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Exercise intensity assessment and prescription in cardiovascular rehabilitation and beyond: why and how: a position statement from the Secondary Prevention and Rehabilitation Section of the European Association of Preventive Cardiology

**Dominique Hansen^{1,2*}, Ana Abreu³, Marco Ambrosetti⁴,
Veronique Cornelissen⁵, Andreas Gevaert^{6,7}, Harel Kempers^{8,10},
Jari A. Laukkanen^{11,12}, Roberto Pedretti¹³, Maria Simonenko¹⁴,
and Matthias Wilhelm¹⁵ Reviewers: Constantinos H. Davos¹⁶,
Wolfram Doehner^{17,19}, Marie-Christine Iliou¹⁸, Nicolle Kränkel^{19,20},
Heinz Völler^{21,22}, and Massimo Piepoli²³**

¹Department of Cardiology, Heart Centre Hasselt, Jessa Hospital, Hasselt, Belgium; ²UHasselt, Faculty of Rehabilitation Sciences, BIOMED-REVAL-Rehabilitation Research Centre, Hasselt University, Agoralaan, Building A, 3590 Hasselt, Belgium; ³Cardiology Department, Hospital Universitário de Santa Maria/Centro Académico de Medicina de Lisboa (CAML), Exercise and Cardiovascular Rehabilitation Laboratory, Centro Cardiovascular da Universidade de Lisboa (CCUL), Lisbon, Portugal; ⁴Cardiac Rehabilitation Unit, ASST Ospedale Maggiore Crema, Crema, Italy; ⁵Research Unit of Cardiovascular Exercise Physiology, Department of Rehabilitation Sciences, Faculty of Kinesiology and Rehabilitation Sciences, KU Leuven, Belgium; ⁶Research Group Cardiovascular Diseases, GENCOR Department, University of Antwerp, Antwerp, Belgium; ⁷Department of Cardiology, Antwerp University Hospital (UZA), Belgium; ⁸Department of Cardiology, Maxima Medical Centre, Veldhoven, The Netherlands; ⁹Department of Industrial Design, Eindhoven University of Technology, Eindhoven, The Netherlands; ¹⁰Institute of Clinical Medicine, University of Eastern Finland, Kuopio, Finland; ¹¹Faculty of Sport and Health Sciences, University of Jyväskylä, Jyväskylä, Finland; ¹²Cardiovascular Department, IRCCS MultiMedica, Care and Research Institute, Sesto San Giovanni, Milano, Italy; ¹³Heart Transplantation Outpatient Department, Cardiopulmonary Exercise Test Research Department, Almazov National Medical Research Centre, St. Petersburg, Russia; ¹⁴Department of Cardiology, Bern University Hospital, University of Bern, Bern, Switzerland; ¹⁵Cardiovascular Research Laboratory, Biomedical Research Foundation, Academy of Athens, Athens, Greece; ¹⁶BCRT—Berlin Institute of Health Center for Regenerative Therapies, Department of Cardiology (Virchow Klinikum), Charité – Universitätsmedizin Berlin, Partner Site Berlin, Germany; ¹⁷Cardiac Rehabilitation and Secondary Prevention Department, Corentin Celson Hospital, Assistance Publique Hôpitaux de Paris Centre Université de Paris, Paris, France; ¹⁸Charité – University Medicine Berlin, Campus Benjamin Franklin, Department of Cardiology, Hindenburgdamm 30, 12203 Berlin, Germany; ¹⁹German Centre for Cardiovascular Research (DZHK), Partner Site Berlin, Berlin D-1220, Germany; ²⁰Klinik am See, Rehabilitation Centers for Internal Medicine, Berlin, Germany; ²¹Department of Rehabilitation Medicine, University of Potsdam, Potsdam, Germany; and ²²Heart Failure Unit, G. da Saliceto Hospital, AUSL Piacenza and University of Parma, Parma, Italy

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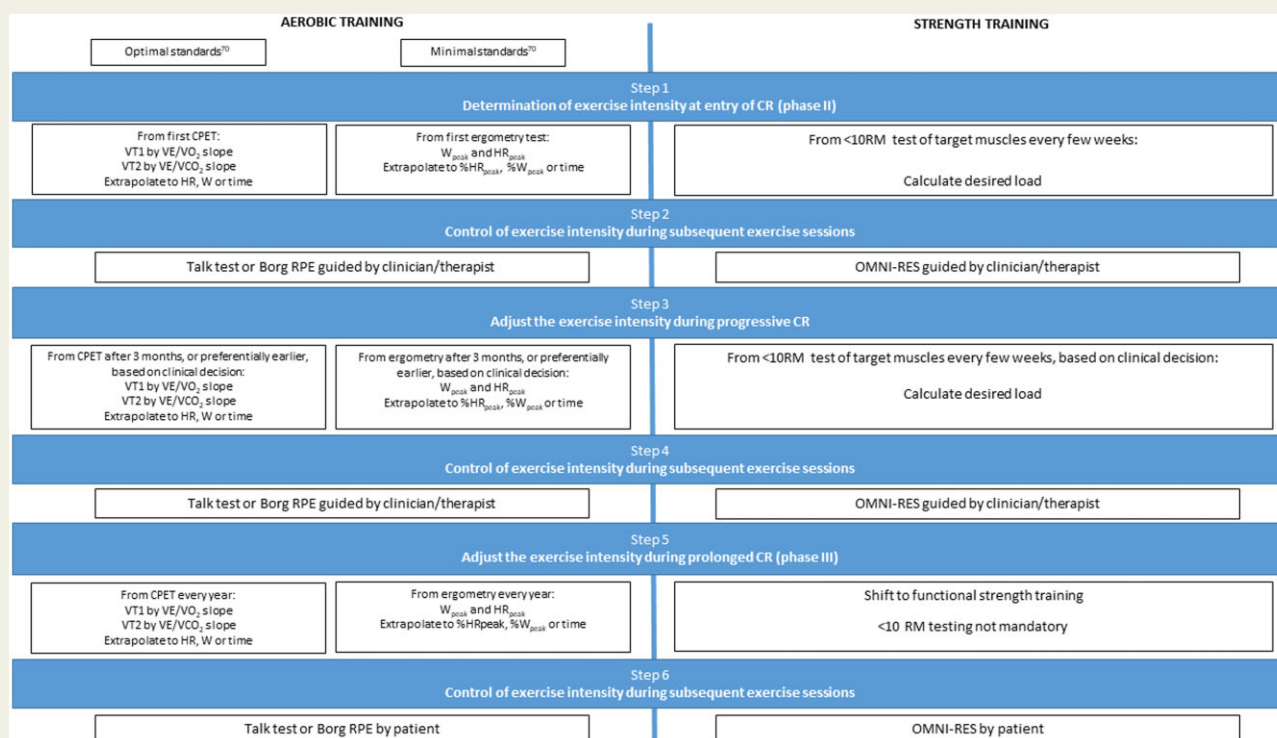
A proper determination of the exercise intensity is important for the rehabilitation of patients with cardiovascular disease (CVD) since it affects the effectiveness and medical safety of exercise training. In 2013, the European Association of Preventive Cardiology (EAPC), together with the American Association of Cardiovascular and Pulmonary Rehabilitation and the Canadian Association of Cardiac Rehabilitation, published a position statement on aerobic exercise intensity assessment and prescription in cardiovascular rehabilitation (CR). Since this publication, many subsequent papers were published concerning the determination of the exercise intensity in CR, in which some controversies were revealed and some of the commonly applied concepts were further refined. Moreover, how to determine the exercise intensity during resistance training was not covered in this position paper. In light of these new findings, an update on how to determine the exercise intensity for patients with CVD is mandatory, both for aerobic and resistance exercises. In this EAPC position paper, it will be explained in detail which objective and subjective methods for CR exercise intensity determination exist for aerobic and resistance training, together with their (dis)advantages and practical applications.

* Corresponding author. Tel: +32 497 875 866, Email: dominique.hansen@uhasselt.be

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Graphical Abstract



The adult Omnibus Resistance Exercise Scale (OMNI-RES) of perceived exertion for resistance training.¹²⁵ Reproduced with permission from Ref.¹²⁵

Introduction

Secondary cardiovascular disease (CVD) prevention integrates cardiovascular rehabilitation (CR) as a central strategy. Multidisciplinary/comprehensive CR leads to significant reductions in hospitalizations, adverse cardiovascular nonfatal events, and mortality rates, as well as improvements in the CVD risk profile and exercise capacity, in patients with CVD.¹⁻⁴ As a result, multidisciplinary CR is a class 1A intervention, which should be offered to every patient with CVD, with specific core components, including exercise.⁵

Exercise training should be prescribed according to the FITT [frequency, intensity, time (duration), and type of exercise] model, including aerobic and resistance training.⁵ As a general advice, for aerobic training, an exercise frequency of at least 3 days/week, preferably 6–7 days/week, at moderate or moderate-to-high intensity is promoted.⁵ In addition, the prescription of resistance training twice a week, at 30–70% of one-repetition maximum (1RM) for the upper body and 40–80% of 1RM for the lower body, with 12–15 repetitions/set, is supported.⁵ Exercise training should be arranged in order to provide an energy expenditure of 1000–2000 kcal/week.⁵

In each exercise training plan, including CR, a proper determination of the exercise intensity is key.⁶ Therefore, in 2013, the European Association of Preventive Cardiology (EAPC) together with the American Association of Cardiovascular and Pulmonary Rehabilitation and the Canadian Association of Cardiac Rehabilitation, published a position statement on the determination

of the exercise intensity in patients with CVD who intend to increase their physical fitness or follow CR.⁷

However, since this publication, many new studies have been published in this field, justifying the need for an updated EAPC position statement on the determination of exercise intensity in CR. First, it has been shown recently that the currently applied objective exercise intensity determination techniques in CR should be revised considerably, as internal inconsistencies were discovered.^{8,9} In addition, a personalized approach based on the patient's preferences and abilities should be followed (e.g. self-selected vs. imposed exercise intensities), particularly in the context of long-term adherence.^{10,11} Certain clinically important aspects in exercise intensity determination are not yet covered, such as how to achieve permanent progression in exercise intensities during prolonged CR programmes, and how to determine the exercise intensity during resistance training. In particular, which exercise intensities should be selected during resistance training is currently a topic of intense debate.¹² Finally, new data have emerged considering the validity and reliability of subjective exercise intensity determination techniques in CVD patients.¹³

As a result, due to these new findings/tendencies, and the lack of guidance in certain aspects of exercise intensity determination in CVD, there is a need for a new EAPC position statement, in which it will be explained:

- why different exercise intensities matter,
- which are the current (objective and subjective) concepts in determining the exercise intensity during aerobic and resistance training,
- how to build in progression in exercise intensities during CR, and

- how to personalize this approach based on the patients' abilities and preferences, by shared-decision making.

This position statement is devoted to cardiologists, physiotherapists, clinical exercise physiologists, nurses, and all specialists who deal with exercise in CVD patients.

Methodology

The accumulation of the current evidence was based on a search strategy of English language published research, consensus documents, and policy documents, by using electronic databases (MEDLINE, EMBASE, and CINAHL), as selected, evaluated, and reviewed by experts from the Section and authors of the original documents. In the development process of this position paper, individuals from CR relevant professional groups were included and the Appraisal of Guidelines for Research and Evaluation tool,¹⁴ as far as derived rating of current CR guidelines,¹⁵ were taken into consideration. Information on the views and preferences of the target population was derived from the literature.¹⁶ From the collected evidence, position statements have been formulated (see Table 1), as well as limitations of the body of evidence, and an agreed approach in exercise intensity determination in CR (see Figure 1). In final, all position statements were carefully aligned with current position papers or guidelines for CR and exercise prescription in CVD.^{5,17}

Exercise intensity in aerobic training: does it matter?

Impact on health outcomes

Several large observational studies have suggested that the relative exercise intensity is more important than the duration to improve life expectancy and lower the risk for chronic diseases in a primary prevention setting. The Copenhagen City Heart Study, for example, followed 5000 individuals over 20 years and analysed data on their self-reported daily cycling habits.¹⁸ It was found that the 'fast' compared to 'slow' cyclists lived longer, were leaner, had a lower blood pressure and cholesterol levels, and a lower diabetes prevalence.¹⁸ In fact, the life expectancy and risk factor burden were unrelated to the total amount of daily cycling.

Whether this also applies to CVD patients, has been studied intensely. There is a considerable variance across randomized controlled trials with regards to the magnitude of improvement in exercise capacity among patients with coronary artery disease (CAD) or heart failure (HF) following CR.¹⁹ Although responders and non-responders could have different phenotypes and genotypes, leading to such variance, the selection of the training modalities could also play a key role. According to a meta-regression analysis, which examined studies that applied continuous exercise intensities as well as high-intensity interval training (HIIT) in CAD and HF patients, higher exercise intensities were independently associated with a greater exercise capacity at CR completion, next to a lower age, male sex, and lower baseline peak oxygen uptake ($\text{VO}_{2\text{peak}}$).¹⁹ For each 10% increase in the applied exercise intensity [$\%\text{VO}_{2\text{peak}}$ or $\%$ peak heart rate (HR_{peak})] across the trials, a greater mean

increase in $\text{VO}_{2\text{peak}}$ by 1.0 mL/kg/min was found ($P=0.04$).¹⁹ However, it is questionable whether these differences in pooled effects between exercise intensities are clinically meaningful at an individual level.^{20,21} Whether or not a different continuous exercise intensity is of paramount importance to affect CVD risk factors in patients with CVD, remains to be studied in greater detail, although the training attendance seems to be greater when lower exercise intensities are selected.^{22,23} The STRRIDE study at least indicated that improvements in the components of the metabolic syndrome was not driven by exercise intensity, but by exercise volume.²⁴

However, although the beneficial effects of aerobic training at a higher continuous intensity are not always obvious, it is important to set the intensity correct, and make significant progression in this intensity during CR (by regular re-assessments), as will be explained later in this manuscript.

High-intensity interval training vs. moderate-intense continuous training

In the last decade, it has been intensely discussed whether HIIT specifically outperforms moderate-intensity continuous training (MICT) with regard to improvements in cardiorespiratory fitness, cardiovascular risk factors, cardiac and vascular function, and quality of life (QoL). There is a fundamental physiological difference between exercising at a continuous moderate intensity vs. HIIT. During HIIT, the calcium release, ATP turnover, and carbohydrate use is significantly greater, when compared with MICT, which leads to a greater accumulation of metabolites, ions, and free radicals. This accumulation is key to the activation of Ca^{2+} /calmodulin-dependent protein kinase II (CaMKII) and AMP-activated protein kinase (AMPK), which collectively stimulate the gene expression for PGC-1 α (peroxisome proliferator-activated receptor gamma coactivator 1-alpha). Ultimately the mitochondrial protein synthesis rates are greater after HIIT vs. MICT, leading to a greater increase in mitochondrial content of the skeletal muscles.²⁵ Eventually, when accumulating several bouts of high-intense exercise in HIIT, the total time spend at this intensity becomes substantial. As a result, in particular, the skeletal muscles will be exposed to intense exercise training. Because respiratory distress/symptoms are prevented to (fully) emerge because of the short duration of the high-intense exercise, and great changes in cardiac output are not mandatory to be able to execute HIIT, this type of exercise training is also feasible for patients with respiratory or cardiac limitations. Multiple studies have been performed in CAD patients and in HF patients with a reduced ejection fraction (EF) (HFrEF) or preserved EF (HFpEF).^{26–30} The most recent and comprehensive meta-analysis evaluated 24 studies ($n=11$ in CAD, $n=11$ in HFrEF, and $n=2$ in HFpEF) with a total of 1080 participants.²⁸ A significantly greater improvement in $\text{VO}_{2\text{peak}}$ was observed after HIIT, compared to MICT [by +1.40 mL/min/kg, in favour of HIIT; 95% confidence interval (CI) 0.69–2.11; $P\leq 0.001$]. This greater improvement in $\text{VO}_{2\text{peak}}$ remained significant in CAD and HFrEF patients, separately. However, when the first study on HIIT in HFrEF patients from Wisloff et al.³¹ was excluded from the analysis, the differences between interventions were no longer significant.²⁸ Also, studies with a sample size of <20 patients in each treatment group showed larger differences between interventions, compared with studies with >50

Table 1 Take home messages and issues to be resolved

Take home messages

For aerobic exercises

The design of the exercise programme should primarily be aimed at optimizing total energy expenditure rather than on one specific training characteristic (e.g. exercise intensity).

A correct determination of the exercise intensity in CVD patients is important as this leads to exercise programmes that are more time-efficient to induce short-term clinical benefits.

In CAD and HF patients, higher exercise intensities are related to relatively greater risks for adverse cardiovascular events, but absolute risk remains low.

The selection of the aerobic exercise intensity should be done in dialogue with the patient in a shared-decision making process.

The commonly used peak indices, such as $\text{VO}_{2\text{peak}}$, HR_{peak} , HRR , and W_{peak} , should be applied with great caution for the prescription of the aerobic exercise training intensity in CVD patients.

The assessment of VT1 and VT2 during CPET, preferably by the nadir of the VE/VO_2 and VE/VCO_2 to WR relationships, provides reliable effort-independent parameters that should be used for the determination of the aerobic exercise intensity in the majority of CVD patients.

The talk test and Borg RPE scale should only be considered as an adjunct to an objective aerobic exercise intensity determination method in CVD patients.

Progression should be made during CR, in which first the desired duration of the exercise session should be achieved before increasing the exercise intensity.

When changes in physical fitness occur as result of CR, the VT1 and VT2 should be re-assessed to re-establish a proper aerobic exercise intensity, if feasible.

For resistance exercises

High-intense dynamic resistance training leads to greater improvements in muscle strength in patients with elevated CVD risk, as opposed to low-intense dynamic resistance training.

When executed properly, high-intense dynamic resistance training is equally safe as low-intense dynamic resistance training, in patients with CVD.

The selection of the resistance exercise intensity should be done in dialogue with the patient in a shared-decision making process.

To properly determine the exercise intensity during resistance training, a $<10\text{RM}$ test can be used to set the initial weight, while the OMNI-RES can be used to track the perceived intensity during the exercise sessions.

To allow further improvements in muscle strength, progressive resistance training is promoted in CR, in which the repetitions, intensity and resting periods can be adjusted in such chronological order.

Issues to be studied/resolved

For aerobic exercises

The impact of different aerobic exercise intensities on CVD risk factors and other health indicators (e.g. cardiac function, vascular function) in CVD patients remains to be studied in isocaloric comparisons.

The medical safety of aerobic exercise interventions with higher exercise intensities remains to be studied during long-term follow-up, in programmes lacking supervision, and patients with pathologies less commonly encountered in CR settings.

For resistance exercises

The clinical benefits of high- vs. low-intense dynamic resistance training, as well as isometric or eccentric resistance training, as an adjunct to aerobic exercise training, remains to be examined in CR.

The haemodynamic impact of high- vs. low-intense dynamic resistance exercise remains to be studied in specific cohorts of patients with CVD.

A standardized approach for the progression in aerobic and resistance training in CR remains to be developed.

The impact of functional resistance training should be studied in prolonged CR.

The impact of self-selected vs. imposed exercise intensities on pleasure and displeasure of exercise, and long-term adherence to exercise training advices, remains to be studied.

patients in each treatment group.²⁸ As a result, it was concluded that large-scale RCT's are needed to clarify these discrepancies.

To date, two large multicentre studies have compared HIIT vs. MICT, one in CAD patients (SAINTEX-CAD, $n = 200$),³² and one in HFrEF patients (SMARTEX-HF, $n = 261$).³³ In the SMARTEX-HF study, only NYHA class II ($\pm 70\%$ of total group) and III ($\pm 30\%$ of total group) patients were included who were stable for at least 6 weeks, and the control group was recommended to exercise regularly without supervision.³³ In contrast to the above-mentioned meta-analyses, in both studies HIIT was not superior to MICT for improving

$\text{VO}_{2\text{peak}}$.^{32,33} The short-term effects of HIIT and MICT on $\text{VO}_{2\text{peak}}$ were sustained after 1 year of follow-up in CAD patients,^{34,35} but partly lost in HFrEF patients.³¹ Therefore, it seems that HIIT could be a more time-efficient manner to improve $\text{VO}_{2\text{peak}}$, as the total exercise duration was significantly shorter, when compared with MICT.^{33,34} Moreover, one key element in a valid comparison between HIIT and MICT is the total energy expenditure of the exercise intervention. Two meta-analyses, one including CAD patients (12 studies, $n = 609$ patients),²⁷ and one including HFrEF patients (13 studies, $n = 411$ patients),²⁹ found that HIIT is not superior to MICT

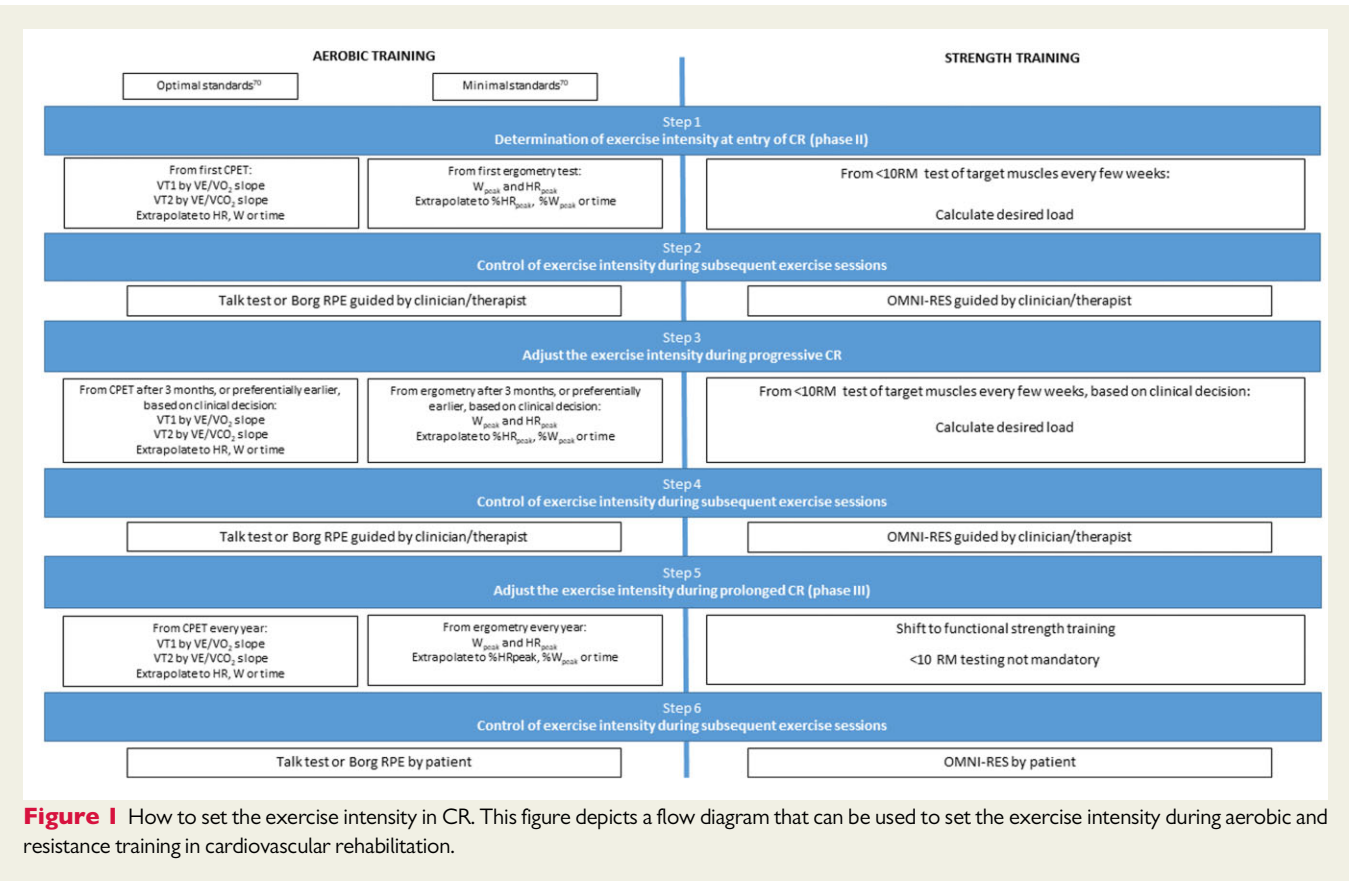


Figure 1 How to set the exercise intensity in CR. This figure depicts a flow diagram that can be used to set the exercise intensity during aerobic and resistance training in cardiovascular rehabilitation.

when isocaloric exercise training programmes were compared. In contrast, in another meta-analysis superior effects on VO_{2peak} were noticed in HIIT vs. isocaloric MICT, but only in programmes with a greater total energy expenditure.²⁸ Two systematic reviews confirmed that the total energy expenditure of the overall programme actually is the strongest predictor of improvements in exercise capacity in HF patients.^{36,37} This observation is well in line with the notion that the number of patients who respond to HIIT, is not significantly greater when compared with MICT.³⁸ In contrast, it is the total volume of exercise that elevates the likelihood to respond sufficiently to the exercise intervention.³⁸ The total energy expenditure of an exercise programme is determined by the product of session frequency and duration, training intensity, and programme length. Hence, also in CAD patients, the design of the exercise programme should be primarily aimed at optimizing total energy expenditure rather than focusing on one specific training characteristic (e.g. exercise intensity).³⁹ Indeed, a greater total exercise volume also predicts greater beneficial changes in adipose tissue mass, blood HDL cholesterol concentrations, and indicators for glycaemic control.⁴⁰ Therefore, CR programmes with too low total training volumes do not cause favourable changes in VO_{2peak} or any other health parameter.⁴¹ For example, such an unfavourable outcome could be expected when patients followed 16 supervised training sessions in which the first exercise sessions lasted for 12 min and increased up to 23 min at the final exercise session, while the exercise intensity increased from 46% of the heart rate reserve (HRR) up to 54% of HRR.⁴¹

The impact of HIIT on other important parameters, related to physical fitness, has also been examined. According to meta-analysis, a significantly greater increase in VO_2 at the first ventilatory threshold (by +0.88 mL/kg/min; 95% CI 0.16–1.60; $P = 0.02$) was observed after HIIT vs. MICT.²⁸ Other cardiorespiratory parameters (e.g. resting HR, peak O_2 pulse, VE/VCO_2 slope, oxygen uptake efficiency slope, and HR recovery after 1 min) responded similarly to HIIT vs. MICT,²⁸ although this remains to be verified in isocaloric comparisons.

In HF (HFpEF and HFrEF) patients, left ventricular function (as indicated by EF) and endothelial function [as indicated by flow mediated dilation (FMD)] were incrementally improved after HIIT, compared to MICT, but for FMD results were no longer significant after excluding patients with HFpEF.²⁸ The cardiovascular risk factors [e.g. body weight, systolic and diastolic blood pressure (BP), LDL- and HDL-cholesterol, triglycerides, and glucose] respond similarly to HIIT vs. MICT.²⁸

Long-term adherence to exercise training

The success of CR is highly dependent on long-term adherence. Therefore, some studies measured the effects of exercise training modalities on QoL, using generic and HF-specific questionnaires. Overall, HIIT and MICT show comparable effects on QoL.²⁸ The adherence to exercise training prescriptions in HIIT vs. MICT in CAD patients has only been assessed in two studies, with comparable outcomes.⁴² In line with these findings, both the SAINTEX-CAD and SMARTEX-HF studies indicate similar drop-out rates for non-medical

reasons in HIIT vs. MICT.^{32,33} Additionally, SMARTEX-HF showed a relatively poor compliance to the prescribed exercise intensity: 51% of patients in the HIIT group exercised at a lower intensity level than prescribed, and 80% of patients in the MICT group exercised at a higher intensity than was intended.³³ In particular, during HIIT the 4-min exercise peaks can be too long for a significant proportion of the patients. This is critically important: according to a meta-regression analysis no single exercise component is a significant predictor of mortality outcomes, but the greatest reductions in total (RR 0.81, $P=0.042$) and cardiovascular mortality (RR 0.72, $P=0.045$) are observed in CR programmes with the highest participant exercise adherence levels.⁴³ As a result, it is important to decide together with the patient what exercise intensities will be applied in a shared-decision making process. This will assist in long-term adherence to the prescribed exercises. However, the most optimal HIIT protocol for CVD patients still remains to be defined, taking into account the variations in the patient's phenotype and preferences, as well as the stage of the CR programme (e.g. early, after a few weeks, after several months of participation).⁴⁴ Moreover, the impact of HIIT on CV prognosis and lifelong adaptations towards an active lifestyle, remains to be demonstrated.⁵

To conclude, the total energy expenditure is instrumental to improve physical fitness and other health parameters in CR, so setting a sufficient exercise intensity is important in this regard.

Impact on medical safety

In apparently healthy, but sedentary individuals, first-exposure high-intensity aerobic training (at $>75\%$ $\text{VO}_{2\text{peak}}$) significantly increases the risk for acute myocardial infarction and, in rare occasions, sudden death.^{45,46} This might be related to acute platelet activation and aggregation, increased formation of thrombin and fibrin, the rise in blood catecholamine concentrations, or increased endothelial shear stress triggering a plaque rupture.^{47–49} In a study covering 25 420 CVD patients, 20 severe cardiac events were reported, of which 5 were related to exercise testing and 15 to exercise training.⁵⁰ The event rate was 1 per 8484 exercise stress tests and 1 per 49 565 patient-hours of exercise training, and the cardiac arrest rate was 1.3 per 1 000 000 patient training hours.⁵⁰ These data clearly indicate that current CR is very safe. However, in this multicentre study, which included 65 centres across France, the impact of the exercise intensity during exercise training was not analysed. A systematic review [$n=1117$ participants (HIIT: $n=547$, MICT: $n=570$)] indicated that HIIT is associated with a relatively low rate of major adverse cardiovascular events in CAD or HF patients (one major cardiovascular adverse event in 11 333 HIIT training hours).⁵¹ Moreover, only one minor cardiovascular adverse event and three non-cardiovascular adverse events (primarily of musculoskeletal origin) were reported as result of HIIT. Another systematic review reported that while HIIT precipitates acute cardiac events at a rate that is six times higher than MICT, comparisons of HIIT vs. MICT indicate that the absolute risk for adverse cardiovascular events and musculoskeletal injury remains, however, low.⁴² However, it must be mentioned that the relatively low number of examined patients precludes robust conclusions on the medical safety of HIIT.

Indeed, in most randomized trials, low-risk and/or clinically stable patients were examined, the exercise interventions were of a relatively short duration (most often up to 3 months), studies were not

powered for safety outcomes and exercise training was supervised: this all mitigates the actual risks of HIIT.^{42,51} Moreover, for some indications (e.g. valve disease, electrophysiological heart diseases, congenital heart disease, etc.) the medical safety of HIIT is not known. In final, safety precautions should also be taken into account during exercise training in the case of nephropathy and retinopathy (e.g. avoid exercise hypertension), peripheral and autonomic neuropathy (e.g. be aware of balance disorders or disturbed BP/HR response to exercise), and foot deformations/wounds (e.g. be aware of orthopaedic symptoms or bacterial infections), thus potentially contra-indicating HIIT.⁵ These arguments may also explain why HIIT is a potential alternative to MICT to allow variation in exercise training but is not formally promoted to all CVD patients.⁵

As a result, to the best and updated knowledge, this position paper suggests that MICT is the most feasible and cost-effective aerobic training modality for current CR activities in all referred populations. HIIT could be prescribed in selected patients (such as stable CAD or HF patients) for specific targets of intervention (e.g. to increase $\text{VO}_{2\text{peak}}$).

Exercise intensity determination in aerobic training: methodology

In 2013, Mezzani *et al.*⁷ proposed a 'threshold-based' rather than a 'range-based' approach for exercise prescription to maximize the benefits of aerobic exercise training in CR. The basis of this concept is that the exercise intensity is determined more accurately when related to physiological principles [i.e. the first and second ventilatory threshold (VT)] than when expressed as a percentage of peak exercise capacity.⁵² In fact, there is considerable inconsistency between exercise intensity prescriptions based on the VT vs. indicators derived from peak exercise parameters in CVD patients,⁸ highlighting the need for standardization and adjustment of the current guidelines. This part summarizes the utility and difficulties of current and novel concepts for the determination of the exercise training intensity.

Objective methods

Indices of peak exercise capacity

The vast majority of CR guidelines recommend that aerobic exercise training intensity is based on indices of peak effort, including % of $\text{VO}_{2\text{peak}}$, % of peak workload (W_{peak}), % of peak HR (HR_{peak}), and % of HR reserve (HRR) (i.e. the difference between peak and resting HR; see Table 2),⁵³ where peak values are usually defined as the highest average value of the last 20–30 s of an incremental symptom-limited cardiopulmonary exercise test (CPET). The most commonly used definitions for maximal or near-maximal effort include a peak respiratory gas exchange ratio (RER) ≥ 1.10 , the occurrence of a VO_2 and/or HR plateau with increasing effort and/or a rating of perceived exertion (RPE) $\geq 18/20$.⁷ Of note, most published and ongoing multicentre trials on exercise intensity in CVD patients have used thresholds of peak indices (e.g. HR_{peak} , HRR) to define the exercise intensity domains. An important problem associated with using these indices of peak exercise capacity for exercise prescription is that not all CVD patients achieve a (near-) maximal effort during CPET. It has been observed that $\sim 15\%$ of the patients do not achieve $\text{RER} \geq 1.10$, in a general outpatient CR population (without claudication)⁸ and

Table 2 Classification of aerobic exercise intensity¹⁷

Intensity	VO ₂ max (%)	HRmax (%)	HRR (%)	RPE scale	Training zone
Low intensity, light exercise	<40	<55	<40	10–11	Aerobic
Moderate intensity exercise	40–69	55–74	40–69	12–13	Aerobic
High intensity	70–85	75–90	70–85	14–16	Aerobic + lactate
Very high intense exercise	>85	>90	>85	17–19	Aerobic + lactate + anaerobic

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HR_{max}, maximal heart rate; HRR, heart rate reserve; RPE, ratings of perceived exertion; VO_{2peak}, peak oxygen uptake.

even more in HF patients (around 46%).⁵⁴ Moreover, a plateau in VO₂ is very often not observed.^{8,55} Another factor hampering the utility of peak indices is the fact that W_{peak} is highly influenced by the ramp rate during a CPET. Its use provides a false positive or negative VO_{2peak} detection in up to ~40% of the cases, reiterating the need for alternative methods to assess or verify peak effort.⁵⁵ Finally, different peak indices cannot be used interchangeably for exercise training prescription. In fact, at the same level of effort, different exercise intensity domains are elicited, with a large inter-individual variation.⁸ For example, the first ventilatory threshold (VT1) occurs at the low-intensity domain (3.7% of cases), moderate-intensity domain (34.9% of cases), high-intensity domain (59.6% of cases), or very hard domain (1.8% of cases).⁸ Moreover, very different distributions in elicited exercise intensity domains are noticed when referring this VT1 to %HR_{peak}, %HRR or %W_{peak}, and when extrapolations are made from the second ventilatory threshold (VT2) to the exercise intensity domains.⁸ Data from other laboratories align with these findings.⁹ Explanations for this observation could include beta-blocker use or chronotropic incompetence, influencing the HR vs. VO₂ relationship,⁵⁶ and a loss of linearity and high variability of the VO₂ vs. workload relationship in CVD patients, and particularly in patients with HF and myocardial ischaemia.^{57,58} However, it must be emphasized that these exercise intensity domains also have been criticized recently in healthy individuals.^{52,59} Moreover, these findings also indicate that when a certain percentage of the VO_{2peak}, HR_{peak}, HRR, or W_{peak} is selected, it is not sure whether this would be physiologically intense enough, or too vigorous, for a significant proportion of CVD patients. Clinicians should also decide whether they base the aerobic exercise intensity on HR or WR (workload-based rehabilitation). The former approach sometimes has the disadvantage that the HR zone between VT1 and VT2 (as explained below) can be very small (e.g. a few beats/min), making it difficult to properly set the target HR during exercise training. Moreover, changes in beta-blocker therapy could further complicate the determination of the target HR during exercise training. Whenever such change in beta-blocker dose has occurred, the new target HR should be set by applying the workload from the last few exercise sessions on the different exercise modes (e.g. bike, treadmill), and note the new elicited HR after ≥5 min of exercise.⁶ The workload-based approach in exercise intensity determination has the disadvantage that it does not automatically change in accordance to changes in exercise capacity (while HR does), so arbitrary increments in the workload must be foreseen during CR to elicit sufficiently effective exercise intensities.

Ventilatory threshold

An approach to avoid using the above-mentioned indices of peak exercise intensity for exercise training prescription is to relate the training intensity to VT1 and VT2. The VT1 represents the exercise intensity corresponding to the transition from purely aerobic metabolism to a point where blood lactate begins to rise in the blood but reaches equilibrium (as a result of progressive activation of anaerobic glycolysis, with stable lactate levels of 1.5–2 mmol/L due to an equal lactate rate of appearance vs. rate of disappearance). To counteract this metabolic acidosis, ventilation (VE) starts to increase at a faster rate than VO₂ until an equilibrium is reached. The VT2, also called the respiratory compensation point or ‘critical power’, represents the exercise intensity at which blood lactate starts to increase rapidly, and could further accumulate by prolonged exercise above this intensity, due to tissue anaerobiosis, resulting in a disproportionate increase in VE relative to CO₂ production (VCO₂) (with lactate levels 3–5 mmol/L and potentially increasing further due to a greater lactate rate of appearance vs. rate of disappearance). The most commonly used methods (see Figure 2) to assess VT1 include the nadir of the VE/VO₂ to work rate (WR) relationship (i.e. the lowest point in the curve before VE/VO₂ starts to increase) and the V-slope method in which the slope of the linear relation between VO₂ and VCO₂ increases (i.e. the increase in VCO₂ becomes faster than the VO₂ increase). VT2 corresponds to the nadir of the VE/VCO₂ to WR relationship (i.e. the lowest point in the curve before VE/VCO₂ starts to increase) and the VE/VCO₂-slope method in which the slope of the linear relation between VE and VCO₂ increases (i.e. the increase in VE becomes faster than the VCO₂ increase). These thresholds could then be extrapolated to the corresponding WR, HR, or exercise time. Typically, from those extrapolations the ‘exercise training zones’ could then be determined: low-intense (at an HR or WR below VT1), moderate-intense (at an HR or WR between VT1 and VT2), and high-intense (at an HR or WR above VT2).

In contrast to the indices of peak exercise capacity, VT1 and VT2 are effort-independent and can be achieved by the vast majority of the general CVD population. Yet, several difficulties may hamper the reliability of the determination of these thresholds. Concerning the V-slope method, a sub-analysis of the HF-Action trial shows that 17% of patients with HF have an indeterminate VT1 on at least one test with a substantial amount of within-subject variability between two consecutive tests.⁶⁰ In addition, a high inter-observer, intra-observer, and inter-site variation is present when determining the VT by the V-slope method.⁶¹ In fact, similar findings have been reported in CAD patients: in 8% and 4% (during cycling or walking exercise tests,

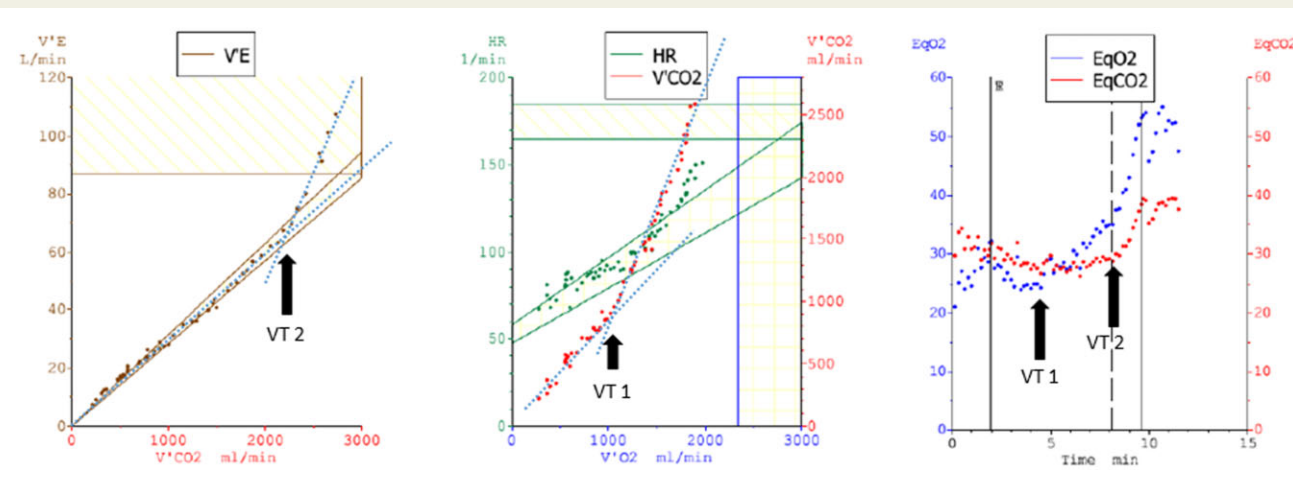


Figure 2 Representative 9-panel Wasserman plot for the determination of VT1 and VT2 in a 46-year old male with obesity. The bold arrows depict the first and secondary ventilatory threshold in this patient case. The dotted lines show where the thresholds (at the cross-points) can be found.

respectively) of these patients, VT1 cannot be determined and a substantial inter-observer variability could be present.⁶ When comparing the V-slope method and the assessment of the nadir of the VE/VO_2 to WR relationship, the latter method shows a slightly lower success rate of determination, but a higher inter-observer agreement,^{6,62} making it more suitable for exercise prescription in HF and CAD patients. The reliability and reproducibility of the assessment of VT2 by the nadir of the VE/VCO_2 to WR relationship is not well established in CVD patients: this method provides lower values than the second lactate turning point, but with acceptable limits of agreement and a success rate of determination of 94%.^{63,64} This suggests that this method is suitable for the follow-up of individual patients in everyday clinical practice. Although critical power tests could be more valid and reproducible to detect the respiratory compensation point or VT2,⁶⁵ the need for repeated exercise testing severely limits its applicability in patients with CVD.

A potential problem with using the VT for exercise training prescription is that it cannot be translated to constant-load exercise training directly. In fact, due to an initial VO_2 on-response delay (lag-time), VO_2 values during CPET correspond to a greater WR than during constant-load exercise. This delay, that can be quantified as the time interval between the onset of the ramp and the onset of the linear increase in VO_2 , is even longer in HF patients,⁶⁶ and varies substantially between subjects.⁶⁷ Since the determination of this delay is difficult and has not been validated in CVD patients, Mezzani *et al.*⁷ proposed, as a rule of thumb, that constant-load exercise prescriptions should be 10 W lower than assessed by a 10 W/min incremental protocol in CVD patients, at least at the start of CR.

On the other hand, exercise intensity prescription, based on VT1 and VT2, could be more effective to improve $\text{VO}_{2\text{peak}}$, as opposed to applying exercise intensities based on $\%\text{VO}_{2\text{peak}}$ or $\%\text{HR}_{\text{peak}}$. In healthy individuals, it was observed that by exercising according to a specific HRR for 12 weeks, 5 out of 12 individuals (42% of total group) experienced a favourable change in relative $\text{VO}_{2\text{peak}}$ ($\geq 5.9\%$), while when individuals exercised according to the VT1–VT2 training zone, relative $\text{VO}_{2\text{peak}}$ improved in all (12/12) subjects ($P < 0.05$ for

interaction effects).⁶⁸ This finding has been reproduced in 39 sedentary healthy adults in another randomized trial,⁶⁹ but remains to be confirmed in CVD patients.

A major limitation, however, is the fact that many CR centres do not have (access to) ergospirometry and directly assessed VO_2 data. As a result, following the EAPC position statement on quality standards in CR,⁷⁰ the minimal requirement would then be to execute a cycle ergometry test, with determination of the exercise intensity based on $\%\text{W}_{\text{peak}}$ or HR_{peak} (though with known limitations), while the ultimate requirement would be to execute a CPET with exercise intensity determination based on VT.

Anaerobic threshold

To determine the onset of anaerobic metabolism during exercise, blood lactate concentrations may also be assessed.⁵² The first lactate threshold (LT1, also known as aerobic threshold) represents the first rise in blood lactate above baseline (often noticed around 1.5–2 mmol/L). The second lactate threshold (LT2, also known as anaerobic threshold) represents a sudden greater increase in blood lactate (often noticed around 3–5 mmol/L).⁵² Although this method may seem attractive in determining the exercise intensity in patients with CVD, some major shortcomings or difficulties prevent the widespread use of this method in many CR centres. For example, there is no consensus what would be the ideal exercise test protocol to determine LT1 and LT2, and there are more than 30 methods described on how to determine LT1 and/or LT2, without internationally supported consensus which method would be most valid.⁵² In addition, at least 3-min step protocols should be used to determine LT1 and LT2 to allow full changes in VO_2 and blood lactate concentrations, while in CVD patients ramp protocols or 1-min protocols are preferred as they are more sensitive to detect changes in $\text{VO}_{2\text{peak}}$ in CVD patients.⁷¹ As a result, in CVD patients the determination of LT1 and LT2 does not seem to offer crucial or even valid information.

Myocardial ischaemia threshold

It is generally conceived that patients with residual myocardial ischaemia should confine to exercise training at an HR or WR which is below the myocardial ischaemic threshold (MIT).⁷ The most common definition of the MIT used in clinical studies is the HR or WR at which a 1 mm horizontal or down-sloping ST segment depression starts to appear during incremental exercise testing.⁷² However, in some individuals the electrocardiography (ECG) is not sensitive enough to detect myocardial ischaemia, but rather a decline in the O₂ pulse trajectory is noticed. Studies show that repeated myocardial ischaemic training sessions (up to 60 min with tolerable ischaemia symptoms) do not induce myocardial injury, significant arrhythmias, or left ventricular dysfunction,⁷³ and may even be more beneficial in a controlled setting for improving the myocardial blood flow.⁷⁴ To further explore the safety and effectiveness of exercise training above the MIT, standardization of its assessment is needed. When using the MIT for exercise training prescription, it is higher during cycling compared to walking/running, while the exercise protocol (ramp or Bruce protocol) does not influence these results.⁷⁵

To conclude, this updated position paper suggests to determine the exercise intensity by assessing VT1 and VT2 during CPET, preferably by the nadir of the VE/VO₂ and VE/VCO₂ to WR relationships, and to allow a training range between these thresholds. If VT cannot be determined due to logistic limitations, clinicians could determine the exercise intensity based on %W_{peak} or %HR_{peak}.

Yet, despite the availability of objective methods to determine the exercise intensity in CR, a need for subjective methods will always remain because clinicians could be in need of simpler tools for patient supervision during exercise sessions.

Subjective methods

When it is impossible to determine a patient's exercise intensity based on a standard exercise test or CPET, the exercise prescription can be guided by using Borg scales and/or subjective tools, such as the 'talk test'.⁷ Whereas individualized exercise prescriptions are typically based on frequency, intensity, time, and type, a subjective exercise intensity determination is an important principle for aerobic exercise prescription because it is a main part of medical safety and training effectiveness. In fact, all possible cardiac-related symptoms indicating exercise-induced serious arrhythmias and myocardial ischaemia or injury, which are usually determined by using New York Heart Association (NYHA) and Canadian Cardiovascular Society (CCS) classifications, have to be taken into account during aerobic training.

The most commonly used subjective methods for the determination of aerobic exercise intensity in CVD patients are the Borg ratings of perceived exertion (RPE, see Table 3) and the talk test.⁷⁷ Several studies showed that the objective measures of effort, such as HR and VO₂, should preferably be used in conjunction with RPE scores in CR settings in clinical practice^{76, 78–80} and in patients receiving β-blocker therapy,⁸¹ to improve the medical safety of exercising and also to achieve significant clinical benefits.

Ratings of perceived exertion

The most widely used instrument to measure perceived exertion or exercise intensity is the Borg's RPE scale. The RPE scale is a subjective means to gauge an individual's aerobic training intensity on the basis of the physical sensations a person experiences during physical

activity including HR, respiratory rate, sweating, and fatigue. It is proposed to supplement a standard CPET with subjective determination of exercise intensity levels, such as RPE.^{82,83} The RPE can be evaluated by the patient at each stage of the CPET on a linear scale with 15 points (6–20). A 0–10 scale for rating exercise intensity may be more intuitive for comprehension by the patient than the 6–20 scale. In both subjective scales, exercise intensity is simply obtained by asking the patient, in his/her perception, the RPE score that best reflects its current aerobic exercise intensity.

Although it is assumed that RPE scores correlate relatively well with both physiological measures of stress and arousal (e.g. HR, VT, and blood lactate) as well as psychological measures of exhaustion,⁸² studies in CVD patients reveal inconsistencies about the strength of the relationship between RPE and various physiological criterion measures, such as HR, blood lactate concentration, (%) VO_{2peak}, VE, and respiratory rate.⁶ The highest correlations between RPE and the physiological criterion measures have been found among male participants (whose VO₂ or VE was measured), and during high-intense exercise.⁷⁷ These findings suggest that RPE is less valid at low-intense exercises.⁷⁷ RPE reported by a patient can be affected by factors other than the physical effort of the exercise, including psychological factors and environmental conditions. In addition, unfamiliarity with exercise training (modes/equipment), low education level, and the use of beta-blockers may cause further difficulties in the interpretation of RPE.^{7,83} As a result, although Borg's RPE scale has been shown to be a valid measure of exercise intensity, its validity may not be as high as previously thought, except under specific conditions.⁷⁷ A more recent systematic review concluded that despite its variability, the RPE Borg scale can be a valid surrogate when peak exercise data are lacking or when HR is not available or usable (e.g. atrial fibrillation, pacemaker, chronotropic incompetence).⁸⁴

Talk test

The talk test has gained popularity as a simple subjective tool for exercise prescription, particularly in home-based CR.⁸⁵ From a

Table 3 20-point Borg ratings of perceived exertion scale⁷⁶

Score	Level of exertion
6	No exertion at all
7	
8	
9	Very light
10	
11	Light
12	
13	Somewhat hard
14	
15	Hard (heavy)
16	
17	Very hard
18	
19	Extremely hard
20	Maximal exertion

physiological point of view, the talk test is based on the swift increase in breathing rate above VT2 that causes difficulty in talking during exercise. For exercise training, patients are instructed to maintain a certain level of exercise while still being able to talk comfortably in full sentences. The self-regulatory nature of the talk test can empower patients for self-management. An important advantage of the talk test is that it does not require any expense and expertise, which further enhances its utility in home-based CR. It could be a relatively simple and safe way of aerobic exercise intensity prescription among CR patients.^{85,86}

The test is suitable in patients with CAD and shows quite good intra-class correlation coefficient values of 0.80, when comparing self-ratings with external observations.^{85,87} However, when comparing with VT1 and/or VT2, the level of agreement demonstrates wide ranges, suggesting poor individual correspondence.^{85,87} Like Borg RPE, the talk test thus can be used as an adjunct practical way to guide exercise intensity in daily activities of CVD patients,⁸⁸ but it cannot replace objective methods to determine the exercise intensity. Another potential limitation is that the talk test is not a practical tool for customizing high-intensity exercise during HIIT and it should therefore be reserved for predominantly moderate intensity exercises. Because the Talk test is based on the swift increase in breathing rate around VT2, it can also not assess VT1 and thus be used for determining a low exercise intensity.

How to determine the exercise intensity during progressive CR (including phase III)?

Continuing the CR programme (into phase III) is important: it results in an increased/maintained functional capacity, quality of life, and physical activity levels, when compared with CVD patients who stop CR after phase II.⁸⁹ This also explains why mortality and/or hospitalization rates are significantly lower in HF and CAD patients following phase III CR programmes, when compared with patients completing phase II CR only.^{90,91}

To achieve the weekly energy expenditure needed to elicit cardiovascular benefits, a steady progression in exercise dose is usually necessary.⁹² It is agreed that patients should progress from moderate- to vigorous-intensity aerobic exercise over the course of a CR programme.^{5,92} As a result, it is proposed to start at VT1 (lower limit of exercise intensity) and progress towards VT2. This approach likely incrementally improves the total increase in exercise capacity obtained by the training programme. The value of an adjustment of exercise dose throughout the training programme has not yet been formally evaluated in clinical trials. Retrospective studies demonstrate that progression of exercise dose during a CR programme is associated with changes in functional capacity.^{93,94} Also for HIIT, a gradual increase in intensity has been described in trials, by starting to exercise at the lower end of the prescribed intensities and gradually increasing to the higher end of the prescribed intensities.⁹⁵ Specifically for the high-intense bouts in HIIT, it can then be decided to go above VT2.

Exercise dose should be increased gradually and frequently, rather than abruptly and sporadically. However, the progression of exercise dose should not be too restricted either, to ensure that CVD patients

meet the final exercise prescription goal.^{5,92} Thus, the exercise progression needs to be individualized for each patient. Factors influencing such exercise progression include patient-related factors (e.g. subjective exertion, physical fitness, comorbidities, age, frailty, CV risk, patient preference), CR team-related factors (e.g. experience, programme policy), and equipment-related factors (e.g. availability of CPET, exercise equipment with automated intensity adjustment based on HR), among others.⁹² Ultimately, shared-decision making should be applied in this process.

All FITT components should be included when prescribing exercise progression, but only one component should be increased at a time for aerobic exercise training.⁹² Increases in intensity and duration of 5–10% per week are generally well tolerated.⁹² As a result, this increase in exercise intensity is very often foreseen between VT1 and VT2, based on objective indicators and also on the patient's willingness and capacity. The exercise duration should first be increased, until the desired session length is attained, before increasing the exercise intensity.⁹² Although this is general advice, it remains however to be validated whether such approach is feasible in very weak or deconditioned patients as well.

Some CR centres habitually include a repeat CPET after several weeks of training to guide the intensity progression. This approach takes into account that changes in aerobic capacity can already occur very early in the programme, with studies showing improvements in $\text{VO}_{2\text{peak}}$ after only 2–4 weeks of exercise training.^{36,37} Of note, the test–retest reproducibility of a repeat exercise test is estimated to be 5–7%.⁹⁶ Thus, changes in exercise capacity below these values should not trigger adaptations in exercise prescription.

It is well established that CR leads to improvements in $\text{VO}_{2\text{peak}}$ and also to increments in VT1 and VT2. Moreover, it has been observed that also HR_{peak} can increase and resting HR can decrease, both in CAD as well as HF patients,²⁸ and that the HR curve during exercise (testing) changes as well.⁹⁷ These data thus indicate that when the physical fitness of the patient changes during CR, the exercise training intensity should be carefully re-assessed. Even more importantly, the training status significantly affects the relation between VT1 or VT2 and the corresponding exercise intensity domains. For example, when comparing physically unfit CVD patients ($\text{VO}_{2\text{peak}} < 15 \text{ mL/min/kg}$) vs. physically fit CVD patients ($\text{VO}_{2\text{peak}} \geq 25 \text{ mL/min/kg}$), VT1 and VT2 fall in significantly different exercise intensity domains.⁸ As a result, clinicians should be careful to use the exercise intensity domains (relying on $\%\text{VO}_{2\text{peak}}$, $\%\text{HR}_{\text{peak}}$, HRR, or $\%\text{W}_{\text{peak}}$) when changes in exercise capacity are elicited as a result of CR.

During prolonged CR (including phase III), it remains important to re-assess VT1 and VT2 to properly determine the exercise intensity, although with a lower frequency (e.g. once a year). The talk test or RPE Borg scale can also be used to direct progression of exercise intensity in MICT programmes, especially in home-based settings. It should however be examined further whether imposed or self-selected exercise intensities would affect the clinical effects of phase III and IV CR.^{10,11,98,99}

Exercise intensity in resistance training: does it matter?

Impact on health outcomes

In contrast to aerobic exercise training, the medical community has long been more hesitant to endorse resistance training for patients with CVD. This hesitation was mainly based on the opinion that BP elevations during resistance training could increase the risk of CV complications, especially in elderly patients. Yet, during the last decade, evidence has been accumulating about the added benefits of resistance training as part of CR. Given that muscle weakness is a strong predictor of premature death in CVD patients,¹⁰⁰ it is obvious that maximizing muscle strength is of paramount importance. Moreover, following cardiac surgery, significant muscle wasting is observed, warranting interventions to regain muscle mass and strength.^{101,102} Moreover, also HF patients experience weakened peripheral muscles.¹⁰³ According to meta-analysis, the addition of resistance training on top of aerobic training leads to greater increments in physical fitness and muscle strength in CVD patients.¹⁰⁴ In addition, resistance training favourably affects bone health,¹⁰⁵ glycaemic control, blood pressure, and lipid profile, at least in the elderly and patients with elevated CVD risk.⁴⁰

In the prescription of resistance training, specific parameters have to be defined. The volume of resistance training is determined by the number of sets, multiplied by the number of repetitions in these sets, and the weight lifted during the muscle contraction. The intensity of a muscle contraction is typically expressed as a percentage of one repetition maximum (%1RM), in which <50% of 1RM is considered as low-intense and >70% of 1RM as high-intense.⁵ Between a set, it is important to allow a sufficient rest interval (usually 1–2 min). In CR, typically dynamic concentric resistance training is applied, while eccentric, isometric, and isokinetic resistance training are less frequently applied.⁵ During concentric resistance training, a contraction and relaxation (going back to start position to initiate a new contraction) duration of 2–4 s is usually proposed, and the number of repetitions per set can vary from 6 up to 25.⁵ In general, in CR it is advised to apply resistance training at an intensity of 30–70% of 1RM for the upper body, and 40–80% of 1RM for the lower body, with 12–15 repetitions per set, multiplied by 2–3 sets per muscle group.⁵ In particular large muscle groups, and muscle groups relevant to activities of daily life, should herein be targeted.

To maximize muscle mass and strength gains, evidence is emerging that dynamic high-intense resistance training (D-HIST) should be preferred above dynamic low-intense resistance training (D-LIST). In several meta-analyses,^{106–108} D-HIST led to significantly greater improvements in muscle strength, as opposed to D-LIST. In healthy older adults, the variables 'training period' ($P = 0.04$) and 'intensity' ($P < 0.01$) as well as 'total time under tension' ($P < 0.01$) had significant effects on muscle strength, with the largest effect sizes for the longest training periods (>50 weeks), intensities of 70–79% of 1RM, and total time under tension of 6.0 s.

These findings are in line with known acute physiological adaptations to resistance exercise stimuli. Changes in the myofibrillar protein synthesis rate are dependent on the contractile intensity of the muscular exercises, revealing only an improvement following a single bout of D-HIST.¹⁰⁹ When D-HIST contractions are executed, the

mitogen-activated protein kinase and mammalian target of rapamycin complex 1-dependent pathways are activated to a significantly greater amount, compared to D-LIST.¹⁰⁹ Such enhanced myofibrillar protein synthesis may lead to greater muscle mass gains, explaining why greater increments in muscle mass are sometimes noted after D-HIST vs. D-LIST.^{106–108} Even if muscle mass gains are comparable after a D-LIST vs. D-HIST, the neurological adaptations are distinct. When comparing a long-term D-HIST intervention (at 80% of 1RM) against a long-term D-LIST intervention (at 30% of 1RM), greater neural adaptations occur after D-HIST (as evidenced by greater increases in percentage voluntary activation and electromyographic amplitude during maximal force production), which may explain the disparate increases in muscle strength, despite similar muscle hypertrophy, following D-HIST vs. D-LIST.¹¹⁰

However, in CVD patients it remains to be established what would be the effects of D-HIST vs. D-LIST (in combination with aerobic training) on changes in muscle mass and strength. As a result, which exercise intensity to select during dynamic resistance training in CR remains a topic of debate.¹²

Impact on medical safety

When CVD patients are exposed to D-HIST, there is a common belief that they may be at an increased risk of acute adverse cardiovascular events. However, during the first phases of CR (phase I and II), patients with CVD are directly guided/supervised by trained clinicians/therapists, well aware of formal contraindications to dynamic resistance training and are able to determine the patient's risk profile.¹² Moreover, rehabilitation or exercise training facilities are specifically designed and equipped to anticipate adverse events during exercise.¹¹¹ This explains, at least partly, why the rates of adverse cardiovascular events during dynamic resistance training are actually very low in CR, or at least not greater as opposed to aerobic training.^{104,112,113} In addition, there is no established relation between the applied dynamic resistance training intensity and the incidence of adverse cardiovascular events during CR in stable and well-screened patients.¹¹⁴

On the other hand, intensive heavy weightlifting, especially when this includes substantial isometric (static) muscle work, can induce the Valsalva manoeuvre. This thus occurs when holding the breath during muscular contraction.¹¹⁵ After the termination of this compressed breathing, a large increase in venous return may be provoked and thus an increase in cardiac output (through a constricted arterial vascular system). This may lead to sharp increments in BP and myocardial oxygen demand. The Valsalva manoeuvre can thus be avoided by teaching patients a proper breathing technique, which includes exhaling during muscular contraction and inhaling when returning to the starting position. Moreover, also the volume of resistance training relates to changes in BP. In older adults, a greater acute response after high-volume resistance training is present, as opposed to low-volume resistance training (but at similar intensities), thus reflecting greater haemodynamic, metabolic and neuromuscular stress, than low-volume resistance training.¹¹⁶

Exercise intensity determination in resistance training: methodology

Objective methods

A distinction should be made between the assessment of muscle strength as a tool to detect and quantify muscle weakness or to evaluate functional status vs. the quantification of muscle strength as the basis of resistance training prescription. This part focusses on ways of assessing muscle strength for exercise prescription in patients with CVD. In the rehabilitation setting, dynamometry could be proposed to set the training load during resistance training. However, this methodology is less attractive because of the high cost of a dynamometer, the technical complexity of executing a strength test, and the difficulty of translating the outcome of dynamometry (expressed as Nm) towards a load during resistance training (kg). Alternatively, a % of 1RM or RM can be used to objectively prescribe the intensity for dynamic resistance training.¹² 1RM is a measure of the maximum weight a patient can lift in one complete repetition for a given exercise in a controlled way through a full range of motion with good posture, whereas RM is the maximum weight that the person can lift for a given number of repetitions of an exercise (e.g. 8RM is the maximum weight that the person can lift eight times). The 1RM is obtained through trial and error by means of free weights or machines, and should ideally be performed for each targeted muscle group.¹¹⁷

As many patients do not have any previous experience with dynamic resistance training before enrolling in CR, patients should first engage in at least one, but preferably more, practice sessions in which they are acquainted with the test equipment and familiarized with a proper and safe execution of the exercise, in order to obtain a reliable score that can be used to prescribe the dynamic resistance exercise, and to track progress over time.¹¹⁸ In this regard, also here it is important to decide together with the patient, in a shared-decision making process, which resistance exercise intensities will be applied to maximize adherence to these prescriptions.

Though studies demonstrate the safety of 1RM testing in patients with mild-to-moderate left ventricular dysfunction and patients enrolled in CR, supporting evidence remains scant. Therefore, a more conservative approach might be followed, especially in the higher-risk patient.^{119,120} So, in patients in which a 1RM test is not suitable, the load-repetition relationship for resistance training, such as a 10RM, may be more appropriate to assess muscular strength.¹²¹ Subsequently, prediction equations are available to estimate the 1RM from these multiple RM tests¹²²:

$$1\text{RM} = \text{applied weight} / (1.0278 - 0.0278 * \text{repetitions})^{123}$$

or

$$1\text{RM} = (1 + 0.0333 * \text{repetitions}) * \text{applied weight}^{124}$$

However, to obtain a good estimation of 1RM, no more than 10 repetitions are allowed during the strength testing (thus leading to a <10RM test).¹²² As these predicted 1RM values are consistently less than the actual 1RM value, the resistance training intensity is not expected to exceed the prescribed load.¹²³

Subjective methods

In the context of dynamic resistance training, it is important to be aware that the same resistance exercise prescribed at a specific % of

1RM may lead to different perceptions of exercise in different patients. Factors such as body weight, coordination, intention, and previous experience with resistance training play a role. The correct dosage therefore also depends largely upon the patient's subjective perception of the exercises. Ratings of perceived exertion are therefore being used to monitor the intensity in a variety of exercise modalities, including dynamic resistance exercise. The RPE can be used effectively to gauge resistance exercise intensity in older adults by the adult Omnibus Resistance Exercise Scale (OMNI-RES, see [Graphical Abstract](#)).^{125,126}

How to determine the exercise intensity during progressive CR (including phase III)?

Consistent improvements in muscular strength have been reported with resistance training interventions, as part of CR, in HF and CAD patients.^{104,127} However, between studies and within the included studies, the magnitude of change in muscle strength varies significantly.^{104,127} As a result, clinicians should thus take into account a significant inter-subject difference in change in muscle strength when determining the exercise intensity when CR progresses. Moreover, most often concentric resistance training has been applied, while the effects of eccentric or isometric resistance training are less well studied.

As explained above, generally initial loads should be light at initiation of CR, with patients completing 12–15 repetitions at 30% of 1RM and 40% of 1RM for the upper and lower body, respectively.⁵ Exercise pace should be slow, allowing at least twice the time for rest/recovery phases as compared to work/contraction phases. Beginning with unilateral exercises can increase strength exercise tolerance. The intensity of the resistance exercises should then be increased up to 70% of 1RM and 80% of 1RM for the upper and lower body, respectively.⁵ Consequently, for optimal training prescription of the muscle groups involved, a periodic evaluation, to accurately adjust the programme, is mandatory. In this respect, the <10RM test can be used once every few weeks.

However, how progression should be made in the build-up of the intensity of resistance training in CR, remains unclear.⁹² Nevertheless, there seems to be consensus that such build-up can only be allowed when it is medically safe (no orthopaedic symptoms, cardiac arrhythmias, or episodes of syncope or dizziness) and patients are able to execute the exercises with proper technique.⁹² Respecting the biological principles of exercise training and considering the need to apply progressive overload so that training adaptations are constantly stimulated, a well-supported approach in the scientific literature is the progression of loads.¹²⁸ This progression involves the increase or variation of the external loads, thus generating larger internal loads (muscle forces or torques) and increasing adaptations over time.¹²⁸ In this regard, three strategies are often used to increase the external load: (i) volume (i.e. number of sets or repetitions), (ii) intensity (amount of resistive load lifted), and (iii) density (i.e. alter rest periods, keeping volume and intensity unchanged).¹²⁸

Table 4 Moving from basic to progressive (functional) resistance training¹²⁸

Basic resistance training	Progressive resistance training
Generic	Specific
Lying/sitting	Standing
Single joint	Multiple joints
Uni-planar or one-dimensional	Multi-planar of three-dimensional
Slow movement	Fast movement
Stable underground	Unstable underground
Without visual deprivation	With visual deprivation
Cyclic	Acyclic
Unilateral	Bilateral
Simultaneous	Alternating
Single task	Double task

How to progress in resistance training, depends on the ultimate goal of the intervention (e.g. increase muscle strength), as well as the acceptance and feasibility (as assessed by the OMNI-RES). In CR, it is believed that, first the desired number of resistance training sets should be achieved, after which the intensity can then be gradually increased, finally followed by adaptations in rest periods.

During prolonged CR (phase III), however, resistance training should be implemented with more focus on functional resistance training targeting those muscle groups needed for facilitating daily life activities. A large body of evidence, at least from healthy (older) individuals, is in support of this concept.¹²⁹ For this purpose, the load progression in resistance training can be achieved by (a combination of) specific adjustments (see Table 4).¹²⁸

This approach remains however to be applied in (prolonged) CR programmes to verify the clinical effectiveness and feasibility. Moreover, it should be examined further whether imposed or self-selected exercise intensities would affect the clinical effects of phase III CR.¹³⁰

Conclusion

From this position statement, it is concluded that:

- the assessment of VT1 and VT2 during CPET, preferably by the nadir of the VE/VO₂ and VE/CO₂ to WR relationships, should be used for the determination of the aerobic exercise intensity in the majority of CVD patients.
- The talk test and Borg RPE scale should only be considered as an adjunct to an objective aerobic exercise intensity determination method in CVD patients.
- To properly determine the exercise intensity during resistance training, a <10RM test can be used to set the initial weight, while the OMNI-RES can be used to track the perceived intensity during the exercise sessions.

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References

1. Rauch B, Davos CH, Doherty P, Saure D, Metzendorf M-I, Salzwedel A, Völler H, Jensen K, Schmid J-P; 'Cardiac Rehabilitation Section', European Association of Preventive Cardiology (EAPC), in cooperation with the Institute of Medical Biometry and Informatics (IMBI), Department of Medical Biometry, University of Heidelberg, and the Cochrane Metabolic and Endocrine Disorders Group, Institute of General Practice, Heinrich-Heine University, Düsseldorf, Germany. The prognostic effect of cardiac rehabilitation in the era of acute revascularisation and statin therapy: a systematic review and meta-analysis of randomized and non-randomized studies—the Cardiac Rehabilitation Outcome Study (CROS). *Eur J Prev Cardiol* 2016;**23**:1914–1939.

2. Long L, Mordi IR, Bridges C, Sagar VA, Davies EJ, Coats AJ, et al. Exercise-based cardiac rehabilitation for adults with heart failure. *Cochrane Database Syst Rev* 2019;**1**:CD003331.

3. Lane R, Harwood A, Watson L, Leng GC. Exercise for intermittent claudication. *Cochrane Database Syst Rev* 2017;**12**:CD000990.

4. Salzwedel A, Jensen K, Rauch B, Doherty P, Metzendorf M-I, Hackbusch M, Völler H, Schmid J-P, Davos CH. Effectiveness of comprehensive cardiac rehabilitation in coronary artery disease patients treated according to contemporary evidence based medicine: update of the Cardiac Rehabilitation Outcome Study (CROS-II). *Eur J Prev Cardiol* 2020;**27**:1756–1774.

5. Ambrosetti M, Abreu A, Corrà U, Davos CH, Hansen D, Frederix I, et al. Secondary prevention through comprehensive cardiovascular rehabilitation: from knowledge to implementation. 2020 update. A position paper from the Secondary Prevention and Rehabilitation Section of the European Association of Preventive Cardiology. *Eur J Prev Cardiol* 2020. doi: 10.1177/2047487320913379.

6. Hansen D, Stevens A, Eijnde BO, Dendale P. Endurance exercise intensity determination in the rehabilitation of coronary artery disease patients: a critical re-appraisal of current evidence. *Sports Med* 2012;**42**:11–30.

7. Mezzani A, Hamm LF, Jones AM, McBride PE, Moholdt T, Stone JA, Urhausen A, Williams MA. Aerobic exercise intensity assessment and prescription in cardiac rehabilitation: a joint position statement of the European Association for Cardiovascular Prevention and Rehabilitation, the American Association of Cardiovascular and Pulmonary Rehabilitation and the Canadian Association of Cardiac Rehabilitation. *Eur J Prev Cardiol* 2013;**20**:442–467.

8. Hansen D, Bonnè K, Alders T, Hermans A, Copermans K, Swinnen H, Maris V, Jansegers T, Mathijs W, Haenen L, Vaes J, Govaerts E, Reenaers V, Frederix I, Dendale P. Exercise training intensity determination in cardiovascular rehabilitation: should the guidelines be reconsidered? *Eur J Prev Cardiol* 2019;**26**: 1921–1928.

9. Pymer S, Nichols S, Prosser J, Birkett S, Carroll S, Ingle L. Does exercise prescription based on estimated heart rate training zones exceed the ventilatory anaerobic threshold in patients with coronary heart disease undergoing usual-care cardiovascular rehabilitation? A United Kingdom perspective. *Eur J Prev Cardiol* 2020;**27**:579–589.

10. Ekkekakis P, Parfitt G, Petruzzello SJ. The pleasure and displeasure people feel when they exercise at different intensities: decennial update and progress towards a tripartite rationale for exercise intensity prescription. *Sports Med* 2011;**41**:641–671.

11. Oliveira BRR, Deslandes AC, Santos TM. Differences in exercise intensity seems to influence the affective responses in self-selected and imposed exercise: a meta-analysis. *Front Psychol* 2015;**6**:1105.

12. Hansen D, Abreu A, Doherty P, Völler H. Dynamic strength training intensity in cardiovascular rehabilitation: is it time to reconsider clinical practice? A systematic review. *Eur J Prev Cardiol* 2019;**26**:1483–1492.

13. Reed JL, Pipe AL. Practical approaches to prescribing physical activity and monitoring exercise intensity. *Can J Cardiol* 2016;**32**:514–522.

14. Brouwers MC, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, Fervers B, Graham ID, Grimshaw J, Hanna SE, Littlejohns P, Makarski J, Zitzelsberger L; AGREE Next Steps Consortium. AGREE II: advancing guideline development, reporting and evaluation in health care. *CMAJ* 2010;**182**:E839–E842.

15. Mehra VM, Gaalema DE, Pakosh M, Grace SL. Systematic review of cardiac rehabilitation guidelines: quality and scope. *Eur J Prev Cardiol* 2020;**27**:912–928.

16. Boyde M, Rankin J, Whitty JA, Peters R, Holliday J, Baker C, Hwang R, Lynagh D, Korczyk D. Patient preferences for the delivery of cardiac rehabilitation. *Patient Educ Couns* 2018;**101**:2162–2169.

17. Pelliccia A, Sharma S, Gati S, Bäck M, Björjesson M, Caselli S, Collet JP, Corrado D, Drezner JA, Halle M, Hansen D, Heidbuchel H, Myers J, Niebauer J, Papadakis M, Piepoli MF, Prescott E, Roos-Hesselink JW, Graham Stuart A, Taylor RS, Thompson PD, Tiberi M, Vanhees L, Wilhelm M, ESC Scientific Document Group. 2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease: the task force on sports cardiology and exercise in patients with cardiovascular disease of the European Society of Cardiology (ESC). *Eur Heart J* 2021;**42**:17–96.

18. Schnohr P, Marott JL, Jensen JS, Jensen GB. Intensity versus duration of cycling, impact on all-cause and coronary heart disease mortality: the Copenhagen City Heart Study. *Eur J Prev Cardiol* 2012;**19**:73–80.
19. Uddin J, Zwisler A-D, Lewinter C, Moniruzzaman M, Lund K, Tang LH, Taylor RS. Predictors of exercise capacity following exercise-based rehabilitation in patients with coronary heart disease and heart failure: a meta-regression analysis. *Eur J Prev Cardiol* 2016;**23**:683–693.
20. Mitchell BL, Lock MJ, Davison K, Parfitt G, Buckley JP, Eston RG. What is the effect of aerobic exercise intensity on cardiorespiratory fitness in those undergoing cardiac rehabilitation? A systematic review with meta-analysis. *Br J Sports Med* 2019;**53**:1341–1351.
21. Swank AM, Horton J, Fleg JL, Fonarow GC, Keteyian S, Goldberg L, Wolfel G, Handberg EM, Bensimhon D, Illiou M-C, Vest M, Ewald G, Blackburn G, Leifer E, Cooper L, Kraus WE; and for the HF-ACTION Investigators. Modest increase in peak VO_2 is related to better clinical outcomes in chronic heart failure patients: results from heart failure and a controlled trial to investigate outcomes of exercise training. *Circ Heart Fail* 2012;**5**:579–585.
22. Oberman A, Fletcher GF, Lee J, Nanda N, Fletcher BJ, Jensen B, Caldwell ES. Efficacy of high-intensity exercise training on left ventricular ejection fraction in men with coronary artery disease (the Training Level Comparison Study). *Am J Cardiol* 1995;**76**:643–647.
23. Lee JY, Jensen BE, Oberman A, Fletcher GF, Fletcher BJ, Raczynski JM. Adherence in the training levels comparison trial. *Med Sci Sports Exerc* 1996;**28**: 47–52.
24. Johnson JL, Slentz CA, Houmard JA, Samsa GP, Duscha BD, Aiken LB, McCartney JS, Tanner CJ, Kraus WE. Exercise training amount and intensity effects on metabolic syndrome (from Studies of a Targeted Risk Reduction Intervention through Defined Exercise). *Am J Cardiol* 2007;**100**:1759–1766.
25. MacInnis MJ, Gibala MJ. Physiological adaptations to interval training and the role of exercise intensity. *J Physiol* 2017;**595**:2915–2930.
26. Pattyn N, Coeckelberghs E, Buys R, Cornelissen VA, Vanhees L. Aerobic interval training vs. Moderate continuous training in coronary artery disease patients: a systematic review and meta-analysis. *Sports Med* 2014;**44**:687–700.
27. Gomes-Neto M, Duraes AR, Reis H, Neves VR, Martinez BP, Carvalho VO. High-intensity interval training versus moderate-intensity continuous training on exercise capacity and quality of life in patients with coronary artery disease: a systematic review and meta-analysis. *Eur J Prev Cardiol* 2017;**24**:1696–1707.
28. Pattyn N, Beulque R, Cornelissen V. Aerobic interval vs. continuous training in patients with coronary artery disease or heart failure: an updated systematic review and meta-analysis with a focus on secondary outcomes. *Sports Med* 2018;**48**:1189–1205.
29. Gomes Neto M, Duraes AR, Conceicao LSR, Saquetto MB, Ellingsen Ø, Carvalho VO. High intensity interval training versus moderate intensity continuous training on exercise capacity and quality of life in patients with heart failure with reduced ejection fraction: a systematic review and meta-analysis. *Int J Cardiol* 2018;**261**:134–141.
30. Araújo BTS, Leite JC, Fuzari HKB, Pereira de Souza RJ, Remígio MI, Dornelas de Andrade A, Lima Campos S, Cunha Brandão D. Influence of high-intensity interval training versus continuous training on functional capacity in individuals with heart failure: a systematic review and meta-analysis. *J Cardiopulm Rehabil Prev* 2019;**39**:293–298.
31. Wisløff U, Støylen A, Loennechen JP, Bruvold M, Rognmo Ø, Haram PM, Tjønnå AE, Helgerud J, Slørdahl SA, Lee SJ, Videm V, Bye A, Smith GL, Najjar SM, Ellingsen Ø, Skjærpe T. Superior cardiovascular effect of aerobic interval training versus moderate continuous training in heart failure patients: a randomized study. *Circulation* 2007;**115**:3086–3094.
32. Conraads VM, Pattyn N, De Maeyer C, Beckers PJ, Coeckelberghs E, Cornelissen VA, Denollet J, Frederix G, Goetschalckx K, Hoymans VY, Possemiers N, Schepers D, Shivalkar B, Voigt J-U, Van Craenenbroeck EM, Vanhees L. Aerobic interval training and continuous training equally improve aerobic exercise capacity in patients with coronary artery disease: the saintex-cad study. *Int J Cardiol* 2015;**179**:203–210.
33. Ellingsen Ø, Halle M, Conraads V, Støylen A, Dalen H, Delagardelle C, Larsen A-I, Hole T, Mezzani A, Van Craenenbroeck EM, Videm V, Beckers P, Christle JW, Winzer E, Mangner N, Woitek F, Höllriegel R, Pressler A, Monk-Hansen T, Snoer M, Feiereisen P, Valborgland T, Kjekshus J, Hambrecht R, Gielen S, Karlsen T, Prescott E, Linke A; SMARTEX Heart Failure Study (Study of Myocardial Recovery After Exercise Training in Heart Failure) Group. High-intensity interval training in patients with heart failure with reduced ejection fraction. *Circulation* 2017;**135**:839–849.
34. Pattyn N, Vanhees L, Cornelissen VA, Coeckelberghs E, De Maeyer C, Goetschalckx K, Possemiers N, Wuyts K, Van Craenenbroeck EM, Beckers PJ. The long-term effects of a randomized trial comparing aerobic interval versus continuous training in coronary artery disease patients: 1-year data from the saintex-cad study. *Eur J Prev Cardiol* 2016;**23**:1154–1164.
35. Taylor JL, Holland DJ, Keating SE, Leveritt MD, Gomersall SR, Rowlands AV, Bailey TG, Coombes JS. Short-term and long-term feasibility, safety, and efficacy of high-intensity interval training in cardiac rehabilitation: the FITR heart study randomized clinical trial. *JAMA Cardiol* 2020;**5**:1382.
36. Ismail H, McFarlane JR, Dieberg G, Smart NA. Exercise training program characteristics and magnitude of change in functional capacity of heart failure patients. *Int J Cardiol* 2014;**171**:62–65.
37. Vromen T, Kraal JJ, Kuiper J, Spee RF, Peek N, Kemps HM. The influence of training characteristics on the effect of aerobic exercise training in patients with chronic heart failure: a meta-regression analysis. *Int J Cardiol* 2016;**208**: 120–127.
38. Gevaert AB, Adams V, Bahls M, Bowen TS, Cornelissen V, Dörr M, Hansen D, Kemps HM, Leeson P, Van Craenenbroeck EM, Kränkel N. Towards a personalised approach in exercise-based cardiovascular rehabilitation: how can translational research help? A 'call to action' from the Section on Secondary Prevention and Cardiac Rehabilitation of the European Association of Preventive Cardiology. *Eur J Prev Cardiol* 2020;**27**:1369–1385.
39. Kraal JJ, Vromen T, Spee R, Kemps HMC, Peek N. The influence of training characteristics on the effect of exercise training in patients with coronary artery disease: systematic review and meta-regression analysis. *Int J Cardiol* 2017;**245**:52–58.
40. Hansen D, Niebauer J, Cornelissen V, Barna O, Neunhäuserer D, Stettler C, Tonoli C, Greco E, Fagard R, Coninx K, Vanhees L, Piepoli MF, Pedretti R, Ruiz GR, Corrà U, Schmid J-P, Davos CH, Edelmann F, Abreu A, Rauch B, Ambrosetti M, Braga SS, Beckers P, Bussotti M, Faggiano P, Garcia-Porrero E, Koudi E, Lamotte M, Reibis R, Spruit MA, Takken T, Vigorito C, Völler H, Doherty P, Dendale P. Exercise prescription in patients with different combinations of cardiovascular disease risk factors: a consensus statement from the EXPERT working group. *Sports Med* 2018;**48**:1781–1797.
41. Nichols S, Taylor C, Goodman T, Page R, Kallvikbacka-Bennett A, Nation F, Clark AL, Birkett ST, Carroll S, Ingle L. Routine exercise-based cardiac rehabilitation does not increase aerobic fitness: a CARE CR study. *Int J Cardiol* 2020;**305**:25–34.
42. Quindry JC, Franklin BA, Chapman M, Humphrey R, Mathis S. Benefits and risks of high-intensity interval training in patients with coronary artery disease. *Am J Cardiol* 2019;**123**:1370–1377.
43. Abell B, Glasziou P, Hoffmann T. The contribution of individual exercise training components to clinical outcomes in randomised controlled trials of cardiac rehabilitation: a systematic review and meta-regression. *Sports Med Open* 2017;**3**:19.
44. Gayda M, Ribeiro PA, Juneau M, Nigam A. Comparison of different forms of exercise training in patients with cardiac disease: where does high-intensity interval training fit? *Can J Cardiol* 2016;**32**:485–494.
45. Bartsch P. Platelet activation with exercise and risk of cardiac events. *Lancet* 1999;**354**:1747–1748.
46. Cadroy Y, Pillard F, Sakariassen KS, Thalamos C, Boneu B, Riviere D. Strenuous but not moderate exercise increases the thrombotic tendency in healthy sedentary male volunteers. *J Appl Physiol* 2002;**93**:829–833.
47. Hilberg T, Menzel K, Glaser D, Zimmermann S, Gabriel HH. Exercise intensity: platelet function and platelet-leukocyte conjugate formation in untrained subjects. *Thromb Res* 2008;**122**:77–84.
48. Ikarugi H, Shibata M, Shibata S, Ishii H, Taka T, Yamamoto J. High intensity exercise enhances platelet reactivity to shear stress and coagulation during and after exercise. *Pathophysiol Haemost Thromb* 2003;**33**:127–133.
49. Thompson PD, Franklin BA, Balady GJ, Blair SN, Corrado D, Estes NAM, Fulton JE, Gordon NF, Haskell WL, Link MS, Maron BJ, Mittleman MA, Pelliccia A, Wenger NK, Willich SN, Costa F 3rd; American College of Sports Medicine. Exercise and acute cardiovascular events placing the risks into perspective: a scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism and the Council on Clinical Cardiology. *Circulation* 2007;**115**:2358–2368.
50. Pavy B, Iliou MC, Meurin P, Tabet JY, Corone S; Functional Evaluation and Cardiac Rehabilitation Working Group of the French Society of Cardiology. Safety of exercise training for cardiac patients. Results of the French Registry of complications during cardiac rehabilitation. *Arch Intern Med* 2006;**166**: 2329–2334.
51. Wewege MA, Ahn D, Yu J, Liou K, Keech A. High-intensity interval training for patients with cardiovascular disease-is it safe? A systematic review. *J Am Heart Assoc* 2018;**7**:e009305.
52. Jamnick NA, Pettitt RW, Granata C, Pyne DB, Bishop DJ. An examination and critique of current methods to determine exercise intensity. *Sports Med* 2020;**50**:1729–1766.
53. Price KJ, Gordon BA, Bird SR, Benson AC. A review of guidelines for cardiac rehabilitation exercise programmes: is there an international consensus? *Eur J Prev Cardiol* 2016;**23**:1715–1733.

54. Chase PJ, Kenjale A, Cahalin LP, Arena R, Davis PG, Myers J, Guazzi M, Forman DE, Ashley E, Peberdy MA, West E, Kelly CT, Bensimhon DR. Effects of respiratory exchange ratio on the prognostic value of peak oxygen consumption and ventilatory efficiency in patients with systolic heart failure. *JACC Heart Fail* 2013;**1**:427–432.
55. Bowen TS, Cannon DT, Begg G, Baliga V, Witte KK, Rossiter HB. A novel cardiopulmonary exercise test protocol and criterion to determine maximal oxygen uptake in chronic heart failure. *J Appl Physiol* 2012;**113**:451–458.
56. Mezzani A, Corra U, Giordano A, Cafagna M, Adriano EP, Giannuzzi P. Unreliability of the %VO₂ reserve versus %heart rate reserve relationship for aerobic effort relative intensity assessment in chronic heart failure patients on or off beta-blocking therapy. *Eur J Cardiovasc Prev Rehabil* 2007;**14**:92–98.
57. Belardinelli R, Lacalprice F, Carle F, Minnucci A, Cianci G, Perna G, D'Eusanio G. Exercise-induced myocardial ischaemia detected by cardiopulmonary exercise testing. *Eur Heart J* 2003;**24**:1304–1313.
58. Niemeijer VM, van't Veer M, Schep G, Spee RF, Hoogeveen A, Kemps HM. Causes of nonlinearity of the oxygen uptake efficiency slope: a prospective study in patients with chronic heart failure. *Eur J Prev Cardiol* 2014;**21**:347–353.
59. Iannetta D, Inglis EC, Mattu AT, Fontana FY, Pogliaghi S, Keir DA, Murias JM. A critical evaluation of current methods for exercise prescription in women and men. *Med Sci Sports Exerc* 2020;**52**:466–473.
60. Bensimhon DR, Leifer ES, Ellis SJ, Fleg JL, Keteyian SJ, Piña IL, Kitzman DW, McKelvie RS, Kraus WE, Forman DE, Kao AJ, Whellan DJ, O'Connor CM, Russell SD. Reproducibility of peak oxygen uptake and other cardiopulmonary exercise testing parameters in patients with heart failure (from the Heart Failure and A Controlled Trial Investigating Outcomes of exercise training). *Am J Cardiol* 2008;**102**:712–717.
61. Myers J, Goldsmith RL, Keteyian SJ, Brawner CA, Brazil DA, Aldred H, Ehrman JK, Burkhead D. The ventilatory anaerobic threshold in heart failure: a multicenter evaluation of reliability. *J Card Fail* 2010;**16**:76–83.
62. Cohen-Solal A, Zannad F, Kavanakis JG, Gueret P, Aupetit JF, Kolsky H. Multicentre study of the determination of peak oxygen uptake and ventilatory threshold during bicycle exercise in chronic heart failure. Comparison of graphical methods, interobserver variability and influence of the exercise protocol. The VO₂ French Study Group. *Eur Heart J* 1991;**12**:1055–1063.
63. Beckers PJ, Possemiers NM, Van Craenenbroeck EM, Van Berendoncks AM, Wuyts K, Vrints CJ, Conraads VM. Comparison of three methods to identify the anaerobic threshold during maximal exercise testing in patients with chronic heart failure. *Am J Phys Med Rehabil* 2012;**91**:148–155.
64. Barron A, Dhutia N, Mayet J, Hughes AD, Francis DP, Wensel R. Test-retest repeatability of cardiopulmonary exercise test variables in patients with cardiac or respiratory disease. *Eur J Prev Cardiol* 2014;**21**:445–453.
65. Poole DC, Rossiter HB, Brooks GA, Gladden LB. The anaerobic threshold: 50± years of controversy. *J Physiol* 2021;**599**:737–767.
66. Meyer K, Schwaibold M, Hajric R, Westbrook S, Ebfeld D, Leyk D. Delayed VO₂ kinetics during ramp exercise: a criterion for cardiopulmonary exercise capacity in chronic heart failure. *Med Sci Sports Exerc* 1998;**30**:643–648.
67. Faude O, Meyer T, Kindermann W. The work rate corresponding to ventilatory threshold during steady-state and ramp exercise. *Int J Sports Physiol Perform* 2006;**1**:222–232.
68. Wolpert AE, Burgos DJ, Janot JM, Dalleck LC. Is a threshold based model a superior method to the relative percent concept for establishing individual exercise intensity? A randomized controlled trial. *BMC Sports Sci Med Rehabil* 2015;**7**:16.
69. Weatherwax RM, Harris NK, Kilding AE, Dalleck LC. Incidence of VO_{2max} responders to personalized vs standardized exercise prescription. *Med Sci Sports Exerc* 2019;**51**:681–691.
70. Abreu A, Frederix I, Dendale P, Janssen A, Doherty P, Piepoli MF. Standardization and quality improvement of secondary prevention through cardiovascular rehabilitation programmes in Europe: the avenue towards EAPC accreditation programme: a position statement of the Secondary Prevention and Rehabilitation Section of the European Association of Preventive Cardiology (EAPC). *Eur J Prev Cardiol* 2020. doi: 10.1177/2047487320924912.
71. Hansen D, Dendale P, Berger J, Meeusen R. The importance of an exercise testing protocol for detecting changes of peak oxygen uptake in cardiac rehabilitation. *Arch Phys Med Rehabil* 2007;**88**:1716–1719.
72. Lalonde F, Poirier P, Sylvestre MP, Arvisais D, Curnier D. Exercise-induced ischemic preconditioning detected by sequential exercise stress tests: a meta-analysis. *Eur J Prev Cardiol* 2015;**22**:100–112.
73. Noel M, Jobin J, Marcoux A, Poirier P, Dagenais GR, Bogaty P. Can prolonged exercise-induced myocardial ischaemia be innocuous? *Eur Heart J* 2007;**28**:1559–1565.
74. Möbius-Winkler S, Uhlemann M, Adams V, Sandri M, Erbs S, Lenk K, Mangner N, Mueller U, Adam J, Grunze M, Brunner S, Hilberg T, Mende M, Linke AP, Schuler G. Coronary collateral growth induced by physical exercise: results of the impact of intensive exercise training on coronary collateral circulation in patients with stable coronary artery disease (EXCITE) trial. *Circulation* 2016;**133**:1438–1448.
75. Noel M, Jobin J, Marcoux A, Poirier P, Dagenais G, Bogaty P. Comparison of myocardial ischemia on the ergocycle versus the treadmill in patients with coronary heart disease. *Am J Cardiol* 2010;**105**:633–639.
76. Borg GA. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc* 1982;**14**:377–381.
77. Chen MJ, Fan X, Moe ST. Criterion-related validity of the Borg ratings of perceived exertion scale in healthy individuals: a meta-analysis. *J Sports Sci* 2002;**20**:873–899.
78. Dunbar CC, Glickman-Weiss EL, Bursztyn DA, Kurtich M, Quiroz A, Conley P. A submaximal treadmill test for developing target ratings of perceived exertion for outpatient cardiac rehabilitation. *Percept Mot Skills* 1998;**87**:755–759.
79. Noble BJ. Clinical applications of perceived exertion. *Med Sci Sports Exerc* 1982;**14**:406–411.
80. Robertson RJ. Exercise testing and prescription using RPE as a criterion variable. *Int J Sport Psychol* 2001;**32**:177–188.
81. Eston R, Connolly D. The use of ratings of perceived exertion for exercise prescription in patients receiving beta-blocker therapy. *Sports Med* 1996;**21**:176–190.
82. Borg G. *An Introduction to Borg's RPE Scale*. New York: Movement Publications; 1985.
83. Gondoni LA, Nibbio F, Caetani G, Augello G, Titon AM. What are we measuring? Considerations on subjective ratings of perceived exertion in obese patients for exercise prescription in cardiac rehabilitation programs. *Int J Cardiol* 2010;**140**:236–238.
84. Casillas JM, Gudjoncik A, Gremaux V, Aulagne J, Besson D, Laroche D. Assessment tools for personalizing training intensity during cardiac rehabilitation: literature review and practical proposals. *Ann Phys Rehabil Med* 2017;**60**:43–49.
85. Saini M, Kulandaivelan S, Devi P, Saini V. The talk test-A costless tool for exercise prescription in Indian cardiac rehabilitation. *Indian Heart J* 2018;**70**:S466–S470.
86. Fletcher GF, Ades PA, Kligfield P, Arena R, Balady GJ, Bittner VA, Coke LA, Fleg JL, Forman DE, Gerber TC, Gulati M, Madan K, Rhodes J, Thompson PD, Williams MA; American Heart Association Exercise, Cardiac Rehabilitation, and Prevention Committee of the Council on Clinical Cardiology, Council on Nutrition, Physical Activity and Metabolism, Council on Cardiovascular and Stroke Nursing, and Council on Epidemiology and Prevention. Exercise standards for testing and training: a scientific statement from the American Heart Association. *Circulation* 2013;**128**:873–934.
87. Sørensen L, Larsen KSR, Petersen AK. Validity of the talk test as a method to estimate ventilatory threshold and guide exercise intensity in cardiac patients. *J Cardiopulm Rehabil Prev* 2020;**40**:330–334.
88. Nielsen SG, Buus L, Hage T, Olsen H, Walsøe M, Vinther A. The graded cycling test combined with the talk test is reliable for patients with ischemic heart disease. *J Cardiopulm Rehabil Prev* 2014;**34**:276–280.
89. Sánchez-Delgado JC, Camargo Sepulveda DC, Cardona Zapata A, Franco Pico MY, Santos Blanco LM, Jácome Hortúa AM, Dutra de Souza HC, Angarita-Fonseca A. The effects of maintenance cardiac rehabilitation: a systematic review. *J Cardiopulm Rehabil Prev* 2020;**40**:224–244.
90. Belardinelli R, Georgiou D, Cianci G, Purcaro A. 10-year exercise training in chronic heart failure: a randomized controlled trial. *J Am Coll Cardiol* 2012;**60**:1521–1528.
91. Hansen D, Mathijs W, Michiels Y, Bonnè K, Alders T, Hermans A, et al. Phase III multidisciplinary exercise-based rehabilitation is associated with fewer hospitalizations due to adverse cardiovascular events in coronary artery disease patients. *Eur J Prev Cardiol* 2020; [e-pub ahead of print].
92. Squires RW, Kaminsky LA, Porcari JP, Ruff JE, Savage PD, Williams MA. Progression of exercise training in early outpatient cardiac rehabilitation: an official statement from the American association of cardiovascular and pulmonary rehabilitation. *J Cardiopulm Rehabil Prev* 2018;**38**:139–146.
93. Amorim H, Cadilha R, Parada F, Rocha A. Progression of aerobic exercise intensity in a cardiac rehabilitation program. *Rev Port Cardiol* 2019;**38**:281–286.
94. Haeny T, Nelson R, Ducharme J, Zuhl M. The influence of exercise workload progression across 36 sessions of cardiac rehabilitation on functional capacity. *J Cardiovasc Dev Dis* 2019;**6**:32.
95. Rognum Ø, Hetland E, Helgerud J, Hoff J, Slørdahl SA. High intensity aerobic interval exercise is superior to moderate intensity exercise for increasing aerobic capacity in patients with coronary artery disease. *Eur J Cardiovasc Prev Rehabil* 2004;**11**:216–222.
96. Keteyian SJ, Brawner CA, Ehrman JK, Ivanhoe R, Boehmer JP, Abraham WT. Reproducibility of peak oxygen uptake and other cardiopulmonary exercise parameters: implications for clinical trials and clinical practice. *Chest* 2010;**138**:950–955.

97. Heber S, Sallaberger-Lehner M, Hausharter M, Volf I, Ocenasek H, Gabriel H, Pokan R. Exercise-based cardiac rehabilitation is associated with a normalization of the heart rate performance curve deflection. *Scand J Med Sci Sports* 2019;**29**:1364–1374.
98. Ekkekakis P. Let them roam free? Physiological and psychological evidence for the potential of self-selected exercise intensity in public health. *Sports Med* 2009;**39**:857–888.
99. Rose EA, Parfitt G. Exercise experience influences affective and motivational outcomes of prescribed and self-selected intensity exercise. *Scand J Med Sci Sports* 2012;**22**:265–277.
100. Kamiya K, Masuda T, Tanaka S, Hamazaki N, Matsue Y, Mezzani A, Matsuzawa R, Nozaki K, Maekawa E, Noda C, Yamaoka-Tojo M, Arai Y, Matsunaga A, Izumi T, Ako J. Quadriceps strength as a predictor of mortality in coronary artery disease. *Am J Med* 2015;**128**:1212–1219.
101. Boujemaa H, Verboven K, Hendriks M, Rummens J-L, Frederix I, Eijnde BO, Dendale P, Hansen D. Muscle wasting after coronary artery bypass graft surgery: impact on post-operative clinical status and effect of exercise-based rehabilitation. *Acta Cardiol* 2020;**75**:406–410.
102. Hansen D, Linsen L, Verboven K, Hendriks M, Rummens J-L, van Erum M, Eijnde BO, Dendale P. Magnitude of muscle wasting early after on-pump coronary artery bypass graft surgery and exploration of aetiology. *Exp Physiol* 2015;**100**:818–828.
103. Melenovsky V, Hlavata K, Sedivy P, Dezortova M, Borlaug BA, Petrak J, Kautzner J, Hajek M. Skeletal muscle abnormalities and iron deficiency in chronic heart failure. An exercise 31P magnetic resonance spectroscopy study of calf muscle. *Circ Heart Fail* 2018;**11**:e004800.
104. Hollings M, Mavros Y, Freeston J, Fatarone Singh M. The effect of progressive resistance training on aerobic fitness and strength in adults with coronary heart disease: a systematic review and meta-analysis of randomised controlled trials. *Eur J Prev Cardiol* 2017;**24**:1242–1259.
105. Gómez-Cabello A, Ara I, González-Agüero A, Casajús JA, Vicente-Rodríguez G. Effects of training on bone mass in older adults: a systematic review. *Sports Med* 2012;**42**:301–325.
106. Raymond MJ, Bramley-Tzerfos RE, Jeffs KJ, Winter A, Holland AE. Systematic review of high-intensity progressive resistance strength training of the lower limb compared with other intensities of strength training in older adults. *Arch Phys Med Rehabil* 2013;**94**:1458–1472.
107. Borde R, Hortobágyi T, Granacher U. Dose–response relationships of resistance training in healthy old adults: a systematic review and meta-analysis. *Sports Med* 2015;**45**:1693–1720.
108. Schoenfeld BJ, Grgic J, Ogborn D, Krieger JW. Strength and hypertrophy adaptations between low- vs. high-load resistance training: a systematic review and meta-analysis. *J Strength Cond Res* 2017;**31**:3508–3523.
109. Holm L, van Hall G, Rose AJ, Miller BF, Doessing S, Richter EA, Kjaer M. Contraction intensity and feeding affect collagen and myofibrillar protein synthesis rates differently in human skeletal muscle. *Am J Physiol Endocrinol Metab* 2010;**298**:E257–E269.
110. Jenkins NDM, Miramonti AA, Hill EC, Smith CM, Cochrane-Snyman KC, Housh TJ, Cramer JT. Greater neural adaptations following high- vs. low-load resistance training. *Front Physiol* 2017;**8**:331.
111. Myers J, Arena R, Franklin B, Pina I, Kraus WE, McInnis K, Balady GJ; American Heart Association Committee on Exercise, Cardiac Rehabilitation, and Prevention of the Council on Clinical Cardiology, the Council on Nutrition, Physical Activity, and Metabolism, and the Council on Cardiovascular Nursing. Recommendations for clinical exercise laboratories: a scientific statement from the American Heart Association. *Circulation* 2009;**119**:3144–3161.
112. Xanthos PD, Gordon BA, Kingsley MI. Implementing resistance training in the rehabilitation of coronary heart disease: a systematic review and meta-analysis. *Int J Cardiol* 2017;**230**:493–508.
113. Marzolini S, Oh PI, Brooks D. Effect of combined aerobic and resistance training versus aerobic training alone in individuals with coronary artery disease: a meta-analysis. *Eur J Prev Cardiol* 2012;**19**:81–94.
114. Lee J, Lee R, Stone AJ. Combined aerobic and resistance training for peak oxygen uptake, muscle strength, and hypertrophy after coronary artery disease: a systematic review and meta-analysis. *J Cardiovasc Transl Res* 2020;**13**:601–611.
115. Niewiadomski W, Pilis W, Laskowska D, Gąsiorowska A, Cybulski G, Strasz A. Effects of a brief Valsalva manoeuvre on hemodynamic response to strength exercises. *Clin Physiol Funct Imaging* 2012;**32**:145–157.
116. Marques DL, Neiva HP, Fial LB, Gil MH, Marques MC. Acute effects of low and high-volume resistance training on hemodynamic, metabolic and neuromuscular parameters in older adults. *Exp Gerontol* 2019;**125**:110685.
117. Health-related physical fitness testing and interpretation (chapter 4). In: Riebe D, ed. *ACSM's Guidelines for Exercise Testing and Prescription*, 10th edn. Philadelphia: Wolters Kluwer; 2018.
118. Levinger I, Goodman C, Hare DL, Jerums G, Toia D, Selig S. The reliability of the 1RM strength test for untrained middle-aged individuals. *J Sci Med Sport* 2009;**12**:310–316.
119. Werber-Zion G, Goldhammer E, Shaar A, Pollock ML. Left ventricular function during strength testing and resistance exercise in patients with left ventricular dysfunction. *J Cardiopulm Rehabil* 2004;**24**:100–109.
120. Haykowsky M, Taylor D, Teo K, Quinney A, Humen D. Left ventricular wall stress during leg-press exercise performed with a brief Valsalva maneuver. *Chest* 2001;**119**:150–154.
121. Williams MA, Haskell WL, Ades PA, Amsterdam EA, Bittner V, Franklin BA, Gulanick M, Laing ST, Stewart KJ; American Heart Association Council on Nutrition, Physical Activity, and Metabolism. Resistance exercise in individuals with and without cardiovascular disease: 2007 update: a scientific statement from the American Heart Association Council on Clinical Cardiology and Council on Nutrition, Physical Activity, and Metabolism. *Circulation* 2007;**116**:572–584.
122. Wood TM, Maddalozzo GF, Harter RA. Accuracy of seven equations for predicting 1-RM performance of apparently healthy, sedentary older adults. *Meas Phys Educ Exerc Sci* 2002;**6**:67–94.
123. Brzycki M. Strength testing—prediction a one rep maximum from reps-to-fatigue. *J Phys Educ Recr Dance* 1993;**64**:88–90.
124. Epley B. *Poundage Chart. Boyd Epley Workout*. Lincoln, NE: Body Enterprises; 1985.
125. Gearhart RF, Lagally KM, Riechman SE, Andrews RD, Robertson RJ. Strength tracking using the OMNI resistance exercise scale in older men and women. *J Strength Conditioning Res* 2009;**23**:1011–1015.
126. Gearhart RF, Lagally KM, Riechman SE, Andrews RD, Robertson RJ. RPE at relative intensities following 12 weeks of resistance exercise training in older adults. *Percept Motor Skills* 2008;**106**:893–903.
127. Gomes-Neto M, Durães AR, Conceição LSR, Roevers L, Silva CM, Alves IGN, Ellingsen Ø, Carvalho VO. Effect of combined aerobic and resistance training on peak oxygen consumption, muscle strength and health-related quality of life in patients with heart failure with reduced left ventricular ejection fraction: a systematic review and meta-analysis. *Int J Cardiol* 2019;**293**:165–175.
128. La Scala Teixeira CV, Evangelista AL, Pereira PEA, Da Silva-Grigoletto ME, Bocalini DS, Behm DG. Complexity: a novel load progression strategy in strength training. *Front Physiol* 2019;**10**:839.
129. Williams TD, Toluoso DV, Fedewa MV, Esco MR. Comparison of periodized and non-periodized resistance training on maximal strength: a meta-analysis. *Sports Med* 2017;**47**:2083–2100.
130. de Oliveira Segundo VH, Piuvezam G, de Azevedo KPM, de Medeiros HJ, Leitão JC, Knackfuss MI. Can people self-select an exercise intensity sufficient to enhance muscular strength during weight training? A systematic review protocol of intervention studies. *Medicine* 2019;**98**:e17290.