# INPLASY PROTOCOL

To cite: Ntallas et al. The effects of exercise on V02peak, Quality of Life and Hospitalization in heart failure patients: A Systematic Review with Meta-analyses. Inplasy protocol 202090031. doi: 10.37766/inplasy2020.9.0031

Received: 07 September 2020

Published: 07 September 2020

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Support: None.

Review Stage at time of this submission: Data analysis.

Conflicts of interest: None.

# The effects of exercise on V02peak, Quality of Life and Hospitalization in heart failure patients: A Systematic Review with Meta-analyses

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**Review question / Objective:** Our systematic review has a specific, clear and measurable objective, that is to assess the effect of exercise training in patients suffering from heart failure, considering VO2peak, hospitalization and quality of life aspects.

Condition being studied: Heart Failure - Exercise Training.

Information sources: The information sources were the three electronic databases searched (PubMed, Cochrane Library, Embase). Where a paper lacked vital information the corresponding author was immediately contacted via e-mail in order to retrieve all the missing data.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 07 September 2020 and was last updated on 07 September 2020 (registration number INPLASY202090031).

# **INTRODUCTION**

**Review question / Objective: Our** systematic review has a specific, clear and measurable objective, that is to assess the effect of exercise training in patients suffering from heart failure, considering VO2peak, hospitalization and quality of life aspects.

**Condition being studied: Heart Failure -Exercise Training.** 

#### **METHODS**

Search strategy: Research Question A: "Does ET enhance V02Peak in HF patients?" Research Question B: "Does ET improve Quality of Life in HF patients?" Research Question C: "Does ET reduce Hospitalization rates in HF patients?" The above three research questions were formed in order to guide this Review. The study framework that was used to guide this review, is the one developed by Kable et al (2012). We searched the databases PubMed, Cochrane Library and Embase. The search terms follow: Heart failure. HFrEF, HFpEF, Reduced ejection fraction, Preserved ejection fraction, Systolic heart failure. Diastolic heart failure. Concestive heart failure, Chronic heart failure, Exercise training, High intensity exercise. Intermittent exercise, Continuous exercise, Strength training, Resistance training, Endurance training, HIT, HIIT, Weight training, Exercise based rehabilitation, Low intensity exercise, V02, VO2, VO2 Peak, VO2 Max, Peak oxygen consumption, VO2 Maximum, Maximum oxygen consumption, Quality of life, QOL, Health related quality of life, HRQOL, Hospital admissions, Hospitalisation, Hospitalization, Rehospitalization, Rehospitalisation.

Participant or population: Heart Failure Patients.

Intervention: Exercise Training.

**Comparator:** Control group.

Study designs to be included: Randomized Controlled Trials (RCT's).

Eligibility criteria: Inclusion Criteria follows: 1) Studies examining the effect of exercise based rehabilitation in heart failure patients. 2) One week of exercise based rehabilitation or more. 3) Randomized controlled trials (RCT's). 4) Studies in Humans. 5) No restriction in Language. 6) No restriction on the exercise type. 7) Patients must be 18 year old or older. Exclusion Criteria: 1) Animal Studies 2) Human studies that did not examine the effect of exercise training in VO2max, QOL or Hospitalization on HF patients. 3) No reviews / systematic reviews and conferences. 4) No restriction in Language 5) Gray Literature (No peer-reviewed studies, Editorials, Letters etc.). 6) Non-RCT's 7) Studies with exercise in the control arm 8) Less than one week of exercise based intervention. 9) Studies on participants under 18 years old. 10) Studies on non HF patients.

Information sources: The information sources were the three electronic databases searched (PubMed, Cochrane Library, Embase). Where a paper lacked vital information the corresponding author was immediately contacted via e-mail in order to retrieve all the missing data.

Main outcome(s): Our analyses revealed that exercise, as a fundamental part of cardiac rehabilitation, increases peak oxygen consumption, which is a key component of physical fitness, and results in decreased hospital admissions and improvement of overall quality of life of Heart failure patients.

Quality assessment / Risk of bias analysis: Our analyses revealed that exercise, as a fundamental part of cardiac rehabilitation, increases peak oxygen consumption, which is a key component of physical fitness, and results in decreased hospital admissions and improvement of overall quality of life of Heart failure patients.

Strategy of data synthesis: A random effect model meta-analysis was used to calculate pre and post mean differences in VO2Peak and QOL due to exercise. Using the same model, we also calculated the Odds ratio for the number of hospitalizations between experimental and control groups of the studies included in the systematic review. Hospital admissions were assessed during the experimental period and also the posttrial follow-up period potentially reported by each RCT. We calculated the 95% confidence interval and heterogeneity between studies using the I<sup>2</sup> statistic. We considered a statistically significant result for heterogeneity when p<0.10, while interpretation of I2 index was made based

on previous guidelines (Higgins and Green 2011). Publication bias was assessed using funnel plots. All analyses and plots production were performed via the Review Manager, Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014 software.

Subgroup analysis: Regarding VO2 peak, we have performed a sub-group analysis with regard to exercise training type, i.e. aerobic versus resistance versus combined (aerobic + resistance) exercise . Unfortunately, a subgroup analysis was not possible for sex. While there are 24 studies that conducted only in males, there is no studies that conducted only in females, most of the included studies in this metaanalysis conducted in both sexes. Therefore, a comparison between males and females is not feasible. Similarly, a sub-group analysis with regard to age is not meaningful, since all of the included studies display an average of age >45 years old as well as several age groups are appeared in some studies. Finally, we believe that a sub-group analysis for VO2 peak with regard to year of publication cannot be adequately interpreted, given that a lot of information with regard to measurements is missing (i.e. technology differences in the devices that used for VO2peak assessments). Regarding quality of life we have performed a sub-group meta-analysis with regard to exercise training type, i.e. aerobic versus resistance versus combined (aerobic + resistance) exercise . Also, we have performed a subgroup meta-analysis with regard to exercise training type, i.e. aerobic versus combined (aerobic + resistance) exercise for hospitalization outcomes, since for this subgroup meta-analysis there was no data for resistance exercise. Finally, for the above-mentioned reasons we were not able to perform a sub-group analysis for sex, age and year of publication of the studies for quality of life and hospitalizations.

### Sensibility analysis: NA.

Language: No restriction.

Country(ies) involved: No restriction.

Keywords: Heart failure; Exercise training; Peak oxygen consumption; V02Peak; Quality of life; Hospitalization.

## **Contributions of each author:**

Author 1 - Konstantinos Ntallas -Conception and design of the study, Literature search, Data collection and analysis, Manuscript preparation.

Author 2 - Petros C. Dinas - Analysis of data, Manuscript preparation, Review of manuscript.

Author 3 - Costas Chryssanthopoulos -Data analysis, Manuscript preparation, Review of manuscript.

Author 4 - George Dallas - Manuscript preparation, Review of manuscript.

Author 5 - Maria Maridaki - Manuscript preparation, Review of manuscript.

Author 6 - Michael Koutsilieris - Manuscript preparation, Review of manuscript.

Author 7 - Anastassios Philippou -Conception and design of the study, Literature search, Manuscript preparation, Review of manuscript.