State-of-the-Art Management of Chronic Systolic Heart Failure

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Disclosures: I have no financial disclosures relevant to this presentation.
Chronic Systolic Heart Failure

- Definition
- Medical Therapy
- Devices
- Atrial Fibrillation with Systolic Dysfunction
- Advanced Heart Failure Considerations
What is Heart Failure?

A complex **clinical syndrome** that results from any structural or functional **impairment of ventricular filling or ejection of blood**.

From the American College of Cardiology / American Heart Association Guidelines
What is Heart Failure?

This clinical syndrome can result from multiple processes:

- Pericardial disorders
- Myocardial disorder (abnormal pump function or abnormal relaxation)
- Endocardium disorder
- Severe heart valve disease
- Metabolic abnormalities

Diastolic Heart Failure (HFpEF)

Systolic Heart Failure (HFrEF; main focus for today’s talk)
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Diuretics
ACEI or ARB
Beta Blockers
Aldosterone antagonist
ARNI
Hydralazine – Nitrates
Ivabradine
Start with a case – Mr. Smith

- Mr. Smith is a 53 year old male with a history of hyperlipidemia and GERD.
Mr. Smith is a 53 year old male with a history of hyperlipidemia and GERD.

He has been experiencing 6 months of progressive dyspnea on exertion. His legs are swollen. He is now sleeping in a recliner chair. He makes an appointment with his doctor.
Start with a case – Mr. Smith

• His primary care physician is concerned about congestive heart failure based on the history.
Start with a case – Mr. Smith

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• Physical examination shows elevated JVP, decreased breath sounds at the bases, an S3 gallop, and pitting edema of the lower extremities.
Start with a case – Mr. Smith

• His primary care physician is concerned about congestive heart failure based on the history.
• Physical examination shows elevated JVP, decreased breath sounds at the bases, an S3 gallop, and pitting edema of the lower extremities.
• Chest xray shows small pleural effusions and mild pulmonary edema
• His primary care physician is concerned about congestive heart failure based on the history.

• Physical examination shows elevated JVP, decreased breath sounds at the bases, an S3 gallop, and pitting edema of the lower extremities.

• Chest xray shows small pleural effusions and mild pulmonary edema

• EKG shows sinus rhythm and a left bundle branch block
Start with a case – Mr. Smith

The echocardiogram shows a dilated left ventricle and severely reduced EF (20%).

LA – left atrium
LV – left ventricle
RA – right atrium
RV – right ventricle
Start with a case – Mr. Smith

• A coronary angiogram was performed showing no obstructive CAD
Start with a case – Mr. Smith

• A coronary angiogram was performed showing no obstructive CAD
• Mr. Smith is diagnosed with a dilated non-ischemic cardiomyopathy with systolic heart failure
Start with a case – Mr. Smith

• A coronary angiogram was performed showing no obstructive CAD
• Mr. Smith is diagnosed with a dilated non-ischemic cardiomyopathy with systolic heart failure
• He is started on furosemide and evidence based heart failure meds and his symptoms improve.
A coronary angiogram was performed showing no obstructive CAD
Mr. Smith is diagnosed with a dilated non-ischemic cardiomyopathy with systolic heart failure
He is started on furosemide and evidence based heart failure meds and his symptoms improve.

Let's talk about these evidence based medications for systolic heart failure
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Diuretics

- Used to relieve symptoms of congestion
- Can improve exercise tolerance
- Not demonstrated to improve mortality
- Typically use loop diuretics
  - Can add thiazide to loop for refractory cases
  - Watch out for hypokalemia
- Don’t forget
  - Low sodium diet (<2000 mg / day)
  - Fluid restriction (< 2 Liters / day)
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Medical Therapy:
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The Renin-Angiotensin-Aldosterone System

This system gets upregulated in heart failure with deleterious results:

- Sodium resorption
- Sympathetic activation
- Fibrosis (scar formation)

The Renin-Angiotensin-Aldosterone System


This system gets upregulated in heart failure with deleterious results:

- Sodium resorption
- Sympathetic activation
- Fibrosis (scar formation)

And therefore blocking this system (with an ACEI or an ARB) is beneficial in systolic heart failure
ACE Inhibitor vs Placebo

Consensus Trial – NEJM 1987

ARB vs Placebo

CHARM-Alternative Trial - LANCET 2003
ACE Inhibitor vs Placebo

- Reduce hospitalization
- Mortality benefit
- Use in all systolic heart failure patients

Don’t combine (ACE typically 1st line and switch to ARB if side effects)

ARB vs Placebo

Alternative Trial - LANCET 2003
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Beta Blockers

• Used to be controversial in heart failure
  • Reduced exercise capacity
  • Reduced cardiac output (can precipitate cardiogenic shock in decompensated HF)
  • General consensus was that BB’s were contraindicated in heart failure

• Subsequently clinical trials have shown significant benefits in heart failure
Beta Blockers

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- Subsequently clinical trials have shown significant benefits in heart failure patients
  - Reduce hospitalization
  - Mortality benefit
  - Use in all systolic heart failure patients

- Carvedilol, metoprolol succinate, or bisoprolol

U.S. Carvedilol Trials – NEJM 1996
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Aldosterone Antagonists (spironolactone or eplerenone)
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Aldosterone Antagonists:
- Reduce hospitalization
- Mortality benefit
- Use in systolic heart failure patients with NYHA functional class II-IV

Only if CrCl >30 and K < 5.0

Aldosterone antagonist vs Placebo

RALES Trial - NEJM 1999
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Angiotensin-receptor-neprilysin inhibitor (ARNI)

What is this??
Angiotensin-receptor-neprilysin inhibitor (ARNI)

What is this??

Valsartan / Sacubitril (Brand name is Entresto)
New medication for systolic heart failure.
This drug is to be used in place of (not in addition to) ACE or ARB.
Angiotensin-receptor-neprilysin inhibitor (ARNI)

What is this??

Valsartan / Sacubitril (Brand name is Entresto)
New medication for systolic heart failure.
This drug is to be used in place of (not in addition to) ACE or ARB.

An ARB
A neprilysin inhibitor:
• blocks neprilysin (which degrades endogenous vasoactive peptides such as brain natriuretic peptide).
• Result is an increase in natriuretic peptides
Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure

John J V. McMurray, M.D., Milton Packer, M.D., Akshay S. Desai, M.D., M.P.H., Jianjian Gong, Ph.D., Martin P. Leftonowitz, M.D., Adel R. Rizkala, Pharm.D., Jean L. Rouleau, M.D., Victor C. Shi, M.D., Scott D. Solomon, M.D., Karl Swedberg, M.D., Ph.D., and Michael R. Zile, M.D.,

for the PARADIGM-HF Investigators and Committees

• valsartan / sacubitril vs enalapril
• 8442 patients, NYHA class II-IV
• EF ≤ 40%
• Valsartan / sacubitril reduced heart failure hospitalization and reduced mortality

Angiotensin-receptor-neprilysin inhibitor (ARNI) Vs ACE inhibitor

Hazard ratio, 0.80 (95% CI, 0.73–0.87) P<0.001
Angiotensin-receptor-neprilysin inhibitor (ARNI)

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<td>In patients with chronic symptomatic HFrEF NYHA class II or III who tolerate an ACE inhibitor or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality.</td>
<td>NEW: New clinical trial data necessitated this recommendation.</td>
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Chronic symptomatic HFrEF NYHA class II or III Tolerating an ACE or ARB

Recommend switching the ACE or ARB to an ARNI
Angiotensin-receptor-neprilysin inhibitor (ARNI)

**Recommendations for Renin-Angiotensin System Inhibition With ACE Inhibitor or ARB or ARNI (Continued)**

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**Chronic symptomatic HFrEF NYHA class II or III**

**Tolerating an ACE or ARB**

- Stop ACEI or ARB. Must wait >36 hours before starting ARNI
- Recommend switching the ACE or ARB to an ARNI
Angiotensin-receptor-neprilysin inhibitor (ARNI)

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**Chronic symptomatic HFrEF NYHA class II or III**
- Tolerating an ACE or ARB

- **Recommend switching the ACE or ARB to an ARNI**
  - Stop ACEI or ARB. Must wait >36 hours before starting ARNI
  - Not recommended in patients with history of angioedema

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2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure
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- Aldosterone antagonist
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- Hydralazine – Nitrates
- Ivabradine
The African-American Heart Failure Trial (A-HeFT)

- African Americans with NYHA class III or IV systolic HF.
- Isosorbide-hydralazine vs placebo

**Hydralazine-Nitrates**

Isosorbide / hydralazine vs placebo

![Graph showing overall survival over days since baseline visit with Isosorbide dinitrate plus hydralazine, hydralazine, and placebo lines, and a p-value of 0.01.](image-url)
The African-American Heart Failure Trial (A-HeFT)

- African Americans with NYHA class III or IV systolic HF.
- Isosorbide-hydralazine vs placebo

Isosorbide / hydralazine:
- Reduce hospitalization
- Mortality benefit
- Use in systolic heart failure patients who are African American with NYHA functional class III-IV
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What is this?
Ivabradine

What is this?

- Medication that lowers heart rate (when in sinus rhythm)
- Selectively blocks the $I_f$ ("funny") current in the sinoatrial node. Blocking this channel reduces the rate at which the SA node fires.

Mitchell A. Psotka, and John R. Teerlink Circulation. 2016;133:2066-2075
Ivabradine

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Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study

6558 patients with systolic HF with EF ≤35% in sinus rhythm with heart rate >70 bpm on beta blocker (if tolerated)

- Randomized to placebo or ivabradine
- Reduction in hospitalizations
- Not statistically significant for reduction in death
**Recommendation for Ivabradine**

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<td>*<em>Ivabradine can be beneficial to reduce HF hospitalization for patients with symptomatic (NYHA class II-III) stable chronic HF/EF (LVEF ≤ 35%) who are receiving GDEM</em>, including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of 70 bpm or greater at rest.**&lt;sup&gt;154-157&lt;/sup&gt;</td>
<td><strong>NEW:</strong> New clinical trial data.</td>
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NYHA class II-III patients  
EF ≤ 35%  
On BB at maximum tolerated dose  
In sinus rhythm with resting HR ≥ 70 bpm

Reasonable to add Ivabradine
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ICD
CRT
CardioMEMS
ReDS
Implantable Cardioverter Defibrillator (ICD)

Primary prevention
- To reduce risk of arrhythmias that can cause sudden cardiac death in systolic HF patients
  - EF ≤ 35% despite optimal medical therapy
  - NYHA class II-III
  - Expected survival of > 1 year

Secondary prevention
- For patients that have had a life threatening sustained arrhythmia such as ventricular tachycardia or ventricular fibrillation
Implantable Cardioverter Defibrillator (ICD)

ICD therapy reduces overall mortality by 23%.

SCD-HeFT. NEJM 2005.
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ICD
CRT
CardioMEMS
ReDS
Cardiac Resynchronization Therapy (CRT)

What is CRT?
- CRT is **pacing** the **right AND left ventricle** at the same time in effort to “resynchronize the right and left ventricle” in patients with dyssynchrony due to a bundle branch block
  - (CRT-P = Biventricular pacing only)
  - (CRT-D = Biventricular pacing AND defibrillator capabilities)

Therefore, only of benefit in select patients:
- **EF ≤ 35% , NYHA class II-IV** AND a **wide QRS on EKG** (LBBB responds best)

What does CRT do?
- Reverse remodel (reverse LV dilatation), improve LVEF, improve mitral regurgitation, improve symptoms, reduce mortality
Cardiac Resynchronization Therapy (CRT)
Cardiac Resynchronization Therapy (CRT)

AFTER CRT
Cardiac Resynchronization Therapy (CRT)

- CRT improves symptoms (not shown)
- CRT reduces cardiac hospitalizations and death

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  - ICD
  - CRT
  - CardioMEMS
  - ReDS
• Passive, wireless, radiofrequency sensor (no battery, no leads)
• Implanted into a distal branch of the descending pulmonary artery
CardioMEMS

Champion Trial, Lancet, 2011
NYHA Class III heart failure (HFrEF and HFpEF) with CHF hospitalization in past 12 months

All patients received the device
   Randomized to management with:
   1) hemodynamic monitoring information is available
   2) control group where access to readings was blocked

Reduction in heart failure hospitalizations at 6 months
Chronic Systolic Heart Failure

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ReDS (remote dielectric sensing)

• Measures lung fluid content (right middle lobe) as a percentage of fluid to lung volume
• If value “too high” the patient is likely hypervolemic and may need increased diuretics
Early data suggests it may help reduce heart failure hospitalizations
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Atrial Fibrillation in Systolic Heart Failure

- Common (the two diagnoses often coexist)
Atrial Fibrillation in Systolic Heart Failure

• Common (the two diagnoses often coexist)
• Can be symptomatic / worsen symptoms
Atrial Fibrillation in Systolic Heart Failure

- Common (the two diagnoses often coexist)
- Can be symptomatic / worsen symptoms
- If associated with rapid ventricular responsive (RVR) can lead to LV dysfunction which may be reversible with rate or rhythm control ("tachycardia induced cardiomyopathy")
Atrial Fibrillation in Systolic Heart Failure

- Common (the two diagnoses often coexist)
- Can be symptomatic / worsen symptoms
- If associated with rapid ventricular responsive (RVR) can lead to LV dysfunction which may be reversible with rate or rhythm control (“tachycardia induced cardiomyopathy”)
- The traditional teaching that rate control is equal to rhythm control in Afib (AFFIRM Trial NEJM 2002) may NOT be true in systolic heart failure patients
Atrial Fibrillation in Systolic Heart Failure

CAMERA-MRI study

- Presented August 2017 at European Society of Cardiology
- Patients with persistent Afib and idiopathic cardiomyopathy (EF ≤ 45%). Randomized to catheter ablation vs ongoing medical rate control
- Endpoint: change in LVEF on cardiac MRI at 6 months.
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Advanced Heart Failure Considerations

Palliative Care
Home Inotropes
Left Ventricular Assist Device
Heart Transplant
Indicators of Advanced Heart Failure:

- Multiple ED visits or Hospitalizations for heart failure (≥ 2 in past year)
- Progressive decline in renal function or hepatic function
- Cardiac cachexia (unintentional weight loss)
- Intolerant of ACEI or ARB (low BP or worsening renal function)
- Intolerant of BB (low BP or worsening HF symptoms)
- Systolic BP consistently < 90 mmHg
- Severe symptoms (SOB with ADL’s, SOB walking one block on level ground)
- Escalating diuretic dose to control volume (high dose loop diuretic, adding metolazone, etc)
- New or worsening hyponatremia
- Frequent ICD shocks
- 6MWT < 300 meters
- Exercise stress showing severe limitation in functional capacity (can’t get out of stage 1)
- Cardiopulmonary stress test suggesting severe cardiac limitation
- Worsening pulmonary hypertension and right sided heart failure
- High 1 year mortality (> 20-25%) predicted by heart failure survival models
- Requiring IV inotropes to support hemodynamics

Adapted from Journal of Cardiac Failure Vol. 21 No. 6 June 2015 by James Fang et al.
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- Palliative Care
  - Home Inotropes
  - Left Ventricular Assist Device
  - Heart Transplant
Palliative care or hospice
• When “advanced therapies” are not an option or not aligned with patient’s goals of care
• Palliative care may improve quality of life, anxiety, depression, and spiritual well-being

Advanced Systolic Heart Failure Considerations
Chronic Systolic Heart Failure

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Palliative Care
Home Inotropes
Left Ventricular Assist Device
Heart Transplant
Advanced Systolic Heart Failure Considerations

Home inotropes

• May make patients feel better, possibly help keep them out of the hospital
• Does NOT reduce mortality
• Can be used either as a bridge (when hopeful for recovery or when waiting for transplant or LVAD) or as a palliative strategy for symptom control
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- Palliative Care
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- Left Ventricular Assist Device
- Heart Transplant
Left ventricular assist device (LVAD)

- In select patients LVAD can improve:
  - Hemodynamics
  - End organ function (or prevent further decline)
  - Symptoms and quality of life
  - Mortality

- Still have numerous complications:
  - GI bleeding
  - Infection
  - Stroke
  - Pump thrombosis

- Bridge to transplant vs destination therapy
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Advanced Systolic Heart Failure Considerations

Heart transplant

- Still the “gold standard” treatment for advanced heart failure
- You are trading one disease for another (immunosuppression, increased infections, increased malignancy)
Back to the case – Mr. Smith

• Mr. Smith was started on carvedilol, Lisinopril, and spironolactone. The doses were uptitrated to maximum tolerated doses.
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• A follow up echo 4 months later showed a somewhat improved ejection fraction at 33%.

Back to the case – Mr. Smith
Mr. Smith was started on carvedilol, Lisinopril, and spironolactone. The doses were uptitrated to maximum tolerated doses.

A follow up echo 4 months later showed a somewhat improved ejection fraction at 33%.

The decision was made to place a CRT-D device (cardiac resynchronization therapy with defibrillator).
Back to the case – Mr. Smith

Repeat echo in 6 months:

With guideline medical therapy and CRT his Ejection Fraction is now 60% (NORMAL)! The patient is NYHA functional class I.
Thank You