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

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The interventions examined in the study were high-frequency and low-frequency exercise training for the rehabilitation of patients with coronary artery disease. The high-frequency programme consisted of two training sessions every day for five days a week, while the low-frequency programme consisted of one training session a day, twice a week. Each training session consisted of cycling on an ergometer (6 minutes warm-up, 20 minutes endurance training with heart rate maintained on 60% to 70% of heart rate reserve, and 4 minutes cool-down) and 45 to 60 minutes sports activities (swimming, walking or jogging, ballsports, calisthenics).

Type of intervention
Rehabilitation.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients aged 30 - 70 years hospitalised for documented coronary artery disease, such as myocardial infarction, angina pectoris, bypass surgery or angioplasty. Patients were excluded if they presented with unstable angina, clinically unstable heart failure, unstable arrhythmias, (such as sustained ventricular tachycardias or exercise induced polymorph ventricular tachycardias), contraindications for exercise training (endocarditis or other systemic infectious disease), other exercise limiting concurrent condition (chronic obstructive pulmonary disease, skeletal or muscular disorders), or a psychosocial indication for inpatient cardiac rehabilitation (severe depression or panic disorder).

Setting
The setting was an outpatient cardiac rehabilitation centre. The economic study was conducted in the Netherlands.

Dates to which data relate
The period of collection of data on effectiveness and resource use was not stated. No price year was reported.

Source of effectiveness data
A single study was used to derive the effectiveness evidence.

Link between effectiveness and cost data
The costing was performed prospectively on the same patient sample as that used in the effectiveness analysis.
Study sample
Power calculations were not reported. Of the 186 eligible patients presenting at the two study hospitals, a sample of 130 subjects was included in the study: 63 patients (mean age: 52±9 years; 83% men) were included in the high-frequency group and 67 patients (mean age: 53±9 years; 93% men) were included in the low-frequency group. The exclusion of 56 eligible patients was mainly due to lack of a reliable baseline measurement and patient refusal to participate in one of the programmes.

Study design
This was a randomised controlled trial, carried out in the departments of cardiology of a general and a university hospital in the Netherlands. Randomisation was performed externally after assessment of baseline data. Length of follow-up was six weeks and five patients dropped out (one in the high-frequency programme and four in the low-frequency programme) for lack of motivation or occurrence of unstable angina.

Analysis of effectiveness
The analysis appears to have been limited to treatment completers only. Several health outcomes were assessed in the analysis: exercise duration, peak workload (Wmax), peak oxygen consumption (peak VO2), peak VO2 adjusted for age and gender, heart rate at peak exercise (peak HR), systolic blood pressure at peak exercise (peak RRsys), diastolic blood pressure at peak exercise (peak RRdia), respiratory exchange ratio at peak exercise (RER peak), serum lactate concentration at peak exercise (peak lactate), ventilatory anaerobic threshold (VAT), relative VAT (VAT as a fraction on Wmax), lipids (total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides) and body weight. Seven dimensions of QoL were also assessed using the RAND-36 instrument: general health, vitality, physical functioning, mental health, health change, social functioning, and bodily pain. Study groups were comparable at baseline in terms of demographics, left ventricular function, exercise capacity, and most QoL parameters. However, three parameters of QoL (mental health, vitality, and social functioning) were statistically different across the study groups.

Effectiveness results
Both programmes improved overall health conditions. However, statistically significant differences (p<0.05) between the high-frequency programme and the low-frequency programme were found in the increase of the following outcome measures: exercise duration (18% versus 12%), Wmax (both for Watt, 18% versus 12%, and Watt/kg, 19% versus 9%), VAT (35% versus 12%), and relative VAT (6% versus 0%).

The authors noted that patients who improved their VAT during high-frequency training were significantly younger than patients who did not improve, while no significant difference in age was found during low-frequency training.

In general, those who improved had better baseline exercise capacity than those who did not show any improvement at six weeks.

The variations in all the remaining outcome measures were not statistically different between the two study groups.

Both programmes improved QoL measures, but there was a trend towards a greater improvement in the high-frequency group and this difference reached statistical significance in terms of two subscales (mental health and health change).

Finally, improvements in physical functioning were significantly greater in the high-frequency group than in the low-frequency group.

Clinical conclusions
Although many health outcomes did not differ across the programmes, the high-frequency training resulted in better improvements in some QoL categories and exercise capacity than the low-frequency programme.
Measure of benefits used in the economic analysis
Health outcomes were left disaggregated and no summary benefit measure was used, thus a cost-consequences analysis was conducted.

Direct costs
Discounting was not relevant due to the short time horizon of the study. The economic analysis included the costs of intake procedures, actual treatment (exercise training, individual counselling and education programme), and exit-procedure. Unit costs and quantities of resources were not reported. The estimation of the costs of the interventions was based on actual rates of treatment duration. The source of the cost data was not reported. Resource use was derived from the trial. The cost/resource boundary adopted in the analysis was not explicitly stated. The period of collection of data on resource use was not reported. No price year was given.

Statistical analysis of costs
Statistical analyses of costs were not performed.

Indirect Costs
Indirect costs were not included in the analysis.

Currency
Euros.

Sensitivity analysis
Sensitivity analyses were not conducted.

Estimated benefits used in the economic analysis
Due to the cost consequences approach, please refer to the effectiveness results reported earlier.

Cost results
The mean costs of intake procedures were Euro 591 and for exit procedures Euro 318.

The costs of the individual counselling were Euro 682 and for the education programme Euro 182, and were similar for both programmes.

Exercise training cost Euro 545 in the high-frequency programme and Euro 273 in the low-frequency programme.

Total costs were Euro 4,455 in the high-frequency programme and Euro 2,273 in the low-frequency programme.

Synthesis of costs and benefits
Costs and benefits were not combined as a cost-consequences analysis was performed.

Authors' conclusions
The authors concluded that the high-frequency training was more effective than the low-frequency programme, due to greater improvements in quality of life and exercise capacity. However, these benefits were gained at a cost which was double that measured in the low-frequency training.
CRD COMMENTARY - Selection of comparators

The rationale for the choice of the comparator was clear. The authors stated that the two programmes were selected, as little evidence was available on the optimal frequency of exercise. You, as a user of this database, should decide whether they represent widely used health interventions in your own setting.

Validity of estimate of measure of effectiveness

The analysis of the effectiveness was based on a randomised controlled trial. Details of the randomisation were not provided and it was also stated that the randomisation process was performed externally. The study groups were not perfectly comparable at baseline and this could have affected the conclusions of the analysis. The drop-out rate was quite low. The authors noted that the adoption of a longer follow-up could have been interesting, but that it was not practically feasible. The authors acknowledged a possible limitation of the analysis, in that the study sample may not have been fully representative of the study population of patients after coronary artery disease, as patients undergoing cardiac rehabilitation usually are highly motivated and are those with a decreased functional capacity or psychosocial problems. In addition, the study sample was predominantly composed of men. A final source of bias may have been the performance of physical activity outside the training programme, which may have negatively affected the high-frequency training.

Validity of estimate of measure of benefit

Health outcomes were left disaggregated and a cost-consequences analysis was carried out, so please refer to the comments in the above field. However, the use of a summary benefit measure reflecting patient preferences for the interventions would have been useful, as quality of life outcomes were already assessed in the analysis.

Validity of estimate of costs

The perspective adopted in the economic analysis was not stated and only the costs strictly associated with the training programme were included in the analysis. Unit costs and quantities of resources were not given and the source of cost data was not stated. Costs were treated deterministically as statistical analyses were not performed. No price year was reported. These limitations hinder the generalisability of the study results to other settings. The overall cost analysis was somewhat limited in terms of methodology and detail.

Other issues

The authors made some comparisons of their findings with those from other studies. The generalisability of the study results to other settings was quite low as no sensitivity analyses were performed and unit costs were not reported. The authors also noted the difficulties of generalising their findings to other populations, as reported earlier. The limitations of the analysis were clearly reported in the discussion of the study.

Implications of the study

The high-frequency training proved to be the most effective rehabilitation programme for patients after coronary artery disease. However, due to its high costs, it should be considered appropriate to limit the programme to those patients with a severely decreased exercise capacity or who are subject to high physical demands in daily life. It also has to be kept in mind that the high-frequency programme benefited mostly younger patients.

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