Diagnosis and Management of Chronic Systolic Heart Failure (HFrEF)

Ebere O Chukwu
Advanced Heart Failure & Transplant Cardiology
Baylor Scott & White
Definition

• A syndrome that results from any structural or functional disorder that impairs the ability of the ventricle to fill with or eject blood.

• Clinically, it is characterized by either congestion (pulmonary or systemic) or a low output state or a combination of both with or without inadequate peripheral oxygen delivery at rest or during stress.

2010 Comprehensive heart failure practice guideline. HFSA.org
Epidemiology

- An estimated 6.5 million Americans ≥20 years of age have HF
- 1 million new cases per year
- 2.6 million office visits in 2015
- Life time risk for CHF (>45y) ranges 20%
- HFrEF and HFpEF present in equal number

Epidemiology

- High readmission rates: 25% at 30 days
  50% at 60 days
- Annual cost was about $30.7 billion (2012)
- Projected to increase by 2030 to $69.7
  (~$244 per US adult)
- Mortality 29.6% at 1 year
- 5 year survival after diagnosis ~50%
Pathophysiology

- Injury to the myocardium
- Fall in cardiac output/increased wall stress
- Activation of the sympathetic (minutes to hours), and RAAS (hours to days)
- Volume expansion, vasoconstriction, HR increase, vascular redistribution (veno constriction, arterial redistribution)
- Ventricular remodeling (*fibrosis*, *apoptosis*, *hypertrophy*, *cellular/molecular alterations*), arrhythmias, pump failure
- Short term beneficial, however over long term will lead to clinical CHF
<table>
<thead>
<tr>
<th>Functional class</th>
<th>Symptoms</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No limitations to physical activity. Ordinary physical activity does not cause fatigue, SOB or palpitations</td>
<td>Climbs $\geq$ 2 flights of stairs with ease</td>
</tr>
<tr>
<td>II (Mild CHF)</td>
<td>Slight limitations to physical activity. Ordinary physical activity leads to fatigue, SOB or palpitations</td>
<td>Can climb 2 flights of stairs but with difficulty</td>
</tr>
<tr>
<td>III (Moderate CHF)</td>
<td>Marked limitations to physical activity. Patient is comfortable at rest, however less than ordinary physical activity leads to fatigue, SOB or palpitations</td>
<td>Can climb $\leq$ 1 flight of stairs</td>
</tr>
<tr>
<td>IV (Severe CHF)</td>
<td>Patient is unable to carry out any physical activity without symptoms of SOB, fatigue or palpitations. Symptoms are also present at rest</td>
<td>Dyspnea/fatigue even at rest</td>
</tr>
</tbody>
</table>
Assessment

- Establish presence of CHF
- Determine Etiology
- Define severity
- Determine therapeutic strategy
- Evaluate response to current therapy
Assessment

- History/PE
- Imaging (CXR, cMRI)
- EKG
- Lab work (including electrolytes, CBC, BNP, TSH)
- Echo
- Risk stratification for ischemia (Nuclear stress test/cath)
- Assess functional capacity
Clinical Assessment

• **Elevated filling pressure/congestion**
  - Shortness of breath (orthopnea, DOE)
  - Fluid retention (JVP, edema, ascites, hepatomegaly)
  - Rales - Not reliable in chronic HF

• **Adequacy of Perfusion**
  - Fatigue
  - Narrow pulse pressure
  - Cool extremities
  - Mental status changes
  - End organ damage (renal insufficiency, hepatic dysfunction)
## Clinical profiles

### Congestion at rest

<table>
<thead>
<tr>
<th>Adequacy of perfusion at rest</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warm and Dry</td>
<td>Yes</td>
<td>Warm and wet</td>
</tr>
<tr>
<td>Normal PCWP</td>
<td>Elevated PCWP</td>
<td></td>
</tr>
<tr>
<td>Compensated</td>
<td>CI normal</td>
<td></td>
</tr>
<tr>
<td>Cold and Dry</td>
<td>Cold and Wet</td>
<td></td>
</tr>
<tr>
<td>PCWP low</td>
<td>PCWP elevated</td>
<td></td>
</tr>
<tr>
<td>CI decreased</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**Stevenson LW**  
Eur J Heart Failure 1999;1: 251-257
Biomarkers

- Naturetic peptides (BNP, Pro-NT BNP)
  - Diagnosis of CHF (*class 1*)
  - Prognostication (*class 1*)
  - Optimize GDMT
  - Not specific for HF, other causes exist
- Troponin
  - Risk stratification (*class IIB*)

Echo

• Most useful diagnostic test in evaluation of the patient with CHF
• What is the LVEF
• Presence of structural LV abnormalities (LVH, dilated or normal LV size, wall motion abnormalities
• Other structural abnormalities such as valvular disease, RV dysfunction
• Obtain at baseline, following appropriate optimization of GDMT, and when there is a major change in clinical status
Treatment

- Improve clinical status
- Improve functional capacity
- Improve quality of life
- Prevent hospital readmissions
- Reduce Mortality

ESC HF guidelines 2016
Drug Therapy

- ACE-I
- ARB
- ARNI
- BB
- Digoxin
- Diuretic
- Hydralazine/nitrate
- Ivabradine
- SGLT2 inhibitors
ACE-inhibitor

- Indicated for use in patients with LV dysfunction, EF < 40%
- Prevention of development of HF in patients with LV dysfunction
- Reduces adverse cardiac remodeling
- Improves survival
- Improves CHF symptoms
- Reduces hospitalizations
- Vasodilates the efferent arterioles => decrease in intraglomerular pressure (expect up to a 30% decrease in GFR/increase in creatinine in some patients)
ACE inhibitors reduce mortality in patients with left ventricular dysfunction

A meta-analysis of five trials involving 12,763 patients with left ventricular dysfunction who were followed for 35 months found that therapy with an angiotensin converting enzyme (ACE) inhibitor significantly reduced mortality (23 versus 26.8 percent, odds ratio 0.80, p <0.0001). There is continuing divergence in the mortality curves during the follow-up that exceeds four years.

### ACE- inhibitor

#### ATLAS trial

<table>
<thead>
<tr>
<th></th>
<th>Low dose</th>
<th>High dose</th>
<th>HR</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cause mortality</td>
<td>44.9%</td>
<td>42.5%</td>
<td>0.92 (0.82-1.03)</td>
<td>0.128</td>
</tr>
<tr>
<td>All cause mortality/hospitalization</td>
<td>83.8%</td>
<td>79.7%</td>
<td>0.88 (0.82-0.96)</td>
<td>0.002</td>
</tr>
<tr>
<td>All cause mortality/CHF hospitalization</td>
<td>60.4%</td>
<td>55.1%</td>
<td>0.85 (0.78 -0.93)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Low dose 2.5 - 5 mg
High dose 32.5 - 35 mg

Parker et al. Circ 1999:100 ; 2312 -2318
ARB

- Symptomatic and asymptomatic patient with LVEF less than 40% who are intolerant to ACE-I (Class 1A)
- May be used as alternative to ACE-I as a first line agent in patients already on ARB for other reasons (Class IIA)
- May be used in persistently symptomatic patients who are already on a BB and an ACE-I
- It is not recommended to use with ACE-I, and aldosterone antagonist
ARBS in Patients Not Taking ACE Inhibitors: Val-HeFT & CHARM-Alternative

Val-HeFT

Survival %

Placebo

Valsartan

p = 0.017

Months

0 3 6 9 12 15 18 21 24 27

CHARM-Alternative

CV Death or HF Hosp %

Placebo

Candesartan

HR 0.77, p = 0.0004

Months

0 9 18 27 36 42

Trouble shooting ACE-i/ARB

- Start low doses, target doses per guidelines
- Close monitoring of renal function (especially potassium)
- Potassium $\geq 5.0$ mEq/L is a concern, however, can use K binders (e.g. Patiromer) concomitantly
- Can expect up to a 0.5mg/dL rise in creatinine
- **Intolerance to ACE-i/ARB due to cardiorenal limitation is a poor prognostic sign**
- **Presence of asymptomatic hypotension is not an indication to stop**
- Stagger with other GDMT agents
Beta Blocker

- Carvedilol
- Metoprolol XL (Toprol)
- Bisoprolol
Beta Blockers

- Recommended for asymptomatic and symptomatic patients with reduced LVEF (< 40%)
- Use drugs shown to be effective in clinical trials (carvedilol, metoprolol XL, bisoprolol)
- Initiate in euvolemic patients (acutely can decrease EF, poorly tolerated in hypervolemia, very sick)
- Dose matters: EF improvement is highest with higher doses (US Carvedilol Trial)
- Optimize dose slowly, increasing dose every 2-4 weeks at small increments with close monitoring
# Effect of Beta Blockade on Outcome in Patients With HF and Post-MI LVD

<table>
<thead>
<tr>
<th>Study</th>
<th>Drug</th>
<th>HF Severity</th>
<th>Target Dose (mg)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>US Carvedilol¹</td>
<td>carvedilol</td>
<td>mild/moderate</td>
<td>6.25-25 BID</td>
<td>↓ 48% disease progression (p= .007)</td>
</tr>
<tr>
<td>CIBIS-II²</td>
<td>bisoprolol</td>
<td>moderate/severe</td>
<td>10 QD</td>
<td>↓ 34% mortality (p &lt;.0001)</td>
</tr>
<tr>
<td>MERIT-HF³</td>
<td>metoprolol succinate</td>
<td>mild/moderate</td>
<td>200 QD</td>
<td>↓ 34% mortality (p = .0062)</td>
</tr>
<tr>
<td>COPERNICUS⁴</td>
<td>carvedilol</td>
<td>severe</td>
<td>25 BID</td>
<td>↓ 35% mortality (p = .0014)</td>
</tr>
<tr>
<td>CAPRICORN⁵</td>
<td>carvedilol</td>
<td>post-MI LVD</td>
<td>25 BID</td>
<td>↓ 23% mortality (p =.031)</td>
</tr>
</tbody>
</table>

Beta-Blocker trouble shooting

- Ensure no reactive airway disease
- May get some symptoms of fluid retention/fatigue with dosing; adjust diuretics/other GDMT to take care of symptoms
- In-class switching if not on GDMT approved BB
- If hypotension:
  - Change from carvedilol to metoprolol XL
  - May be volume depleted, decrease diuretic dose
  - Stagger with ACE-i/ARB/ARNI
Prospective Comparison of ARNI with ACE-I to Determine Impact on Global Mortality in HF

PARADIGM-HF: Main Results

Entresto (Sacubitril-Valsartan)

Neurohormonal Antagonist Therapy: AHA/ACC/HFSA Heart Failure Guideline 2016

Recommendations for Renin–Angiotensin System Inhibition With ACE Inhibitor or ARB or ARNI

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>ACE: A</td>
<td>The clinical strategy of inhibition of the renin-angiotensin system with ACE inhibitors (LOE A) or ARBs (LOE A) or ARNI (LOE B-R), in conjunction with evidence-based beta blockers and aldosterone antagonists in selected patients, is recommended for patients with chronic HFrEF to reduce morbidity and mortality</td>
</tr>
<tr>
<td></td>
<td>ARB: A</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ARNI: B-R</td>
<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>
</tr>
</tbody>
</table>

Trouble shooting Entresto

Cautions for ARNI Therapy: AHA/ACC/HFSA Heart Failure Guideline 2016¹

Recommendations for Renin–Angiotensin System Inhibition With ACE Inhibitor or ARB or ARNI

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>III: Harm</td>
<td>C-EO</td>
<td>ARNI should not be administered to patients with a history of angioedema</td>
</tr>
<tr>
<td>III: Harm</td>
<td>B-R</td>
<td>ARNI should not be administered concomitantly with ACE inhibitors or within 36 hours of the last dose of an ACE inhibitor</td>
</tr>
</tbody>
</table>


- Can reduce or discontinue diuretics in patients with hypotension if volume status okay
- Stagger with other medications
- Careful attention to lab follow up with medication titration (similar to ACE-i/ARB)
Aldosterone Receptor Blocker

- Class II-IV with reduced LV EF (< 35%) while on GDMT with a BB, ACE-I or ARB or ARNI. (Class 1A)
- Patients with LVEF of <40% post MI who have CHF or have a history of DM (EMPHASIS trial, Class 1B)
- Class II patients should have a prior CHF hospitalization or elevated NP
- Creatinine < 2.5 mg/dL in men, < 2.0 mg/dL in women or
- eGFR > 30 mL/min/1.73m²
- Close monitoring of Potassium/renal function required
Aldosterone Blockade in Heart Failure

RALES: Randomized Aldactone Evaluation Study

1663 pts NYHA II, III, and IV, average age 65 and LVEF ≤.35, on ACEI, loop diuretic, ± digoxin randomized to spironolactone 25 mg PO qd vs placebo.

EPHESUS: Improved Survival and Decreased Hospitalization

Event rate at 16 months (%)

Mortality

Mortality or Hospitalization

Eplerenone

Placebo

n=478

n=554

n=993

P value

0.008

0.002

Trouble shooting MRA

- Monitor renal function/potassium closely (3 days after initiation, then 1 week, then monthly for 3 months, then q 3 months)
- Avoid potassium supplements unless K is persistently less than 4.0mEq/L
- Potassium ≥ 5.0 mEq/L is a concern, however, can use K binders (e.g Patiromer) concomitantly
- Avoid MRA in patients with Scr ≥ 2.5 (males), ≥ 2.0 (females) or with an eGFR < 30 mL/min/1.73m^2 (Class IIIB)
- Switch to Eplerenone if gynecomastia with spironolactone
Hydralazine/Nitrate

- Improve morbidity and mortality in self described African American with NYHA class III-IV symptoms who are already on optimal therapy with BB and ACE-I (Class 1A)
- Reasonable for patients on BB and ACE-I and still having CHF symptoms
- Improve morbidity and mortality in patients with symptomatic HFrEF who are ACE-I or ARB intolerant (development of hypotension, renal insufficiency) Class IIA
Hydralazine/Nitrate

Kaplan–Meier Estimates of Overall Survival.

Mortality ▼ by 43%
Ivabradine

- Selective sinus node inhibitor via the $I_f$ channel
- Decreases HR by inhibiting the $I_f$ current without an effect on contractility or relaxation
- Indicated (class IIA) for the use in patients with:
  - Chronic symptomatic systolic HF (LVEF ≥ 35%)
  - Sinus rhythm
  - Maximally tolerated doses of BB or have a contraindication to use
  - Resting heart rate of ≥ 70 bpm
  - CHF hospitalization in the past 12 months
- Reduces risk of HF hospitalization in patients with NYHA class II-III symptoms
- No mortality benefit
Systolic Heart Failure Treatment With the \( I_f \) Inhibitor Ivabradine Trial (SHIFT)\(^1 \)

**CV Death**

- Placebo (491 events)
- Ivabradine (449 events)

HR = 0.91 (95% CI, 0.80-1.03); \( P = .128 \)

**HF Hospitalization**

- Placebo (672 events)
- Ivabradine (514 events)

HR = 0.74 (95% CI, 0.66-0.83); \( P < .0001 \)

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Trouble shooting Ivabradine

- Attempt BB optimization first
- Avoid in patients with
  - bradycardia (< 60 BPM)
  - Acute decompensated CHF
  - Hepatic impairment
  - Hypotensive
DM and CHF

- SGLT2: Dapagliflozin, canagliflozin, empagliflozin, ertugliflozin
- Improve cardiovascular outcomes on top of GDMT
- Mechanisms not defined. Hypothesis:
  - Osmotic diuresis/natriuresis
  - Promote vasodilation
  - Improve myocardial metabolism, improving cardiac efficiency
  - Reduce cardiac fibrosis
- Improvement independent of glycemic control

SGLT2 and CHF

- Dapagliflozin: sodium-glucose cotransporter 2
- HFrEF patients (n = 4744) with DM-II (42%) and without DM-II (58%)
- NYHA class II-IV with LVEF ≤ 40%
- No symptomatic hypotension or SBP < 95 mm Hg
- LVEF NT ProBNP ≥ 600 pg/ml (if hospitalized for heart failure in the past 12 months ≥ 400 pg/ml; if aflutter ≥ 900 pg/ml)
- Mean age 66 years
- eGFR > 30 ml/min/1.73m², SBP > 95 mm Hg
- Median duration of follow up 18.2 months
DAPA-HF.

Trouble shooting SGLT2

• Avoid in patients with DM-1
• Avoid in patients with eGFR < 30
• May need to decrease diuretic (can cause volume depletion)
• Risk of lower limb amputations especially in presence of PAD
• Caution with Canagliflozin in DM pts on digoxin (increases level)
Digoxin

- Indicated for use in patients with HFrEF to reduce heart failure hospitalizations (Class IIA)
- No mortality benefit
- Narrow therapeutic window (0.5-0.9 ng/mL)
- Withdrawal of digoxin in stable patients has been shown in clinical trials to be associated with decompensation
- Data is based on the Dig trial
- Data obtained before the use of GDMT
Diuretic

- Recommended in patients with hypervolemia unless contraindicated (Class 1C)
- Loop diuretics mainstay
- No mortality benefit, activate the SNS/RAAS
- Use lowest dose to maintain euvoolemia
Diuretic Resistance

- High sodium intake
- Poor oral bioavailability
- Use of NSAIDs
- Renal insufficiency
- Compensatory sodium reabsorption in the distal tubules
- Changing to a more potent diuretic
- Can combine loop with thiazide diuretic
Diuretic in CHF

Felker. CHF 2001
ICD therapy is recommended for primary prevention of SCD to reduce total mortality in selected patients with nonischemic DCM. Class 1A

Ischemic heart disease at least 40 days post-MI with LVEF of 35% or less, and NYHA class II or III symptoms on chronic GDMT, who have reasonable expectation of meaningful survival for more than 1 year. Class 1A
ICD Therapy in the SCD-HeFT Trial: Mortality by Intention-to-Treat

<table>
<thead>
<tr>
<th></th>
<th>HR</th>
<th>97.5% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone vs Placebo</td>
<td>1.06</td>
<td>.86-1.30</td>
<td>.53</td>
</tr>
<tr>
<td>ICD vs Placebo</td>
<td>.77</td>
<td>.62-.96</td>
<td>.007</td>
</tr>
</tbody>
</table>

Indications for CRT therapy algorithm.

**Patient with cardiomyopathy on GDMT for ≥3 mo or on GDMT and ≥40 d after MI, or with implantation of pacing or defibrillation device for special indications**

1. **LVEF ≤35%**
   - Evaluate general health status
   - Comorbidities and/or frailty limit survival with good functional capacity to <1 y
   - Continue GDMT without implanted device

2. **Acceptable noncardiac health**
   - Evaluate NYHA clinical status

### NYHA class I
- LVEF ≤30%
- QRS ≥150 ms
- LBBB pattern
- Ischemic cardiomyopathy
- QRS ≤150 ms
- Non-LBBB pattern

### NYHA class II
- LVEF ≤35%
- QRS ≥150 ms
- LBBB pattern
- Sinus rhythm
- LVEF ≤35%
- QRS 120-149 ms
- LBBB pattern
- Sinus rhythm
- LVEF ≤35%
- QRS ≥150 ms
- Non-LBBB pattern
- Sinus rhythm
- QRS ≤150 ms
- Non-LBBB pattern

### NYHA class III & Ambulatory class IV
- LVEF ≤35%
- QRS ≥150 ms
- LBBB pattern
- Sinus rhythm
- LVEF ≤35%
- QRS 120-149 ms
- LBBB pattern
- Sinus rhythm
- LVEF ≤35%
- QRS ≤150 ms
- Non-LBBB pattern
- Sinus rhythm
- LVEF ≤35%
- QRS 120-149 ms
- Non-LBBB pattern
- Sinus rhythm

### Special CRT Indications
- Anticipated to require frequent ventricular pacing (≥40%)
- Atrial fibrillation, if ventricular pacing is required and rate control will result in near 100% ventricular pacing with CRT

Colors correspond to the class of recommendations in the ACCF/AHA Table 1.

Benefit for NYHA class I and II patients has only been shown in CRT-D trials, and while patients may not experience immediate symptomatic benefit, late remodeling may be avoided along with long-term HF consequences. There are no trials that support CRT-pacing (without ICD) in NYHA class I and II patients. Thus, it is anticipated these patients would receive CRT-D unless clinical reasons or personal wishes make CRT-pacing more appropriate. In patients who are NYHA class III and ambulatory class IV, CRT-D may be chosen but clinical reasons and personal wishes may make CRT-pacing appropriate to improve symptoms and quality of life when an ICD is not expected to produce meaningful benefit in survival.
Miscellaneous

• Anemia: Screen for iron deficiency. Give IV iron for IDA (ferritin < 100ng/mL or 100-300 ng/mL if transferrin saturation is < 20%)

• Sleep apnea: Assess for sleep apnea (IIa) CPAP for OSA (IIb). Use of adapto servo ventilation in CSA (class III)

• Antithrombotic therapy for afib/flutter

• Statins if there is evidence of hyperlipidemia

• Patiromer: Binds potassium in the GI tract, increasing fecal potassium excretion and thus lower serum levels. Allows for use of ACE-i/ARB in patients prone to hyperkalemia with these agents
Non-Pharmacologic Measures

- Patient education on self care
- Fluid restrictions: 2 liters/64 oz (ask about fruit)
- Salt restriction (1 teaspoon = 2300 mg of Na). Emphasize reading labels
- Daily Weights: Ensure they have a scale and use it consistently and record weights
- Daily BP: Keep a record
- Stop smoking
- Cardiac Rehab: Associated with improved outcomes in CHF (HF-ACTION). Class IIA recommendation
- Address end of life needs
Recovered EF (HFrecEF)

- TRED-HF trial
- 51 patients with prior history of DCM (mean EF 25%)
- Recovered LV function (mean EF 50%, normal LVEDD, NT ProBNP 72ng/L)
- 25 in the treatment arm weaned off GDMT over 6 months (diuretics => MRA => BB => ACE-I/ARB).
- After 6 months, 25 in the control group had GDMT withdrawn
- Primary end point: Relapse of DCM within 6 months
  - Doubling of ProNT BNP to > 400 ng/L,
  - Clinical evidence of CHF
  - > 10% increase in LVEDD by cMRI
  - Drop in EF by >10% to below 50%

Recovered EF (HFrecEF)

Initial group: 44%
Crossover: 36%
Advanced Heart Failure

- Presence of progressive and/or persistent severe signs and symptoms of heart failure despite optimized medical, surgical, and device therapy.
- Importantly, the progressive decline should be primarily driven by the heart failure syndrome.
**Advanced Heart Failure**

**I-NEED-HELP**

- **I**notropes: Previous or ongoing requirement for dobutamine, milrinone, dopamine, or levosimendan
- **N** NYHA class/ natriuretic peptide
- **E** End-organ dysfunction
- **E** Ejection fraction
- **D** Defibrillator shocks
- **H** Hospitalizations
- **E** Edema/escalating diuretics
- **L** Low blood pressure
- **P** Prognostic medication

Persisting NYHA class III or IV and/or persistently high BNP or NT-proBNP

Worsening renal or liver dysfunction in the setting of heart failure

Very low ejection fraction <20%

Recurrent appropriate defibrillator shocks

More than 1 hospitalization with heart failure in the last 12 months

Persisting fluid overload and/or increasing diuretic requirement

Consistently low BP with systolic <90 to 100 mmHg

Inability to up-titrate (or need to decrease/cease) ACEI, beta-blockers, ARNIs, or MRAs

Crespo-Leiro et al. Eur J Heart Fail 2018; 20: 1505
Advanced CHF

- Inotropic therapy (BTT, Palliative)
- LVAD (BTD, BTT, DT)
- Heart Transplant
- Palliative care/Hospice
- Early referral is imperative
Summary

- HF is a progressive disease with no cure
- Early diagnosis and aggressive therapy (optimizing GDMT) before significant adverse remodeling occurs
- Current approved medications for CHF (GDMT) consist of Beta blockers ACE-i/ ARB, ARNI, aldosterone blocker, hydralazine/nitrate. Dose matters, titrate to doses in clinical trials for benefit
- Relatively low BP alone is not an indication to decrease/or stop GDMT. Follow symptoms and end organ dysfunction
- Follow closely monitoring symptoms, BP, HR, lab work
Summary

- Clinic follow up
  - Signs and symptoms of CHF (including presence of exacerbating factors (CAD, HTN, valvular disease)
  - Compliance with dietary restriction/medication
  - Trend in body weight
  - Functional capacity and activity level
  - Response to therapeutic interventions
  - Prognostication
- Avoid withdrawal of GDMT in patients with recovered EF (TRED-HF trial data) as this can cause harm, even in patients with reverse remodeled LV.
Ebere.Chukwu@bswhealth.org
Intolerance to ACE-i/ARB

On ACEI vs. CRLimit combined: $p < 0.0001$
Inoptropes vs. no Inotropes: $p = 0.0002$
Number of patients remaining at 3-month intervals noted on plot.
## ARB in severe CHF

<table>
<thead>
<tr>
<th>Mean SBP</th>
<th>Mortality</th>
<th>SBP reductions</th>
<th>Valsartan (mortality)</th>
<th>Valsartan HF Hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>90-110 (101)</td>
<td>1.21 (1.03-1.43)</td>
<td>+1.2 ± 12.3</td>
<td>0.82 (0.63-1.06)</td>
<td>0.60 (0.45-0.9)</td>
</tr>
</tbody>
</table>

*Annand IS et al. Circ HF 2008; 1: 34-42*
Adjusted curves grouped by randomization to enalapril or placebo and subsequent early (WRF) status in patients who did not discontinue or dose reduce the study drug in proximity to WRF. Early WRF was defined as a 20% reduction in glomerular filtration rate (GFR) from baseline to 14 days after randomization.
Elevated BNP

Cardiac
- HF, including RV syndromes
- Acute coronary syndromes
- Heart muscle disease, including LVH
- Valvular heart disease
- Pericardial disease
- Atrial fibrillation
- Myocarditis
- Cardiac surgery
- Cardioversion
- Toxic-metabolic myocardial insults, including cancer chemotherapy

Noncardiac
- Advancing age
- Anemia
- Renal failure
- Pulmonary: obstructive sleep apnea severe pneumonia
- Pulmonary hypertension
- Critical illness
- Bacterial sepsis
- Severe burns

Yancy et al. ACC/AHA HF guideline update 2017
Triage of patients with advanced HF and appropriate timing of referral.

1. Age <75*
   - Yes
     - Co-morbidity causing life expectancy <1 year**
       - Yes
         - Advanced HF despite optimal guideline directed management (including CRT/ICD if indicated)
       - No
         - NYHA class II
           - Any of these characteristics:
             - Prior inotrope use
             - LVEF <20%
             - Intolerant of beta-blocker or RAS inhibitor/ARNI
             - Hyponatraemia
             - > 1 admission or unplanned visit to HF clinic for HF in last 12 months
             - SBP <90 mmHg
             - Worsening renal function or SCr > 160 μmol/L
             - Worsening liver function due to HF
             - Haemoglobin <12 g/L
             - Ventricular arrhythmias/ICD shocks
             - Persistent congestions/need for escalating diuretic doses
           - Yes
             - Refer to or discuss with advanced HF center
           - No
             - Manage in local HF service
           - YES
             - NO
               - Re-evaluation in 3-6 months

* >75 years if good functional status apart from HF (mono-organ disease)
** e.g. untreated cancer, dementia, severe COPD