Heart Rate and Cardiovascular Function

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Heart Rate and Cardiovascular Function

HEART RATE

Risk Factor?
Target for therapy?
Increased heart rate shortens life

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Total mortality
Coronary mortality
Cancer mortality
Other mortality
Stroke mortality

Gothenburg study
Eur Heart J 1999;H2

10.004 Healthy Men 45 - 55 y
12 y Follow-up

Healthy Men
45 - 55 y
12 y Follow-up
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**Stages of heart failure**

**Stage A**
- Arteriosclerosis
- Risk Factors
- Coronary Artery Disease
- Ischaemia

**Stage B**
- Plaque Rupture + Thrombosis
- Infarction
- Loss of Contractility
- Dilatation and "Remodeling"

**Stage C**
- Heart Failure
- End-stage Heart Failure

**Stage D**
- End-stage Heart Failure

Heart Failure

Stage B

Stage C

Stage D
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Stages of heart failure and Detrimental effect of ▲ Heart Rate

▲ HR and Ischemia
▲ O2 consumption
▼ Duration of Diastole
▼ Coronary perfusion
▼ Collaterals

▲ HR and Atheroma
▼ Endothelial function
▲ Oxidative stress
▲ Arterial stiffness
▼ Plaque stability

Coronary Artery Disease

Plaque Rupture + Thrombosis

Ischaemia

Infarction

Loss of Contractility

Dilatation and “Remodeling”

Heart Failure

Arteriosclerosis

Risk Factors

End-stage Heart Failure

▲ HR and V Function
▲ O2 demand
▼ Diastolic filling time
▼ Relaxation
▼ Fibrillation threshold
▼ O2 uptake
▼ Contractility
▼ Ventricular efficiency

O2 demand
Diastolic filling time
Relaxation
Fibrillation threshold
O2 uptake
Contractility
Ventricular efficiency
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Effect of Heart Rate increase Ventricular function
Human Papillary Muscle Strips

Böhm et al., Clin Invest, 1992
Heart Rate and Cardiovascular Function

Effect of Heart Rate increase Ventricular function
Human Papillary Muscle Strips

Böhm et al., Clin Invest, 1992
Heart Rate and Cardiovascular Function

Pacing-modulated heart rate and O₂-uptake with and without heart failure

Kindermann et al., Eur Heart J 2002;23:1301.
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Pacing-modulated heart rate and O$_2$-uptake with and without heart failure

Kindermann et al., Eur Heart J 2002;23:1301.
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Hospitalization for Heart Failure in Stable CAD & LD dysfunction

Fox et al. Lancet, 2008; 372: 817-821
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CV death or HF hospitalizations in chronic HF (placebo group in SHIFT)

Increase in risk by 3% per 1 bpm ↑, 16% per 5 bpm ↑

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Mortality in Diastolic Heart Failure

• N=685
• LVEF ≥ 50
• F-up: 1y

Kapoor J et al. J Cardiac Fail 2010
Benefit of Heart rate reduction in heart failure?
Heart rate reduction
Possible benefit in Heart Failure

• Decrease Oxygen demand
• Prolongs diastole (increase coronary blood flow)
• Improves relaxation
• Increase fibrillation threshold
• Increase oxygen uptake
• Increase contractility
• Improves ventricular efficiency
<table>
<thead>
<tr>
<th><strong>Heart Rate Reduction</strong></th>
<th><strong>Limitations</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Exercise</td>
<td>in addition to …</td>
</tr>
<tr>
<td>• Digoxin</td>
<td>no benefit</td>
</tr>
<tr>
<td>• Verapamil, diltiazem</td>
<td>heart failure, AV conduction</td>
</tr>
<tr>
<td></td>
<td>hypotension, other side effects</td>
</tr>
<tr>
<td>• Beta-blockers</td>
<td>hypotension, AV conduction</td>
</tr>
<tr>
<td></td>
<td>asthma, COLD</td>
</tr>
<tr>
<td>• Ivabradine</td>
<td>pure heart rate reduction</td>
</tr>
</tbody>
</table>
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Heart Rate changes in Heart Failure and outcomes

CIBIS I
Circulation
1997;96:2197

Heart Failure
n = 641

Mortality

log[hazard]

Heart rate variation in 2 months

-40 -30 -20 -10 0 10 20

-0.6 -0.5 -0.4 -0.3 -0.2 -0.1 0 0.1 0.2 0.3 0.4 0.5
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Effect of change in HR and achieved HR on clinical outcomes in HF

Meta-regression of beta-blocker trials n=19 537

Correlation of change in HR with relative risk reduction (RRR) in all-cause mortality

\[ r^2 = 0.41 \]

Correlation of final achieved HR with annualized mortality

\[ r^2 = 0.53 \]

Flannery et al. Am J Cardiol. 2008;101:865
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Heart Rate changes in Heart Failure and outcomes

Heart failure trials

Kjekshus J
Eur Heart J 1999;164
Swedberg,
Eur Heart J 20:1999;136
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Heart rate in European surveys: beta-blocker therapy

HF OUTCOME*

ESC HF PILOT**

*Courtesy of Prof Tavazzi
**Courtesy of Prof Maggioni
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HF registries: more than 50% of patients have HR ≥70 bpm

HF OUTCOME*
3480 patients

ESC PILOT HF**
2450 patients

 Patients (%)

≥70  >75  >80

HF OUTCOME*
3480 patients

ESC PILOT HF**
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 Patients (%)

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*Courtesy of Prof Tavazzi
**Courtesy of Prof Maggioni
## Heart Rate and Cardiovascular Function

### Ivabradine in BB patients with advanced heart failure

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Basal Mean ± SD</th>
<th>Change mean ± SD</th>
<th>95% confidence Interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (bpm)</td>
<td>87</td>
<td>74.1 ± 10.4</td>
<td>-10.1 ± 11.1</td>
<td>[-12.5 ± -7.8]</td>
<td>p &lt;0.001</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>85</td>
<td>28.6 ± 5.4</td>
<td>+ 5.3 ± 6.1</td>
<td>[4.0 ± 6.6]</td>
<td>p &lt;0.001</td>
</tr>
<tr>
<td>LVESV (ml)</td>
<td>80</td>
<td>161.7 ± 60.6</td>
<td>- 18.5 ± 30.0</td>
<td>[-25.2 ± -11.8]</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>86</td>
<td>120.8 ± 15.3</td>
<td>- 0.2 ± 15.7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

G. Jondeau, Heart failure congress Milan 2008
Ivabradine in BB patients with advanced heart failure

Change in Functional Class

G. Jondeau, Heart failure congress Milan 2008
SHIFT: Relationship between heart rate and health related quality of life. Results from SHIFT I Ekman (Goteborg, SE) 

SHIFT: Selective heart rate reduction with Ivabradine improves left ventricular remodeling and function: insights from the SHIFT-Echocardiography sub-study J-C Tardif (Montreal, CA)
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Hospitalization for HF

HR = 0.74 (0.66–0.83)

P < 0.0001

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Death from heart failure

HR = 0.74 (0.58–0.94)

P = 0.014

Conclusions:

• Increased heart rate is a risk factor for Heart Failure
• Increased heart rate is related to outcomes
• Reduction of heart rate improves outcomes
• Heart rate should be used for:
  • Risk stratification
  • Guide medical therapy
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