Effects of Different Types of Exercise Training Followed by Detraining on Endothelium-Dependent Dilation in Patients With Recent Myocardial Infarction

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Background—In coronary artery disease, exercise training (ET) is associated with an improvement in endothelial function, but little is known about the relative effect of different types of training. The purpose of this study was to prospectively evaluate the effect of different types of ET on endothelial function in 209 patients after a first recent acute myocardial infarction.

Methods and Results—Endothelial function was evaluated before and after 4 weeks of different types of ET and after 1 month of detraining by measuring flow-mediated dilation and von Willebrand factor levels at baseline and after ET. Patients were randomized into 4 groups: group 1, aerobic ET (n=52); group 2, resistance training (n=54); group 3, resistance plus aerobic training (n=53); and group 4, no training (n=50). At baseline, flow-mediated dilation was 4.5±2.6% in group 1, 4.01±1.6% in group 2, 4.4±4% in group 3, and 4.3±2.3% in group 4 (P=NS). After ET, flow-mediated dilation increased to 9.9±2.5% in group 1, 10.1±2.6% in group 2, and 10.8±3% in group 3 (P<0.01 versus baseline for all groups); it also increased in group 4 but to a much lesser extent (to 5.1±2.5%; P<0.01 versus trained groups). The von Willebrand factor level after ET decreased by 16% (P<0.01) similarly in groups 1, 2, and 3 but remained unchanged in group 4. Detraining returned flow-mediated dilation to baseline levels (P<0.01 versus posttraining).

Conclusion—In patients with recent acute myocardial infarction, ET was associated with improved endothelial function independently of the type of training, but this effect disappeared after 1 month of detraining. **(*Circulation*. 2009;119:1601-1608.)**

Key Words: coronary disease ■ endothelium ■ exercise ■ myocardial infarction

Endothelial dysfunction seems to be particularly relevant in patients with coronary atherosclerosis and acute and chronic myocardial ischemia,[1,2] and the presence of severe endothelial dysfunction is associated with a less favorable prognosis.[3,4] Exercise training for patients with coronary artery disease is now generally accepted as a nonpharmacological intervention to improve endothelial function[5–7]; its positive influence on endothelial and vascular function may explain, in part, the beneficial effects of exercise training on cardiovascular outcomes.[8] However, despite its importance, there is still controversy regarding the level and format of exercise that can yield optimal beneficial effects.[9] Indeed, studies on the effect of exercise training on endothelial function in patients with coronary artery disease focused mainly on aerobic training.[6,7] Practical issues such as the optimal intensity, volume, and, overall, modalities of exercise training are still unclear.[9]

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The recent update statement from the American Heart Association[10] focused on the beneficial impact of resistance training in patients with cardiovascular disease, including those with coronary artery disease. Nevertheless, the effects of resistance training on vascular function remain unclear.[11–17]

There are very few data for coronary patients,[10,18] and the available information generally focuses on the effect of associated resistance and aerobic training.[18] No study has compared the impact of resistance and aerobic training on endothelial function. In a previous study,[19] we demonstrated that, in patients who had had a recent acute myocardial infarction, aerobic training significantly improved endothelial dysfunction, although this beneficial effect was lost after 1 month of detraining. In the present trial, using the same noninvasive method of flow-mediated vasodilatation to assess endothelial function, we evaluated the effect of different types of exercise training (aerobic, resistance, and aerobic and resistance combined) on endothelial function in patients who had had a recent acute myocardial infarction and the impact of 1 month of detraining after completion of all modalities of training. We completed the endothelial evaluation by measuring the levels of von Willebrand factor

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(vWF), an established biomarker of endothelial dysfunction,[20] throughout all phases of our study.

Methods

Patients

We considered all consecutive male and female patients <70 years of age who were referred for a cardiac rehabilitation program between March 31, 2003, and March 31, 2005, after a first uncomplicated acute myocardial infarction (absence of mechanical complications, residual ischemia, left ventricular failure, severe ventricular and/or supraventricular hyperkinetic arrhythmias) in the preceding 3 weeks. Inclusion criteria were the following: the ability to exercise (baseline symptom-free capacity of ≥75 W on bicycle ergometry), absence of previous cardiovascular events, absence of diabetes and/or hypertension, nonsmoker or ex-smoker for >10 years, left ventricular ejection fraction ≥45%, and no echocardiographic evidence of ventricular hypertrophy. We excluded patients taking calcium antagonists; patients with hemodynamically significant valvular heart disease; those who had had cardiopulmonary bypass surgery; and patients with chronic lung disease, systemic and/or hematologic illnesses, and hepatic or renal insufficiency (creatinine >2.5 mg/dL).

Of the 854 patients referred for the rehabilitation program, 228 (26.7%) met the inclusion criteria. All patients underwent coronary angiography immediately after admission to hospital, and 76% underwent coronary angioplasty with stent positioning during or immediately after the acute phase of myocardial infarction. All patients were being treated with β-blockers, angiotensin-converting enzyme inhibitors, statins, and aspirin at the time of the investigation.

Protocol

The protocol was approved by the local ethics committee. Written informed consent was obtained from all patients before randomization.

The baseline evaluation included the patient's clinical history and examination, resting ECG, chest x-rays, blood chemistry (total and high- and low-density lipoprotein cholesterol [Friedwald's formula], triglycerides, baseline and postprandial glycemia, glycohemoglobin, hematocrit, and liver and kidney function tests), transthoracic echocardiogram, and a familiarization baseline maximal cardiopulmonary exercise test, reaching a respiratory exchange ratio >1.10. On the following day, brachial vasoreactivity was evaluated, and after a few hours, the cardiopulmonary exercise test was repeated.

Evaluation of Arterial Vasoreactivity

Endothelial function was assessed with the noninvasive technique proposed by Celermajer et al.[21] Brachial artery reactivity was evaluated by 2-dimensional ultrasonography (SONOS 5500, Hewlett-Packard, Palo Alto, Calif) with a linear, high-resolution probe (12.5 MHz). The patient's arm was fixed in an adjustable swivel device to ensure that the forearm remained in an identical position during the tests. All images were taken by the same investigator who was blinded to the patient's study group randomization. The brachial artery was visualized in a longitudinal section 2 to 10 cm from the medial elbow crease. Focusing and gains were optimized for the best axial resolution to visualize the m line of the posterior and the anterior wall. Flow was monitored by pulsed Doppler with a 65° angle correction relative to the artery and by positioning the 2-mm volume sample in the center of the vessel. The baseline scan of the vessel was performed after the patient had been lying supine for 10 minutes in a quiet room. The patient was fasting, and the last intake of medications had been 24 hours before. The pneumatic cuff under the elbow was then inflated to 260 mm Hg for 5 minutes. When the cuff was deflated, the measurements were repeated during the phase of reactive hyperemia (flow-mediated dilation [FMD]). Images were acquired continuously for 90 seconds after cuff deflation. Ten minutes after the end of hyperemia, having once again ensured that arterial diameter had returned to normal, the patient was given 0.3 mg sublingual nitroglycerin to assess endothelium-independent vasodilatation, and images were acquired after 5 minutes. The ECG was monitored continuously in all patients. Images were digitalized and recorded on an optical disk for offline analysis.

Venipuncture was performed in the morning on patients who had been fasting for >12 hours and had rested for at least 20 minutes to obtain venous blood for measurement of metabolic parameters and vWF. ELISAs were used to determine the plasma levels of vWF (Asserachrom, Diagnostica Stago, Asnières sur Seine, France).

Data Analysis

Data were analyzed by 2 experienced evaluators blinded to the patient's clinical picture, the stage of study, and each other's interpretation. Once the images for analysis were chosen, the boundaries for diameter measurements were identified manually with electronic calipers. Measurements were taken from the center of the m line of the anterior wall to the center of the posterior wall in end diastole, incident with the R wave on a continuously recorded ECG. Ten cardiac cycles were analyzed by each observer for each scan, and the measurements were averaged. Measurements were performed at baseline, during FMD, and after the nitroglycerin test. Changes in vessel diameter were calculated for each subject as the percentage variation of the arterial diameter under different stimuli compared with the baseline diameter.

Intraobserver variability was assessed by measuring the images stored on the optical disk in the first 10 patients 3 months after recording; the mean was 1.3% (range, 0% to 2.4%). Interobserver variability was 1.9% (range, 0.6% to 2.7%). In a preliminary study, when these procedures were performed at the same time on 2 different days in 10 healthy volunteers, the average intrasubject variability was not different (1.7%; range, 0.4% to 2.8%). These findings compare favorably with those in prior reports.[21,22]

Exercise Training Program

After the baseline evaluation, patients were randomized to receive aerobic training (group 1 [G1], 58 patients), resistance training (group 2 [G2], 57 patients), aerobic and resistance training combined (group 3 [G3], 57 patients), or no training in the control group (group 4 [G4], 56 patients).

Patients in G1 underwent moderate aerobic training 4 times a week for 4 weeks. Each session included a 10-minute warmup, 40 minutes of cycling on a cycle ergometer with telemetry monitoring and an intensity set at 75% of peak exercise heart rate measured in the second ECG stress testing, and a 10-minute cool-down. G2 patients underwent controlled resistance training 4 times a week for 4 weeks, according to the indications of the American Heart Association.[23] The patients were trained at 60% of pretraining maximum voluntary contraction, which was determined for all exercises in the circuit. Each of these sessions began and ended with a 10-minute warmup/cool-down and stretching period. Training consisted of 4 sets of 10 resistance exercises repeated 10 to 12 times for a total of 40 exercises, 30 with weights and rubber bands, each taking 45 seconds to 1 minute, with recovery intervals of 15 to 30 seconds and alternating upper and lower body. Subjects were instructed in the correct lifting technique and in preventing the Valsalva maneuver. The intensity and duration of the exercise program were progressively increased. During these sessions, aerobic/endurance exercise was avoided. G3 patients alternated controlled resistance and controlled aerobic training sessions (2 sessions of resistance training and 2 sessions of aerobic training a week). G4 patients avoided regular physical activity.

Cardiac rhythm was continuously monitored on a 4-channel (patient) telemetry system in all trained patients and in all sessions throughout the trial. Average heart rate while exercising during the training period was 100±11, 99±12, and 101±10 bpm in G1, G2, and G3 patients, respectively (P=NS). Patients also were encouraged to increase their daily physical activity level on the nontraining days by walking more, climbing stairs, and so forth. Patients in the aerobic, resistance, and combined exercise groups performed 92±3%, 95±2%, and 94±4% of the scheduled sessions, respec-

Table 1. Study Population

	Aerobic Training (n=52)		Resistance Training (n=54)		Combined Training (n=53)		Control (n=50)		
	n	%	n	%	n	%	n	%	*P*
Men	39	75	39	73	40	75.5	37	74	NS
Women	13	25	15	27	13	24.5	13	26	NS
Anterior AMI	11	21	12	22	12	23	11	22	NS
Inferior AMI	34	65	34	63	35	66	32	64	NS
Non–Q-wave AMI	7	13.5	8	15	6	11	7	14	NS
Coronary angiography									
No stenoses	2	4	3	5.5	1	2	2	4	NS
1 vessel	24	46	23	42.5	24	45	25	50	NS
2 vessels	20	38.5	23	42.5	21	40	17	34	NS
3 vessels	6	11.5	5	9	7	13	6	12	NS
PTCA	38	73	41	75.9	39	73.5	38	76	NS
Age, y	56±6		57±8		55±9		58±7		NS
EF, %	57±7		58±9		56±10		59±6		NS
CPK during AMI, U/L	1532±1121		1602±935		1498±876		1670±1020		NS

AMI indicates acute myocardial infarction; PTCA, percutaneous transluminal coronary angioplasty; EF, left ventricular ejection fraction; and CPK, creatine phosphokinase.

tively. During detraining, no patients underwent structured sessions of physical activity. Patients completed home daily physical activity registers about their total physical activity during both the training and detraining phases. No patients left the program at any point during the study.

Follow-Up

All tests were repeated after 1 month, and the results were compared with those of the baseline tests. The training program in trained patients was stopped at this point. The arterial vasoreactivity and ergometric tests were repeated again after 1 month in all groups of patients to evaluate the impact of detraining. Pharmacological therapy remained unchanged throughout the study except in 6 G1 patients, 3 G2 patients, 4 G1 patients, and 6 G4 patients. We excluded these 19 patients, so our complete sample at follow-up included 209 patients.

Statistical Analysis

Statistical analyses were performed with SPSS software (version 17.0 for Windows; SPSS Inc, Chicago, Ill). Data are presented as mean±SD. Baseline values were compared by use of 1-way ANOVA to determine whether there were significant differences among the 4 groups, followed by a Tukey posthoc multiple comparison test. Repeated-measures ANOVA, followed by the Tukey posthoc test, was used to study whether the magnitude of brachial artery reactivity differed among the trained groups and control group over time (baseline, after 1 month, and after 2 months). Linear regression analysis was used to determine the relationship between FMD and vWF level changes after training. A value of $P<0.05$ was considered statistically significant.

The authors had full access to and take responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

Compliance to training was 92±7%. No adverse events occurred during the training sessions.

Baseline

No significant differences were found between G1, G2, G3, and G4 patients regarding age, gender, site, and dimension of myocardial infarction or left ventricular ejection fraction (Table 1). In line with our inclusion criteria, the sample considered was at low cardiac risk; the majority of the

Table 2. Metabolic Parameters at Baseline and Follow-Up

	G1, Aerobic Training (n=52)		G2, Resistance Training (n=54)		G3, Combined Training (n=53)		G4, Control (n=50)	
	Time 0	Follow-Up (1 mo)	Time 0	Follow-Up (1 mo)	Time 0	Follow-Up (1 mo)	Time 0	Follow-Up (1 mo)
Total cholesterol, mg/dL	161±18	163±22	159±24	163±21	166±25	158±25	160±13	165±19
HDL cholesterol, mg/dL	48±12	49±8	47±10	45±14	46±12	48±10	46±7	47±9
LDL cholesterol, mg/dL	94±12	95±15	92±18	91±20	93±16	95±10	94±8	96±12
Triglycerides, mg/dL	142±59	154±34	144±66	140±44	144±57	151±39	139±40	145±37
Glycemia, mg/dL	89±9.3	92±8.2	84±11.3	85±8.2	81±10.5	87±12	87±7	90±9.9
Body mass index, kg/m^2	26.5±2.4	27±3.1	25.9±2.8	26.3±3.2	26.3±2.5	25.9±3.3	25.7±3.4	26.2±3.8

HDL indicates high-density lipoprotein; LDL, low-density lipoprotein.

Table 3. Ergometric Parameters During Exercise Testing at Baseline and Follow-Up

	G1, Aerobic Training (n=52)		G2, Resistance Training (n=54)		G3, Combined Training (n=53)		G4, Control (n=50)	
	Time 0	Follow-Up (1 mo)	Time 0	Follow-Up (1 mo)	Time 0	Follow-Up (1 mo)	Time 0	Follow-Up (1 mo)
Heart rate, bpm	132±8	128±9	129±9	132±7	129±9	132±7	127±8	135±9
Blood pressure, mm Hg	178±14	182±18	185±19	180±22	177±23	186±24	183±17	188±25
Time, min	13.4±2.7	18±2.9*	13.2±2	17.6±2.5*	12.9±2.7	18.3±2.5*	13.4±2.7	14.2±3.7
Peak Vo_2, mL · kg^{-1} · min^{-1}	22.0±1.2	25.7±1.6*	22.4±1.2	25.9±1.4*	21.7±1.5	26.2±1.6*	22.3±1.3	22.8±1.6

*P<0.01.

patients had limited extension of coronary artery disease, and only 11.5% of G1, 9% of G2, 13% of G3, and 12% of G4 patients had angiographically demonstrated 3-vessel disease (P=NS). None of the metabolic parameters considered or body mass index was significantly different among the different groups (Table 2). Likewise, peak exercise heart rate, blood pressure, and peak Vo_2 were similar among the 4 groups at initial cardiopulmonary exercise testing (Table 3).

Brachial Arterial Vasoreactivity

At the initial evaluation, the baseline diameter of the brachial artery did not differ significantly among the 4 groups (Table 4). After cuff release, the brachial artery diameter increased similarly in all groups (Table 4). In G1 patients, the FMD increased by 4.5±2.6%; in G2 patients, by 4.01±1.6%; in G3 patients, by 4.4±1.4; and in G4 patients, by 4.3±2.3 (P=NS by ANOVA). Nitroglycerin (provoking endothelium-independent vasodilatation) induced similar, statistically significant (P<0.01) vasodilatation in all groups (Table 4); the percentage change was 14.1±5.3% in G1, 13.8±3.6% in G2, 13.6±4.7% in G3, and 13.1±4.6% in G4 (P=NS by ANOVA) (Table 4).

Follow-Up

All 209 patients completed the follow-up. No adverse events occurred in any of the groups during follow-up. As shown in Table 2, no significant differences were found among the 4 groups in any of the metabolic parameters considered. After 1 month, peak $\dot{V}o$ increased significantly in all trained groups, whereas it remained unchanged in G4 patients (Table 3).

Brachial Arterial Reactivity

The diameter of the brachial artery at rest did not change significantly between study entry and the 1-month evaluation in any of the groups.

After 1 month, there was a significant improvement in brachial artery endothelium-dependent relaxation in trained patients (Table 4 and Figure 1). The FMD increased in G1, G2, and G3 patients (P<0.01). The FMD also improved in G4 patients (P<0.05) but to a lesser extent than in the patients in the other 3 groups (P<0.01 by ANOVA).

No significant variations were observed in endothelium-independent function after 1 month in any of the groups (Table 4).

In trained patients, the level of vWF decreased by 16% (P<0.01) similarly in G1, G2, and G3 (Table 5) but remained unchanged in G4. Changes in FMD were correlated with changes in vWF levels (r^2=0.74 in G1, r^2=0.71 in G2, and r^2=0.69 in G3; P<0.01; Figure 2).

Detraining

After 1 month of detraining, work tolerance was reduced by 16±2.3% in all trained patients with no differences among G1, G2, and G3 patients. The brachial artery baseline diameter remained essentially the same, but FMD was significantly lower after detraining than at the end of the training period (Table 4, Figure 1). Endothelium-independent vasodilatation, however, was unchanged (Table 4).

Functional capacity in G4 patients remained unchanged, and no significant variations were observed in brachial artery reactivity throughout the study (Table 4).

Discussion

To the best of our knowledge, the present study is the largest to compare the effect on endothelial function, assessed by FMD, of different types of exercise training in post–myocardial infarction patients. Several interesting findings emerged from our trial.

First, in accordance with previous reports,[19,24] an important degree of endothelial dysfunction (assessed by FMD) was found in a large, homogeneous group of patients 3 weeks after an acute myocardial infarction. In fact, the mean percent

Table 4. Brachial Reactivity Results at Baseline and Follow-Up

	G1, Aerobic Training (n=52)			G2, Resistance Training (n=54)			G3, Combined Training (n=53)			G4, Control (n=50)		
	Baseline	Follow-Up (1 mo)	DT	Baseline	Follow-Up (1 mo)	DT	Baseline	Follow-Up (1 mo)	DT	Baseline	Follow-Up (1 mo)	DT
Baseline diameter, mm	4.2±0.66	4.1±0.57	4.1±0.62	4.1±0.58	4.2±0.7	4.1±0.52	4.05±0.4	4.1±0.7	4.0±0.6	4.2±0.6	4.1±0.7	4.1±0.6
FMD%	4.5±2.6	9.9±2.5*	4.7±1.6*	4.01±1.6	10.1±2.6*	4.8±1.8*	4.4±4	10.8±3*	4.7±2.5*	4.3±2.3	5.1±2.5†	5.3±2.8
NGT%	14.1±5.3	13.5±4.1	13.6±3.9	13.8±3.6	13.9±4.2	14.1±5.1	13.6±4.7	12.9±5.6	14.2±3.7	13.1±4.6	12.9±5.2	13.7±5.8

DT indicates detraining; FMD%, percent change after FMD; and NGT%, percent change in arterial diameter after the nitroglycerin test.
*P<0.01; †P<0.05.

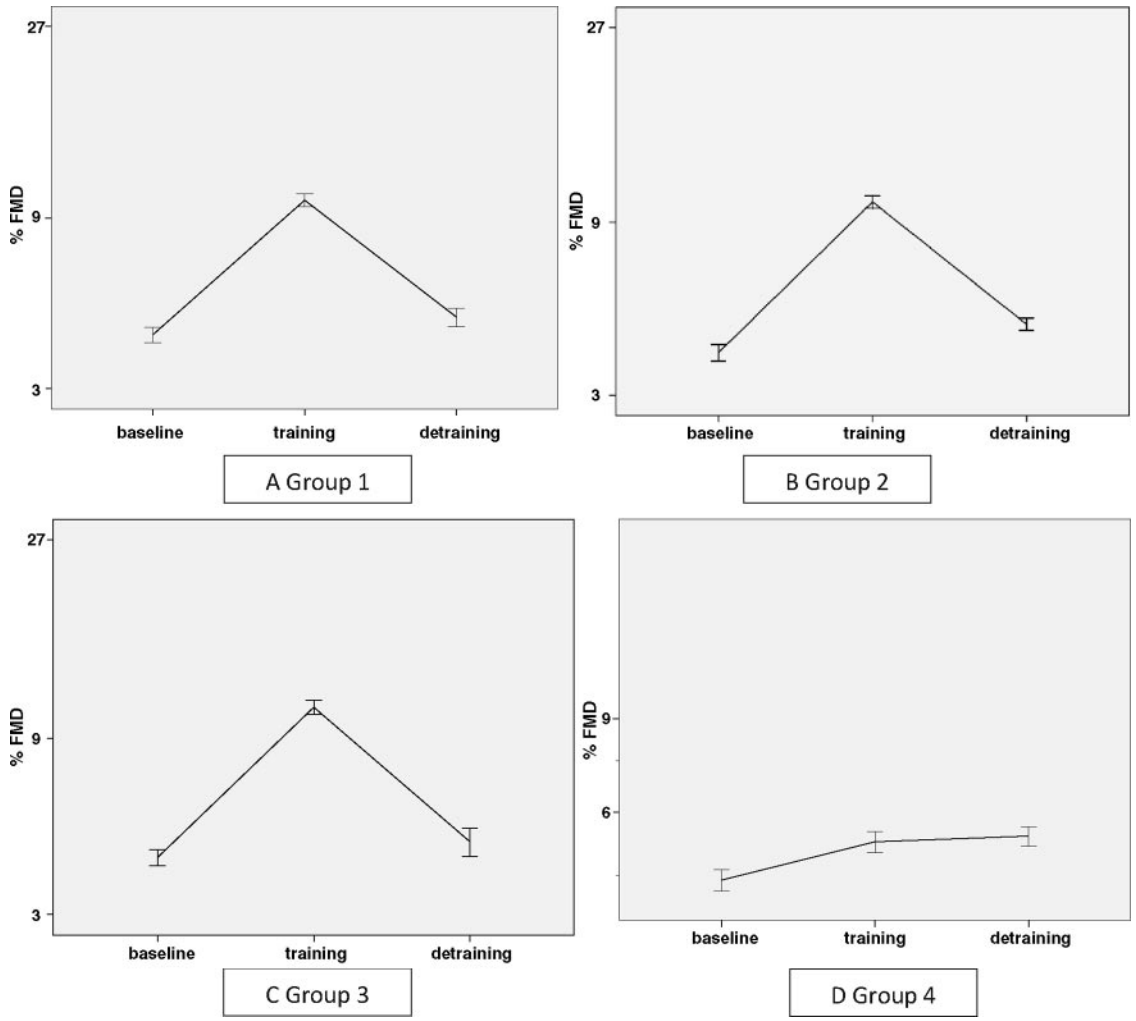

Figure 1. Percent change in FMD during the brachial reactivity study in the 3 groups that underwent training (G1, aerobic training; G2, resistance training, G3, combined aerobic and resistance training) vs a control group (G4). FMD was significantly increased after 1 month of physical training (*$P<0.01$ vs baseline, **$P<0.01$ for intergroup comparison [G1-G2-G3 after training vs control group]) and reduced after 1 month of detraining. Values are mean±SE.

FMD was significantly inferior (4.2%) to a value considered normal in healthy subjects (≈10%).[22]

Second, in line with previous results,[7,19] exercise helped to restore endothelial function as shown by the improvement in indexes of systemic endothelial function in all trained patients, whereas no significant changes in endothelium-independent vasodilatation were apparent. This adaptation appears to be predominantly endothelium dependent[9]; in fact, exercise increases shear stress, which is a strong physiological stimulus for the release of nitric oxide (NO).[25] The mechanism is likely to involve a chronic increase in NO bioavailability mediated by an increase in the expression of NO synthase[26] and by an increase in antioxidant enzymatic activity,[27] which reduces the degradation of NO synthase. A small improvement also was observed in the control group, probably secondary to spontaneous recovery after the acute event and perhaps to the effect of optimized medical treatment.[28] These findings provide evidence of the important contribution of exercise to the improvement of endothelial function and when, in postinfarction patients, optimized treatment, with a potential impact on the endothelium, is provided.

Table 5. vWF Results

	vWF, %		
	At Baseline	At 1 mo	Detraining
G1 (aerobic, n=52)	102±12	86±8.6*	98±14†
G2 (resistance, n=54)	105±15	87±9.4*	101±16†
G3 (combined, n=53)	108±11	91±11*	102±13†
G4 (control, n=50)	109±14	109±15	102±14

*$P<0.01$; †$P<0.05$.

Third, the main goal of our study was to determine the impact of different types of exercise on endothelial dysfunction. In our patients, all types of exercise were useful for correcting the endothelial dysfunction without any difference among aerobic, resistance, or combined training.

Aerobic exercise is known to have an effect on endothelial function in patients with coronary artery disease,[7,19] and its benefit is considered one of the reasons for the decrease in mortality and morbidity associated with physical training.[9] In

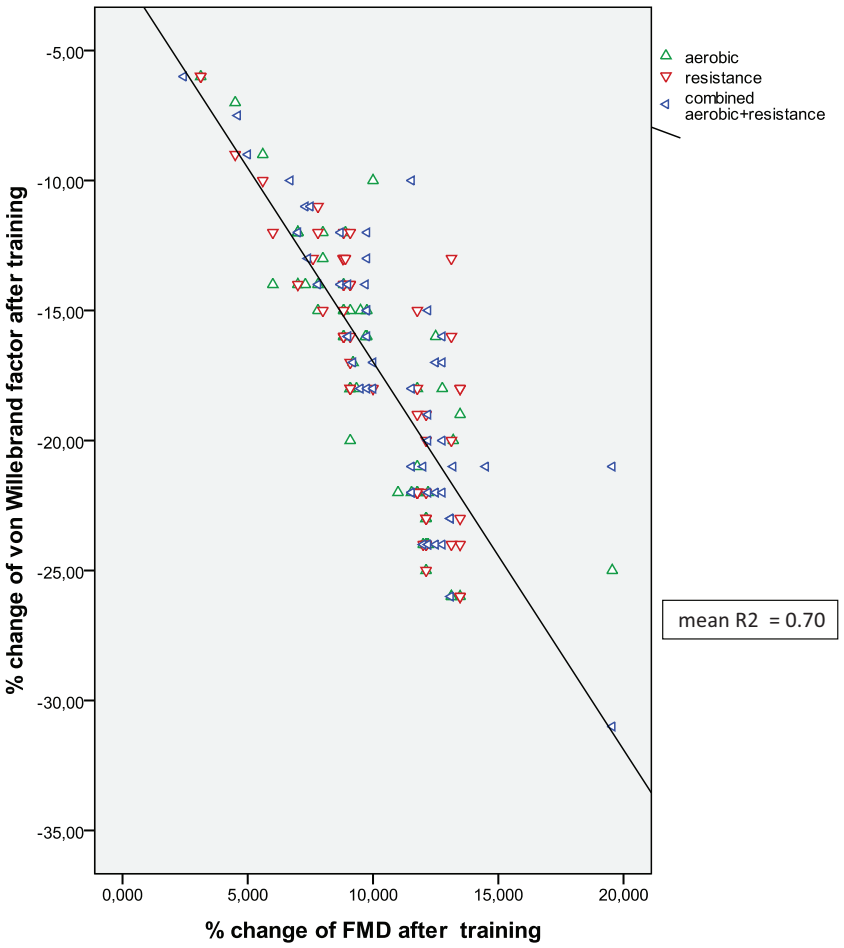

Figure 2. Relation between percent change in vWF and percent change in FMD after training.

patients with coronary artery disease, data are lacking about a similar benefit from resistance training when not combined with aerobic exercise. There is growing evidence to support the notion that dynamic resistive exercise is efficient in heart failure patients,[10,11] whereas in patients with cardiovascular risk factors, resistance exercise is inversely associated with all-cause mortality and the prevalence of metabolic syndrome.[29] In addition, although some studies showed a positive effect of resistance training on endothelial function in patients with heart failure[13–15] and in diabetics[16] and 1 study suggested that resistance training may provide cross-protection against the oxidative stress generated by aerobic exercise,[17] the influence of this type of exercise in isolation on both peripheral and central artery compliance remains unclear. One of the reasons for the inconsistency of the results is that the studies included a limited number of patients. Consequently, the interpretation of the reported results of resistance training on endothelial function is frequently complicated by the lack of sufficient power and nonrandomized trial design. To clarify whether resistance training is indeed beneficial to endothelial function and arterial compliance, it could be useful to encourage patients and professionals to include this type of training systematically in cardiac rehabilitation programs. This would also be fundamental in helping patients to adhere to their exercise training program over the long term; in fact, a varied program is recommended to prevent boredom. The use of unsophisticated and very simple equipment for resistance training such as elastic rubber bands could lead to better adherence over the long term to activities prescribed subsequently for home training. In our trial, the maximal oxygen uptake increased similarly in all trained patients. It is generally accepted that resistance training can improve oxygen uptake, albeit to a lesser extent.[10] In contrast, a much greater increase in aerobic capacity has been shown with circuit training, a type of interval training in which resistance exercises are associated with endurance/aerobic exercises with very short rest periods, thereby combining the benefits of both a cardiovascular and a strength training workout. In our resistance training program, we used short rest periods between exercises as in classic circuit training, but we avoided all endurance exercises. In a previous report,[30] the effect of resistance training on oxygen uptake in elderly subjects was comparable to that of endurance training; in this study, the degree of improvement in V_{O_2} was very similar to that in our patients.

An important question is why, in our present trial, the effect of resistance training on FMD was similar to that of aerobic training and combined training. In fact, although combined training could have the effect of increasing shear stress and thus increasing NO release, there are no data on a similar effect from resistance training.[10] It might be expected that an increase in shear stress could result not only from increased blood flow but also from other hemodynamic variables such as an increased heart rate and blood pressure,

as well as metabolic effects that would act throughout the vasculature.[10]

It is also possible to speculate that the intensity of exercise plays a major role in the stimulation of NO release. In our trial, particular attention was given to the intensity of all types of exercise, and all the sessions were controlled by telemetry to maintain the precisely prescribed intensity. The relationship between intensity of exercise and endothelial function is controversial. In 26 healthy young men, Goto et al[31] found that moderate-intensity aerobic exercise increased endothelium-dependent vasodilatation, whereas high-intensity exercise increased oxidative stress. In contrast, in a recent study of 26 patients with heart failure, high-intensity aerobic interval training resulted in a greater cardiovascular effect and greater improvement in endothelial function than did moderate continuous training.[32] In our study, exercise intensity was maintained at 75% of the heart rate during aerobic training and at 60% of pretraining maximum voluntary contraction during resistance training; this is moderate-intensity exercise,[10] which could be sufficient to improve endothelial function with both aerobic and resistance training without any long-term negative effects. In fact, Miyachi et al[33] reported that high-intensity resistance training (80% of pretraining maximum voluntary contraction) for 4 months reduced central arterial compliance in a group of 14 healthy men. We did not observe a greater improvement after combined exercise. It has been speculated that the volume of exercise could influence vascular reactivity.[34] In our study, the total number of sessions was identical in all 4 trained groups; this identical volume of exercise could explain the identical results on endothelial function.

We found that vWF, a validated indicator of endothelial dysfunction,[20] decreased by 16% without any significant differences among the trained groups. The positive correlation between the improvement in FMD and the decrease in vWF levels confirms the close relationship between vWF and endothelial function.[35] DeJong et al[36] found that an acute bout of resistance training improved fibrinolytic potential in men with coronary artery disease without any significant changes in vWF levels. In contrast, the levels of plasma vWF antigen and activity were enhanced after acute intense exercise.[37] The differences between these findings and those of our study could be explained by the intensity and duration of exercise; although intense and acute exercise could have unfavorable effects on vWF, both moderate and chronic resistance and aerobic exercise seem to have a favorable impact on endothelial function. This hypothesis is supported by the results of a study by Wang et al[38] showing, in 30 sedentary subjects, that short-term strenuous exercise increased vWF factor levels in both the control and trained groups, whereas at rest and immediately after exercise, vWF binding was reduced by training. In this trial, deconditioning reversed the effects of training on resting and postexercise state, mirroring the results of our study, in which all the beneficial effects on endothelial function were lost after 1 month of detraining. Our data confirm that 1 month of detraining is sufficient for both resistance and aerobic training to lose all positive effects on endothelial function. Our results agree with previously reported findings in patients with coronary heart disease[19] and heart failure[15] 4 and 6 weeks, respectively, after the end of training. These data imply that good, long-term adherence to training programs is necessary to maintain vascular benefits on endothelial dysfunction. This aspect is probably particularly important in patients with coronary artery disease in whom the correction of endothelial anomalies could help to slow the progression of atherosclerosis.[5,9]

Finally, no complications were observed in any of the patients throughout the trial during either the exercise sessions or postexercise recovery. This finding confirms the safety of resistance training[20] in post–myocardial infarction patients.

Conclusions

The present study demonstrates that all types of exercise (aerobic, resistance, and their combination) are safe and effective strategies for correcting endothelial dysfunction in patients after a recent myocardial infarction. These findings could help to encourage variety in the prescription of exercise and ultimately to promote better adherence to long-term physical training.

Disclosures

None.

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CLINICAL PERSPECTIVE

Physical exercise is a simple, physiological method for improving endothelial function in patients with ischemic heart disease. It is, however, not yet understood whether endothelial function can be improved only by classic aerobic exercise or by other types of exercise such as resistance training known to have many physiological benefits (eg, on muscle function). We therefore investigated endothelial function in a population of patients who had recently had a myocardial infarct, comparing 159 patients, divided into 3 groups, who underwent different types of training (aerobic, resistance, and their combination) with a control group of 50 patients who did not follow an exercise training program. Endothelial function was analyzed by measuring flow-mediated dilation. Our data clearly showed that the benefit of training, provided that it was of a certain intensity and duration, on endothelial dysfunction was independent of the type of exercise (aerobic, resistance, or combined). After 4 weeks of training, flow-mediated dilation improved significantly in all 3 trained groups. Although there was also a slight, spontaneous improvement in the control group, presumably related to the time passed since the infarct, the improvements in the trained groups were very substantial. All types of exercise were well tolerated and did not cause any complications in our patients. This is an additional reason, besides the already-mentioned beneficial effects of physical activity, for encouraging patients to carry out several types of physical activity to promote better long-term adherence to exercise programs.

Effects of Different Types of Exercise Training Followed by Detraining on Endothelium-Dependent Dilation in Patients With Recent Myocardial Infarction

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