Heart Failure: Issues Unique to Women

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Disclosures

RO1 HL 120857
RO1 AR 30582
R21 AG 045228

American Heart Association
Learn and Live

www.RochesterProject.org
Objectives

- The HF epidemic and its transition
- Case mix changes and HF in women
- Are the current guidelines adequate?
Heart failure is a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood.
Two new epidemics of cardiovascular disease are emerging: Heart failure and atrial fibrillation. Hospital admissions for heart failure have climbed steadily, so that this condition has become the single most frequent cause of hospitalization in persons 65 years of age and older. 

Braunwald E, NEJM, 1997
Hospital Discharges for Heart Failure
United States: 1979-2005 – Source: NHDS, NCHS and NHLBI

AHA Heart Disease and Stroke Statistics 2009 update
Epidemic: Merriam-Webster

- “An outbreak or product of sudden rapid spread, growth...a natural population suddenly and greatly enlarged.”

- Can be due to increased incidence and/or increased survival

- **Investigation:** what is the respective responsibility of each of these factors in the genesis of the HF epidemic?
# Incidence of Heart Failure in the Framingham Heart Study

<table>
<thead>
<tr>
<th>Period</th>
<th>Men</th>
<th></th>
<th>Women</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Incidence of heart failure</td>
<td>Rate</td>
<td>Incidence of heart failure</td>
<td>Rate</td>
</tr>
<tr>
<td></td>
<td>Rate/100,000 person-yr</td>
<td>ratio</td>
<td>Rate/100,000 person-yr</td>
<td></td>
</tr>
<tr>
<td>1950-1969†</td>
<td>627 (475-779)</td>
<td>1.00</td>
<td>420 (336-504)</td>
<td>1.00</td>
</tr>
<tr>
<td>1970-1979</td>
<td>563 (437-689)</td>
<td>0.87 (0.67-1.14)</td>
<td>311 (249-373)</td>
<td>0.63 (0.47-0.84)</td>
</tr>
<tr>
<td>1980-1989</td>
<td>536 (448-623)</td>
<td>0.87 (0.67-1.13)</td>
<td>298 (247-350)</td>
<td>0.60 (0.45-0.79)</td>
</tr>
<tr>
<td>1990-1999</td>
<td>546 (463-665)</td>
<td>0.93 (0.71-1.23)</td>
<td>327 (266-388)</td>
<td>0.69 (0.51-0.93)</td>
</tr>
</tbody>
</table>

*All values were adjusted for age (<55, 55-64, 65-74, 75-84 and ≥85 yr; values in parentheses are 95% CI
†This period served as the reference period

Levy et al: NEJM, 2002
## Incidence of Heart Failure in Olmsted County

<table>
<thead>
<tr>
<th>Period</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Incidence of heart failure</td>
<td>RR (95% CI)</td>
</tr>
<tr>
<td></td>
<td>Rate/100,000 person-yr</td>
<td></td>
</tr>
<tr>
<td>1979-1984</td>
<td>360 (323-396)</td>
<td>1</td>
</tr>
<tr>
<td>1985-1990</td>
<td>390 (354-425)</td>
<td>1.07 (0.94-1.22)</td>
</tr>
<tr>
<td>1991-1995</td>
<td>375 (340-409)</td>
<td>1.01 (0.88-1.15)</td>
</tr>
<tr>
<td>1996-2000</td>
<td>383 (351-415)</td>
<td>1.04 (0.92-1.18)</td>
</tr>
</tbody>
</table>
Mortality of HF in Framingham

Levy et al: NEJM, 2002

P<0.01

P<0.02
Mortality of Heart Failure in Olmsted County

5-year mortality (%)

Men

Women

P<0.05

1979-1984
1985-1990
1991-1995
1996-2000

JAMA, 2004
HF epidemic
Results of the Investigation

- Incidence stable or decreasing (among Caucasians)
- Incidence is not greater in women
- Survival improved
- Prevalence increased
Objectives

- The HF epidemic and its transition
- Case mix changes and HF in women
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Home of Mayo Clinic Rochester and Olmsted Medical Center
Geographically isolated from other providers of medical care
Linkage of all medical, surgical and tissue diagnoses
Assessing LV function in the community
Doppler Echocardiography

Systolic function
- EF ≥50% preserved
- EF <50% reduced

Diastolic function
- Normal diastolic function
- Mild diastolic dysfunction
- Moderate diastolic dysfunction
- Severe diastolic dysfunction

Mitral inflow
- DT >140 ms
- 0.75 < E/A <2
- E/A ≤0.75

Doppler tissue imaging of mitral annular motion
- E/e' <10
- E/e' ≥10

Velocity (m/s)
- 0.15
- 0
- 2.0
Systolic and Diastolic Function
556 Patients With HF in the Community

- HFPpEF 55%
- HFrEF 45%

- Isolated DD
  (EF ≥50% and DD) 44%

Bursi et al: JAMA, 2006
Prevalence of Diastolic HF
HF with EF $\geq$ 50%
## HF in the Community

<table>
<thead>
<tr>
<th></th>
<th>Overall n=556</th>
<th>HFpEF n=308</th>
<th>HFrEF n=248</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr, mean±SD)</td>
<td>76±13</td>
<td>77±13</td>
<td>73±14*</td>
</tr>
<tr>
<td>Women (%)</td>
<td>50</td>
<td>57*</td>
<td>42*</td>
</tr>
<tr>
<td><strong>Comorbidity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior MI (%)</td>
<td>43</td>
<td>36</td>
<td>50*</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>62</td>
<td>58</td>
<td>67*</td>
</tr>
<tr>
<td>COPD (%)</td>
<td>35</td>
<td>38</td>
<td>30</td>
</tr>
<tr>
<td>Conditions ≥3 (%)</td>
<td>69</td>
<td>70</td>
<td>68</td>
</tr>
</tbody>
</table>

Bursi et al: JAMA, 2006
Women, HF, and HFpEF

- Slight female predominance among patients with HFpEF ~55%
- However, the incidence of HF overall is lower in women
- If women make up more than 50% cases of HFpEF, then there is a disproportionate burden of HFpEF in women
- When women have HF, in 63% of the cases, it presents as HFpEF
HFpEF: it’s complicated…
Diagnostic challenges

- Flow based Doppler methods (E/A, DT) (reliability?)
- TDI (E/e’) (better, not ideal)
- Pulmonary pressures likely important
- Strain and torsion are research tools

...HFpEF itself is a heterogeneous entity
Sex-specific cardiovascular structure and function in heart failure with preserved ejection fraction

Mauro Gori¹, Carolyn S. P. Lam²,³, Deepak K. Gupta¹, Angela B. S. Santos¹, Susan Cheng¹, Amil M. Shah¹, Brian Claggett¹, Michael R. Zile⁴, Elisabeth Kraigher-Krainer⁵, Burkert Pieske⁵, Adriaan A. Voors⁶, Milton Packer⁷, Toni Bransford⁸, Martin Lefkowitz⁸, John J V McMurray⁹ and Scott D. Solomon¹*, for the PARAMOUNT Investigators

- 279 pts with HFpEF (57% women)
- Female sex associated with higher prevalence of abnormal LV geometry and worse diastolic function indices
What about outcomes?
Mortality adjusted for age, sex, etiology of HF, hypertension, diabetes, AF

Meta-analysis Global Group in Chronic Heart Failure (MAGGIC) Eur Heart J 2012;33:1750-1757
Adjusted hazard ratios comparing pts with HFpEF and HFrEF fraction by age

Meta-analysis Global Group in Chronic Heart Failure (MAGGIC) Eur Heart J 2012;33:1750-1757

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Number of deaths</th>
<th>Number in group</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;55</td>
<td>847</td>
<td>6624</td>
</tr>
<tr>
<td>55–74</td>
<td>5617</td>
<td>25882</td>
</tr>
<tr>
<td>≥75</td>
<td>5510</td>
<td>15280</td>
</tr>
</tbody>
</table>
Hospitalizations

- OPTIMIZE HF Registry
- Fonarow et al JACC 2007
- No difference between HFpEF and HFrEF in readmission rates (~30% at 60 days)
HFpEF

- HFpEF is more likely to occur in women
- The case mix of HF is changing as the prevalence of HFpEF relative to HFrEF is increasing
- HFpEF disproportionately and increasingly affects women…
  ...elderly women…vulnerable to hospitalizations
Objectives

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### Treatment Advances HFrEF

<table>
<thead>
<tr>
<th></th>
<th>1987</th>
<th>2005</th>
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<tbody>
<tr>
<td>ACE/ARB</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Beta Blockers</td>
<td>Just Starting</td>
<td>X</td>
</tr>
<tr>
<td>Aldo Antag</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AICD</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>CRT</td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

### Treatment Advances HFpEF

<table>
<thead>
<tr>
<th></th>
<th>1990</th>
<th>2005</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretics</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>? BB/ACE/Ca</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>↓ HR in AFib</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>? Maintain NSR</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>


*Trials using comparable and efficacious agents for HFrEF have generally been disappointing when used in patients with HFpEF. Thus, most of the recommended therapies for HFpEF are directed at symptoms, especially comorbidities, and risk factors that may worsen cardiovascular disease.*
“…major concern that the majority of RCTs failed to randomize a sufficient number of the elderly, women, and underrepresented minorities, thus, limiting insight into these important patient cohorts.”
Learnings and Gaps about in HF In Women

- Case mix transitioning and burden shifting towards elderly women presenting with HFpEF
- Outcomes poor, particularly in the elderly
- No specific treatment for HFpEF
- Not enough data for HFpEF and for women!

CALL for ACTION!
Thank You