Physical activity and exercise training in preventive cardiology

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Abstract

Physical activity (PA) and exercise training (ET) are central and indispensable components for primary and secondary prevention of cardiovascular disease (CVD). In healthy individuals, PA reduces all-cause and CV mortality and has confirmed beneficial effects on the cardiovascular risk profile. In secondary prevention, PA counselling and ET are two of the core components of a multidisciplinary cardiac rehabilitation (CR) program. Exercise-based CR is an established strategy in the secondary prevention of CV disease. It improves survival, reduces hospital admissions, improves cardiorespiratory fitness (CRF), and quality of life (QoL). However, these beneficial effects require regular attendance under professional supervision and adherence to recommended guidelines. In patients with heart disease, proper patient assessment with a standardized exercise test as a basis for a tailored ET prescription is required. In healthy subjects this is advocated only in selected groups.

Current guidelines recommend at least 150 min/week of moderate-intensity continuous aerobic PA in both healthy individuals as well as those with cardiac disease. In healthy adults, alternatively intensity can be increased and volume can be halved. High intensity interval training (HIIT) is a relatively new training modality and may be used complementary to continuous training in selected patient groups. HIIT seems to be superior compared to moderate continuous exercise in patients with cardiac metabolic disease with regard to effects on the CV risk profile, endothelial function, improvement in cardiorespiratory fitness, and a reverse cardiac remodelling in patients with heart failure.

One of the major challenges in preventive cardiology is the improvement of long-term adherence to PA recommendations. The aim of this article is to give an overview from the preventive cardiologist’s point of view with a focus on endurance ET prescription for the audience of sports and exercise medicine physicians.

Keywords: physical activity, exercise training, cardiac rehabilitation, cardiorespiratory fitness, interval training

Zusammenfassung


Die aktuellen Richtlinien empfehlen mindestens 150 Minuten/Woche moderat-kontinuierliche körperliche Aktivität sowohl für Gesunde wie auch für Patienten mit einer Herzkrankung. Als Alternative kann bei Gesunden die Intensität erhöht und stattdessen die Dauer halbiert werden. Hochintensives Intervalltraining (HIIT) stellt bei speziellen Patientengruppen eine relativ neue Trainingsmodalität dar, die komplementär zum etablierten kontinuierlich-moderaten Training angesehen wird. Studien zeigen, dass HIIT der etablierten moderat-kontinuierlichen Trainingsmodalität überlegen sein könnte in Bezug auf Effekte auf das kardiovaskuläre Risikoprofil, die Endothelfunktion, die Verbesserung der kardiorespiratorischen Fitness und nicht zuletzt in Bezug auf den Effekt auf das kardiale Remodelling bei Herzensuffizienz.


Schlüsselwörter: körperliche Aktivität, strukturiertes Training, kardiale Rehabilitation, kardiorespiratorische Fitness, Intervalltraining
Cardiovascular disease (CVD) remains the leading global cause of death, accounting for 17.3 million deaths per year worldwide. [1] Physical inactivity has been identified as one of the leading risk factors for global mortality causing an estimated 3.2 million premature deaths globally. [2] Physical activity (PA) is defined as any body movement produced by the contraction of skeletal muscles that results in a substantial increase in caloric requirement over resting energy expenditure. [3,4] In 1953, Morris and colleagues showed that London’s double-decker bus drivers had a higher rate of coronary events compared to conductors. This was attributed to the physically more active job of the conductors compared to the physically inactive bus drivers. [5] This seminal study was the first who confirmed the beneficial effects of PA in cardiovascular (CV) health. Nowadays, multiple population-based trials have confirmed that there is an inverse correlation between PA and all-cause/CV mortality: even doses as low as 15 min of PA per day appear to reduce CV disease risk and all-cause mortality with the greatest health gains due to the first 15–29 min of daily activity in previously inactive individuals. [6–8] A recently published study found a strong negative association of cardiorespiratory fitness (CRF) level in middle aged healthy subjects with health care costs later in life. [9] Over the last six decades the concept that PA and/or structured exercise training (ET) reduce CV mortality has been extended to patients with manifest heart disease (i.e. patients with coronary artery disease (CAD), after percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), and heart failure (HF) patients). [10] ET is a type of PA consisting of planned, structured, and repetitive bodily movement done to improve and/or maintain CRF. [3,4] Cardiac rehabilitation (CR) has the potential to improve survival and reduce hospital admissions, if attended on a regular basis. [11] Exercise-based CR is an established strategy in the secondary prevention of CV disease.

In a large meta-analysis published this year, which collected follow-up data of 14,486 patients with CAD and included 63 prospective randomized clinical trials, exercise-based CR was associated with a substantial reduction in cardiovascular mortality and hospital admissions. The majority of analysed studies showed higher levels of health-related quality of life (QoL) following exercise-based CR compared to control subjects. [12] However, achievement of sustainable effects on hard endpoints have been challenged recently. Amongst other studies from the United Kingdom (UK), the RAMIT trial is the largest randomized controlled trial on comprehensive CR after myocardial infarction. This trial has failed to show beneficial effects on all-cause mortality, cardiac or psychological morbidity, risk factors, health-related QoL or activity. [13] The study had major limitations. Besides being underpowered for the assessment of mortality, the prescribed ET volume was only half of what current recommendations state. Additionally, ET was not tailored based on a maximum exercise test, due to routine sub-maximal exercise testing in the UK at the entry of a CR program. Consequently, the overall increase in CRF was only about one third (0.52 MET, metabolic equivalent) of the mean increase reported in a recent meta-analysis (1.55 MET).

These low training volumes and small increases in CRF may partially explain the reported inefficacy of UK CR to reduce patient mortality. [14–16]

In heart failure patients mortality reduction, reduction of re-hospitalization rate and the improvement in CRF is of utmost importance. [17,18] In a recent meta-analysis including 33 trials with 4740 HF patients, exercise-based CR revealed no increased risk of all-cause mortality compared to controls, but reduced the risk of hospital admissions and conferred improvements in health-related QoL. [19] Furthermore, two recent meta-analyses have emphasized the importance of aerobic endurance training on reverse left ventricular remodelling. [20,21] In chronic HF patients, the development of a catabolic metabolic state is another aspect of interest. Skeletal myopathy is a major limitation of exercise capacity. Muscle wasting is an independent predictor of mortality in CHF and is beneficially influenced by ET on a regular basis. [22,23] Most patients included in exercise-based HF studies had systolic dysfunction (HFrEF). However, >50% of patients with HF have heart failure with preserved ejection fraction (HfPEF), which is particularly common in older patients with HF and in women. [24,25] Mortality data in HfPEF patients are currently lacking. Recent data revealed that ET in patients with HfPEF is associated with an improvement in CRF and QoL. [26] The ExDHF study demonstrated that a structured ET in patients with HfPEF has additional beneficial effects on LV diastolic function compared to patients who received usual care. [27] Taking all these aspects into account, it is comprehensible that PA counselling and a tailored as well as an initially supervised ET are two of the core components of a multidisciplinary secondary prevention program. [28]

**Physiological effect of exercise**

The beneficial effects of exercise on CV risk factors like body composition, blood pressure, blood glucose and lipid profile are well known. [29–32] There seems to be an intensity-dependent effect with more favorable effects regarding body composition, visceral fat and lipid profile at higher exercise intensities. [33,34] Other aspects of interest are the molecular changes that occur in the CV system in response to ET. A byproduct of regular physical exercise is the increase in shear stress of blood flowing through the main arteries leading to the production of vascular nitric oxide (NO) by the up-regulation of endothelial nitric oxide synthase (eNOS). [35] NO induces vasodilation, which results in the lowering of peripheral resistance and increased perfusion of the skeletal muscles. Furthermore, endothelial progenitor cells are activated by ET, which preserve normal endothelial function and stimulate vasculogenesis, and induce multiple metabolic changes in the myocardium resulting in improved tolerance for ischemia and reperfusion injury. [36–40] Last but not least, arterial stiffness, which is associated with several pathologies like systolic hypertension and HF is lower in subjects who regularly exercise compared to sedentary controls. [41,42]

**Risk assessment and Exercise testing**

In healthy subjects aiming to participate in regular PA – particularly those aged 35 years or older- a self-assessment of

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Introduction

“Lack of activity destroys the good condition of every human being, while movement and methodical physical exercise save it and preserve it.” – Plato, Greek philosopher

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Cardiorespiratory fitness as surrogate marker of mortality

Cardiorespiratory fitness (CRF, measured as peak VO₂) is a marker of aerobic exercise capacity and can be expressed as metabolic equivalents (MET), with 1 MET corresponding to 3.5 mL of oxygen per kilogram of body weight per minute (mL/kg/min), the typical resting energy requirement for basal homeostasis.

In addition, CRF is an important surrogate marker of survival and well-being in healthy subjects and those with CV disease, respectively. There is an inverse correlation of CRF and mortality. Each 1-MET increase in CRF is associated with a significant reduction in mortality and CAD events, which compares favorably with the survival benefit conferred by low-dose aspirin, statins, Beta-blockers, and angiotensin-converting enzyme inhibitors after acute myocardial infarction. [56,57]

Exercise prescription

The principles of PA promotion and ET prescription are intended to guide health/fitness on the one hand, and to individually tailor ET for the apparently healthy adult as well as adults with certain chronic (cardiac) diseases on the other. The American College of Sports Medicine (ACSM) recommends in its companion evidence-based position stand to employ the FITT-VP principle to prescribe ET (Table 1). [4]

Intensity guidance can easily be made by self-assessment (e.g. rate of perceived exertion (RPE), i.e., “Borg Scale”). [58] Alternatively, peak heart rate (HR) can be determined with an incremental self-test. Based on this, training intensities can indirectly be calculated (Table 2). If CPET is available, the first and second ventilatory threshold can directly be determined. In summary, training should be guided based on workload and training zones and not on heart rate, particularly in cardiac patients.

Generally, PA promotion should be part of a structured lifestyle counselling program. [4,47] PA promotion as well as ET prescription is not only reserved to exercise physiologists and specialists in preventive medicine, but should also be done in the doctor’s office by general practitioners (GP) and sports and exercise physicians. In Switzerland, several institutions such as the Swiss society of Sports Medicine propose physical activity promotion in primary care (PAPRICA) to emphasize that GP’s play an essential role in PA promotion. [59]

In healthy adults, current European guidelines recommend an aerobic PA volume of 150–300min/week of at least moderate-intensity (Zone II, Table 2) to provide a reduction in all-cause and cardiovascular mortality. As a time-efficient alternative 60–90min/week of high-intensity may be performed, or an equivalent combination of the two types of training. [60] While PA in the primary preventive setting can be seen as an effective monotherapy, in secondary prevention it is in concert with optimal medical therapy which it cannot replace.

In patients with known CVD (including CAD, HF), aerobic ET is recognized as a class I, level of evidence A indication. [60] Among others, PA counselling and ET are two additional core components of a multidisciplinary CR program. [28] A moderate intensity continuous ET (i.e., starting at 50% of maximal work load and gradually increasing to 80% in CAD, and starting at the 1st and gradually increasing to the 2nd ventilatory threshold in HF patients, respectively, Figure 1A), scheduled as 30 min session 3–5 times per week, under close supervision are recommended. [47,60]

Additionally, there is growing evidence that high-intensity interval training (HIIT) may be equivalent or even more effective than moderate-intensity continuous exercise training (MICE) and can be performed safely with impressive improvements in CRF and QoL in CAD patients as well as in chronic HF patients, in whom reverse cardiac remodeling was found with HIIT. [61–64] In patients with lifestyle-induced cardio metabolic disease significant beneficial effects on the cardiovascular risk profile, oxidative stress and inflammation, as well as increases in the availability of NO by HIIT were shown. [65]

Currently, the most commonly used HIIT model consists of 4 times 4 min high intensity intervals (at 80% of maximal work load or above the 2nd ventilatory threshold) and active recovery phases of 3 min at low intensity (at 50% of maximal

<table>
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<th>Table 1: FITT-VP principle for exercise prescription [4]</th>
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<td>– Frequency (how often)</td>
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<td>– Type (mode or what kind)</td>
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<td>– Additional: total Volume (amount) and Progression (advancement)</td>
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workload or below the 1st ventilatory threshold, Figure 1B). The current recommendation is to use HIIT complementary, but not as a replacement for the more established MICE. In much deconditioned HF patients a low intensity interval training with short bouts (10 to 30 seconds, at 50% of maximal work load, or below the 1st ventilatory threshold) and longer recovery periods is recommended (Figure 1C).

In patients with CAD, an additional resistance training (RT) seems to be more effective than endurance training alone. Recommended is an expansion of endurance ET to a dynamic RT 2 times/week (not pure isometric training) in all clinically stable patients with and without HF. A combined ET/RT does not lead to a cardiac remodeling with a more pronounced LV dilatation than ET alone. In chronic HF patients, Inspiratory muscle weakness (IMW) is highly prevalent. In selected patients, the addition of inspiratory muscle training results in improvements in inspiratory muscle strength, CRF, ventilator response to exercise, and QoL.

Conclusions

PA and ET are central and indispensable components of a comprehensive strategy for the primary and secondary prevention of CAD. PA advice has to be part of a structured lifestyle counselling program and should increasingly take place in the doctor’s office and be promoted by general practitioners (GP), particularly in primary prevention. Current international PA recommendations should be applied which have shown to result in sustainable effects. Exercise-based programs contribute to a decreased morbidity and mortality, particularly in patients with CAD with or without HF. Subjects/patients assessment need to be tailored and should include high quality ET recommendations and therapy, delivered by specialists in sports and exercise medicine. Continuous training and interval training can be used complementarily in patients with heart disease.

Perspective

One of the major challenges in preventive cardiology is the improvement of long-term adherence (‘patient empowerment’). Adherence to behavioral advice is associated with a
substantially lower risk of recurrent cardiovascular events, particularly regarding ET recommendations. [73] Future directions with great potential are home-based and smartphone-based CR programs. Comparing home-versus center-based CR programs, there seems to be no difference regarding mortality risk, improvement in CRF, as well as modifiable risk factors, and health-related QoL outcomes in patients with CAD or HF. Additionally, there is no difference with regard to healthcare costs produced by the two forms of cardiac rehabilitation. [74,75] The addition of cardiac tele-rehabilitation to conventional center-based CR may even be more effective and efficient than center-based CR alone, particularly with regard to sustainability of PA level. [76,77]

**Practical implications**
- Physical activity (PA) reduces all-cause and cardiovascular (CV) mortality and has beneficial effects on the cardiovascular risk profile in healthy individuals
- PA advice should increasingly take place in the doctor’s office and be promoted by general practitioners, particularly in primary prevention
- In secondary prevention, PA counselling and structured exercise training are two core components of a multidisciplinary cardiac rehabilitation (CR) program
- Exercise-based CR is an established strategy in the secondary prevention of CV disease and improves survival, reduces hospital admissions, improves cardiorespiratory fitness (CRF), and quality of life
- High intensity interval training (HIIT) can be used complementary to moderate continuous training and may be even superior in patients with cardio metabolic disease with regard to effects on the CV risk profile, endothelial function, improvement in CRF, and a reverse cardiac remodelling in patients with heart failure

**Schlussfolgerungen für die Praxis**
- Körpliche Aktivität ist beim Gesunden mit einer Mortalitätsreduktion und einem günstigen Einfluss auf das kardiovaskuläre Risikoprofil vergesellschaftet
- Die Beratung bezüglich körperlicher Aktivität sollte vermehrt auch in der Arztpraxis durch den Grundversorger stattfinden, speziell in der Primärprävention
- In der Sekundärprävention sind Beratung bezüglich körperlicher Aktivität und strukturiertes Training zwei Kernkomponenten eines multidisziplinären kardialen Rehabilitationssprogrammes
- Bewegungs-basierte kardiale Rehabilitationssprogramme sind etabliert in der Sekundärprävention und senken die Mortalität, verhindern Re-Hospitalisationen, verbessern die kardiorespiratorische Fitness und die Lebensqualität
- Hochintensives Intervalltraining (HIIT) kann komplementär zum etablierten moderat kontinuierlichen Training eingesetzt werden und könnte bei Patienten mit kardio-metabolischer Erkrankung gar überlegen sein in Bezug auf Effekte auf das kardiovaskuläre Risikoprofil, die Endothelfunktion, die Verbesserung der kardiorespiratorischen Fitness und nicht zuletzt in Bezug auf den Effekt auf das kardiale Remodelling bei Herzensuffizienz

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