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Do Responses to Exercise Training in CF Depend on Initial Fitness Level?

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Abstract

Question: To evaluate the responses to an exercise program with respect to initial fitness in subjects with CF.

Material/patients: 72 subjects (42 female) aged 10 to 43 years (Forced Expiratory Volume in 1 sec, FEV_1, of 62.0±26.7%pred) were included. Participants were divided into three groups based on Peak Oxygen Uptake (VO_{2peak} %pred.) Subjects participated in a multifaceted rehabilitation program, including 5-times-a-week exercise training, for 6 weeks. Exercise and ventilatory capacity were determined by a maximal incremental cycling test. VO_2, workload (W) and peak heart rate (HR) at peak and submaximal were used as parameters for exercise capacity and responsiveness to training.

Results: Lung function values were significantly different between groups ($p<0.05$) and increased after training ($p<0.05$) only in groups with lower initial fitness level. Responsiveness to training showed differences between groups ($p<0.05$) at peak and VAT ($p<0.05$) with higher improvements in subjects with lower initial fitness level.

Answer: The improvements in exercise parameters in CF at peak and VAT depended on the fitness level at baseline, independent of lung function. These improvements seen after training were comparable to those seen in healthy persons, suggesting that responsiveness to exercise is similar in CF and in healthy untrained persons.

Introduction

Exercise or regular physical activities have a number of potential beneficial effects in CF, including improved aerobic capacity, flexibility, coordination, muscular strength, lung function and quality of life (1-4). Despite the knowledge about the beneficial effects of exercise training and the factors leading to exercise intolerance in CF, there have been few studies on the effects of exercise training on exercise capacity with respect to subjects' baseline fitness level.

In healthy populations, the initial level of fitness seems to determine the physiological training response. Healthy people with lower peak oxygen uptake (VO_{2peak}) can improve more than those who are already trained or physically active (5). In subjects with CF a positive relationship between physical activity and VO_{2peak} has been found. (6, 7). However, little information is available concerning the benefits of an exercise program in relation to disease severity or fitness levels in CF. Cerny et al. (8) found a similar improvement in exercise capacity in subjects with moderate and severe pulmonary disease after an inpatient hospitalization, but a greater improvement in lung function in the severely affected subjects.

We recently showed a positive relationship between initial fitness level and improvement in maximal exercise capacity in CF (9). These studies suggest that responsiveness to exercise training in people with CF depends on initial fitness level and lung function, with greater benefits in those people with lower fitness level and lung function. However, it is still unclear if similar responses to exercise training occur at submaximal workloads Thus, the objective of the present study was to examine the physiological training responses in CF at maximum and submaximal workloads in relation to pre-training fitness level.

Material and Methods

Subjects

72 participants (42 female) with CF aged 10 to 43 years were included (Table1). The data were assessed during a 6 week in-patient rehabilitation course in a specialized CF institution. Participants were in stable condition, and home medication (inhaled or oral antibiotics, bronchodilators, pancreatic enzyme supplements and vitamins) was continued unchanged throughout the rehabilitation.

Individuals were included if 1) age was ≥10 years, 2) height was ≥ 120 cm, 3) their overall health was stable throughout the study period and 4) they had no acute exacerbation in the 4 weeks prior to the in-patient program. Exclusion criteria were 1) untreated CF-related diabetes, 2) heart problems, 3) 24-hour oxygen (O_2) requirement, 4) intravenous antibiotic therapy in the 4 weeks prior to the program, or if 5) their ventilatory anaerobic threshold (VAT) could not be identified. Subjects were divided into three groups based on their initial fitness level. For allocation the same reference equation was used as in the study of Nixon et al (10, 11). The "high fitness level group" (HFL) consisted of those subjects with a VO_{2peak} of ≥ 82% of predicted, "middle fitness level group" (MFL) was those with initial VO_{2peak} between 59-81% of predicted, and the "low fitness level group" (LFL) were those participants with a VO_{2peak} ≤58% of predicted (10).

The study was approved by the Ethics Committee of the Medical Chamber of Schleswig-Holstein and written informed consent was obtained for each subject, from the parents or guardians prior to the rehabilitation course.

Study design and methods

All measurements were carried out in the first 2 days after admission (T1) and in the last 2 days (T2) before discharge. Measurements of lung function were performed according to the guidelines of the European Respiratory Society (12). FEV_1 and Vital Capacity (VC) and Maximum Expiratory Flow rate at 25% of Vital Capacity (MEF_{25}) were measured by spirometry (Master screen, Jaeger, Wuerzburg, Germany) and values were expressed as a percentage of the normal values (12). Maximal voluntary ventilation (MVV) was calculated as FEV1 (l) x 35 (13).

All subjects completed an incremental cycling test (CPET) (Examiner, Lode B.V. Groningen, The Netherlands) to determine cardio-pulmonary parameters at peak and submaximal exercise capacity. After a 3 minute rest period and after 3 minutes of unloaded cycling, work rate was increased every minute by 10-20 W (Godfrey protocol), depending on patient's height and physical fitness (14). Participants were encouraged to make a maximal effort, and the test was continued until the subject could no longer maintain a pedaling cadence of 60 rpm.

The following measurements were made breath by breath (Master Screen CPX, Viasys Healthcare GmbH, Hoechberg, Germany): Oxygen Uptake (VO2 in ml/min, ml/kg/min), Minute Ventilation (VE in l) Respiratory Rate (f in min), Tidal Volume (VT in ml), Respiratory Exchange Ratio (RER, VCO_2/VO_2), Oxygen pulse (O2Pulse in ml) and Ventilatory Equivalent for Oxygen (EQO2). Breathing reserve (VE/MVV in %) at maximal and submaximal workloads were calculated. Heart rate (HR) was measured continuously on a 12 lead ECG. Workload (W in Watt, Watt/kg) was determined as the highest work level reached at peak or Ventilatory Anaerobic Threshold (VAT). The peak exercise variables were specified as the highest value in the last 30 seconds before stopping the test. Before each exercise test the metabolic cart was calibrated with gases of known concentration (O2: 21.0%, CO2: 5.0%, N_2: 74%).

A test was accepted as near maximal or truly maximal if any of the following objective criteria were met: a) heart rate $\geq$ 90% of age-predicted maximum; b) RER at test termination $\geq$ 1.05; c) VE_{peak} at test termination $\geq$ 65% of MVV (13, 15).

To determine outcome variables at the VAT, excess carbon dioxide method (ExCO2), and the modified V-Slope method were used (16, 17). Two experienced persons independently determined the VAT using these methods and results were compared with the data identified with computer algorithm methods.

Exercise Training Program

Participants exercised 5 times weekly under the supervision of a specialised sport-therapist for 6 weeks. Each training session lasted 45 minutes and consisted of different sport activities depending on age and fitness level (jogging, walking/Nordic-Walking, ball and running games, stretching, balance training, resistance training and swimming). Training intensity during jogging/walking sessions was between 80-90% of the VAT and was monitored with a portable heart rate monitor (Polar Electro, Finland).

The exercise program was part of an intensive treatment regimen. All subjects received daily chest physiotherapy for 30 to 60 minutes once to twice a day and a high energy diet with nutritional supplements according to disease severity and nutritional status.

Statistical Analysis

Data are presented as mean ± standard deviation (SD). The data were evaluated with repeated-measures analyses of variance (MANOVA) with fitness level as between-group factor and training as within-group factor. If a significant result was noticed for the between-group factor a Scheffé post-hoc test was used to compare groups. In case of significance for the factor "training" a Wilcoxon`s signed rank test was applied for within-group comparison. The strength of the correlation between initial VO2peak (ml/kg/min) and △ VO2 (ml/kg/min), $VO2_{VAT}$ and $VO2_{peak}$ (ml/kg/min), and FEV1 and △ VO2 (ml/kg/min) were calculated by Pearson's Correlation coefficient. All statistical analyses were computed with SPSS Ver. 15.0 (SPSS Inc, Chicago, IL.). A p-value of < 0.05 was considered statistically significant.

Results

Characteristics of the participants are shown in Table 1. Subjects of MFL and LFL were older than those of HFL ($p < 0.05$, Table 1). No significant differences between the groups were found for height and weight at T1 and at T2 ($p > 0.05$). All groups gained weight and BMI during the program ($p < 0.001$) and. showed similar improvements (T x FL, $p > 0.05$). At T1 und T2 the lung function values differed between groups ($p < 0.05$). FEV1, VC, MEF25 and MVV were higher in HFL ($p < 0.05$) compared to MFL and LFL. MFL showed better values in all lung function parameters compared to LFL ($p < 0.05$). At the end of the inpatient course a significant interaction "training*fitness level" was found (T x FL $p < 0.05$, Table 1). Improvements in MFL and LFL were higher than in HFL. Lung function values in HFL did not change significantly ($p > 0.05$). An improvement in MEF_{25} was seen only in MFL ($p < 0.05$). The baseline and post-training values for fitness measures are shown in Table 2 and 3. Fitness at peak and VAT differed between groups ($p < 0.05$; Table 2, 3). With the exception of HF_{peak}, all peak fitness values in HFL and MFL group were significantly higher compared to LFL ($p < 0.05$). Fitness values in HFL were non-significantly better than those of MFL ($p > 0.05$). The respiratory measurements at peak included significantly lower VE and VT in LFL compared to MFL and HFL ($p < 0.05$). No differences were found between the groups HFL and MFL. Younger subjects of HFL group showed the highest values for f whereas the values of MFL and LFL were nearly identical. VE/MVV increased with reduction in physical fitness, and values especially in MFL and LFL group were higher than those of healthy people at maximum exercise. RER and EQO2 were similar between groups.

As in peak exercise capacity, the HFL group showed better fitness values at VAT than MFL and LFL. There was no significant difference between the groups HFL and MFL except for WVAT (Watt/kg) ($p < 0.05$), whereas the LFL group had the lowest fitness values compared to HFL and MFL ($p < 0.05$). The respiratory parameters at VAT were similar between groups ($p > 0.05$). VE/MVV increased with decreased fitness level and differed significantly between groups ($p < 0.05$). VE/MVV increased significantly from pre to post-training in MFL and LFL.

Table 1 Subjects characteristics and lung function by fitness level

	HFL (n=8)		HFL vs. MFL[c]	MFL (n=32)		MFL vs. LFL[c]	LFL (n=32)		HFL vs. LFL[c]	Factor Training	Factor T x FL
	T1[a]	T2		T1	T2		T1	T2			
Age (yrs)	16.1±5.4		p=0.239	21.3±6.9		**p=0.026**	26.4±8.4		**p=0.004**		
Height (cm)	158.8±9.9		p=0.349	165.8±9.5[b]		p=0.962	166.0±11.5		p=0.214		
Weight (kg)	50.4±10.8	51.6±10.9*	p=0.658	53.9±8.2	55.3±8.4**	p=0.568	51.3±10.8	52.5±10.3**	p=0.972	**p=0.000**	p=0.556
BMI	19.8±2.3	20.3±3.1**	p=0.972	19.5±2.1	20.1±2.0***	p=0.155	18.5±2.8	18.9±2.5***	p=0.338	**p=0.000**	p=0.592
FEV1 (%pred)	96.4±15.1	100.5±7.3	**p=0.012**	74.1±20.6	78.6±22.4**	**p=0.000**	41.4±16.0	43.3±16.6*	**p=0.000**	**p=0.000**	**p=0.029**
VC (%pred)	103.9±15.3	101.8±9.4	**p=0.007**	83.5±12.8	87.4±12.6**	**p=0.000**	61.3±15.3	63.6±14.3*	**p=0.000**	**p=0.028**	**p=0.041**
MEF25 (%pred)	58.9±28.9	64.3±22.9	**p<0.05**	43.1±36.7	48.0±40.3*	**p=0.000**	12.0±7.0	12.6±8.5	**p=0.000**	**p=0.022**	**p=0.040**
MVV (l)	97.5±28.9	102.9±29.4	p=0.270	90.0±29.1	95.0±31.2**	**p=0.000**	51.4±22.0	53.9±22.5*	**p=0.000**	**p=0.000**	**p=0.032**

[a] Abbreviations as in text described. HFL = High Fitness Level Group; B = MFL = Middle Fitness Level Group; LFL = Low Fitness Level Group; FL = Fitness Level; T = Training Results are expressed as mean ± standard deviation

[b] Within groups (Wilcoxon-Test) * = p<0.05, ** = p<0.01, *** = p<0.001, NS = non-significant

[c] Between groups (Mann-Whitney-U-Test)

In all groups, with exception of HR_{peak} and HR_{VAT}, the fitness level values improved from baseline by 6 weeks. However, there was a significant "training*fitness level" interaction, reflecting different changes between the groups ($p < 0.05$, Table 2, 3). Fitness variables at peak and VAT improved significantly in MFL and LFL ($p < 0.05$) but only minor changes were seen in HFL ($p > 0.05$) after training.

There were only small non-significant improvements in respiratory parameters and a positive time effect was observed only for the VE/MVV at VAT ($p<0.05$). The Wilcoxon`s signed rank test revealed a significant result only in LFL group ($p<0.05$). In Spearman's correlations a positive relationship was found ($r = 0.432$, $p < 0.05$) between initial VO_{2peak} (ml/kg/min) and △ VO2 (ml/kg/min). No significant correlation emerged between FEV1 (%pred) and △ VO2 (ml/kg/min, $r = 0.202$, $p = 0.79$, Figure 1, 2). FEV1 (%pred) was found to correlate positively with $VO2_{peak}$ (ml/min, $r = 0.6$ $p < 0.05$, Figure 3).

Tab. 2 Maximal exercise test results by fitness level

	HFL (n=8)		HFL vs. MFL[c]	MFL (n=32)		MFL vs. LFL[c]	LFL (n=32)		HFL vs. LFL[c]	Factor Training	Factor T x FL
	T1[a]	T2		T1	T2		T1	T2			
VO2peak (ml/min)	1935.5±418.8	2006.3±390.8	p=0.636	1737.9±400.1	1898.4±377.7***	**p<0.001**	1147.2±340.0	1312.4±381.5***	**p=0.000**	**p=0.000**	**p=0.023**
VO2peak (ml/kg/min)	36.8±6.3	37.7±3.8	p=0.079	32.1±4.6	34.2±4.8**	**p<0.001**	22.3±4.1	24.9±4.6***	**p=0.000**	**p=0.000**	**p=0.026**
Wpeak (Watt)	148.8±43.2	160.3±34.6	p=0.749	132.7±35.1	157.0±37.9***	**p<0.001**	85.5±32.3	99.7±39.5***	**p=0.000**	**p=0.000**	**p=0.33**
Wpeak (W/kg)	3.0±0.6	3.1±0.3	p=0.239	2.5±0.4	2.8±0.4***	**p<0.001**	1.7±0.4	1.9±0.5***	**p=0.000**	**p=0.000**	**p=0.020**
O2pulse (ml/b)	10.9±2.8	11.2±2.1	p=0.658	10.3±2.3	11.0±2.2***	**p<0.001**	7.5±2.2	8.5±2.3***	**p=0.000**	**p=0.000**	**p=0.023**
HRpeak (b/min)	177.8±10.9	176.6±12.7	p=0.431	168.5±8.9	173.4±10.4	**p<0.001**	152.5±13.5	155.4±16.9	**p=0.000**	p=0.749	p=0.218
VE (l/min)	69.8±18.9	71.5±20.7	p=0.738	61.9±16.1	70.8±18.7***	**p<0.001**	39.6±10.2	46.9±12.8***	**p=0.000**	**p=0.000**	p=0.107
VT (l)	1.6±0.2	1.7±0.4	p=0.944	1.6±0.5	1.7±0.4	**p=0.044**	1.1±0.4	1.2±0.4	**p=0.043**	p=0.418	p=0.706
f (min)	44.9±11.0	47.4±12.9	**p=0.047**	39.6±7.9	43.0±8.3*	**p=0.038**	37.5±10.4	41.2±10.6**	**p=0.027**	**p=0.007**	p=0.943
VE/MVV (%)	73.7±19.8	67.4±46.6	p=0.853	72.2±20.7	77.7±19.9*	**p=0.024**	83.7±21.0	96.3±23.2**	**p=0.029**	**p=0.033**	p=0.169
RER	1.13±0.11	1.13±0.10	p=0.560	1.15±0.11	1.20±0.11***	**p=0.033**	1.09±0.07	1.14±0.09	p=0.867	**p=0.006**	p=0.087
EQO2	36.9±9.0	35.8±9.1	p=0.995	36.0±6.2	37.4±6.4	p=0.880	35.4±6.6	36.5±.3	p=0.959	p=0.659	p=0.446

[a] Abbreviations as in text described, HFL = High Fitness Level Group; B = MFL = Middle Fitness Level Group; LFL = Low Fitness Level Group; FL = Fitness Level; T = Training Results are expressed as mean ± standard deviation

[b] Within groups (Wilcoxon-Test) * = p<0.05, ** = p<0.01, *** = p<0.001, NS = non-significant

[c] Between groups Mann-Whitney-U-Test

Tab. 3 Submaximal exercise test results by fitness level

	HFL (n=8)		HFL vs. MFL[c]	MFL (n=32)		MFL vs. LFL[c]	LFL (n=32)		HFL vs. LFL[c]	Factor Training	Factor TxFL
	T1[a]	T2		T1	T2		T1	T2			
VO2VAT (l/min)	1332.4±350.9	1458.0±239.0	p=0.508	1183.1±279.0	1352.7±293.7**	**p=0.000**	873.8±228.8	977.8±277.3**	**p=0.000**	**p=0.001**	**p=0.016**
VO2VAT(ml/kg/min)	26.3±5.3	27.3±3.5	p=0.078	22.1±4.1	24.2±3.8*	**p=0.000**	16.5±3.4	18.5±3.6**	**p=0.000**	**p=0.000**	**p=0.020**
WVAT (Watt)	106.4±37.2	114.3±19.0	p=0.223	84.7±25.8	102.4±26.3***	**p=0.000**	61.8±22.6	68.3±27.0**	**p=0.000**	**p=0.000**	**p=0.046**
WVAT (Watt/kg)	2.0±0.5	2.1±0.2	**p=0.015**	1.6±0.4	1.8±0.4**	**p=0.000**	1.1±0.3	1.3±0.4**	**p=0.000**	**p=0.000**	**p=0.039**
O2pulse (ml/b)	8.9±2.5	9.3±1.9	p=0.248	8.5±1.8	9.3±2.1***	**p=0.000**	6.6±1.7	7.6±2.0***	**p=0.000**	**p=0.000**	**p=0.025**
HRVAT (b/min)	149.1±15.2	152.1±11.3	p=0.304	140.4±13.6	145.9±12.8	**p=0.018**	132.6±14.8	133.7±17.9	**p=0.005**	p=0.182	p=0.669
VE (l/min)	37.2±8.1	42.9±7.8*	p=0.987	37.5±9.4	41.5±9.5*	**p=0.016**	28.0±6.3	33.6±9.8***	**p=0.020**	**p<0.001**	p=0.874
VT (l)	1.3±0.3	1.4±0.5	p=0.684	1.4±0.5	1.5±0.4	**p=0.009**	1.0±0.4	1.1±0.4	p=0.293	p=0.075	p=0.809
f (min)	29.8±6.7	33.1±7.4	p=0.507	27.2±6.4	28.7±5.7	p=0.417	29.9±9.8	31.0±8.0	p=0.945	p=0.081	p=0.565
VE/MVV (%)	39.3±11.4	41.3±8.1	p=0.694	44.3±13.9	47.1±15.4	**p=0.000**	61.6±18.1	66.8±17.7*	**p=0.002**	**p=0.041**	**p=0.047**
RER	1.00±0.05	1.00±0.06	p=0.431	1.01±0.05	1.05±0.07**	p=0.150	0.99±0.05	1.02±0.05*	p=0.969	**p=0.013**	p=0.259
EQO2	29.2±6.5	29.9±7.0	p=0.635	31.9±4.7	31.2±4.6	p=0.192	33.5±5.9	35.8±6 .8	p=0.119	p=0.682	p=0.478
VO2VAT % VO2peak	68.2±6.5	73.1±4.2	p=0.920	69.1±9.0	71.3±8.4	p=0.092	74.2±9.4	73.3±9.1	p=0.616	p=0.228	p=0.492

[a] Abbreviations as in text described, Abbreviations as in text described, HFL = High Fitness Level Group; B = MFL = Middle Fitness Level Group; LFL = Low Fitness Level Group; FL = Fitness Level; T = Training Results are expressed as mean ± standard deviation.

[b] Within groups (Wilcoxon-Test) * = p<0.05, ** = p<0.01, *** = p<0.001, NS = non-significant

[c] Between groups (Mann-Whitney-U-Test)

Discussion

To date, little information has been available concerning the influence of disease severity on the benefits of an exercise program in CF. Cerny et al (8) showed a significant improvement in lung function in severely affected subjects with CF after a two week exercise program during hospitalization for treatment of CF pulmonary exacerbations, during which time they also received intravenous antibiotics and intensive airway clearance. The authors found a significant improvement in peak work capacity (PWC) in subjects with moderate-to-severe pulmonary function abnormality and those with severe abnormalities, but the improvements were equivalent between groups. In their study the participants were allocated into groups based on a pulmonary lung function score including several lung function parameters, and not on initial fitness. We recently reported greater improvement of VO_{2peak} in those subjects with CF with a lower fitness level and lower lung function (9). Participants in that study performed the same type of training during an in-patient rehabilitation course, but in contrast to the present study, we did not report on changes of pulmonary parameters during exercise, nor did we examine the effects on cardio-pulmonary parameters at submaximal workloads. The results of this study are an extension of the recently published study (9).

The results of this 6 week exercise training study demonstrated a beneficial effect on peak and submaximal exercise capacity, lung function, and, to a smaller degree, on ventilatory parameters in CF, with a wide range of fitness levels and lung function impairment. The improvement in exercise tolerance is consistent with the literature on exercise in CF (1, 2, 4, 9, 18). Furthermore, our study demonstrated that the initial level of fitness had significant effects on maximal and submaximal fitness parameters. Higher improvements were observed in VO_{2peak} in MFL (+9.6%) and LFL (14.9%) compared to HFL (+5.1%) and at VAT by 11.9% in LFL, 9.5% in MFL and 6.1% in HFL, respectively.

Our results are in line with previous studies in healthy non-CF people showing an inverse relationship between the levels of fitness at baseline and the magnitude of improvement in VO_{2peak} and suggest a normal training response in CF (5, 13). These findings are particularly of interest because Nixon et al. and Pianosi et al. have shown that the likelihood of survival is greater in CF with higher level of aerobic fitness (10, 19). As expected, $VO2_{peak}$ was found to correlate with FEV1 (Fig. 3), but FEV1 had no effect on △VO2. This lack of a relationship of lung function parameters, specifically FEV1, to changes in $VO2_{peak}$was surprising and indicates that the responsiveness to training in CF is independent of severity of lung disease (Fig. 2, 3).

The beneficial effects of the exercise program may be seen primarily as physiologic training effects and can be explained largely by cardiovascular adaptations (improved cardiac output and oxygen extraction to the tissue) (13, 15) . The increase in O2pulse, despite unchanged heart rate, suggests an increase in cardiac stroke-volume, and therefore true improvement in cardiopulmonary fitness, and not just a better effort on the post-training test (13). Aerobic training alone has been shown to increase strength in children with CF (20). Although skeletal muscle strength was not tested in the present study, improvements of peak and submaximal exercise capacity could be associated with a greater strength improvements especially in the LF group (18, 20) . Furthermore a better nutritional status may have a positive effect on lung function and exercise capacity (21, 22).

When the $VO2_{peak}$ of our participants was compared to published normative data of healthy, non-CF populations, a lower VO_{2peak} was observed in all CF groups (13) . Some factors can explain these lower values. In our study, cycle ergometer testing was used to assess the exercise capacity, which may result in lower VO_{2peak} than treadmill testing (13). Cycle exercise may be unfamiliar to subjects with CF who are unfit and or with impaired skeletal muscle strength and this may result in leg fatigue before cardiopulmonary or ventilatory limitation is reached (13).

Normal individuals use 50-70% of the ventilatory capacity at peak exercise. The VE/MVV at peak exercise in our subjects was higher (> 70%), which suggests that the ventilatory limit has been reached before the subjects reached their cardiovascular limit (13, 15). The fact that MFL and LFL increased their already high VE/MVV after training suggests that these less fit subjects might also have increased their tolerance of dyspnea (23). Heart rates at peak exercise in all groups were low compared with normal values at maximum (13, 15) supporting a physiological limitation due to a ventilatory capacity, in addition the aforementioned factors.

The VAT is a useful, reproducible method to determine aerobic fitness in healthy adults and children as well as in CF, and especially for those who cannot perform a maximal incremental cycling test (24, 25). In healthy untrained people the VAT occurs at intensities between 50-60% VO_{2peak} and rarely surpasses 60% of $VO2_{peak}$ (26). However, VAT occurred at a higher percentage of VO_{2peak} in subjects with chronic disease reaching up to 75% VO_{2peak}, and could be explained by an attenuated rise of VO2 above VAT or an exceptional low exercise tolerance (13). The VAT % VO2peak in our subjects was between 68% and 74% $VO2_{peak}$. The phenomenon of an attenuated rise of VO2 above VAT might partly explain the higher percentage of VAT. Other factors such as altered gas exchange, slowed oxygen uptake kinetics and an early onset of peripheral muscle weakness might contribute to the higher values (26, 27).

Lung function values increased significantly only in MFL and LFL. Daily chest physiotherapy was part of the intensive care program. The present study did not include a randomized parallel-group design. Thus, is difficult and somewhat speculative to discuss whether the exercise program or the chest physiotherapy or nutritional supplementation has a more pronounced effect on changes in lung function (21, 28).

Some limitations of the study should be taken into account in the discussion of the results. The subjects were recruited and the collection of data was done during an in-patient rehabilitation course, which could be seen as a bias of selection. Possibly more people with CF with advanced lung function and /or low exercise tolerance take part in this additional type of therapy compared with those with a better lung function and /or only slightly reduced exercise tolerance. This may be one explanation for the low number of participants in the HFL group.

Because of the many facets of the in-patient rehabilitation course (medical treatment, nutritional supplementation, exercise, airway clearance therapy, psychological counselling, and CF-specific education of children, adolescents, adults and their families), it is difficult to assign the greatest effect for the observed changes to any single factor.

We asked the participants about their habitual physical activity at home with a short self-administered questionnaire. However, this questionnaire has not been validated, so we do not know how the subjects' habitual activity levels compare group-to-group.

In conclusion, this study demonstrated that a 6 week exercise training program increased peak and submaximal exercise capacity in people with CF with a wide range of lung function and fitness levels. The responses to training showed differences between groups, with the initial fitness level determining those responses. A correlation was found between initial fitness level at peak and effect on △VO2 but not between initial FEV1 and △VO2. The improvements in exercise parameters at VAT were higher in participants with lower pre-training fitness level and lung function. The changes in fitness seen in the present study were similar to the changes observed in healthy persons who undertake exercise training, suggesting that people with CF, regardless of disease severity, respond similarly to exercise as healthy untrained persons.

Figure 1

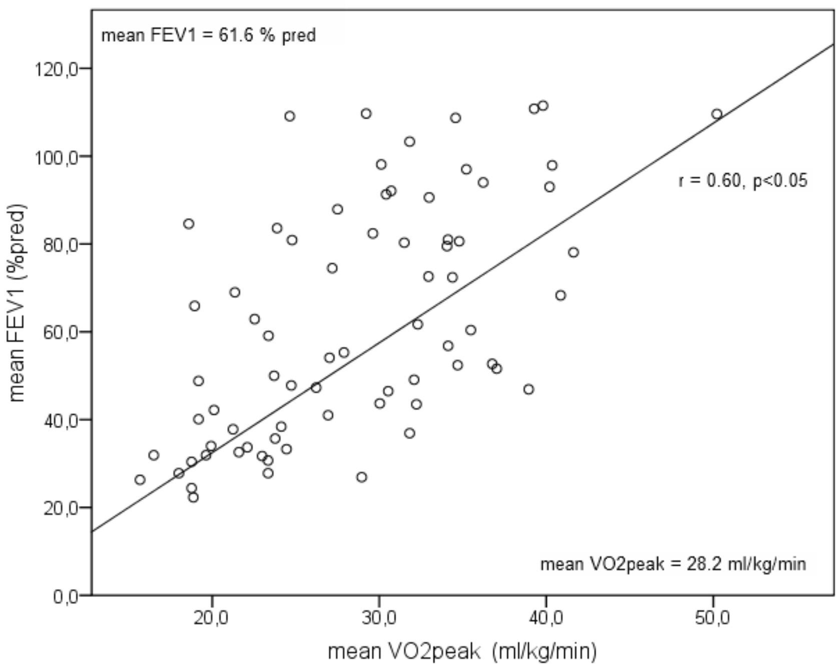

Fig 1 Relationship between VO2peak (ml/kg/min) and FEV1 (%pred) at baseline

Figure 2

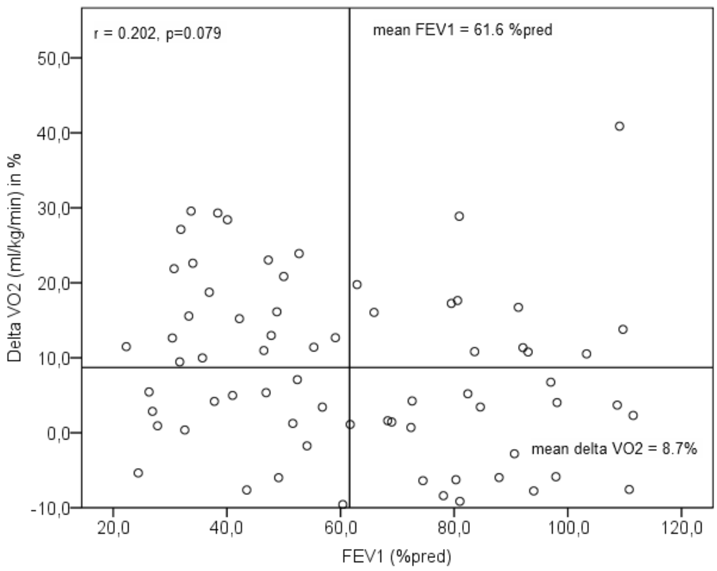

Fig 2 Relationship between delta VO2 (ml(/kg/min) and FEV1 at baseline

Figure 3

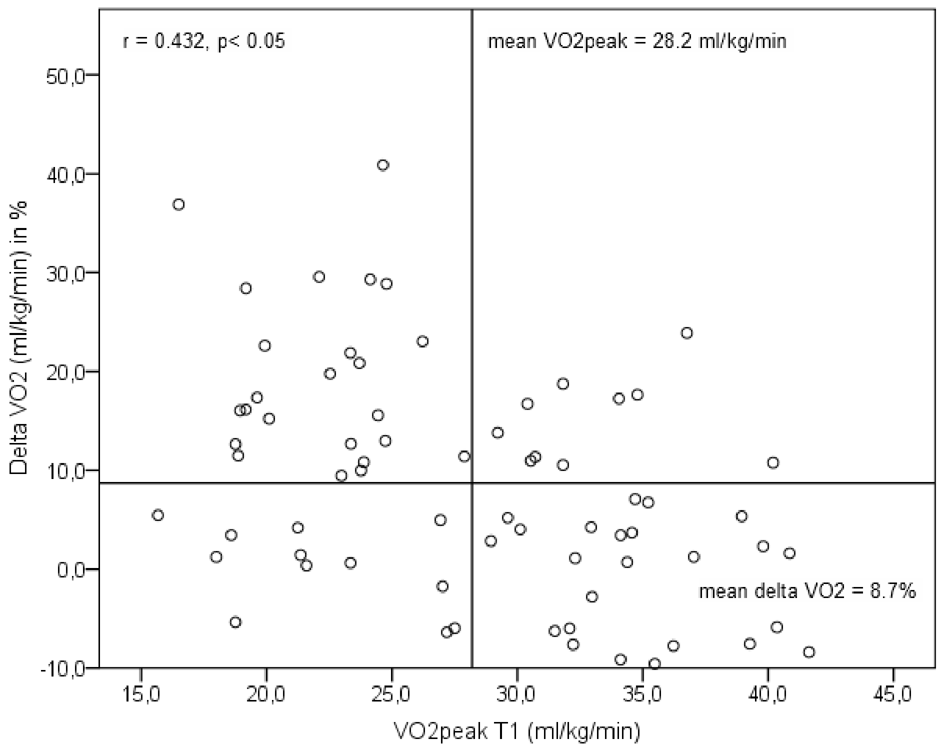

Fig 3 Relationship between VO2peak at baseline and delta VO2 (ml/kg/min)

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