Co-morbidity in Heart Failure: A Public Health Concern

CHF often related to Age, Diabetes, Obesity - so frequent co-morbidity leads to expensive hospitalisation

Peter Sleight, John Radcliffe Hospital Oxford UK
A cardiologist, feeling like Daniel in the Lion’s Den – so go to sleep, this isn’t a surgical talk!
Definition of HF

A pathophysiological state in which the heart is unable to pump blood at a rate sufficient to meet the metabolic needs of the body.

HF is a chronic condition.

Framingham classification does not require measurement of EF.
Stages of HF as Defined in the ACC/AHA Guidelines for the Evaluation and Management of Chronic Heart Failure in the Adult

Health

Lipids
- Blood Pressure
- Smoking
- Obesity
- Diabetes

A  CV Disease

B  LV Remodeling and Dysfunction

C  Overt HF

D  Terminal HF and Death

Owan et al Prog Cardiovasc Dis 2005
HF - Important pathophysiologic mechanisms

Patient factors
- Genetics, ethnicity, sex
- Age
- Use of alcohol, tobacco, toxic drugs

Coexisting conditions
- Hypertension
- Diabetes
- Renal disease
- Coronary artery disease
- Anemia – target of 11G
- Obesity
- Sleep apnea
- Depression

20% Lifetime risk for HF after age 40

Framingham Heart Study

Lifetime risk for HF for given index age is cumulative through age 94 years

EURO Heart Failure Survey

Overall population

Measurement of LV function

Overall population: 10,701

LV systolic dysfunction: 6,806

- LV systolic dysfunction: 53.7% (3,658)
- Preserved systolic function: 46.3% (3,148)

Preserved systolic function: EF ≥40%
Normal / Mild dysfunction

Eur Heart J. 2004;25:1214
Overall prevalence of Heart Failure, and the Age- and Sex-Specific Prevalences of DHF and SHF - EPICA Study

Differences and Similarities between

Preserved EF (diast. HF)     Reduced EF (SHF)

Differences
• Older
• More women
• Less CAD and MI
• More hypertension
• Smaller, thicker LV
• Greater BMI

Similarities
• Diabetes
• Tobacco
• Lipids
• AF
Survival in DHF and SHF in the Community

A = Olmsted County, Minn Study
B = Framingham Heart Study
C = Helsinki Aging Study
D = Cardiovascular Health Study

Owan et al Prog Cardiovasc Dis 2005
Hospital Re-Admission Rates in HF

Similar for both systolic & diastolic HF

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>HF-DHF</th>
<th>HF-SHF</th>
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<tbody>
<tr>
<td>Philbin et al 2000</td>
<td></td>
<td>44</td>
<td>42</td>
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<td>Malki et al 2002</td>
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<tr>
<td>Smith et al 2003</td>
<td></td>
<td>46</td>
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<tr>
<td>Dauterman et al 2001</td>
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<td>58</td>
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</tr>
</tbody>
</table>

Incidence of All Cause and Cardiac Death with Diastolic Dysfunction

Note that all-cause death is also related to Diastolic HF

Bella et al. Circulation 2002
Treating “diastolic heart failure”

The theory: hundreds of papers!

The evidence: virtually none!!
Hypertension is the No. 1 risk factor for HF

Framingham Heart Study

<table>
<thead>
<tr>
<th>Disease</th>
<th>Population-attributable risk (%)</th>
<th>Hazard ratio M</th>
<th>Hazard ratio W</th>
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<tbody>
<tr>
<td>HTN</td>
<td>60</td>
<td>2.1</td>
<td>3.3</td>
</tr>
<tr>
<td>MI</td>
<td>40</td>
<td>6.3</td>
<td>6.0</td>
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<tr>
<td>Angina</td>
<td>20</td>
<td>1.4</td>
<td>1.7</td>
</tr>
<tr>
<td>VHD</td>
<td>0</td>
<td>2.5</td>
<td>2.1</td>
</tr>
<tr>
<td>LVH</td>
<td>0</td>
<td>2.2</td>
<td>2.8</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0</td>
<td>1.8</td>
<td>3.7</td>
</tr>
</tbody>
</table>

VHD = valvular heart disease

Diabetes: A frequent comorbidity with HF

- Framingham data show ↑ HF in diabetic adults age 45 to 74 years
  - 2x ↑ in men; 5x ↑ in women

  - HF prevalence in 1994: 22.4%
  - Annual HF incidence: 7.9%
  - Similar incidence by sex and race
  - Significant ↑ with age and diabetes-related comorbidities

- National registry of >100,000 patients hospitalized with HF
  (mean age 72.4 years)
  - 44% had diabetes

Diabetes is the No. 1 risk factor for HF in women with coronary disease

HERS study

- Diabetes: 3.1
- Atrial fibrillation: 2.9
- Myocardial infarction >1 event: 2.5
- Creatinine clearance <40: 2.3
- Systolic BP ≥140: 2.1
- Current smoking: 1.9
- BMI >35: 1.9
- Left bundle branch block: 1.6
- LV hypertrophy: 1.5

Adjusted hazard ratio

Increasing risk for HF in women with CHD: Impact of diabetes, renal insufficiency, obesity

HERS study; 2391 women with CHD and no HF at baseline

CrCl (ml/min) = creatinine clearance

Obesity and the Risk of Heart Failure

Kenchaiah S et al: NEJM 2002
Heart Failure Pathophysiology
Important pathophysiologic mechanisms in HF

Cardiac abnormalities

Structural
- Myocardium or myocyte
  - Myocardial relaxation
  - Abnormal excitation-contraction coupling
  - β-Adrenergic desensitization
  - Hypertrophy
  - Necrosis
  - Fibrosis
  - Apoptosis

- Left ventricular chamber
  - Remodeling
    - Dilation
    - Increased sphericity
    - Aneurysmal dilatation or wall thinning
    - Concentric hypertrophy

- Coronary arteries
  - Obstruction
  - Inflammation

Functional
- Mitral regurgitation
- Intermittent ischemia or hibernating myocardium
- Induced arterial and ventricular arrhythmias
- Altered ventricular interaction

Important pathophysiologic mechanisms in HF

Biologically active tissue and circulating substances

- RAAS
- SNS (norepinephrine)
- Vasodilators (bradykinin, nitric oxide, prostaglandins)
- Natriuretic peptides
- Cytokines (endothelin, tumor necrosis factor, interleukins)
- Vasopressin
- Matrix metalloproteinases

RELATIVE HAZARD OF VASCULAR EVENTS AND HEART FAILURE BY BASELINE N-BNP LEVEL

Major vascular event

Major coronary event

Stroke

Heart failure
ABSOLUTE BENEFITS OF SIMVASTATIN (S) VERSUS PLACEBO (P) ON FIRST MVE AND MCE IN PARTICIPANTS SUBDIVIDED BY BASELINE N-BNP LEVEL

MVE risk reductions (SE):
- Events avoided/1000: 60 (10), 45 (12), 69 (14), 64 (18), 76 (24)
- P-value: <0.0001, <0.001, <0.0001, <0.001, 0.002

MCE risk reductions (SE):
- Events avoided/1000: 34 (6), 26 (8), 37 (9), 32 (12), 31 (20)
- P-value: <0.0001, <0.001, <0.00001, <0.001, 0.002

Proportion with first event (%)
EFFECTS OF SIMVASTATIN ALLOCATION ON MAJOR CORONARY EVENTS IN PARTICIPANTS SUBDIVIDED BY N-BNP

<table>
<thead>
<tr>
<th>Baseline feature</th>
<th>SIMVASTATIN (10269)</th>
<th>PLACEBO (10267)</th>
<th>Rate ratio &amp; 95% CI</th>
<th>STATIN better</th>
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<tr>
<td>N-BNP (pg/ml)</td>
<td></td>
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</tr>
<tr>
<td>&lt;386</td>
<td>124 (4.4%)</td>
<td>221 (7.8%)</td>
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</tr>
<tr>
<td>≥386 &lt;1172</td>
<td>148 (6.1%)</td>
<td>208 (8.6%)</td>
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</tr>
<tr>
<td>≥1172 &lt;2618</td>
<td>157 (7.5%)</td>
<td>237 (11.2%)</td>
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</tr>
<tr>
<td>≥2618 &lt;5759</td>
<td>188 (11.0%)</td>
<td>234 (14.0%)</td>
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</tr>
<tr>
<td>≥5759</td>
<td>281 (23.1%)</td>
<td>312 (25.5%)</td>
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<td></td>
</tr>
<tr>
<td>ANY</td>
<td>898 (8.7%)</td>
<td>1212 (11.8%)</td>
<td>0.4</td>
<td>27% SE 4 reduction (2P&lt;0.00001)</td>
<td>0.6</td>
</tr>
</tbody>
</table>
ACC/AHA stages of systolic HF and treatment options

Stage A
- High risk with no symptoms

Stage B
- Structural heart disease, no symptoms

Stage C
- Structural disease, previous or current symptoms

Stage D
- Refractory symptoms requiring special intervention
  - Hospice
  - VAD, transplantation
  - Inotropes
  - Aldosterone antagonist, nesiritide
  - Consider multidisciplinary team
  - Revascularization, mitral-valve surgery
  - Cardiac resynchronization if bundle-branch block present
  - Dietary sodium restriction, diuretics, and digoxin
  - ACE inhibitors and β-blockers in all patients
  - ACE inhibitors or ARBs in all patients; β-blockers*
  - Treat hypertension, diabetes, dyslipidemia; ACE inhibitors or ARBs*
  - Risk-factor reduction, patient and family education

*In appropriate patients

NEW THERAPEUTIC OPTIONS FOR END-STAGE HEART FAILURE

Importance of Neuro-humoral Blockade
Including aldosterone blockade
– but all are under-used
Positive inotropes useful for short term
Stem-cell therapy becomes promising
Prognosis improving – but still poor!

Still a role for Cardiac Surgeons!
- Valves, LVADs, Transplantation
Neurohormonal model of HF

Injury to myocytes and extracellular matrix

- Neurohormonal activation – RAAS, SNS
- Increased cytokine expression
- Immune and inflammatory changes
- Altered fibrinolysis

Ventricular remodeling

- Oxidative stress
- Apoptosis
- Altered gene expression
- Energy starvation

Electrical, vascular, renal, pulmonary muscle, and other effects

Heart failure

Diabetes pathogenesis accelerates HF

Diabetes

- Activated sympathoadrenal system
- Activated RAAS
- Hyperglycemia

- Cardiomyocyte death
- Cardiac fibrosis
- Activation of protein kinase C

- Decreased myocardial contractile strength
- Decreased intracellular calcium removal

- Systolic dysfunction
- Diastolic dysfunction

Heart failure

RAAS in CV continuum: Pivotal role of $\text{AT}_1$ receptors in the failing heart

Angiotensin receptor blockade in the CVD continuum

Coronary heart disease

Plaque rupture

Myocardial infarction

Dilation/Remodeling

End-stage heart failure

Endothelial dysfunction

Atherosclerosis

Risk factors

Hypertension
Hyperlipidemia
Diabetes

Implications for β-blockade in diabetes and HF

• HF is a frequent, often fatal complication of diabetes

• β-Blockers are safe and well tolerated by patients with HF and diabetes

• β-Blockade benefits diabetic patients by decreasing hospitalizations for HF and improving survival

• It is time to remove existing barriers for use of β-blockers in patients with HF and diabetes

SENIORS: Design

Study of the Effects of Nebivolol Intervention on Outcomes and Rehospitalization in Seniors with heart failure

- 2128 patients with HF or LVEF ≤35%
- ≥70 years of age (mean, 76 years)
- Randomly assigned to
  - Nebivolol titrated to 10 mg once daily over 16-week maximum (n = 1067)
  - Placebo (n = 1061)
- Primary outcome: Composite of all-cause mortality or CV hospital admission (time to first event)
- Follow-up: median 21 months

SENIORS: Primary and secondary outcomes

All-cause mortality or CV hospital admission (primary outcome)

Time (months)

Event-free survival (%)

HR 0.86 (0.74–0.99)  
P = 0.039

Nebivolol  
Placebo

All-cause mortality (main secondary outcome)

Time (months)

HR 0.88 (0.71–1.08)  
P = 0.214

Nebivolol  
Placebo

No. of events:

Nebivolol  332 (31.1%)  
Placebo  375 (35.3%)

169 (15.8%)  
192 (18.1%)

HR = hazard ratio

SENIORS: Clinical relevance

- Confirms data indicating β-blockade benefits elderly HF patients
- Extends evidence for benefit of β-blockade to a broad range of elderly patients (age >70 years) with HF, including those with mild or preserved LV function
- As in previous large trials, both all-cause mortality and CV hospital admissions show a similar and consistent effect with β-blockade

Impact of RAAS modulation on mortality in HF patients with renal insufficiency

Minnesota Heart Survey

Post-discharge mortality (mean follow-up 15 mo)

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Odds ratio (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>≥90</td>
<td>1</td>
</tr>
<tr>
<td>60–89</td>
<td>1.5 (1.0-2.4)</td>
</tr>
<tr>
<td>30–59</td>
<td>2.5 (1.6-3.9)</td>
</tr>
<tr>
<td>&lt;30</td>
<td>3.7 (1.9-7.0)</td>
</tr>
</tbody>
</table>

P values:
P = 0.65
P = 0.04
P = 0.002
P = 0.17

ACEI/ARB Rx at discharge

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>% mortality</th>
</tr>
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<tbody>
<tr>
<td>≥90</td>
<td>64</td>
</tr>
<tr>
<td>60–89</td>
<td>68</td>
</tr>
<tr>
<td>30–59</td>
<td>63</td>
</tr>
<tr>
<td>&lt;30</td>
<td>48</td>
</tr>
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4926 patients hospitalized with HF

Growing HF epidemic: Threefold increase over past decade - Ageing, Obesity, Diabetes

Annual prevalence/1000 patients

Inappropriate Reflexes in CHF

Myocardial damage causes lower BP than normal.

Sensed by Baroreceptors

CNS interprets this as caused by Haemorrhage

- so switches on reflex mechanisms to retain fluid and raise BP, which are harmful!

Why sympathetic & RAAS blockades work so well
Relative Risk of Total Mortality

Cumulative Incidence (%)

RR = 0.85 (95% CI, 0.75-0.96)
P = 0.008

Months Since Randomization

Placebo 3313 3064 2983 2830 2418 1801 1213 709 323 99 2 0 0
Eplerenone 3319 3125 3044 2896 2463 1857 1260 728 336 110 0 0 0
Relative Risk of Sudden Cardiac Death

**All Patients**

- **Placebo**
- **Eplerenone**

Relative Risk (RR): 0.79 (95% CI, 0.64-0.97)  
*P* = 0.03

**Patients with Baseline Ejection Fraction ≤ 30%**

- **Placebo**
- **Eplerenone**

Relative Risk (RR): 0.67 (95% CI, 0.50-0.91)  
*P* = 0.009
Frequency of Congestive Heart Failure According to Age from 1950 to 1993

Number of patients with CHF

Increase since 1950 (%)

Age

55-64 65-74 75-84 >85

% Change

- 1950
- 1993

Number of patients with CHF

Frequency of Congestive Heart Failure According to Age from 1950 to 1993
Lifetime Risk for Chronic Heart Failure

Lloyd-Jones DM et al: Circulation 2002
Causes for the Increase in Heart Failure

- Ageing population
- Better treatment and prognosis of arterial hypertension
- Survival after myocardial infarction
Mode of Death by NYHA Class in MERIT

NYHA II
- SD: 64%
- CHF: 12%
- Other: 24%
- Nuber of death: n=103

NYHA III
- SD: 59%
- CHF: 26%
- Other: 15%
- Nuber of death: n=232

NYHA IV
- SD: 33%
- CHF: 56%
- Other: 11%
- Nuber of death: n=27
EFFECTS OF SIMVASTATIN ALLOCATION ON MAJOR VASCULAR EVENTS IN PARTICIPANTS SUBDIVIDED BY N-BNP

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<tr>
<td>&lt;386</td>
<td>379 (13.4%)</td>
<td>540 (19.0%)</td>
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</tr>
<tr>
<td>≥386 &lt;1172</td>
<td>410 (16.8%)</td>
<td>503 (20.8%)</td>
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<tr>
<td>≥1172 &lt;2618</td>
<td>405 (19.4%)</td>
<td>547 (25.8%)</td>
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</tr>
<tr>
<td>≥2618 &lt;5759</td>
<td>417 (24.5%)</td>
<td>499 (29.9%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥5759</td>
<td>422 (34.8%)</td>
<td>496 (40.6%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANY</td>
<td>2033 (19.8%)</td>
<td>2585 (25.2%)</td>
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</table>

24% SE 3 reduction (2P<0.00001)
### EFFECTS OF SIMVASTATIN ALLOCATION ON STROKE IN PARTICIPANTS SUBDIVIDED BY N-BNP

<table>
<thead>
<tr>
<th>Baseline Feature</th>
<th>SIMVASTATIN (10269)</th>
<th>PLACEBO (10267)</th>
<th>Rate Ratio &amp; 95% CI</th>
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<tr>
<td>N-BNP (pg/ml)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>&lt;386</td>
<td>98 (3.5%)</td>
<td>117 (4.1%)</td>
<td>0.4 ± 0.01</td>
<td>STATIN better</td>
<td></td>
</tr>
<tr>
<td>386 ≤ N-BNP &lt;1172</td>
<td>91 (3.7%)</td>
<td>92 (3.8%)</td>
<td>0.9 ± 0.1</td>
<td>STATIN better</td>
<td></td>
</tr>
<tr>
<td>1172 ≤ N-BNP &lt;2618</td>
<td>89 (4.3%)</td>
<td>135 (6.4%)</td>
<td>0.6 ± 0.05</td>
<td>PLACEBO better</td>
<td></td>
</tr>
<tr>
<td>2618 ≤ N-BNP &lt;5759</td>
<td>89 (5.2%)</td>
<td>123 (7.4%)</td>
<td>0.8 ± 0.07</td>
<td>PLACEBO better</td>
<td></td>
</tr>
<tr>
<td>5759 ≤ N-BNP</td>
<td>77 (6.3%)</td>
<td>118 (9.7%)</td>
<td>0.5 ± 0.08</td>
<td>PLACEBO better</td>
<td></td>
</tr>
<tr>
<td>ANY</td>
<td>444 (4.3%)</td>
<td>585 (5.7%)</td>
<td>0.7 ± 0.09</td>
<td>PLACEBO better</td>
<td></td>
</tr>
</tbody>
</table>

25% SE 5 reduction (2P < 0.00001)
EFFECTS OF SIMVASTATIN ALLOCATION ON VASCULAR DEATHS IN PARTICIPANTS SUBDIVIDED BY N-BNP

<table>
<thead>
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</tr>
<tr>
<td>&lt;386</td>
<td>87 (3.1%)</td>
<td>112 (3.9%)</td>
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</tr>
<tr>
<td>≥386 &lt;1172</td>
<td>101 (4.1%)</td>
<td>122 (5.0%)</td>
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<td>134 (6.4%)</td>
<td>178 (8.4%)</td>
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<td></td>
</tr>
<tr>
<td>≥2618 &lt;5759</td>
<td>168 (9.9%)</td>
<td>200 (12.0%)</td>
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</tr>
<tr>
<td>≥5759</td>
<td>291 (24.0%)</td>
<td>325 (26.6%)</td>
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</tr>
<tr>
<td>ANY</td>
<td>781 (7.6%)</td>
<td>937 (9.1%)</td>
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</tbody>
</table>

17% SE 4 reduction (2P<0.0001)
### Effects of Simvastatin Allocation on Non-Vascular Deaths in Participants Subdivided by N-BNP

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<tr>
<td>&lt;386</td>
<td>98 (3.5%)</td>
<td>106 (3.7%)</td>
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</tr>
<tr>
<td>≥386 &lt;1172</td>
<td>119 (4.9%)</td>
<td>137 (5.7%)</td>
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<td></td>
</tr>
<tr>
<td>≥1172 &lt;2618</td>
<td>121 (5.8%)</td>
<td>115 (5.4%)</td>
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</tr>
<tr>
<td>≥2618 &lt;5759</td>
<td>114 (6.7%)</td>
<td>108 (6.5%)</td>
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<td></td>
</tr>
<tr>
<td>≥5759</td>
<td>95 (7.8%)</td>
<td>104 (8.5%)</td>
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<td></td>
</tr>
<tr>
<td>ANY</td>
<td>547 (5.3%)</td>
<td>570 (5.6%)</td>
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</tbody>
</table>

5% SE 6 reduction
Fig. 1 The causes of heart failure according to population-attributable risk, based on the analysis of data from the Framingham Heart Study and Framingham Offspring Study reported by Levy et al.\textsuperscript{15} The size of the globe indicates the prevalence of the factor.
Improving Outcomes in Heart Failure: New Insights From Vascular Biology
Preserving Ventricular Function – The Emerging Importance Of Diastolic Heart Failure

Robert S. McKelvie, MD, PhD, FRCP(C)
McMaster University and
Hamilton Health Sciences - General Campus
Hamilton, Ontario, Canada
Changing Population Demographics and the Effect on the Number of Persons with Heart Failure

- New HF cases per year in 2000: 348,000
- New HF cases per year in 2040: 772,000
- % of Population: 16.5, 16.5, 12.7, 11.3, 9.2

Owan et al. Prog Cardio Dis 2005.
Prevalence of Heart Failure

- USA (CHS): 8.8% (4.8% with decreased LV systolic function, 54% with preserved LV systolic function)
- Finland (Helsinki): 8.2% (4.2% with decreased LV systolic function, 51% with preserved LV systolic function)
- England (Poole): 7.5% (5.1% with decreased LV systolic function, 68% with preserved LV systolic function)
- Sweden (Vasteras): 7.5% (3.1% with decreased LV systolic function, 46% with preserved LV systolic function)
- Denmark (Copen.): 6.4% (4.5% with decreased LV systolic function, 70% with preserved LV systolic function)
- Spain (Asturias): 59% (40% with decreased LV systolic function, 71% with preserved LV systolic function)
- Portugal (EPICA): 4.2% (1.7% with decreased LV systolic function, 40% with preserved LV systolic function)
- Netherlands (Rotter.): 1.5% (1.1% with decreased LV systolic function, 71% with preserved LV systolic function)

Age range: 66-103 (Mean range: 78), 75-86, 70-84, 75, ≥50 (Mean range: 60), >40 (Mean range: 68), >25 (Mean range: 65), 55-95 (Mean range: 65)

~57% have HF-PSF
## Proposed Criteria for Diastolic Heart Failure

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>- CHF signs/symptoms</td>
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<tr>
<td>- EF $\geq$ 45%</td>
<td>- EF $\geq$ 50%</td>
</tr>
<tr>
<td>- Hemodynamic or echo evidence of diastolic dysfunction</td>
<td>- Definite or probable if within 72 h of CHF</td>
</tr>
<tr>
<td>- Slow isovolumic LV relaxation</td>
<td>- Possible if not</td>
</tr>
<tr>
<td>- Slow early LV filling</td>
<td>- Hemodynamic evidence of diastolic dysfunction</td>
</tr>
<tr>
<td>- Reduced LV diastolic distensibility</td>
<td>- Definite: abnormal diastolic indices on cardiac catheterization</td>
</tr>
<tr>
<td>- Increased LV chamber stiffness or muscle stiffness</td>
<td>- Probable or possible if no evidence</td>
</tr>
</tbody>
</table>
Pharmacologic Strategies to Prevent CHF

Reduce Blood Pressure - evidence stronger now

Reduce LV Hypertrophy

Prevent CHD & Myocardial Infarction

Reduce Neuro-Humoral drive – incl. Aldosterone

Avoid Cardiomyopathy
All Heart Failure

Kaplan-Meier Rates

Days of Follow-up

RR=0.77 (0.68-0.87)

p<0.0001
HF increases risk of CV death: 4.35, 95% CI (3.56-5.31) p<0.0001
Worse Outcome with Hypokalaemia in HOPE

Primary Outcome (MI/Stroke/CV Death)

K< 3.5 mmol = 22.6%

K normal = 15.5% p = 0.023

K> 5.0 mmol = 15.7% p = 0.4

Hazard Ratio for Hypokalaemia = 1.44

Mann, Yi, Sleight et al, J Clin. Nephrol 2004
Implications of HOPE K Data

Diuretic induced Hypokalaemia is associated with increased risk

Hypokalaemia & risk is reduced by ACE - with no serious hyperkalaemia

After ALLHAT diuretic induced hypokalaemia may increase

A thiazide/ACE combo is safe & logical
HOSPITALIZATION

-36%

p<0.05

Stewart S, Horowitz J. Circulation 2002
Heart Failure in the UK

- 900,000 people have heart failure
  - 1 in 35 aged 65-74yrs
  - 1 in 15 aged 75-84 years
  - 1 in 7 aged 85 and over
- 40% die within one year of diagnosis and 10% per annum thereafter
- 2% of all NHS bed days and 5% of all emergency admissions.
20% Lifetime risk for HF after age 40

Framingham Heart Study

Lifetime risk for HF for given index age is cumulative through age 94 years