Hemodynamic improvement upon levosimendan treatment in low cardiac output patients following coronary artery bypass graft

M. Buerke, K. Krohe, M. Russ, C. Schneider, H. Lemm, R. Prondzinsky, I. Friedrich, H. Bushnaq, R. Silber, K. Werdan

Department of Medicine III & Department of Cardio-Thoracic Surgery
Martin Luther-University
Halle/Saale, Germany
The authors DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.
## Low cardiac output syndrome

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Clinical parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac dysfunction</td>
<td>CI &lt; 2.2 l/min/m²</td>
</tr>
<tr>
<td>Hypotension</td>
<td>RRsys &lt; 80 mmHg</td>
</tr>
<tr>
<td>Increased afterload</td>
<td>SVR &gt; 1000 dyn<em>sec</em>cm⁻⁵</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>HR &gt; 100 /min</td>
</tr>
<tr>
<td>Oliguria</td>
<td>&lt; 0.5 ml/kg/h</td>
</tr>
<tr>
<td>Acidosis</td>
<td>pH &lt; 7.35</td>
</tr>
<tr>
<td>Centralisation</td>
<td>Dyspnea NYHA IV, cyanosis, cold limbs</td>
</tr>
</tbody>
</table>

- Female gender, age > 70 years, diabetes mellitus, 3-V-CAD, emergency or re-do surgery, STEMI (Rao et al.)
- Pulmonary & arterial Hypertension (Cortrufo et al.)
- Aortic clamp time (Kawamura et al.)
- Preexisting impaired renal function (Maganti et al.)
Vicious cycle of low cardiac output syndrome

Myocardial Dysfunction

- Systolic
- Diastolic

Cardiac Output
- Stroke Volume

Systemic Perfusion

Hypotension

- Hypoxemia
- LVEDP

Pulmonary Congestion

Compensatory vasoconstriction

Fluid Retention

Coronary Perfusion pressure

ISCHEMIA

Progressive myocardial Dysfunction

DEATH
Predictors of Low Cardiac Output Syndrome After Isolated Aortic Valve Surgery

- Prevalence of LCOS: 3.9%
- Mortality: 38%

Maganti et al. 2004

Outcome of low cardiac output syndrome
• Sensitizes cardiac troponin C towards $\text{Ca}^{2+}$
• Improves $\text{Ca}^{2+}$-dependent reconfiguration of the troponin complex leading to increased actin-myosin-crosslinks resulting in higher myocardial contractility
Levosimendan – earlier studies

**Follath et al. 2002 (LIDO-Studie)**
Hemodynamic improvement (CI +30%, PCWP -20% after 24h)
(Levo: 28%, Dobutamin: 15%)
Mortality after 30 and 180 days (Levo: 7,8%, Dobutamin: 17%)

**Christoph, ..., Buerke et al. 2007**
Levosimendan vs. IABP in cardiogenic shock

**Ruß, ..., Buerke et al. 2007**
Hemodynamic improvement following levosimendan treatment in patients with acute myocardial infarction and cardiogenic shock

**Ruß, ..... Buerke et al. 2010**
Right ventricular function in myocardial infarction complicated by cardiogenic shock: improvement with levosimendan
Treatment option for acute heart failure

1. **Increased inotropy without**
   - proarrhythmogenic effects,
   - effects on repolarisation,
   - increase of oxygen consumption.

2. **Decrease afterload by vasodilation due to ATP-dependent K⁺-channel activation**

3. **Anti-Stunning-Effects**

Hepatic metabolism, $T_{1/2} \sim 1h$, $T_{1/2}$ of metabolisms $\sim 72h$
Study design

CABG + LCOS → Levosimendan

epinephrine, norepinephrine, dobutamine

-24h | 0 | 3h | 24h | 48h | 72h | 96h

N=41, March 2006 to February 2009
<table>
<thead>
<tr>
<th><strong>Patient characteristics</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender, (male / female)</strong></td>
</tr>
<tr>
<td><strong>Age, years, mean (range)</strong></td>
</tr>
<tr>
<td><strong>BMI, mean (range) Kg/m^2</strong></td>
</tr>
<tr>
<td><strong>Hypertension, n (%)</strong></td>
</tr>
<tr>
<td><strong>Dyslipidemia, n (%)</strong></td>
</tr>
<tr>
<td><strong>Diabetes mellitus, n (%)</strong></td>
</tr>
<tr>
<td><strong>Previous AMI, n (%)</strong></td>
</tr>
<tr>
<td><strong>Known heart failure, n (%)</strong></td>
</tr>
<tr>
<td><strong>Cardiac risk factors (n=4), n/patient</strong></td>
</tr>
<tr>
<td><strong>Prior STEMI n (%)</strong></td>
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<tr>
<td><strong>1-vessel disease n (%)</strong></td>
</tr>
<tr>
<td><strong>2-vessel disease n (%)</strong></td>
</tr>
<tr>
<td><strong>3-vessel disease n (%)</strong></td>
</tr>
<tr>
<td><strong>Ejection fraction (echocardiography)</strong></td>
</tr>
<tr>
<td><strong>Prior Dialysis/acute renal failure, n (%)</strong></td>
</tr>
<tr>
<td><strong>APACHE score TP 0</strong></td>
</tr>
<tr>
<td><strong>IABP before, during and after CABG</strong></td>
</tr>
</tbody>
</table>
## Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF reduced (&lt;30%)</td>
<td>30</td>
<td>73,17</td>
</tr>
<tr>
<td>EF moderate reduced (&lt;50%;&gt;30%)</td>
<td>5</td>
<td>12,19</td>
</tr>
<tr>
<td>EF normal (&gt;50%)</td>
<td>6</td>
<td>14,63</td>
</tr>
<tr>
<td>surgery</td>
<td>24</td>
<td>58,54</td>
</tr>
<tr>
<td>Re do surgery</td>
<td>15</td>
<td>36,59</td>
</tr>
<tr>
<td>survival</td>
<td>23</td>
<td>56,1</td>
</tr>
</tbody>
</table>
Overall effects – HR & BP

**Heart rate**

- Time after application (h): -24, 3, 24, 48, 72, 96
- Levo

**Blood pressure**

- RRsys, RRdia, MAP
- Time after application (h): -24, 3, 24, 48, 72, 96

Overall effects – HR & BP

**Heart rate**

- Time after application (h): -24, 3, 24, 48, 72, 96
- Levo

**Blood pressure**

- RRsys, RRdia, MAP
- Time after application (h): -24, 3, 24, 48, 72, 96
Overall effects – CI & SVR, PVR

Cardiac index

Systemic / pulmonary resistance

![Graphs showing changes in cardiac index and systemic/pulmonary resistance over time.](image-url)
Overall effects – PAM, RAP, PCWP & CPI

PAM RAP PCWP

Cardiac power index

PAM, RAP, PCWP & CPI
Outcome effects – MAP & CPI

**Mean arterial pressure**

- Non-Survivors
- Survivors

**Cardiac power index**

- Non-Survivors
- Survivors

Time after application (h)

Mean arterial pressure (mmHg)

Cardiac power index (W/m²)
Gender effects – HR & MAP

Heart rate

Mean arterial pressure

Time after application (h)
Gender effects – CI & PVR

Cardiac index

Pulmonary vascular resistance

Time after application (h)

CI & PVR for Females and Males
Adverse effects of levosimendan

Known adverse effects:
- Hypotension
- Bleeding
- Impaired renal function

Blood pressure

Creatinine clearance
Conclusions

In patients with low cardiac output syndrome..

- Levosimendan improves hemodynamic effects.
- Levosimendan has beneficial effects on left and right ventricular failure.
- Levosimendan treatment did not result in profound hypotension, worsening of renal function or increased bleeding.

Levosimendan is an useful option to treat patients with low cardiac output syndrome after coronary artery bypass surgery.
Thank you for your attention