Congestive Heart Failure: Update on Effective Monitoring and Treatment

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Outline
- Diagnosis and Staging
- Diastolic Heart Failure
- Evidence-Based Treatment of Systolic HF
- Other Systolic Heart Failure Medications
- Devices
- Surveillance with BNP or Telemonitoring

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.
- 3 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?

1. EF < 35% on echo
2. BNP > 300 on blood test
3. S3 on exam
4. All of the above
5. 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

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 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
Strategies that apply to all CHF Patients

- Salt restriction
- Daily weight monitoring
- Exercise
- Diuretics for symptoms
- Avoid NSAIDS

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Question 2: Which of the following improve survival in diastolic heart failure?
1. ACE-I
2. ARB’s
3. Beta blockers
4. Ca-channel blockers
5. All of the above
6. 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

![Graph showing outcomes](image)

Massie B. et al., NEJM 2008

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
- NICE guideline (Europe) recommends cardiac rehabilitation, though limited evidence

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

1. ACE inhibitors
2. Beta-blockers
3. They’re equally effective
4. 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= over 7000 patients
- 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.

Shlipak MG, Ann Intern Med 2003
**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


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

1. Atenodol
2. Carvedilol
3. Metoprolol
4. Propranolol
5. B and C
6. 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**

Ramani G et al., Mayo Clin Proc 2010
**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

**Nurses or Clinical Pharmacists can Assist Beta Blocker Titrination**

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**Other Therapies in Systolic Heart Failure**
- Diuretics
- Aldosterone Antagonists- spironolactone, eplerenone
- 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

Pitt B. et al., NEJM 1999

Enormous Rise in Spironolactone Use

Figure 1. Rate of Prescriptions for Spironolactone among Patients Recently Hospitalized for Heart Failure Who Were Receiving ACE Inhibitors.

Endline shows the observed prescriptions per 1000 patients during one four-month interval. The line beginning in the second interval of 1999 shows projected prescription rates derived from unconditional autoregressive integrated moving average (ARIMA) model, with 1 bars representing the 95 percent confidence intervals.

Juurlink DN et al., NEJM 2004
Epidemic of Hyper-K Followed

What Happened?

- It’s in the fine print…
- RALES methods- inclusion if patients Cr < 2.5
- Initial AHA Guideline- 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

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
- AHA guidelines have since changed – now more cautionary on spironolactone use.

Shlipak MG et al., Ann Intern Med 2003

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; a 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 HF cause of 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 compared 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
  - expectation of survival > 1 year
  - Not for class 4 HF - prognosis too poor to benefit
  - Of course, NYHA classes are very subjective!
• Prior MI patients appear to have higher SCD risk, among those with Systolic HF

Rationale for CRT
(Cardiac Resynchronization Therapy)

• Cardiac dys-synchrony:
  - no consensus definition; QRS > 0.12 is a proxy
  - implies RV and LV not in harmony
  - Usually evaluated in patients with persistent symptoms
• 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
  McAlister FA, JACC 2004

AHA Indications for CRT

• EF < 35% and Sinus Rhythm (class I evidence)
• NYHA Class 3-4 on optimal treatment
  - NICE guidelines emphasize symptoms despite maximal efforts at medical therapy
• QRS > 0.12 – proxy for cardiac dys-synchrony
• If Atrial Fibrillation present, class IIa evidence

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What is BNP-Guided Therapy?
- Periodic BNP measures with therapy adjusted to maximally lower the BNP
- Trials conducted to compare this strategy with “usual care” without BNP
- Each trial had a specific BNP or Nt-proBNP target—either absolute or % change
- Medical adjustments aimed to lower BNP levels
- Trials targeted dosing of ACE-I/ARB, beta blockers, spironolactone, diuretics
- Industry funded studies: possible publication bias

Porapakkham P. et al., Arch Intern Med 2010

BNP-Guided Therapy
- Meta-analysis of 8 trials
- 1,726 out patients followed for an average of 16 months
- All with EF < 50%
- Decreased mortality (0.76; 0.63-0.91)
- However, benefit appeared attributable to more intensive medical treatment

Porapakkham P. et al., Arch Intern Med 2010

Mortality Benefit Likely from Increased Medication Dosing

NICE guideline suggests BNP monitoring if patients or providers reluctant to escalate treatment

Porapakkham P. et al., Arch Intern Med 2010

Telemonitoring
- Another method in use to monitor patient symptoms and volume status
- Has been widely adopted by some healthcare orgs. such as the VA
- In NIH-funded trial (Chaudhry et al. NEJM 2011):
  - N=1653 patients recently hospitalized for heart failure
  - Randomization to telemonitoring or usual care
  - No change in death (11.1% vs. 11.4%) or readmission (49.3% vs. 47.4%)
Thank you!
Any Questions?