Chronic Congestive Heart Failure: Update on Effective Monitoring and Treatment

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Outline
- Diagnosis and Staging
- Diastolic Heart Failure
- ACE Inhibitors, ARBs, and Beta Blockers
- Other Systolic Heart Failure Medications
- Devices and End-Stage Heart Failure

Heart Failure Epidemiology
- Only cardiovascular outcome that continues to increase
- Lifetime risk ~20%
- Complicated to manage with multiple other comorbidities
- Treatments improve survival and reduce morbidity substantially.
- 4 classes of medications improve survival
- 2 classes of medications improve symptoms
Why is Heart Failure Challenging to Manage?

- Patients are very complicated and often frail
- CHF travels with many other comorbidities:
  - CAD, hypertension, diabetes, CKD
- Polypharmacy
- Diastolic heart failure becoming more common

Question 1: Which of the following establishes a HF diagnosis?

- a) EF < 35% on echo
- b) BNP > 300 on blood test
- c) S3 on exam
- d) All of the above
- e) None of the above

Heart Failure is a Clinical Diagnosis

- **Essential Symptoms**: dyspnea, fatigue, orthopnea
- **Signs**: rales, edema, JVD, S3
- **Physical exam**: does not distinguish systolic vs. diastolic
- Helpful features include:
  - **Chest X-Ray**: pulmonary congestion
  - Elevated BNP or Nt-proBNP
  - Echo showing diastolic or systolic dysfunction

Diastolic vs. Systolic Heart Failure

- **Diastolic HF**:
  - Official term is “Heart Failure with Preserved Ejection Fraction”
  - Abbreviated as HFpEF
  - Pronounced “huff-puff”
- **Systolic HF**:
  - Official term is “Heart Failure with Reduced Ejection Fraction”
  - Abbreviated as HFrEF
  - Pronounced “huff-ruff”
NYHA Functional Classes

**Classes assume a prior diagnosis of heart failure**

I. No limitation on ordinary physical activity
II. Slight limitation – ordinary physical activity
III. Marked limitation - < ordinary physical activity
IV. Symptoms or discomfort at rest

Problems with these classes:
- Patients vary across stages, going up and down
- All class 4 at time of hospitalization

New AHA (2009) Classification of Heart Failure

A. **Risk factors** for heart failure- no clear signs/symptoms
B. **Asymptomatic LV disease** - LVH, diastolic dysfunction, valve disease, low EF
C. **Symptomatic heart failure**- dyspnea at rest or exertion, fluid retention
D. **Advanced heart failure**- inotrope requirement, consideration for assist device or transplant

- Can only progress down the classes
- Emphasizes prevention over staging

Stages, Phenotypes and Treatment of HF

Strategies that apply to all CHF Patients

- Initial ECHO
- Repeat only if major changes
- Salt restriction
- Daily weight monitoring
- Exercise
- Diuretics for symptoms
- Avoid NSAIDS
- Monitor:
  - Volume status
  - Electrolytes, renal function
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Question 2: Which of the following improve survival in diastolic heart failure?

a) ACE-I
b) ARB’s
c) Beta blockers
d) Ca-channel blockers
e) All of the above
f) None of the above

What is Diastolic Heart Failure?

- “Stiff heart syndrome” - heart cannot relax in diastole to allow the left ventricle to fill
- Causes increased pressure in the left atrium, and pulmonary edema
- Defined by EF, yet actual stroke volume may be same as SHF
- Same signs and symptoms as systolic HF
- Especially common in women and elderly

Diastolic HF: Good and Bad News

Good news:
- More favorable prognosis than SHF
- Simpler regimen, as diuretics cornerstone of therapy

Bad news:
- Often progresses to SHF
- No therapies improve DHF survival
ARBS/ACE-Is Do Not Improve Survival

• I-PRESERVE TRIAL

ACC/AHA Guidelines for DHF Treatment

• BP control (SBP < 130)
• Rate/rhythm control in AF
• Diuretics for pulmonary congestion
• Revascularization and other treatment for coronary ischemia
• European guideline recommends cardiac rehabilitation, though limited evidence

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Question 3: Which is the most important treatment for heart failure?

a) ACE inhibitors  
33%

b) Beta-blockers  
18%

c) They’re equally effective
18%

d) Neither
ACE Inhibitors

- Improve symptoms and reduce hospitalizations
- Decrease mortality risk for all heart failure stages
- Class effect- all ACE inhibitors
- Aim for target dose (ATLAS finding)

Meta-Analysis of ACE Trials

- 30 RCTs- ACE-I vs. placebo
- N= 3,870 + 3,2,35
- Mortality
  - 0.77 (0.67-0.88)
- Death or hospitalization for heart failure
  - 0.65 (0.57-0.74)
- Specific ACE-I’s with benefits in RCT’s:
  - Benzapril
  - Enalapril
  - Ramipril
  - Captopril
  - Lisinopril

Kidney Function and ACE Inhibitors in Heart Failure

- Clinical trials show benefit if estimated GFR > 30
- No evidence for lower GFR levels
- Expect the creatinine to rise at least 30%
- Even creatinine doubling is OK- typically returns near baseline
- Worry about K increase (keep < 5.5); balance the K with diuretic dose.
- Continue ACE-Is as eGFR declines unless cannot control K.

ARBs in Systolic Heart Failure

- Generally equivalent to ACE inhibitors
- Use for patients with cough on ACE inhibitors
- Combination of ACE and ARB?
  - Decreases hospitalization risk; increases adverse effect risk (increased K)
  - No survival difference
  - Generally, not recommended, as safety probably lower in actual practice

Shlipak MG, Ann Intern Med 2003

Question 4: Which of the following beta blockers improves survival?

a) Atenodol
b) Carvedilolol
c) Metoprolol
d) Propranolol
e) B and C
f) All of the above (class effect)

Beta Blockers in Systolic Heart Failure

- Beta blockers improve symptoms and increase ejection fraction by 5-10%
- Beta blockers decrease mortality in systolic heart failure, from both pump failure and arrhythmic causes
- Unlike ACE inhibitors, not a class effect
- Metoprolol or Carvedilol (U.S.)
- Bisoprolol in Europe

Heart Failure Survival

Challenge of Titrating Beta Blockers in Heart Failure Patients

- Both metoprolol and carvedilol require subtle dose increases at 2 week intervals
- Can take up to 6 visits to reach target
- Hypo-tension is not a contra-indication unless symptomatic
- Carvedilol may be more difficult to titrate dose up.
- Benefit greatest at maximum dose
- Unfortunately, many patients left at the low starting dose
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Other Therapies in Systolic Heart Failure

- Diuretics
- Aldosterone Antagonists- spironolactone, eplerenone
- Hydralazine/Nitrates
- Digoxin

Diuretics

- Rapid relief of dyspnea and fluid retention
- Aim for lowest dose that reaches “dry weight”
- Therapeutic goals:
  - Improved dyspnea and orthopnea
  - Minimal pre-tibial edema
- Patients can manage the dose and schedule

Diuretic Refractory Patients

- Periodic thiazide (metolazone)
  - e.g. 3x/week doses
  - watch for hypo-Na+, hypo-K+
- Change the loop diuretic- furosemide (Lasix), bumetanide (Bumex), Torsemide (Demadex)
- Long-acting nitrates also useful for symptoms
- Occasional IV diuretics may be required- intestinal edema can block po absorption
Aldosterone Antagonists (spironolactone, eplerenone)

- Improve survival and reduce hospitalization - RALES trial
- Only studied in NYHA class 3-4 heart failure patients on ACE inhibitors
- K allowed up to 5.6; very few hyper-K complications
- 1/3 on beta blockers

**Rales Trial**

HR = 0.70

Pitt B. et al., NEJM 1999

**Enormous Rise in Spironolactone Use**

**What Happened?**

- It’s in the fine print...
- RALES methods - inclusion if patients Cr < 2.5
- 2005 and 2013 AHA Guidelines - spironolactone recommended in NYHA III heart failure if Cr < 2.5
- RALES table 1 - actual Cr levels 1.2 ± 0.3
  - ~80% had Cr ≤ 1.5
  - ~ all had Cr < 2.0
  - average furosemide dose of 80mg

**Epidemic of Hyper-K Followed**

Juurlink DN et al., NEJM 2004
Case Details of Hyper-K on Spironolactone

- Case reviews of critical or fatal hyper-K (≥ 6.5) Schepkers et al., Am J Med 2001
- Mean Cr of 2.1; all on ACE-I also
- Often in setting of other illness-decreased oral intake
- Lessons learned:
  - Caution in using spironolactone if eGFR < 45, or Cr ≥1.5
  - Stop spironolactone in acute illness

Guideline Recommendations on Aldosterone Antagonists

- AHA HF guidelines (2005, 2009, 2013) have oscillated on aldosterone antagonists
  
  **AHA Class I:**
  - Recommended for HF patients EF< 35%
  - eGFR> 30; K < 5.0
  
  **AHA Class III (harmful):**
  - eGFR< 30, K > 5.0

**My recommendation:** Use extreme caution if eGFR 30-45
- QOD dosing: cutting dose by ½
- Advise patients to stop using when PO intake is reduced or acutely ill

Hydralazine and Nitrates


- 1,040 African American patients
- Hydralazine vs. Placebo
- Trial halted early
- HR= 0.57, p= 0.01

Hydralazine/Nitrates

- Recommended (Class I) for “self-described” African Americans
  - Reduced EF
  - Class III/IV symptoms
  - Already treated with ACE, BB

- Consider (Class 2A) in patients who cannot tolerate ACE/ARB
**Digoxin in Systolic HF**
- Remains widely used in heart failure, especially if atrial fibrillation present
- DIG Study – huge trial of digoxin vs. placebo
  - clearly no survival benefit; HR=0.99
  - Decreased risk of first hospitalization (28% lower)
- Trial included both SHF and DHF patients
- Trial conducted before beta blockers widely used in heart failure

**Digoxin in Systolic HF**
- Often, digoxin-induced bradycardia hinders use of beta blockers.
- In these cases, stop digoxin and initiate beta blockers.
- When using digoxin, do not increase dose > 0.125mg; alternate day dosing in CKD.
- AHA Guidelines: “clearly, if digoxin was a new drug, it would not gain approval in HF”.

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**Rationale for Implantable Cardiac Defibrillators (ICDs) in CHF**
- Ventricular arrhythmia - common cause of heart failure death
- ICDs can reverse VT/VF and save the patient
- VT/VF risk is highest in end-stage CHF patients; but those patients unlikely to survive to gain benefit
- Challenge for selecting ambulatory patients for ICDs:
  - VT/VF risk high enough to benefit
  - CHF moderate, so patient might live a few years
ICD’s in Secondary Prevention
- Studied in Systolic HF patients
- Patients who survived prior sudden death or unstable VT event
- ICD’s clearly improve survival
- Must be consistent with goals of care for patient/family – critical role for the PCP

ICDs in Primary Prevention
- Risk/benefit tradeoff
- Recommended for patients with EF < 35% AND:
  - moderate HF symptoms on appropriate treatment
  - expectation of survival > 1 year
  - Not for class 4 HF - prognosis too poor to benefit, unless as a bridge to transplant
- Prior MI patients appear to have higher SCD risk, among those with Systolic HF

Rationale for CRT
(Cardiac Resynchronization Therapy)
- Cardiac dys-synchrony:
  - Concern in patients with EF < 35%
  - RV and LV may not be in harmony
  - Suspect dyssynchrony in patients with persistent symptoms despite ideal treatment
- Causes: decrease ventricle filling, decrease EF, increase MR
- CRT: activates LV/RV together with bi-ventricular pacer
- Meta-analysis:
  - decrease in mortality by 25%
  - detectable after 3 months
  
Ideal Candidates for CRT
- EF < 35% and persistent symptoms
- 3 additional ECG criteria:
  - Sinus rhythm
  - LBBB
  - QRS > 150mg
- Class I: all 3 ECG criteria
- Class 2A: 2 of 3 ECG criteria
- Class 2B: 1 of 3 ECG criteria

McAlister FA, JACC 2004
End-Stage Heart Failure

**European Definition of Class D/Advanced HF**
- Severe symptoms at rest or with minimal exertion
- Hospitalized in last 6 months
- Treatment already optimized
- Poor functional status

**Clinical correlates of Advanced HF**
- Weight loss
- Worsening kidney function
- SBP<90
- Intolerance to ACE and/or BB
- Na<133
- Increasing diuretic requirement
- Frequent ICD shocks

Additional Support for End-Stage Heart Failure Patients

**Consider:**

**Specialized strategies (HF specialist):**
- Mechanical circulatory support
- Inotrope infusions
- Transplant or surgery referral

**Hospice/End-of-Life Care (Palliative care):**
- Comfort care
- Turn off the ICD

Thank you!
Any Questions?