Effects of exercise training on left ventricular volumes and function in patients with nonischemic cardiomyopathy: Application of magnetic resonance myocardial tagging

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Background Exercise training is now an accepted component of the therapeutic regimen in patients with heart failure and underlying ischemia, but few data are available on the effects of training in patients with nonischemic dilated cardiomyopathy.

Methods Twenty-four patients (mean age 55 ± 9 years, mean ejection fraction 26.6% ± 10%) were randomized to an exercise (n = 12) or a control (n = 12) group. Patients in the exercise group underwent 5 45-minute sessions of supervised training per week. Before and after the 2-month study period, exercise testing with respiratory gas exchange and lactate analysis was performed, left ventricular volumes and ejection fraction were measured with magnetic resonance imaging, and left ventricular rotation and relaxation velocities were measured with a novel magnetic resonance imaging tagging technique.

Results Training resulted in increases in peak oxygen uptake (VO_2) (21.7 ± 4 mL/kg/min to 25.3 ± 5 mL/kg/min, $P < .05$) and VO_2 at the lactate threshold (12.8 ± 4 mL/kg/min to 19.0 ± 5 mL/kg/min, $P < .01$). No differences were observed within or between groups in left ventricular end-diastolic volume, end-systolic volume, or ejection fraction. Velocity of left ventricular rotation during systole was unchanged in both groups, and relaxation velocity was higher after training in the exercise group (21.2 ± 5 degrees/s versus 29.7 ± 12 degrees/s, $P < .05$).

Conclusion Training resulted in increases in peak VO_2 and VO_2 at the lactate threshold. Left ventricular volumes and systolic function (ie, ejection fraction and rotation velocity) were unchanged with training, suggesting that training in patients with dilated cardiomyopathy does not lead to further myocardial damage. However, the increase in relaxation velocity after exercise training indicates an improvement in diastolic function. The latter finding suggests an additional potential benefit of exercise training in patients with dilated cardiomyopathy. (Am Heart J 2002;144:719-25.)

During the last decade, numerous studies have shown the benefits of exercise training in patients with chronic heart failure (CHF). Included in a growing list of these benefits are increases in exercise tolerance, improved skeletal muscle metabolic capacity, improved endothelial function, enhanced quality of life, and a reduction in the abnormally heightened ventilatory response to exercise.[1-3] Largely because of these studies, exercise programs are now a well-established component of the therapeutic regimen for patients with CHF.[3,4] Early reservations about potential adverse effects of training on the myocardial remodeling process in postinfarction CHF[5,6] have largely been allayed by recent studies with echocardiography, pulsed Doppler, and magnetic resonance imaging (MRI) of the left ventricle in humans before and after training.[1,3,7-10] In contrast to some early reports in humans and animals,[5,6,11] these studies have shown that training does not lead to further ventricular dilatation, infarct expansion, or ventricular asynergy. However, nearly all the available data have come from patients with reduced ventricular function after myocardial infarction, underlying ischemia, or both, and few data are available on the effects of exercise training in nonischemic dilated cardiomyopathy (DCM). Such data are particularly important at this time, given that patients with DCM represent a significant proportion of the

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Table I. Demographic and clinical characteristics at baseline

	Exercise group (n = 12)	Control group (n = 12)
Age (y)	52.8 ± 12	58.2 ± 6
Height (cm)	173 ± 6.3	171 ± 4.8
Weight (kg)	75.6 ± 15	77.8 ± 14
Ejection fraction (%)	28.5 ± 10	24.9 ± 10
Maximal oxygen uptake (mL/kg/min)	21.7 ± 3.8	19.5 ± 2.7
Pulmonary function		
Forced expiratory volume (one second) 1	2.85 ± 0.96	2.71 ± 0.67
Forced expiratory volume (% of normal)	84.6 ± 24.5	90.7 ± 16.5
Forced vital capacity, 1	3.77 ± 1.01	3.28 ± 0.80
Forced vital capacity (% of normal)	90.5 ± 19.8	90.2 ± 16.5
Peak expiratory flow	5.81 ± 1.14	6.31 ± 1.94
Medications		
Digoxin	5	6
ACE inhibition	12	11
Diuretics	10	10
β-Blockers	9	9
Others	5	4

population of patients with CHF, the prevalence of which remains high.[12]

The aforementioned studies have used echocardiography and MRI to assess the remodeling process after an infarction. Echocardiography provides an assessment of cardiac motion in terms of radial displacement and systolic shortening, and standard MRI permits the measurement of more precise and specific myocardial segments.[13,14] However, rotational displacement during systole and diastole cannot be easily imaged with these techniques. Because different points of the myocardium are analyzed during the cardiac cycle, significant errors can occur in the determination of radial displacement. Recently, novel myocardial tagging techniques with MRI have been developed that make labeling of specific myocardial regions possible and that quantify torsional motion of the ventricle during contraction (twisting) and filling (untwisting). These techniques have the potential to provide greater insight into the behavior of the ventricle in response to exercise training. In this study, we used conventional MRI to more precisely quantify left ventricular volumes and ejection fraction and the previously mentioned MRI tagging techniques to assess systolic and diastolic function in patients with DCM before and after exercise training.

Methods

Twelve patients (10 male and 2 female, mean age 52.8 ± 12 years) participated in the exercise group, and 12 patients (10 male and 2 female, mean age 58.2 ± 6 years) participated in the control group, all after having given informed consent. Clinical characteristics of the 2 groups are outlined in Table I. All patients had nonischemic DCM documented with both echocardiography and angiography. All had stable symptoms before randomization, and all were New York Heart Association classification II or III. Stability was assured with the absence of congestion, symptoms, and significant changes in weight for at least 2 months. Seven patients in the exercise group and 8 patients in the control group were smoking at the time of the study. All patients were limited by fatigue, dyspnea, or both on baseline exercise testing, and none had clinical evidence of pulmonary disease.

Exercise testing

On the day of testing, patients in both groups were requested to abstain from food, coffee, and cigarettes for 3 hours before the test. Standard pulmonary function tests were performed. Maximal exercise testing was performed on an electrically braked cycle ergometer with an individualized ramp protocol.[15] Briefly, this test entails choosing an individualized ramp rate to yield a test duration of approximately 10 minutes. The patient's subjective level of exertion was quantified every minute with the Borg 6 to 20 scale.[16] All tests were continued to volitional fatigue/dyspnea. Respiratory gas exchange variables were acquired continuously throughout exercise with the Schiller CS-100 metabolic system (Baar, Switzerland). Gas exchange variables analyzed included oxygen uptake, carbon dioxide production, minute ventilation, respiratory rate, tidal volume, oxygen pulse, and respiratory exchange ratio. The lactate threshold was determined by 2 experienced observers (JM and PD) blinded to study group.

Exercise training

After stabilization was ascertained and initial testing was performed, patients randomized to the exercise group participated in a training program as outpatients at the Kantonsspital in Chur, Switzerland. Five sessions per week for a duration of 45 minutes on a cycle ergometer were performed; exercise intensity was targeted to maintain a level commensurate with 60% to 80% of maximal oxygen uptake and a continuous perceived exertion rating between 13 and 15 (Borg 6 to 20 scale). Exercise intensity was progressed throughout the 2-month study period on an individualized basis as tolerated. Heart rate and perceived exertion levels were recorded every 5 minutes. All exercise sessions were supervised directly by a medical resident.

Magnetic resonance imaging

Cine-MRI was performed with a commercially available 1.0 Tesla MRI scanner (Philips Gyroscan ACS/NT, Best, The Netherlands) with subjects in the prone position. Details of this procedure have been described by our group previously.[9]

Myocardial tagging

All subjects underwent imaging while prone with a conventional 1.5T magnetic resonance system (Philips Gyroscan ACS/NT, Best, The Netherlands) with a cardiac surface coil (16-cm diameter). An electrocardiogram was recorded, and respiratory motion was monitored with a strain gauge. After 2 short scans to localize the longitudinal heart axis, 3 short-

axis planes (basal 1 cm below the valvular annulus, equatorial at mid distance between basal and apical planes, and apical 1 cm caudal to the endocardium of the apex) were imaged and labeled with a rectangular grid (spacing 8 mm) with the complementary spatial modulation of magnetization (CSPAMM) technique. A total of 16 images was acquired for each imaging plane beginning at end diastole and ending during the next diastole. Temporal resolution was 35 ms and spatial resolution 1.4 mm × 1.4 mm, with slice thicknesses of 8 mm. Motion artifacts were reduced with measurement during a breath hold. With a scan duration of 12 to 16 seconds, the breath hold was possible for all patients. One set of images was acquired for tagging of the horizontal lines, and 1 set of images for the vertical lines. A rectangular grid was achieved with multiplication of the 2 images.

The intersection points of the tagging lines were marked and traced semiautomatically in each image with a custom-written evaluation program. Epicardial and endocardial borders were defined manually in the last image. The position of the border relative to the intramyocardial grid-crossing points was calculated and then automatically determined in all other images with the motion of the grid-crossing points. From the intersection points of the lines, 72 endocardial, midmyocardial, and epicardial points were calculated with the centerline method. End diastole was defined as the first image after the R wave, and end systole as the image with the smallest cavity area. The left ventricle was divided into 4 segments with the septal insertion point of the right ventricle and the center of gravity of left ventricle as reference points. With a slice-following tagging sequence (eg, CSPAMM), all images were compensated for through plan motion.

Systolic rotation (degrees) was defined as the systolic component of circular motion of a midmyocardial region around the center of gravity. Clockwise rotation was described as negative, counterclockwise rotation as positive. Diastolic rotation (degrees) was defined as the diastolic component of circular motion around the center of gravity. Velocity of rotation (degrees/s) was calculated as the angle of rotation between 2 cardiac phases divided by the time between those phases. Velocity of rotation was also normalized for maximal systolic rotation (s^{-1}).

Statistical analysis

Statistical Graphics Corporation software (Bethesda, Md) was used to perform multivariate analysis of variance procedures between patients randomized to exercise and control groups. Post hoc procedures were performed with the Bonferoni method. Data are presented as mean ± SD.

Results

No differences were observed between the 2 groups initially in clinical or demographic data, including age, height, weight, pulmonary function, medication status, or peak oxygen uptake (Table I). No untoward events occurred during any of the exercise testing or training procedures. During monitored stationary cycling during the course of the 2-month study period, the percentage of maximal heart rate maintained was 75% ± 12%.

Maximal exercise testing

Exercise testing responses before and after the study period are presented in Table II. Both groups achieved mean maximal respiratory exchange ratios >1.1 and mean perceived exertion levels > 19.0, suggesting that maximal efforts were generally achieved. No differences were observed within or between groups in maximal heart rate or blood pressure. The exercise group showed a 17% increase in peak oxygen uptake (VO_2) (21.7 ± 3.8 mL/kg/min vs 25.3 ± 5.2 mL/kg/min, $P < .05$), a 14% increase in exercise time ($P < .05$), and a 22% increase in peak watts achieved. No differences were observed among control subjects in these measures of exercise tolerance.

Marked increases in exercise responses were observed at the lactate threshold after training. VO_2 at this point increased from 12.8 ± 4.0 mL/kg/min to 19.0 ± 5.1 mL/kg/min (a 48% increase, $P < .01$). Exercise time increased from 4.0 ± 2.1 minutes to 7.7 ± 2.4 minutes ($P < .01$), and watts achieved increased from 55.0 ± 32 to 104.2 ± 42 ($P < .01$). Concomitant increases in heart rate, minute ventilation, CO_2 production, and lactate were observed at this point.

MRI measurements of ventricular function

Left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), ejection fraction, and mass measured with MRI are presented in Table III. LVEDV was unchanged in the exercise group (192.7 ± 46 mL vs 192.0 ± 54 mL). Although LVEDV decreased somewhat among control subjects, the change was not significant (240.6 ± 97 mL vs 222.6 ± 95 mL). LVESV was slightly but not significantly lowered in both groups after the study period. Ejection fraction and left ventricular mass were similarly unchanged in both groups. No differences were observed within or between groups in posterior or septal wall thickness measured at end diastole.

Rotation and relaxation velocities

Left ventricular rotation and relaxation velocities measured by MRI tagging are presented in Table IV. Exercise training had no effect on left ventricular rotation velocity (39.5 ± 11 degrees/s vs 39.3 ± 11 degrees/s). Similarly, rotation velocity did not change among control subjects (38.1 ± 9 degrees/s vs 37.7 ± 10 degrees/s). Relaxation velocity was significantly higher after training in the exercise group (21.2 ± 5 degrees/s vs 29.7 ± 12 degrees/s, $P < .05$), whereas this response was not different among control subjects.

Discussion

Enthusiasm for exercise training in patients with CHF initially evolved from studies in the late 1980s

Table II. Exercise and gas exchange data

	Exercise (n = 12)		Control (n = 12)		*P* value between groups
	Pre	Post	Pre	Post	
Rest					
Heart rate (beats/min)	73 ± 17	77 ± 12	78 ± 11	71 ± 23	.47
Systolic BP (mm Hg)	146 ± 21	137 ± 27	144 ± 16	139 ± 14	.81
Diastolic BP (mm Hg)	90 ± 10	85 ± 13	93 ± 11	89 ± 12	.92
Lactate threshold					
Heart rate (beats/min)	105 ± 20	125 ± 14*	119 ± 16	120 ± 19	.06
Systolic BP (mm Hg)	169 ± 34	169 ± 37	162 ± 18	159 ± 19	.81
Diastolic BP (mm Hg)	94 ± 20	92 ± 17	99 ± 8	90 ± 13	.47
VO_2 (mL/min)	964.4 ± 334	1432 ± 456†	949.5 ± 201	1045.8 ± 337	.06
VO_2 (mL/kg/min)	12.8 ± 4.0	19.0 ± 5.1†	12.4 ± 2.6	13.1 ± 3.3	.02
Minute ventilation	24.5 ± 8.3	40.3 ± 13.5†	24.5 ± 6.7	22.4 ± 11.0	.03
CO_2 production (mL/min)	806.9 ± 335	1394 ± 505†	787.2 ± 189	934.2 ± 350	.04
Respiratory exchange ratio	0.82 ± 0.01	0.96 ± 0.09†	0.83 ± 0.08	0.88 ± 0.03	.1
Lactate (mmol/L)	1.11 ± 0.4	1.53 ± 0.56	1.08 ± 0.26	1.38 ± 0.48	.07
Exercise time (min)	4.0 ± 2.1	7.7 ± 2.4†	4.2 ± 1.2	5.1 ± 1.9	.02
Perceived exertion	10.9 ± 2.8	11.6 ± 2.3	11.5 ± 2.2	11.4 ± 2.2	.6
Watts	55.0 ± 32	104.2 ± 42†	55.8 ± 19	66.7 ± 34	.05
Maximal exercise					
Heart rate (beats/min)	153 ± 22	155 ± 17	152 ± 18	157 ± 19	.83
Systolic BP (mm Hg)	197 ± 40	193 ± 37	187 ± 23	180 ± 24	.82
Diastolic BP (mm Hg)	105 ± 18	96 ± 17	102 ± 8	95 ± 11	.79
VO_2 (mL/min)	1623.3 ± 368	1885.3 ± 457	1520.4 ± 362	1653.9 ± 388	.58
VO_2 (mL/kg/min)	21.7 ± 3.8	25.3 ± 5.2*	19.5 ± 2.7	20.8 ± 2.7	.3
Minute ventilation	55.7 ± 11.7	71.2 ± 18.1	57.3 ± 13.2	57.8 ± 16.0	.1
CO_2 production (mL/min)	1812.9 ± 308	2230.2 ± 468*	1779.3 ± 302	1930.6 ± 386	.35
Respiratory exchange ratio	1.11 ± 0.05	1.19 ± 0.09	1.18 ± 0.07	1.17 ± 0.10	.35
Lactate (mmol/L)	2.65 ± 1.02	3.59 ± 0.82	2.18 ± 0.87	2.78 ± 1.29	.63
Exercise time, (min)	9.2 ± 1.9	10.5 ± 2.6*	9.2 ± 2.0	9.6 ± 2.7	.09
Perceived exertion	19.5 ± 0.65	19.5 ± 0.5	19.7 ± 0.46	19.3 ± 0.47	.26
Watts	134.6 ± 36.4	164.2 ± 48.8	130.4 ± 35.4	137.5 ± 36.5	.35

Data expressed as mean ± SD.
*$P < .05$ within group.
†$P < .01$ within group.

Table III. Left ventricular volumes, mass, and ejection fraction determined by MRI

	Exercise		Control		*P* value between groups
	Pre	Post	Pre	Post	
LVEDV (mL)	192.7 ± 46	192.0 ± 54	240.6 ± 97	222.6 ± 95	.7
LVESV (mL)	139.9 ± 46	132.2 ± 52	188.1 ± 98	169.2 ± 91	.07
Ejection Fraction (%)	28.5 ± 10	33.0 ± 11	24.9 ± 10	27.1 ± 10	.16
LV mass (g)	236.4 ± 50	230.7 ± 57	269.1 ± 78	273.5 ± 82	.06

Values presented as mean ± SD. *LVEDV*, Left ventricular end-diastolic volume; *LVESV*, left ventricular end-systolic volume.

and early 1990s largely on the basis of favorable peripheral adaptations with no apparent effects on left ventricular properties.[4,17,18] This enthusiasm was dampened somewhat by the publication of data in humans[5] and animals[6,11] that suggested that exercise training in the presence of reduced ventricular function after a myocardial infarction caused further myocardial damage via infarct expansion and ventricular dilatation. However, the available evidence during the last 10 years in humans has been consistent in the demonstration that training does not lead to further myocardial damage in such patients.[1,3,7-10,19] Nearly all of the studies in CHF however, have been performed in patients with underlying ischemic heart disease; the

Table IV. Rotation and relaxation velocities measured by magnetic resonance tagging in the exercise and control group

	Exercise group		Control group		*P* value between groups
	Pre	Post	Post	Pre	
Rotation	39.5 ± 11	39.3 ± 11	38.1 ± 9	37.7 ± 10	.98
Relaxation	21.2 ± 5	29.7 ± 12*	22.5 ± 4	20.9 ± 3	.01

Values expressed as mean ± SD.
*$P < .05$ within group.

effects of training in patients with nonischemic dilated CHF are largely unknown.

In this study, patients randomized to the exercise group showed a 17% increase in peak VO_2 and a considerable (48%) increase in VO_2 at the lactate threshold. It should be noted that although the increases in measures of exercise capacity were significant within the trained group, the absence of between-group differences at peak exercise suggest that our study was underpowered. The training effects we observed were consistent across the sample in the exercise group (ie, all patients in the exercise group had increased peak VO_2). This finding contrasts the recent observations of Belardinelli et al[20] who reported that training was only effective in patients with DCM with abnormal Doppler filling patterns. Studies assessing the effects of training in patients with CHF with mixed etiologies have observed that favorable training effects often occur only in some patients,[17,18,21] but these studies have generally not specified the pattern of training responses by etiology. Although the magnitude, degree, or time course of the response to exercise training may be influenced by exercise intensity, severity of CHF, or etiology of CHF, the difference in the response of our patients with DCM versus those of Belardinelli et al[20] suggests that this is an area that requires further study.

The only study, to our knowledge, that has compared exercise training responses between patients with ischemic CHF and nonischemic, dilated CHF was the recent report of Webb-Peploe et al.[22] After 8 weeks of training, only those patients with CHF and an etiology of DCM showed a significant increase in peak VO_2 (7.0 mL/kg/min vs 2.9 mL/kg/min increase in patients with DCM and ischemia, respectively, after training). In addition, whereas end-diastolic and end-systolic dimensions were reduced after training in patients with DCM, patients with ischemia who trained exhibited echocardiographic evidence of reduced septal excursion and shortening rate. Patients with ischemia also had more complications, such as fluid retention and incidence of rhythm disturbances. Although the patients with DCM in that study responded similarly to ours (eg, 27% increase in peak VO_2, no change in left ventricular dimensions, no complications), the responses among the patients with ischemic CHF differed from our previous findings[9,10,19] and the findings of other investigators.[1,3,7,8,17,18] In the latter studies, left ventricular volumes, ejection fraction, and mass remained unchanged after training regimens of various intensities, including high intensity training.

In terms of exercise training and its effects on ventricular volumes, this study confirms recent observations in patients with CHF and an ischemic etiology[7-10,19] in that training does not lead to further volume expansion. Interestingly, our control subjects exhibited trends for reductions in left ventricular end-diastolic and end-systolic volumes (7.5% and 10.0% reductions in end-diastolic and end-systolic volumes, respectively). Although few previous data are available specifically in patients with DCM, this study, along with that of Belardinelli et al,[20] suggests that the effects of training in patients with DCM are similar to those observed in the growing body of data among patients with reduced ventricular function after a myocardial infarction.[3,7-10,19] Specifically, we did not observe any differences in LVESV, LVEDV, or ejection fraction after exercise training. The application of MRI to address this question represents an advance over previous studies, in that MRI has been shown to be more precise and reproducible than other imaging techniques and is less dependent on geometric assumptions necessary for echocardiography.[23-26]

We also used a novel myocardial tagging technique to assess the effects of training on myocardial rotation and relaxation velocities. This technique is based on MRI and permits the labeling of specific myocardial regions for imaging cardiac motion. Echocardiography, radionuclide ventriculography, and standard MRI assess cardiac motion only in terms of radial displacement or systolic shortening, which can lead to errors because the base of the ventricle moves toward the apex during systole (translational motion) and shows rotational movement during systole and diastole that cannot easily be imaged with previous techniques. In patients with volume overload as the result of aortic stenosis, prolonged systolic rotation with enhanced torsional motion has been observed and diastolic untwisting is prolonged.[27] The insignificant change in ejection frac-

tion in this study, along with the similar rotation velocity in the exercise group before and after the training period, concurs with studies among patients with CHF with an ischemic etiology, showing that training does not alter ventricular contractility.[1,3,9,10,17-19] Our findings, along with other recent studies,[1,3,28] confirm the general impression that increases in peak VO_2 after training in CHF are largely the result of peripheral factors. A new finding in this study was the higher relaxation velocity that occurred in the trained group. This suggests an improvement in diastolic filling (ie, peak filling rate [early or late fraction], isovolumic relaxation time, improved deceleration, or some combination of these). In the Belardinelli et al[20] study of 55 patients with DCM, the improvement in peak VO_2 after training was correlated with an increase in early filling rate and a decrease in atrial filling rate. These investigators also reported that peak VO_2 was significantly increased only among patients with a Doppler pattern of abnormal relaxation.

We are unaware of other investigations addressing adaptations of the ventricle to exercise training specifically among patients with DCM. The absence of any further dilatation, the lack of change in systolic shortening and ejection fraction, and the higher relaxation velocity we observed suggest that training is associated only with an improvement in diastolic function. Several studies have suggested that diastolic function, particularly mitral flow velocity and the ratio of early to late mitral flow velocity, is a critical determinant of exercise tolerance. Some,[29,30] but not all,[31,32] studies among healthy individuals have suggested that exercise training enhances left ventricular diastolic filling at rest. Although a paucity of data exists assessing the effects of exercise training on diastolic dysfunction in CHF, both clinical and experimental evidence exists that would suggest training may have beneficial effects on diastolic function. Diastolic dysfunction is frequently the consequence of aging, hypertrophy, ischemia, or their combination, and exercise training has been shown to have favorable effects on the manifestations of all of these factors.[33]

Limitations

Two noteworthy limitations exist in this study. First, the exercise training period may have been too short to assess the true effects of training on the remodeling process. The 2-month training period was used because 1 to 2 months is the typical rehabilitation period in the central European programs; however, myocardial remodeling is an ongoing process, with at least some adaptations taking years to manifest themselves. Second, the study may have been underpowered to detect between-group changes in myocardial volumes and function. Because so few data exist on ventricular adaptations to training among patients with DCM, the study was powered on the basis of changes in peak VO_2 in our previous studies.[2,9,10]

Clinical implications

These results provide further evidence for the safety and efficacy of exercise training among patients with CHF; training results in a significant increase in a peak VO_2 and a marked increase in VO_2 at the ventilatory threshold, it does not adversely affect ventricular volumes or systolic function (rotation velocity or ejection fraction), and it may enhance diastolic filling. Although exercise training as a treatment option for these patients has gained acceptance during the last decade, data among patients with a nonischemic etiology or DCM are lacking. Although these results require confirmation, they provide further basis for the concept that an improvement in exercise capacity with exercise training could translate to improvements in quality of life,[7,18] lower rates of mortality and hospital readmission for worsening heart failure,[24] and possibly a reduced propensity for ventricular arrythmias in patients with DCM.[34]

References

1. Piepoli MF, Flather M, Coats AJS. Overview of studies of exercise training in chronic heart failure: the need for a prospective randomized multicenter European trial. Eur Heart J 1998;19:830-41.
2. Myers J, Dziekan G, Goebbles U, et al. Influence of high-intensity exercise training on the ventilatory response to exercise in patients with reduced ventricular function. Med Sci Sports Exerc 1999;31: 929-37.
3. Gianuzzi P, Tavazzi L, Meyer K, et al. Recommendations for exercise training in chronic heart failure patients. Working Group on Cardiac Rehabilitation & Exercise Physiology and Working Group on Heart Failure of the European Society of Cardiology. Eur Heart J 2000;22:125-35.
4. Agency for Health Care Policy and Research Clinical Practice Guidelines. Cardiac rehabilitation. Washington, DC: US Department of Health and Human Services; 1995.
5. Jugdutt BI, Michorowski BL, Kappagoda CT. Exercise training after anterior Q wave myocardial infarction: importance of regional left ventricular function and topography. J Am Coll Cardiol 1988:89: 402-12.
6. Gaudron P, Hu K, Schamberger R, et al. Effect of endurance training early or late after coronary artery occlusion on left ventricular remodeling, hemodynamics, and survival in rats with chronic transmural myocardial infarction. Circulation 1994;89:402-12.
7. Gianuzzi P, Cora U, Gattone M, et al. Attenuation of unfavorable remodeling by exercise training in postinfarct patients with left ventricular dysfunction: results of the Exercise in Left Ventricular Dysfunction (ELVD) trial. Circulation 1997;96:1790-7.
8. Gianuzzi P, Tavazzi L, Temporelli PL, et al. Long-term physical training and left ventricular remodeling after anterior myocardial infarction: results of the exercise in anterior myocardial infarction (EAMI) trial. J Am Coll Cardiol 1993;22:1821-9.
9. Dubach P, Myers J, Dziekan G, et al. Effect of exercise training on myocardial remodeling in patients with reduced ventricular func-

tion following myocardial infarction: application of MRI. Circulation 1997;95:2060-7.
10. Myers J, Goebbels U, Dzeikan G, et al. Exercise training and myocardial remodeling in patients with reduced ventricular function: one-year follow-up with magnetic resonance imaging. Am Heart J 2000;139:252-61.
11. Oh BH, Ono S, Glipin E, et al. Altered left ventricular remodeling with B-adrenergic blockade and exercise after coronary reperfusion in rats. Circulation 1993;87:608-16.
12. Zannad F, Briancon S, Juilliere Y, et al. Incidence, clinical and etiologic features, and outcomes of advanced chronic heart failure: the EPICAL study. J Am Coll Cardiol 1999;33:734-42.
13. American Medical Association, Council on Scientific Affairs. Magneic resonance imaging of the cardiovascular system: present state of the art and future potential. JAMA 1988;259:253-9.
14. Benjelloun H, Cranney GB, Kirk KA, et al. Interstudy reproducibility of biplane cine nuclear magnetic resonance measurements of left ventricular function. Am J Cardiol 1991;67:1413-20.
15. Myers J, Buchanan N, Walsh D, et al. Comparison of the ramp versus standard exercise protocols. J Am Coll Cardiol 1991;17: 1334-42.
16. Borg GAV. Psychophysical bases of perceived exertion. Med Sci Sports Exerc 1982;14:377-81.
17. Sullivan MJ, Higgenbotham MB, Cobb FR. Exercise training in patients with severe left ventricular dysfunction. Hemodynamic and metabolic effects. Circulation 1988;78:506-15.
18. Coats AJS, Adanopoulos S, Radaelli A, et al. Controlled trial of physical training in chronic heart failure. Circulation 1992;85: 2119-31.
19. Dubach P, Myers J, Dziekan G, et al. Effect of high intensity exercise training on central hemodynamic responses to exercise in men with reduced left ventricular function. J Am Coll Cardiol 1997;29: 1591-8.
20. Belardinelli R, Georgiou D, Cianci G, et al. Exercise training improves left ventricular diastolic filling pressure in patients with dilated cardiomyopathy: clinical and prognostic implication. Circulation 1995;91:2775-84.
21. Wilson JR, Groves J, Rayos G. Circulatory status and response to cardiac rehabilitation in patients with heart failure. Circulation 1996:94:1567-72.
22. Webb-Peploe K, Chua TP, Harrington D, et al. Different response of patients with idiopathic and ischaemic dilated cardiomyopathy to exercise training. Int J Cardiol 2000:74:215-24.
23. American Medical Association, Counsel on Scientific Affairs. Magnetic resonance imaging of the cardiovascular system: present state of the art and future potential. JAMA 1988;259:253-9.
24. Benjelloun H, Cranney GB, Kirk KA, et al. Interstudy reproducibility of biplane cine nuclear magnetic resonance measurements of left ventricular function. Am J Cardiol 1991;67:1413-20.
25. Semelka RC, Tomei E, Wagner S, et al. Normal left ventricular dimensions and function: interstudy reproducibility of measurements with cine MR imaging. Radiology 1990;174:763-8.
26. Pattyama PMT, Lamb HL, van der Velda E, et al. Left ventricular measurements with cine and spin-echo imaging: a study of reproducibility with variance component analysis. Radiology 1993;187: 261-8.
27. Stuber M, Scheidegger MB, Fischer SE, et al. Alterations in the local myocardial motion pattern in patients suffering from pressure overload due to aortic stenosis. Circulation 1999;100:361-8.
28. Hambrecht R, Niebauer J, Fiehn E, 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 1995;25:1239-49.
29. Levy WC, Cerequeira IB, Abrass RS, et al. Endurance exercise training augments diastolic filoling at rest and during exercise in healthy young and older men. Circulation 1993;88:116-26.
30. Senior DG, Waters KL, Cassidy M, et al. Effect of aerobic training on left ventricular diastolic filling. Conn Med 1989;53:67-70.
31. Shapiro LM, Smith RG. Effect of training on left ventricular structure and function: an echocardiographic study. Br Heart J 1983; 50:534-9.
32. Sadaniantz A, Yurgalevitch S, Amuda JM, et al. One year of exercise training does not alter resting left ventricular systolic or diastolic function. Med Sci Sports Exerc 1996;11:1345-50.
33. Hagberg JM. Physical activity, fitness, health, and aging. In: Bouchard C, Shephard RJ, Stephens T, editors. Physical activity, fitness, and health. Champaign: Human Kinetics; 1994. p. 993-1006.
34. Mager G, Reinhardt C, Kleine M, et al. Patients with dilated cardiomyopahy and less than 20% ejection fraction increase exercise capacity and have less severe arrhythmia after controlled exercise training. J Cardiopulm Rehabil 2000;20:196-8.