Chronic Heart Failure Management & New Treatment Modalities

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Disclosures

• I have no financial conflicts of interest to report with any manufacturer of medications or medical devices
Question 1: Which of the following diagnostic findings is most specific for decompensated heart failure with reduced ejection fraction (HFrEF)?

A. Dyspnea
B. Presence of S3 gallop
C. Lower extremity edema
D. BNP of 250
E. History of T2DM
Question 2: Which of the following is correct with regards to natriuretic peptide testing in heart failure?

A. BNP is not a good prognostic marker for patients with heart failure
B. NT-proBNP is a cleavage product of preproBNP
C. There is evidence that BNP-guided therapy is superior to a symptom guided therapy in patients >75 y/o
D. BNP is a highly sensitive test
E. There is evidence that serial BNP testing reduces mortality
F. NT-proBNP is a good screening test for chronic heart failure
**Question 3:** A 50 y/o African-American woman with chronic HFrEF, ischemic, EF 30%, with AICD, ACC/AHA stage C, presents to clinic for follow-up. She has no shortness of breath, no chest pain, no leg swelling, no early satiety. She is on optimal doses of losartan, carvedilol, spironolactone, aspirin, rosuvastatin. She does not smoke. She had a transthoracic echocardiogram 6 months ago showing a EF of 30%, moderate left atrial enlargement, dilated LV, mild mitral regurgitation. Her exam shows a BP of 115/65 and HR of 60. Her labs are unremarkable. Her ECG shows normal sinus rhythm with a QRS of 100 ms. Which of the following recommendations is appropriate today?

A. Repeat an echocardiogram today to evaluate the EF and mitral valve
B. Switch carvedilol to metoprolol tartrate
C. Counsel her on an exercise training program
D. Refer to Cardiology for Cardiac Resynchronization Therapy
E. (A) and (C) are both correct
F. (A), (B), and (C) are correct
Heart Failure Definitions

• Results from disorders of the pericardium, myocardium, endocardium, valve, or great vessels, or metabolic abnormalities
  – Most have impaired LV function

• Heart Failure with reduced EF (HFrEF)
  – EF≤40%
  – Also referred to as systolic HF

• Heart Failure with preserved EF (HFpEF)
  – EF≥50%
  – Also referred to as diastolic HF
  – Subset of patients
    • HFpEF, borderline, EF of 41-49%
    • HFpEF, improved, EF > 40 %
Why Heart Failure is Important

• Lifetime risk of developing HF is 20% in Americans > 40 y/o
• Incidence stable
  – > 650,000 new HF annually
• Incidence increases with age
• Prevalence continues to rise
  – 1/5 Americans will be ≥ 65 by 2050 and HF prevalence highest in this group
• Health disparities
  – African-Americans have highest risk for HF
• **Mortality**
  – Survival has improved, absolute mortality is about 50% within 5yr of diagnosis (ARIC study)
  – From 1993 to 2005 30 d mortality decreased from 12.6% to 10.8% **BUT** post-discharge mortality increased from 4.3% to 6.4%

• **Hospitalization & Economic burden**
  – Primary diagnosis in >1million hospitalizations annually
  – 1/9 deaths mention HF on death certificate
  – Total cost exceeds $30 billion annually, half spent on hospitalizations in 2013
  – HF-related hospitalization was $23,077 per patient in 2013

• **Risk factors**
  – HTN, T2DM, Metabolic syndrome (prevalence exceeds 20% of age > 20 y/o), Atherosclerotic disease
Pathophysiology
Heart Rate and HF

- ↑ Oxygen consumption
- ↓ diastolic preload
- ↓ coronary perfusion
- ↑ oxidative stress
- ↑ cardiac hypertrophy

Ischemia
Remodeling
Atherosclerosis
<table>
<thead>
<tr>
<th>NYHA Functional Class</th>
<th>ACC/AHA Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Class I:</strong> No limitations of physical activity; ordinary activity does not cause undue fatigue, palpitations, dyspnea</td>
<td><strong>Stage A:</strong> at high risk for HF; no identified structural or functional abnormality; no signs or symptoms</td>
</tr>
<tr>
<td><strong>Class II:</strong> Slight limitation of physical activity; comfortable at rest but ordinary activity results in fatigue, palpitations, dyspnea</td>
<td><strong>Stage B:</strong> Developed structural heart disease that is associated with development of HF but without signs or symptoms</td>
</tr>
<tr>
<td><strong>Class III:</strong> Marked limitation of physical activity, less than ordinary activity results in fatigue, palpitations, dyspnea</td>
<td><strong>Stage C:</strong> Symptomatic heart failure associated with underlying structural heart disease</td>
</tr>
<tr>
<td><strong>Class IV:</strong> Unable to carry on any physical activity; symptoms present at rest; if physical activity undertaken discomfort is increased</td>
<td><strong>Stage D:</strong> Advanced structural heart disease and marked symptoms of HF at rest despite maximal medical therapy</td>
</tr>
</tbody>
</table>
Initial Approach

• History
  – Symptoms:
    • Dyspnea (sensitive 83 not specific 54)
    • **Specific: h/o MI (89), orthopnea (89), edema (72)**
    • PND, early satiety
  – Co-morbidities
    • HTN, T2DM, CAD, CKD, COPD, Anemia
  – Medications
    • TZD (i.e. pioglitazone, rosiglitazone)
    • NSAIDs
  – SHx/FHx
    • 3-generational FHx for idiopathic Dilated CM
    • Smoking associated with 2x risk of admission for multiple admissions for HF and Alcohol has 5x risk

• Exam
  – Blood pressure (checking for orthostasis), volume status
  – JVD has 55-65% sensitivity and 74-80% specificity for increased filling pressures and HJR
  – **+S3 has low sensitivity but high specificity (85-95%)**
  – Ascites, LE edema, Hepatomegaly
Lab & Diagnostic Testing

• Laboratory testing
  – CBC, CMP, UA, Lipid panel, TSH
  – 12 lead ECG
  – **Screening for HIV, hemochromatosis
  – BNP/NT-ProBNP

• Diagnostic testing
  – CXR (specific 82%, not sensitive)
  – 2-dimensional echocardiogram
  – (Testing for Ischemic heart disease)
Biomarkers and HF
What is BNP?

Stress

Cardiac Myocyte

ProBNP

BNP (active)

NT-proBNP
BNP role in chronic HF

• BNP and NT-proBNP are sensitive (92-93%) and can help rule out heart failure
• BNP has prognostic value and can be used for risk stratification
• BNP-guided therapy
  – Controversial
## NP Testing

<table>
<thead>
<tr>
<th></th>
<th>BNP</th>
<th>NT-proBNP</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100 pg/mL</td>
<td>HF unlikely</td>
<td></td>
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<tr>
<td>&gt;400 pg/mL</td>
<td>HF likely</td>
<td></td>
</tr>
<tr>
<td>100-400 pg/mL</td>
<td>“Clinical Judgment”</td>
<td></td>
</tr>
<tr>
<td>NT-proBNP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;300 ng/mL</td>
<td>HF unlikely</td>
<td></td>
</tr>
<tr>
<td>Age &lt; 50, NT-proBNP &gt;450 pg/mL</td>
<td>HF likely</td>
<td></td>
</tr>
<tr>
<td>Age 50-75, NT-proBNP &gt;900 pg/mL</td>
<td>HF likely</td>
<td></td>
</tr>
<tr>
<td>Age &gt;75, NT-proBNP &gt;1800 pg/mL</td>
<td>HF likely</td>
<td></td>
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</table>

BNP and Prognosis
NP and Risk Stratification

• What is a significant change?
  - 40% for BNP, and 25% for NT-proBNP
Pre-discharge BNP and prognosis

- Prospective study
- 114 patients, average age 70, LVEF 37%
- BNP at admission mean was 1015
- BNP at discharge mean was 457
# Changes in BNP levels

<table>
<thead>
<tr>
<th>Elevated BNP</th>
<th>Cardiac:</th>
<th>Non-cardiac:</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>HF</td>
<td>Advancing age</td>
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<tr>
<td></td>
<td>ACS</td>
<td>Anemia</td>
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<td></td>
<td>Valvular disease</td>
<td>Renal failure</td>
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<td></td>
<td>Atrial fibrillation</td>
<td>Critical illness</td>
</tr>
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<td></td>
<td>Myocarditis</td>
<td>Sepsis</td>
</tr>
<tr>
<td></td>
<td>Cardioversion</td>
<td>Toxic-metabolic (burns, chemotherapy)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Decreased BNP</th>
<th>Therapy:</th>
<th>Obesity</th>
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<tr>
<td></td>
<td>Diuresis</td>
<td></td>
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<tr>
<td></td>
<td>ACEi/ARB</td>
<td></td>
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<tr>
<td></td>
<td>β-blocker</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MRB</td>
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<td></td>
<td>Exercise</td>
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</table>
BNP-directed therapy?

- Many RCTs have studied this topic but remains controversial
- Most trials showed that patients in biomarker-guided arm had more up-titrations in therapies
- PROTECT study, reduction in NT-proBNP had reduction in composite outcome
- Most trials had small sample sizes
TIME-HF

• Randomized controlled trial
• Enrolled 622 patients randomized to NT-proBNP guided therapy to symptom guided therapy
• Patient characteristics:
  – Average age 76 but subgroups of patients age 60-74 and ≥75
  – LVEF 30%
  – NT-proBNP 4000-4500
• Outcomes: 18 mo survival free of all-cause hospitalizations and quality of life
Discussion

• Patients in NT-proBNP guided group had more up-titration in medications
• No differences in survival but significant HF-free hospitalization in NT-proBNP group
• Subgroup analysis shows patients <75 had more benefit from NT-proBNP guided therapy
• In patients >75, the NT-proBNP group had more therapy-adverse events
• Several meta analysis draw different conclusions likely related to heterogeneity
• PRIMA-II (2014, in-hospital BNP guided therapy)
ACC/AHA 2013 Recommendations

NP testing

- In ambulatory patients with dyspnea, measurement of BNP or NT-proBNP is useful to support clinical decision making regarding the diagnosis of HF (IA)
- Measurement of BNP or NT-proBNP is useful for establishing prognosis or severity of disease in chronic HF (IA)
- BNP or NT-proBNP guided HF therapy can be useful to achieve optimal dosing of GDMT in select clinically euvoletic patients in well-structured HF disease management program (IIa,B)
- Usefulness of serial measurement of BNP or NT-proBNP to reduce hospitalizations or mortality is not well established (IIb,B)
Looking to the future: Home BNP monitoring? HABIT trial

- Prospective observational study
- 163 patients with HF had weight and BNP (finger stick) levels measured for 60 days
B

PID=0060-0008, Age=76, Gender=M, NYHA=II, LVEF=24
PID=0071-0012, Age=60, Gender=F, NYHA=II, LVEF=20

Graph showing BNP (pg/ml) and weight (lb) over days.
BNP, TTE and HF

• Do not order serial echocardiography for the assessment of chronic heart failure unless the patient’s clinical status changes.

• Do not routinely repeat echocardiography in asymptomatic patients with mild mitral regurgitation and normal left ventricular size and function.

• Reserve the B-type natriuretic peptide (BNP) test to differentiate between a cardiac and pulmonary cause of dyspnea when the diagnosis is unclear; do not routinely measure BNP in patients with typical signs and symptoms of heart failure.
Chronic Heart failure Predictor Models
Talking with Patients

• Seattle Heart Failure
  – https://depts.washington.edu/shfm/

• Heart failure risk calculator (1, 3 yr mortality)
  – http://www.heartfailurerisk.org/

• GWTG-HF – In-patient mortality
Therapies for chronic HFref
Question 4: A 40 y/o Caucasian gentleman was recently diagnosed with HFpEF, non-ischemic in etiology, EF 35%, ACC/AHA stage C. In clinic today, he reports no dyspnea, chest pain, or worsening edema. He is currently on Lisinopril 40mg daily, Carvedilol 25mg twice daily, Spironolactone 25mg daily, and Furosemide 40mg daily. He does not smoke or drink alcohol. Exam shows a BP of 118/75, HR 60; cardiac exam shows a normal S1,S2 no S3 with a regular rate, JVP of 6 cm H2O, and mild pitting edema at the ankles. His labs show a K of 4.0 and Cr of 1.0 mg/dL, Hb of 10.0 (MCV 85) and a ferritin of 60. A fasting lipid panel shows a TC of 180 mg/dL, and a HDL of 40  ECG shows normal sinus rhythm with a QRS of 100 ms. Based on recent evidence, which of the following could provide mortality benefit for this patient?

A. Add warfarin to achieve an INR of 2.0-3.0
B. Give IV iron supplementation
C. Add Aliskiren
D. Add Ivabradine
E. Switch Lisinopril to Valsartan-Sacubitril
F. Add Hydralazine-Isosorbide dinitrate (Bidil)
G. Add Atorvastatin
Pharmacotherapy: What we Know

• Medications that improve mortality:
  – ACEi, ARB (but not combination in HFrEF) (IA)
  – β-blocker (carvedilol, metopolol succinate, bisoprolol) (IA)
  – Hydralazine/Isosorbide dinitrate (IA)
    • African-American
    • NYHC III-IV
  – Aldosterone antagonist (**avoid in men Cr>2.0 and women Cr>2.5 and K>5.0) (IA)

• Medications for symptoms of volume overload (I,C):
  – Loop Diuretics
    • Furosemide
    • Torsemide
    • Bumetanide
  – Sequential Nephron blockade
    • Metolazone
    • Chlorthiazide (IV)

• Medications for re-hospitalization (IIa,B):
  – Digoxin
Other therapies

• Anticoagulation (III,B)
  – Not recommended in patients with chronic HFrEF without evidence of AF, prior thromboembolic event, or cardioembolic source

• Statin (III,B)
  – No benefit solely for HF outcomes

• Omega-3 fatty acids (IIa,B)
  – Can use as adjunctive therapy in NYHC II-IV for HFrEF, HFpEF to reduce mortality and cardiovascular hospitalization
  – GISSI-HF trial
  – Unclear optimal dosing

• Calcium Channel Blockers
  – Should not be routinely given for HFrEF (III, A)
    • DHP (Amlodipine, Felodipine) – no clear survival benefit
    • Non-DHP (Diltiazem) – avoid in HFrEF
Anemia & Depression

• Anemia
  – Common finding in chronic HF
  – Associated with increased mortality in HF
  – Epo-stimulating agents?
    • RED-HF trial – Role of Darbapoetin
    • No mortality benefit, possible harm
  – Iron supplementation?
    • FAIR-HF, included patients with and without anemia but Fe deficiency (ferritin<100), NYHC II-III
    • IV iron replacement
    • Showed significant improvement in symptoms

• Depression
  – One study suggests that even 3mo after discharge, 63% patients had depression symptoms after discharge
Non-Pharmacologic therapy

• Specific education to facilitate HF care (IB)
  – Education improves knowledge, self-monitoring, mediation adherence, days in hospital, and time to hospitalization

• Social support
  – Salt restriction of 1.5 g/day (stage A/B), <3 g/day for C/D* (IIa)
  – CPAP for patients with HF and OSA (IIa,B)
    • Increases LVEF and improves functional status
    • Weight loss
  – Exercise program (IA)
  – Fluid restriction? (stage D HF)
Exercise and HF

• Several RCTs of exercise in HF have been done but low powered
• Large study, HF-ACTION, published in 2009 randomized 2331 patients (EF 25%, ischemic 52%) to either exercise training for 3 mo or usual care
• After adjusting for CAD, 11% reduction in all-cause mortality, CV disease mortality and hospitalizations
  – Improved self-reported health status
  – Reduction in depressive symptoms
• Current ACC/AHA recommendations (2013):
  – Exercise training (or regular physical activity) is recommended as safe and effective to improve functional status (IA)
  – Cardiac rehabilitation can be useful in clinically stable patients with HF to improve functional capacity, exercise duration, quality of life, mortality – (IIb,B)
Devices

• ICD (IA)
  – Primary prevention of SCD to reduce total mortality in patients with non-ischemic DM or ICM at least 40d post-MI, LVEF <35%, NYHC II or III on chronic GDMT with meaningful survival for more than one year

• CRT
  – LVEF<35%, sinus rhythm, LBBB with QRS>150ms and NYHC II-IV on GDMT (IA for NYCH III/IV, IB for NYHC II)
SHIFTing to the heart rate
Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study

Karl Swedberg, Michel Komajda, Michael Böhm, Jeffrey S Borer, Ian Ford, Ariane Dubost-Brama, Guy Lerebours, Luigi Tavazzi, on behalf of the SHIFT Investigators*

Lancet 2010, 376; 875-885

• Raised HR at rest is a risk factor for mortality
  – In patients with CAD, HR>70 bpm had 34% increased risk for CV death
  – Rate increased in in patients treated with β-blockers

• RCT evaluated role of Ivabradine, a SA node inhibitor ($I_f$ current)
  – Does not modify myocardial contractility and intracardiac conduction
## Results

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Ivabradine Rate</th>
<th>Placebo Rate</th>
<th>RR</th>
<th>NNT(H)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV death + hospitalization</td>
<td>24%</td>
<td>29%</td>
<td>0.83</td>
<td>20</td>
</tr>
<tr>
<td>Hospital admission for worsening HF</td>
<td>16%</td>
<td>21%</td>
<td>0.76</td>
<td>20</td>
</tr>
<tr>
<td>All adverse events</td>
<td>45%</td>
<td>48%</td>
<td>0.94</td>
<td>33</td>
</tr>
<tr>
<td>Symptomatic Bradycardia</td>
<td>5%</td>
<td>1%</td>
<td>5.0</td>
<td>25</td>
</tr>
</tbody>
</table>
Discussion Points

• Patients on optimal doses of β-blocker at beginning of trial?
  – At baseline, 89% on β-blockers
  – Only 56% of patients receiving 50% or more of target β-blocker dose

• Does demonstrate the importance of HR in HF

• Benefit in patients with HR>70 bpm with Ivabradine
Launching the ASTRONAUT into the ATMOSPHERE
Effect of Aliskiren on Postdischarge Mortality and Heart Failure Readmissions Among Patients Hospitalized for Heart Failure
The ASTRONAUT Randomized Trial

JAMA, March 20, 2013—Vol 309, No. 11

• What is Aliskiren?
  – Direct renin inhibitor
  – First designed to test BP reduction
  – FDA approved Aliskiren in 2006 for HTN

• Patient characteristics
  – 1639 patients randomized
  – Mean age was 65 years; LVEF 28%
  – 41% patients had DM, 76% with HTN
  – Patients on Diuretics (96%), b-blockers (82.5%), ACEi/ARB (84.2%), MRB (57%)
## Results

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Aliskiren group</th>
<th>Placebo group</th>
<th>RR</th>
<th>ARR(I)</th>
<th>NNT(H)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV death + hospitalization</td>
<td>24.9%</td>
<td>26.5%</td>
<td>0.94</td>
<td>1.6%</td>
<td>NS</td>
</tr>
<tr>
<td>(at 6mo)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P-value 0.41</td>
</tr>
<tr>
<td>CV death + hospitalization</td>
<td>35.0%</td>
<td>37.3%</td>
<td>0.94</td>
<td>2.3%</td>
<td>NS</td>
</tr>
<tr>
<td>(at 12mo)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P-value 0.36</td>
</tr>
<tr>
<td>Incidence of Hyperkalemia</td>
<td>20.9%</td>
<td>17.5%</td>
<td>1.19</td>
<td>3.4%</td>
<td>NS</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P-value 0.09</td>
</tr>
<tr>
<td>Renal impairment/failure</td>
<td>16.6%</td>
<td>12.1%</td>
<td>1.37</td>
<td>4.5%</td>
<td>22</td>
</tr>
<tr>
<td>Hypotension</td>
<td>17.1%</td>
<td>12.6%</td>
<td>1.36</td>
<td>4.5%</td>
<td>22</td>
</tr>
</tbody>
</table>
Figure 2. Kaplan-Meier Analyses of the Cumulative Event Rate for Cardiovascular Death or Heart Failure Hospitalization at 6 Months

![Graph showing cumulative event rate over time for different groups with placebos and aliskiren.](image)

HR, 0.92 (95% CI, 0.76-1.12), P = .41

<table>
<thead>
<tr>
<th>No. at risk</th>
<th>Aliskiren</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>808</td>
<td>807</td>
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<td></td>
<td>762</td>
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<td>679</td>
<td>655</td>
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<tr>
<td></td>
<td>597</td>
<td>578</td>
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</table>

For the analysis of events within 6 months, a Cox-regression model was used. Error bars indicate 95% CIs for the Kaplan-Meier estimate at day 190.
Discussion (1)

- No significant benefit of Aliskiren at 12mo on CV death/hospitalization for HF
- Effect of T2DM?
  - Sub-group analysis
  - DM patients had higher risk of death versus non-diabetics with lower risk of death
At 6 months:
HR (DM) = 1.13
HR (non-DM) = 0.80
P-value 0.08

At 12 months:
HR (DM) = 1.16
HR (non-DM) = 0.80
P-value 0.03
Discussion (2)

• Too many subgroups?
• Definition of DM in the analysis?
• Aliskiren should not be used or used with caution when added to other agents that block RAAS axis

• ATMOSPHERE trial on-going to evaluate ACEi monotherapy versus Aliskiren monotherapy versus combination therapy
Redefining the HF PARADIGM
• PARADIGM-HF study, published NEJM 9/2014
• Inhibition of neprilysin counteracts neurohormonal overactivation
• Prior study looked at ACE+NEPi but had significant risk of angioedema
• This trial looked at combination ARB (valsartan) and AHU377 (sacubitril a NEPi)
Study Design

• Double-blinded, randomized controlled Trial
• Enrolled 8442 patients with NYHA class II-IV HF with EF <40%
• Average age 64 y/o
• Outcomes: Primary was composite CV death or hospitalization from HF
• Trial stopped early, follow-up 27 months
<table>
<thead>
<tr>
<th>Outcome</th>
<th>LCZ696 Group</th>
<th>Enalapril Group</th>
<th>RR</th>
<th>ARR(I)</th>
<th>NNT(H)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV death + hospitalization</td>
<td>21.8%</td>
<td>26.5%</td>
<td>0.82</td>
<td>4.7%</td>
<td>21</td>
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<tr>
<td>Death from CV cause</td>
<td>13.3%</td>
<td>16.5%</td>
<td>0.81</td>
<td>3.2%</td>
<td>31</td>
</tr>
<tr>
<td>First hospitalization for worsening HF</td>
<td>12.8%</td>
<td>15.6%</td>
<td>0.82</td>
<td>2.8%</td>
<td>36</td>
</tr>
<tr>
<td>Symptomatic hypotension</td>
<td>14.0%</td>
<td>9.2%</td>
<td>1.52</td>
<td>4.8%</td>
<td>21</td>
</tr>
<tr>
<td>Cough</td>
<td>11.3%</td>
<td>14.3%</td>
<td>0.79</td>
<td>3.0%</td>
<td>33</td>
</tr>
<tr>
<td>Angioedema</td>
<td>0.2%</td>
<td>0.1%</td>
<td>2.0</td>
<td>0.1%</td>
<td>P-value 0.19</td>
</tr>
<tr>
<td>Elevated Cr ≥2.5 mg/dL</td>
<td>3.3%</td>
<td>4.5%</td>
<td>0.73</td>
<td>1.2%</td>
<td>83</td>
</tr>
<tr>
<td>Elevated serum K ≥6.0</td>
<td>11.3%</td>
<td>14.3%</td>
<td>0.79</td>
<td>3.0%</td>
<td>33</td>
</tr>
</tbody>
</table>
Hazard ratio, 0.80 (95% CI, 0.73–0.87)
P<0.001

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>LCZ696</th>
<th>Enalapril</th>
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<tr>
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<td>853</td>
</tr>
<tr>
<td>1260</td>
<td>249</td>
<td>236</td>
</tr>
</tbody>
</table>
Other Therapies

- Vasopressin antagonists (Tolvaptan)
- Sildenafil
- Endothelin receptor antagonists
- Relaxin
- Cardiac myosin activators
- Gene therapy
- Ranolazine (HFpEF)
The Future...Targeted Gene Therapy

Vector binds to cell membrane

Modified DNA injected into vector

Vector is packaged in vesicle

Vesicle breaks down releasing vector

Gene therapy using an adenovirus vector

Vector (adenovirus)

Vector injects new gene into nucleus

Cell makes protein using new gene

Viral DNA New gene Viral DNA

U.S. National Library of Medicine
Adherence to Medication

• Despite proven benefit of ACEI/ARB, b-blockers, mortality still high
• Adherence to medication is a predictor of clinical outcome
• Data from 2006-2008 National Ambulatory Medical Care Survey (NAMCS)
  – Average age 73 y/o (51% females), BMI 30 kg/m2
  – Common comorbid conditions: HTN, DM, COPD, Cancer, Chronic renal insufficiency
• Most were Medicare (67%); South (43%), Mean time spent with physician was 15 min
• No EMR in 58%
# NAMCS 2006-2008

<table>
<thead>
<tr>
<th>Category</th>
<th>Count (Percentage)</th>
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<tbody>
<tr>
<td>Health education given</td>
<td>622 (41)</td>
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<tr>
<td>Diet and nutrition</td>
<td>272 (19)</td>
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<tr>
<td>Exercise</td>
<td>188 (13)</td>
</tr>
<tr>
<td>Stress management</td>
<td>42 (2)</td>
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<tr>
<td>Tobacco cessation</td>
<td>39 (26)**</td>
</tr>
</tbody>
</table>

**Medications**

<table>
<thead>
<tr>
<th>Type</th>
<th>Count (Percentage)</th>
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<tbody>
<tr>
<td>Diuretic agents</td>
<td>667 (42)</td>
</tr>
<tr>
<td>β-blockers</td>
<td>649 (38)</td>
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<tr>
<td>ACEI/ARBs</td>
<td>542 (32)</td>
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<tr>
<td>Calcium channel blockers</td>
<td>189 (11)</td>
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<tr>
<td>Inotropic agents</td>
<td>214 (14)</td>
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<td>Vasodilators</td>
<td>214 (7)</td>
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<td>Antiarrhythmic agents</td>
<td>143 (4)</td>
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<tr>
<td>Median number of medications</td>
<td>6 (IQR, 2–8)</td>
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</table>
Medications and Clinic Visits

- No differences in medication use and sex, race, DM, or CRI
- Patients with COPD/Asthma less likely to receive β-blocker
Quality Improvement Measures
Grady Heart Failure Clinic
Multidisciplinary approach

• Many QI initiatives to improve adherence and education regarding HF
• GHS is 1,000-bed tertiary care teaching hospital
  – HF is the #1 DRG
  – 1200 HF admissions/yr
• HF admission rate 22 % before HF task force initiative (national 24% in medicare pts)
• Increasing use of a multidisciplinary approach
• Specialized HF clinics can improve adherence to evidence based treatments
HF Clinic

• Coordination with cardiology and primary care
• Patient seen by NP in the hospital and provide 30 day supply of medication, direct 1:1 self-education about HF (ACC/AHA core measures), and follow-up within 7-10 days
• Patient seen by either NP or attending physician and a pharmacist to reinforce education and up-titrate GDMT and self-management skills
• After HF task force the admission rate reduced by 25% (over 6 months)
  – Patient follow-up is a limitation (40% no-show rate despite giving appointments, calling, and giving medications)
  – Next step will be to address barriers
Conclusions

• HF is a complex syndrome and despite evidence based treatment mortality is increasing
• BNP and NT-proBNP can be helpful in prognosis and risk stratification for HF and given the sensitivity can help distinguish HF from other causes of dyspnea
  – Always use with clinical judgment
• Transthoracic echocardiograms should not be routinely performed unless there is a change in clinical status
• Realize there are several new medications that may have a role in treating HFrEF
  – Direct Renin inhibitors
  – Ivabradine
  – Angiotensin Receptor-Neprilysin Inhibitor
• There is an important role of education and exercise in the management of HF
• QI projects and multidisciplinary HF clinics are becoming available and can increase adherence to medications, help in education, and reduce hospital admissions
Acknowledgments

• HF clinic task force group
  – Nurcan Ilksoy, MD, FACP, FSHM (Emory Internal Medicine & Geriatrics)
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  – Diane Wirth, NP
  – Jasmine Johnson, NP
  – Mary-Katherine Cheeley, PharmD
  – Kristi Quaroli, PharmD
• Jada Bussey-Jones, MD, FACP
• Ted Johnson, MD, MPH
4. Parrinello et al. Water and Sodium in Heart Failure: A spotlight on congestion. *Heart Fail Rev* June **2014**.


