HEART TO HEART

Dr. Alicia Ross
Dr. Claire Kassakian

AN INTERDISCIPLINARY CONVERSATION ON HEART FAILURE
NO CONFLICTS OF INTEREST
Heart failure is predominantly a condition of aging
- Prevalence from 6% in those 60-79 years of age
- Increases to 14% in those >80 years of age
- More than **50% of hospitalization occurs in people >75** years of age
- Likely due to HF risk factors (CAD, HTN) that increase with age as age-related maladaptive changes
OBJECTIVES

- Discuss best practices in HF
- Discuss updates in best practices in HF
- Address renal considerations in management of HF
WHY SHOULD CARDIOLOGISTS AND NEPHROLOGISTS TALK?
Multimorbidity is the concurrence of multiple chronic conditions
- 90% of heart failure patients have at least 3 comorbid conditions
- 50% have at least 5 comorbid conditions

Comorbid conditions have been implicated in its pathophysiology
- Lung disease, diabetes, obesity and chronic kidney disease - promotion of inflammation and microvascular dysfunction

Hospitalization and mortality are frequently driven by noncardiovascular causes in both HFpEF and HFrEF

Optimization of HF therapy will have direct effect on therapeutic strategies on the management of concurrent conditions

Gap in knowledge resulting from exclusion of older adults with multimorbidity from major HF randomized controlled trials

Importance of considering the potential effects of multimorbidity on prognosis
- Therapeutic interventions (medications and procedure) may be immediate and significant, whereas potential benefits, usually realized over years, may be attenuated (especially in those with a limited life expectancy)
CENTRAL ILLUSTRATION: Domain Management Approach to HF in the Geriatric Patient

**Medical**
- Evaluate stage and etiology of HF
- Consider challenges in pharmacological treatment; focus on polypharmacy; consider deprescribing
- Consider impact of comorbidities: sleep apnea, kidney disease, diabetes
- Assess for malnutrition

**Physical Function**
- Screen for frailty: slowness, weakness, shrinking, inactivity, exhaustion
- Evaluate mobility; consider fall risk

**Mind and Emotion**
- Evaluate cognition; if impaired, evaluate impact on self-management skills
- Screen for depression; consider treatment

**Social Environment**
- Inquire about extent of social support at home; consider engaging community-based care services
- Inquire about financial resources for prescription medications

GOALS OF THERAPY

- Reduce Morbidity
  - Symptoms
  - Health related QOL and functional status
  - Rates of hospitalization

- Reduce Mortality
Mild to Moderate (HFrEF or HFpEF)
CASE 1

75 year old man with stage 3b CKD (baseline Cr ~2) with proteinuria (~3g/d), HFREF (‘21 ECHO w/ EF 35% w/o valve lesions), AFib on Coumadin, HTN, DM complicated by chronic b/l lower extremity wounds, obesity (BMI 37) and BPH (w/ prior outlet obstruction) presenting to clinic with progressive SOB and weight gain (18lb).

BP 162/88 HR 74. Exam with JVP of 7cm, symmetric rales and 2+ pretibial edema.

UA:
2+ Alb
5-10 hyaline casts, 5-10 granular casts

9.7
128 111 46
5.4 25 3.4

BNP 265
Trop.02
MEDICATIONS

- Amlodipine 5mg daily
- Lisinopril 30mg daily
- Furosemide 40mg daily
- Atorvastatin 40mg QHS
- Propranolol ER 60mg daily
- Warfarin
- Metformin 500mg daily
- Glimepiride 1mg daily
- Omeprazole 20mg daily
- Doxazosin 2mg QHS
- Finasteride 5mg QHS
75 year old man with stage 3b CKD (baseline Cr ~2.1) with proteinuria (~3g/d), HFrEF (EF 35% without valvular lesions), AFib on Coumadin, DM (on oral agents, previously on Victoza) complicated by chronic lower extremity wounds, HTN, and BPH (w/ prior outlet obstruction) presenting to clinic with progressive SOB and weight gain (18lb). BP 162/88 HR 74. Exam with symmetric rales and 2+ pretibial edema.

UA:
2+ Alb
5-10 hyaline casts, 5-10 granular casts

BNP 265
Trop.02
APPROACH TO HFREF

1) Identify the cause of disease
   - Ischemic
   - Valvular
   - Hypertensive
   - Cardiomyopathy
     - ETOH, chemotherapy-associated, arrhythmia-induced, cardiac sarcoidosis, cardiac amyloidosis, abnormal thyroid function, genetic
Kaplan–Meier Curves for the Probability of Death from Any Cause.

Hazard ratio, 0.86 (95% CI, 0.72–1.04)
P=0.12
Death from Cardiovascular Causes, and Death from Any Cause

FRAILTY

- weakness
- weight loss
- sarcopenia
- cognitive decline
- functional decline

Mae Thamer PhD 1, James S. Kaufman MD 2, Yi Zhang PhD 1, Qian Zhang MPH 1, Dennis J. Cotter MSE 1, R. 2, Heejung Bang PhD 2

Predicting Early Death Among Elderly Dialysis Patients: Development and Validation of a Risk Score to Assist Shared Decision Making for Dialysis Initiation

Oregon Geriatric Society
APPROACH TO HFREF

- Address Volume

- Guideline Directed Medical Therapy
  - Neurohormonal therapy
  - Hypertension management
  - ACEI/ARB/ARNI
  - Beta-blocker
  - Aldosterone antagonists
  - Hydralazine/nitrates
APPROACH TO HFREF – OTHER MANAGEMENT COMPONENTS

- Anemia
  - ESA therapy in CKD patients
- Sleep Disordered Breathing
- DMII
  - SGLT2 Inhibitors are no longer just for diabetics...
- Device Therapy
  - Ventricular arrhythmias and ICDs
  - Bradycardia and pacers
CASE 2

- 75 yo man with HTN, HFpEF (EF 60%), CAD s/p PCI, TAA s/p TEVAR, AFib on Eliquis, severe AS s/p TAVR, and DMII with multiple hospitalizations for volume overload & AKI (including one episode where he required a week of dialysis) presents to clinic with increasing LEE and exertional dyspnea. BP 118/58 HR 105 Weight stable. On exam, lungs clear, mild abdominal distention, trace pretibial edema with 1+ edema at ankles.

Medications:
Metoprolol Succinate 100mg QD
Metformin 1g BID
Eliquis 2.5mg BID
Glipizide 10mg BID
Lasix 40mg daily
Clopidogrel 75mg daily
Atorvastatin 80mg Qhs
WHAT IS OUR INITIAL APPROACH TO MANAGEMENT HERE?

- A) Exact same plan as if this patient had HFrEF
- B) Consult Cards and get Renal on board
- C) Address key factors that contribute to the patient's acute decompensation
- D) Consider the patient's kidneys and their perfusion
- E) C and D
“NO BP, NO PEE PEE”

PRELOAD AND AFTERLOAD TARGETS IN HFPEF
APPROACH TO HFPEF: MANAGEMENT
Angiotensin–Neprilysin Inhibition in Heart Failure with Preserved Ejection Fraction


Isosorbide Mononitrate in Heart Failure with Preserved Ejection Fraction


Hazard ratio 0.89
(95% CI 0.77–1.03, p=0.118
Adjusted hazard ratio 0.86, p=0.051

Proportion with cardiovascular death or hospital admission for CHF (%)

Number at risk
Candesartan 1524
1458
1377
833
182
Placebo 1509
1441
1359
824
195
WHAT IS OUR INITIAL APPROACH TO MANAGEMENT HERE?

- Volume management
  - Loop diuretics
  - Aldosterone antagonists
- Management of Hypertension
- Management of arrhythmias
  - Rate versus rhythm control of atrial fibrillation
CASE #3

- 63 year old man with hypertension, dilated cardiomyopathy s/p ICD for primary prevention, stage 3a CKD, OSA (compliant with CPAP), and obesity presents to clinic for routine follow-up. Recent echo – Mildly dilated LV with LVEF 30%; nl RV size and systolic fxn; normal valvular function, grade 2 diastolic dysfunction, RVSP 49 mm Hg; dilated IVC that does not collapse with inspiration

Medications
Lisinopril 20mg BID
Carvedilol 37.5mg BID
Spironolactone 25mg daily
Torsemide 40mg daily
Aspirin
Atorvastatin 40mg daily

13.4  140  37
4.5  1.5  111

NT pro BNP 1087
NEW THERAPIES IN HF

- Angiotensin receptor neprilysin inhibitor
- Sacubitril-Valsartan (Entresto)
- SGLT2 Inhibitors
ANGIOTENSIN RECEPTOR NEPRILYSIN INHIBITOR

NEPRILYSIN

- A neutral endopeptidase
- Degrades endogenous vasoactive peptides, including natriuretic peptides

Neprilysin inhibition results in higher levels of natriuretic peptides leading to:

- Vasodilation
- Sodium excretion
- Possible improvement in ventricular remodeling
PARADIGM-HF

- Randomized, double-blind trial in HFrEF
- LVEF <40%
- NYHA Functional class II, III, IV
- Sacubitril-valsartan (200 mg twice daily, ARB component equivalent to 160 mg of valsartan twice daily or enalapril 10 mg twice daily)

Trial was stopped early after a median follow-up of 27 months because of prespecified boundary for early termination for benefit was crossed.
WHAT ARE THE NUMBERS:

- 4.7% reduction CV death or HF hospitalization
  - NNT 21
- 2.8% reduction in deaths
  - NNT 35
- Symptomatic hypotension more common (14 vs 9%)
- Not associated with worsening renal function
- Median LVEF increased from 28.2% to 37.8%
- NT proBNP declined from 816 to 455 pg/mL

NNT for HFrEF treatments in their landmark trials

- 18 for ACEI inhibitors
- 24 for ARB
- 8 beta-blockers
- 15 for mineralocorticoid antagonists
- 14 for ICD
- 14 for CRT

Change in the NT-proBNP Concentration.

<table>
<thead>
<tr>
<th>Weeks since Randomization</th>
<th>Enalapril</th>
<th>Sacubitril–valsartan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>-10</td>
<td>-15</td>
</tr>
<tr>
<td>2</td>
<td>-20</td>
<td>-25</td>
</tr>
<tr>
<td>3</td>
<td>-30</td>
<td>-35</td>
</tr>
<tr>
<td>4</td>
<td>-40</td>
<td>-45</td>
</tr>
<tr>
<td>5</td>
<td>-50</td>
<td>-55</td>
</tr>
<tr>
<td>6</td>
<td>-60</td>
<td>-65</td>
</tr>
<tr>
<td>7</td>
<td>-70</td>
<td>-75</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>Enalapril</th>
<th>Sacubitril–valsartan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>394</td>
<td>397</td>
</tr>
<tr>
<td>1</td>
<td>359</td>
<td>355</td>
</tr>
<tr>
<td>2</td>
<td>351</td>
<td>363</td>
</tr>
<tr>
<td>3</td>
<td>350</td>
<td>365</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>348</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>349</td>
</tr>
</tbody>
</table>

Angiotensin–Neprilysin Inhibition in Heart Failure with Preserved Ejection Fraction

MULTICENTER, DOUBLE-BLIND, ACTIVE-COMPARATOR TRIAL (PARAGON-HF)

4822 Patients with NYHA class II–IV heart failure and EF ≥45%

Sacubitril–valsartan
97 mg + 103 mg (twice daily)
(N=2419)

Valsartan
160 mg (twice daily)
(N=2403)

Total hospitalizations for heart failure and cardiovascular death

894 events
Rate ratio, 0.87; 95% CI, 0.75–1.01; P=0.06

1009 events

Patients receiving sacubitril–valsartan more likely to have hypotension and angioedema but less likely to have hyperkalemia

S.D. Solomon et al. 10.1056/NEJMoa1908655
Copyright © 2019 Massachusetts Medical Society
Time-to-Event Curves for Primary Composite Outcome and Its Components

A Total Hospitalizations for Heart Failure and Death from Cardiovascular Causes

B Total Hospitalizations for Heart Failure

C Death from Cardiovascular Causes
CLINICAL PEARLS – GDMT/ARNI

- HOW TO START?
- ARNI/ACEI/ARB – better tolerated when patient is “wet”
- Beta-blockers – better tolerated when patient is “dry”
- Must have 36 hours off of ACEI prior to starting ARNI (Washout period)
- Assess tolerability in 2 weeks
- Monitor BP, electrolytes and renal function after initiation and during titration
SGLT2 INHIBITORS:
SGLT2 INHIBITORS:
SGLT2 INHIBITORS:
SGLT2 INHIBITORS:
SGLT2 INHIBITOR STUDIES:

- CANVAS
  - Canagliflozin

- DECLARE
  - Dapagliflozin

- EMPA-REG OUTCOM
  - Empagliflozin

- DAPA-HF
  - Dapagliflozin
DAPA-HF

- Multicenter
- Randomized
- Placebo-controlled trial
- 4744 pts on standard HF therapy
- NYHA Class 2-4 HF
- EF of 40% or less
DAPA-HF

Safety Outcome

Rates of Adverse Events

<table>
<thead>
<tr>
<th></th>
<th>Volume depletion</th>
<th>Renal dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dapagliflozin</td>
<td>7.5% (N=178)</td>
<td>6.5% (N=153)</td>
</tr>
<tr>
<td>Placebo</td>
<td>6.8% (N=162)</td>
<td>7.2% (N=170)</td>
</tr>
</tbody>
</table>

P = 0.40
P = 0.36
CASE 4

84 yo man with CAD s/p CABG (2015) and PCIs (2019), LV/LAA thrombus, AFib s/p cardioversion (on DOAC), AS s/p TAVR, HFrEF, anemia, CKD, DMII, and prior prostate cancer presenting to clinic with persistent complaints of fatigue and poor exercise tolerance previously hopeful to have improved after TAVR. +Intermittent subjective orthostasis. No CP, orthopnea, or edema. Admits to feeling overwhelmed by ongoing decline in his physical strength.

BP 110/64 HR 105 98% RA 73kg (stable). Irregularly irregular with distant heart sounds. Pretibial edema.
MEDICATION LIST

- Lasix 40mg daily
- Lisinopril 30mg daily
- Multivitamin daily
- Atorvastatin 80mg QHS
- Eliquis 2.5mg twice daily
- Clopidogrel 75mg daily
- Nitro 0.4mg tablet PRN CP
- Trazodone HCL 50mg QHS
- Epogen (SQ every 2 wks)
- Vitamin D3 2000 IU daily
- MTV daily
- Glucosamine tablet twice daily
- Glipizide
- Metformin 1000mg BID
Polypharmacy = >5 medications

- Associated with falls, disability and hospitalization
- Exacerbated cognitive impairment
- Nearly universal in patients with heart failure
  - Diuretics
  - (Potassium)
  - ACEI/ARB/ARNI
  - Beta-blockers
  - Aldosterone antagonists
  - (SGLT2 inhibitors)
  - Antiplatelet/anticoagulation/statins

- Majority of clinical trials have excluded older adults, yet guidelines recommend them
- Risk of adverse events rise exponentially
  - Drug-drug interaction (warfarin and NSAIDs; ACEI/spironolactone)
  - Drug-disease interactions (NSAIDs and heart failure)
  - Drug – person interactions (digoxin use in older people)
Drugs that May Exacerbate an Underlying Disease State in Older Adults

May Exacerbate Heart failure
- Antiarrhythmic medications
- Alpha 1 blockers
- Dihydropyridine calcium channel blockers

May increase blood pressure and AKI
- NSAIDS
- Herbal supplements

May increase risk of Syncope
- Peripheral alpha-1 blockers

May increase risk of BI bleeding
- Aspirin
Deprescribing

Process of medication withdrawal or dose reduction under health care supervision to reduce unnecessary or potentially harmful medication use with the goal of improving outcomes.
RCT of Deprescribing Related Interventions

- Very few published
- Statin discontinuation in patients with life expectancy < 1 year
  - No difference in death at 60 days (median survival was 7 months)
  - Improved quality of life, decreased medication burden
- Reduction in anti-HTN therapy by algorithm in patients with mild cognitive impairment
  - No improvement in cognitive, psychological or general daily functioning but no increase in adverse events
- Meta-analysis suggested potential mortality reduction
- More studies are needed
TRED-HF

- Open-label, pilot
- Previous diagnosis of dilated cardiomyopathy with LVEF 40% or lower, absence of current symptoms
- Currently on BB, ACEI, ARB, MRI or combination of drugs
- Current LVEF of >50% and normal LV size and NT pro BNP < 250
- Randomized to continued treatment vs Reduction or cessation of medical therapy
- Primary endpoint was relapse of dilated cardiomyopathy within 6 months
### CV Medications and Commonly Associated Events Resulting from Drug Withdrawal

<table>
<thead>
<tr>
<th>Drug Withdrawn</th>
<th>Adverse Drug Withdrawal Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha 1-blocker</td>
<td>Increase in BP, urinary complaints</td>
</tr>
<tr>
<td>ACEI inhibitor</td>
<td>Increase in BP</td>
</tr>
<tr>
<td>Antianginal</td>
<td>Chest pain</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>Chest pain, tachycardia</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Tachycardia</td>
</tr>
<tr>
<td>Diuretic agents</td>
<td>Increased vascular congestion</td>
</tr>
</tbody>
</table>
CASE 5

81 year old woman with CKD, HTN, DMII (on oral agents), anemia (on ESA therapy), severe OSA (intolerant of CPAP), HFpEF, and HLP presenting with SOB with minimal exertion, orthopnea, edema, and weight gain of 8 pounds in 1 week. She continues to struggle with baseline mobility issues; she continues to use a WC when out of the house and uses a cane inside the house and has been resistant to increasing her diuretic dosing due to urinary urgency. Doing well with sodium discretion until COVID restricted her food options.

3 weeks after this appointment, she is hospitalized with hypoxic respiratory failure and acute on chronic HF. She is discharged to rehab.
REHAB-HF CLINICAL TRIAL

- 349 patients, >60 years of age
- Admitted for acute decompensated heart failure regardless of ejection fraction
- Must be able to walk at least 4 m at enrollment (with or without aid of an assistive device)
- Functionally independent before admission
- Expected to be discharged to home

- 97% were frail or pre-frail
- Key goal was to increase each patient’s endurance (duration of walking); doing this safely first addressing deficits in balance, strength, and mobility
REHAB-HF

- Multicenter Randomized, controlled trial to evaluate a transitional tailored, progressive rehab
- Strength
- Balance
- Mobility
- Endurance
- Started in the hospital and continued after discharge for 36 outpatient sessions
- Primary outcome was Short Physical Performance Battery at 3 months
- Secondary outcomes was 6 month rate of rehospitalization for any cause
TAKE AWAY POINTS

- **HFrEF**: Cause of HF (ischemic? Revascularization may not reduce mortality) Volume 1st. Then HTN, goal-directed therapies. Other targets (arrhythmia, anemia, sleep disordered breathing)
- **HFpEF**: Not as much promising data on pharmacologic intervention as in HFrEF. Volume 1st. Don’t reduce preload too aggressively or you may see AKI “no BP no pee pee”
- **New HF agents**: ARNI is the new ACE/ARB. SGLT2 inhibitors are really diuretics.
  - ARNI (Sacubitril/valsartan) requires careful monitoring for hypotension and worsening renal function
- **Polypharmacy and multimorbidity** are nearly universal in patients with HF
  - Potential benefits of therapeutic interventions may be attenuated in those with a limited life expectancy
- Multidisciplinary approach to geriatric patients with heart failure is key!