Effect of Cardiac Rehabilitation on Functional Capacity in Left Ventricular Assist Device Patients: A Systematic Review and Meta-Analysis

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Introduction

• Exercise-based cardiac rehabilitation (EBCR) has been demonstrated to improve functional capacity in patients with heart failure (HF) as demonstrated by increased
  - peak oxygen consumption (peakVO$_2$) and
  - 6-minute walk distance (6MWD)

• However, there are limited data regarding the impact of EBCR in patients with left ventricular assist devices (LVAD), this despite the routine prescription of EBCR in pivotal LVAD trials
The purpose of this investigation was to evaluate the effect of exercise training on functional capacity in LVAD patients participating in cardiac rehabilitation.
Design

We conducted a systematic review and meta-analysis to evaluate the impact of EBCR on measures of functional capacity in LVAD recipients including:

- peak VO$_2$
- 6MWD
Methods

We searched PubMed, Cochrane Library, Web of Science, and CINAHL for eligible studies reporting use of EBCR in LVAD patients through February 15, 2016 using the following keywords:

1. heart assist device
2. left ventricular assist device
3. ventricular assist device
4. assistive device
5. cardiac rehabilitation
Methods cont’

• Inclusion criteria
  - Studies assessed the impact of EBCR in LVAD recipients greater than 18 years of age
  - Studies included a standard therapy (ST) group for comparison

• Exclusion criteria included
  - Non-English language publication
  - Published abstracts without full text publication
  - Lacking endpoint outcomes such as peak VO₂ and 6MWD
Methods cont’

• Data from selected studies were extracted

• A meta-analysis of randomized trials was performed comparing EBCR versus ST, using a random effects model with DerSimonian Liard weighting

• Analysis employed weighted mean difference (WMD) and intention-to-treat (ITT) principle

• Study quality, publication bias, and heterogeneity were assessed
Results

• Six trials with a total of 183 patients (EBCR: 125; ST: 58)

• Mean age was 50.8 years (EBCR: 50.9 yrs. ST: 50.8 yrs.) and 82.5% were males

• Duration of follow up ranged from one month to 18 months

• Start of exercise rehabilitation ranged from during hospitalization to 10 months post-LVAD implantation

• Median rehabilitation period varied from six to 10 weeks
• Overall, the most common indication for LVAD was bridging to heart transplantation

• EBCR training frequency ranged between 3-5 times weekly

• EBCR was associated with improved peak VO$_2$ in all but 2 trials (n=18) and showed QOL improvement in all trials except one

• Meta-analysis was performed on 3 randomized studies involving 61 patients (EBCR: 39, ST: 22)
Impact of EBCR on peak VO$_2$

### Impact of EBCR on peak VO$_2$ in LVAD recipients

<table>
<thead>
<tr>
<th>Study</th>
<th>WMD (95% CI)</th>
<th>EBCR group N, mean (SD)</th>
<th>ST group N, mean (SD)</th>
<th>% Weight (D+L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kerrigan/2014</td>
<td>3.50 (1.04, 5.96)</td>
<td>18, 15.3 (4.4)</td>
<td>8, 11.8 (2)</td>
<td>52.35</td>
</tr>
<tr>
<td>Hayes/2012</td>
<td>-0.50 (-5.38, 4.38)</td>
<td>7, 14.8 (4.9)</td>
<td>7, 15.3 (4.4)</td>
<td>19.59</td>
</tr>
<tr>
<td>Laoutaris/2011</td>
<td>4.50 (0.60, 8.40)</td>
<td>14, 19.3 (4.5)</td>
<td>7, 14.8 (4.2)</td>
<td>28.06</td>
</tr>
<tr>
<td>D+L Subtotal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(I-squared = 25.6%, p = 0.261)</td>
<td>3.00 (0.64, 5.35)</td>
<td>39</td>
<td>22</td>
<td>100.00</td>
</tr>
</tbody>
</table>

### Test of WMD
- Test of WMD (D+L) = 0, z = 2.49, p = 0.01
- Test of WMD (I+V) = 0, z = 3.20, p = 0.001

**NOTE:** Weights are from random effects analysis

**Abbreviations:**
- D+L: DerSimonian Laird
- EBCR: exercise-based cardiac rehabilitation
- I-V: inverse variance
- LVAD: left ventricular assist device
- ST: standard therapy
- peak VO$_2$: peak oxygen consumption
- WMD: weighted mean difference
Impact of EBCR on 6MWD

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<tr>
<th>Study</th>
<th>WMD (95% CI)</th>
<th>EBCR group N, mean (SD)</th>
<th>ST group N, mean (SD)</th>
<th>% Weight (D+L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kerrigan/2014</td>
<td>46.40 (-8.19, 100.99)</td>
<td>18, 402 (89.3)</td>
<td>8, 356 (51.6)</td>
<td>47.04</td>
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<tr>
<td>Hayes/2012</td>
<td>42.00 (-77.88, 161.88)</td>
<td>7, 531 (131)</td>
<td>7, 489 (95)</td>
<td>9.76</td>
</tr>
<tr>
<td>Laoutaris/2011</td>
<td>79.00 (22.04, 135.96)</td>
<td>14, 527 (76)</td>
<td>7, 448 (55)</td>
<td>43.20</td>
</tr>
<tr>
<td>D+L Subtotal</td>
<td></td>
<td>60.06 (22.61, 97.50)</td>
<td>39</td>
<td>100.00</td>
</tr>
<tr>
<td>Test of WMD = 0 (D+L), z = 3.14, p = 0.002</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>I-V Subtotal</td>
<td></td>
<td>60.06 (22.61, 97.50)</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Test of WMD = 0 (I+V), z = 3.14, p = 0.002</td>
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</tbody>
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NOTE: Weights are from random effects analysis

- ST: standard therapy
- EBCR: exercise-based cardiac rehabilitation
- LVAD: left ventricular assist device
- WMD: weighted mean difference
- 6MWD: six minute walk distance

Abbreviations: D+L: DerSimonian Liard; EBCR: exercise-based cardiac rehabilitation; I-V: inverse variance; LVAD: left ventricular assist device

Impact of EBCR on 6MWD in LVAD recipients

ST better | EBCR better

-100 | 0 | 100
Results cont’

- Meta analysis demonstrated that EBCR was associated with significantly greater peak VO$_2$ compared to ST

- 6MWD improvement was significantly greater in the EBCR group compared to ST group

- No significant heterogeneity was observed
Conclusions

• Our meta-analysis shows that exercise-based cardiac rehabilitation is associated with greater improvement in functional capacity compared to standard therapy.

• Given the small number of patients, further research into the clinical impact of exercise-based cardiac rehabilitation in LVAD patients is necessary.