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Exercise training in chronic heart failure

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Abstract: The syndrome of heart failure (HF) is a growing epidemic that causes a significant socio-economic burden. Despite considerable progress in the management of patients with HF, mortality and morbidity remain a major healthcare concern and frequent hospital admissions jeopardize daily life and social activities. Exercise training is an important adjunct nonpharmacological treatment modality for patients with HF that has proven positive effects on mortality, morbidity, exercise capacity and quality of life. Different training modalities are available to target the problems with which HF patients are faced. It is essential to tailor the prescribed exercise regimen, so that both efficiency and safety are guaranteed. Electrical implanted devices and mechanical support should not exclude patients from exercise training; however, particular precautions and a specialized approach are advised. At least 50% of patients with HF, older than 65 years of age, present with HF with preserved ejection fraction (HFPEF). Although the study populations included in studies evaluating the effect of exercise training in this population are small, the results are promising and seem to support the idea that exercise training is beneficial for HFPEF patients. Both the short- and especially long-term adherence to exercise training remain a major challenge that can only be tackled by a multidisciplinary approach. Efforts should be directed towards closing the gap between recommendations and the actual implementation of training programmes.

Keywords: exercise training, heart failure

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Introduction

The syndrome of heart failure (HF) is a growing epidemic that causes a significant socio-economic burden. In developed countries, 1–2% of the adult population is diagnosed with HF, but prevalence reaches 10% among persons 70 years of age or older [Mosterd and Hoes, 2007]. Despite considerable progress in the management of patients with HF, mortality and morbidity remain a major healthcare concern [Corra *et al.* 2005], and frequent hospital admissions jeopardize daily life and social activities.

The recent 2012 European guidelines for the diagnosis and treatment of acute and chronic heart failure have incorporated a class IA recommendation for regular aerobic exercise in patients with HF to improve functional capacity and symptoms [McMurray *et al.* 2012]. The current therapeutic armamentarium, consisting of a titrated drug regimen, and carefully selected electrical implantable devices, still falls short when it comes to improving exercise tolerance. Exercise training specifically targets this shortcoming and is considered one of the most effective measures to improve patients' wellbeing.

In contrast to HF with reduced ejection fraction (HFREF), the therapeutic approach of patients with preserved ejection fraction (HFPEF) is largely limited to symptomatic treatment. Since patients with HFPEF constitute around 50% of the current HF population [Kitzman *et al.* 2001], there is an urgent need for progress. With regard to the application of exercise training, a similar gap in evidence is seen. Nevertheless, positive results from recently conducted pilot trials [Alves *et al.* 2012; Haykowsky *et al.* 2012; Edelmann *et al.* 2011; Kitzman *et al.* 2010], will hopefully serve as an impetus to explore further this treatment modality for patients with HFPEF.

This review will briefly discuss the pathophysiological rationale for exercise training. The impact of exercise training on hard endpoints, as well as exercise capacity and quality of life (QoL), are addressed. Practical issues (i.e. evaluation of exercise capacity and prescription of exercise training) will be described, as well as the emerging role of exercise training for patients with HFPEF and HF patients with devices, such as the implantable cardioverter-defibrillator (ICD), cardiac resynchronization therapy (CRT) or assist devices. Endurance exercise at moderate intensity is still the most applied training modality for HF patients. Nevertheless, new training modes are tested and are progressively introduced into the clinical arena. For those readers who are interested in basic molecular changes as plausible explanations for exercise-derived benefits, we would like to refer to the recently published review by Gielen and colleagues [Gielen *et al.* 2010].

Targets for exercise training

The Fick equation explains the relationship between exercise capacity and cardiac performance: $VO_2 = Q\ (CaO_2 - CvO_2)$ (VO_2: oxygen consumption; Q: cardiac output; CaO_2: arterial oxygen content; CvO_2: venous oxygen content) and clearly shows that exercise capacity depends on central cardiac, as well as peripheral mechanisms. The correlation between peak oxygen consumption (VO_2peak) and resting left ventricular ejection fraction (LVEF) is poor in patients with chronic heart failure (CHF) [Franciosa *et al.* 1981]. Therefore, cardiac reserve during exercise, as well as peripheral factors implicated in oxygen transfer (peripheral vascular function), oxygen uptake and utilization (skeletal muscle), increased ergoreceptor activity and ventilatory inefficiency need to be taken into account.

Exercise training in CHF patients decreases circulating catecholamine levels [Passino *et al.* 2006], has anti-inflammatory [Gielen *et al.* 2003; Conraads *et al.* 2002] and antioxidative effects [Linke *et al.* 2005], reduces natriuretic peptide concentrations [Conraads *et al.* 2004], and increases shear stress and nitric oxide bioavailability [Ennezat *et al.* 2001], all leading to reduced peripheral vasoconstriction, improved endothelial function and enhanced endothelial repair [Hambrecht *et al.* 1998; Hornig *et al.* 1996]. Regular physical training also tackles muscle wasting and restores the anabolic/catabolic imbalance [Mann and Reid, 2003; Hambrecht *et al.* 1995], as well as hyperactive muscle ergoreflexes [Piepoli *et al.* 1996]. These changes parallel observed training-induced increases in VO_2peak.

The effects of exercise on central haemodynamic function are less well established. Most studies show no significant effect on resting LVEF. However, Hambrecht and colleagues demonstrated that in patients with stable CHF, 6 months of aerobic exercise training led to a small, but significant improvement in stroke volume, with a concomitant reduction in peripheral resistance and left ventricular end-diastolic diameter [Hambrecht *et al.* 2000], suggesting training-induced reverse remodelling, compared with usual care. Belardinelli and colleagues demonstrated that aerobic exercise improves myocardial contractility and diastolic filling in patients with ischaemic cardiomyopathy and reduced LVEF [Belardinelli *et al.* 1996, 1998]. In 2007, a meta-analysis of 14 trials (including 812 patients) showed that aerobic exercise at moderate intensity led to a significant improvement of LVEF (weighted mean difference [WMD] = 2.59%, 95% confidence interval [CI] = 1.44–3.74%), left ventricular end-diastolic volume (LVEDV; WMD = −11.49 ml, 95% CI = −19.95 ml to −3.02 ml), and left ventricular end-systolic volume (WMD = −12.87 ml, 95% CI = −19.95 ml to −3.02 ml), compared with usual care [Haykowsky *et al.* 2007]. The combination of enhanced preload, improved myocardial contractility and augmented vascular reserve has been suggested as an explanation for the increase in LVEF that is seen after aerobic training. Therefore, based on this information, reverse remodelling with exercise training seems possible in clinically stable individuals with HF. Overall the magnitude of the improvement in LVEF was consistent with the magnitude of benefits seen with CRT and angiotensin-converting enzyme inhibitors [McAlister *et al.* 2004; Konstam *et al.* 1992].

Impact of exercise training

Hard endpoints: mortality, morbidity and safety

Based on the analysis of 801 patients enrolled in nine randomized controlled clinical trials, the ExTraMATCH collaborative group calculated a 35% ($p < 0.05$) lower risk for mortality and a 28% ($p < 0.05$) lower risk for the composite endpoint of mortality or hospitalization in favour of exercise [Piepoli *et al.* 2004]. Smart and Marwick conducted a meta-analysis on 11 randomized clinical trials (including 729 patients) and found a 39% lower relative risk for mortality in the exercise group [Smart and Marwick, 2004].

However, none of the studies included in these meta-analyses had sufficient power to address hard endpoints. In addition, most of them were small single-centre trials. Therefore, the results of the HF-ACTION trial (Heart Failure – A Controlled Trial Investigating Outcomes of exercise TraiNing) were eagerly awaited. HF-ACTION is until now the largest multicentre, randomized controlled trial, designed to measure the effects of exercise training on clinical outcomes and safety in patients with stable systolic HF [O'Connor *et al.* 2009]. A total of 2331 patients (72% men, mean age 59 years) with LVEF ≤ 35%, in the New York Heart Association functional class II–IV, and under optimal medical treatment, were randomized 1:1 to either the training group (36 sessions of supervised, moderate-intensity training followed by home-based training) or the usual care group. After a median follow-up time of 30 months, and after adjustment for predefined prognostic predictors, the primary composite endpoint of all-cause mortality or all-cause hospital stay was significantly reduced (–11%, $p = 0.03$) in the training group.

Although HF-ACTION confirmed the safety of exercise training in HF patients – still considered at increased risk – the results did not actually meet the expectations of those active in the field. Several explanations for the observed gap between anticipation and results have been put forward; these include usual care crossover but also the high percentage of patients in both groups using evidence-based medical treatment. The major flaw, however, was the very low level of adherence to the prescribed exercise regimens, resulting in a smaller than expected improvement in aerobic capacity. The median improvement in VO_2peak after 3 months was only 0.6 ml/kg/min (or 4%) in the training group, which is inferior to results reported in other, smaller studies: a mean increase in VO_2peak of 2.16 ml/kg/min has been derived from the data of 848 randomized patients [Rees *et al.* 2004].

Only 30% of the patients reached the target number of 120 min training per week after 10–12 months. Optimization of short- and long-term adherence to exercise training is recognized as a major goal and appropriate strategies are needed [Conraads *et al.* 2012]. Findings of a recent *post hoc* analysis of the HF-ACTION data demonstrating a clear association between improvement in exercise capacity and volume of exercise, underscore the relevance of compliance ($n = 959$) [Keteyian *et al.* 2009]. Furthermore, a clear relation between a change in VO_2peak and clinical outcomes was found. Swank and colleagues concluded that in the HF-ACTION population every 6% increase in VO_2peak (adjusted for other significant predictors) was associated with a 5% lower risk of the primary endpoint (hazard ratio [HR] = 0.95; CI = 0.93–0.98; $p < 0.001$) and a 7% lower all-cause mortality (HR = 0.93; CI 0.90–0.97; $p < 0.001$) [Swank *et al.* 2012]. Supporting the relevance of exercise-induced increased aerobic capacity, Tabet and colleagues showed in a prospective study that absence of improvement in VO_2peak following an exercise training programme is a strong and independent predictor for adverse cardiac events [Tabet *et al.* 2008].

In their systematic review Smart and Marwick reported no exercise-related deaths during over 60,000 h of exercise training by HF patients [Smart and Marwick, 2004]. However, none of the studies incorporated in this meta-analysis included safety as a primary objective. The HF-ACTION trial confirmed the earlier findings of the smaller, single-centre studies stating that regular aerobic-type exercise training is safe and generally well tolerated in patients with chronic, stable HF [Keteyian *et al.* 2010; McKelvie, 2008]. Overall, the adverse event rates during the entire study period did not differ between the exercise and control groups. The most frequent reported adverse events were worsening HF (26.1% in the exercise group *versus* 29.0% in the usual care group), ICD firing (22.2% *versus* 23.4%) and serious adverse arrhythmia (defined as sustained ventricular tachycardia lasting longer than 30 s, ventricular fibrillation, supraventricular tachycardia with rapid ventricular response lasting longer than 30 s, cardiac arrest or bradycardia, heart rate < 50/min, symptomatic, and not related to medication; 14.4% *versus* 14.0%). The relatively young age (59 years of age) of patients enrolled in the study compared with the general HF population needs to be taken into account and caution is necessary when generalizing these results to other populations.

'Surrogate' endpoints: exercise capacity and QoL

Maximal aerobic capacity is a strong and independent prognostic factor in patients with HF [Corra *et al.* 2012; Tabet *et al.* 2008] and determines the amount of activities of daily life a patient can perform independently. The latter translates directly into QoL. Since 1990, several single-centre clinical exercise trials have indicated that regular aerobic exercise has the potential to at least partly reverse exercise intolerance [Keteyian *et al.* 2010]. In 2004, a systematic review of randomized controlled trials on exercise training in CHF patients (848 patients) demonstrated a mean increase of 2.16 ml/kg/min in VO_2peak, and an improvement in terms of health-related QoL in seven out of nine studies [Rees *et al.* 2004]. The HF-ACTION trial included the evaluation of the effects of exercise training on the self-reported health status among patients with HF. After 3 months, a modest, but significant, improvement in health status, using the Kansas City Cardiomyopathy Questionnaire (KCCQ), was seen in the exercise group (5.2 *versus* 3.3 points in usual care, $p < 0.001$). This improvement persisted over time and the effect was similar for the KCCQ subscales, that is, physical limitations, symptoms, QoL and social limitations.

Evaluation of exercise capacity: cardiopulmonary exercise testing with ventilatory gas analysis

Maximal or symptom-limited cardiopulmonary ergometer or treadmill testing, with ventilatory gas analysis (CPET), is considered the cornerstone for safe and efficient exercise prescription, particularly in HF patients. Whereas an in-depth description of the practicalities involved in conducting CPET, as well as its interpretation are beyond the scope of this paper, the relevance of the latter test for prognostication (i.e. VO_2peak, VE/VCO_2 slope, oscillatory breathing [Arena *et al.* 2007]), treatment adjustment (indication for heart transplantation [Corra *et al.* 2002]) and for a tailored exercise prescription [Conraads and Beckers, 2010], deserves to be emphasized. Such information cannot be derived from submaximal exercise testing, such as the 6-min walking test [Guazzi *et al.* 2009].

With regard to safety, again the HF-ACTION trial provides a wealth of information. Out of 4411 exercise tests, 0 deaths per 1000 exercise tests and 0.45 nonfatal major cardiovascular events per 1000 exercise tests (95% CI = 0.11–1.81) were reported. There were no exercise test-related ICD discharges requiring hospitalization [Keteyian *et al.* 2009]. More detailed information on the principles of CPET and the assessment of functional capacity can be found in a recent extensive review [Balady *et al.* 2010].

Prescription of a training programme: types of exercise

Apart from lifestyle changes, including the promotion of common daily activities, both American and European guidelines on HF advise the participation by stable HF patients in a structured exercise training programme [McMurray *et al.* 2012; Bonow *et al.* 2012]. Contraindications for participation in an exercise training programme are listed in Table 1.

Up until now, there are no clearly delineated practical guidelines for exercise prescription in the setting of HF, resulting in a variety of centre-specific approaches for these patients. The programmes differ in a number of characteristics: type (endurance, resistance and strength), intensity (aerobic *versus* anaerobic); method (continuous *versus* intermittent/interval); setting (hospital/centre-based *versus* home-based); application (systemic, regional and respiratory muscle) and control

Table 1. Contraindications for participation in an exercise training programme.

Cardiac	Decompensated or unstable heart failure, New York Heart Association functional class IV Exercise training-induced myocardial ischaemia, hypotension, nonsustained or sustained ventricular tachycardia, atrial fibrillation (until resolved) Severe valvular dysfunction (regurgitation or stenosis)
Extracardiac	Active inflammatory disease, including peri- or myocarditis Cerebrovascular disease preventing exercise testing or training Musculoskeletal disease preventing exercise testing or training Severe obstructive lung disease Uncontrolled diabetes mellitus, thyroid dysfunction Hypo- or hyperkalaemia, hypovolaemia Pulmonary embolism Deep venous thrombosis/thrombophlebitis

(supervised *versus* nonsupervised) [Piepoli *et al.* 2011]. In order to optimize the benefits of exercise training for patients with HF, an individualized programme addressing both peak aerobic capacity (prognosis), as well the ability to continue submaximal exercise during prolonged time (QoL and independent functionality) should be designed.

Three different training modalities have been proposed in different combinations: (a) endurance or aerobic exercise training (continuous and interval); (b) strength/resistance training; (c) inspiratory muscle training.

Endurance or aerobic exercise training

Aerobic or endurance training (i.e. cycling, walking, rowing) is the most investigated training modality in CHF patients, and is recommended as baseline activity [Vanhees *et al.* 2012; Davies *et al.* 2010; Flynn *et al.* 2009; O'Connor *et al.* 2009]; cycling is usually preferred because of the reproducible power output, the possible low workloads and reduced injury rate. Traditionally, the first ventilatory anaerobic threshold (VAT) (50–60% of VO_2peak) was identified as the maximum training intensity for HF patients, avoiding exercise-related risks and adverse events [Myers, 2008; Meyer *et al.* 2005a, 2005b].

However, since CHF patients need a higher percentage of their VO_2peak (compared with normal individuals) to perform daily life activities [Kervio *et al.* 2004; Riley *et al.* 1992], and since one of the main targets of exercise training is to allow these patients to perform daily tasks with less effort, training intensities above the VAT have progressively been tested and introduced. The respiratory compensation point (RCP) (65–90% of VO_2peak [Mezzani *et al.* 2010]), which is strictly related to the so-called 'critical power' or the limit between high intensity and severe intensity of effort, is now accepted as the limit for prolonged aerobic exercise without additional risk for patients with HF [Carvalho and Mezzani, 2011; Mezzani *et al.* 2009]. Figure 1 illustrates the VAT and RCP during an incremental exercise test. Nowadays, exercise intensities between 70% and 80% of VO_2peak are prescribed [Roveda *et al.* 2003; Dubach *et al.* 1997]. Nevertheless, in HF patients with significantly reduced pretraining VO_2peak and/or high exercise-related risks, aerobic training intensities as low as 40% of VO_2peak have proven to be effective [Demopoulos *et al.* 1997; Belardinelli *et al.* 1995].

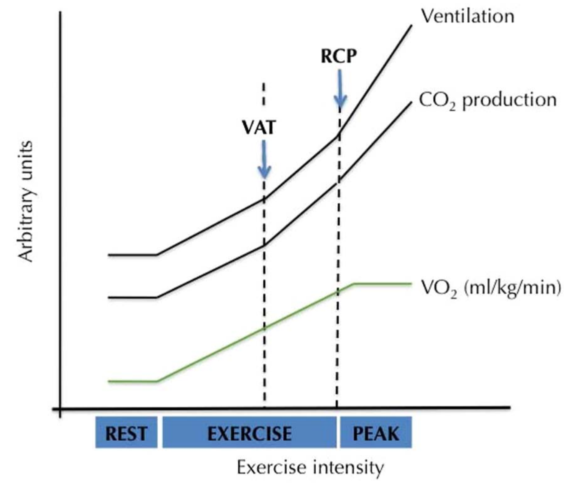

Figure 1. VAT and RCP during an incremental exercise test. RCP, respiratory compensation point; VAT, ventilatory anaerobic threshold.

Session duration should be progressed according to patients' tolerance, with a minimum goal of 30 min/session, at least three times a week [Flynn *et al.* 2009; O'Connor *et al.* 2009]. However, patients with recent haemodynamic instability, lower exercise capacity or fatigue should start with shorter exercise bouts (i.e. 10 min), which can be repeated several times a day.

During training sessions, the rate of perceived exertion (RPE) (Borg scale 6–20) should be used as an adjunctive measure of exercise intensity. Carvalho and colleagues evaluated the reliability of the RPE Borg scale for exercise training monitoring in HF patients on beta-blockers, showing that values of 11–13 (i.e. perceived exertion ranging between 'light' and 'somewhat hard') corresponded with an energy expenditure between the VAT and RCP [Carvalho *et al.* 2009]. Noteworthy is the fact that indoor workloads cannot reliably be extrapolated to outdoor exercise, since environmental conditions can aggravate the exercise.

In 2007, Wisloff and colleagues compared the effect of aerobic interval training (AIT), consisting of 4-min training intervals at high intensity (90–95% of peak heart rate), separated by 3-min active pauses (walking at 50–70% of peak heart rate), total exercise time 38 min, three times weekly, with moderate continuous training (MCT), which consisted of walking continuously at 70–75% of peak heart rate, for 47 min (to compare isocaloric sessions) [Wisloff *et al.* 2007]. The study population consisted of 27 postinfarction HF patients (aged 75.5 ± 11.1 years) (LVEF 29%). The investigators demonstrated that interval training led to greater improvements in aerobic capacity (improvement in VO_2peak 46% *versus* 14%, $p < 0.001$), reverse left ventricular remodelling, endothelial function and QoL. Recently, the same group of investigators published results on the safety of AIT in cardiac patients (however not exclusively HF patients) [Rognmo *et al.* 2012]. It was concluded that the risk of a cardiovascular event is low after both high-intensity exercise and moderate-intensity exercise in a cardiovascular rehabilitation setting. A randomized multicentre trial (SMARTEX-HF study) is currently enrolling HF patients to compare the efficacy and safety of AIT *versus* MCT [Stoylen *et al.* 2012]. This trial is expected to provide a more solid basis for future recommendations on training modes.

Strength/resistance training

To complete daily life tasks, HF patients are often hindered by skeletal muscle weakness, particularly at the level of the upper limbs. Although there is only limited information available on the effect and safety of dynamic resistive exercises in HF patients, experience is growing and results are encouraging. It has been shown that dynamic resistance training has anti-inflammatory effects, improves insulin resistance and counteracts loss of skeletal muscle mass and strength, thereby improving QoL [Bjarnason-Wehrens *et al.* 2004; Cheetham *et al.* 2002; Conraads *et al.* 2002; Singh *et al.* 1999]. Standard exercise training protocols usually involve a combination of aerobic and resistance training. Beckers and colleagues demonstrated in HF patients that combined exercise training had a more pronounced effect on submaximal exercise capacity, muscle strength and QoL than pure endurance training, without unfavourable effects on left ventricular remodelling and outcome parameters [Beckers *et al.* 2008].

HF patients are advised to train smaller muscle groups (including upper and lower body muscle groups) in a dynamic way, avoiding Valsalva manoeuvres, and at low-to-moderate intensity. Training intensity should be determined on the basis of the one repetition maximum (1-RM), the highest weight that one can lift once with correct form, throughout a complete range of motion. Usually, exercise is implemented at 50–70% of the 1-RM [Williams *et al.* 2007; Bjarnason-Wehrens *et al.* 2004]. Sustained maximal isometric exercise (i.e. weight lifting) is contraindicated in these patients, because of the excessive rise in blood pressure and the lowering of the stroke volume.

Inspiratory muscle training

Respiratory muscle dysfunction, characterized by respiratory muscle fibre atrophy, deoxygenation and impaired mitochondrial oxidative capacity has been predominantly observed in patients with advanced HF [Wong *et al.* 2011; Meyer *et al.* 2001]. Winkelmann and colleagues demonstrated in 2009 that adding inspiratory muscle training (IMT), using respiratory muscle-specific training devices, to aerobic training in 24 patients with HF and inspiratory muscle weakness resulted in an additional improvement in inspiratory muscle performance, VO_2peak and functional status compared with aerobic training without IMT [Winkelmann *et al.* 2009]. Laoutaris and colleagues recently showed that combined aerobic/resistance/inspiratory training in 27 patients with HF is safe, and resulted in incremental benefits in peripheral and respiratory muscle weakness, cardiopulmonary function and QoL, compared with the effects of aerobic training alone [Laoutaris *et al.* 2012]. Although these results are promising, the study populations are small and the outcomes need to be addressed in larger randomized studies.

HFPEF

At least 50% of HF patients older than 65 years present with HFPEF [Kitzman *et al.* 1991]. The prevalence of HFPEF increases rapidly, and morbidity and mortality rates are almost comparable to HFREF [Bhatia *et al.* 2006; Owan *et al.* 2006].

The clinical manifestations of both patient groups are largely similar and characterized by exercise-related complaints of dyspnoea and fatigue, with a major impact on QoL [Kitzman *et al.* 1991, 2002].

The pathophysiological background of exercise intolerance in patients with HFPEF is less well understood and seems to differ substantially from HFREF. Tan and colleagues demonstrated that patients with HFPEF present a combination of systolic and diastolic abnormalities [Tan *et al.* 2009]; this combination is more obvious during exercise than at rest and includes reduced myocardial systolic strain, rotation, left ventricular suction, longitudinal function and delayed untwisting. Kitzman and colleagues provided evidence to suggest that the observed reduction in VO_2peak in patients with HFPEF is primarily due to reduced cardiac output, secondary to an inability to increase the end-diastolic and stroke volume *via* the Frank–Starling mechanism [Kitzman *et al.* 2010]. Other investigators have shown that, similar to patients with HFREF, peripheral factors, such as abnormal blood flow distribution [Esposito *et al.* 2010], impaired vascular reserve [Borlaug *et al.* 2010], and skeletal muscle dysfunction [Wilson *et al.* 1993], also contribute to exercise intolerance in HFPEF patients.

Haykowsky and colleagues demonstrated recently that both reduced arteriovenous oxygen difference and reduced cardiac output contribute significantly to the exercise intolerance observed in elderly HFPEF patients [Haykowsky *et al.* 2011]. Moreover, the arteriovenous oxygen reserve was an independent predictor of VO_2peak, which strongly suggests that peripheral factors at least partly determine the limited exercise tolerance in these patients. Interventions that increase heart rate, skeletal muscle perfusion and/or oxygen extraction by active working muscles could improve peak exercise performance in elderly HFPEF patients. The same group of researchers was able to demonstrate in a group of 40 stable, compensated HFPEF patients (mean age 69 ± 6 years), that a 4-month endurance training programme consisting of walking and cycling significantly improved VO_2peak compared with a controlled usual care group (16.3 ± 2.6 *versus* 13.1 ± 3.4, respectively, $p = 0.002$). The peak arteriovenous oxygen difference was higher after the training programme and was the main contributor of the observed improvement in VO_2peak [Haykowsky *et al.* 2012]. These findings were confirmed by the Ex-DHF study (a multicentre, prospective randomized control trial in 64 patients with HFPEF). After a 3-month training programme, consisting of supervised endurance/resistance training, there was an improved functional capacity and QoL. This benefit was associated with an improved left ventricular diastolic function and reversed left atrial remodelling. The exercise training programme was safe and the positive effect on exercise capacity was at least as large as reported in patients with HFREF [Edelmann *et al.* 2011]. Although the study populations included in these studies are small, the results are promising and seem to support the idea that exercise training is beneficial for HFPEF patients. However, large randomized controlled studies are still needed to evaluate outcomes, effectiveness and safety of various training modalities.

Patients with implanted devices

The number of patients implanted with an electrical device (i.e. ICD or CRT) is steadily increasing. Exercise training in patients with an ICD and/or CRT can substantially increase QoL and exercise capacity and seems to be safe [Vanhees *et al.* 2004]. Vanhees and colleagues evaluated the effect of a 3-month training programme in 92 ICD patients, compared with a control group of 473 patients [Vanhees *et al.* 2001]. A total of 23 out of 34 ICD patients had a LVEF below 40%, compared with 41 out of 320 patients of the control group (68% *versus* 13%, $p < 0{,}001$). The training programme resulted in a 21% increase in VO_2peak in the ICD group, which was comparable with earlier study results [Vanhees *et al.* 2004]. Only one inappropriate ICD shock was reported. Conraads and colleagues studied the effect of endurance training after CRT implantation in 17 patients (mean age 59 ± 9 years) with HF and dyssynchrony [Conraads *et al.* 2007]. Patients were randomized to CRT with ($n = 8$) or without ($n = 9$) exercise training. The observed increase in VO_2peak was significantly greater in the trained *versus* the untrained CRT patients (40% *versus* 16%, $p = 0.005$), thus demonstrating an additive effect of CRT and exercise training. Apart from the favourable effect on exercise capacity, exercise training can also have a positive effect on anxiety in ICD patients as well [Belardinelli *et al.* 2006; Fitchet *et al.* 2003]. The importance of this effect is underscored by a prospective study of van den Broeck and colleagues who demonstrated that anxiety predicted a 70% increase in the risk of arrhythmias in type D (or distressed) patients with an ICD [van den Broeck *et al.* 2009].

We think there is a strong rationale to provide exercise programmes for ICD and CRT patients. However, some precautions have to be taken into account. Inappropriate shocks should be avoided at all time. Therefore, the maximum training heart rate should be at least 20 bpm below the ICD-intervention heart rate. Activities with pronounced arm–shoulder movements should be avoided, especially during the first 2 months after implantation. Before starting an exercise training programme, a CPET is indispensable in patients with an ICD and/or CRT. Besides definition of a tailored training heart rate, the heart rate response to exercise and the occurrence of exercise-induced arrhythmias must be assessed. Patients will feel safer and more comfortable if such reassurance is provided. In patients with an implanted CRT-D, adaptation of the tracking rate and rate response during maximal or near maximal effort may be necessary to avoid loss of biventricular pacing at high intrinsic heart rates.

Despite technical progress in the development of ventricular assist devices (VAD), patients who need mechanical support are often severely debilitated and suffer from skeletal muscle wasting and pronounced physical deconditioning. Up until now, scientific information on the safety and effect of exercise training in patients with VADs is limited. Laoutaris and colleagues examined the effect of exercise training (45 min of moderate-intensity aerobic exercise, 3–5 times/week) + high-intensity inspiratory muscle training (2–3 times/week) on top of 30–45 min daily walking in 10 patients with a left-ventricular assist device (LVAD) or a biventricular assist device (BiVAD) [Laoutaris *et al.* 2011]. The control group consisted of five patients with an LVAD or BiVAD (30–45 min daily walking). Exercise training appeared safe. VO_2peak (19.3 ± 4.5 *versus* 16.8 ± 3.7 ml/kg/min, $p = 0.008$), QoL and inspiratory lung capacity (2.4 ± 0.9 *versus* 1.7 ± 0.7, $p = 0.008$) improved compared with baseline measurements; in the control group no significant improvement was seen. Early initiation of exercise training was possible, but the beneficial effects of training were also determined at a later stage after implantation. Up until now, no standard exercise training programme for VAD patients has been established. At the time of writing, it seems prudent to organize exercise training for VAD patients in specialized centres, supervised by a skilled rehabilitation team. Patients should be closely monitored for signs of exercise intolerance or assist device dysfunction. Exercises that irritate the driveline outlet(s) must be avoided, as well as shaking movements and strong vibrations.

Adherence

Despite the evidence on the benefits of exercise training in patients with HF and the importance (class I level of recommendation) that is attributed to cardiac rehabilitation programmes in all major evidence-based guidelines [Komajda *et al.* 2005], this nonpharmacological treatment stays largely underutilized. A recent inventory study on the use of cardiac rehabilitation in Europe demonstrated that only 14% of HF patients eligible for inclusion in a cardiac rehabilitation programme actually were enrolled. This issue is not typical for the HF population, but it is also recognized in the cardiovascular patient population as a whole throughout Europe [Bjarnason-Wehrens *et al.* 2010]. A low level of adherence is one of the most plausible explanations for the lower than expected increments in terms of VO_2peak observed in the HF-ACTION trial. Only 31.5% of the patients enrolled in the study completed 36 supervised training sessions (median completion time was 3.9 months, interquartile range 3.4–4.8 months), and only approximately 40% of patients in the exercise group reported weekly training volumes at or above the recommended 90 min/week at month 3, or 120 min/week from month 3 to month 12 [Keteyian *et al.* 2009].

Explanations for low adherence and compliance to strategies that introduce lifestyle changes can be found at three levels [Conraads *et al.* 2012]: the system level (i.e. socio-economic factors, limited availability of cardiac rehabilitation programmes), the physician level (i.e. low referral and lack of education on the importance of exercise training), and the patient level (i.e. low level of education or inadequate social support [Beckie and Beckstead, 2010]).

Several strategies have been proposed, but up until now, there is little evidence for interventions to improve adherence [Tierney *et al.* 2012]. Education alone is not enough; interventions could benefit from cognitive behavioural therapy and strategies that improve patients' ownership. For the interested reader we would like to refer to a recently published paper of the Study Group on Exercise Training in Heart Failure of the Heart Failure Association of the European Society of Cardiology, which includes several recommendations and strategies to optimize implementation and adherence to exercise training in HF [Conraads *et al.* 2012].

Conclusion

Exercise training is an important adjunct nonpharmacological treatment modality for patients with HF that has proven positive effects on mortality, morbidity, exercise capacity and QoL. Different training modalities are available to target the problems with which HF patients are faced. It is essential to tailor the prescribed exercise regimen, so that both efficiency and safety are guaranteed. Electrical implanted devices and mechanical support should not exclude patients from exercise training; however, particular precautions and a specialized approach are advised. Future research should aim at the development of more effective training modalities and the assessment of higher intensity regimens. In addition, efforts should be directed towards closing the gap between recommendations and the actual implementation of training programmes. One of the major challenges lies within optimizing both short- and especially long-term adherence to exercise training.

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