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November 2008

Absence of Exercise Capacity Improvement After Exercise Training Program

A Strong Prognostic Factor in Patients With Chronic Heart Failure

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Background—Exercise training is established as adjuvant therapy for chronic heart failure, but the prognostic value of improvement in exercise capacity after exercise training has never been evaluated.

Methods and Results—In this prospective bicentric study, all chronic heart failure patients with left ventricular ejection fraction <45% who underwent an exercise training program in a cardiac rehabilitation center between January 2004 and September 2006 were consecutively included. Improvement in exercise capacity was assessed by change in peak oxygen consumption (δPVo_2) and in PVo_2 expressed as a percentage of predicted PVo_2 ($\delta\%PPVo_2$) measured before and after the training program. We included 155 patients (54±12 years old, male 81%, left ventricular ejection fraction=29.5±7.1%). Patients underwent 19±9 training sessions. PVo_2 and $\%PPVo_2$ were significantly increased after the training program (14% and 13%, respectively, $P<0.001$ for both). After 16±6 months follow-up, 27 patients had a cardiac event (death [n=12], cardiac transplantation [n=5], hospitalization for acute heart failure [n=10]). Univariate analysis revealed that among 17 significant predictors of cardiac events, the 2 more powerful ones were level of B-type natriuretic peptide at baseline ($P<0.0001$) and improvement in exercise capacity as assessed by δPVo_2 and $\delta\%PPVo_2$ ($P<0.0001$). Multivariate analysis revealed B-type natriuretic peptide level and $\delta\%PPVo_2$ as only independent predictive factors of outcome ($P=0.01$). The risk ratio of cardiac events for nonresponse versus response to the training program (defined as median $\delta\%PPVo_2<6\%$) was 8.2 ($P=0.0006$).

Conclusions—Among patients with chronic heart failure, the lack of improvement in exercise capacity after an exercise training program has strong prognostic value for adverse cardiac events independent of classical predictive factors such as left ventricular ejection fraction, New York Heart Association class, and B-type natriuretic peptide level. **(*Circ Heart Fail*. 2008;4:00-00.)**

Key Words: heart failure ■ exercise

Exercise training has been established as adjuvant therapy in congestive heart failure (CHF) and is recommended as a useful intervention for CHF patients.[1] Indeed, numerous studies have documented that exercise training is associated with improvement in functional capacity and quality of life.[2–4] However, some patients performing an exercise training program (ETP) do not show any improvement in exercise capacity and peak oxygen consumption (PVo_2). It is not known whether this population is at higher risk. We aimed to prospectively assess the prognostic value of improvement (or lack of improvement) in exercise capacity, after an ETP in patients with CHF.

Clinical Perspective see p ***

Methods

All CHF patients with left ventricular systolic dysfunction (left ventricular ejection fraction [LVEF]≥45%) who were able to undergo an ETP in a cardiac rehabilitation center (Les Grands Près or Lariboisière hospitals) between January 2004 and September 2006 were prospectively included in the study. Patients with recent acute heart failure (<1 month) with noncardiovascular causes of exercise limitation, primary valve disease, congenital heart disease, hypertrophic or restrictive cardiomyopathy, active myocarditis, had acute coronary syndrome within the past 2 weeks, or were under planned coronary revascularization or cardiac surgery were excluded.

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Patients at inclusion underwent Doppler echocardiography, measurement of hemoglobin, creatininemia and B-type natriuretic peptide (BNP) levels, and a cardiopulmonary exercise test. The cardiopulmonary exercise test was repeated after the completion of the program.

Doppler Echocardiography

M-mode, 2D images, and flow and tissue Doppler recordings were obtained for all patients with use of a Doppler transthoracic echocardiograph (GE Vivid 5 or 7 manufactured in Horten, Norway). Two-dimensional imaging examinations were performed as usual in parasternal long- and short-axis views and apical 4- and 2-chamber views.

LV end-diastolic diameters were measured in the TM mode from the longitudinal long- or short-axis view. Doppler recordings were obtained in the apical 4-chamber view. The sample volume was positioned at the tips of the mitral leaflets to measure the transmitral pulsed Doppler velocity: E and A were the peak values reached in early diastole and after atrial contraction, respectively. The sample volume was positioned at the lateral mitral annulus (apical 4-chamber view) to measure tissue Doppler velocity Ea corresponding to early diastolic displacement. LV systolic and diastolic volumes and LVEF were derived from biplane apical (2- and 4-chamber) views with a modified Simpson rule algorithm.[5] Systolic pulmonary artery pressure was calculated from tricuspid or pulmonary insufficiency according to the Bernouilli law.

Cardiopulmonary Exercise Test

Exercise was performed on a bicycle with 10 W/min workload increments up to exhaustion (peak respiratory exchange ratio always>1). Respiratory gas analysis involved use of a cardiopulmonary exercise test-D Medical Graphics system. V_O, carbon dioxide production (V_{CO_2}), and ventilation (V_E) were measured on a breath-by-breath basis. The percent predicted peak oxygen consumption (%PV_{O_2}) was calculated as PV_{O_2} divided by maximal predicted V_O using the values reported by Wasserman et al.[6] The ventilatory threshold (V_T) was measured by classical methods.[7] The V_E/V_{CO_2} slope was calculated by automatic linear regression fitting with the breath-by-breath values obtained throughout the whole exercise.[8] Ventilatory threshold could not be determined in only 6 patients.

Improvement in exercise capacity was assessed by the change in PV_{O_2} and %PPV_{O_2} between admission and after completion of the training program (δPV_{O_2} and δ%PV_{O_2}, respectively). The chronotropic reserve was defined as the difference between the heart rate at peak exercise and at rest. Heart rate recovery (HRR) was defined as the difference between the heart rate at peak exercise and 1 minute after recovery time.[9]

Exercise Training

Patients underwent 3 to 5 training sessions per week for 4 to 8 weeks in a cardiac rehabilitation center (Les grands près or Lariboisière hospitals). Each session included 30 minutes of segmental gymnastics and 40 minutes of cycling on an ergometric bicycle. Exercise training intensity was determined by a training heart rate equal to the heart rate observed at the ventilatory threshold at the initial cardiopulmonary exercise test evaluation. Blood pressure and heart rate were measured at rest, in the middle of the cycle ergometer session, and 5 minutes after the end of each session, during the recovery time. Patients who underwent <8 sessions were excluded from the study.

Statistical Analysis

Normally distributed continuous data are presented as mean±SD. Nonnormally distributed continuous variables are presented as median and 25th to 75th percentiles (BNP plasma level and number of exercise training sessions). Variables were compared using the Student *t* test or the Mann–Withney *U* test for nonnormally distributed variables. Univariate analysis of clinical, echocardiographic, and ergometric parameters at baseline and as well as of change in exercise capacity as assessed by δPV_{O_2} and δ%PV_{O_2} after the training program was done. The primary end point was time to death or cardiac event including heart transplantation and hospitalization for acute heart failure. Patients who did not reach this end point by 2 years were censored. The Kaplan–Meier estimator was used to depict survival-free of cardiac event in the 2 groups that were compared by the log-rank test. Multivariate analysis consisted of Cox models, including the main clinical, echocardiographic, and ergometric parameters after exclusion of collinear factors. A $P<0.05$ was considered significant. All analyses involved use of STAT VIEW 5.0 (StatView Software).

Follow-Up

Outcomes were assessed directly by contacting the patient, the family, or the patient's practitioner. Death, hospitalization for acute heart failure (adjudicated by a physician unaware of the study), and cardiac transplantation were considered cardiac events. A minimal follow-up of 12 months was required for surviving patients. No patients but 2 were lost to follow-up.

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

Results

Baseline Characteristics

Of 165 patients initially included, 10 did not complete the ET program because of orthopaedic limitations or poor motivation, for a final sample of 155 patients. The mean age was 53±12 years, 81% were male, 91% were in sinus rhythm, the etiology of the cardiopathy was ischemic in 55% of the cases, mean LVEF was 29.5±7.1%. Most of the patients received diuretics, angiotensin-converting enzyme, or angiotensin II receptor blocker inhibitors and β-blocker treatment (bisoprolol: n=110, mean daily dose=3.5±2.0 mg; carvedilol: n=33, mean daily dose=23±10 mg). Half of the population received a statin (55%) or spironolactone (53%). Patients' characteristics are in Table 1. T1, AQ:4

Patients Underwent 20 (10 to 30) Training Sessions

No serious cardiac events occurred during the training program. The exercise tolerance of trained patients improved, with a significant increase in V_T, PV_{O_2}, and %PV_{O_2} (+1.4 mL kg^{-1} min^{-1}, +2.2 mL kg^{-1} min^{-1}, and +7.1%, $P<0.0001$ for all).

Outcome

Mean follow-up was 16±6 months. Of the 155 patients included, 27 had a cardiac event: 12 died, 5 underwent cardiac transplantation, and 10 others were hospitalized for acute heart failure. Patients with a cardiac event during follow-up were more often in atrial fibrillation; were more symptomatic at rest; had lower LVEF and hemoglobin level and higher level of filling pressure, BNP and creatininemia levels; and had significantly lower exercise capacity, with lower PV_{O_2} and %PPV_{O_2}, and significantly lower chronotropic reserve and HRR than patients without a cardiac event (Table 1).

Analysis of Survival Without Cardiac Event

Univariate analysis revealed that clinical data (New York Heart Association [NYHA] functional class, sinus rhythm), echocardiographic parameters (LVEF, E/A, and E/Ea ratio and systolic PAP), biological parameters (hemoglobin level), and ergometric parameters (heart rate at peak exercise,

Table 1. Patients' Characteristics

	Overall Population (n=155)	Cardiac Event (n=27)	No Cardiac Event (n=128)
Male, n (%)	125 (81)	22 (81)	102 (80)
Age, y	53±12	57±16	53±11
Ischemic aetiology n (%)	85 (55)	19 (70)	66 (52)
Diabetes, n (%)	32 (20)	6 (23)	26 (18)
Sinus rhythm, n (%)	143 (91)	22 (81)*	121 (95)
LVEF, %	29.5±7.1	25.6±6.1*	30.8±6.7
NYHA class, n			
I–II, n (%)	90 (58)	11 (40)*	79 (62)
III–IV, n (%)	65 (42)	16 (60)*	49 (38)
LVEDD, mm	63±8	64±11	63±7
E/A ratio	1.5±0.8	1.9±1.0*	1.3±0.7
E/Ea ratio	10.6±4.1	12.5±5.8*	10±3.4
Systolic PAP, mm Hg	36±10	42±12*	33±7
Plasma BNP level, pg/mL	331 (169–228)	580 (680–1196)*	284 (137–676)
Creatininemia Level, micromoles/L	108±31	120±39*	104±28
Haemoglobin level, g/dL	12.9±1.6	12.3±1.7*	13.1±1.5
Ventilatory threshold, mL O_2 kg^{-1} min^{-1}	12.1±3.2	11.1±2.8	12.4±3.2
PVo_2, mL O_2 kg^{-1} min^{-1}	16.2±4.4	14.1±4.0*	16.7±4.3
$\%PPVo_2$, %	55±13	50±14*	56±13
RER	1.1±0.02	1.1±0.03	1.1±0.02
HR at rest, bpm	76±15	76±20	75±13
HR at peak exercise, bpm	120±23	111±22*	122±23
Chronotropic reserve, bpm	44±21	33±16*	47±21
HRR, bpm	13±12	5±12*	15±12
Workload (W)	83±26	71±17*	85±27
V_E/Vco_2 slope	36±8.2	41±7*	35±8
No. ET sessions	20 (10–30)	14 (10–27)	20 (9–30)
Treatment			
diuretics, n (%)	130 (91)	25 (92)	115 (90)
ACE-I or ARB, n (%)	152 (98)	26 (96)	126 (99)
β-blockers, n (%)	143 (91)	24 (88)	119 (93)
Bisoprolol, n (dose [mg])	110 (3.5±2.0)	21 (3.6±2.9)	89 (3.5±2.5)
Carvedilol, n (dose [mg])	33, (23±10)	3 (25±31)	30 (22±13)
Spironolactone, n (%)	84 (53)	19 (70)	65 (51)
Statins, n (%)	86 (55)	17 (63)	69 (54)

Data are n (%) or mean±SD for normally continuous distributed variables and median (25th to 75th) for nonnormally distributed ones (BNP plasma level and number of exercise training sessions).

LVEF indicates left ventricular ejection fraction; LVEDD, left ventricular end diastolic diameter; PAP, pulmonary artery pressure; PVo_2, peak oxygen consumption; $\%PPVo_2$, percent of predicted peak oxygen consumption; RER, respiratory exchange ratio; HR, heart rate; HRR, heart rate recovery; δPVo_2, change in PVo_2 before and after exercise training program; $\delta\%PPVo_2$, change in % predicted peak oxygen consumption before and after training program; ET, exercise training; ACE, angiotensin converting enzyme; ARB, angiotensin II receptor blocker inhibitor; NYHA, New York Heart Association.

*$P<0.05$ for comparison cardiac event vs no cardiac event groups.

chronotropic reserve and HRR, maximal workload, PVo_2 and $\%PPVo_2$, V_E/Vco_2 slope) before the training program were significantly predictive of prognosis (Table 2). The main prognostic factors were BNP level at admission ($P<0.0001$) and the improvement of exercise capacity after the training program completion as assessed by δPVo_2 and $\delta\%PPVo_2$ ($P=0.0007$ and $P<0.0001$, respectively). T2

Multivariate analysis of NYHA functional class, LVEF, sinus rhythm, BNP level at admission, and $\delta\%PPVo_2$ revealed only BNP level and $\delta\%PPVo_2$ independently predictive of cardiac events ($P=0.01$ for both; Table 3). With PVo_2 at admission entered in the model, the results were unchanged. Kaplan–Meier survival analysis confirmed that the occurrence of a cardiac event was significantly different between patients with and without improvement in exercise capacity after the training program (Figures 1 and 2). T3 F1–2

The risk ratio of cardiac events after the training program in terms of response and nonresponse (defined as median

Table 2. Univariate Predictors of Cardiac Events

	χ^2	*P*
Age	1.2	0.27
NYHA class (I–II vs III–IV)	7	0.001
Ischemic etiology	3.6	0.06
Diabetes	0.4	0.5
Nonsinus rhythm	8.1	0.003
LVEF	11	0.01
LVEDD	0.01	0.9
E/A ratio	8.1	0.004
E/Ea ratio	5	0.02
Systolic PAP	8.3	0.02
Plasma BNP	15	<0.0001
Creatininemia level	3.0	0.08
Hemoglobin level	4.0	0.04
Ventilatory threshold	3.3	0.06
PVo_2	7.8	0.005
$\%PPVo_2$	6.2	0.01
HR at rest	0.2	0.6
HR at peak exercise	4.0	0.03
Chronotropic reserve	8.0	0.04
HRR	9.8	0.001
Workload	6.5	0.01
VE/Vco_2 slope	5.4	0.04
δPVo_2	15.8	0.0007
$\delta\%PPVo_2$	26	<0.0001
No. ET sessions	2.5	0.1

LVEF indicates left ventricular ejection fraction; LVDD, left ventricular end diastolic diameter; PAP, pulmonary artery pressure; PVo_2, peak oxygen consumption; $\%PPVo_2$, percent of predicted peak oxygen consumption; HR, heart rate; HRR, heart rate recovery; δPVo_2, PVo_2 change before and after exercise training program; $\delta\%PPVo_2$, change in percent predicted peak oxygen consumption before and after training program; NYHA, New York Heart Association; ET, exercise training.

$\delta\%PPVo_2<6\%$) was 8.2 (95% CI, 2.7 to 27.5, $P=0.0006$). The results remained the same if patients who underwent transplantation were considered as being alive until the time of the transplantation.

Comparison of Response and Nonresponse With ETP

Compared with patients who responded to the ETP, those who did not were more often admitted to hospital in atrial fibrillation, had a slightly lower LVEF, and performed a slightly lower number of training sessions. No significant difference was found in age, frequency of diabetes, BNP level at admission, NYHA functional class at rest or exercise capacity at admission. The chronotropic reserve and HRR did not significantly differ between the 2 groups at admission (Table 4). By contrast, after completion of the training program, nonresponsive patients showed a significantly lower chronotropic reserve and HRR than responders (43±22 versus 52±17 bpm and 10±9 versus 15±8 bpm, $P=0.01$ and $P=0.02$, respectively). T4, AQ:5

Table 3. Multivariate Predictors of Cardiac Events

	χ^2	*P*	RR (95% CI)
$\delta\%PPVo_2$	5.6	0.01	0.87 (0.77–0.99)
BNP level	7.5	0.01	1.002 (1.001–1.004)
LVEF	1	0.2	0.92 (0.81–1.05)
NYHA (III–IV vs I–II)	1.3	0.24	0.42 (0.07–2.43)
Sinus rhythm	0.9	0.3	0.38 (0.05–2.69)

$\delta\%PPVo_2$ indicates change in percent of peak oxygen consumption before and after exercise training program; LVEF, left ventricular ejection fraction; RR, relative risk.

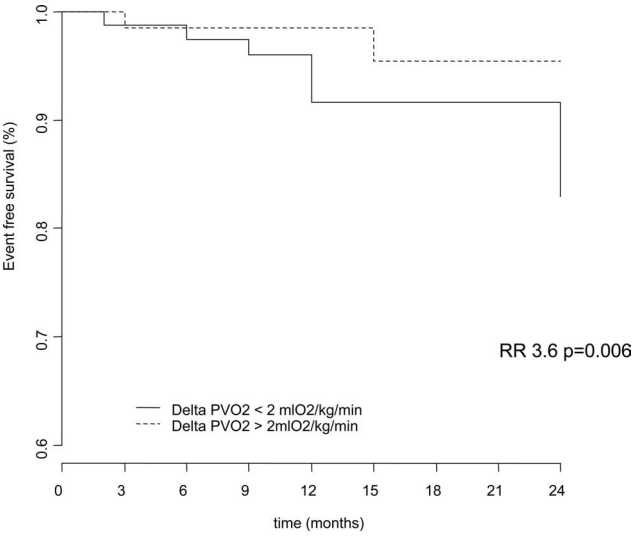

Figure 1. Kaplan–Meier curves for cardiac event-free survival according to the median value of δPVo_2 after an exercise training program in patients with chronic heart failure.

Discussion

CHF patients with LV dysfunction were followed for 16±6 months, on average, after completing the ETP. Most of the patients were treated by β-blockers and angiotensin-

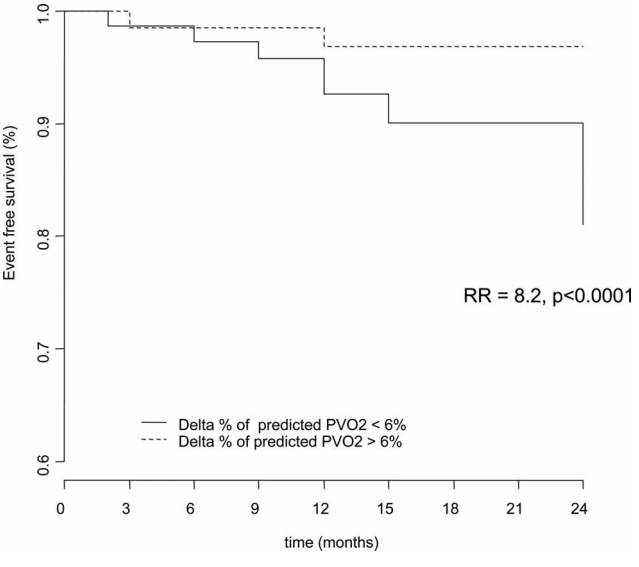

Figure 2. Kaplan–Meier curves for cardiac event-free survival according to the median value of $\delta\%PPVo_2$ after an exercise training program in patients with chronic heart failure.

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Table 4. Characteristics of Patients With or Without Improvement in Exercise Capacity After Exercise Training Program

	Patients With Improvement (n=77)	Patients Without Improvement (n=78)
Male, n (%)	61 (80)	63 (81)
Age, y	52±12	55±13
Ischemic etiology, n (%)	37 (48)	47 (60)
Diabetes, n (%)	32 (20)	18 (23)
Sinus rhythm, n (%)	75 (97)*	69 (89)
LVEF, %	31±6	28±7*
NYHA class		
I–II	47 (61)	45 (58)
III–IV	30 (39)	33 (42)
LVEDD, mm	63±8	64±11
E/A ratio	1.4±0.8	1.4±0.8
Systolic PAP, mm Hg	34±6	37±11
BNP, pg/mL	507 (221–790)	260 (114–655)
Creatininemia level, micromoles/L	103±28	109±31
Haemoglobin, g/dL	13.2±1.5	12.7±1.6
Ventilatory threshold, mL O_2 kg^{-1} min^{-1}	12.1±3.2	12.1±3.2
Chronotropic reserve, bpm	47±20	43±21
HRR, bpm	14±11	11±15
PVo_2, mL O_2 kg^{-1} min^{-1}	16.2±4.4	16.3±4.0
$\%PPVo_2$, %	54±13	58±14
RER	1.1±0.03	1.1±0.02
VE/Vco_2 slope	33±8	37±7
No. ET sessions	20 (10–30)*	16 (9–30)
Bisoprolol, n (dose, mg)	66 (3.5±2.6)	57 (3.7±2.9)
Carvedilol, n (dose, mg)	12 (26±39)	8 (21±12)
Events, n (%)	3 (4%)*	24 (31)

Data are n (%) or mean±SD for normally continuous distributed variables andmedian (25th to 75th) for nonnormally distributed ones (BNP plasma level and no. exercise training sessions).

LVEF indicates left ventricular ejection fraction; LVDD, left ventricular diastolic diameter; HRR, heart rate recovery; PVo_2, peak oxygen consumption; $\%PPVo_2$, percent of predicted peak oxygen consumption; RER, respiratory exchange ratio; ET, exercise training; NYHA, New York Heart Association.

converting enzyme or angiotensin II receptor blocker inhibitors. Classical parameters, such as NYHA functional class, LVEF, sinus rhythm, exercise capacity assessed by PVo_2 or $\%PPVo_2$, and BNP level had significant prognostic value for cardiac events. However, for the first time, lack of improvement in exercise capacity in response to a training program, as defined as median change in $\%PPVo_2<6\%$, was a strong prognostic factor of cardiac events, independently of PVo_2, BNP level, and LVEF at admission.

Exercise capacity is associated with prognosis in healthy populations as well as in patients with ischemic cardiomyopathy[10–12] and in patients with LV dysfunction.[13,14]

After a rehabilitation program, the prognostic value of change in PVo_2 has been evaluated only in patients with coronary artery disease without LV dysfunction. Indeed, Vanhees et al[15] showed in a population of 417 patients after myocardial infarction or coronary bypass surgery that a 1% greater increase in PVo_2 after training was associated with decreased cardiovascular mortality of 2%.

In the setting of CHF, several studies have shown that an increase in PVo_2 during a long follow-up is associated with improvement in outcome.[16–19] However, in these studies, the 2 exercise test evaluations were separated by a long time (4 months to 3 years). The time-related changes in exercise tolerance were related to many factors such as medical treatment adaptations, spontaneous disease evolution, and exercise activity. None of these studies specifically assessed the prognostic value of change in exercise tolerance after completion of an ETP, and none compared the prognostic value of δPVo_2 with BNP level at admission.

Belardinelli et al[20] showed in patients with ischemic cardiomyopathy and LV dysfunction that exercise training was associated with improved myocardial perfusion, coronary collateral score, and prognosis. However, the results suggested that this improvement in prognosis was held only for patients with significant improvement in PVo_2 after completion of the training program, but the number of trained patients (n=50) was not sufficient to draw conclusions. Therefore, we aimed to assess the prognostic value of change in PVo_2 after completion of a training program in patients with overt heart failure in the context of modern medical treatment. Our study confirms the prognostic value of well-known parameters such as the NYHA functional class, PVo_2, BNP level, and LVEF at admission for patients with CHF. However, our results provide important additional information: among well-treated patients, the lack of significant improvement in exercise capacity after a usual and short exercise program (19 sessions, on average) worsens the prognosis independently of the already-known predictive factors. In our study, the rate of ischemic etiology is in keeping with large epidemiological studies.[21] The improvement of exercise capacity is not significantly different in ischemic and nonischemic patients. Moreover, ischemic etiology worsens usually the prognosis; probably because of the relatively small population, we observed only a trend. It is possible that with a greater number of patients, ischemic etiology may also have appeared as predictive of outcome.

In a given patient, predicting the response to an exercise program is difficult. Indeed, the risk profile at admission for patients who responded or not to the exercise program was similar: patients who did not respond had a slightly lower LVEF and were more often in atrial fibrillation at admission than responders, but NYHA functional class at rest, exercise capacity, chronotropic reserve, HRR, and BNP level at admission, did not significantly differ. However, patients who did not respond to the exercise program showed, after ETP completion, a lower chronotropic reserve and HRR than responders. Chronotropic incompetence reflects a modulation of autonomic tone with a desensitization of the β-adrenergic receptor and more severe cardiovascular perturbations in patients with moderate to severe CHF.[22,23] The decrease in heart rate immediately after exercise is considered a function of the parasympathetic nervous system.[24] Low chronotropic reserve was associated with low HRR after completion of the

training program among patients who did not respond to the training program as compared with responders and may be related to high autonomic dysfunction which has a well-known association with cardiovascular risk.[25,26]

Thus, patients with CHF could well benefit from an ETP: (1) it improves exercise capacity and quality of life; (2) it promotes, as Belardinelli et al[20] suggested, a favorable outcome for patients who undertake such a training program (the large U.S. National Institutes of Health-sponsored study [HF-ACTION] is under way and should provide a definitive answer); and (3) the response to an exercise program helps to stratify the risk for CHF patients.

AQ: 6

Limitations

This study is a prospective survey involving a relative small population. Therefore, these results should be replicated in a larger study. Moreover the average age of the patients included is lower than in most drug heart failure trials[27,28] but is consistent with exercise heart failure trials.[2,29]

The reasons for no improvement in exercise capacity after completion of the ETP in some patients remains unclear. Our results favor a high autonomic dysfunction in these patients. Because transthoracic echocardiography was not repeated after completion of the training program, we could not assess evolution of LVEF in these patients. However, many studies have shown short training programs to have no or limited effect on LV remodeling.[2,29–31] In the same way, total peripheral resistance and endothelial function were not assessed in our patients. Further studies are necessary to better understand why some patients significantly improve exercise capacity after a training program and others do not. Furthermore, patients were classically trained at a moderate continuous intensity.[2,29] Hence, our results are not applicable to an interval trained patients.[32]

Conclusion

In CHF patients, the lack of improvement in exercise capacity after an ETP has strong prognostic value for cardiac events independent of LVEF, NYHA status, and BNP level. Patients who do not significantly improve in exercise capacity after such a training program should be carefully monitored.

AQ: 7

Disclosures

None.

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CLINICAL PERSPECTIVE

Exercise training is established as adjuvant therapy for chronic heart failure, but the prognostic value of improvement (or absence thereof) in exercise capacity after exercise training has never been evaluated. We reported in 155 chronic heart failure patients with left ventricular ejection fraction $<45\%$ followed 16 ± 6 months, that an increase in percentage of predicted peak $Vo_2<6\%$ after a short exercise training program (defining a nonresponsive group of patients) is associated with a poor outcome independently of other prognostic factors such as New York Heart Association class, left ventricular ejection fraction, and B-type natriuretic peptide level. Thus, we believe that in clinical practice chronic heart failure patients with systolic left ventricular dysfunction should undergo an exercise training program, which may lead to improved exercise capacity and quality of life. Absence of improvement allow stratification of these patients into a higher risk group, suggesting that future studies focus on methods to improve their prognosis.

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