Eccentric cycling: A promising modality for patients with chronic heart failure.

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Abstract

Introduction

Chronic heart failure (CHF) is characterized by dyspnea and poor exercise tolerance, which decreases aerobic capacity ($\dot{V}O_2$peak), a measure strongly correlated with quality of life and mortality. In healthy populations, eccentric (ECC) cycling can be performed at a lower oxygen demand for matched workload, compared to concentric (CON) cycling, but few studies have previously investigated ECC cycling in CHF. We hypothesized that, when matched for external workload (Watts), an ECC cycling bout would be performed at a lower cardiorespiratory load ($\dot{V}O_2$) than CON in patients with CHF.

Methods

Eleven CHF patients (10 males) with impaired left ventricular systolic function (ejection fraction 31±12%) completed a CON $\dot{V}O_2$peak test, with the subsequent ECC and CON protocols set at 70% of individual maximal CON power (Watts). Oxygen consumption ($\dot{V}O_2$), respiratory exchange ratio (RER), minute ventilation ($\dot{V}_E$), heart rate (HR) and rate pressure product (RPP) were compared between conditions.

Results

ECC was performed at a lower $\dot{V}O_2$ (12.3±1.3 vs. 14.1±0.8 mL.kg^{-1}min^{-1}, P=0.01), RER (0.92±0.02 vs. 0.96±0.01, P=0.01) and $\dot{V}_E$ (36.5±4.4 vs. 40.2±2.0 L/min, P=0.04) in comparison to CON, despite both conditions being performed at matched workloads. Heart rate (101±5 vs. 96±1 bpm; P=0.06) and RPP (13,539±788 vs. 11,911±227 bpm.mmHg^{-1}, P=0.15) were not significantly different between conditions.

Conclusion

When matched for external workload, ECC cycling can be performed with a lower oxygen demand than CON in patients with CHF. Eccentric cycling is a promising modality for cardiac rehabilitation in severely deconditioned patients with CHF.

Keywords: exercise, cardiac rehabilitation, oxygen uptake, exercise rehabilitation.

Introduction

Chronic heart failure (CHF) is a major global health burden (28). By 2030, the prevalence of CHF is expected to increase a further 23% due to rising levels of obesity and diabetes, alongside improved survival following myocardial infarction (19, 29). Hallmark symptoms of CHF are dyspnea and fatigue on exertion (7), leading to impaired functional independence, compromised quality of life and increased morbidity and mortality (32).

It is well established that peripheral abnormalities represent a locus of fatigue in CHF. The sequelae of CHF involving sympathetic nervous system activation, increased inflammatory cytokine release and excessive peripheral vasoconstriction (21), are associated with a generalized skeletal muscle myopathy, which worsens as the disease progresses (3). First conceptualized in 1996 by Coats et al. (8), the ‘muscle hypothesis’ proposes that the activation of skeletal muscle metaboreceptors may underpin exertional dyspnea and fatigue, and by way of a feedback loop, contribute to deteriorating left ventricular function. This creates a vicious cycle whereby worsening exercise intolerance and subsequent deconditioning induce further exacerbation of the condition.

However, such abnormalities in skeletal muscle function and blood flow are amenable to exercise-mediated improvement (10, 18, 24, 25). Exercise training has shown to increase aerobic capacity ($\dot{V}O_2$peak) in patients with CHF (13, 15, 31), a significant clinical finding given that this measure is a strong prognostic indicator (9, 26). Exercise-based rehabilitation programs are now an established component of CHF management worldwide, decreasing hospitalizations, increasing health-related quality of life and possibly reducing long-term mortality (31).

Conventionally, exercise training for patients with CHF has utilized concentric exercise such as cycling, in which prime movers (e.g. knee extensors) shorten in pedalling. However, it can be challenging to prescribe concentric cycling (CON) at an intensity sufficient to induce peripheral adaptations, without causing dyspnea and fatigue in patients with more severe CHF. An exercise modality that enables a greater localized stimulus to the muscle, without increased cardiovascular demand, may provide an alternative pathway to attenuate skeletal muscle abnormalities in CHF.

Eccentric cycling (ECC) possesses unique characteristics that differ from CON, making it a potentially efficacious and clinically relevant alternative for CHF patients. In healthy young males, at the same mechanical intensity (Watts), metabolic intensity ($\dot{V}O_2$) is significantly lower when cycling eccentrically versus concentrically (36). The mechanisms underpinning this phenomenon are not fully understood, but are likely the result of complex molecular events resulting in less adenosine triphosphate (ATP) usage during ECC versus CON exercise (20, 33).

As skeletal muscle has been identified as a key locus of exercise intolerance in patients with CHF (34, 35), ECC may enable exercise to be performed at higher mechanical intensities resulting in clinically important peripheral adaptations, without eliciting significant symptoms. However, there is a paucity of literature comparing the acute effects of ECC and CON cycling in patients with CHF, particularly studies in which the intensity of the sessions is well matched. The aim of this study was to compare, in patients with CHF, the oxygen demand associated with ECC and CON cycling performed at matched workloads. We hypothesized that, when matched for power output (W), patients with CHF would be able to perform an ECC cycling bout at a lower $\dot{V}O_2$ in comparison to CON.

Methods

Participants

Eleven participants with CHF NYHA class I to III with a reduced left ventricular systolic function (ejection fraction <45%) who provided written informed consent were recruited from Fiona Stanley Hospital. Ethics approval for the study was provided by the Royal Perth Hospital Human Research Ethics Committee (HREC 14-160). Medical screening, performed by a cardiologist, occurred before participants were accepted into the study. Participants were excluded from the study if they met any of the following criteria: resting hypertension (>165/95 mmHg), severe obstructive aortic valve stenosis, severe heart rhythm disorder excluding safe participation in exercise, severe pulmonary hypertension (>70 mmHg), venous thromboembolic history within the past three months, musculoskeletal comorbidity limiting functional capacity beyond the CHF itself or inability to provide informed consent. As this was a trial of patients undergoing routine medical therapy, heart failure medications did not constitute exclusion. There were no changes in medication regimens or episodes of heart failure decompensation during the course of the study.

Experimental design

Participants performed a medically supervised graded exercise test (GXT) on a conventional electronically braked recumbent cycle ergometer (Corival, Lode BV, Groningen, The Netherlands) with breath by breath $\dot{V}O_2$ and minute ventilation ($\dot{V}_E$) measured via indirect calorimetry (Vyntus CPX, Jaeger, CareFusion, Germany) and respiratory exchange ratio (RER) calculated automatically. Heart rate (HR) and rhythm were constantly monitored by 12-lead electrocardiogram (ECG). Stages were three minutes in duration and cycling was maintained at a cadence of 60 revolutions per minute (rpm) with workload increased by 20 W increments. Blood pressure was measured manually in the final minute of each stage and the assessment was terminated when the participant reached volitional exhaustion.

Seven days after the GXT, participants performed an ECC cycling session. To familiarise the participants with ECC cycling, each engaged in a short (three minute) familiarisation ECC cycling bout consisting of 30 s without any load, followed by one minute at 30% of W_{max} (from GXT) and then one minute aiming for 70% W_{max} and a further 30 s without any load. When HR and $\dot{V}O_2$ had returned to baseline levels, participants performed a three minute warm-up (30% of W_{max}), followed by five minutes at a workload equivalent to 70% of maximum CON workload (W) achieved during the GXT. Due to the oscillatory nature of ECC cycling, the ECC session was always conducted first with workload averaged across each 30 s period. This way, we were able to alter the workload during every 30 sec during the CON session, to match the two conditions for power output (see Figure 1). Seven days later, a CON session was performed, during which workload was matched to the ECC session. The ECC and CON sessions were performed at the same time of day to help ensure medications influenced the sessions equally.

In the current study, we matched the ECC and CON sessions based on workload, similar to our previous work by Penailillo et al. (36). Because of the limited exercise capacity of the participants in the present study, we minimized the exercise time to 5 min, but set the intensity at 70% W_{max} to compare between ECC and CON. Our pilot studies in healthy young participants showed that when eccentric cycling duration is ~ less than 5 minutes, muscle damage characterized by delayed onset muscle soreness and prolonged strength loss is minimal. Based on this observation, we surmised that 5-min eccentric cycling would not induce significant muscle soreness in our CHF cohort. The workload chosen in this study equated to ~75% VO_2peak, which is at the upper end of the range for continuous aerobic exercise prescription for patients with CVD, as recommended by the ACSM (2).

Eccentric cycling (ECC) protocol

On arrival at the lab participants were attached to a 12-lead ECG and resting HR, rhythm and BP recorded. Participants were given an explanation as to how to operate the ECC ergometer. Eccentric cycling was performed on a recumbent ergometer (Eccentric Trainer, Metitur, Ltd, Jyväskylä, Finland) with a 1.5 kW motor that powered the cranks in reverse. A target power output line was calculated for each participant and displayed on a screen. Actual power output was visually and numerically displayed on screen as a feedback mechanism for participants. Cadence was set at 40 rpm to account for the difficulty in performing higher cadence ECC cycle ergometer contractions.

A metabolic cart (Vyntus CPX, Jaeger, CareFusion, Germany) was used to measure oxygen uptake and participants performed a three minute warm up, aiming for a power output correlating to 30% W_{max} achieved during GXT. Following this, participants were instructed to increase their wattage to 70% of W_{max} for a further five minutes. Heart rate, $\dot{V}O_2$ (ml.kg.$^{-1}$.min^{1}), $\dot{V}_E$ and RER were averaged across 10 s epochs with BP recorded at 1:30 and 4:30 of the five minute protocol. This was followed by a three minute cool down during which participants were instructed to keep their legs turning without applying any resistance.

Concentric (CON) cycling protocol

One week following the ECC session, participants completed a CON session using the conventional recumbent cycle ergometer mentioned above, with resistance (W) adjusted every 30 s to match workload attained during the ECC session. Participants were instructed to cycle at 40 rpm. Identical measurements to those outlined in the ECC session were recorded.

Other measures

A visual analogue scale (VAS; 10-cm line, 0: no pain, 10: worst possible pain) was used to assess exercise muscle soreness in the quadriceps muscles pre, immediately post, 1, 24, 48 and 72 hours after each exercise session as a marker of muscle damage. Blood lactate (BLa) was measured before, immediately after and five minutes after each exercise by obtaining blood samples from the fingertip using a Lactate Pro 2 (Arkay Inc., Japan).

Statistical analyses

An *a-priori* sample size calculation was calculated from Meyer. et al. (27), using an effect size of 3.74, power of 0.8 and p = 0.01. This calculation indicated that a minimum sample size of 8 was required. All results were analysed using SPSS (Version 20.0, IBM, USA) and expressed as means ± SD. As CON workload was manipulated every 30 s in order to closely match it to the ECC workload of the previous session, average values for the final 10 s of each 30 s epoch for $\dot{V}O_2$, HR, RER and $\dot{V}_E$ were recorded. These values were averaged across each minute of the exercise session to provide an overall average for the five minute protocol. Statistical analyses for the above measures were conducted using these values. Paired, two tailed *t*-tests were used to analyse the differences in outcome measures between the two exercise protocols. For all analyses, statistical significance was set at $p \leq 0.05$.

Results

Participant characteristics

Participant characteristics are presented in Table 1. Five participants had ischemic cardiomyopathy and six had non-ischemic cardiomyopathy as their primary diagnosis. Medications remained unchanged throughout the course of the study. Each participant completed all sessions without any adverse responses.

Comparison of ECC and CON sessions

Respiratory variables

Across the exercise period, $\dot{V}O_2$ was lower (P=0.01) in ECC (12.3 ± 1.3 $ml.kg^{-1}.min^{-1}$) than CON (14.1 ± 0.8 $ml.kg^{-1}.min^{-1}$, Figure 2).

Respiratory exchange ratio (RER) was lower during ECC (0.92 ± 0.02) than CON (0.96 ± 0.01, P=0.01). Similarly, $\dot{V}_E$ was also significantly lower during ECC (36.5± 4.4 vs. 40.2±2.0 L/min, P=0.04). The average change in blood lactate (BLa) from pre to immediately post exercise was similar between conditions (1.5 ± 3.7 vs. 2.7 ± 3.8 mmol/L, P=0.46).

Hemodynamic variables

Heart rate (HR) was not statistically different during ECC (101 ± 5 bpm) and CON (96 ± 1 bpm, P=0.06). Similarly, there were no differences in mean arterial pressure (92 ± 1 vs. 89 ± 2 mmHg, P=0.34) or rate pressure product (RPP) (13,539 ± 788 vs. 11,911 ± 227 $bpm.mmHg^{-1}$, P=0.15) between conditions.

Muscle soreness

No significant difference in muscle soreness existed between ECC and CON before and immediately after exercise (0.82 ± 1.4 vs. 0.82 ± 1.3 cm). Muscle soreness was significantly higher 24 hours (3.0 ± 3.1 vs. 0.5 ± 0.9 cm, P=0.02) and 48 hours after ECC exercise compared to CON (2.1 ± 2.1 vs. 0.9 ± 0.7 cm, P=0.01), but this difference diminished 72 hours post-exercise (0.5 ± 2.0 vs. 0.0 ± 0.4 cm, P=0.38).

Discussion

The principal finding of this study is that, when matched for workload, $\dot{V}O_2$ was significantly (~13%) lower during ECC compared to CON cycling in patients with CHF. This is consistent with previous research in healthy populations reporting lower $\dot{V}O_2$ responses to ECC than CON when matched for workload (1, 11, 36). ECC did not evoke significantly higher cardiovascular demand, with similar HR, BP and RPP responses, to CON. The corollary is that, for a given $\dot{V}O_2$, higher workloads can be attained during ECC. Exercise that elicits a higher localized muscular stimulus, in the absence of increased cardiovascular demand, is a clinically relevant finding for patients with CHF in whom skeletal muscle maladaptations contribute significantly to exercise intolerance and impaired aerobic capacity (14).

Some previous studies have compared ECC and CON in clinical populations (4, 5, 17, 27, 38, 40). These studies are broadly consistent with our data, in that they report higher power outputs during ECC. Besson et al. (4) concluded that ECC was a safe alternative to CON in CHF, inducing functional improvements in 6 min walk time following a seven week ECC training program. Using the same protocol, the group conducted a follow up study concluding that ECC induced similar improvements in maximal capacity and superior strength (triceps surae) increases compared to CON (5). However, in both studies, workload (W) was subjectively matched between conditions. Theodorou et al. (40) assessed the effect of ECC exercise in participants with CHF via stair descending and ascending exercise. Eccentric and isometric torque was reported to be greater in the ascending group, with concentric torque similar between conditions. Although, the aforementioned studies used a between-subjects design and individual differences may partially explain the results. The present study is therefore the first, to our knowledge, to closely match intensity between conditions and use a within-subjects design, allowing valid comparisons to be made between the acute responses to ECC and CON cycling in individuals with CHF.

In addition to a lower $\dot{V}O_2$ response, we also observed significantly lower $\dot{V}_E$ and RER values during ECC. These results indicate that, when matched for workload, ECC can be performed with a lower respiratory demand compared to CON. One of the mechanisms that may be responsible for the lower oxygen demand involves actin-myosin cross-bridge cycling. During ECC contractions some cross-bridges are forcibly detached, allowing ATP to be stored, thereby lowering metabolic cost (33). Achieving a similar exercise workload with a significantly lower oxygen demand is a clinically relevant and novel finding for CHF patients, who commonly experience dyspnea, impaired skeletal muscle function and exercise intolerance.

We reported a slightly increased HR during the ECC bout (~5 bpm, not statistically significant). This is in contrast to two previous studies in healthy individuals, where a lower hemodynamic burden (e.g. HR, BP) was reported during ECC compared to CON exercise (11, 36). We speculate that our findings reflect the unfamiliar ECC cycling stimulus, which our previous work shows can potentially exaggerate HR response, and that HR during ECC cycling decreases with repeated exposures (36). Previous work by Penailillo et al. (36)

indicated that the HR response to an initial bout of ECC exercise is exaggerated, with subsequent bouts of ECC at identical workloads eliciting a 12% lower HR response. The mechanisms underlying this are currently not well understood, however the authors speculated that this may be due to elevated metabolic stress or cycling efficiency experienced during an initial ECC session. Meyer et al. (27) examined coronary artery disease patients with preserved ventricular function and found HR during ECC was consistently higher than during CON across a 20-min protocol following 5 and 8 weeks of a training program. In contrast, significantly lower HRs during ECC were recorded by Besson et al. (4) in ECC trained patients with CHF. In a similar population, who also underwent a training program, Theodorou et al. (40) also reported lower HRs in the descending stair group following 6 weeks of training, although no statistical analysis was provided. However, the subjective quantification of workload in these studies complicates interpretation of the results. In the present study, HR responses during ECC were not significantly different compared to CON at matched workloads. This may be related to the medication regimes of our participants, which attenuate HR and BP responses to exercise. Additionally, the difference between ECC and CON HR responses has been demonstrated to be intensity-dependent, with HR during concentric exercise increasing more steeply with increasing workload (11). It is therefore possible that the workload performed in this study was too light to reveal significant differences in HR between the two conditions. Similarly, BP and RPP responses did not significantly differ between the conditions. Given that RPP is an index of myocardial oxygen demand (16), this finding has important implications and indicates that ECC exercise can be performed with a similar hemodynamic response to CON exercise in patients with CHF.

Average levels of BLa were higher following CON, although this did not reach statistical significance. These results are consistent with Perry et al. (37) and Dufour et al. (11) who reported that ECC BLa did not accumulate in healthy populations until participants had reached higher intensities (300 W) of cycling. Due to the low aerobic capacity in our participants (in comparison to healthy populations), average power output did not exceed 90W during the exercise conditions. The average absolute (pre/post) change in BLa was therefore small but, importantly, was not higher under the ECC condition.

Muscle soreness was significantly higher 24 and 48 hours after ECC compared to CON, despite the fact that we matched cadence at 40 rpm for both conditions, as ECC is better tolerated at slower speeds (6). These findings concur with those of Penailillo et al. (36) and Elmer et al. (12) Although eccentric contractions demonstrate mechanical efficiency through recruitment of fewer muscle fibers for a given level of tension (22, 39), increased muscle soreness occurs due to connective tissue damage and inflammation (23). Only responses to a single bout of ECC and CON were investigated in this study and we were therefore unable to examine the repeated bout effect, whereby muscle soreness decreases significantly following subsequent ECC bouts (30).

Several limitations of the present study are germane. Due to the highly specific nature of our sample, our results cannot necessarily be extrapolated to all patients with cardiac-related conditions. Also, although several females underwent the screening process, only one satisfied the inclusion criteria. Thus, these results may not necessarily translate to females. The order of the exercise sessions was unable to be randomized because we needed to carefully assess ECC responses in order to match subsequent CON sessions. However, our approach did allow us to match the conditions for power output, allowing valid comparisons to be made.

The present study investigated the responses to ECC and CON. Currently, this form of exercise requires relatively expensive ECC ergometers, which may be a barrier to its uptake for many cardiac rehabilitation programs. However, cycling is only one form of ECC exercise. Walking down hill, controlled lowering into a chair or lowering weights are all functional eccentric based movements requiring little expense while taking advantage of the unique properties of ECC contractions. Future studies should investigate if our promising results related to ECC are also applicable to these more accessible exercise options.

In conclusion, this study has confirmed that, when matched for workload, ECC is performed at a lower oxygen demand in comparison to CON in patients with CHF. Furthermore, this can be attained with a similar hemodynamic demand. These findings suggest that greater external workloads may be achieved eccentrically, for a given oxygen demand thereby creating a foundation for further research. As functional capacity is severely restricted in patients with CHF, ECC exercise has potential to enhance much needed peripheral adaptations and functional capacity.

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Conflict of Interest

The results of this study do not constitute endorsement by the American College of Sports Medicine. The authors also wish to declare that the results of this study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

Figure legend

Figure 1: Power outputs (W) during the 5 minute exercise protocol in the ECC and CON conditions.

Figure 2: Difference in power output (W), $\dot{V}O_2$ (ml.kg^{-1}.min^{-1}), RER (ml.kg^{-1}.min^{-1}), and $\dot{V}_E$ (L/min) between ECC and CON. Data are expressed as a percent (%) of ECC, illustrating a significantly higher power output (W), with a lower $\dot{V}O_{2,}$ RER and $\dot{V}_E$ during the ECC condition compared to the CON session.

* P<0.01, # P<0.05

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