Heart Failure: An Ounce of Prevention vs a Pound of Cure

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General Principles of HF Prevention

- Maintain healthy life-style habits
- Avoid excessive alcohol
- Have regular ‘flu shot
- Identify those at risk
- Prevent myocardial infarction
- Treat hypertension, DM, lipids
- Correct ischemia
- Correct valvular regurgitation
- Correct uncontrolled A Fib
Systolic Hypertension Trials

- SHEP: 170/77 mmHg
- Syst-China: 170/86
- Syst-Eur: 174/86

Treatment effect (mmHg)

HF outcome

RRR (%)

CI’s 0.33-0.65, P=0.13

P=0.12
SHEP
Fatal & Hospitalized nonfatal HF

1=Placebo 2=Active Therapy
Age 80-89 yrs
p=0.04 NNT=28

Kostis et al. JAMA 1997;278:212-6
Heart Failure Endpoint in UKPDS 38

Absolute risk %
(per 1000 pt yrs)

P=0.0043  RR=0.44 (99% CI 0.20 to 0.94)
VALUE: Analysis of Results Based on BP Control at 6 Months

Pooled Treatment Groups

<table>
<thead>
<tr>
<th>Event</th>
<th>Controlled patients(n = 10755)</th>
<th>Non-controlled patients(n = 4490)</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatal/Non-fatal cardiac events</td>
<td></td>
<td></td>
<td>0.75</td>
<td>0.67–0.83</td>
</tr>
<tr>
<td>Fatal/Non-fatal stroke</td>
<td></td>
<td></td>
<td>0.55</td>
<td>0.46–0.64</td>
</tr>
<tr>
<td>All-cause death</td>
<td></td>
<td></td>
<td>0.79</td>
<td>0.71–0.88</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td></td>
<td></td>
<td>0.86</td>
<td>0.73–1.01</td>
</tr>
<tr>
<td>Heart failure hospitalisations</td>
<td></td>
<td></td>
<td>0.64</td>
<td>0.55–0.74</td>
</tr>
</tbody>
</table>

*SBP < 140 mmHg at 6 months

**\(P < 0.01\).

ARB BASED BP LOWERING REGIMENS

<table>
<thead>
<tr>
<th>Condition</th>
<th>Trials</th>
<th>Events/participants ARB</th>
<th>Events/participants Control</th>
<th>Difference in BP* (mean, mm Hg)</th>
<th>Relative risk (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>4</td>
<td>396/8412</td>
<td>500/8379</td>
<td>-2/-1</td>
<td>0.79 (0.69-0.90)</td>
<td>0.46</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>4</td>
<td>435/8412</td>
<td>450/8379</td>
<td>-2/-1</td>
<td>0.96 (0.85-1.09)</td>
<td>0.43</td>
</tr>
<tr>
<td>Heart failure</td>
<td>3</td>
<td>302/5935</td>
<td>359/5919</td>
<td>-2/-1</td>
<td>0.84 (0.72-0.97)</td>
<td>0.26</td>
</tr>
<tr>
<td>Major cardiovascular events</td>
<td>4</td>
<td>1135/8412</td>
<td>1268/8379</td>
<td>-2/-1</td>
<td>0.90 (0.83-0.96)</td>
<td>0.78</td>
</tr>
<tr>
<td>Cardiovascular death</td>
<td>4</td>
<td>491/8412</td>
<td>511/8379</td>
<td>-2/-1</td>
<td>0.96 (0.85-1.08)</td>
<td>0.34</td>
</tr>
<tr>
<td>Total mortality</td>
<td>4</td>
<td>887/8412</td>
<td>943/8379</td>
<td>-2/-1</td>
<td>0.94 (0.86-1.02)</td>
<td>0.59</td>
</tr>
</tbody>
</table>

BP LOWERING REGIMENS IN HF

Difference in BP (mmHg) -5/-2  -2/-1  -4/-3
ACEI vs P  ARB vs P  more vs less

P = placebo
More vs less BP lowering regimens

Heart Failure

Cumulative Event Rate

Rel Risk  95% CI
2.04  1.79-2.32

$z = 10.95, \ p < 0.0001$

ALLHAT

Cumulative Event Rates for Heart Failure by ALLHAT Treatment Group

<table>
<thead>
<tr>
<th></th>
<th>HR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/C</td>
<td>1.38 (1.25-1.52)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>L/C</td>
<td>1.19 (1.07-1.31)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Number at risk:
- Chlorthalidone: 15,255, 14,528, 13,898, 13,224, 11,511, 6,369, 3,016, 384
- Amlodipine: 9,048, 8,535, 8,185, 7,801, 6,785, 3,775, 1,780, 210
- Lisinopril: 9,054, 8,496, 8,096, 7,689, 6,698, 3,789, 1,837, 313
# BENEFITS OF LOWERING BP

<table>
<thead>
<tr>
<th>Condition</th>
<th>Average % Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke Incidence</td>
<td>35-40</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>20-25</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>50</td>
</tr>
</tbody>
</table>

In stage 1 HTN and additional CVD risk factors, achieving a sustained 12 mmHg reduction in SBP over 10 years, will prevent 1 death for every 11 patients treated.
Simvastatin and HF

Fig. 1. Kaplan–Meier curves for new adverse experience of clinical heart failure in patients with coronary artery disease but no previous evidence of heart failure.
STATINS AND PROVE IT

Scirica et al. JACC 2006;47:2326-31
STATIN TRIALS METANALYSIS

Hospitalization for HF n=27,546 patients

Scirica et al. JACC 2006;47:2326-31
All Heart Failure

Kaplan-Meier Rates

Days of Follow-up

RR=0.77 (0.68-0.87) p<0.0001

Prevention of HF in HOPE

Rate (%) of developing heart failure

**Age**
p < 0.0001

**BMI**
p < 0.0014

**Systolic Blood Pressure (SBP)**
p < 0.0001

**Pulse Pressure (PP)**
p < 0.0001

Baseline Characteristics Independently Associated with Heart Failure in HOPE

- CAD
- MAU
- Diuretic use
- LVH
- Age (for 10-year difference)
- Diabetes
- TC > 5.2, no tx
- CABG
- Stroke/TIA
- No ramipril
- PVD
- BMI (for 4-unit difference)
- Heart rate (for 10-beat difference)
- Pulse pressure (for 10 mm Hg difference)

## Prevention of HF in HOPE

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Ramipril</th>
<th>RR (95% CI)</th>
<th>Test of Interaction (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>534 (11.5%)</td>
<td>417 (9.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age (yrs)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65</td>
<td>184 (8.7%)</td>
<td>139 (6.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65+</td>
<td>350 (13.8%)</td>
<td>278 (10.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Systolic BP (mmHg)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;139</td>
<td>220 (9.5%)</td>
<td>203 (8.6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>139+</td>
<td>314 (13.5%)</td>
<td>214 (9.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Heart Rate (bpm)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;71</td>
<td>294 (10.8%)</td>
<td>231 (8.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>71+</td>
<td>240 (12.4%)</td>
<td>186 (9.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>136 (11.3%)</td>
<td>117 (9.2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>398 (11.5%)</td>
<td>300 (8.9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>299 (10.4%)</td>
<td>219 (7.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>235 (13.3%)</td>
<td>198 (11.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Known Hypertension</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>247 (9.8%)</td>
<td>192 (7.9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypert</td>
<td>287 (13.4%)</td>
<td>225 (10.2%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Prevention of HF in HOPE

Hospitalisation for heart failure

RRR: 39%
p = 0.002

Placebo Annual Event Rate: 0.4%
## PEACE

### Table: Post hoc analyses

<table>
<thead>
<tr>
<th>Outcome Description</th>
<th>Trandolapril (N)</th>
<th>Placebo (N)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death from cardiovascular causes, nonfatal MI, or stroke (outcome in HOPE)</td>
<td>396 (9.5)</td>
<td>420 (10.2)</td>
<td>0.93 (0.81–1.07)</td>
<td>0.32</td>
</tr>
<tr>
<td>Death from cardiovascular causes, nonfatal MI, or cardiac arrest (outcome in EUROPA)</td>
<td>346 (8.3)</td>
<td>356 (8.6)</td>
<td>0.96 (0.83–1.12)</td>
<td>0.62</td>
</tr>
<tr>
<td>CHF</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>As primary cause of hospitalization or death</td>
<td>115 (2.8)</td>
<td>152 (3.7)</td>
<td>0.75 (0.59–0.95)</td>
<td>0.02</td>
</tr>
<tr>
<td>As primary cause of hospitalization</td>
<td>105 (2.5)</td>
<td>134 (3.2)</td>
<td>0.77 (0.60–1.00)</td>
<td>0.05</td>
</tr>
<tr>
<td>As primary cause of death</td>
<td>15 (0.4)</td>
<td>25 (0.6)</td>
<td>0.59 (0.31–1.13)</td>
<td>0.11</td>
</tr>
<tr>
<td>Stroke</td>
<td>71 (1.7)</td>
<td>92 (2.2)</td>
<td>0.76 (0.56–1.04)</td>
<td>0.09</td>
</tr>
<tr>
<td>Onset of new diabetes†</td>
<td>335 (9.8)</td>
<td>399 (11.5)</td>
<td>0.83 (0.72–0.96)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

* CI denotes confidence interval, MI myocardial infarction, CHF congestive heart failure, PEACE the Prevention of Events with Angiotensin Converting Enzyme Inhibition Trial, HOPE the Heart Outcomes Prevention Evaluation, and EUROPA the European Trial on Reduction of Cardiac Events with Perindopril in Stable Coronary Artery Disease.

† The analysis included 3432 patients in the trandolapril group and 3472 patients in the placebo group and excluded patients with diabetes at baseline.
Benefits greater in LVEF < 0.28
Enalapril Beneficial in LV Dysfunction with Hypertension

SOLVD Combined Trials CHF Hospitalization Results

Patients with DBP $\geq 90$ mmHg

Patients with a History of Hypertension

Patients with SBP $\geq 140$ mmHg

All Patients

FIGURE 2. Hospitalization for congestive heart failure in three hypertension subgroups and the total SOLVD cohort.

Kostis AJH 1995;8:909-14
S3 and JVP Predict HF Hospitalization
SOLVD Prevention

S3
RR 1.57
(adj RR 1.34)

JVP
RR 1.84
(adj RR 1.54)

Risk Factors for HF Development

- Hypertension*
- Ischemic heart disease*
- Diabetes*/metabolic syndrome
- Hyperlipidemia*
- Smoking*
- Obesity
- Older age
- Male gender
- Ethnicity
- Physical inactivity
- Heavy alcohol consumption
- Excessive salt intake
- Cardiotoxic agents
- Family history/genetics
- Low ejection fraction*
- Impaired diastolic function
- Left ventricular hypertrophy
- Elevated neurohormonal biomarkers
- Abnormal ECG
- Increased cardiothoracic ratio
- Microalbuminuria
- Elevated resting heart rate

* Most important targets for prevention

The Heart Failure Continuum

Risk Factors
- Hypertension
- Dyslipidemia
- Diabetes
- Smoking
- Family History

Canadian Cardiovascular Society

Patients at Risk of Developing HF

• Clinical assessment is recommended in all patients to identify known or potential risk factors for HF (eg hypertension, IHD, diabetes, hyperlipidemia, smoking)
  (Class I, Level C)

• All modifiable risk factors for HF, including those for CAD, such as hypertension, diabetes mellitus and hyperlipidemia, should be treated according to current national guidelines
  (Class I, Level A)

Practical Tips

• Poor adherence to preventive measures is common. Reassess regularly to ensure targets achieved/maintained

• Patients at high risk for HF should receive influenza vaccine (yearly) and pneumococcal vaccine (if not in last 6 yrs)
Hypertension, LV Hypertrophy and HF Risk

- Presence of hypertension increases risk of HF, eg Framingham Study
- Presence of LVH increases risk of HF and risk is independent of association with hypertension
- Treatment of hypertension clearly reduces risk of HF, eg BP Lowering Treatment Trialists’ Collaboration

**Practical Tips**

- BP goal <140/90mmHg in most individuals
- <130/80mmHg in diabetes and/or kidney disease and perhaps in patients with multiple risk factors
Ischemic Heart Disease and HF Risk

- 52% of HF diagnoses in general population attributed to CAD
- 40% of patients who have experienced an MI will develop HF over time
- 8-fold increase in risk of subsequent death when a new MI occurs in patients with established HF
- 1/3 of all deaths in HF are preceded by an ischemic event
- Target dyslipidemia, hypertension, diabetes, smoking. Treat aggressively

Diabetes Mellitus and HF Risk

- DM increases risk 2 to 4 fold compared to patients without DM
- DM is well established risk factor for CAD/IHD
- DM may produce HF independently of CAD (diabetic CM)
- While increased HbA1C is associated with increased HF, no study to date has shown improved glycemic control reduces HF
- Canadian Diabetes Association recommends HbA1C ≤7.0% in most patients with DM

Heart Failure and Diabetes

**Recommendation**

- Treat elevated blood glucose to achieve:
  - HbA1C ≤ 7.0%
  - fasting/preprandial blood glucose 4.4 mmol/L to 7.0 mmol/L  
  (Class I, Level A)

**Practical Tips**

- Oral antidiabetic therapy should be individualized; no compelling evidence exists to recommend one agent over another
- Metformin may be considered a first-line agent if the eGFR is > 30 mL/min but should be discontinued temporarily if renal function worsens significantly
Hyperlipidemia and HF Risk

- Elevated TG and elevated TC/HDL are associated with increase in HF risk
- Statin therapy may reduce HF risk

Practical Tips

- Hyperlipidemia should be treated aggressively
- In patients at high risk for HF, target LDL may be <2.0mmol/L
- Statins may be the preferred drug

Smoking and HF Risk

- Smoking may account for 17% of new HF cases
- Smoking has a direct and independent relationship with the development of asymptomatic ventricular dysfunction
- Smoking cessation can reduce morbidity and mortality by 30% within 2 years in patients with HF

Practical Tip

- Smoking cessation is an important strategy to prevent HF

Patients with Asymptomatic LV Dysfunction

- ACE inhibitors should be used in all asymptomatic patients with LV dysfunction and LVEF <40%  
  (Class 1, Level A, LVEF <35%; Class I, Level B, LVEF 35-40%)

- Beta-blockers should be considered in all asymptomatic patients with LV dysfunction and LVEF < 40%  
  (Class I, Level B, prior MI; Class IIa, Level C, no prior MI)

Heart Failure Management

Prevention and treatment of heart failure (HF)

To prevent HF: treat all cardiac RFs; if low LVEF, prescribe ACEI +/- beta-blocker

If HF symptoms but LVEF >40%, treat cause, eg, hypertension, ischemia
Consider ACEI/ARB, beta-blocker

If systolic HF but LVEF <40%

For all symptomatic patients with systolic HF:
- Tailored diuretic prescription
- Education on:
  - HF syndrome
  - Warning signs and symptoms
  - Self-monitoring
  - Drug therapy
  - Prognosis

ACEI + Beta-blocker

Titrate to target doses

Intolerance
Prescribe ARB

Intolerance
Prescribe ARB
Consider nitrate/hydralazine

Clinically stable
Continue prescription

Persistent symptoms
Add ARB
Digoxin/nitrates
↑ or combine diuretics
Spironolactone

If LVEF <30%, consider ICD referral

If QRS >120ms, consider CRT referral

If refractory, consider transplant

NYHA class III
NYHA class IIIb-IV

Prevention of Heart Failure: Key Points

• Actively review patients in your practice for heart failure risk factors
• Aggressively treat the most important target risk factors to prevent the development of heart failure
• Prescribe proven ACE-I and beta blocker for most patients with known LV systolic dysfunction