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1.3 Cardiovascular diseases. Risk factors and physical activity

Cardiovascular diseases are the leading cause of death worldwide, with coronary heart disease (CHD) at the forefront, along with its associated conditions such as acute myocardial infarction and heart failure. Physical activity aims to improve the cardiovascular risk profile in both primary and secondary prevention. When multiple risk factors are present, the risk of a cardiovascular event is significantly increased.

Diabetes

Even in individuals with diabetes, where ubiquitous atherosclerosis leads to macro- and microangiopathy throughout the entire vascular tree, more glucose-4 transporters (GLUT-4 transporters) are transported from the endoplasmic reticulum to the cell membrane during and after physical exertion, resulting in increased glucose uptake into the cell. This process is independent of insulin and insulin receptors. Long-term improvements in glucose metabolism (HbA1c) are achieved through endurance training (-0.73%), general strength training (-0.57%), or a combination of both (-0.51%), as shown by meta-analyses of intervention studies.

In the Look-AHEAD study (n = 5,145 overweight type 2 diabetics, mean age 59 years, 60% women), patients in the intervention group achieved significant weight loss (n = 2,570, recommendation of >175 minutes of physical activity per week, dietary modification with calorie reduction to 1200-1800 kcal/day and meal replacements at the start of therapy). As waist circumference decreased, HbA1c levels, physical fitness, and all other cardiovascular risk factors improved significantly, except for LDL cholesterol levels. Despite these differences, there was no significant difference between the groups regarding the primary endpoint, cardiovascular morbidity and mortality, especially the incidence of myocardial infarction as an expression of macroangiopathy. However, the effect on microangiopathy was crucial. The risk of advanced nephropathy (GFR <30 ml/min/1.73 m² or GFR <45 ml/min/1.73 m² and albumin/creatinine ratio ≥30 mg albumin/g creatinine or GFR <60 ml/min/1.73 m² and albumin/creatinine ratio >300 mg/g) was significantly reduced by intensive lifestyle intervention. This effect was predominantly observed when there was weight reduction, reduction in systolic blood pressure, and reduction in HbA1c levels.

Lipids

Training interventions only show moderate effects on the lipid profile. Physical activity can increase HDL cholesterol, and an effect on triglycerides is almost always observed. A recent meta-analysis of endurance training intervention studies (intensity: 65-80% VO2max, duration: 40-50 minutes per session, frequency: 3-4 times per week, intervention duration: 26-40 weeks) confirms this, showing an 8% reduction in triglycerides ($p = 0.0004$) and a 4% increase in HDL cholesterol ($p = 0.0061$). The effect on LDL cholesterol is minimal; however, physical activity reduces subfractions of LDL particles, such as the particularly atherogenic small-dense LDL particles (sdLDL particles), and increases the size of LDL particles, which is believed to have an antiatherogenic effect. In secondary prevention after myocardial infarction, the primary focus is on consistently lowering LDL cholesterol to < 70 mg/dL, which can usually only be achieved through medication due to the limited effects of physical training. It should be noted that HDL cholesterol decreases with a low-fat diet, and simultaneous physical training can only partially compensate for this.

Arterial Hypertension

In 2015, 1.13 billion people worldwide were affected by arterial hypertension, an established cardiovascular risk factor for coronary heart disease (CHD). Optimal blood pressure control is essential for hypertensive patients with CHD and is primarily achieved through medication. Physical activity and dietary modification complement this therapy, with physical activity lowering blood pressure by improving vascular elasticity, endothelial function, sympathetic nervous system hormone status, and the renin-angiotensin system.

Training intervention studies have shown that both endurance and general strength training can lower blood pressure. In a large meta-analysis from 2013, 93 of these studies ($n = 5{,}223$; including normotensive, pre-hypertensive, and hypertensive patients) were summarized. On average, systolic blood pressure decreased by 4 mmHg and diastolic blood pressure decreased by 3 mmHg through endurance training. The effect was greatest in hypertensive patients (-8 mmHg systolic). The importance of blood pressure during physical exertion should be particularly considered. In patients with CHD, blood pressure should be optimally controlled, which should be regularly monitored during exercise stress tests (ergometry).

Coronary Heart Disease (CHD)

Physical activity improves the prognosis in CHD in addition to the effects of pharmacological therapy. This effect is partially mediated through the reduction of the aforementioned risk factors and improved exercise tolerance, but the mechanisms are more diverse than previously known.

Exercise tolerance in exercise stress testing is a crucial prognostic parameter after myocardial infarction (MI):

In a prospective observational study of 12,169 male cardiac patients, with an average age of 55 years (7,096 patients with a history of MI, 3,077 patients with a history of bypass surgery, and 1,996 patients with ischemic heart disease), patients with high exercise tolerance (VO2 peak > 22 ml/kg/min) had a 61% lower likelihood of cardiac death compared to patients with low exercise tolerance (VO2 peak < 15 ml/kg/min) after an average follow-up of 8 years. Patients with moderate fitness (VO2 peak 15-22 ml/kg/min) already had a 38% lower relative risk of cardiovascular mortality compared to those with severely limited exercise capacity.

Maximum exercise tolerance, measured as VO2 peak, is also an independent predictor of cardiovascular mortality in women after myocardial infarction. In a study by Kavanagh et al., a 1 ml/kg/min increase in VO2 peak was associated with a 10% decrease in cardiovascular mortality in women with CHD (including 2,380 with a history of MI).

Cardiac rehabilitation with structured training is essential for improving exercise tolerance after myocardial infarction, while medication therapy has little or no effect in this context. Patients who participated in a rehabilitation program had a 26% lower risk of cardiac death compared to patients without the program, according to a 2016 Cochrane meta-analysis (including 14,486 CHD patients with a history of MI, PCI, or bypass surgery) (RR 0.74; 95% CI 0.64-0.86). So that every patient benefits from sports therapy, the program must be adapted to its capacity. In a recent study, patients with a good improvement in VO2peak before and significantly lower mortality after rehabilitation.

The prognosis of CHD is significantly influenced by the extent of physical activity. The more active patients with CHD are, the lower the risk of overall and cardiovascular mortality. The study by Stewart et al. clearly demonstrates this "dose-response effect". 15,486 patients with stable CHD and a history of myocardial infarction, percutaneous coronary intervention (PCI), or surgical revascularization provided information on their current physical activity through questionnaires, with a mean follow-up of 3.7 years. Doubling the extent of physical activity (measured in MET-hours per week) showed a 10% reduction in overall mortality (multivariable-adjusted relative risk [RR] 0.90; 95% confidence interval [CI]: 0.87–0.93) and an 8% reduction in cardiovascular mortality (multivariable-adjusted RR 0.92; 95% CI: 0.88–0.96). Patients who were active for 10-20 MET-hours per week had a 50% lower mortality compared to inactive patients. Even further increase in activity beyond 20 MET-hours per week improved survival by an additional 20%.

Intensity: Moderate Continuous Training versus Interval Training. Improving Exercise Tolerance

The optimal intensity for improving exercise tolerance in patients with coronary heart disease (CHD) is still debated. Until about 10 years ago, only moderate-intensity continuous training (MICT) was recommended. However, according to recent studies, high-intensity interval training (HIIT) or even more intense training can be considered as an alternative for well-tolerated patients. The effects of higher intensity training appear to be superior to the established MICT. This is crucial since improved exercise tolerance is associated with better prognosis.

In a recent review, the effects of HIIT (n = 456) and MICT (n = 488) on exercise tolerance were examined. Among 953 patients in 17 randomized controlled trials (RCTs), 123 had CHD, 633 had a history of myocardial infarction (MI), 477 had undergone percutaneous coronary intervention (PCI), and 361 had undergone bypass surgery. The duration of interventions ranged from 4 weeks to 12 months, with training frequencies ranging from ≥2-5 times per week to ≥4 times per day. The intensity of HIIT followed the guidelines (≥85% VO2 peak or ≥85% heart rate reserve [HRR] or ≥90% of maximum heart rate [HR]), alternating with lower intensity periods. MICT was performed at intensities of 50-75% VO2 peak or 50-75% HRR or 50-80% of maximum heart rate. The primary endpoint of the studies was maximum oxygen consumption (VO2 peak).

Of the 17 studies, 16 showed the superiority of HIIT (VO2 peak SMD 0.34 ml/kg/min; 95% CI [18.20-18.66]; $p < 0.001$; I2 = 28%). The effect was dependent on the duration of the intervention, with training programs lasting less than 6 weeks showing no significant effect, and interventions lasting over 12 weeks not providing additional benefits compared to those between 7-12 weeks.

Indeed, the direct comparison in the SAINTEX study demonstrated that both MICT and HIIT significantly improved exercise tolerance in 200 patients with coronary heart disease (CHD). The intervention lasted for 12 weeks with 3 training sessions per week. In both the MICT group (target training intensity 70-75% of maximum heart rate) and the HIIT group (target: intervals of 4 minutes at 90-95% of maximum heart rate), VO2 peak significantly increased: +22.7 ± 17.6% in the HIIT group and +20.3 ± 15.3% in the MICT group. There was no difference between the groups after 12 weeks or in the 1-year follow-up. This was discussed in terms of the actual achieved training heart rates converging, as the average heart rate in the MICT group exceeded the target (80% of maximum heart rate), while in the HIIT group, it was lower (average of 88% of maximum heart rate) because many patients were unable to sustain 90-95% of maximum heart rate for 4 minutes.

However, the current review by Hannan et al. is in line with previous meta-analyses, which showed that HIIT resulted in, on average, 1.5-1.8 ml/kg/min higher VO2 peak compared to moderate continuous training. Both forms of training were considered safe in terms of cardiac events, as neither of the intervention groups experienced cardiac events leading to hospitalization. However, only 13 out of the 17 studies reported the occurrence of any incidents.

From when to be active after myocardial infarction?

Cardiac remodeling following a myocardial infarction leads to changes in the ventricle, including increased inflammation, cellular migration, and ultimately the formation of myocardial scars. Impairment of left ventricular function (EF) and an increase in end-systolic and end-diastolic volumes are associated with significantly higher mortality rates.

The temporal influence of physical training on cardiac remodeling has been relatively underexplored. A meta-analysis by Haykowsky et al. summarized the temporal effect of cardiac rehabilitation measures on remodeling in patients after a myocardial infarction. The included studies (n = 647 post-infarction patients, average age 55 years, with a moderately impaired EF of 44% on average) involved endurance training of moderate intensity, ranging from 60% to 80% of VO2peak. The training sessions had a duration of 20-80 minutes, and the interventions lasted for 1-6 months.

The most significant anti-remodeling effects were observed when training commenced as early as 1 week after discharge in myocardial infarction patients and continued for at least 6 months. In terms of end-systolic volume (an important predictor of cardiac mortality after a myocardial infarction) and left ventricular function, the training needed to be extended by one month for every week it was initiated after the optimal time point of 1 week post-hospital discharge, to achieve the same effects.

Patients with stable coronary heart disease (CHD) are generally advised to engage in daily targeted physical training lasting 20 minutes, performed at their optimal heart rate with moderate intensity. Longer durations of 30 to 60 minutes per day are desirable. Strength training can be added twice a week to prevent muscle loss. It is important to note that beyond these recommendations, everyday physical activity should still be incorporated.

Patients with CHD and other heart diseases may initially struggle to sustain the full 20 minutes of exercise. In such cases, starting with 5 to 10 minutes of training, twice a day, can be beneficial. Patients must be made aware that training sessions of 1 to 2 times per week in cardiac groups are not sufficient. A minimum of 3 training sessions per week is recommended, exceeding the guidelines for primary prevention.

Immediately after a myocardial infarction, physical activity should be tailored to the individual's previous fitness level, disease progression, potential heart failure, and any accompanying conditions. Ideally, daily activity should start with low volume and intensity but occur multiple times throughout the day to gradually acclimate the body to exertion.

Competitive Sports in Coronary Heart Disease

Patients with coronary heart disease (CHD) who are interested in competitive sports form only a small group. These patients, for instance, want to know whether they are medically allowed to participate in competitions. If a patient wants to participate in competitions, the likelihood of cardiac events during (intense) exertion should be analyzed. This includes assessing the severity of CHD, systolic function, wall motion abnormalities with myocardial scars, arrhythmias (during exertion and at rest), and any associated symptoms. If none of these factors are present, the patient can participate in competitions. Otherwise, they should refrain from engaging in competitive sports due to the high likelihood of cardiac events.

For patients at low risk, all sports are generally permissible, and there are no sport-specific restrictions. In special cases, individual consideration is necessary, such as for ultramarathons, prolonged exertion like marathons, exertion at high altitudes, or in extreme heat that can lead to significant electrolyte imbalances or hypoxia.

Cardiac Rehabilitation and Long-Term Programs

According to guidelines, phase II of cardiac rehabilitation after a myocardial infarction should ideally start immediately after hospital discharge. Depending on the patient's preference, psychosocial aspects, local conditions, and availability, it can be done on an outpatient or inpatient basis.

The contents of cardiac rehabilitation include education (lifestyle measures, optimization of risk factors), exercise therapy, as well as psychological and psychosocial topics.

After completing outpatient or inpatient rehabilitation, patients with coronary heart disease (CHD) should participate in structured long-term programs, such as one of the over 6000 cardiac exercise groups in Germany. Outpatient cardiac exercise is conducted under medical supervision. It requires a prescription from a physician, which needs to be approved by the responsible payer (health insurance, pension insurance) beforehand. With the Form 56, 90 training sessions can be prescribed, which must be completed within 24 months. The training consists of a combination of endurance, general strength, and coordination exercises. The groups are usually divided into a training group (capacity > 1 watt/kg body weight) and an exercise group (< 1 watt/kg body weight).

The sole activity in a cardiac exercise group, however, is not sufficient in the long term to achieve the goal of daily minimum 20-minute moderate-intensity exercise. While walking or ergometer training are most commonly performed, especially in older patients, the choice of suitable sport depends on the patient's preference, local conditions, and current fitness level. The more a patient can enthuse themselves about "their" activity, the longer they will continue to do it - and it is precisely this long-term commitment that is crucial.