

# INPLASY PROTOCOL

To cite: Wang et al.  
Effectiveness of Exercise-  
Based Cardiac Rehabilitation  
for Patients With Left  
Ventricular Assist Device: A  
Systematic Review and Meta-  
Analysis. Inplasy protocol  
202340073. doi:  
10.37766/inplasy2023.4.0073

Received: 20 April 2023

Published: 20 April 2023

**Corresponding author:**  
Yongnan Li

lyngyq2006@foxmail.com

**Author Affiliation:**  
Department of Cardiac  
Surgery, Lanzhou University  
Second Hospital.

**Support:** National Key R&D  
Program of China  
(2021YFC2701704).

**Review Stage at time of this  
submission:** Completed but  
not published.

**Conflicts of interest:**  
None declared.

## Effectiveness of Exercise-Based Cardiac Rehabilitation for Patients With Left Ventricular Assist Device: A Systematic Review and Meta-Analysis

Wang, YJ<sup>1</sup>; Lu, SJ<sup>2</sup>; Wu, YN<sup>3</sup>; Wei, SL<sup>4</sup>; Li, J<sup>5</sup>; Shao, KM<sup>6</sup>; Wu, XY<sup>7</sup>;  
Li, YN<sup>8</sup>.

**Review question / Objective:** P:Patients With Left Ventricular Assist Device; I:Exercise-Based Cardiac Rehabilitation; C:standard therapy (ST); O:the clinical impact of EBCR in LVAD patients (6MWD and peak V-o<sub>2</sub> in patients with advanced HF who under-go LVAD implantation).

**Eligibility criteria:** Studies were included in the systematic review and meta-analysis if they (1) assessed the impact of EBCR in LVAD recipients; (2) included a standard therapy (ST) group for comparison; and (3) enrolled adult subjects (>18 years of age). Exclusion criteria included (1) non-English language publication; (2) published abstract without full-text publication; (3) studies assessing the effect of cardiac rehabilitation on LVAD recipients without an ST group; (4) studies assessing the effect of different treatment strategies of cardiac rehabilitation without an ST group; and (5) studies lacking endpoint measures such as peak Vo<sub>2</sub> and 6-minute walk distance (6MWD). Standard therapy was defined as LVAD recipients who were not given any individualized/structured exercise prescription apart from advice to walk regularly by their physicians (30-45 min/d). The EBCR group was defined as participation in a structured cardiac rehabilitation program with a clearly defined protocol.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 April 2023 and was last updated on 20 April 2023 (registration number INPLASY202340073).

### INTRODUCTION

**Review question / Objective:** P:Patients With Left Ventricular Assist Device; I:Exercise-Based Cardiac Rehabilitation;

C:standard therapy (ST); O:the clinical impact of EBCR in LVAD patients (6MWD and peak V-o<sub>2</sub> in patients with advanced HF who under-go LVAD implantation).

**Rationale:** PubMed, Web of Science, CINAHL, and Cochrane Library databases were searched for randomized studies assessing the impact of EBCR in patients following LVAD implantation compared with standard therapy (ST). Using pre-defined criteria, appropriate studies were identified and selected. Data from selected studies were extracted in a standardized fashion and a meta-analysis was performed using a random-effects model with DerSimonian Liard weighting. Analysis employed weighted mean difference (WMD) as the effect size and intention-to-treat (ITT) principle. Study quality, publication bias, and heterogeneity were assessed.

**Condition being studied:** Left ventricular assist devices (LVADs) are being increasingly used to support patients with advanced heart failure (HF), both as a bridge to recovery and as destination therapy. It is well-known that LVADs improve survival, functional capacity, and quality of life (QOL) in patients with advanced HF. However, compared with recipients of heart transplants, many patients with LVADs continue to experience exercise intolerance. Exercise-based cardiac rehabilitation (EBCR) has been shown to be safe and effective in patients with HF. Exercise-based cardiac rehabilitation improves peak oxygen uptake ( $Vo_2$ ), functional capacity, and QOL and reduces HF symptoms and hospitalizations. However, there are very limited data on the safety and efficacy of EBCR in patients with LVADs. We therefore systematically reviewed the literature and performed a meta-analysis to evaluate the impact of EBCR in LVAD recipients. This meta-analysis and systematic review suggest that EBCR in advanced HF patients receiving LVADs is associated with significant improvement in exercise capacity as assessed by peak  $Vo_2$  and 6MWD. Therefore, LVAD recipients should be encouraged to participate in supervised EBCR. However, given the small number of patients, there is an urgent need for large well-designed multicenter studies assessing the clinical benefits of EBCR in

the burgeoning population of HF patients with LVADs.

## METHODS

**Search strategy:** A systemic literature review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. Two authors separately searched PubMed, Web of Science, CINAHL, and Cochrane Library databases for studies assessing the effect of cardiac rehabilitation in patients following LVAD implantation from May 1949 through April 2023. We used the following key words in various combinations: heart assist device; ventricular assist device; assistive device; and cardiac rehabilitation. The bibliographies of selected manuscripts and review articles were also manually searched for additional studies that were not identified in the original search. Titles and abstracts were screened to identify studies for full-text review. Studies assessing the effect of EBCR in patients following LVAD implantation and fulfilling the pre-defined inclusion and exclusion criteria were selected for inclusion in the review and quantitative analysis.

**Participant or population:** Patients With Left Ventricular Assist Device.

**Intervention:** Exercise-Based Cardiac Rehabilitation.

**Comparator:** Standard therapy (ST).

**Study designs to be included:** Unlimited.

**Eligibility criteria:** Studies were included in the systematic review and meta-analysis if they (1) assessed the impact of EBCR in LVAD recipients; (2) included a standard therapy (ST) group for comparison; and (3) enrolled adult subjects (>18 years of age). Exclusion criteria included (1) non-English language publication; (2) published abstract without full-text publication; (3) studies assessing the effect of cardiac rehabilitation on LVAD recipients without an ST group; (4) studies assessing the effect of different treatment strategies of cardiac

rehabilitation without an ST group; and (5) studies lacking endpoint measures such as peak Vo<sub>2</sub> and 6-minute walk distance (6MWD). Standard therapy was defined as LVAD recipients who were not given any individualized/structured exercise prescription apart from advice to walk regularly by their physicians (30-45 min/d). The EBCR group was defined as participation in a structured cardiac rehabilitation program with a clearly defined protocol.

**Information sources:** PubMed, Web of Science, CINAHL, and Cochrane Library databases.

**Main outcome(s):** The clinical impact of EBCR in LVAD patients (6MWD and peak V·o<sub>2</sub> in patients with advanced HF who under-go LVAD implantation).

**Additional outcome(s):** 6MWD and peak V·o<sub>2</sub> in patients with advanced HF who under-go LVAD implantation.

**Data management:** Data extraction was completed by two independent investigators ). A standardized data extraction form was used for collecting the baseline from each incorporated study including lead author, publication year, country or district, maternal and so on. Any disagreement was settled by consensus and consultations with experienced reviewers.

**Quality assessment / Risk of bias analysis:** Using the Joanna Briggs Institute case series checklist to qualify the article.

**Strategy of data synthesis:** Data from selected studies were extracted and a meta-analysis of randomized trials was performed comparing EBCR versus ST using the random effects model with DerSimonian Liard weighting. Analysis employed weighted mean difference (WMD) as the effect size and intention-to-treat (ITT) principle. Publication bias was analyzed visually using funnel plot. The Cochrane Q statistic was calculated and used to determine the heterogeneity of

included studies for each endpoint. I<sup>2</sup> index values of 25% to 50%, 51% to 75%, and >75% were considered as low, moderate, and high heterogeneity, respectively. An exclusion sensitivity analysis was performed when necessary and a 2-sided P value of < .05 was considered statistically significant for all analyses.

**Subgroup analysis:** Data from selected studies were extracted and a meta-analysis of randomized trials was performed comparing EBCR versus ST using the random effects model with DerSimonian Liard weighting.

**Sensitivity analysis:** The Cochrane Q statistic was calculated and used to determine the heterogeneity of included studies for each endpoint. I<sup>2</sup> index values of 25% to 50%, 51% to 75%, and >75% were considered as low, moderate, and high heterogeneity, respectively. An exclusion sensitivity analysis was performed when necessary and a 2-sided P value of <0 .05 was considered statistically significant for all analyses.

**Language restriction:** Only English articles will be included.

**Country(ies) involved:** China.

**Keywords:** cardiac rehabilitation; heart failure; left ventricular assist device; meta-analysis.

**Contributions of each author:**

Author 1 - Yujin Wang - Author 1 drafted the manuscript.

Email: 5942194@qq.com

Author 2 - Sijie Lu - The author provided statistical expertise.

Email: 625362881@qq.com

Author 3 - Yawen Wu - The author contributed to the development of the selection criteria, and the risk of bias assessment strategy.

Author 4 - Shilin Wei - The author read, provided feedback and approved the final manuscript.

Email: weishilinv@qq.com

---

**Author 5 - Jian Li - The author read, provided feedback and approved the final manuscript.**

**Email: [lijian5556@foxmail.com](mailto:lijian5556@foxmail.com)**

**Author 6 - Kangmei Shao - The author read, provided feedback and approved the final manuscript.**

**Email: [328963894@qq.com](mailto:328963894@qq.com)**

**Author 7 - Xiangyang Wu - The author read, provided feedback and approved the final manuscript.**

**Email: [xuxyok@163.com](mailto:xuxyok@163.com)**

**Author 8 - Yongnan Li - The author read, provided feedback and approved the final manuscript.**

**Email: [lyngyq2006@foxmail.com](mailto:lyngyq2006@foxmail.com)**