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# Influence of high-intensity exercise training on the ventilatory response to exercise in patients with reduced ventricular function

[Clinical Sciences: Clinical Investigations]

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## ABSTRACT^

Influence of high-intensity exercise training on the ventilatory response to exercise in patients with reduced ventricular function. *Med. Sci. Sports Exerc.,* Vol. 31, No. 7, pp. 929-937, 1999.

Background: Exercise training increases exercise capacity in patients with reduced ventricular function in part through improved skeletal muscle metabolism, but the effect training might have on abnormal ventilatory and gas exchange responses to exercise has not been clearly defined.

Methods: Twenty-five male patients with reduced ventricular function after a myocardial infarction were randomized to either a 2-month high-intensity residential exercise training program or to a control group. Before and after the study period, upright exercise testing was performed with measurements of ventilatory gas exchange, lactate, arterial blood gases, cardiac output, and pulmonary artery and wedge pressures.

Results: In the exercise group, peak [latin capital V with dot above]$O_2$ and [latin capital V with dot above]$O_2$ at the lactate threshold increased 29 and 39%, respectively, whereas no increases were observed among controls. Maximal cardiac output increased only in the exercise group (1.7 L·min$^{-1}$, $P < 0.05$), and no changes in rest or peak exercise pulmonary pressures were observed in either group. At baseline, modest inverse relationships were observed between pulmonary wedge pressure and peak [latin capital V with dot above]$O_2$ both at rest ($r = -0.56$, $P < 0.05$) and peak exercise ($r = -0.43$, $P < 0.05$). Maximal [latin capital V with dot above]E/[latin capital V with dot above]$CO_2$ was inversely related to maximal cardiac output ($r = -0.72$, $P < 0.001$). Training did not have a significant effect on these relationships. Training lowered [latin capital V with dot above]E/[latin capital V with dot above]$O_2$, heart rate, and blood lactate levels at matched work rates throughout exercise and tended to lower maximal Vd/Vt. The slope of the relationship between [latin capital V with dot above]E and [latin capital V with dot above]$CO_2$ was reduced after training in the exercise group (0.33 pre vs 0.27 post, $P < 0.01$), whereas control patients did not differ.

Conclusions: Exercise training among patients with reduced left ventricular function results in a systematic improvement in the ventilatory response to exercise. Training increased maximal cardiac output, tended to lower Vd/Vt, and markedly improved the efficiency of ventilation. Peak [latin capital V with dot above]$O_2$ and ventilatory responses to exercise were only modestly related to pulmonary vascular pressures, and training had no effect on the relationships between exercise capacity, ventilatory responses, and pulmonary pressures.

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Exercise intolerance is a hallmark of chronic congestive heart failure (CHF). In recent years, the physiologic mechanisms underlying reduced exercise capacity in this condition have been the source of a great deal of investigation (19,31,46). Chronically reduced blood flow (22,24,53), skeletal muscle metabolic derangements (44,52), deconditioning (4), pulmonary abnormalities (26), and neurohumoral dysfunction (3) combine in varying degrees to underlie the major cause of morbidity in CHF, reduced exercise tolerance. Many of these abnormalities mimic those associated with deconditioning. Recent controlled trials have demonstrated that exercise training can improve some of these abnormalities in patients with reduced ventricular function (10,11,16,17). Some (10,11), but not all (21,41), studies have observed increases in maximal cardiac output after training, but it appears that the major benefit of training in CHF may be reversal of skeletal muscle metabolic abnormalities (16,17).

A pathophysiologic feature of CHF that has gained particular interest in recent years is abnormal ventilatory responses to exercise. These ventilatory abnormalities contribute to dyspnea in CHF and are a major cause of exercise intolerance (26,32,47). Mechanisms that have been proposed to explain this response include increased intrapulmonary pressures (14,20,35), elevated physiologic dead space (32,40,47,50), early metabolic acidosis (8,51), altered ventilatory control (33,34,37), and abnormal breathing patterns including rapid, shallow respiration (20,32,40,51). Despite a great deal of research directed toward this area in the 1990s, a complete explanation for the mechanism(s) underlying these abnormal ventilatory responses to exercise is lacking (26). Two recent studies have reported small improvements in markers of abnormal ventilation after training in CHF

(6,45), but there have been no controlled trials to date that have addressed this issue in detail.

In the present study, we sought to further elucidate the mechanisms underlying abnormal ventilatory responses to exercise in patients with reduced ventricular function and to study the effects a program of exercise training would have on them. Accurate evaluation of these mechanisms, including ventilation/perfusion matching, ventilatory control, metabolic acidosis, and breathing patterns, requires the simultaneous measurement of ventilatory gas exchange, intrapulmonary pressures, cardiac output, and arterial blood gases. These variables were acquired simultaneously during upright exercise before and after a 2-month high-intensity residential training program among patients with reduced ventricular function after a myocardial infarction.

## METHODS

Patients. Twelve male patients (mean age 56 ± 5 yr) participated in the exercise group, and 13 male patients (mean age 55 ± 7 yr) participated in the control group. Clinical characteristics of the two groups are outlined in Table 1. All had sustained a myocardial infarction, and some had undergone bypass surgery. The hospital course in all patients included the diagnosis of heart failure. Before their hospitalization, none of the patients had a previous history of heart failure. Patients exhibiting angina or ECG signs of ischemia during exercise were excluded from the study. The presence of reduced ventricular function was documented by signs, symptoms, and an angiographically determined ejection fraction < 40%. All were limited by fatigue or dyspnea on baseline exercise testing, and none had clinical evidence of pulmonary disease. All patients were New York Heart Association Functional Class II or III. Six patients in the exercise group and five in the control group had mild to moderate mitral regurgitation. The study was approved by the Investigational Review Board at the Kantonsspital, Chur. Written informed consent was obtained, and all patients had stable symptoms for at least 1 month before randomization.

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TABLE 1. Patient characteristics.

Study design. After myocardial infarction or bypass surgery, patients were stabilized for approximately 1 month. At the time of randomization, patients in both groups underwent initial testing (maximal exercise testing with gas exchange, lactate, and hemodynamic measurements). These tests were repeated after 2 months. Randomization was performed using a list of random numbers. After stabilization, each patient's pharmacologic regimen remained constant throughout the study period.

Exercise training. After stabilization and initial testing, patients in the exercise group resided in a rehabilitation center in Seewis, Switzerland for a period of 8 wk. Seewis is a small village in the mountains with an elevation of 3500 feet. The center has its own staff of physicians, consisting of a medical director and three interns/residents. Program components included education, exercise, and low-fat meals prepared three times daily by the center's cook. Two outdoor walking sessions daily for a duration of approximately 1 h were performed, once in the morning and once in the afternoon. Walking intensity was stratified into four levels based on clinical status, exercise capacity, and performance on a 500-m walking test (50-m increase in altitude) on a nearby hill. The patients were accompanied by a physician during these walking sessions. Exercise leaders carried two-way radios for communication with the center in case of emergency. A van equipped with emergency equipment remained in close proximity to the group.

In addition to these walking periods, the patients performed four 45-min periods of monitored stationary cycling per week. The cycling sessions were designed to elicit an intensity equal to roughly 60-80% of the patient's heart rate reserve and were increased progressively over the 2 months as tolerated. Control patients remained at home to convalesce, received usual clinical follow-up, and were encouraged not to exercise beyond a level associated with normal activities of daily living.

Exercise testing. Before randomization, each patient performed a preliminary exercise test to help ascertain clinical stability and to habituate the patients to the testing procedure, apparatus, etc. The data from this preliminary test was not used in the study analysis. On the day of testing, patients were requested to abstain from food, coffee, and cigarettes for 3 h before the test. Standard pulmonary function tests were performed. Maximal exercise testing was

performed on an electrically braked cycle ergometer using an individualized ramp protocol. Briefly, this test entailed choosing an individualized ramp rate to yield a test duration of approximately 10 min (30). The ramp rates ranged between 10 and 15 $W \cdot min^{-1}$. A 12-lead electrocardiogram was monitored continuously, and blood pressure was measured manually every minute during exercise and throughout the recovery period. The patient's subjective level of exertion was quantified every minute by using the Borg 6-20 scale (2). All tests were continued to volitional fatigue/dyspnea; no patients were limited by angina.

Respiratory gas exchange variables were acquired continuously throughout exercise using the Schiller CS-100 metabolic system. Gas exchange variables analyzed were oxygen uptake, carbon dioxide production, minute ventilation, respiratory rate, tidal volume, oxygen pulse, respiratory exchange ratio, and the ventilatory equivalents for oxygen ([latin capital V with dot above]E/[white square with S]$O_2$) and carbon dioxide ([white square with S]E/[white square with S]$CO_2$). The gas exchange data were obtained breath-by-breath and expressed as rolling 30-s averages printed every 10 s. The lactate threshold was determined visually by consensus among two experienced reviewers (blind to group and pre/post test identity) using a computerized plot of the oxygen uptake versus lactate relationship.

Resting and peak exercise cardiac output and pulmonary pressures were determined in the catheterization laboratory. These procedures in our laboratory have been described in detail previously (11). Briefly, using standard sterile preparation procedures, a thermodilution catheter was positioned in the pulmonary artery via an antecubital vein under fluoroscopic guidance. A 5-fr introducer sheath was then inserted into the radial artery and connected to a pressure transducer for monitoring arterial pressure and sampling arterial blood. The patient was then helped off the catheterization table and onto a cycle ergometer placed in the catheterization laboratory. The hemodynamic system was recalibrated after the patient had rested in the upright position for 5 min. Maximal ramp exercise with gas exchange analysis was performed as described above. Cardiac output was measured using the Fick equation as (oxygen uptake/arteriovenous oxygen difference). Arterial blood gas samples were obtained at rest and peak exercise using an electrode system (ABL System Series, Roche Laboratories, Basel, Switzerland). The ratio of ventilatory dead space to tidal volume (Vd/Vt) was calculated at rest and peak exercise using the following equation (28): (Equation 1) where $PaCO_2$ is the arterial

carbon dioxide tension, and $PeCO_2$ is the mixed expired carbon dioxide tension. Arterial blood lactate samples were drawn every minute throughout the test, and whole blood was analyzed after the test using an enzymatic colorimetric method (Roche Laboratories).

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Equation 1

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Statistics. Statistical Graphics Corporation Software (Bethesda, MD) was used to perform multivariate analysis of variance procedures comparing gas exchange responses between groups. This procedure considered both inter- and intra-group comparisons, and interactions among the factors (group and test) for each dependent variable. *Post hoc* multiple comparison procedures were performed using the Scheffe method. Clinical and demographic data were compared using unpaired *t*-tests and chi-square analysis. Relationships between gas exchange variables and hemodynamic responses to exercise were assessed by simple linear regression. Data are expressed as mean ± SD.

## RESULTS^

No differences were observed between groups initially in clinical or demographic data, including age, height, weight, resting blood pressure, pulmonary function, ejection fraction, or maximal oxygen uptake (Table 1). No untoward events occurred during any of the exercise testing or training procedures. During monitored cycling sessions over the 2 months, the mean percentage of maximal heart rate maintained was 83 ± 6%, the mean percentage of maximal workload was 78 ± 7%, and perceived exertion averaged 15.2 ± 2. Two patients in the exercise group and one in the control group did not undergo invasive hemodynamic exercise testing during either the initial or follow-up test due to either clinical reasons or technical difficulties. Thus, pulmonary capillary wedge pressure, pulmonary artery pressure, cardiac output, a-[white square with S]$O_2$ difference, and Vd/Vt are presented for 10 patients in the exercise group and 12 patients in the control group; for all other gas exchange and hemodynamic data, the numbers were 12 and 13 for exercise and control groups, respectively.

Maximal exercise testing. Both groups achieved maximal respiratory exchange ratios greater than 1.20 and perceived exertion levels of roughly 19 on both tests, suggesting maximal efforts were generally achieved (Table 2). No patient in either group was limited by angina, and none exhibited ECG evidence of ischemia during baseline exercise testing. Arterial oxygen saturation remained above 90% at peak exercise during both tests in all but one patient, who exhibited small decreases to 87 and 89% on pre- and post-testing, respectively. No differences were observed within or between groups in maximal heart rate or blood pressure. The exercise group demonstrated a 29% increase in maximal oxygen uptake (19.4 ± 3.0 to 25.1 ± 4.8 $mL \cdot kg^{-1} \cdot min^{-1}$, $P < 0.01$) (Fig. 1). Concomitant increases in maximal minute ventilation, $CO_2$ production, exercise time, and Watts achieved were observed in the exercise group. No differences between tests were observed among control patients in maximal oxygen uptake, exercise time, or Watts achieved.

TABLE 2. Exercise and gas exchange data.

Figure 1-Study design.

Oxygen uptake at the lactate threshold increased significantly (39%, $P < 0.01$) in the exercise group, whereas a small decrease was observed among controls. Similar increases in exercise time and Watts achieved at the lactate threshold were observed among patients in the exercise group, whereas the control group demonstrated small decreases in these variables. No differences were observed within or between groups for heart rate, systolic or diastolic blood pressure, respiratory exchange ratio, lactate, or perceived exertion at this point.

Maximal cardiac output increased in the exercise group from 12.0 $L \cdot min^{-1}$ before training to 13.7 $L \cdot min^{-1}$ after training ($P < 0.05$). This was accompanied by a widening of the maximal arteriovenous oxygen difference from 13.1 ± 1.3 to 14.8 ± 1.6 mL $O_2 \cdot 100\ mL^{-1}$ ($P < 0.05$). These variables did not differ among controls. No differences were observed within either group before or after the study period in resting ejection fraction or resting or maximal exercise mean arterial, wedge, right atrial, or pulmonary artery pressures, stroke volume, pulmonary vascular resistance, or systemic vascular resistance.

Relationships between hemodynamic responses, gas exchange variables, and work rate. By ANOVA, significant main effects were observed in the exercise group for reductions in [white square with S]E/[white square with S]$O_2$ ($P < 0.01$), perceived exertion ($P < 0.001$), heart rate ($P < 0.001$), and lactate ($P < 0.01$) at matched time points (work rates) throughout exercise (Figs. 2 and 3). Trends were also observed for reductions in [white square with S]E/[white square with S]$CO_2$ and the oxygen uptake/work rate relationship ($P = 0.06$ for both). Among controls, none of these relationships differed significantly with the exception of a reduction in heart rate ($P < 0.05$). The slope of the relationship between [white square with S]E and [white square with S]$CO_2$ was reduced after training among patients in the exercise group (0.33 pre vs 0.27 post, $P < 0.01$, Fig. 4), whereas control patients did not differ. The ratio of maximal tidal volume to respiratory rate (Vt/RR) improved slightly after training in the exercise group (0.053 ± 0.02 to 0.049 ± 0.02 $L/breath \cdot min^{-1}$), whereas control patients increased slightly (0.053 ± 0.02 to 0.054 ± 0.02 $L/breath \cdot min^{-1}$); these differences were not significant between groups ($P = 0.65$). A similar response in Vt/RR was observed in each group throughout submaximal exercise. The reduction in minute ventilation during exercise in the trained group was mediated primarily by a reduction in respiratory rate (Fig. 3).

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Figure 2-Influence of exercise training on oxygen uptake, perceived exertion, heart rate, and lactate at matched ramp work rates during exercise. *Open squares* indicate baseline values; *closed circles* indicate posttraining. A main effect ($P < 0.01$) was observed for all except oxygen uptake.

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Figure 3-Influence of training on ventilatory responses to exercise at matched ramp work rates during exercise. *Open squares* indicate baseline values, *closed squares* indicate posttraining. A significant reduction was observed for [white square with S]/[white square with S]$O_2$ ($P < 0.01$).

Figure 4-The slope of the relationship between minute ventilation and [white square with S]$CO_2$ before (*open circles*) and after (*closed circles*) training in the exercise group. (0.33 pre vs 0.27 post, $P < 0.01$).

Figure 5 illustrates the relationships between resting and peak exercise pulmonary wedge pressures and peak [white square with S]$O_2$ among patients in both groups before randomization. Modest but significant inverse correlations were observed both at rest ($r = -0.56$, $P < 0.01$) and peak exercise ($r = -0.43$, $P < 0.05$). Maximal minute ventilation was correlated with [white square with S]$CO_2$ on both the pre ($r = 0.71$, $P < 0.001$) and post ($r = 0.85$, $P < 0.001$) tests. Maximal ventilation was not significantly related to pulmonary wedge pressure at rest ($r = -0.17$) or peak exercise ($r = -0.30$). The relationships between maximal [white square with S]E/[white square with S]$CO_2$ and maximal cardiac output, Vd/Vt, pulmonary wedge pressure and pulmonary artery pressure are illustrated in Figure 6. Maximal [white square with S]E/[white square with S]$CO_2$ was strongly inversely related to maximal cardiac output ($r = -0.72$, $P < 0.001$) and modestly related to mean maximal pulmonary capillary wedge pressure ($r = 0.53$, $P < 0.05$) and maximal Vd/Vt ($r = 0.54$, $P < 0.05$), but was unrelated to maximal pulmonary artery pressure ($r = 0.09$). Maximal [white square with S]E/[white square with S]$CO_2$ was also inversely related to peak [white square with S]$O_2$ ($r = 0.47$, $P < 0.05$). When these relationships were reassessed after the training or control periods, no appreciable differences were observed.

Figure 5-The relationships between resting and maximal exercise pulmonary wedge pressures and peak oxygen uptake among patients in both groups before randomization.

Figure 6-The relationships between maximal exercise [white square with S]E/[white square with S]$CO_2$ and maximal cardiac output, maximal pulmonary capillary wedge pressure (PCW), maximal Vd/Vt, and maximal mean pulmonary artery pressure (PA) in both groups at baseline.

## DISCUSSION^

Although excessive ventilatory responses to exercise in patients with reduced ventricular function have been the subject of a great deal of study in recent years, an understanding of the mechanisms and their treatment remains incomplete. Pharmacologic intervention with inotropic therapy or vasodilators has been shown in some studies (7,43), but not in others (12,38), to improve this response. Cardiac transplantation has been shown to partially reverse abnormal ventilatory responses to exercise (25). One treatment option that has gained acceptance in recent years in patients with heart failure is exercise training (1,6,10,11,16,17,45). This is a departure from past decades in which these patients were generally excluded from formal exercise training programs due to concerns about safety and reservations about whether they could derive any benefits. A substantial body of evidence has now been published in the 1990s documenting the efficacy and safety of exercise training in these patients (1).

The mechanisms underlying the abnormal ventilatory response to exercise in heart failure have generally been thought to include heightened pulmonary pressures, ventilation/perfusion mismatching, early metabolic acidosis, abnormal ventilatory control, deconditioning,

and abnormal breathing patterns (5,26,32,46). Although it has been suggested that an improvement in the ventilatory response to exercise may be among the benefits of training in these patients (6,45), there have been no controlled trials to address the mechanism(s) underlying an improvement, if one exists. A mechanistic assessment of this issue requires an invasive exercise test, including the measurement of changes in cardiac output, pulmonary artery wedge pressure, lactate, arterial blood gases, and ventilatory gas exchange.

Response to exercise training. The high-intensity training stimulus employed in the present study yielded considerable increases in peak [latin capital V with dot above]$O_2$ (29%) and concomitant increases in [latin capital V with dot above]$O_2$ at the lactate threshold (39%), Watts achieved, and exercise time (Table 2). These increases in peak [latin capital V with dot above]$O_2$ and other variables are substantially larger than those in the aforementioned trials (6,19,45). Although no differences were observed within or between groups in resting ejection fraction, maximal cardiac output increased by 1.7 $L \cdot min^{-1}$ in the trained group, which contrasts with several studies in CHF showing either no change (17,21,41) or a more modest increase in cardiac output, the order of 1.0 $L \cdot min^{-1}$ (6,45). Presumably, the marked training effects we observed were due not just to the high-intensity training stimulus but also to the fact that the exercise program was residential, permitting a relatively captive environment within which exercise, diet, and other factors could be controlled to a greater degree than a more typical outpatient program.

Ventilatory response to exercise. The ventilatory requirement for exercise is defined by three factors according to the alveolar gas equation: 1) metabolic $CO_2$ production (expressed as [latin capital V with dot above]E/[latin capital V with dot above]$CO_2$); 2) the $PaCO_2$ set point; and 3) the fraction of dead space ventilation (expressed as Vd/Vt). As other investigators have observed in patients with CHF (47,51), arterial $PCO_2$ remained normal throughout exercise in the present study (falling from 34.0 ± 3.8 to 30.9 ± 4.2 mm Hg), and [latin capital V with dot above]E and [latin capital V with dot above]$CO_2$ were tightly coupled, suggesting that neural and chemoreceptor control of ventilation were normal. Exercise training reduced the slope of the relationship between [latin capital V with dot above]E and [latin capital V with dot above]E/[latin capital V with dot above]$CO_2$ (Fig. 4). [latin capital V with dot above]E/[latin capital V with dot above]$CO_2$ was characteristically shifted upward (Table 2 and Figure 3), which reflects a heightened Vd/Vt (50). The heightened

ventilatory response to exercise is also evidenced by an elevated [latin capital V with dot above]E/[latin capital V with dot above]$O_2$, particularly on the initial test (Fig. 3).

Ventilation/perfusion mismatching. Ventilation/perfusion mismatching has been identified as a major factor contributing to an increase in physiologic dead space (Vd/Vt) in CHF (26,31,46,47). Underlying this response is reduced pulmonary perfusion caused by an attenuated cardiac output response to exercise (47). The inverse association between the ventilatory requirement for exercise ([latin capital V with dot above]E/[latin capital V with dot above]$CO_2$) and maximal cardiac output in the present study (Fig. 6) suggests that decreased pulmonary perfusion did in fact underlie an increased physiologic dead space by increasing ventilation/perfusion mismatching. A better matching of ventilation to perfusion, and thus a reduction in Vd/Vt, could in theory be accomplished by either an improvement in cardiac output or a reduction in physiologic dead space. We hypothesized that an increase in maximal cardiac output with training observed in some previous studies (10,11,17) would parallel a reduction in physiologic dead space. Although a substantial increase in maximal cardiac output occurred in the trained group, we did not observe a significant reduction in the ratio of dead space to tidal volume, making improved ventilation/perfusion mismatching an unlikely explanation for the improved ventilatory response to exercise.

Efficiency of ventilation. The significant reductions in [latin capital V with dot above]E/[latin capital V with dot above]$O_2$ (Fig. 3) and the reduction in the slope of the relation between [latin capital V with dot above]E and [latin capital V with dot above]$CO_2$ (Fig. 4) clearly confirm a beneficial effect of exercise training on the ventilatory response to exercise. These measures are well-recognized indices of ventilatory efficiency and have been used as markers of the severity of CHF (32,50).

Breathing pattern. The alveolar gas equation also defines a condition in which a reduction in tidal volume would raise the [latin capital V with dot above]E/[latin capital V with dot above]$CO_2$ [[latin capital V with dot above]E/[latin capital V with dot above]$CO_2$ = 863/($PaCO_2$ × (1 - Vd/Vt] and contribute to hyperventilation. Rapid, shallow respiration is characteristic of the response to exercise in patients with CHF (20,31,32,40,51), and it has been suggested that this breathing pattern reflects an effort on the part of the patient to reduce the work of breathing (20). Clark and associates (5) recently observed that hyperventilation during exercise was not due to

*anatomic* dead space *per se* in patients with CHF, but rather due to an altered ventilatory pattern (ratio of tidal volume to breathing rate). Initially, our patients demonstrated a ratio of tidal volume to breathing rate which was similar to that observed in previous studies among patients with CHF (5,32), and training had only a slight effect on this relationship. The overall reduction in the ventilatory requirement for work ([latin capital V with dot above]E/[latin capital V with dot above]$O_2$) we observed after training was attributable mainly to a lower respiratory rate, whereas tidal volume remained relatively unchanged (Fig. 3). Training had only minimal effects on the breathing pattern.

Metabolic acidosis. Numerous investigators have associated early lactate accumulation in the blood with metabolic acidosis, hyperventilation, and exercise intolerance in patients with CHF (8,31,47,51). Lactate that accumulates in the blood during exercise must be buffered to maintain physiological pH, and the bicarbonate buffering process yields a secondary source of $CO_2$, which stimulates ventilation. Previous studies have demonstrated that exercise training causes a delay in the ventilatory threshold in normal subjects (9,36) and in patients who have sustained a myocardial infarction (18,42). A delay in the threshold of hyperventilation would be particularly important in patients with CHF, because dyspnea is such an important limitation to their daily activities (23). Whether training causes a reduction in lactate production or an increase in the rate of lactate clearance has been debated, but clearly training delays lactate accumulation during exercise (29). Our data confirm the work of others (6,42) with respect to both a delay in the lactate threshold (Table 2) and an overall reduction in the slope of the relationship between blood lactate and work rate throughout exercise (Fig. 2). Because ventilation is an important component of perceived effort (39), it follows that a marked reduction in perceived exertion was observed throughout exercise after training (Fig. 2).

Pulmonary pressure. Historically, the predominant explanation for exertional dyspnea in patients with CHF has been higher than normal pulmonary wedge pressures, causing reflex hyperventilation (14,20,26,35). However, more recent studies have consistently shown that the two are unrelated during exercise (9,12,31,46). Although our patients were clinically stabilized such that many did not exhibit excessive wedge pressures initially, we similarly observed only modest relationships between rest and exercise wedge pressures and peak [latin capital V with dot above]$O_2$ (Fig. 5) and the ventilatory response to exercise (Fig. 6). As reported by others (12,13), there was a

significant, though modest, inverse relationship between pulmonary wedge pressure at rest and peak [latin capital V with dot above]$O_2$ (Fig. 5). Unlike previous studies, however, we observed a significant inverse relationship between peak [latin capital V with dot above]$O_2$ and pulmonary wedge pressure during exercise, though the relationship was weak ($r = -0.43$, $P < 0.05$).

These data confirm the relatively weak relations between intrapulmonary pressures, peak [latin capital V with dot above]$O_2$, and the ventilatory requirement for exercise (12,31,46), suggesting that stimulation of pulmonary receptors do not underlie abnormal ventilatory responses to exercise. The influence of exercise training on pulmonary vascular pressures has been disputed. Some studies have demonstrated increases in left ventricular filling pressures during exercise after training in this population (21,41), whereas others have shown decreases (41,49) and others have observed no change (11,21,48). We did not observe any changes in pulmonary wedge pressure, pulmonary artery pressure, or pulmonary vascular resistance in either the trained or control groups, and the relationships between pulmonary pressures, exercise capacity, and ventilation were similar before and after the study period in both groups.

Limitations. The present population differed somewhat from other recent studies in that the patients had newly diagnosed ventricular dysfunction after a myocardial infarction. The findings may have been different had the disease been more chronic or had the ventricular dysfunction been more severe. Our observations cannot be attributed entirely to exercise training because there is some spontaneous improvement in exercise tolerance during the 1-2 months after a myocardial event (15). The accurate measurement of physiologic dead space during exercise is a difficult undertaking, even using direct blood gas samples to quantify $PaCO_2$; this measurement is influenced by the variability of the blood gas sample and how the increments in gas exchange data are averaged. Recent studies have demonstrated that inspiratory muscle strength is a determinant of peak [latin capital V with dot above]$O_2$ in CHF, and that these muscles can be trained (27). We did not measure this parameter, and the effect of aerobic training on inspiratory muscle strength is unknown. Finally, it is unclear whether more standard outpatient rehabilitation or home programs would be as effective in improving ventilatory and gas exchange responses to exercise. Although the patients in the present study were consecutive, it is likely that some patients exposed to such

a high intensity regimen would drop out, become injured, or be unable to complete the program for safety reasons.

## SUMMARY ^

The present data demonstrate that exercise training among patients with reduced left ventricular function after a myocardial infarction or surgery results in a systematic improvement in the ventilatory response to exercise. Training increased peak [latin capital V with dot above]$O_2$, increased maximal cardiac output, tended to lower Vd/Vt, and markedly improved the efficiency of ventilation. Training reduced lactate levels in the blood throughout exercise and delayed the lactate threshold, and these responses largely explained the reduced ventilatory response to exercise after training. Peak [latin capital V with dot above]$O_2$ and ventilatory responses to exercise were only modestly related to pulmonary vascular pressures, and training had no effect on the relationships between exercise capacity, ventilatory responses, and pulmonary pressures. The favorable influence of exercise training on ventilatory responses to exercise in the present study provides further support for the use of this modality in patients with reduced ventricular function.

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