Annals of Internal Medicine

Established in 1927 by the American College of Physicians

ARTICLE

Exercise Training in Patients with Heart Failure A Randomized, Controlled Trial

Steven J. Keteyian, PhD; Arlene B. Levine, MD; Clinton A. Brawner, BS; Takeshi Kataoka, MD; Felix J. Rogers, DO; John R. Schairer, DO; Paul D. Stein, MD; T. Barry Levine, MD; and Sidney Goldstein, MD

15 June 1996 | Volume 124 Issue 12 | Pages 1051-1057

Objective: To assess the benefit of exercise training in patients with heart failure caused by left ventricular systolic dysfunction and to further describe the physiologic changes associated with exercise training in these patients.

Design: Randomized, controlled trial.

Setting: Urban outpatient clinic.

Patients: 40 men with compensated heart failure who were receiving standard medical therapy were randomly assigned to an exercise-training group or to a control group that did not exercise. Fifteen of the 21 patients assigned to exercise training and 14 of the 19 patients assigned to the control group completed the study.

Intervention: Patients assigned to exercise training participated in a program of three exercise sessions per week for 24 weeks.

Measurements: Symptom-limited exercise tests with gas exchange analysis done just before randomization, at week 12, and at week 24.

Results: At week 24, the following changes (mean ± SE) were seen in patients in the exercise group and patients in the control group, respectively: exercise duration, 2.8 ± 0.6 minutes and 0.5 ± 0.5 minutes; peak oxygen consumption (VO_2), 231 ± 54 L/min and 58 ± 38 L/min; peak ventilation, 12 ± 3 L/min and minus4 ± 3 L/min; peak heart rate, 10 ± 4 beats/min and minus2 ± 4 beats/min; and peak power output, 20 ± 6 W and 2 ± 5 W. Differences between the increases occurring in the exercise group and the changes occurring in the control group were significant ($P < 0.05$). Among patients in the exercise group, 85% of the increase in peak VO_2 occurred by week 12, and 46% of the increase in peak VO_2 was caused by the increase in peak heart rate.

Conclusions: Exercise training does not appear to be contraindicated in patients with compensated heart failure. Exercise training improved exercise tolerance, as measured by increases in peak VO_2, exercise duration, and power output. This improved exercise tolerance was caused in part by an increase in peak heart rate.

The role of exercise training in the treatment of heart failure remains a paradox, because exercise intolerance is a characteristic finding in patients with this condition. Improved exercise performance after exercise training has been seen in patients with heart failure, but such training is not yet widely incorporated into clinical

practice. In addition, the mechanisms by which this improvement occurs are uncertain. Factors that may explain the improvement include an increase in cardiac output [1, 2], an improvement in skeletal muscle metabolism [3-5], and an increase in peak blood flow to the exercising limb that is caused by a decrease in vascular resistance [1, 2, 5].

Five randomized trials [5-9] have assessed exercise performance after exercise training in patients with symptomatic heart failure. Two trials that assessed cardiorespiratory fitness as measured by oxygen consumption (VO_2) showed a 22% improvement in peak VO_2 after 4 weeks of exercise training [6] and a 31% improvement after 6 months of exercise training [5]. Two other trials [7, 8] showed an increase in exercise duration after 12 weeks of exercise training, and a fifth trial [9] recently found no significant increase in peak VO_2 after exercise training.

We sought to assess the benefit of exercise training in patients with heart failure caused by left ventricular systolic dysfunction and to further describe the physiologic changes associated with exercise training. Functional capacity and cardiorespiratory fitness were measured before and after exercise training in patients with compensated heart failure who were receiving standard medical therapy. Patients were randomly assigned either to a group that participated in a program of three supervised exercise sessions per week for 24 weeks (exercise group) or to a control group that did not exercise.

Methods

Patients

▲ Top
▪ Methods
▼ Results
▼ Discussion
▼ Author & Article Info
▼ References

Forty men with compensated heart failure and left ventricular dysfunction were randomly assigned to the exercise group (n = 21) or the control group (n = 19). Randomization was done according to a computer-generated randomization list. Patients were recruited from the outpatient heart failure clinic of a tertiary care hospital or from the office of a cardiologist practicing in the community. Patients meeting the eligibility criteria for the study first received a brief explanation of the study from their cardiologist. Patients willing to participate in the randomized trial were then referred. The hospital's institutional review board approved our study, and all patients provided written informed consent.

Inclusion criteria were New York Heart Association class II or III, a resting ejection fraction of 35% or less as measured by echocardiography or gated equilibrium radionuclide angiography, and no change in medical therapy for 30 days before randomization. Exclusion criteria were atrial fibrillation, acute myocardial infarction within the previous 3 months, angina pectoris at rest or induced by exercise, current enrollment in another clinical trial, and current participation in a regular exercise program (at least twice weekly). Patients were classified as having ischemic cardiomyopathy if they had had a myocardial infarction or had angiographic evidence of coronary artery disease that could explain the extent of ventricular dysfunction. If they did not meet these criteria, they were classified as having idiopathic dilated cardiomyopathy.

Study Design

Exercise tests were completed before and after a 30-day prestudy period. The prestudy period was used to document the stability of exercise tolerance, clinical conditions, and prescribed medications. Immediately after completing the second exercise test, patients were randomly assigned to the exercise group or the control group. Each patient's assignment was sealed in an envelope until completion of the second exercise test. Exercise testing was repeated at weeks 12 and 24 for patients in both groups. Each patient's physician was asked not to change a patient's drug regimen during the study, if possible. Patients in the control group were instructed to maintain their normal daily activity habits and not to begin an exercise regimen. Controls were contacted by telephone every 2 to 3 weeks to assess compliance, cardiac-related symptoms, and continued avoidance of a regular activity program.

Exercise Testing

Symptom-limited, maximal exercise tests were completed using an upright stationary cycle ergometer (Monark, Stockholm, Sweden), starting at a power output of 25 W and increasing by 25 W every 3 minutes. Tests were discontinued when dyspnea or calf, thigh, or generalized fatigue developed. Patients were monitored by electrocardiography (Q-3000, Quinton Instruments, Seattle, Washington) at rest, during exercise, and during 8 minutes of recovery. Blood pressure, heart rate, rating of perceived exertion (categorized on the Borg scale; range, 6 to 20), and a 12-lead electrocardiogram were obtained after 30 minutes of supine rest, within the last 25 seconds of each stage of exercise, and during peak exercise.

Air expired during exercise testing was analyzed using a Horizon II Metabolic System (Sensormedics, Yorba Linda, California). Direct measurement and calculations were used to determine peak VO_2, carbon dioxide production (VCO_2), ventilation, oxygen (O_2) pulse, and respiratory exchange ratio. Expired air was sampled at a rate of 10 per second and reported as a 15-second average. Exercise tests in the exercise group and the control group represented peak effort, as evidenced by ratings of perceived exertion that were generally 16 or more and respiratory exchange ratios that were greater than 1.1.

Ventilatory derived anaerobic threshold (V-AT) was determined using the V-slope method, originally defined by Beaver and colleagues [10] and later simplified by others [11-13]. This measure, in which VCO_2 is plotted as a function of VO_2, can be used to detect the beginning of excess carbon dioxide production caused by the buffering of H^+ that arise from lactic acid. Two independent, experienced reviewers blinded to the patients' group assignment and testing periods determined V-AT. For four patients in the exercise group and five patients in the control group, a reviewer could not determine V-AT in at least one of each patient's three exercise tests. We also computed the slope of the relation between ventilation and VCO_2 as a marker of the severity of heart failure [14].

Exercise Training

Each exercise training session lasted 43 minutes. During each session, patients completed a 5-minute, slow warm-up phase, a 33-minute aerobic phase (three different types of exercise equipment were used for 11 minutes each), and a 5-minute cool-down phase. Exercise equipment included motor-driven treadmills, stationary cycles, rowing machines, and arm ergometers. Patients attended the exercise training program three times per week. Using the heart rate reserve method [15], we set exercise intensity at 60% for the first 2 weeks and then increased it, as tolerated, to as high as 80%. A rating of perceived exertion of 12 to 14 was also used to guide exercise intensity. Heart rate and rhythm were monitored during exercise using a single-lead electrocardiography telemetry system.

Statistical Analysis

Of the 40 patients entered into the study, only those who also completed the exercise tests at weeks 12 and 24 were considered in the data analysis. The 5 patients who dropped out for nonmedical reasons were asked to return for follow-up testing, but they refused. We compared patient characteristics at baseline using an unpaired *t*-test or the Fisher exact test. We used univariate repeated-measures analysis of variance with the Greenhouse-Geisser [16] sphericity correction to determine whether a significant ($P < 0.05$) difference in the change across time occurred between the two groups. For variables for which a significant (or a tendency toward a significant) time-group interaction was detected, we used analysis of variance to assess a within-group time effect and used a Student two-sample *t*-test to assess a group effect. For the latter two analyses, we used the Bonferroni multiple testing adjustment to reduce the α level accordingly. Values are expressed as means ± SE. The SAS software package (SAS Institute, Cary, North Carolina) was used for all analyses.

Results

Compliance, Medical Therapy, and Safety

Among patients who completed the study, no differences in demographic characteristics were seen between the two study groups after randomization

▲ Top
▲ Methods
▪ Results
▼ Discussion
▼ Author & Article Info

▼ References

(Table 1). Of the 40 patients randomly assigned at baseline, 29 completed the study and 11 dropped out (Table 1). Regardless of the reason for drop out, patients with ischemic cardiomyopathy tended to drop out more frequently (7 of 16 patients [44%]) than did patients with dilated cardiomyopathy (4 of 24 patients [17%]) ($P = 0.08$). In addition, ejection fraction tended to be lower in patients who dropped out than in those who did not (18% ± 5% compared with 23% ± 8%; $P = 0.09$), and patients who dropped out tended to be older (61 ± 10 years compared with 54 ± 11 years; $P = 0.07$). No differences were seen in New York Heart Association class (II compared with III) between patients who completed the study and those who dropped out.

View this table: Table 1. **Baseline Patient Characteristics***
[in this window]
[in a new window]

Fifteen patients in the exercise group completed the study. Two patients dropped out because of noncardiac medical conditions (progressive, limiting arthritis in one patient and newly diagnosed cancer in the other) that developed within 1 month of the start of the exercise program. One patient developed atrial fibrillation between week 12 and week 24; 3 other patients stopped exercising for personal reasons before week 12 and refused follow-up testing. Fourteen of the 19 patients in the control group completed the study. Two dropped out for personal reasons and refused follow-up testing, 1 developed atrial fibrillation between week 12 and week 24, 1 was hospitalized at week 22 for an acute myocardial infarction, and 1 died suddenly.

At baseline, the drug regimens of the exercise and control groups were similar (Table 1); drugs included digoxin, diuretics, and an angiotensin II-converting enzyme (ACE) inhibitor. During the 24-week study, minor changes in medications occurred among patients in the exercise group. In three patients, the dose of an ACE inhibitor was increased; in two, the dose of a long-acting nitrate was increased; in three, the dose of a diuretic agent was changed; and in one, digoxin therapy was stopped. In two controls, the dose of an ACE inhibitor was decreased; in one, the ACE inhibitor dose was increased; and in one, digoxin therapy was discontinued. No patients began receiving an ACE inhibitor, a diuretic agent, or a long-acting nitrate during the study.

Of the 15 patients in the exercise group, 14 regularly attended the exercise training sessions. One patient regularly attended the exercise program for the first 12 weeks, but between weeks 12 and 24, the patient attended 30% of exercise sessions. In this patient, however, peak VO_2 increased by more than 20%. All 14 controls who completed the study reported avoiding participation in any regular physical activity program during the 24-week study. Overall, 138 symptom-limited graded exercise tests and 1150 exercise training sessions were completed without incident.

Rest and Submaximal Exercise

No significant differences over time were seen between the exercise and control groups in resting heart rate, heart rate during exercise at 50 W, ventilation at 50 W, or resting systolic or diastolic blood pressures. Among patients in the exercise group, the heart rate during exercise at a standardized submaximal power output of 50 W was significantly decreased over time (– 8 ± 3 beats/min; $P = 0.025$). A similar decrease was not seen in the control group (0 ± 3 beats/min; $P > 0.2$).

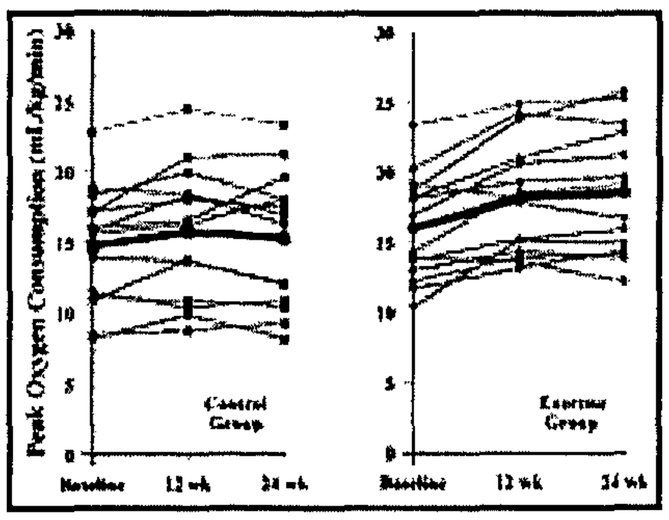
Peak Exercise

Four measures of exercise tolerance—absolute peak VO_2 ($P < 0.05$), relative peak VO_2 ($P < 0.05$), exercise duration ($P < 0.01$), and peak power output ($P < 0.05$)—were significantly increased over time in the patient group compared with the control group (Table 2); Figure 1 and Figure 2. No significant difference in V-AT over time was seen between the two groups. Among patients in the exercise group, absolute peak VO_2 and peak VO ($_2$) relative to body mass increased over time by 16.3% and 15.6%, respectively. Age tended to be related to the observed change in peak VO_2 ($r = – 0.49$; $P = 0.08$), and 85% of the increase in peak VO_2 occurred by

week 12. Among patients in the control group, absolute and relative peak VO_2 changed by 4.7% and 3.5%, respectively.

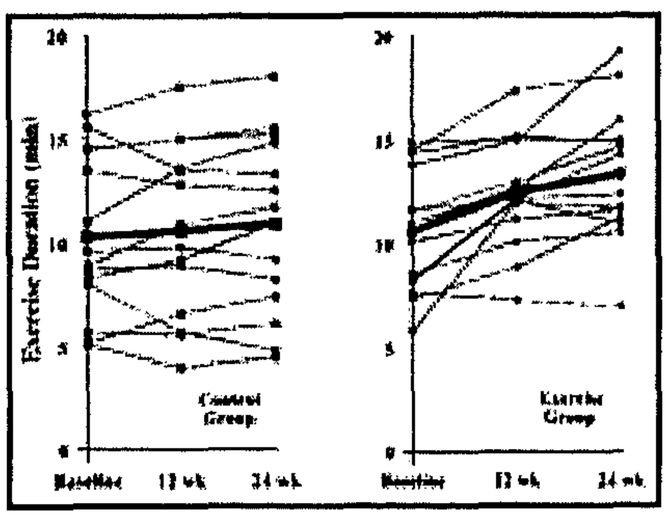
View this table:
[in this window]
[in a new window]

Table 2. **Changes in Cardiorespiratory Responses during Peak Exercise in Patients in the Exercise Group and Patients in the Control Group***



View larger version (28K):
[in this window]
[in a new window]

Figure 1. **Peak oxygen consumption in patients with compensated heart failure who did not have exercise training (control group, *n* = 14) and who did have exercise training (exercise group, *n* = 15).** The heavy line represents the mean value across time, with a significant difference noted between groups (analysis of variance; $P < 0.05$).



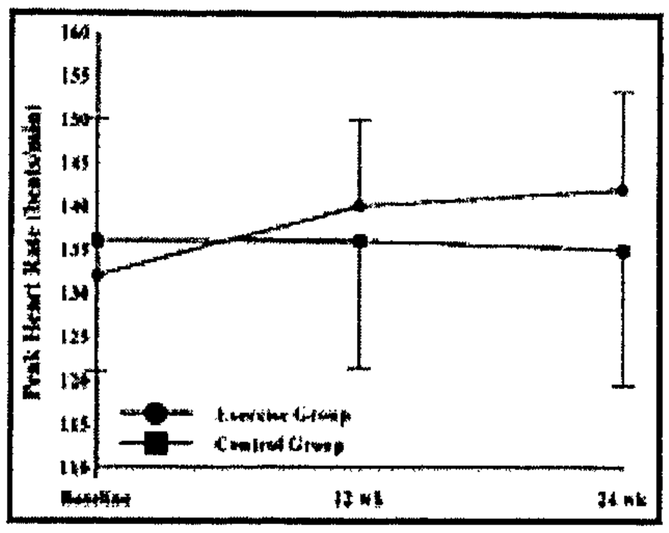
View larger version (25K):
[in this window]
[in a new window]

Figure 2. **Exercise duration in patients with compensated heart failure who did not have exercise training (control group, *n* = 14) and who did have exercise training (exercise group, *n* = 15).** The heavy line represents the mean value across time, with a significant difference noted between groups (analysis of variance; $P < 0.05$).

Among patients in the exercise group, the increase in peak VO_2 tended to be greater in those with idiopathic dilated cardiomyopathy (305 ± 60 mL/min) than in those with ischemic cardiomyopathy (121 ± 67 mL/min) (P = 0.07). No other differences were seen among patients in the exercise group, relative to the etiology of heart failure.

The difference in the change in peak ventilation over time between patients in the exercise group and patients in the control group was significant ($P < 0.01$). However, the change in the slope for ventilation to VCO_2 over time did not differ between groups (exercise group, –1.3 ± 0.9; control group, –2.2 ± 1.0). Peak ventilation increased by 12 ± 3 L/min in the exercise group ($P = 0.001$) and decreased by 4 ± 3 L/min in the control group ($P = 0.2$).

In addition, a significant difference ($P < 0.05$) was seen in the change over time in peak heart rate between the exercise group (132 ± 6 beats/min to 142 ± 5 beats/min; difference, 10 ± 4 beats/min) and the control group (136 ± 7 beats/min to 135 ± 8 beats/min; difference, –2 ± 4 beats/min) (Figure 3). Peak rate pressure product, O_2 pulse, rating of perceived exertion, respiratory exchange ratio, and systolic and diastolic blood pressures did not significantly differ between groups.



View larger version (15K):
[in this window]
[in a new window]

Figure 3. **Peak heart rate in patients with compensated heart failure who had exercise training (exercise group, *n* = 14) and did not have exercise training (control group, *n* = 13).** A significant difference over time was seen between groups (analysis of variance; $P < 0.05$). Values are expressed as means with 95% CIs.

Discussion

▲ Top
▲ Methods
▲ Results
▪ Discussion
▼ Author & Article Info
▼ References

In this randomized trial, we showed that moderately to vigorously intense exercise training safely improved exercise capacity in patients with compensated heart failure and left ventricular systolic dysfunction. Our observations of improved exercise duration, power output, and VO_2 after 24 weeks of exercise training are consistent with findings of previous uncontrolled [1, 17] or crossover [2, 18] trials involving similar types of patients. The 16% improvement in VO_2 that we found is also consistent with the 22% increase reported by Jette and colleagues [6] but is less than the 31% increase reported by Hambrecht and coworkers [5]. In our exercise group, 85% of the improvement in peak VO_2 had occurred by week 12.

Chronotropic incompetence is characteristic of patients with heart failure, and peak heart rate is a determinant of exercise capacity [19]. Our study suggests that chronotropic incompetence may be reversed, in part, by exercise training. This finding differs from those in previous reports, which showed no change in peak heart rate after exercise training [1, 5, 20]. In fact, increased peak heart rate accounted for 46% of the increase in peak VO_2 that occurred in the exercise group. We did not differentiate, however, between an increase in peak heart rate caused by a physiologic adaptation (such as a change in $ß_1$ receptor sensitivity) and an increase caused by an improved ability on the part of the exercise-trained patients to put forth greater effort. The absence of any differences between groups for rating of perceived exertion and respiratory exchange ratio (see Table 2) suggests that the increase in peak heart rate was probably not caused by an improved ability on the part of exercise-trained patients to put forth greater effort during testing. We have previously reported [21] a similar degree of heart rate-related improvement in exercise performance in heart transplant recipients participating in exercise training soon after surgery. The increased peak heart rate in such patients was thought to reflect a training-induced strengthening of the skeletal muscles of the legs, which allowed the patients to continue cycle testing until they reached a higher peak heart rate.

Not all of the increase in peak VO_2 can be explained by the increase in peak heart rate. Sullivan and colleagues [1] reported a trend toward an increased stroke volume at peak exercise after training that was accompanied by an increased peak single-leg blood flow and a trend toward an increased leg arteriovenous O_2 difference. An increase in peak cardiac output [2, 5] and a decrease in both systemic vascular resistance [5] and plasma norepinephrine levels [2] have been reported after exercise training. These changes were associated with an increase in vagal tone, which is presumed to be a result of a correction of the autonomic imbalance that is known to be present in patients with heart failure [2].

Abnormal skeletal muscle function and metabolism have also been implicated as a cause of exercise intolerance in patients with heart failure [22-24]. Although additional evidence assessing the effects of exercise training on skeletal muscle metabolism is needed, training may improve oxidative capacity [5] and

muscle energetics during submaximal exercise [3, 4, 25].

Peak ventilation, power output, and exercise duration also improved in our exercise group. Exercise duration is often used as a measure in clinical trials to evaluate the efficacy of certain drugs. Although exercise duration may not be a valid marker of exercise capacity [26, 27], our exercise group did show more than a 2-minute increase compared with the control group. This increase in exercise duration exceeds the 0.5- to 1.5-minute increases that have been previously shown in clinical trials evaluating ACE inhibitors [18, 28] or digoxin [7, 28].

The absence of a significant improvement in absolute V-AT over time in our exercise group compared with controls differs from the findings of the one randomized trial that has assessed this variable in patients with heart failure [5]. Hambrecht and colleagues [5] showed a 23% increase in absolute V-AT after 6 months of exercise training. Improved function during submaximal exercise is clearly an important consideration in these patients, who often have symptoms of exercise intolerance. Their ability to do standard or routine daily activities with fewer or less severe symptoms and a reduced heart rate response is a useful and functional outcome. Previous investigators have shown that in patients with heart failure, improved exercise capacity is associated with improved New York Heart Association class [20], quality-of-life scores [7], and patient-scored symptoms of breathlessness or fatigue [2].

Our study had some limitations. Randomization was done after patients completed the exercise test at the end of the 30-day prestudy period. Therefore, persons conducting the exercise tests at weeks 12 and 24 were aware of group assignment. Bias at these times was possible but unlikely, because an effort was made to have all patients exercise to their peak effort.

Evidence that peak effort was achieved is found in both the rating of perceived exertion and the respiratory exchange ratio. In addition, any possible learning effect associated with familiarization with testing was minimized by the inclusion of an exercise test at the beginning and the end of the 30-day prestudy period and by the use of a control group.

At study entry, most patients were receiving standard medical therapy, but minor changes that could have affected exercise performance did occur throughout the 24 weeks. The ACE inhibitor dose was increased in three patients in the exercise group and was decreased in two patients in the control group. These drugs can increase exercise duration [18], but in these five patients, such an effect would have been minimal. In each patient, the dose was changed and therapy with the drug was not stopped or started.

Although no exercise-related adverse events occurred during our study, the small sample size limited our ability to quantitate risk. Our findings on safety, however, are consistent with those of previous exercise trials that had similar sample sizes and reported few, if any, training-related complications [1, 2, 5-917, 18, 20]. No data are available on the long-term effect of regular exercise training on morbidity or mortality in patients with heart failure.

On the basis of our findings and the work of other investigators, we conclude that there seem to be no cardiac-related contraindications to exercise training in patients with stable heart failure caused by left ventricular systolic dysfunction. Exercise training improved peak VO_2, peak heart rate, peak ventilation, peak power output, and exercise duration. Much (46%) of the increase in peak VO_2 that occurred in the exercise group was caused by the increase in peak heart rate. However, further study is needed on the long-term benefit of exercise training in these patients, including the effect of training on the ability of patients to do routine activities of daily living.

Drs. Levine, Levine, and Goldstein: Henry Ford Heart and Vascular Institute, 2799 West Grand Boulevard, Detroit, MI 48202. Dr. Rogers: 2295 Riverside Drive, Trenton, MI 48183.

Dr. Schairer: 37799 Professional Center Drive, Suite 105, Livonia, MI 48154.

Author and Article Information

From Henry Ford Heart and Vascular Institute, Detroit, Michigan.
Grant Support: In part by a grant from Astra Merck.
Requests for Reprints: Steven J. Keteyian, PhD, Henry Ford Heart and Vascular Institute, Suite 1107, 2921 West Grand Boulevard, Detroit, MI 48202.
Current Author Addresses: Drs. Keteyian, Kataoka, and Stein and Mr. Brawner: Henry Ford Heart and Vascular Institute, 2921 West Grand Boulevard, Suite 1107, Detroit, MI 48202.

▲ Top
▲ Methods
▲ Results
▲ Discussion
▪ Author & Article Info
▼ References

References

▲ Top
▲ Methods
▲ Results
▲ Discussion
▲ Author & Article Info
▪ References

1. Sullivan MJ, Higginbotham MB, Cobb FR. Exercise training in patients with severe left ventricular dysfunction. Hemodynamic and metabolic effects. Circulation. 1988; 78:506-15.

2. Coats AJ, Adamopoulos S, Radaelli A, McCance A, Meyer TE, Bernerdi L, et al. Controlled trial of physical training in chronic heart failure. Exercise performance, hemodynamics, ventilation, and autonomic function. Circulation. 1992; 85:2119-31.

3. Adamopoulos S, Coats AJ, Brunotte F, Arnolda L, Meyer T, Thompson CH, et al. Physical training improves skeletal muscle metabolism in patients with chronic heart failure. J Am Coll Cardiol. 1993; 21:1101-6.

4. Stratton JR, Dunn JF, Adamopoulos S, Kemp GJ, Coats AJ, Rajagopalan B. Training partially reverses skeletal muscle metabolic abnormalities during exercise in heart failure. J Appl Physiol. 1994; 76:1575-82.

5. Hambrecht R, Niebauer J, Fiehn E, Kalberer B, Offner B, Hauer K, et al. Physical training in patients with stable chronic heart failure: effects on cardiorespiratory fitness and ultrastructural abnormalities of leg muscles. J Am Coll Cardiol. 1996; 25:1239-49.

6. Jette M, Heller R, Landry F, Blumchen G. Randomized 4-week exercise program in patients with impaired left ventricular function. Circulation. 1991; 84:1561-7.

7. Koch M, Douard H, Broustet JP. The benefit of graded physical exercise in chronic heart failure. Chest. 1992; 101:231S-4S.

8. Kostis JB, Rosen RC, Cosgrove NM, Shindler DM, Wilson AC. Nonpharmacologic therapy improves functional and emotional status in congestive heart failure. Chest. 1994; 106:996-1001.

9. Killavuori K, Toivonen L, Naveri H, Leinonen H. Reversal of autonomic derangements by physical training in chronic heart failure assessed by heart rate variability. Eur Heart J. 1995; 16:490-5.

10. Beaver WL, Wasserman K, Whipp BJ. A new method for detecting anaerobic threshold by gas exchange. J Appl Physiol. 1986; 60:2020-7.

11. Sue DY, Wasserman K, Moricca RB, Casaburi R. Metabolic acidosis during exercise in patients with chronic obstructive pulmonary disease. Use of the V-slope method for anaerobic threshold determination. Chest. 1988; 94:931-8.

12. Dickstein K, Barvik S, Aarsland T, Snapinn S, Millerhagen J. Validation of a computerized technique for detection of the gas exchange anaerobic threshold in cardiac disease. Am J Cardiol. 1990; 66:1363-7.

13. Schneider DA, Phillips SE, Stoffolano S. The simplified V-slope method of detecting the gas exchange threshold. Med Sci Sports Exerc. 1993; 25:1180-4.

14. Buller NP, Poole-Wilson PA. Mechanism of the increased ventilatory response to exercise in patients with chronic heart failure. Br Heart J. 1990; 63:281-3.

15. American College of Sports Medicine. Guidelines for Exercise Testing and Prescription. 4th ed.

Philadelphia: Lea & Febiger; 1991:148-9.

16. Geisser S, Greenhouse SW. An extension of Box's results on the use of the F distribution in multivariate analysis. Annals of Mathematical Statistics. 1958; 29:885-91.

17. Arvan S. Exercise performance of the high risk acute myocardial infarction patient after cardiac rehabilitation. Am J Cardiol. 1988; 62:197-201.

18. Meyer TE, Casadei B, Coats AJ, Davey PP, Adamopoulos S, Radaelli A, et al. Angiotensin-converting enzyme inhibition and physical training in heart failure. J Intern Med. 1991; 230:407-13.

19. Smith RF, Johnson G, Ziesche S, Bhat G, Blankenship K, Cohn JN. Functional capacity in heart failure. Comparison of methods for assessment and their relation to other indexes of heart failure. The V-HeFT VA Cooperative Studies Group. Circulation. 1993; 87(6 Suppl):VI88-93.

20. Lee AP, Ice R, Blessey R, Sanmarco ME. Long-term effects of physical training on coronary patients with impaired ventricular function. Circulation. 1979; 60:1519-26.

21. Keteyian S, Shepard R, Ehrman J, Fedel F, Glick C, Rhoads K, et al. Cardiovascular responses of heart transplant patients to exercise training. J Appl Physiol. 1991; 70:2627-31.

22. Sullivan MJ, Green HJ, Cobb FR. Skeletal muscle biochemistry and histology in ambulatory patients with long-term heart failure. Circulation. 1990; 81:518-27.

23. Myers J, Froelicher VF. Hemodynamic determinants of exercise capacity in chronic heart failure. Ann Intern Med. 1991; 115:377-86.

24. Mancini DM, Walter G, Reichek N, Lenkinski R, McCully KK, Mullen JL, et al. Contribution of skeletal muscle atrophy to exercise intolerance and altered muscle metabolism in heart failure. Circulation. 1992; 85:1364-73.

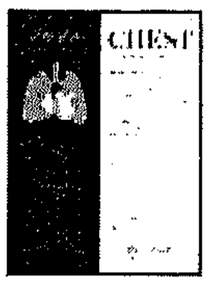
25. Minotti JR, Johnson EC, Hudson TL, Zuroske G, Murata G, Fukushima E, et al. Skeletal muscle response to exercise training in congestive heart failure. J Clin Invest. 1990; 86:751-8.

26. Chandrashekhar Y, Anand IS. Can common exercise indices determine peak exercise oxygen consumption and anaerobic threshold during stress testing in patients with chronic congestive heart failure? Indian Heart J. 1993; 45:493-5.

27. Cohen-Solal A, Caviezel B. Cardiopulmonary exercise testing in chronic heart failure. Heart Failure. 1994; April/May:46-57.

28. Comparative effects of therapy with captopril and digoxin in patients with mild to moderate heart failure. The Captopril-Digoxin Multicenter Research Group. JAMA. 1988; 259:539-44.

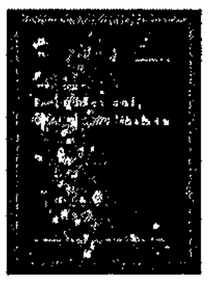
This article has been cited by other articles:



Cardiac Rehabilitation Following Percutaneous Revascularization, Heart Transplant, Heart Valve Surgery, and for Chronic Heart Failure
Chest, June 1, 2003; 123(6): 2104 - 2111.
[Abstract] [Full Text] [PDF]

Circulation ▸HOME

I. L. Pina, C. S. Apstein, G. J. Balady, R. Belardinelli, B. R. Chaitman, B. D. Duscha, B. J. Fletcher, J. L. Fleg, J. N. Myers, and M. J. Sullivan
Exercise and Heart Failure: A Statement From the American Heart Association Committee on Exercise, Rehabilitation, and Prevention
Circulation, March 4, 2003; 107(8): 1210 - 1225.
[Full Text] [PDF]

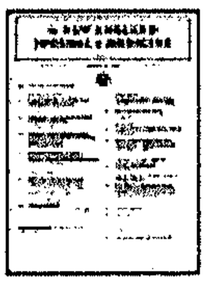


AMERICAN JOURNAL OF Respiratory and Critical Care Medicine ▸HOME

ATS/ACCP Statement on Cardiopulmonary Exercise Testing
Am. J. Respir. Crit. Care Med., January 15, 2003; 167(2): 211 - 277.
[Full Text] [PDF]

JOURNAL WATCH (GENERAL) ▸HOME

EXERCISE TRAINING GOOD FOR HEART FAILURE
Journal Watch (General), July 5, 1996; 1996(705): 7 - 7.
[Full Text]



The NEW ENGLAND JOURNAL of MEDICINE ▸HOME

P. A. Ades
Cardiac Rehabilitation and Secondary Prevention of Coronary Heart Disease
N. Engl. J. Med., September 20, 2001; 345(12): 892 - 902.
[Full Text] [PDF]

European Heart Journal ▸HOME

Recommendations for exercise training in chronic heart failure patients
Eur. Heart J., January 2, 2001; 22(2): 125 - 135.
[PDF]

Journal of Applied Physiology ▸HOME

C. T. Pu, M. T. Johnson, D. E. Forman, J. M. Hausdorff, R. Roubenoff, M. Foldvari, R. A. Fielding, and M. A. F. Singh
Randomized trial of progressive resistance training to counteract the myopathy of chronic heart failure
J Appl Physiol, June 1, 2001; 90(6): 2341 - 2350.
[Abstract] [Full Text]

European Heart Journal ▸HOME

K. Meyer
Exercise training in chronic heart failure: is it really safe?

Eur. Heart J., June 2, 1999; 20(12): 851 - 853.
[PDF]

Circulation ▸HOME

K. L. Grady, K. Dracup, G. Kennedy, D. K. Moser, M. Piano, L. W. Stevenson, and J. B. Young

Team Management of Patients With Heart Failure : A Statement for Healthcare Professionals From the Cardiovascular Nursing Council of the American Heart Association

Circulation, November 7, 2000; 102(19): 2443 - 2456.
[Full Text] [PDF]

Journal of Applied Physiology ▸HOME

A. Maiorana, G. O'Driscoll, C. Cheetham, J. Collis, C. Goodman, S. Rankin, R. Taylor, and D. Green

Combined aerobic and resistance exercise training improves functional capacity and strength in CHF

J Appl Physiol, May 1, 2000; 88(5): 1565 - 1570.
[Abstract] [Full Text]
