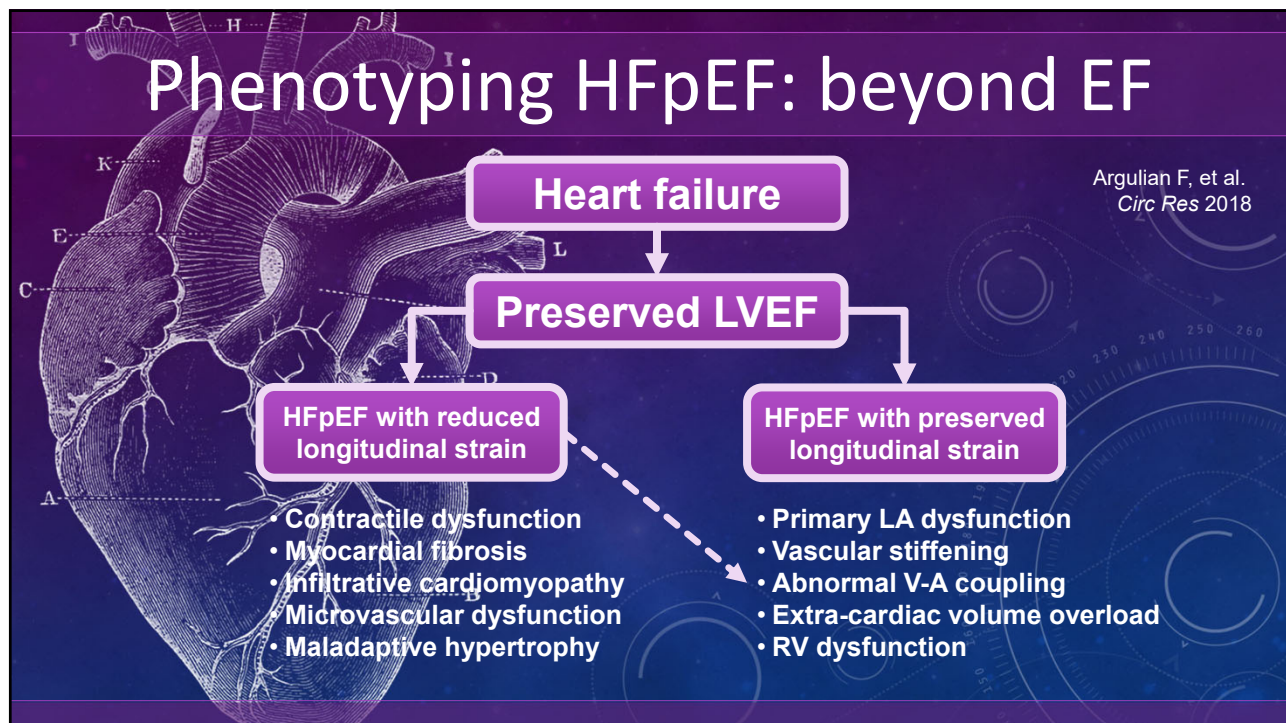
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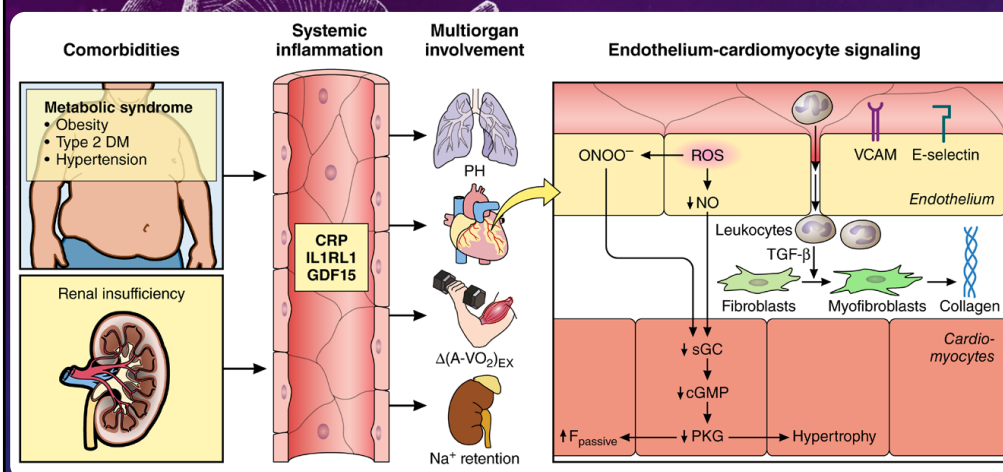
Treatment of “myocardial” HFpEF

- Potential ARNI responders: PARAGON subgroup analyses
 - ✓ LVEF < 55-60%
 - ✓ Recently hospitalized for HF within the last 6 months
 - ✓ Already treated with MRA (congested phenotype)
 - ✓ May work better in women compared to men
 - ✓ Avoid in pts with low BP, combined post- and pre-capillary pulmonary hypertension, amyloid, restrictive CM, constriction
- MRAs: TOPCAT subgroup analysis: LVEF on lower end of normal
- Myosin inhibition: in patients with HCM + obstruction

Solomon SD, et al. *NEJM* 2019; Solomon SD, et al. *Circulation* 2020
 Vaduganathan M, et al. *JACC* 2020; Jering K, et al. *JACC Heart Fail* 2021
 McMurray JJV, et al. *Circulation* 2020; Solomon SD, et al. *Eur Heart J* 2016; Olivetto I, et al. *Lancet* 2020

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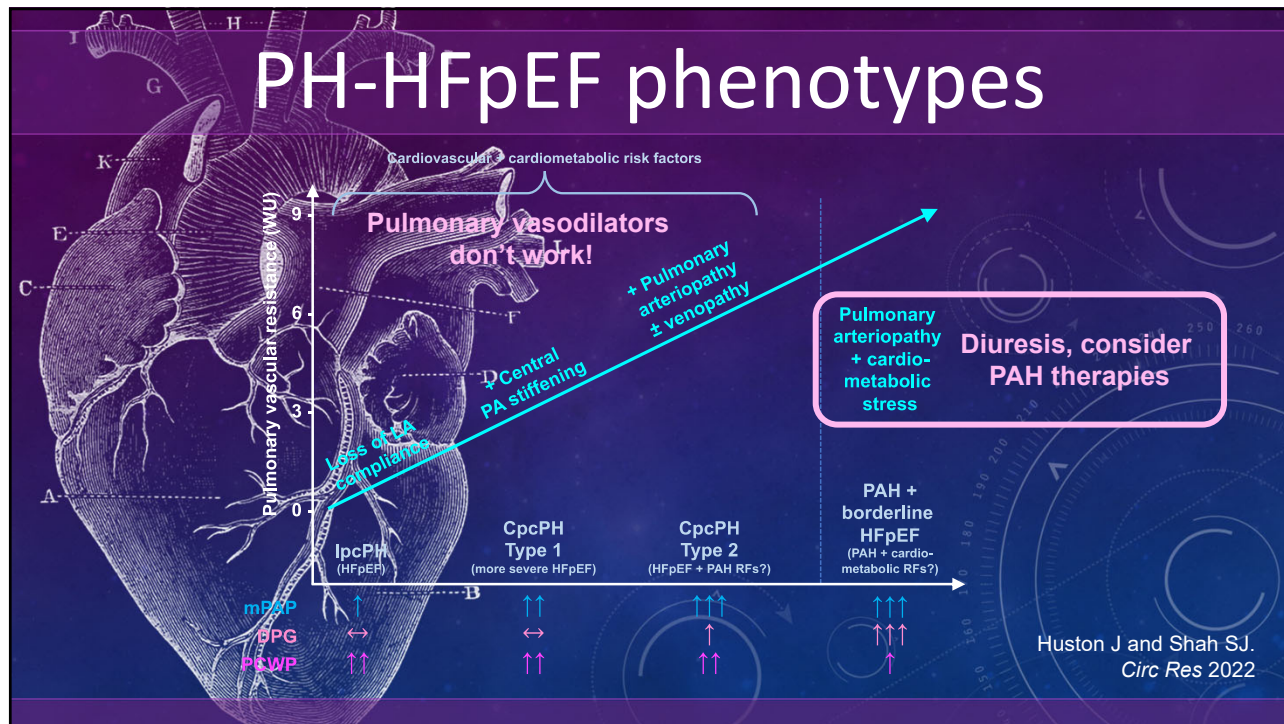
Comorbidity-inflammation in HFpEF



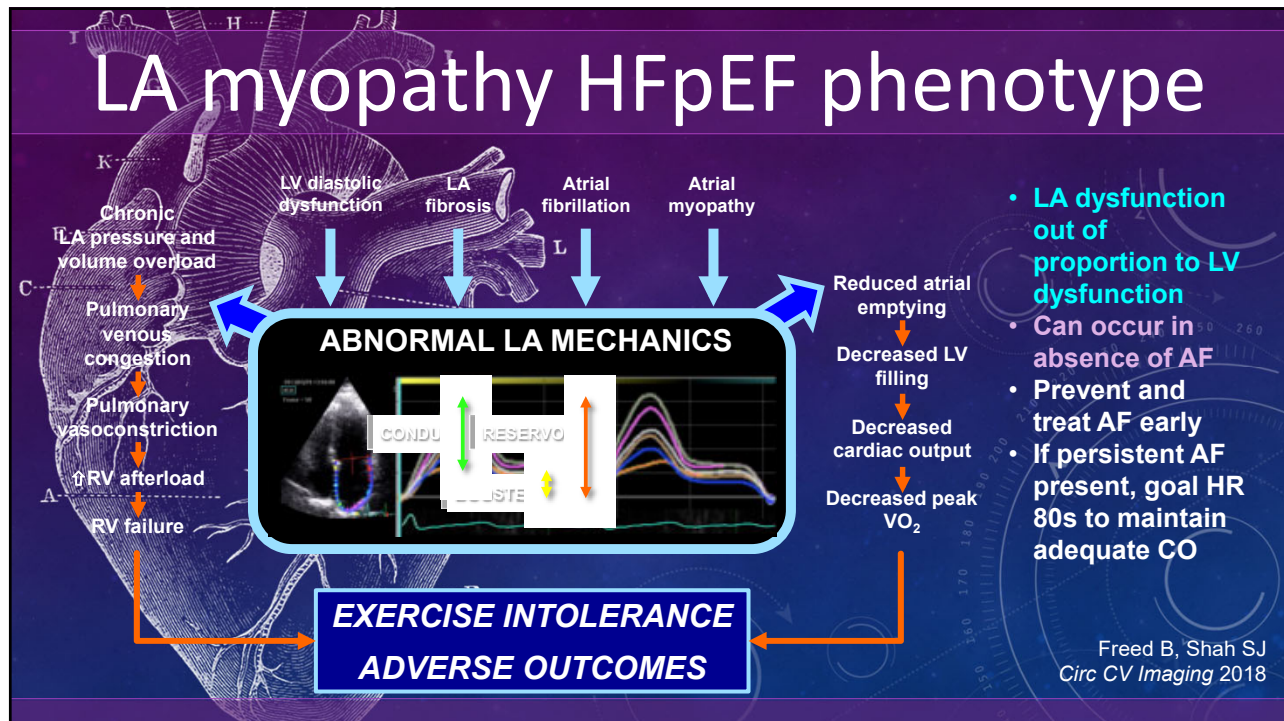
- 75% of HFpEF patients have coronary microvascular dysfunction (CMD)
- Treatment still to be defined... consider testing for at treating symptomatic CMD

Shah SJ... Paulus W. *Circulation* 2016; Shah SJ, et al. *Eur Heart J* 2018

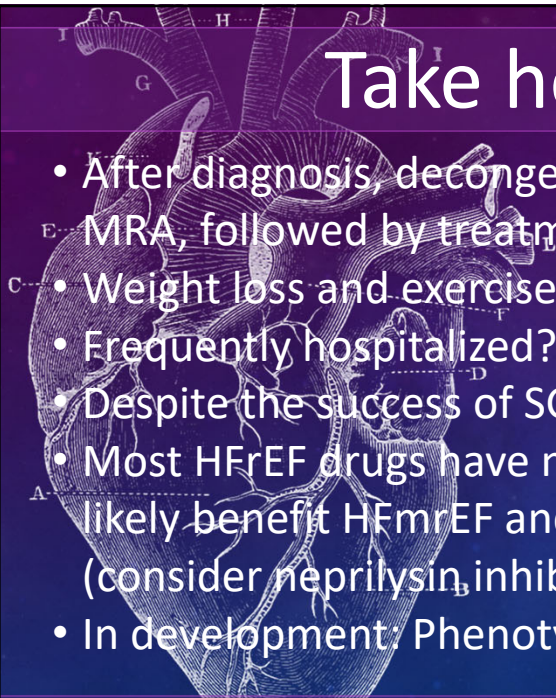
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Take home points

- After diagnosis, decongest (if needed) with SGLT2i and MRA, followed by treatment of comorbidities
- Weight loss and exercise training are beneficial
- Frequently hospitalized? Consider implantable PA monitor
- Despite the success of SGLT2i, Rx of HFpEF far from ideal
- Most HFrEF drugs have not worked for HFpEF overall, but likely benefit HFmrEF and HFpEF with LVEF < 55-60% (consider neprilysin inhibition)
- In development: Phenotype-based, targeted treatment

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Shah Lab – Northwestern University

thank you

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