

Exercise-Based Cardiac Rehabilitation: Impact on Myocardial Function measured by Global Longitudinal Strain

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Abstract: Measures of cardiovascular (CV) health and function are improved by exercise. However, it might be challenging to determine the short-term efficacy of an exercise intervention when conventional metrics steadily improve. Reductions in left ventricular global longitudinal strain (LVGLS) are a powerful predictor of future cardiac dysfunction and death. LVGLS is a very sensitive cardiac imaging tool that can identify myocardial dysfunction before more conventional assessments. Because of its sensitivity, LVGLS may provide a practical way to monitor the short-term impact of an exercise intervention on CV function, giving practitioners valuable data to enhance patient care in exercise environments. It's unknown, nevertheless, how exercise affects LVGLS. This systematic review and meta-analysis aimed to determine the effect exercise has on LVGLS across a range of populations. Included studies assessed LVGLS pre–post an exercise intervention (minimum 2 weeks) in adults 18 years and over, and were published in English from 2000 onwards. Study-level random-effects meta-analyses were performed using Stata (v16.1) to calculate summary standardized mean differences (SMD) and 95% confidence intervals (CI). 39 studies met selection criteria, with 35 included in meta-analyses (1765 participants). In primary analyses, a significant improvement in LVGLS was observed in populations with CV disease (SMD=0.59; 95% CI 0.16–1.02; p=0.01), however, no significant effect of exercise was observed in CV risk factor and healthy populations. In populations with CV disease, LVGLS could be used as an early biomarker to determine the effectiveness of an exercise regime before changes in other clinical measures are observed.

Keywords: Physical Activity, Cardiac Function, Cardiovascular Imaging

Introduction

Numerous health, fitness, and performance metrics are improved by exercise across a range of demographics (American College of Sports Medicine 2013; Anderson 2016). Exercise is a key component of treatment for cardiovascular (CV) disease and related risk factors in order to enhance health outcomes and avoid CV events (Sharman et al. 2019; Hordern et al. 2012). Exercise is also advised in healthy individuals to avoid developing chronic illnesses in the future (American College of Sports Medicine 2013).

CV disease is the leading cause of death across Europe (45% of all deaths) (European Heart Network 2017), with an estimated cost to the European Union of €210 billion a year (Timmis et al. 2020). Populations at the greatest risk of CV disease include those with pre-existing risk factors such as hypertension (HTN), type 2 diabetes (T2DM), high cholesterol, obesity, history of smoking or alcohol abuse, physical inactivity, and a family history of CV disease.

Global longitudinal strain (GLS) is a highly sensitive CV imaging measure that detects early signs of myocardial dysfunction prior to clinical abnormalities and symptoms arising. GLS measures

myocardial deformation along the longitudinal cardiac axis, with reductions in GLS a strong prognostic indicator of future CV dysfunction and mortality. Given the sensitivity of LVGLS, it could offer practitioners a viable way to determine the effectiveness of an exercise regime prior to changes in more traditional measures of CV health and function occurring.

Methods

The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement guidelines.

Literature search

Candidate studies published between 2000 and 2020 were searched on November 24, 2020 via Medline, Scopus, eMbase, SPORTDiscus. Search terms included "exercise", "physical activity", "global longitudinal strain", "speckle tracking".

Selection criteria

Included studies assessed LVGLS before and after an exercise intervention (minimum 2 weeks) in adults aged 18 years and over. Exclusions: inadequate description of intervention, same population in different papers, or missing data. Studies measuring acute effects following a CV event without a control group were excluded from secondary meta-analyses.

Data extraction and quality assessment

Data were extracted regarding demographics, study characteristics, exercise protocols, and outcomes. Quality assessment was performed using the QUADAS-2 tool to assess risk of bias.

Data analysis

Percentage change in LVGLS was calculated: $[(\text{post LVGLS} - \text{pre LVGLS})/\text{pre LVGLS}] \times 100$. Primary meta-analyses included RCTs, N-RCTs, and crossover studies with a non-exercising control group. Secondary analyses included exercise group data from all study types. Analysis was performed using Stata (v16.1) with a random-effects model.

Results

39 studies were included in the review, with 35 included in the meta-analyses (1765 participants). Average exercise intervention spanned 20.7 ± 19.9 weeks with 3.9 ± 1.5 sessions per week. 53.8% prescribed aerobic exercise only.

Primary meta-analyses

- **CV disease:** A moderate effect of exercise was observed compared to controls (SMD = 0.59; 95% CI 0.16–1.02; $p=0.01$).
- **CV risk:** No significant effect (SMD = 0.07; 95% CI -0.15–0.29; $p=0.56$).
- **Healthy:** No significant effect (SMD = -0.20; 95% CI -0.73–0.33; $p=0.45$).

Secondary meta-analyses

Across all clinical populations (CV disease, CV risk, CKD), an SMD of 0.45 was observed (95% CI 0.23–0.66). In non-clinical populations (healthy and athletic), an SMD of 0.20 was observed (95% CI 0.08–0.32).

Sub-group exploratory analysis

There was no significant difference between exercise intervention lengths ($p=0.06$) or modalities (aerobic only vs. combined, $p=0.38$) on the change in LVGLS.

Clinical Significance

A 10% relative change in LVGLS is considered clinically significant. Two CV disease studies and two CV risk studies reported clinically significant increases following exercise. No exercising group observed a clinically significant reduction in LVGLS, suggesting exercise does not negatively impact it.

Discussion

This is the first study to analyze the effect of exercise on LVGLS across diverse populations. In populations with overt CV disease, exercise significantly increased LVGLS. This provides insight into how cardiac rehabilitation improves myocardial function. Reductions in LVGLS are markers of early dysfunction; therefore, increases are vital for promoting function. The lack of significant change in primary analyses of CV risk and healthy populations might be due to several factors. In risk groups (HTN, T2DM), exercise may have led to a reduction in medication, which complicates the strain results. In healthy groups, the inclusion of resistance training studies (which show less central adaptation) may have diluted the results. Exploratory analysis suggests any aerobic exercise performed for a minimum of 2 weeks may be sufficient to increase LVGLS.

Strengths and Limitations

Strengths: high number of studies, systematic search, active control arms. Limitations: Lack of individual participant data, inter-vendor variability (different machines/software), poor reporting of exercise intensity in some studies, and evidence of publication bias in healthy and CKD groups.

Conclusion

In populations with overt CV disease, exercise significantly increased LVGLS, suggesting it could be used as an early biomarker to determine the effectiveness of an exercise regime before changes in other clinical measures are observed. Similar findings were not observed in primary analyses of CV risk and healthy populations. Secondary meta-analyses suggest exercise may be used as a therapeutic intervention to increase LVGLS in CV diseased, CV risk, CKD, and athletic populations. Further RCTs are warranted for at-risk CV populations.

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