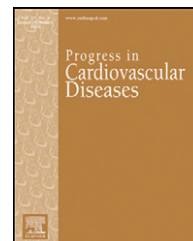


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Exercise Training in Patients with Heart Disease: Review of Beneficial Effects and Clinical Recommendations

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ABSTRACT

Over the last decades exercise training has evolved into an established evidence-based therapeutic strategy with prognostic benefits in many cardiovascular diseases (CVDs): In stable coronary artery disease (CAD) exercise training attenuates disease progression by beneficially influencing CVD risk factors (i.e., hyperlipidemia, hypertension) and coronary endothelial function. In heart failure (HF) with reduced ejection fraction (HF_{rEF}) training prevents the progressive loss of exercise capacity by antagonizing peripheral skeletal muscle wasting and by promoting left ventricular reverse remodeling with reduction in cardiomegaly and improvement of ejection fraction. Novel areas for exercise training interventions include HF with preserved ejection fraction (HF_{pEF}), pulmonary hypertension, and valvular heart disease. In HF_{pEF}, randomized studies indicate a lusitropic effect of training on left ventricular diastolic function associated with symptomatic improvement of exercise capacity. In pulmonary hypertension, reductions in pulmonary artery pressure were observed following endurance exercise training.

Recently, innovative training methods such as high-intensity interval training, resistance training and others have been introduced. Although their prognostic value still needs to be determined, these approaches may achieve superior improvements in aerobic exercise capacity and gain in muscle mass, respectively.

In this review, we give an overview of the prognostic and symptomatic benefits of exercise training in the most common cardiac disease entities. Additionally, key guideline recommendations for the initiation of training programs are summarized.

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Abbreviations and Acronyms

CAD = coronary artery disease
CR = cardiac rehabilitation
CV = cardiovascular
CVD = cardiovascular disease
EF = ejection fraction
EDV = end diastolic volume
ESV = end systolic volume
HIIT = high intensity interval training
HF = heart failure
HFpEF = heart failure—preserved ejection fraction
HFrEF = heart failure—reduced ejection fraction
LV = left ventricular
MI = myocardial infarction
OMT = optimal physical therapy
PA = physical activity
PCI = percutaneous coronary intervention
PAH = pulmonary arterial hypertension
VO ₂ = oxygen consumption
PH = pulmonary hypertension

CV mortality was also extended to patients with manifest heart disease: 1) In coronary artery disease (CAD) patients a consistent 18%–20% reduction in all-cause mortality was confirmed in meta-analyses.^{2,3} After an acute coronary syndrome the effects seem to be even more pronounced leading to a 40% decline in 6-month mortality.⁴; 2) In heart failure (HF) with reduced ejection fraction (HFrEF), a European meta-analysis of pooled patient data from randomized studies found a significant reduction of total mortality by 35% and of hospitalization by 28%.⁵ This was, however, not confirmed in a prospective large-scale multicenter study, probably as a result of lower-than-expected adherence to the prescribed training programme.⁶ It is clear, however, that training programs result in a 15%–25% increase in exercise capacity, a concomitant improvement of New York Heart Association (NYHA) functional class, and a reversal of left ventricular remodeling with reduction of cardiomegaly; 3) Recently, the beneficial training effects on symptoms, exercise capacity and left ventricular diastolic function were also confirmed in HF with preserved ejection fraction (HFpEF) in the ExDHF study⁷; And 4) Training as a therapeutic concept is also being extended to patient groups which were formerly advised not to engage in recreational PA or structured exercise programs (e.g., patients with pulmonary

“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)]

The antique wisdom on the benefits of regular exercise for health was based on the observation that well-trained individuals were less likely to become sick. Today, large-scale population-based trials have confirmed that there is indeed a correlation between leisure-time PA and all-cause/cardiometabolic (CV) mortality: 15 min of exercise per day confers a 14% mortality reduction.¹ A 4% reduction can be added for each additional 15 min of daily exercise time.¹

During the last 50 years the concept that exercise reduces

hypertension,⁸ valvular and congenital heart disease). Clinical research in these areas is just beginning and although first proof-of-concept studies confirmed safety and efficacy it is too early to extrapolate the findings to prognostic improvements.

Exercise training has multiple physiologic effects on the CV system, most notably a reduction of resting heart rate as a result of increased parasympathetic tone, an improved vascular endothelial function with augmented flow-mediated vasodilation during exercise, an increased vasculogenesis through endothelial progenitor cells, and multiple metabolic changes in the myocardium resulting in improved tolerance for ischemia and reperfusion injury.^{9,10,11}

Beneficial clinical and prognostic effects of exercise training in heart disease

Contrary to former textbook recommendations, there are in fact only a few cardiac pathologies in which patients do not derive a symptomatic or prognostic benefit from regular training programs. The list of clear contraindications includes unstable angina, and recent myocardial infarction, uncontrolled cardiac arrhythmia, symptomatic severe aortic stenosis or other valvular disease, decompensated symptomatic HF, and acute myocarditis or pericarditis.

Relative contraindications usually lead to temporary suspension of training programs and should be corrected before the exercise training is reinitiated. Most relevant are uncontrolled tachy- and bradyarrhythmias, severe arterial hypertension (systolic blood pressure >200 mm Hg, diastolic blood pressure >110 mm Hg), electrolyte disorders or uncorrected severe anemia.

In this review, only key indications for exercise-based cardiac rehabilitation (CR) can be briefly discussed. We will therefore focus on (1) stable CAD, (2) post-infarction rehabilitation, and (3) HF (both HFrEF and HFpEF). As novel and upcoming indications for exercise training, we assess training in valvular heart disease, congenital heart disease, and pulmonary hypertension.

Stable coronary artery disease

The oldest account that physical exercise can improve the symptoms of ischemic heart disease comes from the physician, who first described the clinical syndrome of angina pectoris, William Heberden. He reported that a patient with angina pectoris was nearly cured of his symptoms after sawing wood every day for half a year. As this observation would at best qualify for a class C recommendation in modern guidelines we need to look into prospective clinical studies.

Prognostic benefits of exercise training in coronary artery disease

In a large, high-quality meta-analysis, Taylor and colleagues collected clinical follow-up data in 8940 patients with CAD included in 48 prospective randomized clinical exercise training studies.² Exercise-based CR, was associated with a significant decrease in all-cause mortality by 20% (odds ratio 0.80; 95% confidence interval 0.68 to 0.93) and in cardiac

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