Heart Failure with Preserved Ejection Fraction

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Learning Objectives

1. Compare and contrast heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF) in clinical presentation and prognosis
2. Prepare diagnostic tools for patients with suspected heart failure.
3. Construct treatment plans for patients, using Guideline Directed Medical Therapy (GDMT) specific to HFpEF
4. Formulate a plan to implement strategies to prevent hospital readmissions in patients with heart failure.
What is **congestive** heart failure?

**Clinical Syndrome**
- Impaired ventricular filling &/or ejection
  - Dyspnea
  - Fatigue
  - Edema

ACC/AHA: Largely a clinical diagnosis based on a careful history and physical exam

J Am Coll Cardiol 2013;62:e147–239

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**Ejection Fraction**

Systolic Failure

Diastolic Failure

LA aorta LV

Diastolic Failure

LA aorta LV
ACC/AHA 2013 Heart Failure Definitions

• Heart Failure with Reduced Ejection Fraction (HFrEF): EF < 40%

• Heart Failure with Preserved Ejection Fraction (HFpEF): EF > 50%
  – HFpEF, borderline: EF 40-49%
    • AKA HF w/mid-range EF (HFmrEF)
  – HFpEF, improved: EF > 40%
    • Patient with HFrEF previously whose EF recovers

J Am Coll Cardiol 2013;62:e147–239

AES Question
AES #1

Which of the following is false regarding HFpEF?

A. It causes half of all heart failure hospitalizations in the United States
B. Women are more likely than men to have HFpEF
C. HFpEF and HFrEF have similar morbidity and mortality
D. HFpEF and HFrEF cannot be differentiated based on symptoms

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Heart Failure with Preserved Ejection Fraction

- 1 in 5 US adults > 40 years will develop heart failure
- Leading cause of hospitalizations, > 1 million admissions yearly
- Half of all patients with HF have HFpEF
  - Two thirds of elderly patients with HF have HFpEF
  - Patients aged < 65 years are more likely to be obese and diabetic
HFpEF versus HFrEF

- 5-year overall survival 35%
- Similar morbidity
  - Hospitalization
  - Symptom burden
  - Quality of life
- Patients with HFpEF are more likely to die of non-cardiovascular causes

Pathophysiology

- Diastolic and systolic dysfunction
  - Impaired relaxation, increased ventricular stiffness
- Multi-system disease, systemic inflammation
- Endothelial dysfunction
- Arterial stiffness
- Chronotropic incompetence

Nat Rev Cardiol. 2014 Sep;11(9):507-15
HFpEF Diagnosis

- Symptoms and signs of heart failure
  - Other causes excluded
- Normal ejection fraction (EF > 50%)
- Evidence of cardiac dysfunction (echo, right heart cath)

“Other causes excluded”

<table>
<thead>
<tr>
<th>Non HF causes</th>
<th>HF not caused by HFpEF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic lung disease</td>
<td>Restrictive cardiomyopathy</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>Hypertrophic cardiomyopathy</td>
</tr>
<tr>
<td>Anemia</td>
<td>Constrictive pericarditis</td>
</tr>
<tr>
<td>Upper airway obstruction</td>
<td>Severe valvular disease</td>
</tr>
<tr>
<td>Ascites/decompensated liver failure</td>
<td>Right HF from other causes (RV infart, idiopathic pulmonary HTN, arrhythmogenic RV)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>High-output heart failure</td>
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</tbody>
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HFpEF Evaluation

- Labs: CBC, CMP, TSH, UA
- ECG: CAD, LVH, dysrhythmia
  - 50% have atrial fibrillation, lifetime risk 67%
  - 70% have underlying CAD
- CXR
- Cardiac stress testing

https://commons.wikimedia.org/w/index.php?curid=61614661

AES Question
**AES #2**

Ms. Diana Stoleck is a 68 YOF with COPD, obesity, HTN and T2DM. She was admitted to the hospital for acute hypoxic respiratory failure. Her BP is 170/105 and O₂ is 92% on 2L O₂. On exam, her heart rate is regular, there is no murmur, you hear scattered mild wheezes and rales in the lower 1/3 of the lungs bilaterally and see mild LE edema. HJR is present. A CXR shows vascular congestion. BNP is 78 pg/ml. Which of the following is false?

A. A BNP <100 may be used to reliably exclude HFpEF in ambulatory patients  
B. Obese patients with acute decompensated heart failure (ADHF) may have a BNP <100  
C. Symptomatic ambulatory patients with HFpEF may have a BNP <100  
D. NT-proBNP and BNP are equally useful for diagnosing heart failure
BNP: B-type Natriuretic Peptide: “Basically Not Perfect”

- BNP may be normal
  - Purely exertional symptoms
  - BNP < 100pg/mL in 30% of symptomatic ambulatory patients
  - 15% of obese patients with acute heart failure BNP < 100
- Low specificity
- Higher levels = worse prognosis
- NT-proBNP no advantage over BNP

Test Name | LR+ | LR-
--- | --- | ---
CXR: pulmonary venous congestion | 14 | 0.5
Hepatojugular reflux | 6 | 0.8
Jugular venous distension | 4.9 | 0.7
N-terminal proBNP > 340 pmol/L | 4.3 | 0.2
BNP > 150 pg/ml | 3.1 | 0.2
Rales | 2.7 | 0.5
Paroxysmal nocturnal dyspnea | 2.6 | 0.7
BNP > 30 pg/ml | 2.5 | 0.05
Lower extremity edema | 2.3 | 0.6
Orthopnea | 2.2 | 0.7

https://www.essentialevidenceplus.com/content/diagcalc/155
AES #3

You suspect Ms. Stoleck has heart failure and you obtain a transthoracic echocardiogram. Her results show an EF of 65%, left ventricular hypertrophy (LVH) with a normal ventricle size, a pulmonary artery pressure of 40 and no evidence of diastolic dysfunction. What do you tell her?

A. She is unlikely to have HFpEF because she has no evidence of diastolic dysfunction
B. Her elevated PA pressure suggests HFpEF is not the cause of her dyspnea
C. Her echo findings support a diagnosis of HFpEF
D. Her LVH is unlikely related to her symptoms
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Unpair Diastolic Dysfunction and HFpEF

• Diastolic dysfunction ≠ HFpEF  
  – A physiologic finding  
• 1/3 of patients with HFpEF do not have diastolic dysfunction observed on echocardiography  
  – Received aggressive treatment  
  – Purely exertional symptoms  
• 1/3 of patients have diastolic dysfunction without HFpEF
Echocardiography

- **EF > 50%**
- Diastolic dysfunction: 70%
  - E/e’ ratio
  - Delayed relaxation
  - Increased stiffness
- LVH: 50-60%
- Normal LV cavity size
- Increased left atrial size: 65%
- Increased pulmonary artery pressure (>35mmHg)

AES Question

!?
Ms. Stoleck responds well to IV diuresis and is ready for discharge. Which of the following medications improves outcomes for patients with HFpEF?

A. Metoprolol Succinate  
B. Lisinopril  
C. Isosorbide mononitrate  
D. A & B  
E. None of the above
Barriers to Practice

Guideline Directed Medical Therapy for HFpEF?

<table>
<thead>
<tr>
<th>HFrEF</th>
<th>HFpEF</th>
</tr>
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<tbody>
<tr>
<td>ACEI/ARB</td>
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<tr>
<td>Beta-blockers</td>
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</tr>
<tr>
<td>Digoxin</td>
<td>Digoxin</td>
</tr>
<tr>
<td>Aldosterone antagonists</td>
<td>Aldosterone antagonists</td>
</tr>
<tr>
<td>Sacubitril-valsartan</td>
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</table>

Goals of Treatment

- Alleviate symptoms
- Optimize comorbidities
- Reduce hospitalizations
Exercise – Just Do it

- Exercise improves symptoms, QOL and decreases hospitalizations, SOR A

- 2019 Cochrane review, N=5783, 44 trials, exercise-based cardiac rehabilitation vs placebo
  - Total hospitalizations 16.5% vs 23.7%; NNT=14
  - Improvement in exercise capacity, symptoms and quality of life

- 2015 MA of 6 RCTs exercise vs placebo, N=276 HFpEF patients
  - Improved quality of life and exercise capacity

Diuretics

- Relief of symptoms in patients with volume overload, SOR A
- Loop more titratable than thiazide
  - Oral furosemide ~50% bioavailability, significant inter- and intra-patient variance
  - 1mg bumetanide ~ 10mg torsemide ~ 40mg furosemide
- Avoid over-diuresis
  - Reliance on preload for diastolic filling and cardiac output
- Avoid NSAIDs
Sodium and Fluid Restriction

- ACC/AHA recommend daily sodium <3g and 1.5-2L fluids per day, SOR C
  - 2018 SR, 9 trials, N=479, no benefit sodium restriction
  - Small RCTs of inpatient sodium and fluid restriction show no benefit
  - SODIUM-HF (Study of Dietary Intervention Under 100mmol in Heart Failure; NCT02012179) pending
- High sodium diets can mitigate diuretic effect
- Fluid restrict if patients are hyponatremic

JAMA Intern Med. 2018 Dec 1;178(12):1693-1700

Nitrates and NSAIDs: Just Say No

- Long-acting nitrate therapy associated with worse clinical outcomes in HFpEF when compared to placebo, SOR B
  - Dose-related decreased levels of activity and more adverse events
- NSAIDs
  - Increased cardiovascular risk
  - Limit response to diuretics
Optimize Comorbidities

- HTN
- DM2
- Obesity
- Atrial fibrillation

Hypertension

- Treat per evidence-based hypertension guidelines, SOR C
  - ACC/AHA recommends <130/80 for HF patients
  - No evidence that better BP control improves outcomes in HF patients
  - May use ACE-I/ARB, thiazide, non-dihydropyridine CCB, BB per other indications

Diabetes

• Lancet 2019 MA of SLGT-2 inhibitors, N=34,322
  – Reduces risk of CV-related death and hospitalization among patients with HF by 29% (HR 0.71, 95% CI 0.61–0.84), NNT 47
  – Empagliflozin or canagliflozin in addition to metformin
• Dapagliflozin reduces r/o hospitalization, NNT=125

• GLP-1 agonists cardiovascular benefit for high CV-risk patients
  – Liraglutide, semaglutide, dulaglutide

• Avoid TZDs

Lancet. 2019;393(10166):31-39
Diabetes Care 2019 Jan; 42(Supplement 1): S90-S102.

Obesity

• More than 80% of patients with HFP EF are overweight or obese
• Associated with greater morbidity
• 2016 RCT of a 20 weeks exercise and diet program
  – Patients with HFP EF, BMI>30, N=100, avg 22 lb. weight loss
  – Improved exercise tolerance and HF symptoms
Obstructive sleep apnea (OSA)

- Up to 80% of patients with HFpEF
- No difference in major CV outcomes, but...
  - Patients feel better
  - 70% reduction in MVA
- Order sleep study in patients with HFpEF and
  - Daytime somnolence
  - Snoring/witnessed apnea


Atrial Fibrillation and HFpEF

- More than 2/3 of patients with HFpEF have AF
- Worse outcomes, HFpEF dependent on
  - Filling time
  - Atrial kick
- Consider rhythm control, particularly younger patients
  - Improved symptoms and quality of life
Reduce readmissions

- > 1 million HF admissions every year
  - 1 in 4 patients readmitted within 30 days
- Structured home visits, telephone support, telemonitoring and multidisciplinary HF clinics all reduce readmissions and mortality
  - Home visits: HF readmissions 49%, NNT 7; all-cause mortality 23% NNT=9
  - HF clinics: HF readmissions 30%, NNT=8; all-cause mortality 44%, NNT=18
  - Meta-analyses include HFrEF > HFpEF, ? HFpEF specific effect

Transitions of Care - Components

- AHA/ACC recommendations:
  - Very-early post-discharge contact (24-72 hours)
  - Early office follow up – 1-2 weeks
  - Medication reconciliation
  - Patient education starting in hospital
  - Health record communication with the patient and clinicians
  - Interdisciplinary coordination

Cochrane 2015, Issue 10. Art. No.: CD007228
TOPCAT trial: Spironolactone in HFpEF

- RCT spironolactone vs placebo in HFpEF, N=3445
  - Patients: > 50 years w/ symptomatic heart failure, EF ≥ 45%
    - Recruited from Americas and Russia
  - Composite outcome: CV-death, aborted cardiac arrest or HF-hospitalization
  - Mean follow-up 3 years
  - No difference in primary outcome
    - Decreased hospitalization 12.0% vs. 14.2%; NNT= 45
  - Patients from Americas: primary outcome 27.3% vs 31.8% spironolactone vs placebo, NNT=22

NEJM. 2014 Jul 10; 371(2):181
Spironolactone in HFpEF

- ACC/AHA weak recommendation. Consider if:
  - Hospitalization in the past year or BNP > 100
  - Serum potassium < 5.0
  - Estimated GFR is > 30
- Start 12.5mg daily, goal 25-50mg
  - Check serum potassium and creatinine in 1-3 weeks after initiation/dose changes
  - Decrease dose if potassium is >5.5, stop if > 6

Practice Recommendations

- BNP is useful to exclude HFpEF in low-risk patients however a normal level does not exclude HFpEF in high-risk patients, SOR C
- Obtain a transthoracic echocardiogram to confirm HFpEF in a patient with clinical signs and symptoms of heart failure and an ejection fraction ≥ 50%, SOR C
- Recommend exercise training to patients with HFpEF, SOR A
- For patients with HFpEF and T2DM already on metformin, add a SLGT-2 inhibitor if additional glucose-lowering therapy is required, SOR A
- Consider transitional care interventions for patients with frequent HF hospitalizations, SOR B