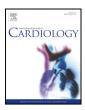
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#### Review

# The effects of resistance training on muscle strength, quality of life and aerobic capacity in patients with chronic heart failure – A meta-analysis

Catherine Giuliano <sup>a,b</sup>, Amalia Karahalios <sup>c</sup>, Christopher Neil <sup>a,b,e</sup>, Jason Allen <sup>a,b</sup>, Itamar Levinger <sup>a,b,d,\*</sup>

<sup>a</sup> Clinical Exercise Science Research Program, Institute of Sport, Exercise and Active Living (ISEAL), Victoria University, Melbourne, Australia

<sup>b</sup> Western Health, Melbourne, Australia

<sup>c</sup> Centre for Epidemiology and Biostatistics, Melbourne School of Population and Global Health, The University of Melbourne, Australia

<sup>d</sup> Department of Cardiology, Austin Health, Melbourne, Australia

<sup>e</sup> Department of Medicine-Western Precinct at the University of Melbourne, Australia

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#### ABSTRACT

*Background:* Resistance training (RT) has been utilised to target muscle dysfunction associated with Chronic Heart Failure (CHF). However, there is limited meta-analysis evidence to support its use as a standalone therapy. This meta-analysis examined the effects of RT on muscle strength (one repetition maximum, 1RM and Peak Torque), aerobic capacity (VO<sub>2peak</sub> and 6 min walk distance) and quality of life (QoL) in patients with CHF. *Methods:* We searched Medline, EMBASE, Cochrane and CINAHL for studies published up to July 2016, combining terms related to the population (eg, *heart failure, CHF*) with terms for the intervention (eg, *resistance, strength*)

*training*) and the outcomes (eg, *QoL*, *VO*<sub>2</sub> *peak*, *strength*, *aerobic capacity*). *Results*: Ten studies including 240 participants were included in our meta-analysis (aged 48–76 years, Ejection Fraction 18–37%). Training duration ranged from 8 to 24 weeks and intensity up to 80% of 1RM. RT increased 1RM (standardised change score = 0.60; 95% Confidence Interval: 0.43, 0.77) but not strength measured via peak torque at  $60^{\circ}/s^{-1}$  and  $180^{\circ}/s^{-1}$ . RT increased VO<sub>2peak</sub> (CSMD: 2.71 ml/kg/min; 1.96, 3.45) and QoL (CSMD: -5.71; -9.85, -1.56).

*Conclusion:* RT as a single intervention can increase muscle strength, aerobic capacity and QoL in patients with CHF and may offer an alternative approach, particularly for those unable to participate in aerobic training. The effect of RT on muscle strength is mainly during slow controlled movements and not during rapid movements. Older adults and patients with advanced CHF are underrepresented in RT trials and future studies should seek to optimise their inclusion.

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#### 1. Introduction

Chronic Heart Failure (CHF) is a dynamic and progressive syndrome, which develops secondary to structural or functional abnormalities of cardiac tissue. It leads to the inability of the heart to supply enough blood to meet the body's metabolic needs and causes breathlessness, fatigue and reduced exercise tolerance [1]. Life expectancy in patients with CHF is increasing however, many of these recovered years are spent with debilitating burden of symptoms [2], high incidence of hospitalisations [3,4] and a poor ultimate prognosis [4].

Treatment for patients with CHF is alike other terminal illnesses and is primarily focussed on managing symptoms and maintaining quality

emily.karahalios@unimelb.edu.au (A. Karahalios), Christopher.neil@wh.org.au (C. Neil), [ason.allen@vu.edu.au (J. Allen), Itamar.levinger@vu.edu.au (I. Levinger). of life (QoL). Exercise training is an integral component of this paradigm [5–7] due to its capacity to ameliorate symptoms [8], reduce hospital admissions [9] and improve functional capacity, which translate into improved QoL [8,10–12]. Traditional approaches to exercise rehabilitation have largely focussed on aerobic-based training given its ability to increase aerobic capacity (VO<sub>2peak</sub>) [13–15]. However, it is now accepted that exercise intolerance in CHF is not exclusively due to central cardiovascular factors and consequently, clinicians are moving beyond a centrally focussed treatment approach. Specifically, the "muscle hypothesis" argues that abnormalities in peripheral muscle tissue initiate deleterious feedback loops and become drivers for disease progression [16]. Adding to the fact that muscle mass is strongly correlated with  $VO_{2peak}$  [17,18] it has been argued that targeting muscle dysfunction may interrupt these maladaptive feedback loops and improve exercise tolerance [19].

Resistance training (RT) is normally employed for conditioning skeletal muscle tissue however, it was largely overlooked for patients with CHF prior to 1990's due to concerns that high cardiac afterload

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Corresponding author at: Institute of Sport, Exercise and Active Living (ISEAL), Victoria University, PO Box 14428, Melbourne, VIC 8001, Australia.
 *E-mail addresses:* Catherine.giuliano@vu.edu.au (C. Giuliano),

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may adversely affect left ventricular remodelling [8,20]. More recently, modern methods of hemodynamic measurement have allayed these concerns by confirming the integrity of the left ventricle during RT [12,21]. With confirmation of safety and acknowledgment of the wider health and fitness benefits, RT is now supported in clinical practice guidelines for people with cardiovascular disease [22]. There are however, several unresolved limitations to these guidelines, which continue to impact on clinical decision making.

Firstly is the question of applicability of current best practice guidelines to patients with CHF. The joint council Scientific Statement from the American Heart Association recommends RT for individuals with and without cardiovascular disease [22]. The guideline presents a consensus of evidence supporting the safety and efficacy of RT through large randomised controlled trials and metaanalyses. However, these data are largely derived from patients with cardiovascular diseases other than CHF, or in patients with few comorbidities or risk factors. In specific reference to CHF, the guidelines are based on only a small number of individual studies [23,24]. The precision of estimates of effects derived from such studies is limited and authors acknowledged the need for further evidence. The consequences of overly generalised guidelines for cardiovascular disease is particularly problematic in CHF, since it is the end stage of other cardiovascular conditions and as such, patients often suffer from multi-organ and co-morbid disease which can further challenge management. For instance, Havranek et al. [25]. reported an incidence of diabetes and chronic obstructive pulmonary disease of 40% and 33%, respectively, in elderly patients with CHF.

Secondly, patients with CHF are generally older than those with other cardiovascular conditions, yet this age discrepancy is largely unaddressed in these guidelines. The Framingham Heart study reported a mean age of diagnosis of 76.4 years for CHF [26], compared to 56 or 65 years for the median age of first myocardial infarction, for men and women respectively [27]. Patients with CHF, particularly those who are elderly, are a heterogeneous group and differ significantly from patients with other cardiovascular diseases. The complexity of the illness merits exclusive exercise recommendations for treatment. It is for this reason, that explicit medical guidelines exist for patients with CHF which pay specific attention to the management of comorbidities, as well as issues related to older age [28].

Finally, the focus for cardiac rehabilitation remains heavily on aerobic or centrally focussed training and limited evidence exists to support RT as an effective standalone therapy. It was previously reported that RT has a smaller effect compared to aerobic training in increasing peak VO<sub>2</sub> in patients with CHF [29], however RT produces greater improvements in skeletal muscle strength and endurance [30]. The American Heart Association acknowledges the potential benefits of RT for cardiovascular health, weight management and prevention of disability and falls, however, given the extensive benefits of aerobic training, RT was not recommended to be used as its substitute [22]. Some clinicians and researchers have argued that many patients have insufficient capacity to tolerate aerobic exercise, such as those who are elderly or have more advanced CHF and that RT may be a suitable alternative for these patients [31–33].

Systematic reviews and meta-analysis are the reference standard for developing clinical practice guidelines because of their methodological rigour and assessment of potential bias. To our knowledge only one meta-analysis has analysed the effects of RT versus usual care in patients with CHF [34], however this study did not analyse muscular strength. Therefore, the purpose of this meta-analysis was to systematically review randomised controlled trials (including quasi-randomised designs) and meta-analyse the effects of RT, as a single intervention, on muscle strength, aerobic capacity and QoL in patients with CHF.

#### 2. Methods

#### 2.1. Search strategy

With the support from a clinical librarian, we developed search strategies to identify controlled trials of RT in patients with CHF. Specifically, we focussed on the effect of RT on muscle strength (1 repetition maximum, 1RM, and/or peak isokinetic torque), aerobic capacity (measured by VO<sub>2</sub> peak and/or 6 min walk distance [6MWD]), and QoL measured using the Minnesota Living with Heart Failure questionnaire. We searched CINAHL, Medline, EMBASE, and Cochrane databases up to 10th July, 2016. In brief, the search strategy combined terms related to the population (eg, heart failure, cardiomyopathy, CHF) with terms for the intervention (eg, resistance training, strength training, circuit training) and the outcomes (eg, QoL, VO<sub>2peak</sub>, muscle strength, aerobic capacity). The full electronic search strategy for Medline is presented in Appendix 1. Next, we hand searched the reference lists of retrieved papers to identify additional relevant studies. Unpublished studies or eligible abstracts (i.e. from conferences and research meetings) that did not have full text available were not included.

#### 2.2. Eligibility criteria

The inclusion criteria for studies were: (i) controlled trials (including quasirandomised design); (ii) adult participants > 18 years with CHF, where a diagnosis was based on clinical signs or left ventricular ejection fraction less than 40%; (iii) intervention of interest was progressive RT, and included regimes designed for targeted muscle training, or those in which high central cardiovascular strain or aerobic stimulus was specifically avoided; (iv) the comparison group was a non-exercise control group (i.e. studies comparing RT to another mode of exercise were excluded); and (v) the outcome of interest was aerobic capacity measured using the 6 min walk distance (6MWD), and/or  $VO_{2peak}$ . QoL measured using the Minnesota Living with Heart Failure Questionnaire; and/or muscle strength measured using 1RM and/or peak isokinetic torque measurements (Fig. 1). In the case of suspected duplication of data across publications, authors were contacted for confirmation and only the largest study was included.

#### 2.3. Data extraction

CG and AK extracted the data from the included studies and IL resolved discrepancies. The following data were extracted: (i) the characteristics of the participants in the control and intervention group i.e. sample size, mean (standard deviation) age, sex, New York Heart Association Class (NYHA), ejection fraction (%), mean height (meters) and mean

#### Participants

- Adults with Chronic Heart Failure
- Diagnosis based on clinical signs or left ventricular ejection fraction <40%</li>

#### Intervention

 Progressive resistance exercise training, including circuit, or other modified strength training regimes

#### Comparison

Control group (i.e. not another mode of exercise)

#### **Outcome measures**

- Aerobic capacity
  - o 6 Minute Walk Distance
  - VO<sub>2 peak</sub>
- Quality of Life
  - Minnesota Living with Heart Failure Questionnaire
  - Muscle Strength
    - 1 Repetition Maximum (RM)
      Book Looking the Torong and the Second Se
    - Peak Isokinetic Torque measurements

#### **Study Design**

Controlled trials (including quasi-randomised)

Fig. 1. Eligibility criteria for study inclusion.

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