Chapter 5
Differential effects of high- versus low-frequency exercise training in rehabilitation of patients with coronary artery disease.

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ABSTRACT

Objectives
To study the influence of frequency of exercise training during cardiac rehabilitation on functional capacity [i.e. peak oxygen consumption (VO$_2$) and ventilatory anaerobic threshold (VAT)] and Quality of Life (QoL).

Background
Although the value of cardiac rehabilitation is now well established, the influence of the different program characteristics on outcome has received little attention, and the effect of frequency of exercise training is unclear. Functional capacity is regularly evaluated by peak VO$_2$, but also parameters of sub-maximal exercise capacity, e.g. VAT, should be considered, because especially sub-maximal exercise capacity is important in daily living.

Methods
Patients with coronary artery disease (n=130, 114 men; mean age 52 ± 9 years) were randomised to either a high- or low-frequency program of 6 weeks (10 or 2 exercise sessions per week of 2 hours, respectively). Functional capacity and QoL were assessed before and after cardiac rehabilitation. Also global costs were compared.

Results
Compared to baseline mean exercise capacity increased in both programs: for high- and low-frequency respectively, peak VO$_2$=15 and 12%, Wmax=18 and 12%, VAT= 35 and 12% (all p<0.001). However, when the programs were compared only VAT increased significantly more during the high-frequency program (p=0.002). During the high-frequency program QoL increased slightly more and more individuals improved in subjective physical functioning (p=0.014). We observed superiority of the high-frequency program especially in younger patients. Mean costs were estimated at 4455 and 2273 EURO, resp. for high- and low-frequency program.

Conclusions
High-frequency exercise training is more effective in terms of VAT and QoL, but peak VO$_2$ improves equally in both programs. Especially younger patients seem to benefit from the high-frequency training.
Cardiac rehabilitation is a well-established treatment in patients with coronary artery disease. Beneficial effects on exercise capacity and quality of life (QoL), and probability of recurrent events and hospitalisation are reported in various studies using different programs. Although there are some data available regarding different levels of intensity, little or no data exist on the optimal frequency of these programs.

Outcome assessment of cardiac rehabilitation programs and of medication trials is usually focused on peak exercise capacity, especially peak oxygen consumption (peak VO₂). However, the value of peak VO₂ has been recently questioned as outcome-parameter of studies, especially in patients with chronic heart failure. Indeed it has been suggested that sub-maximal, endurance exercise capacity should also be evaluated, for example the anaerobic threshold, because this might reflect better exercise in daily life.

Therefore, the present study compared the effects on both peak VO₂ and ventilatory anaerobic threshold (VAT) of high frequency with low frequency exercise training during outpatient cardiac rehabilitation.

METHODS

Study-design.

Patients, who had been hospitalised with manifestations of documented coronary artery disease (myocardial infarction, angina pectoris, bypass surgery, or angioplasty), were referred to our cardiac rehabilitation centre by the departments of cardiology of a general and a university hospital. They were eligible for the study, if their age was between 30 and 70 years. Exclusion criteria were: unstable angina, clinically unstable heart failure, unstable arrhythmias (e.g. sustained ventricular tachycardias or exercise induced polymorphic ventricular tachycardias), contraindications for exercise training (e.g. endocarditis or other systemic infectious diseases), other exercise limiting concurrent condition (e.g. chronic obstructive pulmonary disease, skeletal or muscular disorders), or a psychosocial indication for inpatient cardiac rehabilitation (severe depression or panic disorder). Patients were randomised either to high frequency or low frequency exercise training during a 6 weeks outpatient (phase II) cardiac rehabilitation program. Randomisation was executed externally after assessment of baseline data and obtaining written informed consent. The study-protocol was approved by the institutional review board and was in accordance with the Helsinki Declaration. Baseline left ventricular function, ejection fraction and wall motion score index, was evaluated by echocardiography (Vingmed CFM 800; Vingmed Sounds, Norway).

Outline of the training programs.

Duration of the rehabilitation stage was 6 weeks. The high frequency program consisted of 2 training-sessions each day, 5 days a week. The low frequency program consisted of 1 training-session a day, twice a week, without advice or prescription of additional exercise outside the program. Each training-session consisted of cycling on an ergometer (6 minutes warm-up, 20 minutes endurance training with heart rate (HR) maintained on 60 to 70% of HR Reserve, 4 minutes cool-down) and 45 to 60 minutes
sports-activities (swimming, walking or jogging, ballsports, callisthenics). All patients joined the education program and participated in relaxation therapy and breathing technique instructions for once a week (teaching awareness of respiration and of bodily tension). Spouses were also invited to join two exercise-sessions and an education program. A dietician, social worker and/or psychologist individually counselled patients.

**Exercise testing.**

Exercise capacity was measured both before and at the end of the exercise training program. All patients were familiarised to the exercise testing protocol by a preliminary exercise test with respiratory gas exchange measurement 1-3 days before the baseline exercise test. Graded symptom-limited exercise tests were performed on an electromagnetically braked cycle ergometer (Excalibur, Lode, Netherlands) as previously described in detail. The protocol consisted of a three-minute warm-up period at a workload of 20 Watt. The next stage, the workload was increased to 50 Watt and then by 10 Watt every subsequent minute. Patients were instructed to maintain a speed of 60 to 70 rotations per minute and were encouraged to perform maximally to symptoms of dyspnea or general fatigue to a level of perceived exertion of 19 to 20 according the Borg scale. A complete 12-lead electrocardiogram was monitored continuously. Blood pressure was measured by cuff sphygmanometry pre-exercise, every three minutes during exercise and during 6 minutes post-exercise. A capillary bloodsample was obtained within 45 seconds after peak exercise to measure blood-lactate concentration. During the final exercise test, we obtained also a bloodsample at a sub-maximal exercise stage, i.e. the same exercise stage as peak workload during the baseline exercise test. Patients breathed through a mask with a turbine volume transducer, measuring the volume of inspired and expired air. Respired gases were withdrawn from the mask for determination of O₂ and CO₂ and were analysed breath by breath (Oxycon Champion, Jaeger, Netherlands). The gas-analysers as well as the volume transducer were calibrated before each test. Peak VO₂ was defined as the mean VO₂ of the last minute of the exercise test. Age- and gender-adjusted peak VO₂ was calculated as a fraction of predicted peak VO₂. Respiratory Exchange Ratio (RER) was calculated on line (VO₂ / VCO₂). VAT was determined using the RER = 1 method and was reported in (percentage of) Wmax.

**Quality of life assessment.**

Subjective improvement on health was assessed with the RAND-36, which is a Dutch version of the MOS SF-36 (Medical Outcomes Survey 36-item Short Form health domains). This questionnaire is widely accepted and well validated and was completed before and immediately after the 6-week program. We used seven subscales (perception of general health, vitality, physical functioning, mental health, health change, social functioning, and bodily pain) to evaluate change in QoL.
Calculation of costs.

Costs of both programs were calculated on the basis of the rates of the actual system of calculation. In this system the actual duration of treatment by the various professionals directly determined the calculated costs. The program was subdivided into intake-procedure, actual treatment (exercise training, individual counselling, and education program), and exit-procedure and the approximate mean time of treatment were calculated.

Statistical analysis.

Statistics were obtained using SPSS (PC+, version 5.01 1992). Differences between groups (high versus low frequency and improvement versus no improvement) were analysed using unpaired t-test; differences of program-effect were analysed with MANOVA for repeated measures. Individual effect of training programs was defined as improvement as an increase of more than 50% of SD of the mean baseline parameter and no improvement as a smaller increase than 50%. Differences in individual improvement between both programs were tested with chi-square-test and reported in Risk-Ratio. Correlation between QoL and exercise capacity was reported in Pearson product moment correlation coefficient (R). Significance was expected to occur when (two-tailed) p-values were below 0.05. Group data for each variable are expressed as mean value ± SD.

RESULTS

Overall population.

We randomised 130 of a total of 186 patients who met in- and exclusion criteria. Reasons for non-randomisation were: no reliable measurement of baseline parameters (i.e. exercise tests, echocardiography, or questionnaires) (11 patients), and refusal of participation in one or another program (36 patients preferred one of the two programs, 9 refused because of other reasons). There were no significant differences between both groups in baseline characteristics; i.e. demographic, left ventricular function, exercise capacity, and most parameters on health related QoL (table 1). However on three parameters of QoL we observed a slightly significant difference at baseline, i.e. mental health, vitality and social functioning (p of difference respectively p=0.03, p=0.04, p=0.05). During the program 5 patients dropped-out (high frequency 1 and low frequency 4; p=ns). In one patient (high frequency program) the drop-out was caused by occurrence of unstable angina pectoris, treated by coronary bypass surgery); four patients (low frequency program) stopped attending exercise sessions due to lack of motivation (3x) or due to resumption of work (1x). Other patients attended all exercise session. If patients were not able to join a session, this session was rescheduled. All exercise tests were stopped because of symptom i.e. general fatigue and/or dyspnea with or without some leg discomfort. In none of the patients angina was the reason for termination of the test.
Exercise testing.

Increase of exercise capacity was highly significant during both programs (table 2). Mean increase of peak VO\textsubscript{2} was comparable between both programs, while VAT increased more during high frequency training (p=0.002). Also Wmax and exercise duration increased significantly more during high frequency training. HR, systolic blood pressure, RER and blood lactate concentration during peak exercise did not change during each program (neither were there significant differences between both programs). Most individuals showed an improvement of both Wmax and peak VO\textsubscript{2} during both programs (fig. 1). Peak VO\textsubscript{2} improved in half of the patients during both

<table>
<thead>
<tr>
<th></th>
<th>High-frequency (n=63)</th>
<th>Low-frequency (n=67)</th>
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<tbody>
<tr>
<td>Age</td>
<td>52 ± 9</td>
<td>53 ± 9</td>
</tr>
<tr>
<td>Gender</td>
<td>Male/female 52/11 (83/17%)</td>
<td>52/5 (93/7%)</td>
</tr>
<tr>
<td>Length</td>
<td>175.4 ± 8.2</td>
<td>177.2 ± 7.5</td>
</tr>
<tr>
<td>Weight</td>
<td>80.1 ± 11.0</td>
<td>79.2 ± 10.9</td>
</tr>
<tr>
<td>Last cardiac event</td>
<td>MI 47 (75%)</td>
<td>51 (76%)</td>
</tr>
<tr>
<td></td>
<td>CABG 6 (9%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td></td>
<td>PTCA 6 (9%)</td>
<td>5 (8%)</td>
</tr>
<tr>
<td></td>
<td>Angina 4 (7%)</td>
<td>9 (13%)</td>
</tr>
<tr>
<td>Medication</td>
<td>Beta-blocker 49 (78%)</td>
<td>55 (82%)</td>
</tr>
<tr>
<td></td>
<td>Calcium-antagonist13 (21%)</td>
<td>19 (28%)</td>
</tr>
<tr>
<td></td>
<td>Nitrate 13 (21%)</td>
<td>18 (27%)</td>
</tr>
<tr>
<td></td>
<td>ACE-inhibitor 19 (30%)</td>
<td>17 (25%)</td>
</tr>
<tr>
<td></td>
<td>Diuretics 12 (19%)</td>
<td>13 (19%)</td>
</tr>
<tr>
<td></td>
<td>Digitalis 4 (6%)</td>
<td>5 (8%)</td>
</tr>
<tr>
<td>LVEF</td>
<td>0.48 ± 0.11</td>
<td>0.46 ± 0.10</td>
</tr>
<tr>
<td>Wall Motion Score Index</td>
<td>1.35 ± 0.36</td>
<td>1.31 ± 0.30</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>NYHA I/II/III 47/15/1 (75/23/2%)</td>
<td>50/17/0 (75/25/0%)</td>
</tr>
<tr>
<td>Angina</td>
<td>NYHA I/II 58/5 (92/8%)</td>
<td>53/14 (79/21%)</td>
</tr>
</tbody>
</table>

Table 1. Baseline-characteristics.
Abbreviations: CABG = coronary surgery; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NYHA = functional classification according to New York Heart Association; PTCA = coronary angioplasty.

Figure 1. Percentage of patients with a significant improvement during cardiac rehabilitation on the following parameters: peak VO\textsubscript{2} = peak oxygen consumption; SPhF= quality of life assessed as subjective physical functioning; VAT = ventilatory anaerobic threshold; Wmax = maximal workload. * = significant difference (p<0.01).
### Table 2: Parameters at baseline and after rehabilitation stage, and percentile increase

<table>
<thead>
<tr>
<th></th>
<th>High-frequency</th>
<th></th>
<th>Low-frequency</th>
<th></th>
<th>MANOVA for repeated measures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>after 6 weeks</td>
<td>%</td>
<td>Baseline</td>
<td>after 6 weeks</td>
</tr>
<tr>
<td>Exercise duration</td>
<td>13.0 ± 4.1</td>
<td>15.3 ± 4.4</td>
<td>+18%</td>
<td>13.6 ± 3.7</td>
<td>15.2 ± 4.1</td>
</tr>
<tr>
<td>Wmax</td>
<td>140 ± 41</td>
<td>165 ± 43</td>
<td>+18%</td>
<td>147 ± 37</td>
<td>165 ± 42</td>
</tr>
<tr>
<td>Wmax (Watt/kg)</td>
<td>1.76 ± 0.49</td>
<td>2.09 ± 0.49</td>
<td>+19%</td>
<td>1.82 ± 0.45</td>
<td>1.99 ± 0.49</td>
</tr>
<tr>
<td>Peak VO₂</td>
<td>22.5 ± 6.5</td>
<td>25.8 ± 6.8</td>
<td>+15%</td>
<td>23.4 ± 5.6</td>
<td>26.1 ± 5.8</td>
</tr>
<tr>
<td>Age-adj. peak VO₂ (ml/min/kg)</td>
<td>±0.21</td>
<td>0.83 ± 0.21</td>
<td>+14%</td>
<td>0.75 ± 0.20</td>
<td>0.82 ± 0.21</td>
</tr>
<tr>
<td>Peak HR</td>
<td>135 ± 20</td>
<td>138 ± 19</td>
<td>+2%</td>
<td>134 ± 22</td>
<td>137 ± 20</td>
</tr>
<tr>
<td>Peak RRsys</td>
<td>182 ± 29</td>
<td>185 ± 28</td>
<td>+2%</td>
<td>178 ± 28</td>
<td>182 ± 28</td>
</tr>
<tr>
<td>Peak RRdia</td>
<td>83 ± 11</td>
<td>84 ± 11</td>
<td>+1%</td>
<td>84 ± 12</td>
<td>83 ± 11</td>
</tr>
<tr>
<td>RERpeak</td>
<td>1.12 ± 0.08</td>
<td>1.10 ± 0.07</td>
<td>-2%</td>
<td>1.11 ± 0.08</td>
<td>1.12 ± 0.08</td>
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<tr>
<td>Peak Clactate</td>
<td>6.7 ± 2.3</td>
<td>7.1 ± 2.3</td>
<td>+6%</td>
<td>7.0 ± 1.7</td>
<td>7.0 ± 2.3</td>
</tr>
<tr>
<td>VAT</td>
<td>96 ± 31</td>
<td>130 ± 39</td>
<td>+35%</td>
<td>105 ± 37</td>
<td>118 ± 39</td>
</tr>
<tr>
<td>Relative VAT</td>
<td>0.70 ± 0.14</td>
<td>0.74 ± 0.14</td>
<td>6%</td>
<td>0.72 ± 0.14</td>
<td>0.72 ± 0.14</td>
</tr>
</tbody>
</table>

**Quality of life (RAND-36)**

- General health: 58.3 ± 16.2 → 62.3 ± 14.8; 7% increase
- Vitality: 50.2 ± 19.5 → 59.5 ± 15.9; 19% increase
- Physical functioning: 71.3 ± 19.5 → 80.4 ± 19.7; 13% increase
- Mental health: 59.0 ± 22.1 → 70.2 ± 17.9; 19% increase
- Health change: 56.4 ± 25.7 → 73.3 ± 18.4; 30% increase
- Social functioning: 56.4 ± 22.4 → 70.7 ± 20.5; 25% increase
- Bodily pain: 89.6 ± 30.7 → 93.3 ± 25.6; 4% increase

**Lipids and body weight**

- Total cholesterol (mmol/l): 6.26 ± 1.12 → 5.79 ± 0.97; 8% decrease
- LDL cholesterol (mmol/l): 3.50 ± 0.99 → 3.10 ± 0.82; 11% decrease
- HDL cholesterol (mmol/l): 0.88 ± 0.23 → 0.88 ± 0.21; 0% decrease
- Triglycerides (mmol/l): 2.20 ± 1.01 → 1.98 ± 0.99; 10% decrease
- Body weight (kg): 79.9 ± 10.9 → 79.3 ± 10.4; 1% decrease

Table 2: Parameters at baseline and after rehabilitation stage, and percentile increase

Abbreviations: age-adj peak VO₂ = peak VO₂, adjusted for age and gender; exerc.dur = exercise duration in minutes; ns = p > 0.05.; peak Clactate = serum lactate concentration at peak exercise; peak HR = heart rate at peak exercise; peak RER = respiratory exchange ratio at peak exercise; peak RRdia = diastolic blood pressure at peak exercise; peak RRsys = systolic blood pressure at peak exercise; VAT = ventilatory anaerobic threshold; relative VAT = VAT as fraction of Wmax; Wmax = peak workload.

The last three columns indicate Manova for repeated measures, respectively ‘program x time’ interaction effect, main effect for time, and main effect for ‘program’. Differences in efficacy between both programs are indicated by the ‘program x time’ interaction effect.
Differential effects on exercise capacity of cardiac rehabilitation programs (high and low frequency resp.: 30/60 and 30/62; p=ns), while in contrast significantly more individuals improved their VAT during the high-frequency program (high and low frequency resp.: 35/48 and 19/49; p=0.002) (table 3). Patients who improved their VAT during high frequency training were significantly younger than patients who did not improve (50 ± 9 vs. 56 ± 8 years; p<0.05), while no significant difference in age was observed during low frequency training between both categories (52 ± 10 vs. 53 ± 9 years). The ‘improvement’ group tended to have a better baseline-exercise capacity than the ‘no-improvement’ group during high frequency training (Wmax 151 ± 40 vs. 126 ± 40, peak VO2 23.8 ± 6.8 vs. 21.3 ± 6.3; resp. p=0.065 and p=0.241). In contrast, during the low frequency program the improvement group tended to have a lower baseline exercise capacity (Wmax 146 ± 37 vs. 147 ± 36, peak VO2 22.6 ± 5.1 vs. 24.2 ± 6.1; resp. p=0.937 and p=0.320). This difference between improvement and no-improvement group was also observed concerning peak VO2 and QoL, however this was not significant. Mean endurance exercise capacity increased significantly during both programs. This was reflected not only by a higher VAT but also by a lower HR, RER, and serum lactate concentration at sub-maximal exercise (respectively 124 vs. 128/min, 1.04 vs. 1.07, and 4.7 vs. 5.4 mmol/l; program x time interaction effect, respectively, p=0.047, p<0.001; p=0.134).

**Quality of life.**

Almost all measures of the RAND-36 improved significant in both treatment groups; this tended to be greater during high frequency (table 2). This difference between programs was statistically significant on two sub-scales (mental health and health change). Also, during the high frequency program significantly more individuals reported improvement in subjective physical functioning (fig. 1). Mean improvement in subjective physical functioning was significantly correlated with mean improvement of VAT (r=0.178, p=0.035), but not with improvement on peak VO2 (r=0.090, p=0.169).

<table>
<thead>
<tr>
<th>Improvement</th>
<th>High frequency</th>
<th>Low frequency</th>
<th>Chi (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wmax (Watt)</td>
<td>Yes</td>
<td>49 (79%)</td>
<td>36 (57%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>13 (21%)</td>
<td>27 (43%)</td>
</tr>
<tr>
<td>Peak VO2 (ml/kg/min)</td>
<td>Yes</td>
<td>30 (50%)</td>
<td>30 (48%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>30 (50%)</td>
<td>32 (52%)</td>
</tr>
<tr>
<td>VAT (Watt)</td>
<td>Yes</td>
<td>35 (73%)</td>
<td>19 (39%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>13 (27%)</td>
<td>30 (61%)</td>
</tr>
<tr>
<td>Subjective physical functioning</td>
<td>Yes</td>
<td>23 (40%)</td>
<td>11 (19%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>35 (60%)</td>
<td>47 (81%)</td>
</tr>
</tbody>
</table>

*Table 3: Individual improvement of exercise capacity and quality of life during both programmes. Abbreviations: peak VO2 = oxygen consumption at peak exercise; VAT = ventilatory anaerobic threshold; Wmax = maximal workload. Improvement: yes = individual increase of parameter of > 0.5 SD; no = smaller of no increase.*
**Costs.**

Mean costs of intake and exit procedure were 591 and 318 Euro, respectively; individual counselling approximately 682 Euro and education program 182 Euro. The only difference in costs between both programs was the exercise training; exercise training was in the high frequency program a factor five higher than the low frequency program; respectively 273 and 545 Euro. Total costs of both programs were 4455 and 2273 Euro.

**DISCUSSION**

Cardiac rehabilitation has become a well-established treatment modality in patients with heart disease. Effects have been demonstrated on functional and psychosocial recovery, and on cardiac morbidity and (in meta-analysis) mortality\(^1\-^3\). Studies demonstrated also beneficial effects in various categories of cardiac patients. In addition to post-myocardial infarction patients, also patients with chronic heart failure or after heart transplantation were shown to benefit from such programs\(^17\-^19\). However, most of the programs applied in these studies were not compared in a randomised way, and critical program evaluation, therefore, is crucial, also because development of individual tailor-made programs is demanded nowadays\(^20\).

The present randomised study focused on program evaluation and demonstrated a beneficial effect in favour of high frequency exercise training on QoL and (sub-maximal) exercise capacity. Both qualities assess important issues, which are related to the goal of rehabilitation, namely restoration of normal daily functioning. This superiority of high frequency training was not only clear in mean improvement but also on the number of individuals who experienced significant improvement (of VAT: high and low frequency resp. 35/14 and 19/49). These better results, however, were obtained at the expense of almost twice as much money and the question therefore rises, whether high frequency training should always be preferred. Although high frequency training is common in some centres, low frequency training is mostly used and is known to be effective. The present study confirmed the efficacy of low frequency training demonstrating a mean increase of at least 10% on most parameters. In most patients this increase would be enough to reach their individual rehabilitation targets (e.g. restoration of recreational activities, resumption of work). An additional benefit elicited by high frequency training might be indicated only in specific patients, such as those with a severely decreased exercise capacity or with high physical demands in daily life. It might be speculated, that only in these patients this additional effect will sustain on long term, while in other patients this program effect would disappear. It is however of clinical relevance to evaluate whether the effects of this high frequency program are maintained over a longer period of time. Our results also suggest that particularly younger patient might benefit.

In contrast to peak VO\(_2\), VAT improved significantly more during the high frequency program. Also a differential higher improvement of Wmax (compared with peak VO\(_2\)) was measured during the high frequency program. This discrepancy might
be explained by a higher increase of VAT, by which patients might sustain exercise testing longer due to a later increase of blood lactate concentration. Other potential explanations might be a higher increase of muscular strength and improvement of motor skills improving the energetic efficiency of movement. A higher motivation is unlikely to explain the differential higher increase in Wmax. If patients have a higher motivation, they might sustain a higher level of anaerobiosis and symptoms of fatigue. However, blood lactate concentration, RER, as well as peak HR were comparable between both groups.

The differential effects on peak and endurance exercise capacity raises the question which parameter to prefer in the assessment of an intervention. Several trials in chronic heart failure have also shown disappointing effects on peak VO₂, while parameters reflecting sub-maximal exercise capacity, e.g. QoL or six-minute walk distance, were favourably affected²¹,²². Since most physical activities are on a sub-maximal level, this might explain the observed relation between VAT and QoL (~ subjective physical functioning) observed in this study.

**Study-limitations.** The present study-population can not be automatically considered to be representative for each patient after a recent coronary event due to a referral bias. In general, only a proportion patients are referred for cardiac rehabilitation after a recent coronary event, and often only those with a decreased functional capacity or psychosocial problems. Generally, those referred are highly motivated and this might explain the relative low dropout rate and low initial exercise capacity in the present study. In addition, we included mainly males. This is in line with the population generally referred for cardiac rehabilitation. A low number of female patients was also observed by others and can be partly explained by a lower incidence of coronary artery disease among females. Also, women are less likely to be referred due to several reasons²³. In addition, some ethnic groups might be referred less in some society. This is of particular interest, while ethnicity might influence clinical profile and predict outcome of rehabilitation²⁴. This last issue did, however, not apply to our study. We included only Caucasians and in our region ethnicity has hardly impact on referring patients for cardiac rehabilitation.

Physical activity outside the program might have disturbed the trial. These activities were not controlled for. Physical activity in the low frequency program might have elicited an extra training-stimulus, diminishing the difference between both programs. In contrast, extra physical activity during the high frequency program might have an adverse effect due to over-training. If this were true, it may have decreased the mean physiological benefits of the high frequency program. Symptoms of over-training were not assessed systematically in our study. In addition, a high frequency program might not be feasible for all patients due to other scheduled activities and it might be speculated that a somewhat shorter program would already generate a more pronounced physiological effect.

A relatively short program of 6 weeks was applied in this study, since this is a common length for programs used in Europe¹⁶. Whether the results of this study are applicable to programs with a longer length (for example 3 months) is unknown. However, a longer program with this high frequency exercise training will not be easily applied in clinical practice because of the high costs.
CONCLUSION

High frequency exercise training in cardiac rehabilitation is more effective than low frequency training, as VAT and QoL increased more during high frequency exercise training, while, in contrast, there was no program effect on peak VO$_2$. This differential effect stresses the importance of assessment of VAT, especially when therapy is aimed at improvement of functional capacity in daily life.

References
15. Ware JE, Sherbourne CD. The MOS 36-Item Short-Form Health Survey (SF-36). Med Care 1992; 30; 473-83.


