



# Efficacy of inspiratory muscle training in chronic heart failure patients: A systematic review and meta-analysis

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## ABSTRACT

**Introduction:** Inspiratory muscle training (IMT) offers an alternative to exercise training (EXT) in the most severely deconditioned heart failure patients who are unable to exercise. We conducted a meta-analysis to determine magnitude of change in peak  $\text{VO}_2$ , six minute walk distance (6MWD), Quality of Life measured by the Minnesota Living with Heart Failure Questionnaire (MLWHFQ), maximal inspiratory pressure ( $\text{PI}_{\text{max}}$ ) and ventilatory equivalent for carbon dioxide ( $V_E/\text{VCO}_2$  slope) with IMT.

**Methods:** A systematic search was conducted of randomized, controlled trials of IMT therapy in CHF patients using Medline (Ovid) (1950–February 2012), Embase.com (1974–February 2012), Cochrane Central Register of Controlled Trials and CINAHL (1981–February 2012). The search strategy included a mix of MeSH and free text terms for the key concepts heart failure, inspiratory or respiratory muscle training, exercise training

**Results:** The eleven included studies contained data on 287 participants: 148 IMT participants and 139 sham or sedentary control. Compared to control groups, CHF patients undergoing IMT showed a significant improvement in peak  $\text{VO}_2$  ( $+1.83 \text{ ml kg}^{-1} \text{ min}^{-1}$ , 95% C.I.  $1.33$  to  $2.32 \text{ ml kg}^{-1} \text{ min}^{-1}$ ,  $p < 0.00001$ ); 6MWD ( $+34.35 \text{ m}$ , 95% C.I.  $22.45$  to  $46.24 \text{ m}$ ,  $p < 0.00001$ ); MLWHFQ ( $-12.25$ , 95% C.I.  $-17.08$  to  $-7.43$ ,  $p < 0.00001$ );  $\text{PI}_{\text{max}}$  ( $+20.01$ , 95% C.I.  $13.96$  to  $26.06$ ,  $p < 0.00001$ ); and  $V_E/\text{VCO}_2$  slope ( $-2.28$ , 95% C.I.  $-3.25$  to  $-1.30$ ,  $p < 0.00001$ ).

**Conclusions:** IMT improves cardio-respiratory fitness and quality of life to a similar magnitude to conventional exercise training and may provide an initial alternative to the more severely de-conditioned CHF patients who may then transition to conventional EXT.

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## 1. Introduction

Although considerable progress has been made in optimizing drug management of patients with chronic heart failure (CHF), the social and personal burden of CHF is still characterized by debilitating symptoms, frequent re-hospitalizations and high mortality rates [1]. A specific symptom of CHF is respiratory muscle fatigue due to frequent dyspnea [2]. Exercise-based cardiac rehabilitation is a comprehensive structured intervention since it best addresses the complex interplay of medical, psychological and behavioural factors facing CHF patients [3]. However, some patients do not adapt or drop out of conventional exercise training programs, and others are unable to perform even low levels of physical effort. The most severely impaired patients (New York Heart Association (NYHA) class III/IV) may be, at least initially, exercise intolerant, therefore alternative physical therapies have been employed including functional electrical stimulation [4] and respiratory (inspiratory) muscle training [5].

Respiratory, or inspiratory, muscle training (IMT) has shown potential beneficial effects in CHF patients, such as improving peak

oxygen consumption ( $\text{VO}_2$ ) [6], better performance in functional tests [7], and improved quality of life [8]. IMT therapy may be an alternative treatment for patients who cannot engage in conventional exercise training programs, but the beneficial effects of IMT in the treatment of patients with CHF have yet to be compared to traditional aerobic exercise training programs. Published studies comparing benefits derived from IMT therapy mostly exhibit small sample sizes and somewhat conflicting results. The aim of this work was to conduct a systematic review and meta-analysis of randomized, controlled trials of IMT versus sham or sedentary control. We examined the magnitude of change in peak  $\text{VO}_2$ , six minute walk distance (6MWD), Quality of Life measured by the Minnesota Living with Heart Failure Questionnaire (MLHFQ), maximal inspiratory pressure ( $\text{PI}_{\text{max}}$ ) and of the slope of increase in ventilation over carbon dioxide output ( $V_E/\text{VCO}_2$  slope), comparing the effect sizes with those previously reported following conventional aerobic or resistance exercise training in this patient population.

## 2. Methods

### 2.1. Search strategy

Potential studies were identified by a systematic review librarian. A systematic search was conducted of Medline (Ovid) (1950–February 2012), Embase.com (1974–

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February 2012), Cochrane Central Register of Controlled Trials and CINAHL (1981–February 2012). The search strategy included a mix of MeSH and free text terms for the key concepts heart failure, inspiratory or respiratory muscle training, exercise training, and these were combined with a sensitive search strategy to identify randomized controlled trials. Reference lists of papers found were scrutinized for new references. All identified papers were assessed independently by two reviewers (NS and GD) and a consensus reached by consulting a third reviewer (FG) if required. Searches of published papers were conducted up until February 2012.

## 2.2. Inclusions

Randomized, controlled trials including CHF patients undergoing IMT, for a minimum of 2 weeks, were included in this study. IMT groups were compared with a sedentary (or sham IMT) control group, education or a conventional exercise training group. There were no language restrictions.

## 2.3. Exclusions

Animal studies, review papers and non-randomized controlled trials were excluded. Studies that included participants who were non-heart failure or healthy in either treatment or control groups were also excluded. Authors were contacted to provide missing data or to clarify if data were duplicated in multiple publications by the same author or research group, incomplete data or data from an already included study resulted in exclusion. Studies of physical therapy other than aerobic, strength or IMT (e.g. tai chi) and acute exercise rather than training response studies were also excluded.

## 2.4. Studies included in the review

We examined conference proceedings and the latest editions of relevant journals not yet available on electronic databases. Fig. 1 shows the PRISMA flow diagram, initial screening identified 49 potential reports, 38 studies were excluded, 12 were duplicates, 15 as they were not randomised trials of IMT in heart failure patients and 11 because they were either review articles or had patients that did not meet our inclusion criteria, leaving 11 eligible trials. One group produced four publications each reporting data from different participants (so our data analyses avoided duplication).

## 2.5. Data synthesis

Data relating to primary and secondary outcomes, heart failure patient characteristics and exercise training protocols were reviewed. Information was archived in a

database. The primary outcome measure following intervention was post exercise change in peak  $\text{VO}_2$ , in  $\text{ml kg}^{-1} \text{min}^{-1}$ . Secondary outcomes were changes in 6MWD, MLHFQ,  $\text{P}_{\text{I}_{\text{max}}}$ , and  $\text{V}_E/\text{VCO}_2$  slope.

## 2.6. Statistical analysis

Revman 5.1 (The Nordic Cochrane Centre, Copenhagen, Denmark) was used to conduct meta-analyses for outcome measures following IMT. Data used were continuous and were reported as mean and standard deviation. Revman 5.1 enabled calculation of post-intervention change from baseline for standard deviation, using change in mean values, number of subjects and p value for each group. Mean difference in these data from baseline were analyzed. Study quality was compared by Jadad [9] and PEDro [10] scores and an Egger plot was produced to identify sources of publication bias [11]. We used a 5% level of significance and a 95% confidence interval to report change in outcome measures.

## 3. Results

The eleven included studies [6–8,12–19] contained data of 287 patients: 148 IMT participants and 139 sham or sedentary control participants. Generally, the studies were well matched at baseline for age, NYHA class, gender, peak  $\text{VO}_2$  and medication use (Table 1). Five studies utilised daily training, two studies required patients to train 6 days weekly and four studies required patients to train thrice weekly. Four studies required patients to train for 12 weeks, three studies for 10 weeks, one study was 8 weeks and two were for 6 weeks. Five studies utilized 60%  $\text{P}_{\text{I}_{\text{max}}}$  as the training intensity, one study used 40%  $\text{P}_{\text{I}_{\text{max}}}$  and five used 30%  $\text{P}_{\text{I}_{\text{max}}}$ , most studies adjusted training intensity each week during supervised sessions. All but three studies required patients to complete some of the IMT sessions at home. Control participants trained at 0–15%  $\text{P}_{\text{I}_{\text{max}}}$  or received education (Table 2).

Compared to control groups, CHF patients undergoing IMT showed a significant improvement in peak  $\text{VO}_2$  ( $+1.83 \text{ ml kg}^{-1} \text{min}^{-1}$ , 95% C.I. 1.33 to  $2.32 \text{ ml kg}^{-1} \text{min}^{-1}$ ,  $p < 0.00001$ ) (Fig. 2); in

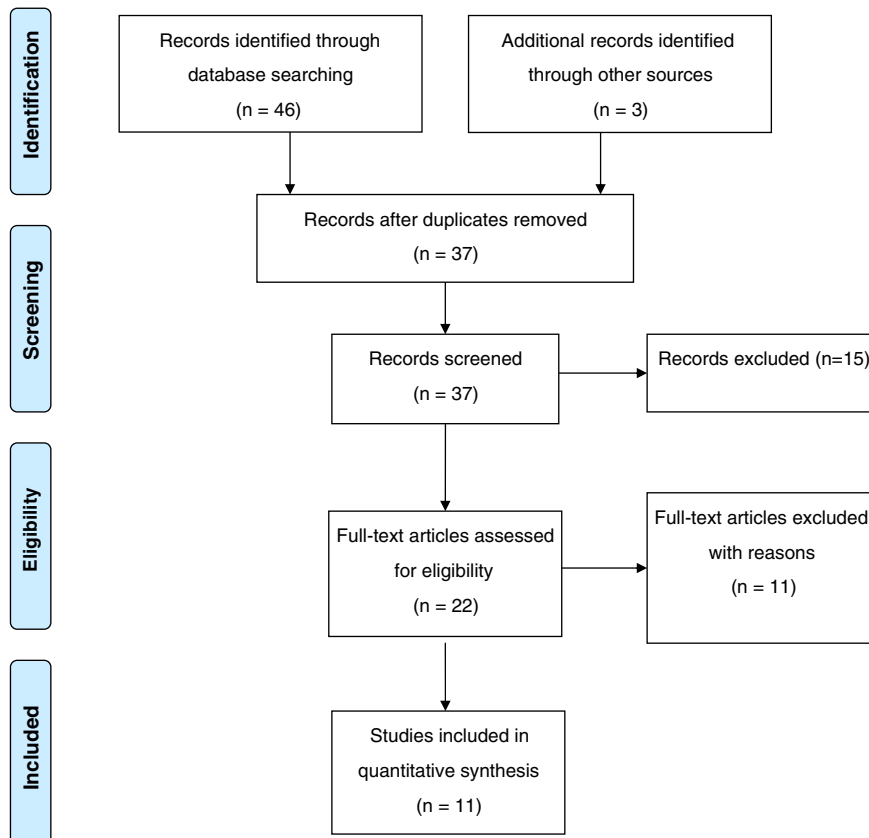


Fig. 1. PRISMA flow diagram.

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