

Is there a beneficial effect difference between age, gender, and different cardiac pathology groups of exercise training at ventilatory threshold in cardiac patients?

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Abstract

Background: Research on cardiac rehabilitation has raised interesting methods and effects without however establishing the share of the profits according to age, sex and cardiac pathology. Yet today, this disease with various pathologies strikes people of all ages and both sexes, and the recommended rehabilitation exercise intensity is often the ventilatory threshold. The aim of this study was to compare benefits of a training program at ventilatory threshold according to age, gender and cardiac pathology.

Methods: One hundred and eighty eight cardiac patients, of whom 62 had coronary artery bypass surgery, 22 artery angioplasty, 54 myocardial infarction and 50 valve replacements, aged 31–82 years, performed spirometric and cardiopulmonary exercise tests before and after a training program. This program consisted of exercise on a cycloergometer for three sessions of 45 min per week for eight weeks at heart rates attenuated at ventilatory threshold (V_{Th}) obtained during a cardiopulmonary exercise test conducted before the training period.

Results: Peak heart rate, peak aerobic power, and peak oxygen uptake determined at V_{Th} increased during the training period in all groups of subjects. Men and adult groups had higher absolute values compared to women and elderly groups. No difference was observed in cardiac pathology groups. Similar improvements of aerobic capacities were observed in age, gender and cardiac pathology groups.

Conclusions: A training program conducted at personalised V_{Th} significantly improves the aerobic physical capacities of all cardiac patients, and inducessimilar benefits whatever the age, gender or cardiac pathology. (Cardiol J 2011; 18, 6: 632–638)

Key words: cardiac rehabilitation, aerobic capacity, gender

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Introduction

Cardiac pathology is often accompanied by risk factors such as arterial hypertension, obesity, hy-

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perlipidemia and physical inactivity which lead to a reduction in the aerobic capacity, particularly in the elderly [1]. Changes in lifestyle and cardiac rehabilitation (CR) make it possible to ensure a better physical, psychological and social conditions for the patient with cardiovascular disease. Today, the prevention of subsequent cardiac events and the maintenance of physical functioning in such patients are major challenges in preventive care [1, 2].

Training at an exercise intensity corresponding to the ventilatory threshold (V_{Th}) is advised after cardiac surgery and during secondary prevention [1, 2]. Endurance exercise such as walking and cycling at V_{Th} are often performed during CR by trained patients [2, 3]. However, although endurance exercise at the V_{Th} has been shown to cause benefits in cardiac patients [2, 4] the breakdown of these benefits during a CR program according to age, gender, and cardiac pathology has yet to be investigated.

On the other hand, while the respiratory gas exchange parameters during a cardiopulmonary exercise test have been examined during the respiratory effect survey to set training intensity [5, 6], other tests, such as the pulmonary function test, constituting an important complementary examination particularly for patients with cardiac disease [7, 8] are not usually investigated. Vargas et al. [7], using the spirometric test, showed a reduction of respiratory function among cardiac patients with coronary artery bypass (CAB) surgery. A significant reduction of ventilatory flows and volumes among all patients with valve replacements was also observed by Vaidya et al. [8]. These results also showed an influence of cardiac pathology on the respiratory function after surgery. In addition, it has been reported by Kristjansdottir et al. [9] that following cardiac surgery, the respiratory system of patients suffers considerable damage, which partly explains the reduction, in some cases, of ventilatory flows and volumes observed during spirometric tests. However, the evaluation of the effects of CR using a spirometric test seems neglected well this follow-up apparatus to the respiratory behavior is often used at rest. However, this apparatus is easier used than a respiratory chain which requires the presence of a cardiologist.

Indeed, the effects of a CR with an exercise intensity equal to V_{Th} on the aerobic capacities in adult and elderly women and men or cardiac pathologies is absent from the literature.

Thus, the purpose of this study was to assess the beneficial effects of exercise training at $V_{\rm Th}$ on pulmonary function and the aerobic capacities in different age, gender and different cardiac pathology groups.

Table 1. Subjects and medications.

Subjects (men/women)	188 (112/76)
Diagnostics:	
Artery angioplasty	22 (16/6)
Coronary artery bypass	62 (36/26)
Myocardial infarction	54 (28/26)
Valve replacement	50 (32/18)
New York Heart Association class:	
1	12
Ш	176
Left ventricular ejection fraction [%]	58 ± 19
> 65%	103
> 55%	26
> 45%	21
> 30%	38
Medications:	
Beta-blockers	86
ACE inhibitors	43
Calcium channel blockers	12
Aspirin	56
Amiodarone	19
Digoxin	21
Diuretics	14
Nitrates	21
Warfarin	27

Methods

To compare the benefits of training at V_{Th} according to age (adult subjects < 65 years vs elderly subjects \geq 65 years), gender (men vs women), or cardiac pathologies (CAB surgery, artery angioplasty [AA], myocardial infarction [MI], and valve replacement [VR]), cardiac patients underwent a standardized training program for three days per week for eight weeks. A pulmonary function test and a cardiopulmonary exercise test were performed at the beginning (T_1) and the end (T_2) of the training program. Data was collected from an echocardiographic examination to determine the left ventricular ejection fraction (LVEF) calculated using Simpson's formula [10]. During the continuous training program, training-related symptoms like dyspnea, pulse and blood pressure were controlled. All patients received written information about the testing procedures, training program and examinations.

Subjects

For this preliminary study, 188 cardiovascular patients aged between 31 and 82 (Table 1) participated one month after their cardiac event. The experi-

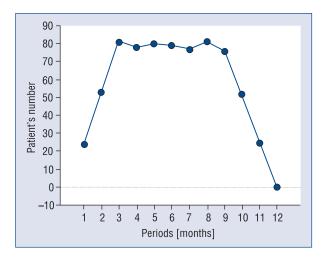


Figure 1. Patient's number at the end of each month from the first month until the last month of the training program.

mental procedures were carried out in accordance with the ethical standards of the Helsinki Declaration of 1975. Before the training program, a medical examination was performed to ensure that the criteria for inclusion were fulfilled. Only adult and elderly patients (men and women) with CAB or AA or MI or VR participated in the training program. After the first test at T_1 , patients with resting LVEF evaluated by means of echocardiography lower than 30%, significant reductions of LVEF, severe exertional ischemia $(\geq 1 \text{ mm ST-segment depression})$, severe exertional arrhythmias, or an exercise limitation due to a non--cardiopulmonary cause (e.g. arthritis) were excluded from this investigation. Other patients excluded were those who had not completed the training program and/or the last test (T_2) . The medical treatment began at least 15 days before the period of training study and was not modified thereafter, so as not to influence the data collected at T_1 and at T_2 (Fig. 1).

Pulmonary function test

The baseline spirometric function was measured (Vmax 2130 spirometer, SensorMedics, Anaheim, CA, USA) in a seated position before the cardiopulmonary exercise test. Forced vital capacity (FVC), forced expiratory volume in one second (FEV₁), FEV₁/FVC ratio, and peak expiratory flow (PEF) were recorded according to body temperature and pressure standard (BTPS).

Cardiopulmonary exercise test

The individualized exercise test protocol used in our laboratory usually resulted in a peak oxygen consumption (VO_{2peak}) test duration of 8–12 min, meeting the classical exercise testing recommendations. All subjects were encouraged to exercise until they felt unable to continue. The cardiopulmonary exercise data was realized on a cycle ergometer (Ergometrics 800S, Sensor Medics, Anaheim, CA, USA) to determine peak heart rate (HR_{peak}), peak power output (PO_{peak}), VO_{2peak}, and V_{Th}. Both inspiratory and expiratory airflow were obtained from the calibrated mass flow sensor (Vmax 2130 Metabolic Measurement System, SensorMedics, Anaheim, CA, USA) and electronically integrated to obtain volume measurements.

Measurements of oxygen uptake and carbon dioxide production were made using a computerized custom gas exchange system. The V_{Th} was determined according to three validated methods as described previously [11, 12] to determine V_{Th} from incremental exercise test data: 1) ventilatory equivalent method (VE/VO₂ method); 2) excess carbon dioxide method (PETCO₂), and 3) modified V-slope method. This point was measured in a double blind design, according to the best agreement between two independent observers. In case of disagreement (i.e. more than a 10% difference between the two observers), a third investigator was asked to assess the thresholds. The value retained was the average of the values in closer agreement. The V_{Th} was designated as the work rate that was most congruent among the different threshold determination methods. To ensure that VO_{2peak} was attained, all three of the following criteria had to be met: 1) maximal HR at a value close to 90% of the theoretical maximal HR; 2) respiratory exchange ratio \geq 1.10; and 3) pedal rate note maintained at 50 rpm at each level of exercise.

Training program

All patients were ambulatory and were trained in a cardiovascular rehabilitation service. The duration of the training program was fixed at three days per week for eight weeks. The duration of the study was one year. The training program started one month after the hospitalization for all patients and consisted of pedalling on electronic cycleergometers at the heart rate target (HR_{target}) corresponding to the V_{Th} [13]. The training schedule was the same for all the patients, and consisted of a 3-min warm-up followed by 10 min of work (at HR_{target}) and 5 min of active recovery on a stationary cycle repeated over a 45-min session. After the completion of the training session, subjects had a 2-min active recovery period followed by 3 min of passive recovery. During training, HR was continuously moni-

	T ₁	T ₂	Change (%)
Number	18	38	
Ages [years]	61.2 -	± 13.4	
Body mass [kg]	74.6 ± 14.0	74.8 ± 12.9	0.4 ± 2.4
PO _{peak} [W]	86±33	$104 \pm 42^{*}$	21±14
V _{Th} [mL/kg/min]	9.8±2.1	11.4±2.4*	17±13
VO _{2peak} [mL/kg/min]	14.2 ± 2.5	16.4±2.8*	16±9
HR₀ [bpm]	77 ± 10	75±11*	-4 ± 10
HR _{peak} [bpm]	109 ± 17	$117 \pm 20^{*}$	13±9
FVC [L]	2.9 ± 1.0	3.1±1.1*	7±13
FEV ₁ [L/s]	2.2 ± 0.7	2.3±0.8*	8±14
FEV ₁ /FVC [%]	73.8±8.9	74.5±11.4	0.3 ± 5.0
PEF [L]	5.5 ± 1.9	$6.0 \pm 1.8^{*}$	11±16

Table 2. Anthropometric characteristics, exercise aerobic capacities and spirometric variables obtained during T_1 and T_2 in all patients.

 PO_{peak} — peak power output; VO_{2peak} — oxygen consumption; V_{T_h} — ventilatory threshold; HR_0 — resting heart rate; HR_{peak} — peak heart rate; FVC — forced vital capacity; FEV_1 — forced expiratory volume in one second; FEV_1/FVC — forced vital capacity/forced vital capacity ratio; PEF — peak expiratory flow values expressed in mean ± SD; *p < 0.001

tored (Sport Tester PE 3000; Polar Electro, Kemple, Finland). The HR monitor was set so that subjects would exercise within \pm 5 bpm of the prescribed intensity (HR_{target}). An alarm sounded to remind patients to train within the preselected range.

Statistical analysis

The software Statview (SAS institute) was used for the statistical analysis. Spirometric parameters (FVC, FEV₁, FEV₁/FVC ratio, and PEF) and aerobic performance (HR₀, HR_{max}, PO_{peak}, VO_{2peak}, V_{Th}) are expressed in average value and standard deviation. Comparison between T₁ and T₂ ANOVA apparied test within age, gender and cardiac pathology group was made to assess the effects of exercise training at V_{Th} . In order to determine if there are differences in pulmonary function or aerobics capacities parameters or beneficial effects of exercise training at V_{Th} in different age, gender and different cardiac pathology groups between independent groups, ANOVA analysis (two factors: physiological parameter and groups) for repeated measurements $(T_1 \text{ and } T_2)$ was used. When the difference was significant, comparisons were then carried out using a post--hoc Newman-Keuls test. A multi-factorial ANOVA was also used to reach possible interactions of age and gender on the beneficial effect of the training program in cardiac pathology groups. The usual threshold of significance (p) was fixed at 0.05.

Results

Of 233 patients during T_1 , only 205 were selected for the study, but 17 patients did not partici-

pate in the whole training program for other reasons. Subjects' LVEF percentages and medications are illustrated in Table 1.

Table 2 shows the anthropometric characteristics, aerobic exercise capacities and spirometric variables obtained during T_1 and T_2 in all patients.

Table 3 shows the increase of pulmonary function (FVC, FEV₁, and PEF; p < 0.001) and exercise aerobic capacity (PO_{peak} , VO_{2peak} , and HR_{peak} ; p < 0.001) variables expressed in absolute values for both age groups between T_1 and T_2 . These variables remained higher in adults compared to elderly patients at T_1 and T_2 . But FEV₁/FVC ratio absolute values were stable and similar in both groups. HR₀ decreased between T_1 and T_2 in each group and were similar in the two groups. For each age group, V_{Th} increased between T_1 and T_2 without significant difference. When the pulmonary function and exercise aerobic capacity variables at T₂ were expressed as percentages (with the values obtained at T_1 considered at 100% for each subject), no significant difference was observed in the variation (value at T_2 – value at T_1) or benefit between age groups.

Table 4 presents the increase of pulmonary function (FVC, FEV₁, and PEF; p < 0.001) and aerobic capacities (PO_{peak}, VO_{2peak}, and HR_{peak}; p < 0.001) variables in absolute values. These values were significantly higher in men compared to women during T₁ and T₂. The V_{Th} was also significantly higher in men than in women from T₁ to T₂. However, no difference was observed between the sexes in FEV₁/FVC ratio. No significant difference was observed in the variation (value at T₂ – value at T₁) or

		T ₁		T ₂	Chang	ge [%]
	Adults	Elderly	Adults	Elderly	Adults	Elderly
Number	102	86				
Age [years]	51±9	73±5**				
Height [cm]	168 ± 9	164±8*				
Body mass [kg]	77 ± 15	72±1*	77 ± 14	$72 \pm 10^{*}$	0.3 ± 2.3	0.6 ± 2.6
PO _{peak} [W]	100 ± 37	70±17**	123 ± 47	$84 \pm 20^{**}$	24 ± 12	19 ± 15
VO _{2peak} [mL/kg/min]	15.1 ± 2.8	$13.2 \pm 1.7^{**}$	17.3 ± 3.1	$15.3 \pm 2.1 * *$	15 ± 14	16 ± 13
V _{Th} [mL/kg/min]	10.2 ± 2.1	$9.2 \pm 1.8^{*}$	11.9 ± 2.4	$10.8 \pm 2.2^{*}$	18 ± 10	17 ± 9
HR₀ [bpm]	77±9	78 ± 12	74 ± 12	76 ± 13	-4 ± 9	-3 ± 12
HR _{peak} [bpm]	116 ± 15	$101 \pm 16^{**}$	126 ± 16	$107 \pm 19^{**}$	9 ± 9	6 ± 10
FVC [L]	3.4 ± 0.9	2.3 ± 0.7 **	3.7 ± 1.0	2.5 ± 0.7 **	8±13	7 ± 14
FEV ₁ [L/s]	2.5 ± 0.7	$1.7 \pm 0.5^{**}$	2.7 ± 0.8	$1.8 \pm 0.5^{**}$	9 ± 14	7 ± 15
FEV ₁ /FVC [%]	76 ± 7	74±8	77±4	74 ± 7	0.5 ± 3.2	0.2 ± 6.5
PEF [L]	6.3 ± 1.9	$4.6 \pm 1.5^{**}$	6.8 ± 1.8	$5.0 \pm 1.6^{**}$	10 ± 15	12 ± 19

Table 3. Anthropometric characteristics, exercise aerobic capacities and spirometric variables obtained during T_1 and T_2 in adults and elderly.

Abbreviations as in Table 2; *p < 0.05; **p < 0.001

Table 4. Anthropometric characteristics, exercise aerobic capacities and spirometric variables obtained during T_1 and T_2 in women and men.

	т	1		T ₂	Chang	ge (%)
	Women	Men	Women	Men	Women	Men
	76	112				
Age [years]	63 ± 14	60 ± 13				
Height [cm]	159 ± 61	71±7***				
Body mass [kg]	68 ± 13	79±12***	68 ± 12	$79 \pm 11^{***}$	0.6 ± 2.8	0.3 ± 2.2
PO _{peak} [W]	66 ± 14	99±35***	79 ± 18	$123 \pm 43^{**}$	19 ± 15	24 ± 13
VO _{2peak} [mL/kg/min]	13.3 ± 2.1	14.8±2.6**	15.4 ± 2.4	17.1±2.9**	19 ± 15	17 ± 13
V _{Th} [mL/kg/min]	9.2 ± 1.9	$10.1 \pm 2.0^{*}$	10.8 ± 2.4	$11.9 \pm 2.2^{**}$	16 ± 9	15 ± 8
HR₀ [bpm]	75 ± 11	78 ± 10	73 ± 12	76 ± 11	-3 ± 9	-4 ± 12
HR _{peak} [bpm]	106 ± 15	$117 \pm 17^{*}$	113 ± 20	$125 \pm 18^{*}$	7±10	8±9
FVC [L]	2.2 ± 0.7	$3.5 \pm 0.9^{***}$	2.4 ± 0.7	$3.7 \pm 1.0^{***}$	8±13	7 ± 14
FEV ₁ [L/s]	1.7 ± 0.5	$2.5 \pm 0.8^{***}$	1.8 ± 0.6	$2.7 \pm 0.8^{***}$	8±13	8 ± 15
FEV ₁ /FVC [%]	77±6	74±9*	77±7	$74 \pm 8^{*}$	0.2 ± 6.5	0.5 ± 3.6
PEF [L]	4.3 ± 1.3	6.4 ± 1.7	4.7 ± 1.4	6.9 ± 1.7	11 ± 18	12 ± 16

Abbreviations as in Table 2; *p < 0.05; **p < 0.001; ***p < 0.001

benefit between gender groups for the pulmonary function or exercise aerobic capacity variables when their values at T_2 were expressed in percentages (with the values obtained at T_1 considered at 100% for each subject).

Table 5 shows there were no significant differences between the cardiovascular pathology groups (AA, CAB, MI, VR) for anthropometric characteristics (age, height and body mass), pulmonary function (FVC, FEV₁, FEV₁/FVC ratio, PEF) or absolute aerobic capacities (HR₀, PO_{peak}, VO_{2peak}, V_{Th}, HR_{peak}) variables. Similar benefit values (as the variation in percentage: value at T_2 – value at T_1 ; with the values obtained at T_1 considered at 100% for each subject) were found in pulmonary function or exercise aerobic capacity variables between cardiac pathology groups. In addition, no difference was observed between pathology groups, even when a multi-factorial ANOVA test was used to determine the possible interactions of age and gender on pathology.

Number 22 Age [years] 60 ± 11 Height [cm] 168 ± 9 Height [cm] 168 ± 9 Tests and change \mathbf{T}_1 \mathbf{T}_2 (%) \mathbf{T}_1 Body mass [kg] 80 ± 16 79 ± 15 -0 ± 2 77 ± 75 PO _{peak} [W] 81 ± 20 98 ± 29 20 ± 9 83 ± 75 PO _{peak} [W] 76 ± 7 75 ± 9 -2 ± 10 78 ± 72 HR _{peak} [bpm] 107 ± 11 117 ± 12 9 ± 5 109 ± 72 Vn. [mL/kg/min] 107 ± 11 117 ± 12 9 ± 5 109 ± 72 Vn. [mL/kg/min] 9 ± 2 11 ± 3 21 ± 12 10 ± 71 FEV, [L/s] 2.8 ± 08 3.2 ± 1.1 8 ± 11 2.8 ± 3.2	CAB group	dn		MI group			VR group	
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n] 76 ± 7 75 ± 9 -2 ± 10 nm] 107 ± 11 117 ± 12 9 ± 5 1 nL/kg/min] 14 ± 2 6 ± 3 19 ± 11 sq/min] 9 ± 2 11 ± 3 21 ± 12 sq/min] 2.8 ± 0.8 3.2 ± 1.1 8 ± 11 2.2 \pm 0.6 2.3 ± 0.7 5 ± 9	83 ± 35 101 ± 42	$2 23 \pm 15$	94 ± 36	13 ± 49	19 ± 14	84 ± 30	102 ± 40	22 ± 15
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2.8±0.8 3.2±1.1 8±11 2.2±0.5 2.3±0.7 5±9	10±2 11±3	14 ± 16	10 ± 2	12 ± 3	20 ± 13	10 ± 2	11 ± 3	18±11
2.2 ± 0.5 2.3 ± 0.7 5 ± 9	2.8 ± 0.9 2.9 ± 1.0	0 9±14	3.2 ± 1.2	3.3 ± 1.3	9 ± 11	2.9 ± 1.2	3.0 ± 1.0	4 ± 15
	2.0 ± 0.6 2.2 ± 0.8	8 11±19	2.4 ± 0.8	2.6 ± 0.7	9 ± 13	2.1 ± 0.9	2.2 ± 1.0	4±9
FEV,/FVC [%] 78±8 77±7 -1±3 74±	74±6 75±6	1 ± 4	74 ± 7	73±9	-0 ± 5	75±8	76 ± 9	1 ± 7
PEF [L] 5.9±1.8 6.3±2.1 7±16 5.2±	5.2±1.9 5.8±2.1	1 13±20	5.7 ± 1.7	6.3 ± 1.8	11 ± 15	5.5 ± 2.1	5.9 ± 1.9	11 ± 15

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Discussion

There was a beneficial effect of a training program at exercise intensity corresponding to the V_{Th} in all cardiac patients for both pulmonary function and aerobic performance parameters, as reported by previous researchers [1–4]. Pulmonary function and aerobic capacities variables absolute values were significantly higher in men and adults compared to women and the elderly respectively. However, there were similar values in cardiac pathology groups for all variables. There were also similar benefits in cardiac patients independent of age, gender, or cardiac pathology for pulmonary function and aerobic capacities variables.

In the present study, adherence to the exercise intensity at individual V_{Th} by all patients independent of age, gender or cardiac pathology was in accordance with the findings of previous investigations [12-14]. In all cardiac patients (Table 2), the averages of body mass were similar during T₁ and T_2 due perhaps to the short duration of the cardiac training program (less than three months for each subject). The increase of FVC and FEV₁ in this study could be explained by the respiratory work during CR allowing a reinforcement of the respiratory muscles or the resistance of the pain, especially in elderly patients and those with VR or CAB surgery [7, 8]. The stable value of FEV₁/FVC ratio could be explained by a concomitant increase of FEV₁ and FVC in all subjects during the CR program [8]. In the present study, the increase in aerobic performance parameters (PO_{peak}, VO_{2peak} , V_{Th} , HR_{peak}) with the decrease in HR₀ in all cardiac patients during the CR program agreed with previous findings [2, 15].

Consistent with previous research, the present cardiac rehabilitation program results (Table 3) in increases of most pulmonary functions (FVC, FEV₁, PEF) and aerobic performance parameter values (PO_{peak}, VO_{2peak}, V_{Th}, HR_{peak}) with higher values in adult groups compared to elderly groups [2, 16]. The difference between adult groups and elderly groups could be due to their differences in anthropometric characteristics (height and body mass) [17]. The lack of difference in improvement observed in FVC, FEV₁, FEV₁/FVC, PEF, VO_{2peak}, V_{Th}, and HR_{peak} between adults and elderly patient groups demonstrates a similar effect of the cardiac training program at the V_{Th} on pulmonary function and aerobic performance parameters in both age groups.

The present study showed no change in body mass in either sex group between T_1 and T_2 , indicating a similar training program effect on this anthropometric characteristic parameter for both sexes (Table 4). However, the differences observed at T_1 and T_2 between men and women in the absolute pulmonary function parameters (FVC, FEV₁, PEF), with higher values in men, could be supported by previous results [2, 12]. In addition, aerobic performance parameter (PO_{peak}, VO_{2peak}, V_{Th}, HR_{peak}) differences between sexes, with higher values in men, could be explained by their different anthropometric characteristics [2, 5]. However, the similar improvement in pulmonary function or aerobic performance parameters in both groups could be due to the same work intensity during the CR program.

The similar absolute values and improvements (Table 5) observed in the pulmonary function and aerobic capacities variables for all cardiac pathology groups showed that cardiac patients had similar changes in these parameters during CR program at exercise intensity corresponding to the individual V_{Th} . The improvement in age, gender or pathology groups would be significantly different if the patients were trained at tolerated exercise intensity [2].

In fact, Ades et al. [2] reported a significant difference in cardiac training program benefit between adults and elderly patients when they were trained at the personalized tolerated exercise intensity. Moreover, a difference was found in CR program benefit when women and men were trained at tolerated exercise intensity [2, 16]. Gayda et al. [18] found a higher benefit of CR program in men using combined aerobic and resistance than that during aerobic training. These results show that the improvement during CR program depends on the exercise intensity.

Conclusions

Personalized cardiac endurance training programs at individual ventilatory threshold exercise intensity induce a significant increase in pulmonary function and aerobic capacity in all cardiac patients.

Although the adults and males demonstrated higher absolute values in pulmonary function and exercise aerobic capacities than the elderly people and women without significant difference in pathology groups, cardiac training improvements are similar irrespective of age, gender or cardiac pathology.

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