

Replacing “Failure” with “Function” in heart failure management

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Session Description

- During this session you will learn about the latest evidence-based guidelines for managing heart failure with reduced, mildly reduced and preserved ejection fraction.
- Pharmacokinetics and dynamics of the newest medications will be covered as well as best practices for titration of guideline directed medical therapy.

Objectives

- Describe the current heart failure definition and classification.
- Review assessment techniques for evaluating patients with heart failure.
- Discuss management strategies for implementing guideline directed medical therapy in diverse clinical settings.

Heart Failure in the United States

6.2 million with HF in the US

\$39.2 billion total cost (direct and indirect)

11 million provider visits annually

50% with heart failure die within 5 years of diagnosis

Defining Heart Failure

A clinical syndrome with symptoms and/or signs due to:



Structural and/or functional cardiac abnormality

verified by an elevated BNP

and/or objective evidence of pulmonary or systemic congestion.

Classifying heart failure

Classification based on LVEF:

HFrEF: symptomatic HF with LVEF $\leq 40\%$

HFmrEF: symptomatic HF with LVEF 41-49%

HFpEF: symptomatic HF with LVEF $\geq 50\%$

HFimpEF: symptomatic HF with a baseline LVEF $\leq 40\%$, a ≥ 10 -point increase from baseline LVEF, and a second measurement of LVEF $> 40\%$

Stages of HF	
Stage A	At risk (-) structural heart disease or symptoms
Stage B	Structural heart disease (-) signs or symptoms
Stage C	Structural heart disease (+) current or prior symptoms
Stage D	Refractory requiring specialized interventions

New York Heart Association Classes

Class	Symptoms
NYHA Class I	No HF symptoms with ordinary physical activity
NYHA Class II	HF symptoms with ordinary physical activity. None at rest.
NYHA Class III	Significant limits in physical activity. Minimal symptoms at rest
NYHA Class IV	Symptoms at rest. HF symptoms with any activity.

Diagnostic evaluation of heart failure

6 minute walk test-
<300 m poor prognostic
indicator

EKG- rate, rhythm,
conduction
abnormalities,
hypertrophy

Echo- ejection fraction,
valve function, wall
motion abnormalities,
wall thickness.

Potential Precipitants of Heart Failure



Coronary artery disease

Hypertension

Anemia

Peripartum

Valve dysfunction

Cardiotoxins (chemotherapy, cocaine, alcohol)

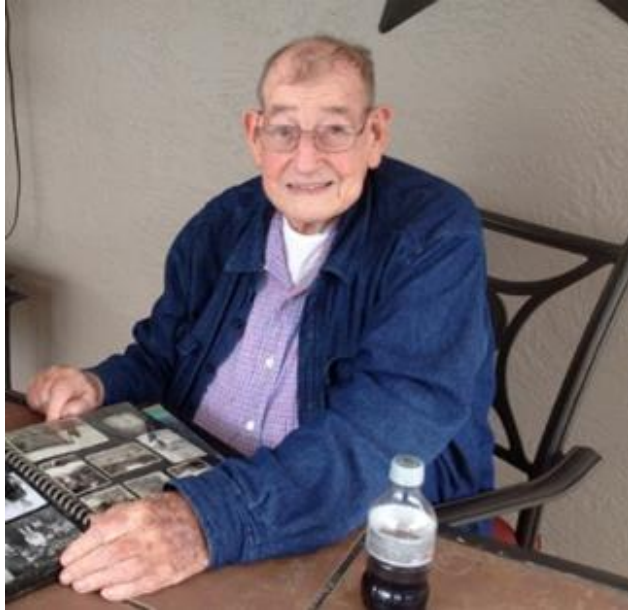
Dysrhythmias(atrial, ventricular)

Endocrine (thyroid, diabetes mellitus)

Restrictive (amyloid, sarcoid, hemochromatosis)

Idiopathic

Viral



What does HF look like?

Key components in
obtaining HF
history:

Somnolence/Confusion

Orthopnea *

Bendopnea

PND

Early satiety

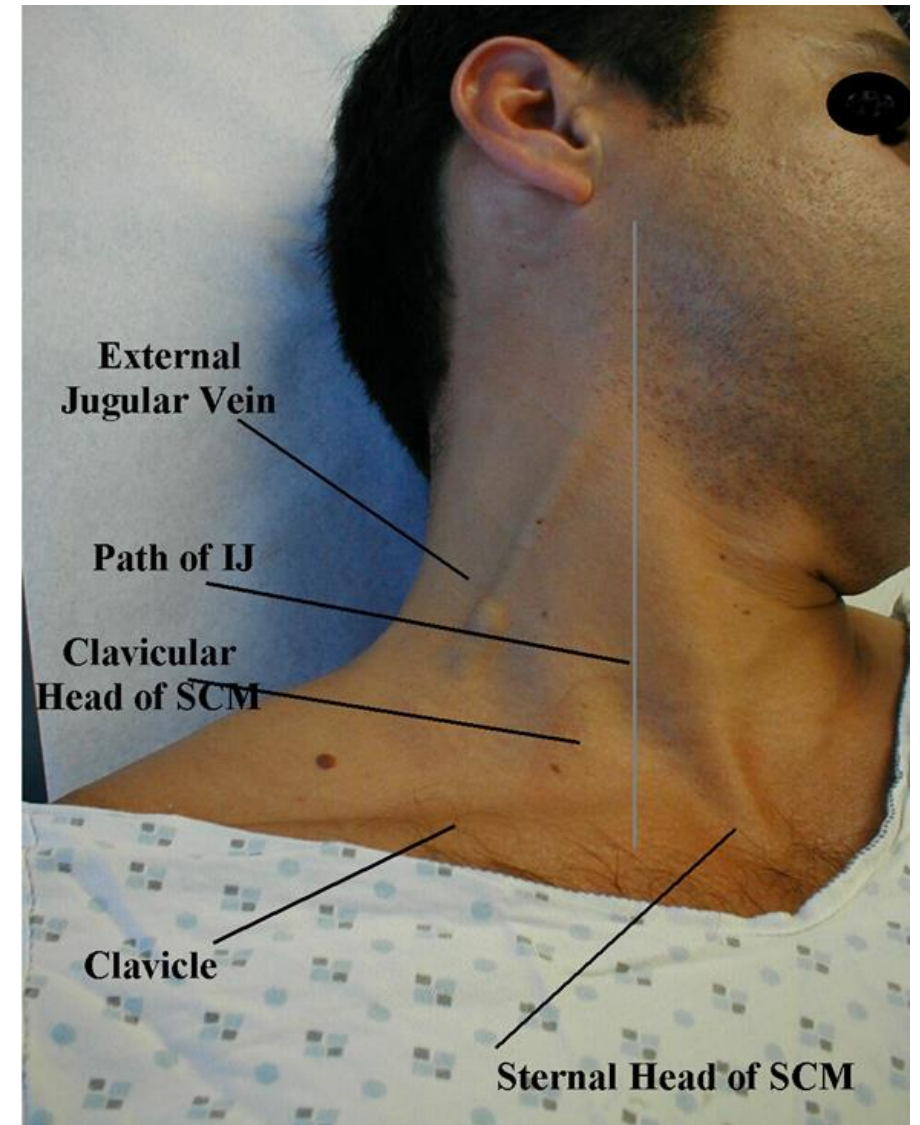
Nausea

Abdominal swelling

Edema

Pertinent physical exam findings- Head to Toe

- General appearance
- VS- Narrow pulse pressure and tachycardia
- Eyes- check sclera and conjunctiva
- Thyroid
- Neck- JVD
- Heart- S3, S4, rhythm irregularity,
- Lungs- rales, rhonchi, wheezes
- Abdomen- hepatjugular reflux, ascites
- Extremities- edema, perfusion
- Skin- temperature, color



Triage tool

Evidence for Congestion

- Orthopnea
- Ascites
- Elevated JVD
- Rales
- +S3
- Edema
- Hepatojugular reflux

Evidence for Low Perfusion

- Cool extremities
- Narrow pulse pressure
- Symptomatic hypotension
- Declining renal function
- Confusion, somnolence

Warm and Dry	Warm and Wet
Cold and Dry	Cold and Wet

Adapted from: Nohria, A., Lewis, EF, and Stevenson, LW. *Medical Management of Advanced Heart Failure. JAMA, 2002, 287: 628-640.*

Determining Risk- In hospital and post discharge events

Systolic BP-
<115 mmHg

Hyponatremia -
<133 mEq/L

Renal function-

- BUN >43 mg/dl strongest predictor of in hospital death
- Cr increase by >0.3 mg/dl

Biomarkers-
Increased troponin
and BNP

Residual congestion

American
College of
Cardiology
Expert Decision
Pathway for
Treatment
Optimization
for HFrEF

- Guideline directed medical therapy (GDMT) for pt with symptoms
- Uptitrate every 2 weeks to reach target dose within 3-6 months
- Persistent edema despite escalating diuretic.
 - Switch to a different loop
 - Add thiazide type diuretic

4 Pillars of HFrEF treatment: GDMT



RAASi/ARNI



Beta Blocker



MRA



SGLT2i

Angiotensin Receptor- Neprilysin Inhibitor (ARNI)

Benefits for HFrEF and HFpEF

- Reduced HF hospitalizations
- Reduced cardiovascular deaths
- Reduced rates of kidney impairment compared to ACEi or ARB

Caution

- Higher rates of hypotension compared to ACEi or ARB



ARNI

Sacubitril/Valsartan

- Dosing:
 - 24-26mg bid
 - 49-51mg bid
 - 97-103 mg bid

Dosing recommendations

Patient Population	Starting Dose	Recommendation for titration
Not previously on ACEi or ARB	24-26 mg bid	Double does every 2-4 week to target as tolerated
Previously on moderate to high dose ACEi or ARB	49-51 mg bid	Double dose every 2-4 weeks as tolerated
Severe kidney impairment	24-26 mg bid	Double dose every 2-4 weeks to target as tolerated

ARNI

36 hr washout period is
MANDATORY if switching from ACE-
I to reduce risk of angioedema

Washout not needed if switching
from ARB

Consider cost and/or coverage
issues

ARNI- Safety considerations

Potential Adverse Effects	Warnings/Precautions	Contraindications
Hypotension	Monitor for angioedema and hypotension	History of angioedema
Hyperkalemia	Monitor kidney function	Concurrent use with ACEi or aliskiren in pts with diabetes
Dizziness	Fetal toxicity- STOP if becomes pregnant	Hypersensitivity to sacubitril or valsartan
Kidney impairment	36 hr washout after last dose ACEi	
Cough		

Target doses for ACE and ARB

ACE inhibitor

- Ramipril 5 mg bid
- Lisinopril 40 mg daily
- Enalapril 10 mg bid

Angiotensin Receptor Blocker

Candesartan 32 mg daily

Valsartan 160 mg bid

Losartan 150 mg daily

Beta Blocker target doses

- Metoprolol succinate 200 mg daily
- Carvedilol 25 mg bid
- Bisoprolol 10 mg daily



Mineralocorticoid
Receptor
Antagonist

Spirolactone 25 mg daily

- Eplerenone 25 mg daily



Key points for monitoring

Potassium should be monitored within one week of starting medication

Consider stopping potassium supplement

Pt. Education

- Discuss high potassium foods (bananas, plant milks, avocados, potatoes)
- Avoid potassium containing salt substitutes

Sodium Glucose co-transporter 2 inhibitors (SGLT2i)

**EMPAGLIFLOZIN
10 MG DAILY**

**DAPAGLIFLOZIN
10 MG DAILY**

SGLT2 inhibitors

Benefits

- Reduction in HF hospitalizations
- Reduction in Cardiovascular mortality
- Treat Type 2 DM with lower risk of hypoglycemia
- Decreased progression of CKD
- Diuretic effect
- Weight loss

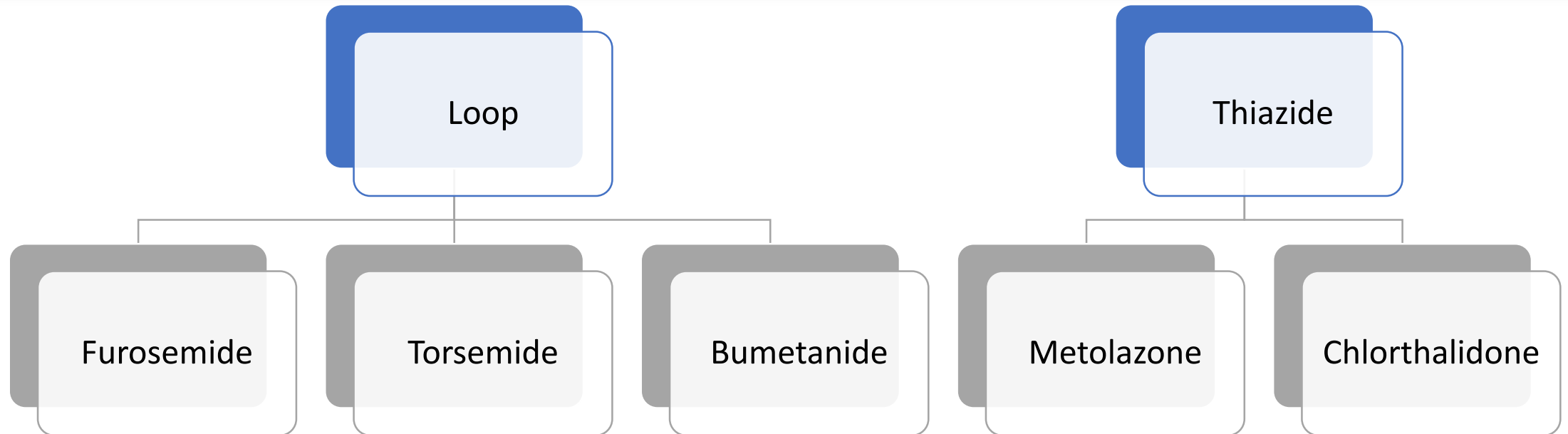
SGLT2i- Safety considerations

Potential Adverse Effects	Warnings/Precautions	Contraindications
UTI (female >male)	Potential volume depletion	Do NOT use with Type 1 DM
Genital mycotic infection (female >male)	Consider stopping 3 days prior to surgery to avoid DKA	Dialysis
Increased urine output	Hold or stop with AKI	Lactation
	Risk of Fournier's gangrene	Hypersensitivity to med

SGLT2i- considerations

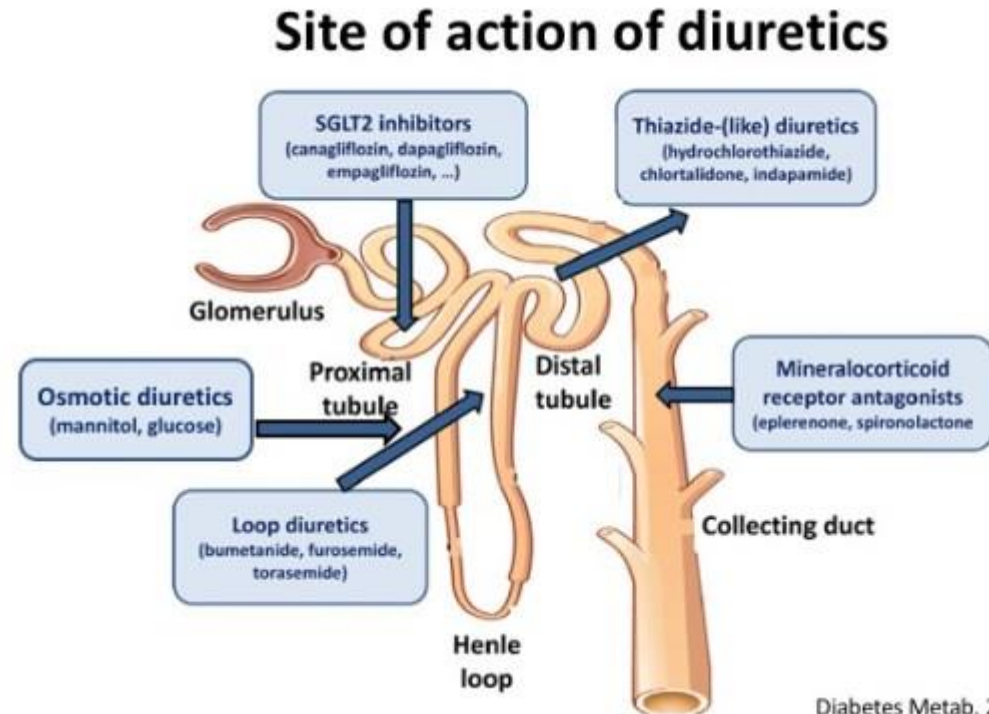
- eGFR \geq 20 ml/min/1.73m² you can use Empagliflozin
- eGFR \geq 25 ml/min/1.73m² you can use Dapagliflozin
- May be able to reduce diuretic dose
- Genitourinary effects
 - At increased risk for UTI, vaginal infections
 - Consider genital hygiene

What about diuretics?



When to use which diuretic?

- Escalating diuretic doses
- Diuretic tolerance
- Adding a thiazide



Diabetes Metab. 2016 Sep;42(4):224-33.

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Hydralazine and Isosorbide dinitrate

- Indications
 - Self identified African American patients
 - Based on data from A-HEFT trial
 - HFrEF with NYHA Class III-IV on optimal tolerated GDMT
- Benefits
 - Improve symptoms
 - Reduce morbidity and mortality.

Hydralazine and Isosorbide Dinitrate

- Hydralazine starting dose 37.5 mg tid
- Isosorbide dinitrate starting dose 20 mg tid
- Combination pill 37.5/10 mg

- Challenges with tid dosing
- Useful if uncontrolled BP
- An alternative if kidney function declines

- Caution in older adults

Ivabradine

Dose: 5 mg bid
(can go up to 7.5 mg bid)

Goal is resting
HR 50-60

Considerations

Increases risk of
atrial fibrillation

Contraindicated with
severe liver disease,
pacemaker, heart block or
sick sinus syndrome and
pregnancy

Ivabradine

- Reduce hospitalizations and cardiovascular death.
- Indications
 - NYHA Class II to III with stable HFrEF
 - If resting HR >70 on maximally tolerated GDMT and patient in sinus rhythm.



Vericiguat

Mechanism

- Soluble guanylate cyclase stimulator which increases levels of cGMP to promote vasodilation

Indication

- Reduce CV death or HF hospitalization after outpatient IV diuretic or recent hospitalization for HF in adults with symptomatic chronic HF and ejection fraction <45%

Vericiguat

Added on to GDMT

Dose 2.5 mg daily up to 10 mg daily taken with food

Double dose every 2 weeks until target

Considerations:

- Hypotension and anemia
- Contraindicated in pregnancy

Vericiguat- Safety considerations

Potential Adverse Effects	Warnings/Precautions	Contraindications
Anemia	Fetal-embryo toxicity	Pregnancy- use contraception for one month after stopping med
Hypotension	Lactation	Concurrent use with other sGC stimulators (tx PH)
	Concomitant use with PED-5 inhibitors	
	Severe hepatic impairment	
	Avoid with eGFR <15 ml/min/1.73m ²	

Digoxin

Indications

- Symptomatic patients on GDMT or unable to tolerate GDMT

Potential benefit

- Reduce HF hospitalizations

Digoxin

Narrow
therapeutic index

Consider creatinine
clearance, age and
lean body wt.

May only need to
be doses a few
days per week.

Treat Iron deficiency

- Definition: iron deficiency in HF differs from other conditions of chronic inflammation
 - Ferritin <100 $\mu\text{g/L}$ or ferritin of 100-299 $\mu\text{g/L}$ with a transferrin saturation $<20\%$.
- Treatment:
 - IV iron is preferred route.
 - IV iron sucrose (maximum dose of 200 mg per setting) or
 - IV Ferric carboxymaltose (maximum dose of 1000 mg per week).

Non-pharmacologic treatment

- Diet- limit sodium to less than 2 gms/day
- Fluid restriction-only implemented for certain conditions
- Activity- exercise to perceived exertion



Medications to AVOID

NSAIDS

- Antagonizes RAAS blockade
- May promote water and sodium retention
- May increase BP in pt with hypertension

Calcium Channel blockers

- Negative inotropic effects
- Non-DHP (diltiazem and verapamil) increased risk of HF hospitalization

Barriers to medication titration

- Hypovolemia
- Hyperkalemia
- Symptomatic hypotension
- Homebound pt
- Established kidney disease
- Reduce diuretic when starting SGLT2i
- Check salt substitutes, potassium supplements
- Reduce diuretic when to titrate ARNi
- Consider telehealth, home health
- Start ARNI/ACEi/ARB at low dose and monitor potassium

29-year-old male graduate student with 3-week h/o URI with cough and persistent DOE, orthopnea and fatigue. Flu, Strep and COVID tests negative

BP 116/64 HR 106 SpO2 92% RA Wt. 200 lbs. BMI 24.3

Tachycardic rate/regular rhythm. No S3 or S4. JVP elevated to angle of jaw, + hepatjugular reflux

Clear to auscultation bilaterally

Soft, nondistended, + hepatomegaly, +BS

Warm, 1+ bilateral lower extremity edema, 2+ distal pulses bilaterally

EKG: Sinus Tachycardia without acute EKG changes

133	28	18	94
3.8	98	0.9	

No medications

NT- Pro BNP 9800 pg/ml

(Normal = Less than 125 pg/ml for age 0-74)

CXR= Cardiomegaly with diffuse infiltrates

Your approach to care

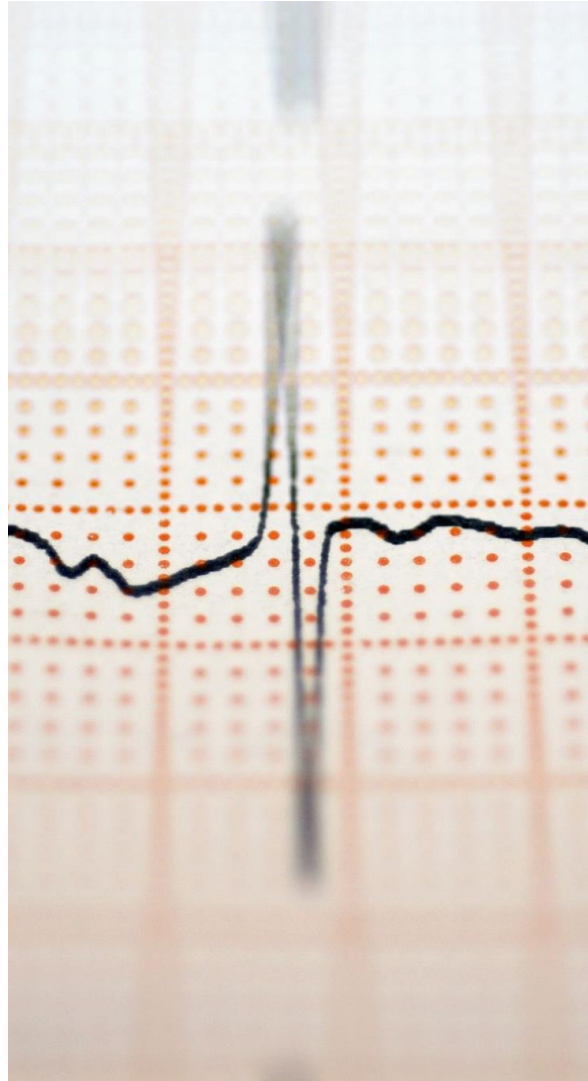
Diagnostic

- Echo

Diurese

- Manage symptoms

Start on GDMT



Heart Failure with Mildly Reduced Ejection Fraction

HFmrEF

(symptomatic HF with LVEF 41-49%)

Treatment

Diuretics to treat symptoms

SGLT2i to reduce HF hospitalization and CV mortality

Consider initiating GDMT with 4 pillars



Heart Failure with Improved Ejection Fraction

HFimpEF

symptomatic HF with a baseline LVEF $\leq 40\%$, a ≥ 10 -point increase from baseline LVEF, and a second measurement of LVEF $> 40\%$



Treatment

- **DO NOT STOP MEDICATIONS**
 - Continue GDMT even in asymptomatic patients
 - Prevent worsening LV dysfunction and/or HF relapse



Heart Failure with Preserved Ejection Fraction

HFpEF

symptomatic HF with LVEF $\geq 50\%$

Heart Failure with *PRESERVED EF*

Recommendations	Evidence
Control blood pressure	IB
Diuretics for overload	IC
Coronary revascularization with angina and/or ischemia if contributing to symptoms	IIa (level of evidence C)
BBs, ACEi and ARBs* with hypertension	IIa (level of evidence C)
Management of AF	IIa (level of evidence C)
*Aldosterone receptor antagonists : EF \geq 45%, elevated BNP or hospitalization within 1 year for HF, GFR >30 ml/min, Scr <2.5 mg/L, K+ <5.0 meq/L	IIb (level of evidence B-R)



Managing comorbidities in HFpEF

Anemia

Metabolic syndrome

Obesity

Sleep disordered breathing

COPD

Kidney dysfunction

66 yo male with a h/o HFpEF EF 55%, Htn, BPH,OSA with obesity

Sx: Fatigue, abdominal distention, bendopnea, worsening lower leg edema. No functioning scale at home.

BP 154/86 HR 88 Afebrile RR 22 SpO2 97% RA Wt. 340 lbs. BMI 41

Regular rate and rhythm. no S3 , + S4. No audible murmur. JVP elevated to earlobe, + HJR

Lungs CTA

Distended, firm, nontender, nondistended, unable to assess hepatomegaly, + BS

Warm, 3+ bilateral lower extremity edema, 2+ distal pulses bilaterally

136	30	17	}	184
4.1	95	1.0		

NT Pro BNP 400

Echo: EF >55% with LVH

EKG; Sinus Rhythm without ischemic changes

Cardiac Meds

Losartan 50 mg daily

Furosemide 120mg bid

Carvedilol 25 mg every 12 hours

Spirolactone 12.5 mg daily



Clinical inertia

- Barriers to dose titration
 - Provider- Patient has stable symptoms
 - Patient declines- “I feel good on current doses.”

Transitions in Care: Pearls for post discharge visit

Patient centered care with a focus on medication reconciliation.

Symptom perception

Physical exam

Symptom management

Precipitants to hospitalization

Intensifying therapy- avoid clinical inertia

73 yo female with a h/o HFrEF EF 20%, Anterior MI in 2017, Htn, COPD and Osteoarthritis and resides in skilled nursing facility

Sx: Orthopnea, dyspnea, lower leg edema and wt gain. EDW= 210 lbs (212 lbs 3 weeks ago)

BP 190/96 HR 102 Afebrile RR 22 SpO2 92% RA Wt. 240 lbs. BMI 41

Rapid rate/irregular rhythm. no S3 , + S4. No audible murmur. JVP elevated to earlobe, + HJR

Crackles 1/3 up on right clear on left

Soft, nontender, nondistended, + hepatomegaly, + BS

Warm, 1+ bilateral lower extremity edema, 2+ distal pulses bilaterally

136	30	17	}	222
4.4	95	1.0		

NT Pro BNP 8,000

Echo: EF 20% with mild MR, anterior wall akinesis, all other walls hypokinetic

EKG; Atrial fibrillation

Ramipril 10mg daily
ASA 81 mg daily
Atorvastatin 40 mg daily
Torsemide 40mg bid
Carvedilol 25 mg every 12 hours
Spironolactone 12.5 mg daily
Nitro 0.4 mg sl prn chest pain

Non-adherence



Non-adherence

Systems level

- Silos of care
- Difficulty getting medication refills
- Poor or challenging communication
- Challenging with patient assistance programs

Therapy

- Polypharmacy
- Adverse effects
- Medication frequency

A small green seedling with several leaves is growing out of a crack in a dark, textured surface, likely asphalt. The background is a soft, out-of-focus light color. The image is partially obscured by a white curved shape on the right side of the slide.

Non-Adherence

- Socioeconomic
 - Challenges with pharmacy access
 - Out of pocket costs of care
 - Limited social support
 - Transportation limits
 - Housing insecurity
 - Food deserts

Non- adherence

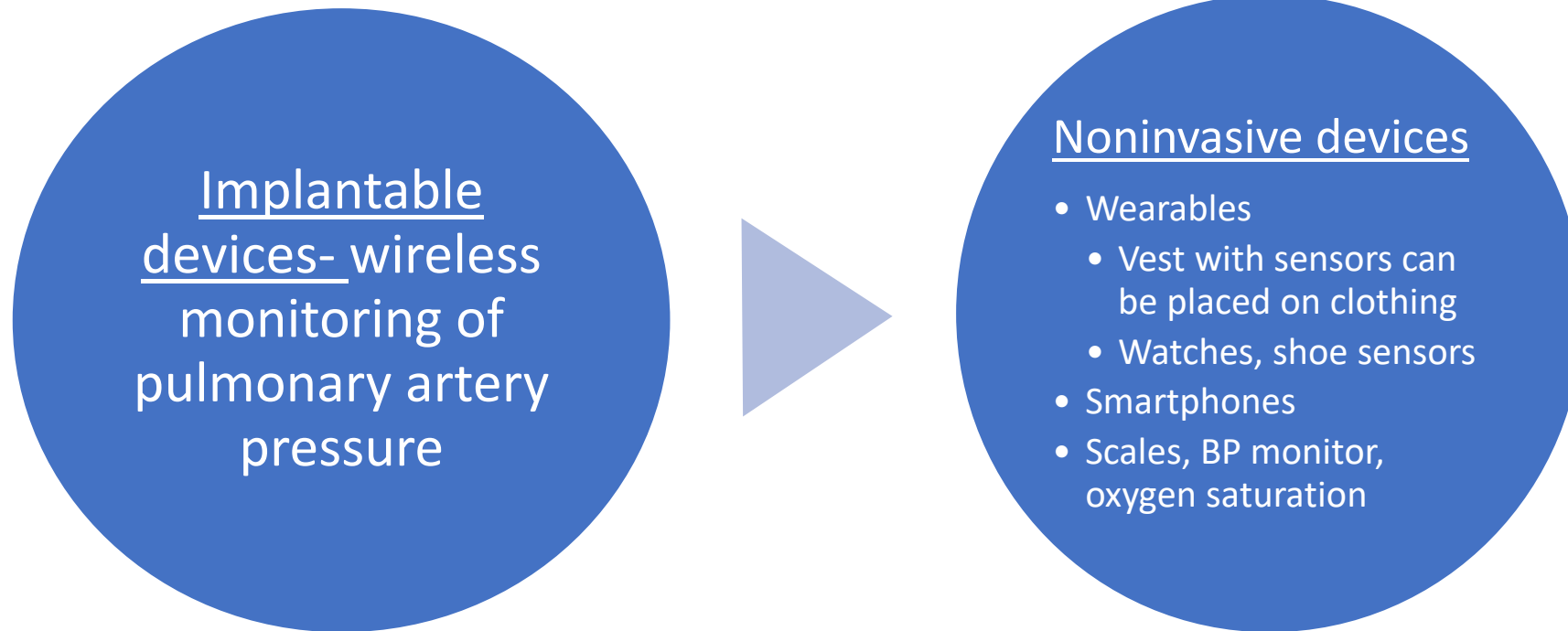
Medical condition

- Complex medical diagnoses
- Mental health diagnoses
- Polypharmacy

Patient

- Limited health literacy
- Physical limitations
- Social isolation

Using Technology in Heart Failure



Tools in medication management

Enhanced pill
boxes/Smart pill
dispensers

Alarm system pill
reminders

Smart package
systems

Bio ingestible sensors
(alert sent to
smartphone and later to
provider via wearable

Polypill

Medication delivery

Electronic prescribing

Pillbox and/or pill
card

Devices

- Implantable Cardioverter/Defibrillator
 - Indications
 - HFrEF with NYHA class II–III symptoms and EF of $<35\%$ at least 40 days post MI.
 - Ischemic cardiomyopathy and NYHA class I symptoms EF $<30\%$.
 - Location
 - Below clavicle
 - Subcutaneous at the side of the chest below the armpit.
- Cardiac Resynchronization Therapy (CRT)
 - Indications
 - Sinus rhythm, EF $<35\%$, QRS duration $>150\text{msec}$ and LBBB morphology

64 yo male hospitalized 4 times/12mo with a h/o NICM, Htn, DM2, Renal insufficiency, S/P ICD now 2 days post discharge.

Sx: PND, Orthopnea, DOE, early satiety, lower leg and scrotal edema.
EDW=198 lbs- 2020

BP 110/80 HR 98 Afebrile SpO2 94% RA Wt. 228 lbs. BMI: 33
Rapid rate/regular rhythm. + S3 , no S4. JVP elevated to angle of jaw, + hepatojugular reflux
Clear to auscultation bilaterally
Ascites with + fluid wave, distended, unable to assess hepatomegaly, diminished BS
Warm, 2+ bilateral lower extremity edema, 2+ distal pulses bilaterally
Self reported scrotal edema

Most recent Echo: EF 25% with Grade II diastolic dysfunction, Mod MR, no focal WMA

EKG; NSR with QRS>130

NT Pro BNP 20,000

135	30	10	}
4.0	98	1.0	

Lisinopril 40mg daily
Furosemide 60 mg bid
Amlodipine 10 mg daily
Carvedilol 25 mg every 12 hours
Lantus insulin 10 units at bedtime
Simvastatin 20 mg po bedtime
Spironolactone 12.5 mg po daily
Digoxin 0.125mg po daily

Advanced Therapies

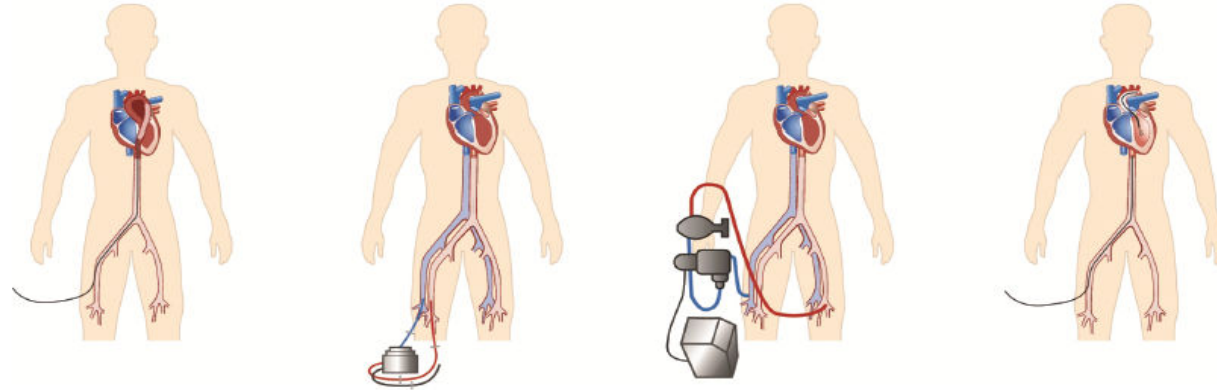
- Mechanical circulatory support (MCS)
- Transplant
- Inotropes



Figure 2: Percutaneous Mechanical Circulatory Support Devices Currently Used For High-risk Percutaneous Coronary Intervention

MCS

LV support



Device	IABP	TandemHeart	VA-ECMO	Impella 2.5/CP
Mechanism	Counterpulsation	Centrifugal flow continuous pump (LA to aorta)	Centrifugal flow continuous pump (RA to aorta)	Axial flow continuous pump (LV to aorta)
Flow/output	0.5–1.0 l/min	2.5–4.0 l/min	4.0–6.0 l/min	2.5–4.3 l/min
Sheath size	7–8 Fr arterial	21 Fr inflow (venous) 15–17 Fr outflow (arterial)	18–21 Fr inflow (venous) 15–22 Fr outflow (arterial)	12–14 Fr
Coronary perfusion	Yes+	No	No	Yes+++
Reduced work/O ₂ demand	Minor	Yes	No	Yes
FDA clearance/approval	510 (k) clearance	510 (k) clearance	510 (k) clearance	Premarket approval
FDA approval safe and effective	No	No	No	Yes
FDA indication	NA	NA	NA	High-risk PCI, AMI and other cardiogenic shock
Approved duration of use	Short days	<6 hours	<6 hours	Up to 6 days
FDA clinical trials	None	Yes	None	Yes, multiple
Safety – aortic valve	0%	0%	Unknown	0%
Safety – stroke	2–6%	0–1%	12%	0–1%
Leg ischemia	+	+++	+++++	++

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IABP = Intra-aortic balloon pump; LA = left atrium; LV = left ventricle; NA = not applicable; PCI = percutaneous coronary intervention; RA = right atrium; VA-ECMO = venous arterial extracorporeal membrane oxygenation. Adapted from: Thiele et al. 2019.⁶⁹ Used with permission from Oxford University Press.

Cardiac transplantation



Inotropes

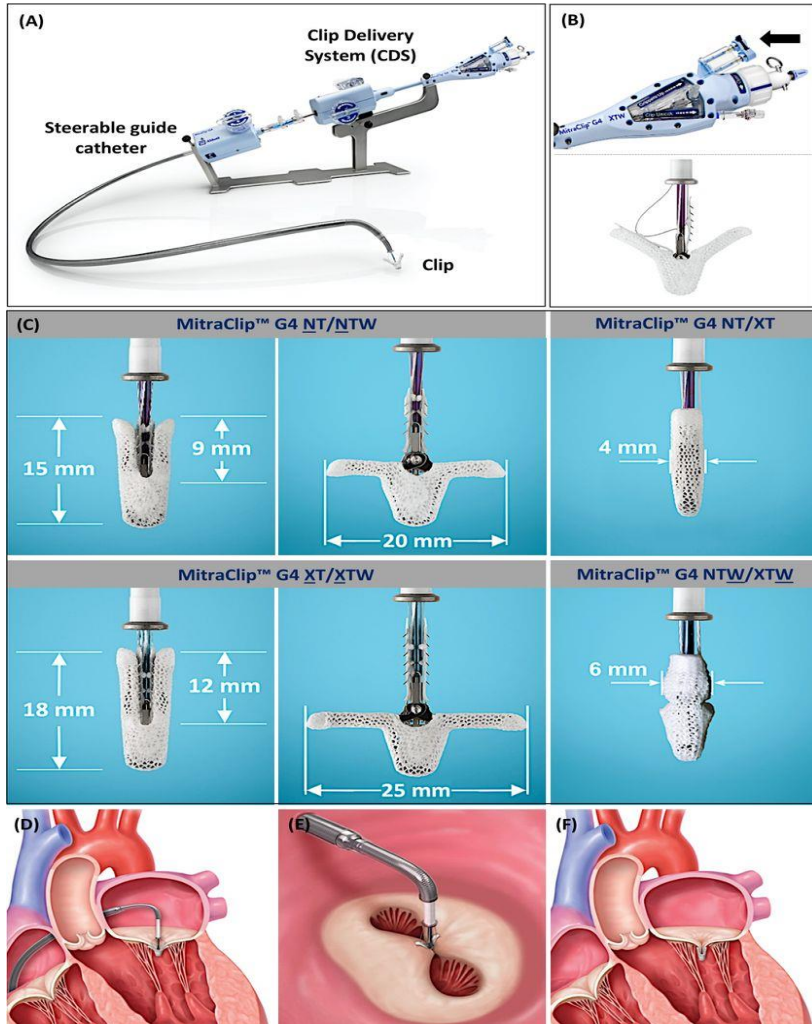
Dopamine-
increase kidney
perfusion

Dobutamine-
increase cardiac
output

Milrinone-
increase cardiac
output

Catheter based therapies

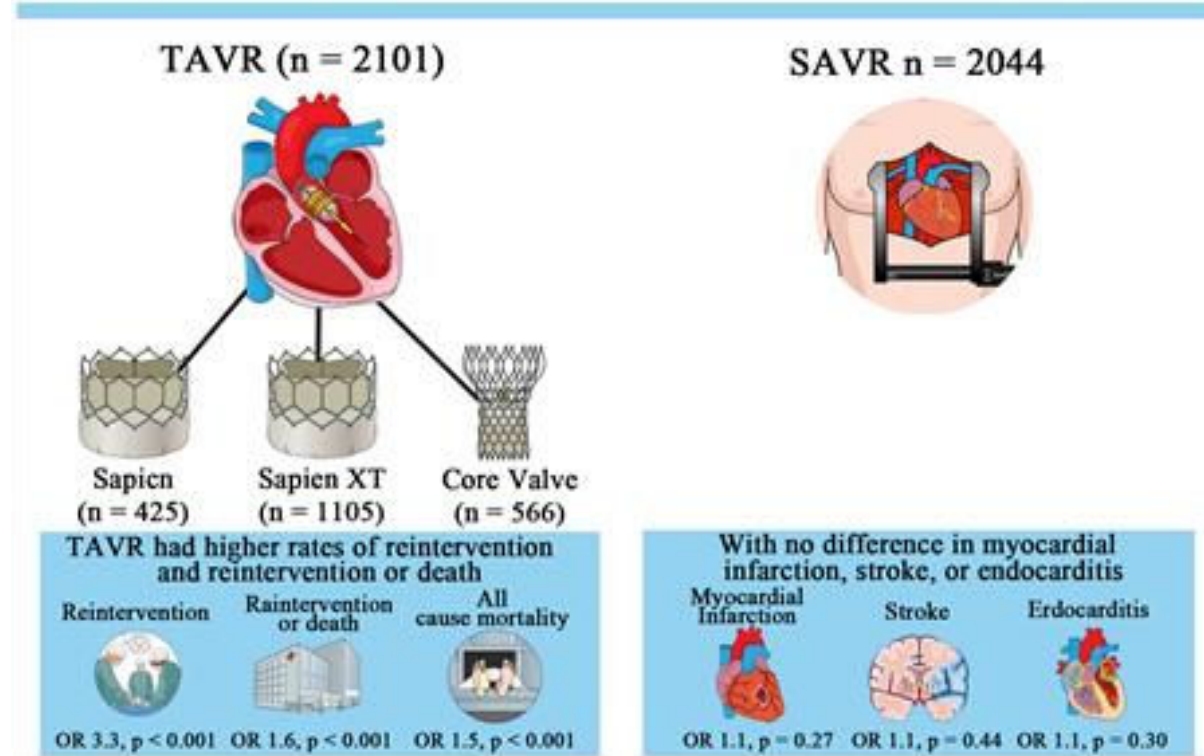
Mitra Clip



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TAVR (Transcatheter Aortic Valve Replacement)

Aortic Valve Reintervention with TAVR vs.SAVR at 5-year follow-up
Meta-analysis of five studies (4145 patients)



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Clinical Trials

Over 800 clinical trials in the US focused on HF.

North Carolina

- 23 active studies
- Focusing on procedures:
 - TAVR
 - Baroflex stimulator
- Medications
 - Finerenone
- Devices
 - Implantable sensors

TreatHF Mobile Application

TreatHF helps clinicians determine which therapies are suggested for their patients with stage C HFrEF and provides guidance on the use of each therapy.

1. Enter patient information on the Evaluation screen.
 1. Indicate patient's current use of background medications, and their response to those medications.
 2. Enter any further indications the patient might have for additional medication or device therapy.
2. View individualized next steps on the Advice screen.
 1. Review advice for titrating current medications.
 2. See what additional medications are suggested for your patient based on their indications.
 3. Email yourself a summary of the next steps as a basis for a medication plan.
3. Reference detailed information regarding each therapy on the Therapy Reference screen.
 1. Access information regarding initiation, titration, monitoring, contraindications and cautions for each medication recommended for the treatment of patients with stage C HFrEF.
 2. View expert consensus guidance on optimizing a medication plan for your patient and improving adherence."

TreatHF app

Indicate for stage C HFrEF Patient:

HF Assessment Parameters

Reset

Select NYHA Class

[NYHA Classes](#)

III

Select LVEF Range

≤35%

Background Medications

RAS Inhibitor ⓘ

Select which type of RAS inhibitor the patient is currently prescribed:

✓ ARNI

ACEI

ARB

None

Evidence-Based Beta Blocker

Select which beta blocker the patient is currently prescribed:

Discussing Goals of Care



Language is important



Advanced Directives



MOST/POLST forms

HF Hospital Followup visit

Pearls for practice

1. Focus on medication reconciliation
2. Address pt perception of symptoms (worse/better/same)
3. Physical Exam findings (compare to before hospitalization)
4. Identify potential precipitants to hospitalization
5. Intensify therapy
6. Followup lab results

What should we be doing in HF care?

- Provide the right meds at the right dose
- Refer when appropriate
- Manage the multi-morbid conditions including social determinants of health
- Enhance community partnerships
- Incorporate innovative technology when available



Implications for Primary Care Practice

Focus
on

Focus on prevention of and early intervention

Engage

Engage patient in shared decision making early in disease trajectory

Define

Define goals of care at each visit.



Questions- email margaret.bowers@duke.edu