

Secondary prevention through cardiac rehabilitation: physical activity counselling and exercise training

Key components of the position paper from the Cardiac Rehabilitation Section of the European Association of Cardiovascular Prevention and Rehabilitation

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Cardiac patients after an acute event and/or with chronic heart disease deserve special attention to restore their quality of life and to maintain or improve functional capacity. They require counselling to avoid recurrence through a combination of adherence to a medication plan and adoption of a healthy lifestyle. These secondary prevention targets are included in the overall goal of cardiac rehabilitation (CR). Cardiac rehabilitation can be viewed as the clinical application of preventive care by means of a professional multi-disciplinary integrated approach for comprehensive risk reduction and global long-term care of cardiac patients. The CR approach is delivered in tandem with a flexible follow-up strategy and easy access to a specialized team. To promote implementation of cardiac prevention and rehabilitation, the CR Section of the EACPR (European Association of Cardiovascular Prevention and Rehabilitation) has recently completed a Position Paper, entitled 'Secondary prevention through cardiac rehabilitation: A condition-oriented approach'. Components of multidisciplinary CR for seven clinical presentations have been addressed. Components include patient assessment, physical activity counselling, exercise training, diet/nutritional counselling, weight control management, lipid management, blood pressure monitoring, smoking cessation, and psychosocial management. Cardiac rehabilitation services are by definition multi-factorial and comprehensive, with physical activity counselling and exercise training as central components in all rehabilitation and preventive interventions. Many of the risk factor improvements occurring in CR can be mediated through exercise training programmes. This call-for-action paper presents the key components of a CR programme: physical activity counselling and exercise training. It summarizes current evidence-based best practice for the wide range of patient presentations of interest to the general cardiology community.

Keywords

Cardiac rehabilitation • Exercise training • Physical activity • Prevention

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Rationale

There has been impressive progress in pharmacological therapies and in sophisticated technology-based diagnostic and therapeutic procedures in cardiovascular diseases in recent years. As a consequence, a greater number of men and women now survive acute events but with a heavier burden of chronic conditions and clinical need.

A management approach based on interventional cardiology and medication is thus not effective: ‘...the burden of established cardiovascular disease may also be reduced by early diagnosis, appropriate disease management, rehabilitation and prevention, including structured lifestyle counselling’ (European Heart Health Charter, Article 7).¹

After an acute event or with chronic heart conditions, patients need structured support to restore their quality of life and to maintain or improve functional capacity. They require counselling to prevent event recurrence by adhering to a medication plan and adopting a healthy lifestyle. Cardiac rehabilitation (CR) can be viewed as the clinical application of preventive care by means of a professional multidisciplinary integrated approach for comprehensive risk reduction and global long-term care of cardiac patients. This is accompanied by a flexible follow-up strategy, and easy access to a specialized team. Thus, CR programmes are recommended (Class I) by the European Society of Cardiology (ESC),^{2,3} American Heart Association (AHA), and American College of Cardiology (ACC)^{4–6} in the treatment of patients with coronary artery disease (CAD) and chronic heart failure.^{7–9} Moreover, it is a cost-effective intervention following an acute coronary event and heart failure, since it improves prognosis by reducing recurrent hospitalization and health care expenditures, while prolonging life.^{10,11}

Despite its well-documented benefits, CR is vastly underutilized. Only about a third of coronary patients in Europe receive any form of CR.^{12,13} The results of the EUROASPIRE audits of preventive care of coronary patients over the last 12 years show adverse lifestyle trends and an increasing prevalence of cardiovascular risk factors in cardiac patients.¹⁴ Moreover, even when implemented, most CR programmes are short-term interventions. Some recent studies on prevention and CR (e.g. EuroAction¹⁵ and GOSPEL¹⁶) have specifically aimed at maintaining beneficial longer term life changes and improving prognosis in cardiac patients.

Structure and aim of the paper

The CR Position Paper¹⁷ adopts a pragmatic approach with practical guidelines on seven clinical conditions: acute coronary syndrome and post primary percutaneous coronary intervention (PCI), stable CAD and elective PCI, cardiac surgery, coronary artery and valve heart surgery, chronic heart failure; cardiac transplantation, diabetes mellitus, and peripheral arterial disease. Core CR components include patient assessment, physical activity counselling, exercise training, diet/nutritional counselling, weight control management, lipid management, blood pressure monitoring, smoking cessation, and psychosocial management.

In this ‘Call for action’ paper, addressed to the wider community of general cardiologists, we aimed to highlight the key aspects of CR: physical activity and exercise training. Many of the multi-risk

factor benefits of the CR programme have been documented to be mediated through regular physical activity and exercise training:^{18–20} increased fibrinolysis and decreased coagulability,²¹ anti-inflammatory effects,²² improved autonomic function,²³ prevention and restoration of age-related decline in endothelium-dependent vasodilatation, which may also help explain the improvement in hyperaemic myocardial blood flow.²⁴ Exercise-related benefits in exercise training slow CAD progression.²⁵ Since peak oxygen uptake is an important predictor of cardiac and all-cause death, a small gain in aerobic power may improve not only functional capacity but also survival prospects.^{26,27} The assessment, counselling, and support in the maintenance of physical activity and exercise training are core tasks for the physicians engaged in the prevention of cardiovascular disease and are addressed here.

The development of the position paper and the present ‘Call for action’ manuscript involved a systematic process of evaluation and synthesis of 2003–2009 guidelines including ESC, ACC/AHA, and the National Institutes of Health. When available, Classification of Recommendations and Level of Evidence are expressed in ACC/AHA format. Thereafter, both well-established aspects of physical activity and exercise training, and less-established or more controversial issues in CR are presented and discussed (Tables 1–3, and ‘Research Needs and Future Directions’ section). Finally, a glossary of the more common terms and concepts used here is provided (Table 4).

Physical activity counselling

Physical activity is defined as any bodily movement produced by contraction of skeletal muscles and resulting in energy expenditure above the basal level and, as such, part of lifestyle intervention. The following points are established/general agreed activities applicable to all conditions in CR (detailed issues specific for each condition are mentioned separately in Table 1):

- Assess physical activity level by history: domestic, occupational, and recreational needs; activities relevant to age, gender, and daily life; readiness to change behaviour; self-confidence; barriers to increase physical activity, and social support in making positive changes.
- Advise individualized physical activity according to patient’s age, past habits, co-morbidities, preferences, and goals.
- Recommend a minimum of 30 min/session of moderately vigorous aerobic activity, on most days of the week, or at least three to four times per week; gradual increases in daily lifestyle activities over time with their incorporation into daily routine.
- Reassure regarding the safety of the recommended protocol.
- Encourage the involvement in leisure activities, positively enjoyable and in group programme because patients tend to revert to their previous sedentary habits over time.
- Educate on the need for lifelong continuation of physical conditioning and the risk of relapses. If any interruption has occurred, physical, social, and psychological barriers to attendance should be explored, and alternative approaches suggested.
- Expected outcomes: increased participation in domestic, occupational, and recreational activities. Improved psychosocial well-being, prevention of disability, enhancement of opportunities for independent self-care; improved aerobic fitness and prognosis.

Table 1 Physical activity counselling specific for different clinical conditions

Components	Established/generally agreed issues	Class (level)
Post-ACS and post primary PCI ^{2–5,44,45}	Assess:	
	Risk must be assessed by physical activity history and exercise testing to guide prescription	I (B)
	Symptom-limited exercise testing after clinical stabilization. Submaximal exercise stress testing in selected cases (Figure 1) ^a	I (C) ^{31–33}
	Recommend:	
	After uncomplicated procedure, physical activity can start the next day. After a large and/or complicated myocardial damage, physical activity should start after clinical stabilization, and be increased slowly, according to the symptoms	I (A)
	In the presence of preserved exercise capacity without symptoms, patient can resume routine physical activity for 30–60 min, such as brisk walking, supplemented by an increase in daily activities (such as walking breaks at work, gardening, or household work); otherwise, the patient should resume physical activity at 50% of maximal exercise capacity and gradually increase	I (B)
	Physical activity should be a combination of activities like walking, climbing stairs, cycling	
Stable CAD and post elective PCI ^{2,45,46}	Assess: exercise capacity and ischaemia threshold by symptom limited exercise stress test (Figure 1). ^a Exercise or pharmacological imaging technique in symptomatic patients with un-interpretable ECG	I (B)
	Recommend: refer to 'Post-ACS and post primary PCI' issues	
Post cardiac surgery, coronary artery ⁴⁷ and valve heart surgery ^{48,49}	Assess: exercise capacity to guide exercise prescription:	I (C)
	Submaximal exercise stress test as soon as possible	
	A maximal exercise test after surgical wound stabilization (Figure 2)	
	Recommend: physical activity counselling according to wound healing and exercise capacity	
	Also refer to 'Post-ACS and post primary PCI' issues	
Chronic heart failure ^{7,8}	Assess: peak exercise capacity by maximal symptom-limited cardiopulmonary exercise testing. For testing protocol, small increments 5–10 W per minute on bicycle ergometer or modified Bruce or Naughton protocols on treadmill are indicated (in order to achieve max. exercise capacity in 8–12 min)	I (B)
	Recommend: at least 30–60 min/day of moderate-intensity physical activity	I (A)
	Also refer to 'Post-ACS and post primary PCI' issues	
Cardiac transplantation ^{50,51}	Assess: exercise capacity (Figure 3). Also refer to 'Post cardiac surgery' and 'Chronic heart Failure' issues	
	Recommend: Long-term dynamic and resistance exercise to prevent many side-effects of immunosuppressive therapy	
	Exercise intensity relies more on the perceived exertion (i.e. around 12–14 Borg scale) or on the anaerobic threshold (if available) than on a specific heart rate; e.g. instruct the patients to start walking 1.5 km five times weekly at a pace resulting in a perceived exertion of 12–14 on the Borg scale. The pace should be increased slowly over time to Nordic walking	
Diabetes mellitus ⁵²	Assess: Functional capacity and exercise-induced ischaemia by maximal symptom-limited exercise stress testing ^a	I (B)
	Recommend: refer to 'Post-ACS and post primary PCI' issues	I (A)
Peripheral artery disease ^{38,53}	Assess: functional capacity (usually markedly impaired, often <50% of the predicted value) and cause of exercise limitation (e.g. claudication)	
	Exclude occult CAD: perform treadmill or bicycle exercise testing to monitor symptoms, S-T segment and T wave changes, arrhythmias, heart rate and blood pressure responses, also useful for exercise prescription	
	Pain free and maximal walking distance on a treadmill (3.2 km/h and 10% slope)	
	Recommend: exercise activities, especially walking, lasting >30 min, ≥3 times/week. Patients should seek to reach their claudication threshold ('walk until near-maximal pain') to stimulate collateral's formation ^a	

^aSee 'Research Needs and Future Directions' section.

Table 2 Exercise training prescription generally applicable

Mode	Continuous endurance: walking, jogging, cycling, swimming, rowing, stair climbing, elliptical trainers, and aerobic dancing
Duration	At least 20–30 min (preferably 45–60 min)
Frequency	Most days (at least 3 days/week and preferably 6–7 days/week)
Intensity	50–80% of peak oxygen consumption (close to anaerobic threshold) or of peak heart rate or 40–60% of heart rate reserve; 10/20–14/20 of the Borg Rating of Perceived Exertion

A progressive increasing training regimen should be prescribed with regular follow-up controls (at least every 3–6 months), to adjust the duration and the level of the exercise to the reached level of tolerance. Peak oxygen consumption (Peak VO₂) by cardiopulmonary exercise testing is the ideal physiologic marker of intensity; practically surrogate intensity markers are here presented.

Exercise training programme

Exercise training is defined as a sub-category of physical activity in which planned, structured, and repetitive bodily movements are performed to maintain or improve one or more attributes of physical fitness and thus it is a structured intervention over a defined period of time. It should be integrated within the physical activity intervention: all the activities highlighted in the previous paragraph should apply also to the exercise training plan.

The following points are established/general agreed issues in exercise training applicable to all clinical conditions (Table 2) (detailed issues specific for each condition are mentioned separately in Table 3):

- Assess exercise capacity by symptom-limited stress testing, either on bicycle ergometer or on treadmill. In the routine clinical setting, this is not always applicable, particularly in the presence of left ventricular dysfunction (ejection fraction <40%) or after recent surgical intervention (because of the surgical wounds) and therefore sub-maximal exercise evaluation and/or 6 min walk test should be considered.²⁸
- Advise individualized exercise training after careful clinical evaluation, including risk stratification.
- Recommend as general advice sub-maximal endurance aerobic (Table 2).
- Educate on the recognition of symptoms induced by effort. Appropriate behaviour and re-definition of exercise training target should be discussed for the individual patient.
- Expected outcomes: increased cardio-respiratory fitness and enhanced flexibility, muscular endurance, and strength; reduction of symptoms, attenuated physiologic responses to physical challenges, and improved psychosocial well-being.
- Programme settings. During the initial phases supervised in-patient or hospital-based exercise training programmes may be recommended in high-risk cardiovascular patients, i.e. those with impaired systolic left ventricular function, those with severe co-morbidities, leading to significant disability, and in those with recent (<1 week) clinical destabilization. This will verify individual responses and tolerability in a safe clinical setting and will promptly

identify signs and symptoms indicating to modify or terminate the programme. The supervision should include physical examination, assessment of exercise-related symptoms or arrhythmias, and monitoring of heart rate and blood pressure before, during, and after exercise training. The supervised period should be prolonged in patients with new symptoms, clinical signs of decompensation, blood pressure abnormalities, and increased supraventricular or ventricular arrhythmia during exercise.

Research needs and future directions

This Position Paper proposes that both general and specific gaps in knowledge to the implementation of physical activity counselling and exercise training as preventive tools in cardiovascular diseases must be addressed to increase their acceptance, feasibility, and sustainability. The general gaps fall into two categories: healthcare provider-related, and specific skills deficit-related.

Most healthcare providers focus on acute disease presentation. They may lack knowledge about current best evidence of the effectiveness of preventive care; lack skills to carry out behavioural interventions; or lack motivation or time to train or deliver such interventions. Patient-related gaps include lack of knowledge of potential benefits of secondary prevention and difficulties with long-term adherence. Health system-related barriers are lack of incentives for preventive care, with no systematic approach to its implementation as well as practical concerns about costs. As a consequence, exercise-related secondary prevention programmes are generally under-funded, with large discrepancies across different European countries.

Approaches to overcome these gaps include continuing education of healthcare professionals about the negative role of sedentary life and their own modelling role in setting a good example with engagement in healthy lifestyles; and incentives and surveys on physical activity programmes and community-based approaches to increase physical activity participation and to evaluate their cost-effectiveness.

Beside these general knowledge gaps, specific knowledge and skills deficits need to be addressed, as summarized next.

- 1 *Exercise tolerance is affected* by age, gender, conditioning status, and the presence of disease or medications. It typically declines by 10% on average per decade in non-athletic adults, and this decline rate appears to hasten with ageing. It is 10–20% greater in men than in women. Consideration of all these determinants is important when functional capacity in a specific individual is assessed. Equations for age-predicted standards have been published but seldom applied.²⁹
- 2 *Learning a new, different behaviour*, like changing from a sedentary to an active lifestyle, requires the modifications of the several small attitudes and behaviours. Thus, both physiological and psycho-social progression are needed to achieve patient behaviour change by first a gradual and simple promotion of physical activity within one's current domestic, occupational, and leisure settings and only thereafter participation in more structured, more vigorous exercise training. Multiple interventions

Table 4 Glossary of terms

Aerobic training: training that improves the efficiency of the aerobic energy-producing systems and that can improve cardio-respiratory endurance
Anaerobic training: training that improves the efficiency of the anaerobic energy-producing systems and that can increase muscular strength and tolerance for acid-base imbalances during high-intensity effort
Aerobic endurance training/endurance activities: activity supported by aerobic metabolism that engages large muscle groups in a rhythmical manner, including such activities as walking, jogging, running, swimming, cycling, aerobic exercise to music, circuit training
Heart rate reserve (HRR): the difference between maximal heart rate and resting heart rate
Maximal oxygen uptake (VO ₂ max): the maximal capacity for oxygen consumption by the body during maximal exertion. It is determined during dynamic exercise from a 'plateauing' of VO ₂ despite work rate continuing to increase. It is also known as aerobic power, maximal oxygen consumption, and cardiorespiratory endurance capacity
Maximal heart rate (HR max): the highest heart rate value theoretically attainable during an all-out effort to the point of exhaustion
Metabolic equivalent (MET): a unit used to estimate the metabolic cost (oxygen consumption) of physical activity. One MET equals the resting metabolic rate of approximately 3.5 mL O ₂ kg ⁻¹ min ⁻¹
Peak heart rate (peak HR): highest HR achieved on a test performed to the limit of tolerance
Peak oxygen uptake (peak VO ₂): highest VO ₂ achieved on a test performed to the limit of tolerance. No additional criteria are needed for its determination
Physical fitness: a set of attributes that people have or achieve that relates to the ability to perform physical activity
Rating of perceived exertion (RPE): a person's subjective assessment of how hard he or she is working. The Borg scale is a numerical scale for rating perceived exertion
Resistance training: training designed to increase strength, power, and muscle endurance by lifting weight
Speed: a skill-related component of physical fitness that relates to the ability to perform a movement within a short period of time
Strength: the ability of the muscle to exert force
Training heart rate (THR): a heart rate (HR) goal established by using the HR equivalent to a selected training level (percentage of VO ₂ max). For example, if a training level of 75% VO ₂ max is desired, the VO ₂ at 75% is determined and the HR corresponding to this VO ₂ is selected as the THR

conducted over time may need to be employed to sustain physical activity behaviour modification. It is not yet evident which strategies have most relevance in promoting physical activity across groups.³⁰

3 *Exercise testing to initiate an exercise training programme in specific clinical conditions.* In general, there is a dearth of studies comparing different aerobic exercise regimens in cardiac patients.³¹ Moreover there are controversial aspects of exercise testing applicable to specific clinical conditions, as discussed in the following paragraphs.

3.1 *Post-ACS and post primary PCI.* Although symptom-limited exercise testing can be safely performed 7 to 14 days after

primary PCI (when an exercise training programme can be initiated),³² its application is scarce in routine clinical practice. The ACC/AHA guidelines recommend pre-discharge sub-maximal exercise testing at 4–6 days after myocardial infarction for prognostic assessment, activity prescription, ECG monitoring, and evaluation of medical therapy.^{28,33} In the training programme, exercise intensity should be set to 70–85% of the peak heart rate. In case of symptomatic exercise-induced ischaemia, patients exercising to a 70–85% ischaemic heart rate, or to the early onset of angina, have been suggested. In asymptomatic exercise-induced ischaemia, exercising to 70–85% of the heart rate at the onset of ischaemia (defined as ≥ 1 mm of ST depression) has been proposed.³¹ Another area of uncertainty concerns the need for continuous ECG monitoring and the opportunity to train above the ischaemic threshold.

3.2 *Stable CAD and post elective PCI.* Symptom-limited exercise testing can be safely performed the day after routine PCI, but scarcely performed.³⁴

3.3 *Chronic heart failure.* Several controversies still need to be addressed.

3.3.1 *Exercise training:* this is recommended for NYHA functional class II or III patients, tailored to the individual's exercise tolerance, because it improves exercise capacity and quality of life. However, ExTraMATCH,¹¹ Cochrane meta-analysis,³⁵ and HF-ACTION trial³⁶ have provided somewhat contradictory results about its effectiveness on morbidity and mortality in stable patients.

3.3.2 *Mixed modalities:* limited information about combined aerobic, strength, interval, resistance, and respiratory exercise training is available. Although the safety of all of these exercise modalities is undisputed, the question about the most effective training mode remains to be answered.

3.3.3 *Heart rate:* this can be used for exercise prescription or to monitor exercise intensity. However, its use is inadequate in patients with severely reduced exercise capacity, chronotropic incompetence, negative chronotropic medications, co-morbidities with an impact on exercise performance, atrial fibrillation, or after heart transplantation.

3.3.4 *ICDs and exercise training:* although exercise training seems feasible and safe in patients with ICD, a supervised setting with qualified staff and constant surveillance is needed in patients with frequent ventricular arrhythmias. Experience is limited and data are available from highly specialized centres. Concerning the intensity of exercise, a heart rate training threshold at ICD detection rate minus 20 b.p.m. has been proposed.³⁷

3.4 *Cardiac transplantation.* although exercise training would theoretically delay or prevent CAD progression in the transplanted heart, evidence is lacking.

3.5 *Diabetes mellitus.* A symptom-limited maximal exercise test is mandatory for all diabetic patients before commencing regular physical activity. Exercise capacity and maximal heart rate need to be determined, to tailor an individual exercise programme.

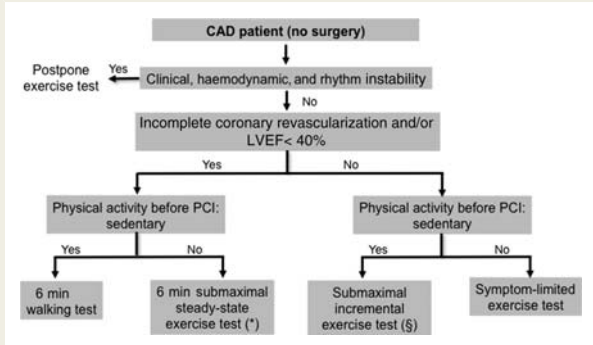


Figure 1 Proposed algorithm for functional evaluation in exercise prescription in coronary artery disease (CAD) patients not treated with cardiac surgery. The following general criteria should be considered in planning an exercise testing modality for exercise prescription. *Safety*: stability of clinical, haemodynamic, and rhythmic parameters (e.g. symptomatic Brady-arrhythmias, persistent or paroxysmal atrial flutter/fibrillation with inadequate rate control, exercise-induced persistent or paroxysmal supraventricular tachycardia, exercise-induced ventricular premature contractions, ventricular tachycardia/fibrillation), ischaemic and angina threshold (in case of incomplete revascularization), degree of left ventricular impairment. *Associated factors*: sedentary habits, orthopaedic limitations, occupational and recreational needs. *Upper limit for terminating submaximal 6 min single stage (steady-state) exercise testing: rating of perceived exertion (Borg scale) 11–13/20 or maximal heart rate = heart rate at standing rest + 20–30 b.p.m.⁵⁴ §Upper limit for terminating sub maximal incremental testing: maximal heart rate = 70% HR reserve or 85% of age-predicted maximal heart rate.⁵⁵

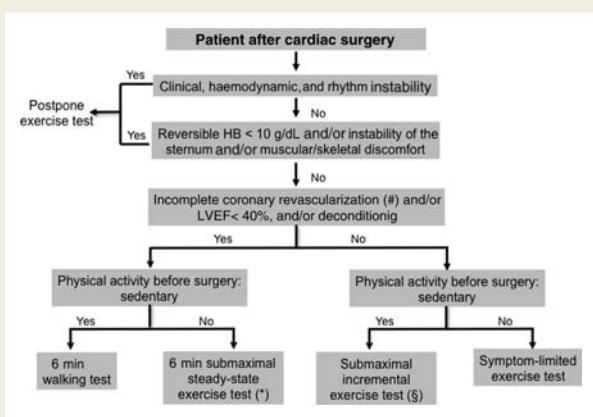


Figure 2 Proposed algorithm for functional evaluation in exercise prescription after cardiac surgery, i.e. coronary artery bypass graft (CABG), valve repair interventions. The following general criteria should be considered in planning exercise testing modality for exercise prescription: *Safety*; *Co-morbidities*: haemoglobin concentration (HB) values; muscular-skeletal discomfort, healing issues at the incision sites; *Associated factors*: deconditioning due to prolonged hospitalization, sedentary habits, orthopaedic limitations, occupational and recreational needs. #Incomplete revascularization in case of CABG (see also legend to Figure 1).

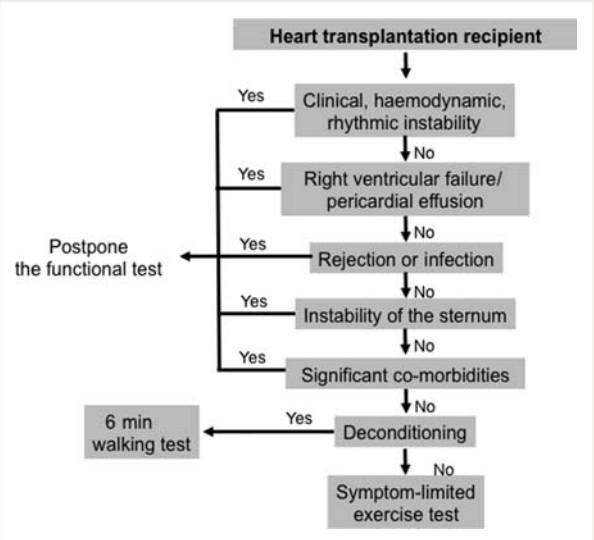


Figure 3 Proposed algorithm for functional evaluation in exercise prescription after heart transplantation. The following general criteria should be considered in planning an exercise testing modality for exercise prescription: *Safety*; *Co-morbidities* [anaemia (HB < 10 gr/dL), kidney failure (creatinine level > 3 mg/dL), neurological disorders, haematological disorders, diaphragmatic failure]; *associated factors* (see also legends to Figures 1 and 2).

3.6 *Peripheral artery disease*. The time course of the response to an exercise training programme is not fully elucidated in peripheral artery disease: clinical benefits have been observed as early as 4 weeks after initiation. They may continue to accrue after 6 months of supervised exercise training, three times per week, and sustained when continued for an additional 12 months. There are no data to support the efficacy of the informal ‘Go home and walk’ advice, however unsupervised exercise training programmes may be adopted [Ib, (B)].³⁸

4. *Resistance training*. As mentioned above, if there is a lack of studies comparing elements of the aerobic training regimen in cardiac patients, there is even less information on resistance exercise training studies.³⁹ General recommendations for training regimens include using 30–40% of the 1-repetition maximum for the upper body and 40–50% of the 1-repetition maximum for lower body exercises, with 12 to 15 repetitions in 1 set repeated two to three times weekly.³¹ Nevertheless, because most of the outcome data discussed above relate to aerobic exercise training, resistance exercise in cardiac patients should be in addition to and not in replacement of the aerobic training component.

According to the most updated recommendations and revisions of the literature,^{40–43} three algorithms for functional evaluation in exercise prescription in CAD patients without cardiac surgery (Figure 1), in patient after cardiac surgery (Figure 2) and after heart transplantation (Figure 3), are proposed. Sub-maximal exercise evaluations and 6 min walk tests are presented as alternatives to symptom-limited stress testing, which should be considered the first choice whenever it is possible.

Conclusion

In CR, all of the goals of secondary prevention are targeted by promoting lifestyle change and patient adherence to pharmacological therapy. While it is clearly understood and accepted that an isolated exercise programme is not CR, physical activity and exercise training must be recognized as the core components from which to build a comprehensive CR programme. Physical activity will be the carrier of change and of maintenance of healthy behaviours in the longer term, with positive consequences on self-confidence and esteem, socialization, return to work, and normalization of daily life activities. In sum, CR programmes, with a core of physical activity and exercise training, promote better quality of life, better control of classical cardiovascular risk factors, and, consequently, a lower rate of events and longer higher quality survival. Advocating for CR programmes for every patient who can benefit must be on every cardiologist's agenda.

Conflict of interest: none declared.

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