Effect of aerobic and resistance exercise on central hemodynamic responses in severe chronic heart failure

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Cheetham, Craig, Daniel Green, Julie Collis, Lawrence Dembo, and Gerard O’Driscoll. Effect of aerobic and resistance exercise on central hemodynamic responses in severe chronic heart failure. J Appl Physiol 93: 175–180, 2002; 10.1152/japplphysiol.01240.2001.—Exercise is now considered an important component of management in chronic heart failure (CHF), but little is known about central hemodynamic changes that occur during different exercise modalities in these patients. Seventeen patients (ejection fraction 25 ± 2%) undertook brachial artery and right heart catheterization and oxygen consumption assessment at rest, during submaximal and peak cycling (Cyc), and during submaximal upper and lower limb resistance exercise. Cardiac output (CO) increased relative to baseline during peak Cyc (P < 0.05) but did not change during submaximal Cyc or upper or lower limb exercise. Heart rate (HR) was lowest during upper limb exercise and progressively increased during lower limb exercise, submaximal Cyc and peak Cyc, with significant differences between each of these (P < 0.01). Conversely, stroke volume (SV) decreased during submaximal Cyc and lower limb exercise and was lower during peak and submaximal Cyc and lower limb exercise than during upper limb exercise (P < 0.05). CHF patients are dependent on increases in HR to increase CO during exercise when SV may decline. Resistance exercise, performed at appropriate intensity, induces a similar hemodynamic burden to aerobic exercise in patients with CHF.

cardiac output; right heart catheterization; stroke volume; heart rate; pulmonary artery wedge pressure

Patients with chronic heart failure (CHF) exhibit impaired exercise tolerance that limits their functional capacity and quality of life. Recent studies suggest that peak exercise oxygen uptake (VO2peak), a measure of cardiopulmonary exercise capacity, strongly predicts prognosis in CHF, exhibiting a higher correlation with mortality than clinical indexes, including pulmonary artery wedge pressure (PAWP) and left ventricular (LV) ejection fraction (15, 19). In addition, improvement in VO2peak is associated with enhanced survival in patients awaiting cardiac transplantation (23).

Although central hemodynamic abnormalities initiate and underlie the disease process, measures of cardiac function correlate poorly with exercise capacity in patients with CHF (19, 23). A number of studies, which have reported skeletal muscle atrophy, changes in fiber type and bioenergetics consistent with anaerobic metabolism, and impaired skeletal muscle blood flow, suggest that peripheral factors may impair oxygen transport and utilization and limit exercise performance in CHF (8, 18). The similarity between these peripheral abnormalities and those that characterize prolonged inactivity or bed rest encouraged initial studies of the effect of exercise training in CHF (2, 6, 7, 11, 24).

It is now well established that a variety of exercise prescriptions can improve VO2peak and other measures of exercise tolerance, reverse skeletal muscle histochemical abnormalities, enhance nutritive blood flow, and possibly improve quality of life and clinical outcome in patients with CHF (3, 5). However, the majority of training studies have used aerobic modalities, which improve cardiorespiratory fitness but are not specifically targeted at the skeletal muscle. Because skeletal muscle abnormalities are an important limitation to exercise tolerance in heart failure (18), and because muscular strength impacts on the capacity to perform tasks of daily living, our laboratory recently examined the effects of an exercise training program designed to combine aerobic cardiorespiratory exercise with muscular resistance training (13, 14). The results of these studies indicate that incorporation of resistance exercise modalities that specifically target the peripheral limitations to exercise tolerance evident in patients with CHF improves cardiorespiratory fitness, skeletal muscle strength, and vascular function.

Despite this promising evidence regarding the benefit of resistance exercise in patients with CHF, surprisingly little is known about the central hemodynamic changes that occur during exercise in severe LV dysfunction (21). Because it is important, in terms of appropriate prescription of exercise programs, to establish the hemodynamic burden associated with different exercise modalities, this study investigated the...
relative effects of typical, clinically relevant aerobic and weight resistance exercise on central hemodynamics.

METHODS

Subjects and screening measures. Patients were recruited from the Advanced Heart Failure Service and Cardiac Transplant Unit at Royal Perth Hospital. Seventeen subjects [16 men, 1 woman, age 57 ± 3 (SE) yr, weight 79 ± 3 kg, body mass index 26 ± 1, \( V_{\text{O}2\text{peak}} \) 17.5 ± 0.9 ml·kg\(^{-1}\)·min\(^{-1}\)] with severe heart failure (12 ischemic, 4 idiopathic, 1 viral etiology), who were in New York Heart Association class III or IV, with LV ejection fraction of 25 ± 2% (radionuclide ventriculography) were recruited. Patients were screened via medical history and physical examination and hematological and biochemical profile, including measurement of serum electrolytes, urea and creatinine, uric acid, liver function, and serum lipids. The following were excluded: smokers, those with renal impairment or proteinuria, those with hepatic impairment, goit, or hyperuricemia, those with hypercholesterolemia (total cholesterol >6.0 mmol/l), or those with hypertension (blood pressure >160/90 mmHg while on their usual medications, listed below. In addition, a preliminary \( V_{\text{O}2\text{peak}} \) test was performed on a treadmill ergometer to assess functional capacity, and patients with preserved exercise capacity (i.e., \( V_{\text{O}2\text{peak}} \) >25 ml·kg\(^{-1}\)·min\(^{-1}\)) or orthopedic limitations to performance were excluded.

Patients were optimized on medical therapy and clinically stable for 3 mo before enrollment. There were no signs of fluid overload (edema, elevated jugular venous pressure, S\(_3\), crackles) at the time of study. Patients were receiving typical heart failure medications: 15 patients were taking angiotensin-converting enzyme inhibitors, 2 an angiotensin II type 1 receptor antagonist, 17 a thiazide or loop diuretic, 5 spironolactone, 13 digoxin, 10 a β-blocking drug (7 carvedilol, 2 sotalol, 1 atenolol), 8 a long-acting nitrate vasodilator, 5 amiodarone, 9 aspirin, 7 warfarin, and 10 lipid-lowering therapy. Medications were not altered in any patient during the course of the trial. The study protocol was approved by Royal Perth Hospital Ethics Committee, and subjects gave written, informed consent.

Study design. Subjects attended the cardiac catheterization laboratory on one occasion after a 6-h fast. Right heart catheterization was performed by using the right internal jugular approach, under fluoroscopic control. After placement of a 9-Fr sheath, an 8.5-Fr continuous cardiac output (CO), oximetric pulmonary artery catheter (model 777HF8, Baxter, Irvine, CA) was inserted, allowing continuous monitoring (Compact, Datex Engstrom, Helsinki, Finland) of pressure in the right atrium [i.e., central venous pressure (CVP)] and pulmonary artery (PAP). Via inflation of a distal balloon, PAWP, an index of left heart preload, was intermittently determined at rest and during each exercise modality. Mixed venous oxygen saturation (in %) was continuously recorded by fiber-optic reflectance spectrophotometry in the pulmonary artery (Vigilance, Baxter), while a pulse oximeter (Compact module, Datex Engstrom) attached to a resting index finger was used to similarly monitor arterial oxygen saturation (in %). A continuous CO measurement device (Vigilance, Baxter), which relies on the principle of thermal filament thermocoulomter, monitored CO in 20-s epochs. Stroke volume (SV) was derived from CO and heart rate (HR). Patients were monitored continuously with an electrocardiograph. Systemic vascular resistance (SVR) was derived from the equation [mean arterial pressure (MAP) – mean CVP]/CO, LV stroke work index (LVSWI) from (MAP × SV × 0.01360), and rate-pressure product (RPP) from [systolic blood pressure (SBP) × HR]. A 21-gauge cannula (model RA-04020, Arrow, Reading, PA) was also placed in the brachial artery of the nondominant arm for the continuous monitoring of arterial pressure waveforms from which SBP, diastolic blood pressure (DBP), and MAP were recorded. All data were streamed from the Datex, Vigilance, and arterial pressure monitors into a data-acquisition system (Powerlab, ADInstruments, Castle Hill, Australia) at 40 Hz and displayed in real time.

Experimental procedures. After the brachial artery and right heart catheterization described above, subjects were placed on a bed in a semirecumbent posture at a trunk-to-lower limb angle of 45°. Oxygen consumption (\( V_{\text{O}2} \)) and hemodynamic variables were then assessed at rest, during submaximal upper and lower limb weight resistance exercise, and during submaximal and peak cycling (Cyc) exercise. Initially, patients rested for 30 min while \( V_{\text{O}2\text{peak}} \) was continuously measured by using mass flow ventilometry and simultaneous mixing chamber analysis of expired gas fractions (Vmax, Sensormedics, Yorba Linda, CA). Gas analyzers and flow probes were calibrated before each test. At the end of this 30-min baseline period, a custom-made portable bilateral leg press device was positioned at the foot of the bed, and subjects were required to perform 100 s of leg press exercise at 40% of their predetermined maximal voluntary contractile (MVC) strength, with one contraction every 4 s. This was followed by a 20-min resting phase during which hemodynamic data returned to baseline. They then performed 100 s of biceps curl exercise, at an intensity of 40% MVC, using their preferred limb, at a rate of one contraction cycle per 4 s. A further 20-min rest phase then ensued for restoration to baseline, followed by incremental recumbent exercise using a cycle ergometer (model 881, Monark, Varberg, Sweden) mounted at the base of the bed. The test began at 20 W, with 20-W increments every 3 min until volitional exhaustion with the subjects instructed to maintain a cadence of 60 rpm. All hemodynamic and gas-analysis variables were continuously monitored throughout each exercise modality, except PAWP, which was recorded twice under steady-state conditions for each modality. PAWP were recorded at end expiration. Waveforms were assessed by two independent observers, blinded to the subject identity and experimental condition.

Analysis of data. At baseline and during each exercise modality, data were averaged over 20-s epochs. The average of the final two of these epochs was calculated to represent steady-state responses to each exercise modality. Peak exercise data for each individual during the cycle ergometer test were calculated from the final two epochs preceding termination of the test, regardless of the total duration of exercise performed. One-way ANOVA was performed with SPSS to determine the effect of exercise modality on each parameter, whereas two-way ANOVA was used to determine the effect of each exercise modality, in patients treated and not treated with β-blockade. Post hoc t-tests were performed to determine significance of differences between each modality and between those treated and not treated with β-blocking medication. Pearson’s product-moment correlation was used to determine the strength of relationship between selected variables. Data are expressed as means ± SE, and \( P < 0.05 \) was considered significant.

RESULTS

All 17 patients completed the upper and lower limb exercise and the first 3 min of cycle ergometer exercise. No adverse symptoms, significant arrhythmias, or ST segment abnormalities were witnessed during or after

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any test. Resting baseline data and responses to each exercise modality are presented in Table 1. Submaximal Cyc and lower limb and upper limb exercise were performed at 52 ± 4, 39 ± 3, and 25 ± 2% of the preliminary treadmill VO2peak, respectively.

Effect of exercise modalities on hemodynamic variables. ANOVA indicated a significant effect of exercise modality on CO (P < 0.05); post hoc tests revealed that CO increased relative to baseline during peak Cyc (P < 0.05) but did not significantly change during submaximal Cyc or upper limb or lower limb exercise. CO during peak Cyc was significantly higher than that during upper limb and lower limb exercise (P < 0.01). Exercise modality significantly influenced HR, VO2, RPP, and MAP data (all P < 0.01, ANOVA), with differences detected by post hoc tests for all modalities of exercise compared with baseline levels for each variable (P < 0.01). Exercise modality did not influence SVR. Exercise HR was lowest during upper limb exercise and increased, in the following order, during lower limb exercise, submaximal Cyc, and peak Cyc, with significant differences between each of these (P < 0.01; Fig. 1).

SV was significantly influenced by exercise modality (P < 0.01, ANOVA); relative to baseline, SV decreased during submaximal Cyc and lower limb exercise (both P < 0.05), but this decrease did not reach significance during peak Cyc (P = 0.054; Fig. 1). Comparison between modalities revealed lower SV during peak and submaximal Cyc and lower limb exercise than during upper limb exercise (all P < 0.05), with no difference between either submaximal or peak Cyc and lower limb exercise. When data from all modalities were pooled, HR and SV revealed a significant inverse correlation (r = −0.62, P < 0.001; Fig. 2).

ANOVA indicated an effect of exercise modality on mean pulmonary arterial pressure (MPAP), PAWP, and CVP. Post hoc tests indicated that each of these variables increased during all modalities relative to baseline (P < 0.05), with the exception of upper limb
exercise. During submaximal and peak Cyc and lower limb exercise, MPAP, PAWP, CVP, and RPP were higher than during upper limb exercise (all \( P < 0.01 \)). LVSWI was also affected by exercise modality (\( P < 0.05 \), ANOVA), with reduction during lower limb and submaximal Cyc (\( P < 0.05 \)), but no change during upper limb or peak Cyc exercise, relative to baseline data. LVSWI was also lower during submaximal Cyc and lower limb compared with upper limb exercise (\( P < 0.01 \)).

**Effect of \( \beta \)-blockade on hemodynamic variable responses to exercise modalities.** Comparisons between selected data are presented according to \( \beta \)-blockade status in Table 2; 10 subjects were treated with \( \beta \)-blocking medication (see \textit{METHODS}), and 7 were untreated. Although HR was generally lower and SV higher at baseline in the group receiving \( \beta \)-blocking medication and, on the average, HR was lower and SV, MPAP, and PAWP higher during exercise, especially at peak Cyc, in those on \( \beta \)-blockade, none of these differences was significant, and medication status did not significantly influence the response of any variable to the exercise modalities (2-way ANOVA).

**DISCUSSION**

The present study describes changes that occur in central hemodynamic variables in response to different, clinically relevant modalities of exercise. Our laboratory has previously established that combined aerobic and resistance exercise training induces physiological adaptations that favor improvement in exercise tolerance and \( V_{O2\text{peak}} \) (13, 14). Specifically, these studies demonstrated that the addition of resistance-type activity to aerobic exercise improved skeletal muscle strength, body composition, aerobic capacity, and vascular function in patients with severe heart failure. The addition of resistance exercise to more traditionally utilized aerobic-type training may, therefore, help target the peripheral limitations to exercise that characterize these patients while simultaneously providing a stimulus to cardiopulmonary adaptations. In these studies, resistance exercise was initially prescribed at an intensity of 40% MVC with subsequent progression to 60% over an 8-wk period. Although the selection of these intensities was based on our laboratory’s clinical experience of exercise tolerance in these severely debilitated patients, precedents in the literature regarding safety of resistance exercise intensities in heart failure are scant (21). The present study, therefore, determined the relative hemodynamic burden associated with traditionally prescribed aerobic exercise, compared with clinically relevant upper and lower limb resistance exercise. The results indicate that submaximal and maximal aerobic exercise induce greater hemodynamic burden than resistance exercise performed at clinically relevant intensities.

Changes in CO to all exercise modalities were relatively modest in the present study. In the only previous study we could find that compared resistance and aerobic exercise hemodynamic responses in CHF patients...

### Table 2. Selected hemodynamic measures during different modalities of exercise in heart failure patients: effect of treatment with \( \beta \)-blockade

| Parameter | Baseline
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<tbody>
<tr>
<td>( V_{O2} ) ml·kg(^{-1})·min(^{-1} )</td>
<td>Upper Limb (Biceps Curl)</td>
</tr>
<tr>
<td>( \beta )-Blockade</td>
<td>3.3 ± 0.2</td>
</tr>
<tr>
<td>No ( \beta )-blockade</td>
<td>3.9 ± 0.3</td>
</tr>
<tr>
<td>CO, l/min</td>
<td>( \beta )-Blockade</td>
</tr>
<tr>
<td>No ( \beta )-blockade</td>
<td>5.3 ± 0.5</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>( \beta )-Blockade</td>
</tr>
<tr>
<td>No ( \beta )-blockade</td>
<td>73 ± 3</td>
</tr>
<tr>
<td>SV, ml/beat</td>
<td>( \beta )-Blockade</td>
</tr>
<tr>
<td>No ( \beta )-blockade</td>
<td>74 ± 8</td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>( \beta )-Blockade</td>
</tr>
<tr>
<td>No ( \beta )-blockade</td>
<td>79 ± 2</td>
</tr>
<tr>
<td>MPAP, mmHg</td>
<td>( \beta )-Blockade</td>
</tr>
<tr>
<td>No ( \beta )-blockade</td>
<td>29 ± 3</td>
</tr>
<tr>
<td>PAWP, mmHg</td>
<td>( \beta )-Blockade</td>
</tr>
<tr>
<td>No ( \beta )-blockade</td>
<td>17 ± 2</td>
</tr>
<tr>
<td>CVP, mmHg</td>
<td>( \beta )-Blockade</td>
</tr>
<tr>
<td>No ( \beta )-Blockade</td>
<td>8 ± 2</td>
</tr>
<tr>
<td>SVR, dyn·s·cm(^{-5} )</td>
<td>( \beta )-Blockade</td>
</tr>
<tr>
<td>No ( \beta )-Blockade</td>
<td>1,159 ± 113</td>
</tr>
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Values are means ± SE. See text for details of significance of differences.
patients, CO measured by two-dimensional echocardiography also increased modestly, to 9.3 l/min during submaximal cycle exercise and to 6.9 l/min during submaximal leg press (17). Predictably, the CO response to exercise in CHF is dependent on the degree of LV impairment; most studies of CHF patients have revealed similar or slightly larger changes during maximal aerobic-type exercise (7, 16, 24), whereas patients with less severe LV dysfunction exhibit higher CO values (1, 9, 12). The patients recruited from the Cardiac Transplant Unit in the present study had severe CHF characterized by reduced ejection fraction and impaired V\textsubscript{0\textsubscript{2peak}}, despite maximal medical therapy. Their impaired CO responses are consistent with the findings from the present study was undertaken to compare the hemodynamic impact of exercise performed at typically prescribed and clinically relevant intensities. The hemodynamic impact of resistance exercise performed at high intensity, or during isometric exercise, in patients with severe LV dysfunction should be investigated in future studies, but in the interim we would endorse the guideline that they be avoided in high-risk cardiac patients (21). Another limitation of the present study involves exercise posture. SV is near maximal in the supine position because the effects of gravity are negated (20), and exercise posture therefore determines the magnitude of SV response. We were conscious of this in the design of the present study and specifically placed patients in a semirecumbent posture during each exercise modality, at a torso angle of 45°. Although this angle approximates that generally used in leg press and biceps curl exercise, it represents a compromise for the cycle exercise, which would normally be performed in a more upright posture. In any event, the adoption of upright posture would be associated with a lower SV at any given workload (20), thereby reinforcing our principal findings.

Conclusions. In contrast to healthy individuals, patients with severe CHF are largely dependent on increases in HR to increase CO; in the present study SV declined during exercise. Reduced contractility and maintained afterload may contribute to this observation. Despite this, resistance exercise prescribed at appropriate intensity is associated with a lower hemodynamic burden than more traditionally administered submaximal aerobic exercise and may have the added advantage of specifically targeting peripheral limitations to exercise performance which characterise CHF patients (13, 14).

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