Cardiac Rehabilitation Program for LVAD Patients

Dr Katherine Fan
Consultant Cardiologist
Grantham Hospital, Hong Kong SAR
Left Ventricular Assist Devices (LVAD)
Improved Survival Following LVAD Implantations

HEART TRANSPLANT

LVAD

Continuous Flow LVAD/BiVAD Implants: 2008 – 2016, n=17633*

P(overall) = .005
P(Era 1 vs Era 2) = .01
P(Era 1 vs Era 3) = .01
P(Era 2 vs Era 3) = .17


85% 1 yr
74% 5 yr
58% 10 yr

1 Yr-82%
2 Yr- 73%

Underlying cause of death:
Event: Death (censored at transplant and device cessation)

Median survival (years):
1982-1991 18.6
1992-2001 10.5
2002-2008 12.2
2009-2015 NA

All pair-wise comparisons significant at p < 0.05
Two-Year Outcomes with a Magnetically Levitated Cardiac Pump in Heart Failure

Significant improved outcome and safety profile
Exercise hemodynamics in CF-LVAD patients

- **Total CO during exercise:**
  - 1. **flow through the pump**
    - Pump speeds- adjusted by ECHO guidance to ensure sufficient circulator support at rest while allowing intermittent AV opening and maintaining normal LV dimensions
    - Pressure difference across the pump ($\Delta P$)
  - 2. **ejection through the aortic valve**
  - Current LVAD mechanics are highly after-load sensitive
  - Complex physiologic response affecting afterloads:
    - Blood volume
    - Heart rate
    - Aortic stiffness
    - Medical therapy
    - Vascular tone
    - Exercise induced peripheral vasodilatation

Jung et al. J Heart and Lung Transplantation 2015;34:489-496
Yet improvements in maximal cardiac works are marginal

• Although continuous flow LVAD support has been documented to significantly improve functional capacity and quality of life compared to pre-implantation values,

• Physical activity and overall energy expenditure and peak VO2 are all attenuated when compared with patients that received a Heart Transplant (considered gold standard treatment for end-stage HF
Possible factors associated with exercise intolerance in LVAD patients

• Device type
• Inability to increase cardiac output during exercise
• Right ventricular dysfunction
• Chronotropic incompetence
• Impaired pulmonary function
• Skeletal myopathy
• Endothelial dysfunction
3 key limiting elements in determining exercise response in heart failure patients

- **Cardiovascular**
  - Once supported- Improvement in hemodynamic status due to increased CO

- **Peripheral (Musculoskeletal)**
  - Deconditioned skeletal muscle
  - Changes in neurohormonal system
  - Endothelial dysfunction
  - Abnormal muscular vasodilation and blood flow changes

- **Central (Respiratory)**
  - Respiratory abnormalities
  - Ventilation/ perfusion mismatch
  - Abnormal gas diffusion
  - Increased dead space and pulmonary pressure
3 key limiting elements in determining exercise response in heart failure patients:

- **Cardiovascular**
  - Once supported: Improvement in hemodynamic status due to increased CO

- **Peripheral (Musculoskeletal)**
  - Deconditioned skeletal muscle
  - Changes in neurohormonal status
  - Endothelial dysfunction
  - Abnormal muscular vasodilation and blood flow changes

- **Central (Respiratory)**
  - Once supported:
    - Improved respiratory muscle strength due to increased skeletal muscle perfusion
    - Reversal of peripheral neurohormonal hyperactivation
    - Ability to increase nutritional intake
Effects of Exercise Training in LVAD Recipients
Pump speed titration:
• Increase in CO
• Improvement in left sided filling pressures

Exercise:
• Increase in CO
• Increase in both right and left filling pressures
• Pump speed titration during exercise:
  • Enhanced pump flow but did not reduce filling pressures
    • Increased venous return exceeding unloading capacity of LVAD

Inadequate rise in output to cope with the increased filling pressures, most likely due to afterload dependency of the pump (demonstrated by fall in SVO2)
Improvements in exercise capacity do not occur spontaneously

Figure 1 Factors affecting maximal exercise capacity in left ventricular assist device (LVAD)–supported patients. CO, cardiac output.
Non-physiologic Responses of CF-LVAD

• The impact of exercise training on submaximal capacity would be more pronounced than the impact on maximal performances.

• Cardiac output will not increase more than slightly due to the fixed speed pump.

• Increased oxygen demand during strenuous exercise will not be fully met.
Skeletal muscle dysfunction plays a critical role: Scientific based

- ET under supervision has potential to improve:
  - **Muscle strength**
    - Necessary to perform short duration activities of daily living (e.g., dressing and showering)
  - Enhance QoL
  - Respiratory efficiency and ventilator response
  - Peripheral vasodilation response
  - Skeletal muscle oxidative capacity
  - Decreased neurohormonal activation
2013 ISHLT Guidelines: all capable LVAD patients should be involved in CR program but not specific about intervention methods

- USA/ European guidelines demonstrate that exercise training improves FC and peak VO2, reduces the VE/ V CO2 slope in HF patients
- Associated with a host of positive physiologic adaptations
  - Enhanced endothelial function
  - Muscle perfusion
  - Oxygen supply
  - Aerobic characteristics in skeletal muscle
- But **NO** guidelines regarding best approach to CR or exercise prescription for patients with LVAD
- **LVAD pts undergo rehabilitation protocols designed for other types of cardiovascular diseases or cardiac surgeries**
Supervised exercise training vs usual care in ambulatory patients with LVAD: a systemic review
Ganga et al. PLOS 2017

3 RCTs, 2 prospective observational studies and 3 retrospective observational studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Supervised ET Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>De Jonge, [20], 2001</td>
<td>2 to 6 min of low level activities alternated with 1 to 2 min of rest. Training sessions with bicycle, treadmill, and rowing machine. Intensity increases based on Bjorg RPE. Duration of exercise gradually increased to 20–40 min/day 3–5 times a week. Strength and endurance training of local muscle groups.</td>
</tr>
<tr>
<td>Laoutaris, [19], 2011</td>
<td>Walk every day for 30–45 min on their own. Participants exercised at home, using bike or treadmill, for 30–45 min at moderate intensity level of 12–14 on Bjorg RPE, 3 to 5 days a week. In addition, they underwent high-intensity inspiratory muscle training (IMT) 2 to 3 times per week in the hospital. Exercise sessions were quantified by confirmation of implementation of home ET protocol during each IMT session 2 to 3 times a week</td>
</tr>
<tr>
<td>Kugler, [13], 2011</td>
<td>Home-based, tailored, every other day, smartcard-guided, cycle ergometer training program supplemented by regular phone calls for psychosocial support and training updates. Exercise sessions were quantified by recording training data (mean training heart rate, mean training workload and RPE) in a smartcard and is based on a protocol in a study by Tegbur et al. [25]</td>
</tr>
<tr>
<td>Hayes, [18], 2012</td>
<td>Participated in Mobilization Protocol (see control group) on days when they did not attend gym. Physiotherapy in gym for 1 hour, 3 days a week for 8 weeks; initially as inpatients, and continuing after hospital discharge. Exercise training included 15 minutes on treadmill, 15 min on stationary bike, and 3 Upper Extremity and Lower Extremity strength training exercises aiming for 2 sets of 10 repetitions. Workload intensity progressed based on RPE and dyspnea.</td>
</tr>
</tbody>
</table>

| Karapolat, [21], 2013 | Flexibility exercises (range of motion, stretching exercise), aerobic sessions lasting 30 minutes, 60–70% of peak VO2, and 12–14 Bjorg RPE, strengthening exercises involving UE and LE muscle groups, breathing exercises and relaxation exercises. Exercise sessions for 90 min, occurring 3 times a week for 8 weeks |
| Compostella, [23], 2014 | Three daily sessions of exercise-based training for 6 days a week. Exercise training includes breathing exercises, aerobic training, and calisthenics. |
| Kerrigan, [12], 2014  | Supervised exercise training program 3 days a week for 6 weeks, completed primarily by treadmill and a secondary modality (cycle ergometer, recumbent stepper) for 30 minutes at a training intensity set at 60% of the heart rate reserve, with patients allowed to progress to an intensity of 80% heart rate reserve |
| Marko, [22], 2014     | Aerobic training with bicycle ergometer and included interval training consisting of alternating high and low periods of training and 3 min warm up and cool down periods. Strength training directed on LE muscles only, with 2 series of 12 repetitions each. Walking training and gymnastics training with coordination, strength and balance training exercises. |
Interventions and Supervision

- Primary mode aerobic ET
- Strength training exercises
- Inspiratory muscle training
- Doses varied:
  - Duration: 2-18 weeks
  - Frequency: 3-6 sessions/week
  - Session length: 20-90 minutes/session
  - Intensity: Bjorg RPE 12-14; 60-80% of HR reserve; 60-70% peak oxygen uptake

- Supervision of ET
- Direct observation in cardiac rehabilitation gym setting
- Monitoring of exercise intensity and frequency through a home monitoring system
- Or both: implementation of supervised ET protocol at home combined with hospital visits (2-3x/week) for direct supervision of inspiratory muscle training
Effects of ET on Peak Oxygen Uptake and QoL

**Effect of Exercise Training on Peak Oxygen Uptake**

<table>
<thead>
<tr>
<th>Study name</th>
<th>Std diff in means</th>
<th>Std diff in and 95% CI</th>
<th>Relative weight</th>
<th>Sample Size</th>
<th>ET</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laoutaris, 2011</td>
<td>0.590</td>
<td>-0.504</td>
<td>1.684</td>
<td>0.291</td>
<td>13</td>
<td>5</td>
</tr>
<tr>
<td>Kugler, 2012</td>
<td>1.065</td>
<td>0.564</td>
<td>1.566</td>
<td>0.000</td>
<td>52</td>
<td>34</td>
</tr>
<tr>
<td>Hayes, 2012</td>
<td>0.301</td>
<td>-0.753</td>
<td>1.354</td>
<td>0.576</td>
<td>14</td>
<td>5</td>
</tr>
<tr>
<td>Kerrigan, 2014</td>
<td>0.284</td>
<td>-0.608</td>
<td>1.176</td>
<td>0.532</td>
<td>19</td>
<td>7</td>
</tr>
<tr>
<td>Random Effects Model</td>
<td>0.736</td>
<td>0.320</td>
<td>1.151</td>
<td>0.001</td>
<td>4</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Fig 2. Forest plot depicting effect of supervised exercise training on exercise capacity measured as peak oxygen uptake (ml/kg/min). ET = exercise training, Gp = group.

**Effect of Exercise Training on Quality Of Life**

<table>
<thead>
<tr>
<th>Study name</th>
<th>Std diff in means</th>
<th>Std diff in and 95% CI</th>
<th>Relative weight</th>
<th>Sample Size</th>
<th>ET</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laoutaris, 2011</td>
<td>0.985</td>
<td>-0.145</td>
<td>2.114</td>
<td>0.008</td>
<td>19</td>
<td>7</td>
</tr>
<tr>
<td>Kugler, 2012</td>
<td>2.159</td>
<td>1.569</td>
<td>2.748</td>
<td>0.000</td>
<td>17</td>
<td>7</td>
</tr>
<tr>
<td>Hayes, 2012</td>
<td>1.711</td>
<td>0.487</td>
<td>2.936</td>
<td>0.006</td>
<td>34</td>
<td>7</td>
</tr>
<tr>
<td>Kerrigan, 2014</td>
<td>1.111</td>
<td>0.167</td>
<td>2.056</td>
<td>0.021</td>
<td>19</td>
<td>7</td>
</tr>
<tr>
<td>Random Effects Model</td>
<td>1.589</td>
<td>0.969</td>
<td>2.209</td>
<td>0.000</td>
<td>16</td>
<td>7</td>
</tr>
</tbody>
</table>

Fig 4. Forest plot depicting effect of supervised exercise training on quality of life in LVAD patients. ET = exercise training, Gp = group.
Exercise performance during first two years after left ventricular assist device implantation
ASAIO J 2017 63(4): 408-413

- Clear long-term improvement in submaximal physical activity
- but in the absence of changes in peak oxygen uptake
- Physical performance continues to improve, indicating that training of peripheral musculature is improved
- Longer continuation of medically guided exercise training in ambulatory setting is warranted
Broaden understanding of what “function” meant to LVAD patients
Alternative Approaches to Understanding Functional Status

• Physical training studies utilized multi-faceted intervention strategies to enhance functional status

• Studies based selection of intervention strategies on other cardiac surgery rehabilitation interventions

• Multiple modality approach addresses physical recovery multi-dimensionally including:
  • Strength and endurance training
  • Inspiratory muscle training
  • Dietary guidance
  • Psychosocial counseling
Multi-modal approach- Frailty

- Frailty defined as impairment in multiple, interrelated organ systems causing decreased homeostatic reserve and increased vulnerability to stress
Frailty and the Selection of Patients for Destination Therapy LVAD
Circ Heart Failure 2012;5:286-293

Frailty
Increased Vulnerability to Stress

LVAD-Responsive Frailty
- Systolic and diastolic dysfunction
- ↑ PCWP and CVP
- ↓ Cardiac output

LVAD-Independent Frailty
- Inflammation
- Anorexia
- Polypharmacy
- Deconditioning
- Sarcopenia
- Malnutrition
- Cognitive deficits
- Injurious falls

Post-Operative Complications
- Prolonged LOS
- Need for ICU care

Impaired Health Status
- Disability
- Loss of ADLs
- Institutionalization

Reduced Survival

Pre-LVAD Frailty
- Aging
- COPD / lung disease
- Cancer
- Diabetes
- Osteoporosis
- Peripheral vascular disease
- Cirrhosis
- Neurologic disease

Post-LVAD Frailty

Patient A
Favorable Outcome
Lower risk for premature death or complications, with marked improvement in functional status

Patient B
Intermediate Outcome
Moderate risk for premature death and complications with some persistent functional limitation

Patient C
Unfavorable Outcome
High risk for premature death and complications with failure to improve functional status
LVAD clinic in Hong Kong
GH Advanced Heart Failure Pathway - Frailty Score Assessment

Physical

- Any “Yes” of the following?
  1) Exhaustion
  2) Poor hand grip
  3) Poor appetite
  4) 6 min walk test <400m
  5) Reduced physical activity

≥3 = physically frail

Cognitive

- Montreal Cognition Assessment - Hong Kong version (HK-MoCA)
  <22

Score 1

Depression

- Hospital Anxiety and Depression Scale (HADS)
  ≥8

Score 1

Total Score = 7
Frailty Conferred Increased Prognostic Significance in Chinese Patients with Advanced Heart Failure

K Fan et al. Presented in Euro Heart Failure 2017

**BACKGROUND**
- Frailty is a state of increased vulnerability to adverse outcomes, reflects biologic rather than chronological age.
- More common in heart failure patients than in general population.
- Strongly associated with increased morbidity & mortality.
- Frailty among Chinese patients with advanced heart failure is unknown.

Frailty was assessed for patients referred for consideration of heart transplantation/LVAD in 3 domains. Total score (0 to 7)

**RESULTS**
- Among 42 patients, frailty scores were collected at baseline & every 3 months.
- Frailty scores were serially followed up for positive clinical outcomes.

34 patients had serial assessments

Significant improvement was found in frailty score from mean 3.29 to 1.53 (p<0.001) after a mean of 9.74 months of medical follow up/surgical intervention.

**KEY IMPROVEMENTS**
- Establishment of an objective, reproducible way to assess advanced heart failure patient's frailty status serially which is invaluable in guiding advanced heart failure therapy decision making.
- Frailty scores help understand the effectiveness of advanced heart failure therapy.

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**Survival Functions**
- Frailty <5
- Frailty >5

P=0.046
Cardiac Rehabilitation Program for End-stage Heart Failure Patients with LVAD in Hong Kong

FU T Y, Fan K …et al. Poster presentation in APCCRC 2018

- Exercise based CPR consisted of cardiorespiratory and strength training
- Once per week for 24 sessions (6 months)
- Outcomes assessed by:
  - Functional: 6MHWT
  - Muscle strength evaluated by isokinetic knee extension strength test defined by 10 repetitive maximum (RM) torque of quadriceps strength

Results:
- 33 LVAD patients recruited into EBCR program (82% men)
- Mean age 48.7 +/- 13.6 years
- Average duration from LVAD to EBCR was 5.3 months
Outcomes of Functional Tests (6 MWT & Muscle Strength)

**6 MIN WALK TEST**

- Baseline: 393.57 meters
- 6M post-LVAD: 382.18 meters
- 6M post EBCP: 440.75 meters

**MUSCLE STRENGTH** (Quadriceps)

- **Pre-EBCR**: 1.76 kg
- **End of EBCR**: 3.49 kg

*Statistically significant difference**
What do “function” mean to our LVAD patients?
Conclusions

- Exercise therapy after LVAD – exercise function similar to mild heart failure
- Based on existing knowledge, it would seem beneficial to incorporate exercise protocols in the interdisciplinary treatment of LVAD patients bridged to recovery, thereby optimizing peripheral factors important in facilitating exercise tolerance
- Exercise training in LVAD should be encouraged as this improves peak VO2 (clinically relevant and improve prognosis)
- Optimizing non-cardiac peripheral parameters to improve ability to perform ADLs should be attempted
- In future, an automatic speed change algorithm/function in response to varied loading conditions may enable LVADs to provide sufficient support even during strenuous exercise
Thank You!
Champion of Life