Responses to constant work exercise in patients with chronic heart failure

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Abstract

Objective—To describe the kinetics of metabolic gas exchange at the onset and offset of low level, constant work exercise in patients with chronic heart failure.

Setting—Tertiary referral centre for cardiology.

Patients—10 patients with chronic heart failure and 10 age matched controls.

Methods—Each subject undertook maximum incremental exercise testing with metabolic gas exchange measurements, and a fixed load exercise test at 25 watts with metabolic gas exchange measurements before, during, and after the test. A monoexponential curve was fitted to the data to describe the kinetics of gas exchange at onset and offset of fixed load exercise.

Outcome measures—Peak oxygen consumption; time constants of onset and offset for metabolic gas exchange variables during constant load exercise.

Results—Peak oxygen consumption (mean (SD)) was higher in controls (26.1 (4.3) v 15.3 (5.3) ml/kg/min; p < 0.001) than in heart failure patients. Oxygen consumption during steady state was the same in both groups (9.2 (1.8) ml/kg/min in controls v 8.6 (1.6) in patients). The time constant of onset was the same in each group, but the time constant of offset was longer in patients (1.29 (0.14) v 0.82 (0.07); p < 0.005). There was a relation between peak oxygen consumption and time constant of offset (R = 0.56; p < 0.001).

Conclusions—The dynamics of gas exchange at the onset of low level exercise are normal in heart failure, but the recovery is delayed. The delay is related to the reduction in exercise capacity. A patient may spend a greater portion of the day recovering from exercise, and may not begin the next bout from a position of true recovery, perhaps contributing to the sensation of fatigue. (Heart 1999;82:482–485)

Keywords: chronic heart failure; metabolic gas exchange; constant load exercise

The syndrome of chronic heart failure is characterised by reduced exercise capacity, as reflected in a reduction in peak oxygen consumption (VO2) on an incremental exercise test, and an increase in the ventilatory response to exercise, characterised by an increase in the ventilatory equivalent for carbon dioxide. These exercise abnormalities may be related to abnormal skeletal muscle behaviour.1

Steady state exercise at a fixed load elicits the same oxygen consumption/kg whether a patient has heart failure or not. The pattern of increase in oxygen consumption to a plateau when a fixed load is applied can be described by a monoexponential equation, as can the pattern of recovery to resting values at the end of the exercise. As it takes a finite time for the circulation to adjust to the exercise load, there is a gap between oxygen demand at the onset of exercise, and the matching of demand to supply in the plateau phase (fig 1). This is known as the oxygen deficit. The pay back at the end of exercise is the relative excess oxygen consumption during recovery. This is the oxygen debt.2

Previous investigators have examined the onset3 4 and offset5 6 of exercise, and found a slower rate of adjustment in patients with heart failure, but have not investigated the behaviour of metabolic gas exchange variables at the onset and offset of fixed load exercise in patients with heart failure. This is the aim of the present study.

Methods

Ethics approval was granted by the local ethics committee, and all subjects gave their informed, signed consent before participating in the study. Ten patients with chronic stable heart failure and 10 age matched controls were studied. No patient had myocardial infarction or an episode of decompensation of their heart failure in the three months preceding the study. Patients with peripheral neuropathy or other locomotor disease or pulmonary disease were excluded from study. All patients...
werereceivingangiotensinconvertingenzyme
inhibitorsanddiuretics.Noneofthecontrols
was taking regular medication.
Subjects attended on two occasions. Height
and weight was measured. On the first occasion,
a maximum incremental treadmill exercise test
was performed using the Bruce protocol.
Expired air was sampled continuously, and
metabolic gas exchange measurements were
performed (MedGraphics cardiorespiratory
diagnostic systems, CardiO2 and CPX/D sys-
tems, using BreezeEx software; Medical Graph-
ics Corp, St Paul, Minnesota, USA). The
system was calibrated before each test. The
ECG was monitored continuously, and blood
pressure measured every three minutes.
On the second visit, subjects performed
cycle ergometer (EM 840, Siemens, Erlangen,
Germany) exercise at a fixed load of 25 watts
for 10 minutes. Metabolic gas exchange data
were recorded continuously for 10 minutes
before and for 10 minutes after the exercise
test.

Table 3 Time constants for the onset and offset of exercise for carbon dioxide production
(V\textsubscript{CO\textsubscript{2}}) and ventilation (\textit{VE})

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients (n = 10)</th>
<th>Controls (n = 10)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>\textit{V\textsubscript{CO\textsubscript{2}}} onset</td>
<td>1.63 (0.81)</td>
<td>1.24 (0.90)</td>
<td>−0.41 to 1.20</td>
</tr>
<tr>
<td>\textit{V\textsubscript{CO\textsubscript{2}}} offset</td>
<td>1.75 (0.58)</td>
<td>1.07 (0.36)</td>
<td>0.23 to 1.14</td>
</tr>
<tr>
<td>\textit{VE} onset</td>
<td>2.18 (1.30)</td>
<td>1.35 (1.43)</td>
<td>−0.45 to 0.21</td>
</tr>
<tr>
<td>\textit{VE} offset</td>
<td>1.87 (0.70)</td>
<td>1.19 (0.38)</td>
<td>0.15 to 1.21</td>
</tr>
</tbody>
</table>

Values are mean (SD).
**p < 0.01, *p < 0.05.

Table 4 Correlations between time constants of onset and offset

<table>
<thead>
<tr>
<th>Variables</th>
<th>O\textsubscript{2} onset</th>
<th>CO\textsubscript{2} onset</th>
<th>\textit{VE} onset</th>
<th>O\textsubscript{2} offset</th>
<th>CO\textsubscript{2} offset</th>
</tr>
</thead>
<tbody>
<tr>
<td>O\textsubscript{2} onset</td>
<td>0.84</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CO\textsubscript{2} onset</td>
<td>0.61</td>
<td>0.91</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>\textit{VE} onset</td>
<td>0.43</td>
<td>0.59</td>
<td>0.72</td>
<td></td>
<td></td>
</tr>
<tr>
<td>O\textsubscript{2} offset</td>
<td>0.52</td>
<td>0.66</td>
<td>0.70</td>
<td>0.93</td>
<td></td>
</tr>
<tr>
<td>CO\textsubscript{2} offset</td>
<td>0.39</td>
<td>0.48</td>
<td>0.56</td>
<td>0.82</td>
<td>0.93</td>
</tr>
</tbody>
</table>

The direct correlations between onset and offset for each variable are highlighted in bold.
\textit{V\textsubscript{O\textsubscript{2}}}, expiratory minute volume.
controls. This is expected in that a given workload must require the same energy expenditure regardless of who performs it. Patients will be exercising at a greater percentage of their maximum capacity. The respiratory exchange ratio, which can be taken as an index of the metabolic cost of exercise, is greater in patients.

We also investigated the possibility that patients may take longer to achieve steady state exercise kinetics than controls, as has been reported previously. By plotting the oxygen consumption data and counting by hand, Chelinsky-Fallick et al found the oxygen deficit to be increased in heart failure. Other investigators have reported prolonged time constants of recovery from maximum exercise.

We designed our experiment to examine the dynamics of onset and offset from submaximal steady state exercise. Our hypothesis was that, perhaps as a consequence of abnormal skeletal muscle metabolism, patients may show delayed recovery from exercise compared with controls and have a greater oxygen debt.

We found no difference between patients and controls at the onset of exercise, but a prolonged recovery time at the end. As a corollary, the oxygen debt was also greater. These abnormalities are related to a reduction in peak exercise capacity, although we measured peak oxygen consumption using treadmill rather than cycle exercise.

We cannot explain why our results for the onset of exercise are not in accordance with other investigators. We were careful to choose a work load that would be below the anaerobic threshold for our patients. Work above the anaerobic threshold results in a progressive increase in $V_o_2$ during steady state exercise, and thus an overestimate of $\tau$ onset. This may account for the prolonged $\tau$ in some studies.

From the patient's perspective, the time course of recovery may be more important. A given activity requires the same expenditure of effort as for a normal person, but this is at the cost of a prolonged recovery time and an increased oxygen debt. A patient spends a greater portion of the day recovering from exercise, and may not begin the next bout from a position of true recovery, contributing to the sensation of fatigue. We have deliberately selected a group of patients with moderately severe heart failure. It will be interesting to see if the relation between prolonged recovery and exercise capacity holds true for patients with milder disease.

Appendix

CALCULATION OF TIME CONSTANTS

The increase of any variable to a plateau during stable exercise is described by the monoexponential function:

$$x(t) = x_e - (\Delta x)e^{-(t\tau_e)/\tau_a}$$

where $\tau_e$ is the time constant of onset. Similarly, the decrease of that variable from its plateau to its resting state at the end of exercise is described by the monoexponential function

$$x(t) = x_t + (x(t_e) - x_t)e^{-(t\tau_e)/\tau_g}$$; $x(t_e)$ is the end of exercise.
where \( \tau_o \) is the time constant of offset. In these formulae, \( t \) is time, and \( t_1 \) and \( t_2 \), respectively, the times at which exercise starts and finishes.

The parameters are found by fitting the formulae to the observations on the basis that individual observations are contaminated by white noise of constant standard deviation, \( \sigma \), to be determined by the fitting procedure. Briefly, if a realisation of the experiment contains \( n \) observations \((t_1, x_1), \ldots, (t_n, x_n)\), then the parameters are found by maximising the likelihood function

\[
\prod_{k=1}^{n} \frac{1}{\sqrt{2\pi}\sigma} \exp \left[ -\frac{(x_k - x(t_k))^2}{2\sigma^2} \right]
\]

or, more conveniently, by minimising the negative log likelihood function

\[
\phi = \frac{1}{2\sigma^2} \sum_{k=1}^{n} (x_k - x(t_k))^2 + n\log\sigma + \frac{n}{2} \log(2\pi)
\]

This minimisation was achieved using the Broyden’s method. The main diagonal of the inverse Hessian of \( \phi \) yields the standard errors in the estimation of the parameters.