REVIEW

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High Intensity Interval Training in Patients with CHD and Preserved Ventricular Function

Hochintensives Intervalltraining bei Patienten mit KHK und erhaltener ventrikulärer Pumpfunktion

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Summary

› **Introduction:** Applicability and effectiveness of high-intensity interval training currently are discussed and investigated as a possible addition to moderate continuous training (MCT) in cardiac rehabilitation (CR). Meanwhile, prospective multi-centre-RCTs and meta-analyses are also available for AIT/HIIT (aerobic interval training/ high-intensity interval training) in patients with CHD and CHF / HFrEF.
› **Method:** We conducted a selective literature search until December 2017. This was focussed on studies to evaluate high-intensity interval training modalities in CR both in general as in patients with CHD.
› **Results:** While early (and often small) studies and the following meta-analyses often showed highly significant positive results for high-intensity interval training in comparison to MCT with regards to the maximum oxygen uptake ($\dot{V}O_2$peak) and other clinically relevant parameters, current prospective multicentre RCTs and meta-analyses show no such significant advantages for high-intensity interval training. Total energy-expenditure (EE) appears to be more relevant for the benefits of such inventions independent of session duration, programme length and training intensity.
› **Discussion:** High-intensity interval training in CR is a safe form of training for CHD patients with preserved left ventricular function showing equivalent improvement of cardiovascular protection factors compared with MCT. It offers a more variable and slightly time saving training option, but requires more intense coaching for the individual patient. Sometimes interval training is not tolerated by CHD-patients. Nevertheless, there is still a need for research in a more precise application and its long-term effects.

Zusammenfassung

› **Einführung:** Die Anwendbarkeit und Effektivität eines hochintensiven Intervalltrainings als mögliche Ergänzung zum moderaten kontinuierlichen aeroben Ausdauertraining (MDT) in der kardiologischen Rehabilitation (CR) steht aktuell im wissenschaftlichen Focus. Aktuell liegen erstmalig prospektive Multizenter-RCTs und Metaanalysen bei Patienten mit koronarer Herzkrankheit (KHK) und chronischer Herzinsuffizienz (CHI/ HFrEF) vor.
› **Methode:** Wir führten eine selektive Literaturrecherche bis Dezember 2017 durch. Die Suche konzentrierte sich auf Studien zur Evaluierung des Intervall-Trainingsmodus einschließlich hochintensiver Intensitäten in der CR insgesamt und insbesondere bei KHK-Patienten.
› **Ergebnisse:** Die ersten, meist kleineren Studien und die daraus resultierenden Meta-Analysen zeigten signifikante Vorteile von hochintensivem Intervalltraining im Vergleich zum MDT zur Verbesserung der körperlichen Leistungsfähigkeit ($\dot{V}O_2$peak) und anderer klinisch relevanter Parameter. Die Ergebnisse aktueller prospektiver multizentrischer RCTs und Metaanalysen bestätigen diese Vorteile für hochintensives Intervalltraining im Vergleich zum MDT nicht. Der Gesamt-Energieumsatz (total energy expenditure, EE) scheint für den Nutzen von aeroben Ausdauertraining relevanter zu sein, unabhängig von Trainingsintensität, -dauer und -modalität für die Effizienz der Intervention.
› **Diskussion:** Hochintensives Intervalltraining in der CR stellt bei KHK-Patienten mit erhaltener linksventrikulärer Pumpfunktion eine sichere und in Bezug auf Verbesserung kardiovaskulärer Schutzfaktoren dem MDT gleichwertige Trainingsform dar. Vorteile sind ein abwechslungsreicheres Trainingsangebot bei gleichzeitiger maßvoller Zeitersparnis. Nachteile sind ein erheblicher Aufwand bei Trainingsdurchführung und eine häufig fehlende Praktikabilität seitens des Patienten. Es besteht weiterhin Forschungsbedarf zur differenzierteren Anwendung und zu Langzeit-Effekten von hochintensivem Intervalltraining.

KEY WORDS:
Cardiac Rehabilitation, Exercise, Endurance Training, Coronary Arterial Disease, High Intensity Interval Training

SCHLÜSSELWÖRTER:
Kardiologische Rehabilitation, Bewegung, Ausdauertraining, koronare Herzerkrankung, Hochintensives Intervalltraining

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Introduction

Definition – History and Primary Prevention

Cardiovascular diseases account for 45% of all deaths, and thus top the list of causes of death in Europe. The total costs resulting from these diseases are about 210 billion € annually in the EU (47). In addition to effective pharmacological and surgical or interventional therapies, training measures to increase the cardiorespiratory performance capacity ($\dot{V}O_2$peak) are, among others, increasingly in the focus of science and rehabilitative applications (31)

Physical training is a clinically-proven, cost-effective, primary intervention for the prevention and treatment of numerous chronic diseases (11). Results of a meta-analysis on primary prevention show that independent of age and gender, there is a significant inverse relationship between exercise intensity and overall mortality (23). In elderly people, a higher training intensity is associated with a greater positive effect on the onset incidence of coronary heart disease (CHD) (20).

Interval training is characterized by alternating exercise and recovery phases. These should be so designed that the highest possible oxygen uptake can be maintained over the longest possible time (10, 11, 44). Interval training is performed at various intensities, whereby the "high intensity" interval training used for about 10 years lies at minimum 85 to 90% of the $\dot{V}O_2$peak or HR_{max}, alternating with recovery phases of the same length, longer, or even shorter, at moderate to low intensity.

High intensity interval training (HIIT) is used for training with rather short (ca 30 sec) intervals, while the current randomized multicenter-studies (RCTs) comprise so-called aerobic interval training (AIT) with longer intervals (4 minutes followed by 3-minute active recovery phases). The latter was designed in Norway and used uniformly in the two current large RCTs in CHD- and CHF-HFrEF patients. (5, 48). Healthy volunteers additionally performed supramaximal exercise (up to 120% $\dot{V}O_2$peak) in the sense of "all-out" protocols (5, 43).

Training by the interval method is thus not clearly defined and offers many design possibilities. It can be adapted to individual needs and capacities via duration and intensity of the exercise and recovery intervals as well as via the relationship between exercise and recovery (1:1, 1:2, 2:1) (5).

The most important advantage of high-intensity interval training is the time efficiency of the training form, despite considerable efforts with respect to performance, monitoring and adaptation of this training form. This is important in light of the fact that "lack of time" is the most-often cited barrier to adherence to regular physical exercise (35, 39). According to single studies of athletes and healthy persons, performance of an HIIT is experienced as more pleasant than moderate aerobic endurance training by the continuous exercise method (MCT) (3). Current studies show that, especially in people with a lack of exercise and low cardiorespiratory fitness, the interest and pleasure in physical activity sinks with the degree of intensity, which counters the actual goal of long-term adherence to physical activity (49).

The beginnings of interval training ("repetition training" or "intermittent exercise") arose in the first decade of the 20th century: in Scandinavia at that time, Holmer introduced the so-called "fartlek" (Swedish for "speedplay") to the training design for endurance athletes. High-intensity interval training is thus not a new form of training in sports. As early as 1976, Saltin et al. described two different interval-training protocols, which can be taken as the models for the further development (38).

The effectiveness of high-intensity interval training in improving the $\dot{V}O_2$peak in healthy individuals has been confirmed among other things by two current meta-analyses. In comparison, high-intensity interval training was more effective than MCT (1.2±0.9mL/Kg-1min-1). The greatest improvement was observed in untrained persons with a low fitness level. Training interventions which lasted longer had a greater effect (27, 46).

Interval Training incl. HIIT /AIT in Cardiac Rehabilitation (CR)

The primary goal of individually-adapted training interventions in CR is a demonstrable favorable influence on the course and prognosis of an existing cardiovascular disease (2). The secondary goals are improvement in physical performance capacity and exercise tolerance by improving cardiorespiratory, muscular and metabolic fitness, reduction of age or disease-related degenerative processes resulting in an improved quality of life and independence for the patient (42).

The highest attainable oxygen uptake ($\dot{V}O_2$peak) is taken as an independent inverse risk marker for morbidity and mortality in cardiovascular and/or metabolic diseases, including CHF-HFrEF (15, 16, 18, 30, 41). Long-term observations of CHD patients show that high cardiovascular performance capacity compared to low capacity is associated on average with a decrease in overall mortality by 65% and cardiovascular lethality by 56% (4). A $\dot{V}O_2$peak raised by 1 ml/kg/min on average is associated in men with an 8-17% and in women with a 10-14% reduction in overall mortality and in total with a 10-16% reduction in cardiovascular lethality (4, 15, 16, 17).

A 12-week CR brought improvement in the performance capacity of 5641 CHD patients of 1 metabolic equivalent (MET), accompanied on average by a reduction of overall mortality by 13% (in patients with initially low physical performance capacity even by 30%). An increase by 1 MET in the first year after CR was associated on average with a 25% reduction in overall mortality (24).

Studies to date consistently show that high training intensities are well tolerated, even in patients with high cardiovascular risk or manifest, stable and pharmacologically-adequate therapy of cardiovascular diseases including CHD, and are not associated per se with an elevated risk for the individual patient (31, 37, 48).

AIT has especially been in the scientific focus of CR for nearly 15 years, after a Norwegian group demonstrated significant clinical improvement in patients with CHD and CHF-HFrEF (36, 48).

In CHD patients, participation in interval training (including HIIT/AIT) or moderate training by the continuous exercise method (MCT) in the modern CR setting is basically coupled with a very low risk of relevant episodes, which does not differ significantly between the two training forms (37). A study conducted in a small and inhomogeneous patient collective did, however, reveal adverse effects (nausea, vagovasal reactions, cardiac arrhythmias and myocardial ischemias) in up to 8% of the patients up to 24 hours after a single high-intensity interval session (21).

In the 1990s, Meyer et al. performed the first studies in Germany with interval training forms using short exercise intervals (exercise phase 30, recovery phase 40 sec) in CHD and especially CHF-HFrEF patients during CR. The protocol used here had long been introduced to German CR (25, 26).

Results of a first meta-analysis on high-intensity interval training (10 studies, n=273 patients with CHD, CHF-HFrEF or existing cardiovascular risk factors) showed an advantage of interval training over MCT in the overall collective. On average, significantly greater improvement in $\dot{V}O_2$peak was attained in 12- to 16-week interval training (+3.03ml/kg/min) (45).

One protocol with long exercise phases, which is often used in current and scientific studies, is the so-called 4×4 minutes AIT protocol mentioned earlier. After a brief warm-up phase at moderate intensity (60% of maximum heart rate, HR_{max}), four 4 -minute exercise intervals (85 to 90 % $\dot{V}O_2$peak or 90-95% HR_{max}) alternate with 2- to 3-minute recovery phases (60-70% HR_{max}) (48). The effectiveness of this protocol has been tested in numerous studies on cardiac patients, especially CHD and CHF-HFrEF patients (6, 14, 28, 29, 40, 42, 43, 45, 48). ›

Moreover, the effectiveness has been confirmed in metabolic syndrome and other cardiovascular risk factors (7,11,45). High-intensity interval training is an effective training modality to improve the $\dot{V}O_2$peak. Moreover, positive effects have been found on anthropometric parameters, arterial blood pressure, LDL and HDL cholesterol and a decreased prevalence of metabolic syndrome (45). Results of current meta-analyses, by contrast, document advantages of MCT in the reduction of resting heart rate and body weight (22, 31). Vascular improvements (endothelial function or "flow-mediated vasodilation" (FMD) of the arm arteries) by high-intensity interval training were also observed (7, 13, 34).

High-Intensity Interval Training in Patients with Coronary Heart Disease (CHD) with Preserved Left-Ventricular Ejection Fraction

Table 2 shows a summary of the results of current studies in which the effectiveness of high-intensity interval training was compared to MCT in CHD patients.

Table 3 shows a summary of the results of current meta-analyses, in which the effectiveness of high-intensity interval training versus MCT is compared in healthy individuals and CHD patients.

After performance of many smaller and inhomogeneous studies, the first meta-analysis comprising exclusively training studies on CHD patients with preserved systolic ejection fraction (9 studies, n=206 patients) revealed a significantly greater improvement in $\dot{V}O_2$peak (+1.60ml/kg/min) in high-intensity interval training compared to MCT. A significant weight loss (-0.78kg) and a reduction of resting pulse were more likely attained with MCT (31). The results of two Australian meta-analyses (6, resp. 10 studies, n=229, resp. n=472), likewise show a significantly greater improvement in $\dot{V}O_2$peak on average by high-intensity interval training (+1.53, resp. +1.78ml/kg/min) compared to MCT (9, 22).

Moholdt et al. were able to confirm in a retrospective univariate "general linear model" that in high-intensity interval training, the actual training intensity (%HR_{max}) is decisive for the efficiency of the training. In 112 CHD patients who trained for 12 weeks with the 4x4 min. protocol, significantly greater improvements in $\dot{V}O_2$peak were achieved in the group which trained on average at the highest intensity (>92% HR_{max}) (29).

A randomized pilot study (n=91) performed in a German rehabilitation clinic examined the effect of the 4x4 min. protocol (AIT) during a 3-week CR compared to MCT (70-75% HR_{max}) in the same training scope. In both groups, the physical exercise capacity was significantly improved ($Watt_{max}$ in AIT +11.9% vs. MCT +8.15%). No advantage was observed for AIT (14).

In Austria, Tschentscher et al. compared two different forms of high-intensity interval training including AIT with MCT. The study group (n=66) was randomized to three different training forms during a 6-week outpatient CR: 1. MCT at 65-85% HR_{max}, 2. "classical" AIT with 4 x 4 min at 85-95% HR_{max} or 3. so-called pyramidal training (PYR) with 3x8 min at 65-95-65% HR_{max}. In all groups, a significant improvement in the maximum attained performance in watts was achieved with 18 training sessions. No difference was determined between the groups (40).

The customary duration of CR in the German-speaking region of three to six weeks does not appear to be long enough to demonstrate differences in the effectiveness of the two training methods. In all of the studies integrated in the meta-analyses, training was conducted over at least 12 weeks. A Norwegian study (n=59 CHD patients) confirms this assumption: after 4-week training, (5/week) the results of AIT and MCT were comparable with respect to improvement in $\dot{V}O_2$peak (28).

In the first large (n=200) multicenter prospective randomized study on CHD patients (SAINTEX-CAD), contrary to the results of earlier studies and meta-analyses, comparable positive effects of AIT and MCT were determined after 12-week training. This was also the case for improvement in $\dot{V}O_2$peak, peripheral endothelial function (FMD of the A. brachialis), for the influence on CV risk factors, quality of life (QoL) and safety aspects (6).

Another meta-analysis with 11 studies and n=594 patients was performed including SAINTEX-CAD, which again found significantly better results for AIT (+1.25ml/min/kg) with respect to improvement in $\dot{V}O_2$peak (12).

Of particular interest in this meta-analysis is a subgroup analysis, in which the authors examined the data of studies which initially matched the training with respect to energy expenditure or isocaloricity. It was proven within studies on AIT that the total energy expenditure (EE) and not the training modality resp. intensity apparently determines the improvement in performance capacity (8, 12). Comparable results were found in another meta-analysis in CHD patients. After correlation to the (total) EE, the influence of the three parameters total training time, duration of training sessions and training intensity no longer showed independent effect strengths (8, 19).

In contrast to this, the influence of training intensity and modality in the studies not matched by EE remains speculation with a hypothetical advantage for high-intensity interval training including HIIT and AIT.

The authors of the SAINTEX-CAD study report that the patients in the AIT group had a tendency to train less intensively than predetermined (88% instead of 90-95% HR_{max}), while the MCT group tended to perform their training more intensively (80% instead of 70-75% HR_{max}) (32). The targeted very high intensity of 90-95% HR_{max} could only be achieved by some of the CHD patients. Results of a subsequent analysis of a small study collective (n=18) of the SAINTEX-CAD study showed significantly higher energy expenditures for MCT compared to AIT (352±90.8 kcal vs. 269±70.7kcal pro session), which may explain the neutral results in the SAINTEX-CAD given above. By contrast, in the originally defined 4x4min protocol isocaloricity (as originally intended by Wisløff et al. in the implementation of this protocol) could be demonstrated – even though here with a trend "in favor of" MCT (317±85.2 vs. 273±65.3kcal) (32). In an editorial on the current meta-analysis, the authors of the SAINTEX-CAD study emphasize that further randomized studies which take EE into account are needed to answer the question whether the EE or the training modalities are the more important. The discussion about the advantages of AIT/HIIT resp. MCT thus remains open and exciting (8).

The maintainability and long-term effects of high-intensity interval training for CHD patients have hardly been studied thus far. A Norwegian study examined the effect of 6-month home-training in 51 patients following an initial 4-week CR (28). The home-training led in the observation period to a significant further increase in $\dot{V}O_2$peak only in the interval group. The authors assume that this effect resulted from the higher intensity of home-training in the group. This could indicate that the patients gain greater confidence in their own performance capacity thanks to the high-intensity training and attempt more at home. A comparable effect was observed in the 1-year follow-up of the AIT group in the SAINTEX-CAD study (33).

Conclusions

Conclusions concerning high-intensity interval training including AIT and HIIT in CHD (with preserved left-ventricular ejection fraction):

1. High-intensity interval training can be optionally integrated in addition to MCT in a training program during CR on an individual basis taking into account the preferences and physical exercise capacity of the individual patient with stable and optimally-treated CHD. It has no greater general risk for stable patients than MCT.
2. But within Phase II CR, the target group appears rather small, especially for AIT and HIIT. The studies confirm that many patients cannot follow the predetermined high-intensity training guidelines. This means that considerable effort is needed for individually adapted implementation and supervision of training in the application of interval training. As part of Phase II CR, high-intensity interval training appears to be suitable for more resilient patients who are willing and motivated to exert themselves more.
3. In the clinical setting, the postulated time advantage of about 30 min/week by isocaloric expenditure in AIT/HIIT compared to MCT is not relevant. HIIT appears to be interesting as part of outpatient or home-based CR, or for independent continuation of effective training in Phase III.
4. High-intensity interval training appears to be counterproductive in patients with pre-existing lack of exercise and low fitness level, particularly at the start, considering the long-lasting adherence to physical exercise to be achieved by the CR.
5. One-year data are only available for SAINTEX-CAD (for AIT positive), in general, however long-term observations which confirm the prognostic importance of this form of training are also missing in all meta-analyses.
6. Through high-intensity interval training in CHD patients, especially as part of CR, there has been increased focus in MCT as well on training intensity and EE, whereby the latter currently appears to have the greatest impetus for improvement of the $\dot{V}O_2$peak.

Conflict of Interest

The authors have no conflict of interest.

Table 1

Overview of the currently used, not-yet uniform terminology and abbreviations in interval and volume-oriented training forms.

INTERVAL TRAINING	
AIT	aerobic interval training
HIT	high-intensity (aerobic) training
HIIT	high-intensity interval training
HAIT	high-intensity aerobic interval training
SIT	sprint or short (term) interval training
VOLUME-ORIENTATED TRAINING	
HVT	high-volume (low intensity) training
MCT/CONT/CT	(moderate) continous training
ET/END	endurance training
MICE	moderate-intensity continous exercise

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Table 2 – 1st part

Summary of the results of current randomized studies (RCTs) comparing the effectiveness of high-intensity interval training versus moderate training by the continuous exercise method (MCT) in CHD patients. (CAD: coronary artery disease; CABG: coronary artery bypass grafting; CEPT: cardiopulmonary exercise test; M/F=male/female; MI=myocardial infarction;

STUDY	DISEASE	SAMPLE SIZE	GENDER	AGE (YRS)	OUTCOME PARAMETER	MAJOR FINDINGS	DROPOUT RATES	VO_2 MEASURE-MENT
Rognmo et al., 2004; Amundsen et al., 2008 (36,50)	CAD	17 (INT 8)	M/F	62	Peak VO_2 (exercise capacity)	peak VO_2 greater in HIIT versus MCT ($p<0.011$)	7 (29.2%)	CPET
Warburton et al., 2005 (51)	CAD (post CABG or MI)	14 (INT 7)	M/F	56	Exercise capacity Anaerobic capacity	No difference between groups	NR	CPET
Moholdt et al., 2009 (28)	Post CABG	59 (INT 28))	M/F	61,1	Peak oxygen uptake Left ventricular function Quality of life Blood markers	HIIT showed further increase in peak VO_2 compared to MCT ($p<0.05$)	21 (30.4%)	CPET
Moholdt et al., 2011 Moholdt et al., 2012 (52, 53)	Post MI	89 (INT 30)	M/F	57	Aerobic capacity	peak VO_2 greater in HIIT versus usual care exercise ($p<0.005$)	38 (35.5%)	CPET
Rocco et al., 2012 (54)	CAD	37 (INT 17)	M	59,7	Peak oxygen uptake PETCO2 Ventilatory anaero-bic limiar	No difference between groups	NR	CPET
Currie et al., 2013 (55)	recent CAD event	22 (INT 11)	M/F	65	Brachial artery flowmediated dilation Cardiorespiratory fitness	No difference between groups ($p>0.05$)	8 (26.7%)	CPET
Keteyian et al., 2014 (56)	MI, CABG, CAD	28 (INT 11)	M/F	59	Peak VO_2 (cardi-orespiratory fitness)	peak VO_2 greater in HIIT versus MCT ($p<0.043$)	39 (28.2%)	CPET
Conraads et al., 2015 (6)	CAD (post CABG or MI and/or PCI)	174 (INT 85)	M/F	58.4	Peak VO_2 Peripheral endo-thelial function Cardiovascular risk factors Quality of life	No difference between the groups ($p>0.05$)	26 (13%)	CPET
Cardozo et al., 2015 (57)	CAD	71 (INT 23)	M/F	64	Peak VO_2 (exercise capacity) VE/VCO slope O_2 pulse	peak VO_2 increa-sing in HIIT and remaining stable in MCT ($p<0.04$)	none (0%)	CPET
Jaureguizar et al., 2016 (58)	CAD	72 (INT 36)	M	58	Functional capacity Quality of life Safety	HIIT significantly greater increase in peak VO_2 and 6-minute walk distance compared to MCT ($p<0.05$)	NR	CPET
Prado et al., 2016 (59)	CAD	35 (INT 17)	M/F	59	Cardiorespiratory fitness	No difference between groups ($p>0.05$)	NR	CPET
Tschentscher et al., 2016 (40)	CAD	60 (INT 20 AIT and 20 PYR)	M/F	62	Peak work capacity	No difference between all 3 groups (p n.s.) with isocaloric exercise training protocols	6 (9.1%)	no CPET

Table 2 – 2nd part

INT=interval training; HIIT=high-intensity interval training; MCT=moderate continuous training; $PETCO_2$=Partial pressure of exhaled carbon dioxide; NR=not reported. PPO=peak power output; PYR=Pyramid training; RCP=respiratory compensation point; SRT=steep ramp test; VAT=ventilatory anaerobic threshold; VCO_2=carbon dioxide production; VE=minute ventilation; VO_2=oxygen uptake;) (modified from 9, 12, 22).

VO_2 MEASUREMENT	HIIT INTENSITY PRESCRIBED	HIIT INTENSITY TRAINED	MCT INTENSITY PRESCRIBED	MCT INTENSITY TRAINED	HIIT TIME TRAINED (MIN)	MCT TIME TRAINED (MIN)	FREQUENCY PER WEEK	DURATION (WEEKS)	SUPERVISION
CPET	80–90% VO_2peak (85–95% HR_{peak})	NR	50-60% of VO_2peak	NR	33	41	2	10	Yes
CPET	85–95% HR/VO_2 reserve	NR	65% HR/VO_2 reserve	NR	30	30	2	16	NR
CPET	90% HR_{max}	92% HR_{max}	70% HR_{max}	74% HR_{max}	NR	46	5	4	NR
CPET	90% HR_{max}	79% HR_{max}	Moderate-to-high	73% ± 10% HR_{max}	NR	NR	2	12	NR
CPET	HR at RCP	80–90% VO_2 peak	HR at VAT	NR	42	60	3	12	Yes
CPET	80–104% at PPO	73% ± 10% HR_{max}	51–56% at PPO	65% ± 4% HR_{max}	NR	NR	2	12	Yes
CPET	80–90% HR reserve	NR	60–80% HR reserve	NR	40	40	3	10	Yes
CPET	90–95% HR_{peak}	88% HR_{peak} or 86% Peak workload	70–75% HR_{peak}	80% HR_{peak} or 63% Peak workload	38	47	3	12	Yes
CPET	90% HR_{peak}	NR	70-75% HR_{peak}	NR	40	40	3	16	Yes
CPET	SRT_{max}	Second month:	HR at VT1 (2nd month: +10% HR at VT1)	First month: 64.2%±8.5% of VO_2peak Second month: 69.5%±8.7% of VO_2peak	40	40	3	8	NR
CPET	HR at RCP	NR	At VAT	NR	52	60	3	12	Yes
no CPET	85-95% HR_{peak}	Start: 77,4± 4,5% HR_{peak} End: 75,8± 57% HR_{peak}	60-70% HR_{peak}	Start: 80,5±6.1% HR_{peak} End: 73.6±7.3% HR_{peak}	25	33	3	6	Yes

Table 3

Summary of the results of current meta-analyses, in which the effectiveness of high-intensity interval training is compared to moderate continuous training (MCT) in healthy individuals and in CHD patients. (CAD=coronary artery disease; CHF=chronic heart failure; AHT=arterial hypertension; INT=interval training; HIIT=high-intensity interval training; MCT=moderate continuous training; NR=not reported; QoL=quality of life.

META-ANALYSIS	DISEASE	STUDIES INCLUDED	SUBJECTS	AGE (YRS)	STUDY SELECTION	OBJEKTIVES	TRAINING SESSIONS	RESULTS	CONCLUSION (ABSTRACT)
Weston et al. 2014 (46)	healthy subjects	38	567	19-34	fitness assessed pre- and post-training training period ≥2 weeks repetition duration 30-60s work/rest ratio <1.0 exercise intensity max. or near max.	VO_2max (%) Peak spint power - in 30-s Wingate test (%) Mean sprint power - in 30-s Wingate test (%)	13 training sessions	in active non-athletic males +6,2%±3,1% in active non-athletic females +3.6%±4.3% in sedentary males +10.0%±5.1% in sedentary females + 7.3 % ± 4.8 % in athletic males + 2.7%±4.6 % HIIT vs. traditional ET -1.6%±4.3% Peak power – Results n.s./unclear Mean power – Results n.s./ unclear	Low-volume HIT produces moderate improvements in the aerobic power of active non-athletic and sedentary subjects. Unclear modifying effects of sex and HIT dose on aerobic power and the unclear effects on sprint fitness
Milanovic et al. 2015 (27)	healthy subjects	28	732	18-45 (25.1 ± 5)	VO_2max assessed pre- and post-training training period ≥2 weeks	VO_2max (mL/kg/ min)	NR	ET +4.9mL/kg/min±1.4mL/kg/min HIIT +5.5mL/kg/min ±1.2mL/ kg/min HIT vs ET +1.2mL/kg/min ±0.9mL/kg/min	Endurance training and HIT both elicit large improvements in the VO_2 max of healthy, young to middle-aged adults, with the gains in VO_2max being greater following HIT when compared with endurance training
Weston et al. 2014 (45)	CAD, CHF, AHT, MBS, Obesity	10	273 (HIIT NR)	NR	randomized trials comparing HIIT and MCT in cardiac, hypertensive or metabolic patients ≥4 weeks	VO_2peak (mL/kg/ min) and (%)	4-16 weeks with 3-6 training sessions/ week	MCT +5.4mL/kg/min (19.4%) HIIT +2,6mL/kg/min (10.3%)	HIIT significantly increases CRF by almost double that of MCT in patients with lifestyle-induced chronic diseases
Pattyn et al. 2014 (31)	CAD	9	206 (HIIT 100)	NR	randomized trials comparing HIIT and MCT in CAD patients ≥4 weeks	VO_2peak (mL/kg/ min) and (%) Body weight (kg)	4-16 weeks with 2-6 training sessions/ week	HIIT vs MCT +1.60 mL/kg/min [p=0.03] MCT vs HIIT -0.78kg [p=0.05]	In CAD patients with preserved and/or reduced LVEF, AIT is superior to MCT for improving peakVO_2, while MCT seems to be more effective in reducing body weight
Elliott et al. 2015 (9)	CAD	6	229 (HIIT 99)	65	randomized trials comparing HIIT and MCT in CAD patients ≥4 weeks	VO_2peak (mL/ kg/min) VO_2peak (mL/kg/ min) at AT Systotic blood pressure (mmHg)	4-16 weeks with 2-6 training sessions/ week	VO_2peak: HIIT vs MCT + 1.60 mL/ kg/min [p < 0.0001] VO_2peakAT: HIIT vs MCT +1.23 mL/kg/min [p<0.0001] RR systol: MCT vs HIIT -3,44mmHg [p=0.077]	In CAD patients HIIT appears more effective than MDT in improvement of aerobic capacity but not for systolic blood pressure
Liou et al. 2016 (22)	CAD	10	472 (HIIT 218)	59	randomized trials comparing HIIT and MCT in CAD patients ≥4 weeks	VO_2peak (mL/ kg/min) Body weight (kg) Resting heart rate (min-1)	4-16 weeks with 2-6 training sessions/ week	VO_2peak: HIIT vs MCT +1.78mL/ kg/min [p=0.009] Body weight: MCT vs HIIT -0.48 kg [p = 0.004] HRrest: MCT vs HIIT -1,80 min-1 [p=0.001]	HIIT improves the mean VO_2peak in CAD patients more than MCT, MCT shows a more pronounced numerical decline in patients' resting heart rate and body weight
Gomes-Nato et al. 2017 (12)	CAD	12	609 (HIIT 218)	58.4	randomized trials comparing HIIT and MCT in CAD patients ≥4 weeks	VO_2peak (mL/ kg/min) VO_2peak (mL/ kg/min) non-isocaloric VO_2peak (mL/kg/ min) isocaloric Change in quality of life (QoL)	4-16 weeks with 2-6 training sessions/ week	VO_2peak: HIIT vs MCT +1.25mL/ kg/min [p=0.003] VO_2peak non-isocaloric: HIIT vs MCT +1.87mL/kg/min [p<0.00001] VO_2peak isocaloric: HIIT vs MCT +0.36 mL/kg/min [p=0.16] QoL: HIIT vs MCT -0.02 [p=0.90]	HIIT may improve VO_2peak and should be considered in CAD patients. This superiority disappeared when isocaloric protocol is compared.