Recovery Kinetics of Oxygen Uptake and Heart Rate in Patients With Coronary Artery Disease and Heart Failure*

Leandro Pavia, MD; Jonathan Myers, PhD; and Rusconi Cesare, MD

**Background:** Patients with congestive heart failure exhibit a prolonged period of recovery to baseline levels of oxygen consumption, but the decline of heart rate during recovery from exercise has been shown to be similar to that in healthy subjects, and the results of studies on the response of ventilation in recovery have been mixed. Patients with coronary artery disease have a reduced exercise capacity, but it is unknown whether the patterns of the decline in oxygen uptake (\(\dot{V}O_2\)), ventilation, or heart rate are similar to those in patients with heart failure.

**Methods:** We performed a cardiopulmonary exercise test with a ramping protocol in 18 healthy subjects, 18 patients with coronary artery disease, 19 patients with class A or B congestive heart failure, and 19 patients with class C congestive heart failure, according to the Weber classification. Peak oxygen uptake and the kinetics of oxygen uptake, ventilation, and heart rate were calculated and expressed as the slope of a single exponential relation between \(\dot{V}O_2\) levels and time during the first 3 min of recovery as

\[ y(\dot{V}O_2) = y_0 A e^{-\frac{x}{t}}. \]

**Results:** A difference in time of recovery of \(\dot{V}O_2\) was found only between healthy subjects and patients with more severe heart failure (class C) \((p < 0.05)\); no significant differences were observed among any of the groups in ventilation or heart rate recovery responses.

**Conclusion:** \(\dot{V}O_2\) recovery time is prolonged only in the presence of more severe heart failure. The presence and degree of heart disease has no effect on ventilation or heart rate recovery time.

*(CHEST 1999; 116:808–813)*

**Key words:** baseline oxygen consumption; congestive heart failure; exercise response; oxygen uptake

**Abbreviations:** \(\dot{V}CO_2\) = carbon dioxide output; \(\dot{V}O_2\) = oxygen uptake; \(V_E\) = minute ventilation

Patients with chronic heart failure have abnormal gas exchange and ventilatory responses to exercise, characterized by reduced peak oxygen uptake (\(\dot{V}O_2\)) levels, an earlier appearance of the ventilatory threshold, a reduced slope of the increase in \(\dot{V}O_2\) vs time, and inefficient ventilation. These abnormalities have been shown to parallel the severity of this condition.1–6 The limited cardiopulmonary reserve in these patients appears to affect not only exercise responses but also the recovery phase. In healthy subjects, the pattern of \(\dot{V}O_2\) in recovery, expressed as \(\dot{V}O_2\) recovery kinetics, is a rapid decline,7,8 and exercise training has been shown to contribute to an even faster decline.9 However, among patients with chronic heart failure, the recovery of \(\dot{V}O_2\) becomes prolonged, a response that worsens as the condition becomes more severe.10–14 In contrast, the response of heart rate in the early recovery period does not appear to be affected by the degree of exercise intolerance.11,13

Patients with coronary artery disease have reduced exercise capacity and their response to exercise is characterized by a reduced submaximal \(\dot{V}O_2\)/work rate ratio, a steeper heart rate/\(\dot{V}O_2\) relation, chest pain, and significant ST segment changes.15,16 The hemodynamic response to exercise is characterized
by a reduction in maximal cardiac output and peak heart rate. However, few data are available in regard to \( V_{O2} \) and heart rate kinetics in recovery among patients with coronary artery disease. The purpose of this study was to evaluate the rates of recovery of \( V_{O2} \), ventilation, and heart rate among patients with coronary artery disease, and to compare their responses to patients with chronic heart failure and healthy subjects.

**MATERIALS AND METHODS**

**Study Group**

Cardiopulmonary exercise data were analyzed in 76 subjects. We collected data from 18 patients with coronary artery disease, 38 patients with chronic heart failure (19 Weber class A or B, and 19 Weber class C), and 20 age-matched control subjects. Among patients with coronary artery disease, 11 had sustained myocardial infarctions, 3 had myocardial infarctions followed by coronary artery bypass grafting, 3 had bypass surgery alone, and 1 had a percutaneous transluminal coronary angioplasty after an acute myocardial infarction. In the patients with class A or B heart failure, the etiology was determined to be ischemia in 13 patients and idiopathic in 6. In class C heart failure, the etiology was determined to be ischemia in 12 patients, idiopathic in 6, and valvular disease in 1.

All patients were tested while they received their usual drug therapy, including angiotensin-converting enzyme inhibitors, diuretics, nitrates, digitals, or calcium antagonists in accordance with the prescription of the referring physician. Patients taking \( \beta \)-blockers were specifically excluded. A standard echocardiogram was performed to assess left ventricular function.

**Exercise Testing**

All patients underwent a maximal cardiopulmonary exercise test with an electromagnetically braked cycle ergometer in the upright position using a ramp protocol. The ramp rates used were 20 W/min in the control group, 20 or 15 W/min in the group of patients with coronary artery disease, and 10 W/min in the group of patients with congestive heart failure. All tests were monitored continuously with two leads, V1 and V5. Ventilatory gas exchange analysis was performed throughout exercise and for 3 min during the recovery period.

The tests were performed using the Medical Graphics Corporation CAD/Net System 2001 device (Hans Rudolph Inc.; Kansas City, MO). A two-way, low-resistance breathing valve (Hans-Rudolph) with a dead space of 90 mL was used, and expired air flow was recorded with a pneumotachometer (Medical Graphics). Before each test, the pneumotachometer was calibrated with a 3-L syringe and the gas analyzer was calibrated with a certified \( O_2/CO_2 \) mixture. \( O_2 \) and \( CO_2 \) were monitored continuously and two leads, V1 and V5. Ventilatory gas exchange analysis was performed throughout exercise and for 3 min during the recovery period.

The system computer calculated \( V_{O2} \) minute ventilation (VE), carbon dioxide output (\( V_{CO2} \)), ventilatory equivalents for \( O_2 \) and \( CO_2 \) (\( Ve/V_{O2} \) and \( Ve/V_{CO2} \), and end-tidal \( O_2 \) and \( CO_2 \) pressures. The criteria for detecting the ventilatory threshold were a systematic increase in the \( Ve/V_{O2} \) ratio without an increase in \( Ve/V_{CO2} \) ratio and a systematic increase in end-tidal \( O_2 \) pressure without a decrease in end-tidal \( CO_2 \) pressure. The constant decay of \( V_{O2} \), VE, and heart rate, expressed as the slope of a single exponential relation among \( V_{O2} \), VE, heart rate, and time during the first 3 minutes of recovery were calculated with the following formula:

\[
y = y_0 + Ae^{-\frac{x}{t}}
\]

where \( y \) was the parameter (\( V_{O2} \), VE, or heart rate, respectively), \( y_0 \) was the parameter at time zero (the beginning of the recovery phase), \( A \) and \( e \) were constants, \( x \) was the time elapsed, and \( t \) was the constant decay. Computer software was used in the calculation (Origin, version 2.5; Microcal; Northhampton, MA).

**Statistical Analysis**

The results are presented as mean ± SD. Differences between groups were assessed by analysis of variance followed by Newman-Keuls tests. Differences were considered significant at \( p < 0.05 \).

**RESULTS**

We found no significant differences in age among the groups (Table 1). \( V_{O2} \) (measured in millimeters per minute), \( V_{CO2} \) (measured in millimeters per kilogram per minute), and workload were significantly higher in the control group (\( p < 0.05 \)) than in the other groups at the ventilatory threshold and peak exercise. Peak heart rate was significantly higher in the control group than the other groups (Table 1). Significant differences also were observed in \( V_{O2} \) (measured in millimeters per kilogram per minute) between the patients with coronary artery disease and class A or B congestive heart failure vs patients with class C congestive heart failure at both the ventilatory threshold (\( p < 0.05 \)) and peak exercise (\( p < 0.05 \)).

We found no significant differences in the slope of the decline in ventilation or heart rate during the recovery phase among the study groups. The slope of recovery of oxygen consumption was more gradual in patients with class C congestive heart failure relative to the other groups (\( p < 0.05 \)) (Table 2). Figure 1 illustrates an example of \( V_{O2} \) kinetics during the recovery phase in a healthy subject, a patient with coronary artery disease, and a patient with class B and C congestive heart failure. Significant but weak negative correlations were observed between the rate of decline in \( V_{O2} \) and variables at the ventilatory threshold, including \( V_{O2} \) (measured in millimeters per minute) (\( r = -0.49 \)), \( V_{CO2} \) (measured in millimeters per kilogram per minute) (\( r = -0.42 \)) and watts (\( r = -0.46 \)) (\( p < 0.05 \) for all three variables). Negative correlations also were found between the recovery \( V_{O2} \) response and peak exercise variables, including \( V_{O2} \) (measured in millimeters per minute) (\( r = -0.60 \)), \( V_{CO2} \) (measured in millimeters per kilogram per minute) (\( r = -0.56 \)), \( V_{CO2} \) (\( r = -0.59 \)), and watts (\( r = -0.52 \); all \( p < 0.05 \)). We discovered no
significant correlation between recovery of \( \dot{V}O_2 \) and age. The recovery times of ventilation and heart rate were not significantly correlated with age or any exercise variables at the ventilatory threshold or peak exercise.

**Discussion**

The findings of the present study suggest that in patients with coronary artery disease, the rate of recovery of \( \dot{V}O_2 \) immediately after maximal exercise is not different from healthy subjects or patients with mild or moderate heart failure; only among patients with relatively severe heart failure is there a prolongation of the time required for \( \dot{V}O_2 \) to recover after exercise. The slope of the increase in \( \dot{V}O_2 \) from rest to a constant submaximal workload has been shown to be prolonged in congestive heart failure,\(^{12}\) a finding that appears to be accentuated as heart failure worsens.\(^{4}\) Our findings suggest that delayed \( \dot{V}O_2 \) responses also occur in recovery from exercise in accordance with the severity of heart failure.

The rate at which \( \dot{V}O_2 \) recovers from exercise has been used as an index of oxidative capacity in healthy subjects.\(^{24,25}\) The rate of decrease in \( \dot{V}O_2 \) has been traditionally related to the oxygen debt after exercise,\(^{26}\) which involves an initial fast component (alactacid) and a second slow component (lactacid).\(^{27}\) More recently, as the mechanisms that mediate post-exercise \( \dot{V}O_2 \) have proven more complex, the term excess postexercise oxygen consumption has been used to absolve this entity from a strict dependence on anaerobic metabolism.\(^{8}\) One factor that contributes to the delayed recovery of \( \dot{V}O_2 \) is the prolonged recovery time of the muscle phosphate/phosphocreatine ratio.\(^{28-31}\) A faster recovery time for this ratio has been demonstrated in athletes.\(^{32}\) Other factors that could delay oxygen kinetics during exercise and recovery in heart failure may involve delays in circulatory transport of oxygen to and from metabolizing tissue,\(^{33,34}\) gas exchange in pulmonary tissues,\(^{2}\) or rate of uptake by the exercising or recovering muscle tissues themselves. The importance of circulatory factors is underscored by the

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<th>Table 1—Characteristics and Exercise Responses of the Study Groups*</th>
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<td>Workload, W</td>
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<td>HR, beats/min</td>
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*Values given as mean ± SD. CAD = coronary artery disease; CHF = congestive heart failure; HR = heart rate.
†p < 0.05 vs CAD.
‡p < 0.05 vs CHF (classes A and B).
§p < 0.05 vs CHF (class C).
‖p < 0.05 vs CHF (class C).
¶p < 0.05 vs CHF (class C).

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<th>Table 2—Recovery Kinetics in Each Group*</th>
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*Values given as mean ± SD. tRec = time constant of decay. See Table 1 for other abbreviations.
†p < 0.05 vs CHF(class C).
observation that the half-time of PCr in recovery is
determined not only by the oxidative capacity of the
peripheral muscles,35,36 but also by blood flow.28,36

Central factors also may help to explain the slower
recovery of VO₂ in patients with heart failure. Ac-
cording to the Fick equation, VO₂ is the product
of cardiac output, i.e., heart rate multiplied by the stroke
volume, divided by the arteriovenous oxygen differ-
ence. During the recovery phase, VO₂ remains ele-
vated in patients with left ventricular dysfunction,
because cardiac output remains high.34,38,39 The
comparatively rapid decrease in arteriovenous oxy-
gen difference when cardiac output remains elevated38,39 suggests that VO₂ during early recovery relies
more on cardiac output than on arteriovenous oxy-
gen difference, unlike that during exercise when both variables contribute more equally to VO₂. Sev-
eral studies have demonstrated an increase in con-
tactility associated with an increase in stroke vol-
ume40–42 or an improvement in myocardial wall
motion immediately after exercise due to endoge-
nous catecholamine stimulation in healthy subjects.43

In patients with left ventricular dysfunction, signifi-
cant increases in stroke volume and ejection fraction
also have been reported during the early recovery
period.34

The pathophysiologic basis for the rapid decline in
arteriovenous oxygen difference after exercise previ-
ously observed may involve redistribution of blood
flow to nonexercising tissues secondary to sympa-
thetic-induced vasoconstriction44–46 or metabolic ac-
idosis-induced vasoconstriction during exercise.47
This phenomenon may represent a compensatory
response for an enhanced peripheral vascular tone to
maintain the systemic arterial BP in the setting of
reduced cardiac output.

Plotnick et al,48 using radionuclide angiography,
demonstrated in both healthy subjects and patients
with coronary artery disease an elevation of cardiac
output and ejection fraction during the early period
of recovery. The absolute values differed between
control subjects and patients with coronary artery
disease, but the trends paralleled one another. In our
study, the VO₂ recovery times in patients with coro-

nary artery disease did not differ from healthy

subjects.

Importantly, VO₂ kinetics during the early recov-
ery phase are considered independent of the exercise
level achieved, particularly if it was above the venti-
latory threshold49 or at > 50% of maximal exercise
capacity.13 This permitted a valid comparison be-
tween the groups in the present study, despite the
large differences in exercise capacity. The negative
correlation between exercise parameters at peak

Figure 1. Representative curves illustrating the decrease in postexercise VO₂ in a healthy subject
(control subject) (top left), a patient with coronary artery disease (CAD) (top right), a patient with class
B congestive heart failure (CHF) (bottom left), and a patient with class C CHF (bottom right).
tRec = recovery time constant decay.
exercise and at the ventilatory threshold confirms our observation that \( \dot{V}O_2 \) responses in recovery are abnormal only in the presence of a severe reduction in exercise capacity and abnormal left ventricular function.

In terms of heart rate kinetics in the early phase of recovery, we did not observe any differences among healthy subjects and our patient groups, we did not observe any significant relationships between heart rate responses in recovery and other exercise variables. This confirms the work of others,\(^{11,13}\) and suggests that the mechanisms that regulate heart rate during recovery are different from those during exercise in which increases in heart rate are the result of increases in sympathetic outflow and decreases in vagal outflow.\(^{16}\)

The kinetics of ventilation during recovery were similar in all groups, which contrasts the findings of some,\(^{10,13}\) but not all previous investigations.\(^{11}\) Two previous reports have shown that \( \dot{V}E \) recovery time is prolonged in heart failure in parallel with the degree of exercise impairment.\(^{10,13}\) Riley\(^{11}\) however, reported that \( \dot{V}E \) recovery time was actually faster in patients with heart failure compared with controls.

In summary, during the early period of recovery, the rate of decline in \( \dot{V}O_2 \) is inversely related to exercise capacity and is slowed only in the presence of class C heart failure. The rate of recovery of heart rate and ventilation is similar among healthy subjects, patients with coronary disease, and patients with heart failure. Clinically, \( \dot{V}O_2 \) kinetics during recovery from exercise appears to be an important marker of the severity of left ventricular dysfunction\(^{10–14}\) and may even have an important role in assessing prognosis in patients with congestive heart failure.\(^{14}\)

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