Treating Heart Failure in Biodiverse Patient Populations: Best Practices and Unveiling Disparities in Blacks

- 12th Annual Leadership Summit on Health Disparities & Congressional Black Caucus Spring Health Braintrust
- April 20-21, 2015
- Keith C. Ferdinand, MD, FACC, FAHA,FASH,FNLA
  - Professor of Clinical Medicine
  - Tulane University School of Medicine
  - Immediate Past-chair National Forum for Heart Disease and Stroke Prevention
Has disclosed the following affiliations. Any real or apparent COIs related to the presentation have been resolved.

Speaker’s Bureau
- None

Grant/Research Support
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Consultant
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Heart Failure (HF): A Major Public Health Burden in the United States

- ~550,000 new cases of HF diagnosed each year\(^1\)
- 2012 prevalence, 8 million US adults >18 years of age (2.8%) had HF
- In the US, HF affects about 3% of the African American population; whereas, this rate is about 2% in the general population\(^2\)
- The annual rates per 1000 population of new and recurrent HF events is:\(^3\)

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Black men</th>
<th>Black women</th>
</tr>
</thead>
<tbody>
<tr>
<td>65-74 years of age</td>
<td>21.1</td>
<td>18.9</td>
</tr>
<tr>
<td>75-84 years of age</td>
<td>52.0</td>
<td>33.5</td>
</tr>
</tbody>
</table>

Forecasting the Impact of Heart Failure in the United States: A Policy Statement From the American Heart Association
Paul A. Heidenreich, Nancy M. Albert, Larry A. Allen, David A. Bluemke, Javed Butler, Gregg C. Fonarow, John S. Ikonomidis, Olga Khavjou, Marvin A. Konstam, Thomas M. Maddox, Graham Nichol, Michael Pham, Ileana L. Piña and Justin G. Trogdon
Circ Heart Fail published online April 24, 2013;
DOI: 10.1161/HHF.0b013e318291329a
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Copyright © 2013 American Heart Association. All rights reserved. Print ISSN: 1941-3289. Online ISSN: 1941-3297
Projected HF: Race/ethnicity 2012-2030

Heidenreich, Albert, NM et al Circ Heart Fail. 2013;6:00-00
Racial Differences in Incident Heart Failure among Young Adults

Kirsten Bibbins-Domingo, Ph.D., M.D., Mark J. Pletcher, M.D., M.P.H., Feng Lin, M.S., Eric Vittinghoff, Ph.D., Julius M. Gardin, M.D., Alexander Arynychyn, M.D., Cora E. Lewis, M.D., O. Dale Williams, Ph.D., and Stephen B. Hulley, M.D., M.P.H.

ABSTRACT
Incident HF White and Black Men/Women in the CARDIA Study.


N=5115
B vs. W P=0.001
Long-term Antihypertensive Therapy Significantly Reduces CV Events

Average reduction in events (%)

Stroke: 35%-40%
Myocardial infarction: 20%-25%
Heart failure: >50%

n=201,566

Heart Failure: Causal Mechanisms

Smoking
Dyslipidemia
Diabetes

Hypertension

Obesity
Diabetes

MI

LVH

Systolic Dysfunction

Diastolic Dysfunction

HF

Normal LV Structure and Function

LV Remodeling

Subclinical LV Dysfunction

Overt Heart Failure

ACC/AHA Stage A ➔ Stage B ➔ Stage C
Diastolic Heart Failure: More Common in African Americans

Etiology of Heart Failure in African American Patients

Hypertension

Coronary Artery Disease

LVH

MI

HF

More common cause of HF cases in blacks

More common cause of HF cases in whites

LVH=left ventricular hypertrophy  HF=heart failure  MI=myocardial infarction

Adapted from Yancy CW. J Card Fail. 2003;9:S210-S215.
Manifestations of Heart Failure in African American Patients

- Prevalence of HF higher in African Americans than in Caucasians
- HF has a more malignant natural history in African American patients
  - Occurs at an earlier age\(^1\)
  - Associated with more advanced LV disease at diagnosis\(^1\)
- Differing etiology in African Americans
  - More likely to be associated with a history of hypertension\(^1\)
  - Incidence of MI is consistently lower\(^1\)
- Worse prognosis in African Americans
  - Higher rate of hospitalization than in Caucasian patients\(^2\)
  - Higher mortality rate than in Caucasians\(^2\)

Etiology of HF in African Americans

HF predominately caused by CAD

HF predominately caused by HTN

Hypertension in African Americans
Potential Physiologic and Hemodynamic Determinants

- Higher salt sensitivity
- Low levels of plasma renin
- Vascular dysfunction
  - vasoconstrictor hyperactivity
  - diminished vasodilatory function
- Greater rates of comorbidity (especially diabetes mellitus)
- Obesity
- Sedentary lifestyle
- Unhealthy diet
- Family history

Thirty-Day Readmission Rates for Medicare Beneficiaries by Race and Site of Care

Karen E. Joynt, MD, MPH
E. John Orav, PhD
Ashish K. Jha, MD, MPH
Blacks and Minority Hospitals – Higher HF Readmissions
A Medicare Population

<table>
<thead>
<tr>
<th></th>
<th>Acute Myocardial Infarction</th>
<th>Congestive Heart Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Patients</td>
<td>Readmission Rate, %</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>42,401</td>
<td>24.8</td>
</tr>
<tr>
<td>White</td>
<td>537,091</td>
<td>22.6</td>
</tr>
<tr>
<td>Site of care</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minority-serving hospital</td>
<td>50,107</td>
<td>25.5</td>
</tr>
<tr>
<td>Non-minority-serving hospital</td>
<td>529,385</td>
<td>22.0</td>
</tr>
</tbody>
</table>

Hospital Readmission by Race/Ethnicity

• For HF, blacks have higher odds of readmission regardless of site of care
  – While patients from minority-serving hospitals had even higher odds of readmissions regardless of race

• In general, whites at non-minority-serving hospitals had lowest risk of readmission


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Print ISSN: 0009-7322. Online ISSN: 1524-4539
Hypertension may be the single most important modifiable risk factor for HF in the US.

Hypertensive men and women have substantially greater risk for developing HF than normotensive men and women.

### Table 18. Medical Therapy for Stage C HF/EF: Magnitude of Benefit Demonstrated in RCTs

<table>
<thead>
<tr>
<th>GDMT</th>
<th>RR Reduction in Mortality (%)</th>
<th>NNT for Mortality Reduction (Standardized to 36 mo)</th>
<th>RR Reduction in HF Hospitalizations (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitor or ARB</td>
<td>17</td>
<td>26</td>
<td>31</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>34</td>
<td>9</td>
<td>41</td>
</tr>
<tr>
<td>Aldosterone antagonist</td>
<td>30</td>
<td>6</td>
<td>35</td>
</tr>
<tr>
<td>Hydralazine/nitrate</td>
<td>43</td>
<td>7</td>
<td>33</td>
</tr>
</tbody>
</table>

BEST: No Survival Advantage with β-blocker Bucindolol in African Americans with HF

Favors β-blockade

BEST African Americans

BEST Non-African Americans

Relative risk of mortality

Heart Failure is Associated with Neurohormonal Excess and Nitric Oxide Insufficiency

- **Neurohormones**
  - Neurohormonal Antagonists
    - Beta Blockers
    - Renin-Angiotensin Antagonists
    - Aldosterone Blockers

- **Endothelial Nitric Oxide**
  - Nitric Oxide Enhancers (NOE)
    - Fixed-dose combination Hyd/ISDN
Oxidative Stress Leads to a “Nitroso-Redox” Imbalance in Heart Failure

Survival in Black Patients and White Patients

**V-HeFT I**

**Black patients**

- Survival, %
- Time, days since randomization
- HR = 0.53 (0.29, 0.98)
- \( P = 0.04 \)

**White patients**

- Survival, %
- Time, days since randomization
- HR = 0.88 (0.63, 1.24)
- \( P = 0.47 \)

<table>
<thead>
<tr>
<th>Patients, n</th>
<th>ISDN/HYD</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>49</td>
<td>79</td>
</tr>
<tr>
<td>ISDN/HYD</td>
<td>43</td>
<td>61</td>
</tr>
<tr>
<td>Placebo</td>
<td>36</td>
<td>44</td>
</tr>
<tr>
<td>Time (days)</td>
<td>28</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>16</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>3</td>
</tr>
</tbody>
</table>

Combination of Isosorbide Dinitrate and Hydralazine in Blacks with Heart Failure

Anne L. Taylor, M.D., Susan Ziesche, R.N., Clyde Yancy, M.D., Peter Carson, M.D., Ralph D'Agostino, Jr., Ph.D., Keith Ferdinand, M.D., Malcolm Taylor, M.D., Kirkwood Adams, M.D., Michael Sabolinski, M.D., Manuel Worcel, M.D., and Jay N. Cohn, M.D., for the African-American Heart Failure Trial Investigators*
A-HeFT Trial

• Objective
  – Demonstrate the safety and efficacy of ISDN/HYD compared with placebo in African American patients with moderate to severe HF concurrently receiving standard HF treatment

• Inclusion Criteria
  – Patients self-identified as African American
  – NYHA class III or IV HF (> 3 months)
  – LVEF ≤ 35% (or ≤ 45% with dilated LV by echo)
  – Standard therapy for HF, including ACEI/ARB + BB (> 3 months)
A-HeFT: All-Cause Mortality

Hazard ratio = .57, Placebo 43% Decrease

P = .01

Hydralazine/Isosorbide Dinitrate Fixed Dose Combination: Decreased Relative Risk of First HF Hospitalization by 39%

AHeFT: Trial Summary  N=1050

All-Cause Mortality (%)
- Placebo + Standard Therapies: 6.2%
- HYD/ISDN + Standard Therapies: 10.2%
- P = 0.012

First HF Hospitalization (%)
- Placebo + Standard Therapies: 16.4%
- HYD/ISDN + Standard Therapies: 24.4%
- P < 0.001

Patient Reported Functional Status
- HYD/ISDN + Standard Therapies: n=85
- Placebo + Standard Therapies: n=130
- P < 0.01

The combination of HYD and ISDN is recommended for African Americans with NYHA class III–IV HFrEF on GDMT IA

A combination of HYD and ISDN can be useful with HFrEF who cannot be given ACE-Is or ARBs IIa B

Ivabradine

- FDA Approved April 15, 2015
- “Funny” current inhibitor for the treatment of heart failure
- Additional agent for blacks?
Conclusions

- HF disparities in by race and ethnicity
  - Start early
  - Persist
  - May worsen
  - Are preventable

- New guidelines and evidence-based best practices to improve outcomes and may help eliminate disparities in HF morbidity and mortality
Thank You!