ΕΘΝΙΚΟ ΚΑΙ ΚΑΠΟΔΙΣΤΡΙΑΚΟ ΠΑΝΕΠΙΣΤΗΜΙΟ ΑΘΗΝΩΝ

ΣΧΟΛΗ ΕΠΙΣΤΗΜΩΝ ΥΓΕΙΑΣ

ΙΑΤΡΙΚΗ ΣΧΟΛΗ

ΤΟΜΕΑΣ ΠΑΘΟΛΟΓΙΑΣ

Α' ΠΝΕΥΜΟΝΟΛΟΓΙΚΗ ΚΛΙΝΙΚΗ

Δ/ΝΤΗΣ ΚΑΘΗΓΗΤΗΣ ΝΙΚΟΛΑΟΣ ΚΟΥΛΟΥΡΗΣ

Π.Μ.Σ. ΚΑΡΔΙΟΠΝΕΥΜΟΝΙΚΗ ΑΠΟΚΑΤΑΣΤΑΣΗ ΚΑΙ ΑΠΟΚΑΤΑΣΤΑΣΗ ΠΑΣΧΟΝΤΩΝ ΜΕΘ

ΔΙΠΛΩΜΑΤΙΚΗ ΕΡΓΑΣΙΑ

ΘΕΜΑ: «TELEREHABILITATION ΣΕ ΧΡΟΝΙΑ ΚΑΡΔΙΑΚΗ ΑΝΕΠΑΡΚΕΙΑ ΚΑΙ ΣΤΕΦΑΝΙΑΙΑ ΝΟΣΟ»

ΤΣΟΥΚΑΤΟΣ ΜΙΧΑΛΗΣ

ΑΘΗΝΑ, 2019

<u>ΤΡΙΜΕΛΗΣ ΕΠΙΤΡΟΠΗ</u>

Επιβλέπων: Κωνσταντίνος Δάβος, ερευνητής Β’

Μέλος: Π. Κατσαούνου, Επ. καθηγήτρια

Μέλος: Ιωάννης Καλομενίδης, αν. καθηγητής

Index

Introduction

Coronary heart disease (CHD) is one of the top causes of death in the developed countries, the top cause of years of life lost globally [1] and it was responsible for ≈1 of every 7 deaths in the United States in 2013.[2] The prevalence of heart failure (HF) is estimated at 1–2% in the western world and the incidence approaches 5–10 per 1000 persons per year.[3]Cardiac rehabilitation (CR) has proven beneficial effects on prevention of CHD, and is highly recommended in clinical guidelines for patients with coronary artery disease(CAD). [4] [5] The benefits of exercise training are well documented and unquestionable therefore, exercise training is strongly recommended in HF patients. [6] Even though CR is highly recommended it is poorly implemented in everyday clinical practice. According to a European survey fewer than half of eligible cardiovascular patients benefit from CR in most European countries. Deficits include absent or inadequate legislation, funding, professional guidelines and information systems in many countries. [7] There are different categories of barriers for exercise in HF such as patient related, social and economic, healthcare system/team, condition related and therapy related. [8] Enabling a comprehensive CR at patients' homes and the introduction of simple training modality could eliminate those adherence hindering factors and increase patient participation in rehabilitation programs. The key to solve the problem of safety and monitoring of homebased physical training of cardiovascular patients and to make this rehabilitation modality theoretically possible is the latest technological advancements in the field of telemedicine which was the reason for the European Society of Cardiology to mention this form of rehabilitation in its current guidelines. [5] [9]

Telerehabilitation is the supervision and performance of a comprehensive CR programme at a distance. The components of telerehabilitation are telemonitoring, teleassessment, telesupport, teletherapy, telecoaching, teleconsulting, and telesupervision of exercise training. Systematic reviews including primary studies comparing cardiac telerehabilitation with centre-based CR have shown that the former to be non-inferior to the latter. [10] [11] Published randomized controlled trials (RCTs) showed that home-based telerehabilitation is well accepted, safe, and effective and has high adherence among HF patients.[1] [2] [13] In this context we can understand that telerehabilitation for cardiopulmonary patients may be helpful to the furthering and popularization of CR and moreover increase the compliance to the recommended guidelines.

1.0 Heart failure

1.1 Definition and classification of heart failure

Heart failure is defined as the inability of the heart to supply the peripheral tissues with the required amount of blood and oxygen to meet their metabolic demands. Pathophysiologically, the cardiac output is in its absolute or relative amount low and/or has a pathological distribution. It leads to a clinical syndrome characterized by symptoms like dyspnea or fatigue, and signs such as elevated jugular venous pressure, tachycardia, or peripheral edema. Heart failure is mostly caused by an underlying myocardial disease; however valve diseases, endocardial, or pericardial abnormalities and heart rate/rhythm disorders may also result in cardiac malfunction. The clinical severity of HF is graded according to the New York Heart Association (NYHA) functional classification based on the clinical symptoms and physical activity of the patient (Table 1).

Another classification of chronic HF was established by the American College of Cardiology and the American Heart Association to complement the NYHA functional classification. This classification is also based on the clinical signs and symptoms of the patient, and comprises concomitant diseases and risk factors, to estimate the progression stage and outcome of the disease (Table 2). [14]

Table 1: New York Heart Association (NYHA) Functional Classification

Class	Severity of symptoms and physical activity
I	No limitation of physical activity. Ordinary physical activity does not cause undue breathlessness, fatigue, or palpitations.
II	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in undue breathlessness, fatigue or palpitations.
III	Marked limitation of physical activity. Comfortable at rest, but less than ordinary physical activity results in undue breathlessness, fatigue, or palpitations.
IV	Unable to carry on any physical activity without discomfort. Symptoms at rest can be present. If any physical activity is undertaken, discomfort is increased.

Demonstration of an underlying cardiac cause is central to the diagnosis of HF. This is usually a myocardial abnormality causing systolic and/or diastolic ventricular dysfunction. However, abnormalities of the valves, pericardium, endocardium, heart rhythm and conduction may also cause HF (more than one abnormality is often present). Identification of the underlying cardiac problem is crucial for therapeutic reasons, as the precise pathology determines the specific treatment used. [6]

Table 2: Classification of Chronic Heart Failure According to the American College of Cardiology

Stage	Description
A: High risk for developing heart failure	Hypertension, diabetes mellitus, family history of cardiomyopathy
B: Asymptomatic heart failure	Previous myocardial infarction, left ventricle dysfunction, valvular heart disease
C: Symptomatic heart failure	Structural heart disease, dyspnoea and fatigue, impaired exercise tolerance
D: Refractory end-stage heart failure	Marked symptoms at rest despite maximal medical therapy

1.2 Epidemiology of heart failure

The prevalence of HF depends on the definition applied, but is approximately 1–2% of the adult population in developed countries, rising to ≥10% among people >70 years of age. Among people >65 years of age presenting to primary care with breathlessness on exertion, one in six will have unrecognized HF. The lifetime risk of HF at age 55 years is 33% for men and 28% for women. [6]

The lifetime risk of developing HF is 20% for Americans ≥40 years of age. In the United States, HF incidence has largely remained stable over the past several decades, with >650,000 new HF cases diagnosed annually. Heart failure incidence increases with age, rising from approximately 20 per 1,000 individuals 65 to 69 years of age to >80 per 1,000 individuals among those ≥ 85 years of age. Approximately 5.1 million persons in the United States have clinically manifest HF, and the prevalence continues to rise.

Heart failure is the primary diagnosis in >1 million hospitalizations annually. Patients hospitalized for HF are at high risk for all-cause rehospitalization, with a 1-month readmission rate of 25%. In 2013, physician office visits for HF cost $1.8 billion. The total cost of HF care in the United States exceeds $30 billion annually, with over half of these costs spent on hospitalizations. [15]

Over the last 30 years, improvements in treatments and their implementation have improved survival and reduced the hospitalization rate in patients with HF although the outcome often remains unsatisfactory. The most recent European data demonstrate that 12-month all-cause mortality rates for hospitalized and stable/ambulatory HF patients were 17% and 7%, respectively, and the 12-month hospitalization rates were 44% and 32%, respectively. In patients with HF (both hospitalized and ambulatory), most deaths are due to cardiovascular causes, mainly sudden death and HF worsening. Hospitalizations are often due to non-cardiovascular causes. Hospitalizations for cardiovascular causes did not change from 2000 to 2010, whereas those with non-cardiovascular causes increased. [6]

2.0 Coronary heart disease

2.1 Definitions

Cardiovascular disease (CVD) is a group of diseases that include both the heart and blood vessels, thereby including CHD and CAD, and acute coronary syndrome (ACS) among several other conditions. Although health professionals frequently use both terms CAD and ACS interchangeably, as well as CHD, they are not the same. Acute coronary syndrome is a subcategory of CAD, whilst CHD results of CAD. On the other hand, CAD is characterized by atherosclerosis in coronary arteries and can be asymptomatic, whereas ACS almost always presents with a symptom, such as unstable angina, and is frequently associated with myocardial infarction regardless of the presence of CAD. Finally, CAD is usually used to refer to the pathologic process affecting the coronary arteries (usually atherosclerosis) whilst CHD includes the diagnoses of angina pectoris, myocardial infraction and silent myocardial ischemia. In turn, CHD mortality results from CAD. [16]

Coronary heart disease is caused by the narrowing of the coronary arteries, leading to an imbalance between the functional requirements of the heart and the capacity of the coronary arteries to supply blood and oxygen. As a consequence, the heart muscle is damaged, which will eventually become clinically apparent with cardiac symptoms. Clinical manifestations of CHD include stable or unstable angina pectoris, myocardial infarction, cardiac arrhythmias, congestive HF, and/or sudden cardiac death. The main cardiac symptoms are thoracic pain and dyspnoea. In the long term, CHD is associated with disability, impaired health-related quality of life(QoL), and premature death. [17]

Moreover according to Charles Steenbergen, and Nikolaos G. Frangogiannis the term ischemic heart disease (IHD) describes a group of clinical syndromes characterized by myocardial ischemia, an imbalance between myocardial blood supply and demand. In most patients with IHD, the cause of myocardial ischemia is a reduction in coronary blood flow due to atherosclerotic CAD. Because of the slow progression of coronary atherosclerosis, and the excess capacity in the major coronary arteries, there is usually a long period of silent coronary disease and gradual luminal narrowing before the appearance of clinical ischemic symptoms. The manifestations of IHD are dependent on the duration, severity, and acuity of the ischemic episodes. A sudden critical reduction in coronary blood flow is the underlying mechanism in ACSs, a spectrum of clinical conditions that encompasses unstable angina, non-ST-elevation myocardial infarction, and ST-elevation myocardial infarction. In contrast, in chronic IHD the presence of flow-limiting coronary lesions restricts the ability of the heart to increase blood supply in response to increases in myocardial oxygen demand, resulting in development of angina pectoris, a transient discomfort in the chest and neighbouring areas. [18]

2.2 Epidemiology of coronary heart disease

The clinical syndromes of CHD cause more deaths, morbidity, and financial burden in western societies than any other group of diseases and is one of the top cause of years of life lost globally.

Coronary heart disease alone caused ≈1 of every 7 deaths in the United States in 2013 and 370.213 Americans died of CHD. Each year, an estimated number of ≈660 000 Americans suffer a new coronary attack (defined as first hospitalized myocardial infarction or CHD death) and ≈305 000 have a recurrent attack. It is estimated that an additional 160.000 silent myocardial infarctions occur each year. Approximately every 34 seconds, 1 American has a coronary event, and approximately every 1 minute and 24 seconds, an American will die of one. [2]

Although CHD mortality rates have declined over the past four decades in western countries, this condition remains responsible for ~one-third of all deaths in individuals over age 35. [16]

3. Cardiac rehabilitation

3.1 Definition, recommendations, contraindications

The term CR refers to coordinated, multidisciplinary interventions designed to optimize a cardiac patient's physical, psychological, and social functioning, in addition to stabilizing, slowing, or even reversing the progression of the underlying atherosclerotic processes, thereby reducing morbidity and mortality. [19]

Cardiac rehabilitation programs are recognized as integral to comprehensive care of CHD patient and have been given a Class IA recommendation from the American Heart Association, the American College of Cardiology, and the European Society of Cardiology, with exercise therapy consistently identified as a central element. [20] [21] [22] [23]

Guidelines from the American College of Cardiology/American Heart Association, European Society of Cardiology and Canadian Cardiovascular Society have included evidence-based recommendations for the use of exercise in the management of HF. According to the American College of Cardiology/ American Heart Association exercise training (or regular physical activity) is recommended as safe and effective, for patients with HF who are able to participate, to improve functional status (Class I, level of evidence A) and CR can be used in clinically stable patients with HF to improve functional capacity, exercise duration, health- related QoL, and mortality (Class IIa, level of evidence B).[15] The Canadian Cardiovascular Society recommends regular exercise to improve exercise capacity, symptoms and QoL in all HF patients (strong recommendation, moderate quality evidence) and regular exercise in HF patients with reduced ejection fraction to decrease hospital admissions (strong recommendation, moderate quality evidence). [24] In the European Society of Cardiology guidelines it is recommended that aerobic exercise is encouraged in patients with HF to improve symptoms and functional capacity (Class I, level of evidence A) and regular aerobic exercise is encouraged in stable patients with HF with a reduced ejection fraction to reduce the risk of hospitalisation from HF (Class I, level of evidence A). [6]

According to the Heart Failure Association and the European Association for Cardiovascular Prevention and Rehabilitation implementation of exercise training requires appropriate patient selection, training protocol identification, intensity, and progression monitoring and is recommended for stable New York Heart Association (NYHA) class I–III HF patients. Moreover they suggest that after hospitalization for exacerbation, early mobilization through an individualized exercise programme may prevent further disability. Both clinical stability and early mobilization are important requisites that help achieve functional self-sufficiency and trust prior to conducting a symptom-limited exercise test and initiating regular exercise training. When clinical stabilization is achieved, appropriate screening for contraindications to exercise is necessary, including medical history, clinical examination, resting electrocardiogram (ECG), a symptom-limited exercise test, and echocardiography (Table 3). Finally, the selection of the exercise modality should take into account the patient's age, concomitant disease(s), leisure and working habits, preferences and abilities, logistical restraints, and the availability of ET facilities and equipment. [25]

Contraindications to CR only apply to the exercise aspect. They include: Unstable angina, acute decompensated congestive HF, complex ventricular arrhythmias, severe pulmonary hypertension (right ventricular systolic pressure > 60 mm Hg), intracavitary thrombus, recent thrombophlebitis with or without pulmonary embolism, severe obstructive cardiomyopathies, severe or symptomatic aortic stenosis, uncontrolled inflammatory or infectious pathology, and any musculoskeletal condition that prevents adequate participation in exercise. [26]

A	**Contraindications to exercise testing and training**
1	Early phase after acute coronary syndrome (up to 2 days)
2	Untreated life-threatening cardiac arrhythmias
3	Acute heart failure (during the initial period of haemodynamic instability)
4	Uncontrolled hypertension
5	Advanced atrioventricular block
6	Acute myocarditis and pericarditis
7	Symptomatic aortic stenosis
8	Severe hypertrophic obstructive cardiomyopathy
9	Acute systemic illness
10	Intracardiac thrombus
B	**Contraindications to exercise training**
1	Progressive worsening of exercise tolerance or dyspnoea at rest over previous 3–5 days
2	Significant ischaemia during low-intensity exercise (,2 METs,50 W)
3	Uncontrolled diabetes
4	Recent embolism
5	Thrombophlebitis
	New-onset atrial fibrillation/atrial flutter
C	**Increased risk for exercise training**
1	>1.8 kg increase in body mass over the previous 1–3 days
2	Concurrent, continuous, or intermittent dobutamine therapy
3	Decrease in systolic blood pressure with exercise
4	NYHA functional class IV
5	Complex ventricular arrhythmia at rest or appearing with exertion
6	Supine resting heart rate >100 b.p.m.
7	Pre-existing co-morbidities limiting exercise tolerance

Table 3: Summary of contraindications to exercise testing and training(A), exercise training(B), and increased risk for exercise training(C) for heart failure patients.

3.2 Benefits of cardiac rehabilitation

A 2011 Cochrane systematic review and meta-analysis that has allowed analysis of 47 studies randomising 10,794 patients with CHD to exercise-based CR or usual care has shown that exercise-based CR reduced overall and cardiovascular mortality in medium to long term (≥12 months) of follow-up, and also reduced hospital admissions in the shorter term follow up (<12 months). Cardiac rehabilitation did not reduce the risk of myocardial infarction, coronary artery bypass graft or percutaneous transluminal coronary angioplasty. In seven out of 10 trials reporting health related QoL using validated measures there was evidence of a significantly higher level of QoL with exercise-based CR than usual care. [26]

The latest updated Cochrane review of exercise based CR for CHD which included 63 RCTs with 14,486 CHD patients showed an absolute risk reduction in cardiovascular mortality from 10.4% to 7.6% for patients after myocardial infarction and revascularisation who received CR compared with those who did not. No significant reduction was apparent in total mortality. The overall risk of hospital admissions was reduced with CR but there was no significant impact on the risk of myocardial infarction, coronary artery bypass graft or percutaneous coronary intervention. In five out of 20 trials reporting health-related QoL using validated measures, there was evidence of significant improvement in most or all of the sub-scales with exercise-based CR compared to control. Four trial-based economic evaluation studies indicated exercise-based CR to be a potentially cost-effective use of resources in terms of gain in quality-adjusted life years. [27]

The above mentioned meta-analyses, although complete, included RCTs of doubtful size and quality, where women, elderly or high risk populations were scarcely represented. Another important issue is that the recent changes in the medical management of CHD with the introduction of statins, ACE inhibitors and dual anti-platelet therapy as well as modern invasive techniques and devices has changed the course of the disease in the recent years. All these, may be serious disadvantages affecting the generalizability of previous findings to all CHD patients, giving the impression that the benefits of exercise-based CR have been over-estimated.

The effectiveness of CR as provided in every day clinical practice is affected by the type of CR offered (i.e. content, duration, intensity and volume) which, often vary within the countries. This is a major problem given that we lack internationally accepted minimal standards for evaluating the quality of CR delivery. The Cardiac Rehabilitation Outcomes Study (CROS) has been designed taking into account all these aspects. CROS was the first meta-analyses to include not only RCTs but also prospective and retrospective controlled cohort studies enrolling patients after an acute coronary event, a CABG or mixed populations with CHD. The studies were included into the meta-analysis only if the patients were participating in a supervised, comprehensive, multi-disciplinary CR starting within 3 months after the index event consisted of at least two weekly sessions of structured physical exercise and one weekly session of the following components: information, motivational techniques, education, psychological support and interventions, social and vocational support. CROS tried to investigate the effectiveness of CR on total mortality in the modern era by including studies published after 1995 when statins were initiated in CHD management. The study included 25 studies with 219,702 patients fulfilling all inclusion criteria. It was published in 2016 and was the first meta-analysis to show a significant reduction in total mortality by 36% - 63% for CR participants after an ACS, by 36% after CABG and by 33% - 48% in mixed CHD populations beyond the beneficial effects of modern medication and devices. For the first time mortality reduction was also related to some minimal standards of CR delivery which has to start early after the acute event, must be structured, multi-component including not only physical training but also educational sessions and psychosocial interventions. [28] A 2014 review on exercise-based CR for HF included 33 trials enrolling 4,740 patients predominantly with reduced ejection fraction HF and class II or III. The review resulted that there was no difference in pooled mortality between exercise-based CR versus no exercise control in trials with up to one-year follow-up. However, there was a trend towards a reduction in mortality with exercise in trials with more than one year of follow-up. Compared with control, exercise training reduced the rate of overall and HF specific hospitalization. Exercise also resulted in a clinically important improvement superior in the Minnesota Living with Heart Failure questionnaire a disease specific health-related QoL measure. These benefits were independent of the participant's age, gender, degree of left ventricular dysfunction, type of CR (exercise only vs. comprehensive rehabilitation), mean dose of exercise intervention, length of follow-up and overall risk of bias and trial publication date. Within these included studies, a small body of evidence supported exercise-based CR for HF due to preserved ejection fraction and when exclusively delivered in a home-based setting. One study reported an additional mean healthcare cost in the training group compared to the control. Two studies indicated exercise-based CR to be a potentially cost-effective use of resources in terms of gain in quality-adjusted life years and life-years saved. The authors conclude that, compared with no exercise control, exercise-based rehabilitation does not increase or decrease the risk of all-cause mortality in the short term (up to 12-months' follow-up) but reduces the risk of hospital admissions and confers important improvements in health-related QoL. This review provides further evidence that exercise training may reduce mortality in the longer term and that the benefits of exercise training appears to be consistent across participant characteristics including age, gender and HF severity. [29]

A 2019 meta-analysis which investigated the effect of CR on health related QoL in patients with CAD included 49 reports from 41 RCTs with 11,747 patients. The conclusion was that receiving CR was shown to improve health related QoL, with exercise, non-exercise, and psychological based interventions playing a vital role. While these improvements in health related QoL were modest they still reflect an incremental benefit in comparison to receiving usual care. [30]

A 2019 contemporary systematic review and meta-analysis of included 44 trials between January 2013 and January 2018 and compared exercise-based CR for HF, with control subjects. Exercise-based CR did not reduce the risk of all-cause mortality but did reduce all-cause hospitalizations and HF specific hospitalizations. Moreover patients reported improved Minnesota Living with Heart Failure questionnaire overall scores. No evidence of differential effects across different models of delivery, including centre versus home-based programs, were found. These benefits appear to be consistent across exercise-based CR program characteristics. [31]

3.3 Exercise characteristics and modalities

Exercise prescription for CHD patients is based on a thorough clinical evaluation including risk evaluation, echocardiography, and exercise testing, and should take into account the patients' fitness, individual preferences, and/or disability status, comorbidities and environmental and external conditions. The individual training intensity is determined as a percentage of symptom-free maximal exercise capacity as measured by the VO_{2peak} and/or by determining the first ventilatory threshold during cardiopulmonary exercise testing (CPET). In clinical practice, maximal work load in watts (Joule per sec) without signs of ischaemia and/or cardiac or respiratory failure and under actual medication may be used for an approximation of exercise capacity. Training intensity is prescribed as percentage of maximal workload and/or percentage of maximal heart rate achieved during the test. [32]

The Heart Failure Association and the European Association of Preventive Cardiology clarify that for stable HF patients appropriate screening for contraindications to exercise is necessary, including medical history, clinical examination, resting electrocardiogram, a symptom-limited exercise test, and echocardiography. If the clinical status of a patient is unclear and/or previous examinations/tests are inconclusive, supplementary investigations such as 24h Holter monitoring, chest X-ray, or stress echocardiography should be considered as appropriate. The selection of the exercise modality should take into account the patient’s age, concomitant disease(s), leisure and working habits, preferences and abilities, logistical restraints, and the availability of exercise training facilities and equipment.

A gentle individualized gradual mobilization of the patient (known as ‘calisthenic exercises’) is advisable as a prologue and preparatory form of exercise, especially for severe HF patients with physical deconditioning or cachexia or after recent clinical instability.

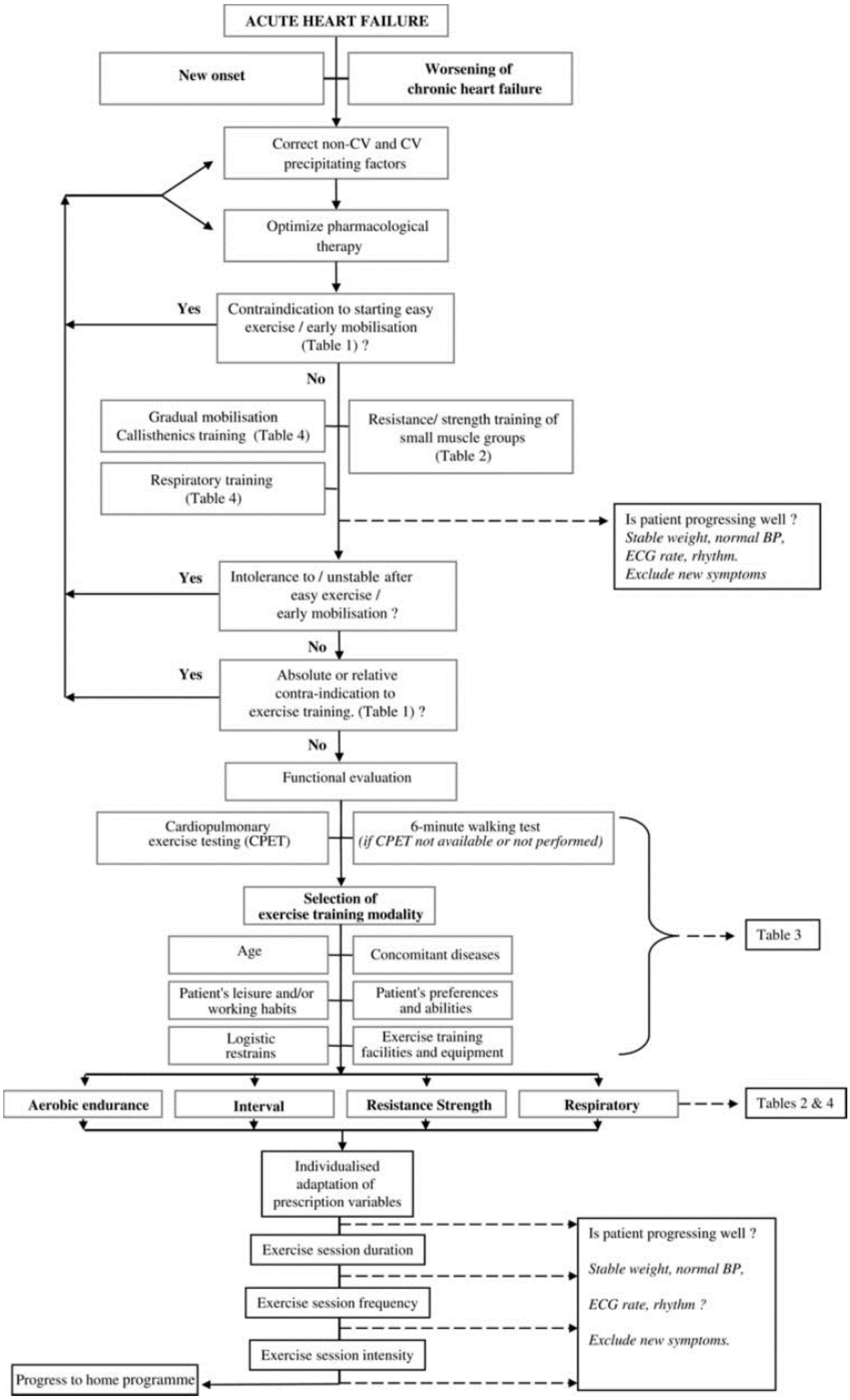

Figure 1: Flow-chart to guide tailoring an exercise training programme according to the individual clinical conditions and needs of the heart failure patient.

Identification of the appropriate and adequate level of training intensity is crucial to obtain the desired benefits while maintaining reasonable control of the related risk. A universal agreement on exercise prescription in chronic HF does not exist; thus, an individualized approach is recommended, with careful clinical evaluation, including behavioural characteristics, personal goals, and preferences. Training protocols vary in a number of variables: intensity (aerobic and anaerobic); type (endurance, resistance, and strength), method (continuous and intermittent/interval), application (systemic, regional, and respiratory muscle), control (supervised and non-supervised), and setting (hospital/centre- and home-based).

Three different training modalities have been proposed with different combinations:

(1) endurance aerobic (continuous and interval); (2) strength/resistance and (3) respiratory (Figure 1). [25]

A 2016 meta-regression analysis which included 17 trials investigated the influence of training characteristics on the effect of aerobic exercise training in patients with chronic HF. The authors concluded that total energy expenditure appeared the only training characteristic with a significant effect on improvement in exercise capacity. However, the results were strongly dominated by one trial (HF-ACTION trial), accounting for 90% of the total patient population and showing controversial results compared to other studies. A repeated analysis excluding the HF-ACTION trial confirmed that the increase in exercise capacity is primarily determined by total energy expenditure, followed by session frequency, session duration and session intensity. These results suggest that the design of a training program requires high total energy expenditure as a main goal. Increases in training frequency and session duration appear to yield the largest improvement in exercise capacity. [33]

A 2016 systematic review and metanalysis who aimed to compare the home based rehabilitation programs with the usual care with centre based CR programs included

19 trials with median follow up of 3months,17 comparisons of home-based CR to usual care (995 patients) and four comparing home and centre-based CR. The results showed that compared to usual care, home-based CR improved VO_{2max} and total Minnesota Living with Quality of Life score with no difference in mortality, hospitalisation or study drop out. Outcomes and costs were similar between home-based and centre-based CR with the exception of higher levels of trial completion in the home-based group. Home-based CR results in short-term improvements in exercise capacity and health-related QoL of HF patients compared to usual care. The magnitude of outcome improvement is similar to centre-based CR. Home-based CR appears to be safe with no evidence of increased risk of hospitalisation or death. These findings supported the provision of home-based CR for HF as an evidence-based alternative to the traditional centre-based model of provision. [34]

A 2018 systematic review and meta-analysis comparing high-intensity interval training to moderate intensity continuous training within CR included seventeen studies, involving 953 participants (465 for high-intensity interval training and 488 for moderate intensity continuous training). The results showed that, high-intensity interval training was significantly superior to moderate intensity continuous training in improving cardiorespiratory fitness overall. The authors concluded that high-intensity interval training is superior to moderate intensity continuous training in improving cardiorespiratory fitness in CR participants. Improvements in cardiorespiratory fitness are significant for CR programs of > 6-week duration. Programs of 7–12 weeks' duration resulted in the largest improvements in cardiorespiratory fitness for patients with CAD. High-intensity interval training appears to be as safe as moderate intensity continuous training for CR participants. [35]

A 2017 systematic review and meta-analysis investigated the effects of high-intensity interval training on aerobic capacity in cardiac patients. The systematic review included 21 RCTs which enrolled a total of 736 patients (81% male, 19% female) with cardiac disease (eleven studies examined patients with CAD and ten studies examined patients with chronic HF). The authors concluded that interval exercise can provide more benefits than continuous in terms of improving peakVO_2 and VO_2 at aerobic threshold in patients with cardiac disease. Interval programs, which increase exercise capacity compared with traditional exercise, are thus preferable. No significant difference between the interval and continuous groups was observed in terms of peak heart rate, peak minute ventilation, VE/VCO_2 slope and respiratory exchange ratio, body mass, systolic or diastolic blood pressure, triglyceride or low- or high-density lipoprotein cholesterol levels, flow-mediated dilation, or left ventricular ejection fraction. [36]

A 2016 systematic review and meta-analysis investigated the effect of resistance training on clinical outcomes in HF. The 27 included studies enrolled a total of 2321 participants, 1172 in an intervention and 1149 in either sedentary controls or aerobic exercise only groups, producing over 31,263 patient-hours of training. Mortality, hospitalization, resting blood pressure and left ventricular ejection fraction were all unchanged with resistance or combined aerobic and resistance training. Peak-VO_2 was improved in combined exercise vs. control and in resistance vs. control. Quality of life was improved in combined vs. control. Six-minute walk test was improved in combined exercise vs. control, and in resistance vs. control. The authors concluded that resistance only or combined training improves peakVO_2, QoL and walking performance in HF patients. [37]

A 2012 systematic review and meta-analysis investigated the efficacy of inspiratory muscle training in chronic HF patients and included 11 studies contained data from 287 patients. Compared to the control group, chronic HF patients undergoing inspiratory muscle training showed a significant improvement in peakVO_2, Minnesota Living with Heart Failure Questionnaire which was used to evaluate the health related QoL, and VE/VCO_2 slope. The authors concluded that inspiratory muscles training improves cardio-respiratory fitness and QoL to a similar magnitude to conventional exercise training and may provide an initial alternative to the more severely de-conditioned chronic HF patients who may then transition to conventional exercise training. [38]

A 2016 systematic review and meta-analysis included 3 randomized controlled trials, examining the effects of combined exercise and inspiratory muscle training versus conventional exercise, on exercise capacity, respiratory muscle strength, and QoL measurements in patients with HF. The results showed that, combined exercise and inspiratory muscle training resulted in improvement of maximal inspiratory pressure weighted mean differences and Minnesota Living with Heart Failure Questionnaire weighted mean differences. Non-significant difference was observed in peakVO_2 for participants in the combined exercise/inspiratory muscles training group compared with the conventional exercise group. No serious adverse events were reported. The authors concluded that combined exercise/inspiratory muscle training may improve maximal inspiratory pressure and QoL in patients with HF and should be considered for inclusion in CR programs. [39]

In a 2013 prospective randomised study the benefits of combined aerobic, resistance, and inspiratory training in patients with chronic HF were investigated. Twenty-seven patients, aged 58 ± 9 years, NYHA II/III with LVEF 29 ± 7% were randomly assigned to a 12-week aerobic training (AT) (n=14) or a combined aerobic, resistance, and inspiratory training (ARIS) (n=13) exercise program. Aerobic training consisted of bike exercise at 70-80% of max heart rate. ARIS training consisted of AT with resistance training of the quadriceps at 50% of 1 repetition maximum (1RM) and upper limb exercises using dumbbells of 1-2 kg as well as inspiratory muscles training at 60% of sustained maximal inspiratory pressure (SPI(max)). At baseline and after intervention, patients underwent cardiopulmonary exercise testing, echocardiography, evaluation of dyspnea, muscle function and QoL scores. The ARIS program as compared to AT alone, resulted in additional improvement of the quadriceps muscle strength and endurance, SPI(max), exercise time, circulatory power (peak oxygen consumption × peak systolic blood pressure), dyspnea and QoL. The authors concluded that ARIS training was safe and resulted in incremental benefits in both peripheral and respiratory muscle weakness, cardiopulmonary function and QoL compared to that of AT.

A 2018 systematic review and meta-analysis investigated the effects of Tai Chi-based CR on aerobic endurance, psychosocial well-being, and cardiovascular risk reduction among patients with CHD. Thirteen studies met the inclusion criteria. Tai Chi groups showed a large and significant improvement in aerobic endurance compared with both active and non-active control interventions. Tai Chi groups also showed a significantly lower level of anxiety and significantly better QoL compared with non-active control groups. The authors concluded that significant effects of Tai Chi have been found in improving aerobic endurance and psychosocial well-being among CHD patients. Tai Chi could be a cost-effective and safe exercise option in CR . However, the effect of Tai Chi on CVD risk reduction has not been amply investigated among CHD patients. [40]

3.4 Adherence to cardiac rehabilitation

In a position statement of the Study Group on Exercise Training in Heart Failure of the Heart Failure Association of the European Society of Cardiology on 2012 the non-adherence of HF patients to exercise is described as the Achilles heel of exercise training after taking into consideration the results of HF-ACTION. This was a 2009 randomized control trial which included 2331 medically stable outpatients with HF and reduced ejection fraction, in which only 40% of patients in the exercise group reported weekly training volumes at or above the recommended 90 min per week at month 3, or 120 min from month 3 to month 12. The non-adherence of these patients affected the benefits of CR. The statement concluded that CR was poorly implemented and even the patients who were enrolled in a supervised exercise training or multidisciplinary CR programme showed low adherence.

Multiple are the barriers and the reasons for non-adherence to physical activity and exercise. The interventions should aim to address all these causes, and all professionals should encourage physical activity when seeing patients in order to emphasize its importance. Even when the amount of time spent exercising as part of a programme is small, supervised and encouraged exercise is likely to lead to a more active lifestyle, so that the effective 'dose' of exercise may be considerably greater than that directly prescribed. [8]

A 2019 systematic review of prospective cohort studies investigated the factors which are associated with non-participation in and dropout from CR programmes. The authors selected 43 studies with a total of 63,425 patients from 10 different countries that met the inclusion criteria. Factors associated with non-participation in and dropout from CR were grouped into six broad categories: intrapersonal factors, clinical factors, interpersonal factors, logistical factors, CR programme factors and health system factors. They found that clinical factors, logistical factors and health system factors were the main factors assessed for non-participation in CR. They also found differences between the factors associated with non-participation and dropout. They concluded that several factors were determinants of non-participation in and dropout from CR. These findings could be useful to clinicians and policy makers for developing interventions aimed at improving participation and completion of CR, such as e-health or home-based delivery programmes. [41]

A 2019 systematic review and metanalysis investigated the quality of interventions to promote patient utilization of CR. Twenty-six RCTs with 5299 patients with myocardial infarction, angina, revascularization, or HF were included. Interventions aimed at increasing utilization of comprehensive phase II CR. Meta-regression analyses suggested that the intervention deliverer (nurse or allied healthcare provider) and the delivery format (face-to-face) were influential in increasing enrolment. There was low-quality evidence that interventions to increase adherence were effective. There was moderate-quality evidence that interventions to increase program completion were effective. The authors concluded that there are effective interventions to increase CR utilization, but more research is needed to establish specific, implementable materials and protocols, particularly for CR completion. [42]

A 2019 systematic review and metanalysis investigated the effect of mobile applications for improving adherence in CR. Eligible studies were the ones which used mobile applications as a stand-alone intervention or as the primary component for the intervention directed at improving CR adherence, without any limitations on outpatient or home-based CR. Eight studies were eligible for this systematic review including 4 RCTs as well as 4 before-after studies of which only one had a control group. Four RCTs and 185 patients in experimental group were included in meta-analysis. The result was that the adherence of patients using mobile applications was 1.4 times higher than the control group. The authors concluded that the use of mobile applications for improving the adherence of the CR might be effective. However, mobile applications are in an initial stage for CR use and more research is needed to validate their effectiveness. [43]

4.0 Telerehabilitation in coronary heart disease and heart failure

4.1 Definitions

The term eHealth encompasses a range of services or systems combining medicine/healthcare and information technology, including:

- clinical information systems (electronic medical records, decision support and monitoring clinical and institutional practice).
- telemedicine and telecare (including disease management services, remote patient monitoring, teleconsultations and homecare).
- integrated regional and national information networks and associated e-referrals and e-prescribing.
- disease registries and other non-clinical systems used for education, public health, patient/disease-related behaviour and healthcare management.
- ‘‘mobile’’ health (mHealth) including the use of mobile devices in collecting health data providing healthcare information to practitioners, researchers and

patients, real-time monitoring of patient's vital signs and direct provision of care.

- ''personalised'' health (pHealth): wearable or implantable micro- and nano-technologies with sensors and/or therapy delivery devices to help facilitate health and social care decision-making and delivery.
- ''Big Data'' large scale integration and analysis of heterogeneous data sources, usually of high volume, velocity, and variety, ideally linked at the individual person level to provide a more holistic view of patient/individual, social and environmental factors that may influence health. [44]

The American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR) in a 2001 statement recognizes the value of advancing technology and the benefits it may provide in the delivery of cardiac and pulmonary rehabilitation services. According to AACVPR, telemedicine refers to the use of electronic communication and information technologies to provide and support clinical care at a distance and telehealth includes activities such as education for healthcare professionals, community health education, public health, research, and administration of health services. [45]

Telecare in HF patients can be defined as monitoring which consists of the transmission of symptoms, signs and/or biological or physiological data from a remote location to another location for data interpretation and decision-making. The most basic form of telecare is structured telephone support, in which providers schedule routine telephone contacts with patients for ongoing assessment. Telecare also encompasses the concept of telemonitoring, in which symptoms and/or physiological data derived from external monitoring devices, home monitoring cardiovascular implantable electronic devices and/or implantable hemodynamic devices are transferred automatically to a healthcare provider via a wireless or broadband connection, with targeted follow-up triggered by variances that exceed pre-set thresholds. Telemonitoring can be conducted manually by health care professionals or automatically by specialized software. In addition to telemonitoring, telecare also includes teleassessment (active remote assessment), telesupport (e.g. supportive tele visits by nurses, psychological support), teletherapy (interactive therapy), telecoaching (support and instruction for therapy), teleconsulting and telerehabilitation.

Telerehabilitation is defined as a supervised remote comprehensive CR and it includes the telecare and telesupervision of exercise training. [46] It offers services that were once scarce or unavailable to the population, improves access to services, facilitates the continuity of care for the vulnerable clientele and saves money and time. Services offered in telerehabilitation are very diverse. They include as mentioned above tele-follow up, teletraining, teleconsultation, teletreatment, and telemonitoring or telesurveillance. [47]

1	Telemonitoring – minimally intrusive, often involving sensors
2	Teleassessment – active remote assessment
3	Telesupport – supportive televisits by nurses, psychological support
4	Teletherapy – actual interactive therapy
5	Telecoaching – support and instruction for therapy
6	Teleconsulting
7	Telesupervision of exercise training

Table 4 Components of telerehabilitation [9]

A 2010 study evaluated a home-based telemonitored CR model (HTCR) using walking training compared with an outpatient-based standard cardiac rehabilitation (SCR) using interval training on a cycle ergometer. The study included 152 HF patients who were randomized to either HTCR or SCR. All patients underwent 8 weeks of CR. Both groups were comparable in terms of demographic and clinical characteristics and medical therapy. The effectiveness of CR was assessed by changes in NYHA class, peak oxygen consumption, 6-min walking test distance, and SF-36 score. All patients in the HTCR group received a device called EHO 3 and a mobile phone. The EHO 3 device enabled recording of ECG data from three pre-cordial leads and transmittal via a mobile phone to the monitoring centre. The mobile phone was also used for voice communication. Before beginning a training session, patients in the HTCR group used the mobile phone to answer a series of questions regarding their present condition, including fatigue, dyspnoea, blood pressure, body mass, and medication taken. Patients then transmitted resting ECG data to the monitoring centre. If no contraindications to training were identified, patients were given permission to start the training session. The EHO 3 system was used to monitor and control training in any place where the patient selected to exercise. The device had training sessions pre-programmed individually for each patient (defined exercise duration, breaks, timing of ECG recording). The planned training sessions were executed with the device indicating what should be done with sound and light signals. The timing of automatic ECG recordings corresponded to peak exercise. If the training session was completed uneventfully, the patient transmitted the ECG recording via the mobile phone to the monitoring centre immediately after the end of every training session. Patients could also transmit an ECG recording at any time, for example if they experienced symptoms like palpitations, chest pain, etc. The ECG recordings were analysed at the monitoring centre, and the safety, efficacy, and accuracy of a particular patient rehabilitation programme were assessed. Using the data on HR during exercise and the patient subjective evaluation of the perceived exertion, consultants were able to adjust the training workload appropriately or, if necessary, to discontinue the session. Telephone contact was also used for psychological support.

Cardiac rehabilitation resulted in a significant improvement of all parameters in both groups. All patients in the HTCR group completed the 8 weeks of CR, whereas 15 patients in the SCR group (20%) discontinued CR. The authors concluded that in patients with HF, HTCR was equally as effective as SCR and provided a similar improvement in quality of life. Adherence to CR seemed to be better for HTCR and home-based telemonitored CR may be a useful alternative form of CR in patients with HF. [12]

4.2 Telerehabilitation compared with usual care and other types of cardiac rehabilitation

In 2017 a randomised trial which was aiming to determine the efficacy and safety of a short-term, real-time, group-based HF rehabilitation program delivered into each participant's home via an online telerehabilitation system was published. The questions in this trial were whether a 12-week, home-based telerehabilitation program conducted in small groups is non-inferior to a traditional centre-based program in terms of the change in 6-minute walk distance and in terms of functional capacity, muscle strength, quality of life, urinary incontinence, patient satisfaction, attendance rates, and adverse events.

This was a two-group, parallel, non-inferiority trial with blinded outcome assessors. Participants were randomised to an experimental group, provided with a 12-week home-based telerehabilitation program delivered twice weekly and a control group, provided with a traditional centre-based program of the same duration and frequency.

The control group received a centre-based rehabilitation program based on current recommended guidelines encompassing education, aerobic and strength training exercise supervised by physiotherapists. The telerehabilitation program was delivered via a synchronous videoconferencing platform across the internet to groups of up to four participants within the home. Two-way audio-visual communication enabled interaction of all parties, and the physiotherapist guided participants through an exercise program similar to the control group. This approach enabled the physiotherapist to watch participants performing the exercises and provide real-time feedback and modification. Telerehabilitation equipment was loaned to participants, as required, including a laptop computer, a mobile broadband device connected to 3G wireless broadband internet, an automatic sphygmomanometer, a finger pulse oximeter, free weights and resistance bands.

This study was the first to test a group-based video telerehabilitation program delivered in the home against a traditional centre-based rehabilitation program for people with chronic HF. According to these results the change in the performance in the six-minute walking test from baseline to week 12 in the experimental group was not inferior compared with that in the control group. There were also no differences between the two intervention groups in most other functional capacity measures, muscle strength, quality of life, urinary incontinence, patient satisfaction and adverse events. The only significant differences were relatively minor, but they did favour the telerehabilitation group. The telerehabilitation group had higher attendance rates compared with the control group. In conclusion, telerehabilitation was not inferior to centre based rehabilitation program in patients with chronic heart failure. [48]

In 2019 a systematic review and meta-analysis of telehealth interventions for the secondary prevention of CHD was published. Multiple databases from 1990 to 30

April 2018 were searched. Studies were considered relevant if they were RTCs evaluating the effects of telehealth interventions on risk factor modification in patients with CHD with at least three months' follow-up compared with CR and/or usual care. Telehealth interventions were defined as having greater than 50% of patient–provider contact for risk factor modification (addressing multiple risk factors) advice being delivered by the telephone, internet, videoconferencing, text messaging or mobile apps. Telehealth intervention could be delivered alone or as an adjunct to CR or usual care. Cardiac rehabilitation referred to face-to face centre-based or community-based CR. Usual care was defined as any routine care for CHD excluding telehealth intervention.

A total of 14,292 studies were screened for possible inclusion and 80 full manuscripts were reviewed. Thirty two papers reporting 30 unique trials with 7283 unique patients were included. The majority of study participants were men (although no trials excluded women) with mean age 61.7±4.3 years who were enrolled after an ACS or revascularization. Telehealth intervention was divided into two types: telehealth delivered alone as an alternative care, and telehealth as an adjunct care to CR and/or usual care. Usual care in the comparison group was varied among the studies, including clinical visits, counselling on medication or secondary preventive behaviours by health professionals, or referring to hospital or community-based CR.

The telehealth interventions which were reported were internet, mobile phones and text messaging, smartphone applications, telephone calls, online monitoring with combination between them in some of the studies. Delivery and amount of contact varied substantially between studies. All trials included at least one face to face assessment. Interventions were delivered by nurses, dieticians, physiotherapists, kinesiologists, psychologists, physiologists, pharmacists, physicians with different combinations between them from study to study. Telehealth intervention time varied from six weeks to 48 months.

The authors concluded that despite the significant variation in the reviewed telehealth interventions, they offer substantial benefits for the secondary prevention of CVD in comparison with usual care and are equivalent to centre-based CR. Reduction of recurrent cardiac events and total cholesterol at medium to long-term duration can be additional benefits for CHD patients when telehealth is combined with usual care and/or CR. Telehealth interventions with a range of delivery modes could be offered to patients who cannot attend CR, or as an adjunct to CR. Telehealth interventions were associated with fewer deaths over time, although it was not statistically significant. According to the reviewers telehealth interventions have the potential to improve cardiovascular risk factors which is the major objective of facility-based CR. Moreover telehealth interventions mostly delivered by phone and/or internet could enhance access to a formal secondary prevention by patients unable to attend centre-based CR and could therefore narrow the current evidence–practice gap in this specific area. [49]

Another 2019 systematic review of recent CR meta-analyses in patients with CHD or HF aimed to review the meta-analyses of supervised, homebased or telemedicine-based exercise CR published between July 2011 and April 2018. Evidence on mortality, hospitalization, peakVO_2, exercise capacity, muscle strength and health-related QoL in patients with CHD or HF referred to CR was obtained by searching six electronic databases. Thirty meta-analyses met the inclusion criteria and were included in this review. Sixteen metanalyses included CHD patients, 12 included HF patients and 2 included both. For the metanalyses in CHD patients the active intervention in 13 of those was CR centre supervised exercise-based; telemedicine-based CR intervention was in two meta-analyses and home-based CR intervention in one meta-analysis. In patients with HF the active intervention in 11 of these meta-analyses was exercise-based CR in a rehabilitation centre and home based CR intervention in one meta-analysis. In the 2 metanalyses for both HF and CHD patients the exercise-based CR in a rehabilitation centre was the main intervention. The authors concluded that the overall observation from these 30 independent CR meta-analyses suggests that the results are sufficiently robust in favour of CR to promote strategies to improve referral rates to CR whether delivered as exercise-based CR, home-based CR or telemedicine-CR. [50]

A 2018 systematic review aimed at reviewing the literature and assessing the efficacy of telerehabilitation for cardiac patients. The systematic review of the literature analysed seven clinical trials involving telerehabilitation for patients with CVD and specifically patients with CAD, HF and diabetes mellitus. The total number of the patients in these seven clinical trials was 1.133. The authors concluded that hybrid CR and home-based rehabilitation using telerehabilitation are feasible and safe alternatives, with high adherence by patients with CVD. They can be added to conventional CR programs or be used in isolation. In addition, they help to improve depression, functional capacity and the physical activity level. [51]

A systematic review and meta-analysis published in 2016 aimed to determine the benefits of telehealth exercise-based CR on exercise capacity and other modifiable cardiovascular risk factors compared with traditional exercise-based CR and usual care, among patients with CHD. Eligible studies were RTCs comparing secondary prevention outpatient (home-based or community-based) telehealth exercise based CR with usual care or non-telehealth centre-based exercise CR, among adults with diagnosed CHD (atherosclerosis, angina pectoris, myocardial infarction or coronary revascularisation). Telehealth exercise-based CR interventions used information and communication technologies (telephone, mobile/smartphone, mobile application, portable computer, internet, biosensors) to deliver or monitor structured exercise training that included prescriptive components such as frequency, level of intensity and duration. Telehealth and centre-based exercise could be delivered alone or as part of comprehensive CR. Usual care could include standard medical care but not structured, prescriptive exercise training.

Outcomes of interest included maximal aerobic exercise capacity, modifiable cardiovascular risk factors, exercise adherence, mortality and clinical events. 11 studies with 1189 patients in total met the eligibility criteria and were included in the review and meta-analysis. The main findings were that telehealth exercise-based CR appeared to be at least as effective, and in some cases more effective, for improving cardiovascular risk factors and functional capacity, although there was some evidence of heterogeneity between studies. Characteristics of the telehealth platforms likely influence the intensity of telehealth exercise base CR interventions and may contribute to the variability. Moreover telerehabilitation overcomes common barriers that limit participation in centre-based programmes and could enhance CR utilisation by providing additional options for patients whose needs are not met by existing services. The challenge according to the authors at the moment was to capitalise on advances in mobile sensor and communication technologies that enable more comprehensive, responsive and interactive intervention delivery. [52]

A 2016 systematic review and metanalysis compared the exercise telemonitoring and telerehabilitation with traditional cardiac and pulmonary rehabilitation. Main objective was to determine whether the benefits of the exercise component of pulmonary rehabilitation and CR using telerehabilitation are comparable to usual-care programmes. Eight CR and one pulmonary rehabilitation trial were included and meta-analyses were performed for peak oxygen consumption, peak workload, exercise test duration, and 6-minute walk test (6MWT) distance. No differences were found in exercise outcomes between usual care and telerehabilitation groups for CR studies, except in exercise test duration, which slightly favoured usual care groups. The pulmonary rehabilitation study which was included showed similar improvements in the 6MWT in both the usual care and the telerehabilitation groups. The authors concluded that telerehabilitation for patients with cardiac conditions provided benefits similar to usual care with no adverse effects reported. Similarly, more studies on telerehabilitation for patients with pulmonary conditions need to be conducted. [53]

A 2015 systematic review investigated the effects of telerehabilitation in patients with cardiopulmonary diseases compared with other CR delivery models for improving physical or functional outcomes in these patients. Inclusion criteria for this review were: the home-based telerehabilitation to be the core component, the intervention to have at least 2 exercise sessions, RTCs were only included and physical or functional outcome measures to be reported in adult patients with CHD, chronic HF, and chronic respiratory disease. Eleven studies were analysed. It appeared that telerehabilitation was no different to other delivery modes for patients with cardiopulmonary diseases, in terms of exercise capacity expressed as 6MWT distance, peak oxygen consumption and QoL. Telerehabilitation appeared to have higher adherence rates compared with centre-based exercise. There has been similar or no adverse events reported in telerehabilitation compared with centre-based exercise. The authors concluded that although telerehabilitation showed promise in patients with cardiopulmonary diseases, compelling evidence was still limited. There was a need for more detailed, high-quality studies and for studies on the use of video-based telerehabilitation. [11]

A 2014 systematic review and metanalysis aimed to determine the effectiveness of telehealth delivered CR compared with centre-based supervised CR. Five databases were searched to April 2014 without language restriction and randomized controlled trials that compared telehealth intervention delivered CR with traditional centre-based supervised CR in adults with CAD were included. Fifteen articles reporting nine trials were reviewed, most of which recruited patients with myocardial infarction or revascularization. No statistically significant difference was found between telehealth interventions delivered and centre-based supervised CR in exercise capacity, weight, systolic and diastolic blood pressure, lipid profile, smoking, mortality, quality of life and psychosocial state. The authors concluded that telehealth intervention delivered CR does not have significantly inferior outcomes compared to centre-based supervised program in low to moderate risk CAD patients. Telehealth intervention offers an alternative deliver model of CR for individuals less able to access centre-based CR. Choices should reflect preferences, anticipation, risk profile, funding, and accessibility to health service. [10]

A 2019 randomised controlled non-inferiority trial examined the effects and costs of real-time remotely monitored exercise-based CR (REMOTE-CR) with centre-based programmes of CR (CBexCR) in adults with CHD. One hundred sixty two participants were randomised to receive 12 weeks of telerehabilitation or centre-based rehabilitation.

REMOTE-CR provided individualised exercise prescription, real-time exercise monitoring/coaching and theory-based behavioural strategies via a bespoke telerehabilitation platform (smartphone and chest-worn wearable sensor, bespoke smartphone, web apps and custom middleware) (Figure 2). During exercise training, participants' physiological (heart and respiratory rate, single lead ECG) and geopositional data were displayed in the smartphone app for self-monitoring, streamed to a web server via 3G/4G/Wi-Fi, and visualised in the web app. Specialists provided real-time individualised audio coaching, feedback and social support throughout (but not prior to) real-time exercise monitoring. Participants received audio communications via earphones to optimise usability and preserve the real-time context of message content. Outside of real-time interaction, participants could review all recorded exercise performance data, set individualised goals and review automated goal achievement feedback to facilitate self-monitoring. REMOTE-CR comprised three exercise sessions per week over 12 weeks and encouragement to be active ≥5 days per week. Prescribed session duration and intensity level ranged from 30 to 60 min (including warm-up and cool-down phases) and 40%–65% heart rate reserve, respectively; intensity level was adjusted to optimise physiological adaptation without inducing abnormal clinical signs or symptoms. Walking was the most accessible exercise mode but participants could choose alternatives if preferred. Exercise prescription was individualised and progressive, based on participants' maximal aerobic exercise capacity ($\dot{V}O_{2max}$), exercise-induced signs and symptoms, age, sex, exercise tolerance and preferences. CBexCR comprised 12 weeks of supervised exercise delivered by clinical exercise physiologists in CR clinics. Exercise prescription was comparable to REMOTE-CR and studies that have established the effectiveness of CBexCR.

This trial resulted that $\dot{V}O_{2max}$ was comparable in both groups at 12 weeks and REMOTE-CR was non inferior to CBexCR. REMOTE-CR participants were less sedentary at 24 weeks while CBexCR participants had smaller waist and hip circumferences at 12 weeks. No other between-group differences were detected. Per capita programme delivery and medication costs were lower for REMOTE-CR. Hospital service utilisation costs showed no statistically significant difference. The authors concluded that REMOTE-CR is an effective, cost-efficient alternative delivery CR model that could—as a complement to existing services—improve overall utilisation rates by increasing reach and satisfying unique participant preferences. [54]

A 2016 randomised, single-blind, non-inferiority trial investigated whether home-based video telerehabilitation is equivalent to centre based programs in patients with HF. Patients with stable HF were recruited to a 12-week exercise-based rehabilitation program in two hospitals. Participants were randomised to telerehabilitation or control groups. The telerehabilitation group received a 12-week, real-time video-based telerehabilitation program delivered into patient's homes via the internet twice-weekly. The control group received a traditional centre based program of the same duration and frequency. Both groups received similar exercise prescription. Participants were assessed by independent blinded examiners at baseline and at completion. The primary outcome was the 6MWT distance at program completion. Quality of life and program attendance rates were secondary outcomes. Post-program assessment on 53 participants (mean age 67 years,75% male) revealed no significant difference between the groups with regard to the 6MWT distance gains. No difference between groups was found for QoL, but higher attendance rates were observed in the telerehabilitation group. The authors concluded that telerehabilitation was non-inferior to centre based exercise in patients with HF and appeared to be an effective alternative. [55]

Figure 2: Remotely monitored exercise-based cardiac telerehabilitation platform schematic.

A 2019 pilot study evaluated the feasibility and usefulness of biomedical sensors in telerehabilitation in patients with HF. Four participants with HF (mean age 66 years) followed the 12-week CR program using telerehabilitation, including sensors to monitor real-time vital signs during sessions. The exercise program included cardiovascular, strengthening and flexibility exercises. Participants were evaluated before the intervention and one month after the end of the program. Functional capacity was measured with CPET, the 6MWT, and the sit to stand test. Quality of life was objectified using the Kansas City Cardiomyopathy Questionnaire. The main outcome demonstrated that real-time biomedical sensors can be safely used by clinicians during a telerehabilitation session. Most participants showed a tendency to improve their physical capacities such as walking distance and lower limb muscular strength. As a main outcome of CR, QoL seems to improve after the 12-week intervention. The authors concluded that this study proved the feasibility of using telerehabilitation with real-time biomedical sensors as an alternative or a complement to the conventional CR program. Use of sensors allowed a safe environment for the patient and an adequate and personalized exercise prescription. Limitation in one-to-one supervision must be challenged in future clinical trials to demonstrate that telerehabilitation could be efficient for cardiac patients requiring more individual supervision than group sessions in a gymnasium. Integrating biomedical sensors to a telerehabilitation platform allowed clinicians to receive real-time transmissions of the ECG signal, oxygen saturation, and heart rate during an exercise program. These clinical data could be helpful to adjust and personalize the intensity of exercises to each patient's condition. [56]

A 2017 RTC aimed to analyse the effect of a home-based specific exercise program, maintenance phase, with a six months period, performed in a virtual reality or conventional environment, on the body composition, eating patterns and lipid profile of subjects with CAD. Patients were randomly assigned to either intervention group 1 (n = 11), whose program encompassed the use of virtual reality; or intervention group 2, a booklet (n = 11) or a control group, only receiving education concerning cardiovascular risk factors (n = 11) during 6 months. Beyond the baseline, at 3 and 6 months the body composition was assessed with a bioimpedance scale and a tape-measure, eating patterns with the semi-quantitative food frequency questionnaire and three months later, the lipid profile with laboratory tests.

The virtual reality intervention group used the Kinect-RehabPlay project, which was developed by the faculty of engineering University of Porto and which relies on software to monitor and evaluate the rehabilitation exercises, which have to be performed by the user and captured by the Kinect sensor, providing him/her with real time feedback about the given challenge. This system provides a virtual physical therapist performing the exercise and providing indications concerning the quality of execution. The participant is also represented as a second avatar, which interactively follows the physical therapist. The software uses the Microsoft Kinect to track individual movement and making a match with a pre-defined pattern. This feature monitored the number of repetitions for each exercise, according to the pre-calculated value, and set it to the individual exercise profile. The same was referenced in the program along with the respective exercise.

The intervention group 1 revealed significant improvements in the waist-to-hip ratio after 6 months and, between the baseline and third month, when compared with the control group. The intervention group 1 also decreased total fat consumption after 6 months and increased high-density lipoprotein cholesterol 3 months after the program end. The authors concluded that he virtual reality format had a positive influence on body composition, specifically on the waist-to-hip ratio, in the first 3 months. [57]

In another 2017 RCT the virtual reality platform Kinect-RehabPlay was used to analyse the effect of a six-month home-based phase III specific exercise program, performed in a virtual reality environment compared to conventional (booklet) environment, on executive function, QoL and depression, anxiety and stress in patients with CAD. This trial was conducted in patients, who had completed phase II CR, randomly assigned to intervention group 1 (IG1), whose program encompassed the use of Kinect (n = 11); or intervention group 2 (IG2), a paper booklet (n = 11); or a control group (CG), only subjected to the usual care (n = 11). The three groups received education on cardiovascular risk factors. The assessed parameters, at baseline, 3 and 6 months, were executive function, control and integration in the implementation of an adequate behaviour in relation to a certain objective, specifically the ability to switch information (Trail Making Test), working memory (Verbal Digit Span test), and selective attention and conflict resolution ability (Stroop test), QoL (MacNew questionnaire), depression, anxiety and stress (Depression, Anxiety and Stress Scale 21).

The results were that he IG1 revealed significant improvements, in the selective attention and conflict resolution ability, in comparison with the CG in the 6 months period and in comparison with the IG2 in the 3 to 6 months period. No significant differences were found in the QoL, depression, anxiety and stress. The authors concluded that the virtual reality format had improved selective attention and conflict resolution ability, revealing the potentiality of CR, specifically with virtual reality exercise, on executive function. [58]

A 2019 randomized clinical trial investigated the effects of a 9-week hybrid comprehensive telerehabilitation program (HTCR) on long-term outcomes in patients with HF. The Telerehabilitation in HF Patients (TELEREH-HF) trial was a multicentre, prospective, open-label, parallel-group randomized clinical trial that enrolled 850 HF patients with NYHA level I-IV and LVEF≤ 40% up to 6 months after hospitalization . Patients from 5 centres in Poland were randomized 1:1 to HTCR plus usual care or usual care only and followed up for 14 to 26 months after randomization. During the first 9 weeks, patients underwent either hybrid HTCR (1 week in hospital and 8 weeks at home) or usual care with observation. The HCTR intervention encompassed telecare, telerehabilitation, and remote monitoring of implantable devices. No intervention occurred in the remaining study period.

Telerehabilitation was carried out by a medical team (physicians, physiotherapists, nurses, and a psychologist), and advanced monitoring systems were used. The monitoring system included a special remote device for supervised exercise training monitored with tele-ECG, which consists of an EHO mini device, blood pressure device, and body-weight scale, a data transmission set via a mobile telephone, and a monitoring centre capable of receiving and storing patients' medical data. The EHO mini devices was able to record ECG data from 3 precordial leads and transmit them via a mobile telephone network to the monitoring centre. The device had training sessions pre-programmed individually for each patient (with defined exercise duration, breaks, and timing of ECG recording). Additionally, if technical requirements were complied with, patients in the HCTR group who had CIEDs received a transmitter which allowed the automatic transmission of data from the implant to a web-based monitoring platform. Remote monitoring relied on data acquired automatically by the device, with unscheduled transmission of any predefined alerts to the medical staff in each centre. The telerehabilitation program encompassed 3 training modalities: endurance aerobic Nordic walking training, respiratory muscle training, and light resistance and strength exercises and it was planned individually for each patient according to the guidelines.

The trial showed that the HCTR intervention did not extend the percentage of days alive and out of the hospital. The mean days were 91.9 (19.3) days in the HCTR group vs 92.8 (18.3) days in the usual-care group, with the probability that HCTR extends days alive and out of the hospital equal to 0.49 vs usual care. During follow-up, 54 patients died in the HCTR arm and 52 in the usual-care arm, with mortality rates at 26 months of 12.5% vs 12.4%, respectively. There were also no differences in hospitalization rates. The HCTR intervention was effective at 9 weeks, significantly improving peak oxygen consumption and QoL and it was well tolerated, with no serious adverse events during exercise. The authors concluded that the positive effects of a 9-week program of HCTR in patients with HF did not increase the percentage of days alive and out of the hospital and did not reduce mortality and hospitalization over a follow-up period of 14 to 26 months. [59]

4.3 Cost of telerehabilitation

A randomized control trial published in 2015 investigated the cost-utility of a cardiac telerehabilitation program. The aim of the intervention was to increase the patients' participation in the program. One hundred fifty one patients participated in this trial. The patient was registered as a user in the information technology platforms and was equipped with a tablet computer giving him or her web access to his or her own personal health record and measurements. The patient received training in the use of the different devices and the digital rehabilitation plan, and a doctor prescribed how often the patient needed to measure blood pressure, pulse, and weight, most often twice a week, whereas steps were measured every day. The data were transmitted via a secure transmission line. Patients, their relatives, and healthcare professionals from the hospital and healthcare centres were able to communicate and share data from the personal health record. In addition, patients and relatives had access to activeheart.dk (a digital toolbox with information on rehabilitation topics, activities, and videos showing patients describing their experiences of being a heart patient and appropriate exercises for after surgery). After 2 weeks in the program, each patient was visited by a project assistant in order to make sure that the patient and relative were confident in using the technology. Healthcare professionals monitored the measured values every week, contacted the patients if the values were abnormal, and discussed rehabilitation activities with the patient. The telerehabilitation program lasted for 3 months. The control group followed a traditional rehabilitation program at the hospital or healthcare centre based on CR guidelines.

Costs of the intervention were estimated with a health sector perspective following international guidelines for cost utility. Quality of life was assessed using the 36- Item Short Form Health Survey. The rehabilitation activities were approximately the same in the two groups, but the number of contacts with the physiotherapist was higher among the intervention group. The mean total cost per patient was 1,700 euros higher in the intervention group. The quality adjusted life-years gain was higher in the intervention group, but the difference was not statistically significant. The incremental cost utility ratio was more than 400,000 euros per quality adjusted life-years gained. The authors concluded that even though the rehabilitation activities increased, the program does not appear to be cost-effective. The intervention itself was not costly (less than 500 euros), and increasing the number of patients may show reduced costs of the devices and make the cardiac telerehabilitation programme more cost-effective. Telerehabilitation can increase participation, but the intervention, in its current form, does not appear to be cost-effective. [60]

Another randomized control trial which was published in 2015 investigated the cost effectiveness of a comprehensive cardiac telerehabilitation programme. One hundred forty CR patients, randomized (1:1) to a 24-week telerehabilitation programme in addition to conventional CR (intervention group) or to conventional CR alone (control group). The incremental cost-effectiveness ratio was calculated based on intervention and health care costs (incremental cost), and the differential incremental quality adjusted life years gained.

The patients in the intervention group received a 24-week internet-based, comprehensive telerehabilitation programme. The programme focused on multiple CR core components and used both physical activity telemonitoring and dietary, smoking cessation, physical activity telecoaching strategies. For the telemonitoring part, intervention group patients were prescribed patient-specific exercise training protocols, based on achieved peak aerobic capacity (peakVO_2) during initial maximal CPET (CPET) and calculated body mass index (BMI). Intervention group patients were instructed to continuously wear an accelerometer and to weekly transmit their registered activity data to the telerehabilitation centre's local server. These data enabled a semi-automatic telecoaching system to provide the patients with feedback, encouraging them to gradually achieve predefined exercise training goals. In addition, patients received e-mails and/or SMSs (text messages) with tailored dietary and smoking cessation recommendations, based on cardiovascular risk factor profiling at study start.

The trial resulted that the total average cost per patient was significantly lower in the intervention group than in the control group with an overall incremental cost of 564.40 €. Dividing this incremental cost by the baseline adjusted differential incremental quality adjusted life years yielded an incremental cost-effectiveness ratio of -21,707 €/QALY. The number of days lost due to cardiovascular rehospitalizations in the intervention group was significantly lower than in the control group. The authors concluded that the addition of cardiac telerehabilitation to conventional centre-based CR is more cost effective and efficient than centre-based CR alone. They commented that the results of this trial might be useful for policy makers to decide how limited health care resources should best be allocated in the era of exploding needs. [61]

4.4 Conclusion

As the global burden of CVD is increasing the need for referral to, access to and participation in effective secondary prevention therapies and rehabilitation services will always be increased. Cardiac rehabilitation has been proven to be an effective tool for the care of patients with CHD and HF and is highly recommended. The benefits of CR include mortality reduction, symptom relief, smoking cessation, exercise tolerance improvement, risk factors modification and overall psychosocial wellbeing. The main challenge of CR at the moment is the need to overcome its currently unsatisfactory accessibility.

A promising solution to these problems seems to be home-based telerehabilitation. According to the available evidence, it is clear that such treatment is technologically and logistically implementable and thus offers an effective and safe way of rehabilitation accepted by patients and the caregiver team. Telemedicine/telehealth has the potential to increase quality of care by enhancing communication between the patient and healthcare professionals or providing access to specialized services for patients who otherwise would not have access to rehabilitation and prevention services.

Telerehabilitation interventions have a range of delivery modes. Internet, mobile phones, text messaging, smartphone applications, telephone calls, online monitoring, portable computers and tablets, biomedical censors, chest wearable devices, earphones are among the modalities that are used in telerehabilitation programs. Telerehabilitation could be offered to patients who cannot attend CR, or as an adjunct to CR. Despite a significant variation in the reviewed telerehabilitation interventions, they offer substantial benefits for the treatment of HF and CHD in comparison with usual care and are equivalent to centre-based CR regarding the benefits in functional capacity, muscle strength, QoL, patient satisfaction, cardiovascular risk factors modification, depression and physical activity level. Reduction of recurrent cardiac events and total cholesterol at medium to long term duration in hybrid CR programmes which combine usual care and/or CR has been observed. The solution to the limitation that telerehabilitation needs a one to one supervision of the patient might be overcome by the use of virtual reality platforms which offer individual supervision. Telerehabilitation is a safe and efficient alternative with high adherence by the patients. The new technologies have a great potential to improve CR delivery and minimize health problems. However, the implementation of these technologies in CR seems to be in the initial stage and there is a need for more detailed and high quality studies. The development of new technologies and devices seems to be a promising opportunity for the improvement of the provision and the efficiency of CR and telerehabilitation.

References

1. Global, regional, and national age–sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *The Lancet*. 2015;385(9963):117-171. doi:10.1016/S0140-6736(14)61682-2

2. Mozaffarian D, Benjamin EJ, Go AS, et al. Executive Summary: Heart Disease and Stroke Statistics—2016 Update: A Report From the American Heart Association. *Circulation*. 2016;133(4):447-454. doi:10.1161/CIR.0000000000000366

3. Mosterd A, Hoes AW. Clinical epidemiology of heart failure. *Heart*. 2007;93(9):1137-1146. doi:10.1136/hrt.2003.025270

4. Knuuti J, Wijns W, Saraste A, et al. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. *European Heart Journal*. August 2019:ehz425. doi:10.1093/eurheartj/ehz425

5. Piepoli MF, Hoes AW, Agewall S, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts)Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur Heart J*. 2016;37(29):2315-2381. doi:10.1093/eurheartj/ehw106

6. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J*. 2016;37(27):2129-2200. doi:10.1093/eurheartj/ehw128

7. Bjarnason-Wehrens B, McGee H, Zwisler A-D, et al. Cardiac rehabilitation in Europe: results from the European Cardiac Rehabilitation Inventory Survey. *European Journal of Cardiovascular Prevention & Rehabilitation*. 2010;17(4):410-418. doi:10.1097/HJR.0b013e328334f42d

8. Conraads VM, Deaton C, Piotrowicz E, et al. Adherence of heart failure patients to exercise: barriers and possible solutions: A position statement of the Study Group on Exercise Training in Heart Failure of the Heart Failure Association of the European Society of Cardiology. *European Journal of Heart Failure*. 2012;14(5):451-458. doi:10.1093/eurjhf/hfs048

9. Piotrowicz E. The management of patients with chronic heart failure: the growing role of e-Health. *Expert Review of Medical Devices*. 2017;14(4):271-277. doi:10.1080/17434440.2017.1314181

10. Huang K, Liu W, He D, et al. Telehealth interventions versus center-based cardiac rehabilitation of coronary artery disease: A systematic review and meta-analysis. *Eur J Prev Cardiolog*. 2015;22(8):959-971. doi:10.1177/2047487314561168

11. Hwang R, Bruning J, Morris N, Mandrusiak A, Russell T. A Systematic Review of the Effects of Telerehabilitation in Patients With Cardiopulmonary Diseases: *Journal of Cardiopulmonary Rehabilitation and Prevention*. 2015;35(6):380-389. doi:10.1097/HCR.0000000000000121

12. Piotrowicz E, Baranowski R, Bilinska M, et al. A new model of home-based telemonitored cardiac rehabilitation in patients with heart failure: effectiveness, quality of life, and adherence. *European Journal of Heart Failure*. 2010;12(2):164-171. doi:10.1093/eurjhf/hfp181

13. Piotrowicz E, Zieliński T, Bodalski R, et al. Home-based telemonitored Nordic walking training is well accepted, safe, effective and has high adherence among heart failure patients, including those with cardiovascular implantable electronic devices: a randomised controlled study. *Eur J Prev Cardiolog*. 2015;22(11):1368-1377. doi:10.1177/2047487314551537

14. Tanai E, Frantz S. Pathophysiology of Heart Failure. In: Terjung R, ed. *Comprehensive Physiology*. Hoboken, NJ, USA: John Wiley & Sons, Inc.; 2015:187-214. doi:10.1002/cphy.c140055

15. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA Guideline for the Management of Heart Failure. *Journal of the American College of Cardiology*. 2013;62(16):e147-e239. doi:10.1016/j.jacc.2013.05.019

16. Sanchis-Gomar F, Perez-Quilis C, Leischik R, Lucia A. Epidemiology of coronary heart disease and acute coronary syndrome. *Ann Transl Med*. 2016;4(13):256-256. doi:10.21037/atm.2016.06.33

17. Müller-Nordhorn J, Willich SN. Coronary Heart Disease. In: *International Encyclopedia of Public Health*. Elsevier; 2017:159-167. doi:10.1016/B978-0-12-803678-5.00090-4

18. Steenbergen C, Frangogiannis NG. Ischemic Heart Disease. In: *Muscle*. Elsevier; 2012:495-521. doi:10.1016/B978-0-12-381510-1.00036-3

19. Leon AS, Franklin BA, Costa F, et al. Cardiac Rehabilitation and Secondary Prevention of Coronary Heart Disease: An American Heart Association Scientific Statement From the Council on Clinical Cardiology (Subcommittee on Exercise, Cardiac Rehabilitation, and Prevention) and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity), in Collaboration With the American Association of Cardiovascular and Pulmonary Rehabilitation. *Circulation*. 2005;111(3):369-376. doi:10.1161/01.CIR.0000151788.08740.5C

20. Balady GJ, Ades PA, Bittner VA, et al. Referral, Enrollment, and Delivery of Cardiac Rehabilitation/Secondary Prevention Programs at Clinical Centers and Beyond: A Presidential Advisory From the American Heart Association. *Circulation*. 2011;124(25):2951-2960. doi:10.1161/CIR.0b013e31823b21e2

21. Smith SC, Benjamin EJ, Bonow RO, et al. AHA/ACCF Secondary Prevention and Risk Reduction Therapy for Patients With Coronary and Other Atherosclerotic Vascular Disease: 2011 Update. *Journal of the American College of Cardiology*. 2011;58(23):2432-2446. doi:10.1016/j.jacc.2011.10.824

22. Authors/Task Force Members:, Perk J, De Backer G, et al. European Guidelines on cardiovascular disease prevention in clinical practice (version 2012): The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts) * Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *European Heart Journal*. 2012;33(13):1635-1701. doi:10.1093/eurheartj/ehs092

23. Wenger NK, Froelicher ES, Smith LK, et al. Cardiac rehabilitation as secondary prevention. Agency for Health Care Policy and Research and National Heart, Lung, and Blood Institute. *Clin Pract Guidel Quick Ref Guide Clin*. 1995;(17):1-23.

24. Ezekowitz JA, O'Meara E, McDonald MA, et al. 2017 Comprehensive Update of the Canadian Cardiovascular Society Guidelines for the Management of Heart Failure. *Canadian Journal of Cardiology*. 2017;33(11):1342-1433. doi:10.1016/j.cjca.2017.08.022

25. Piepoli MF, Conraads V, Corrà U, et al. Exercise training in heart failure: from theory to practice. A consensus document of the Heart Failure Association and the European Association for Cardiovascular Prevention and Rehabilitation. *European Journal of Heart Failure*. 2011;13(4):347-357. doi:10.1093/eurjhf/hfr017

26. Heran BS, Chen JM, Ebrahim S, et al. Exercise-based cardiac rehabilitation for coronary heart disease. In: The Cochrane Collaboration, ed. *Cochrane Database of Systematic Reviews*. Chichester, UK: John Wiley & Sons, Ltd; 2011:CD001800.pub2. doi:10.1002/14651858.CD001800.pub2

27. Anderson L, Thompson DR, Oldridge N, et al. Exercise-based cardiac rehabilitation for coronary heart disease. Cochrane Heart Group, ed. *Cochrane Database of Systematic Reviews*. January 2016. doi:10.1002/14651858.CD001800.pub3

28. Rauch B, Davos CH, Doherty P, et al. 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 Cardiolog*. 2016;23(18):1914-1939. doi:10.1177/2047487316671181

29. Taylor RS, Sagar VA, Davies EJ, et al. Exercise-based rehabilitation for heart failure. Cochrane Heart Group, ed. *Cochrane Database of Systematic Reviews*. April 2014. doi:10.1002/14651858.CD003331.pub4

30. Francis T, Kabboul N, Rac V, et al. The Effect of Cardiac Rehabilitation on Health-Related Quality of Life in Patients With Coronary Artery Disease: A Meta-analysis. *Canadian Journal of Cardiology*. 2019;35(3):352-364. doi:10.1016/j.cjca.2018.11.013

31. Taylor RS, Long L, Mordi IR, et al. Exercise-Based Rehabilitation for Heart Failure. *JACC: Heart Failure*. 2019;7(8):691-705. doi:10.1016/j.jchf.2019.04.023

32. Vanhees L, Rauch B, Piepoli M, et al. Importance of characteristics and modalities of physical activity and exercise in the management of cardiovascular health in individuals with cardiovascular disease (Part III). *Eur J Prev Cardiolog*. 2012;19(6):1333-1356. doi:10.1177/2047487312437063

33. 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. *International Journal of Cardiology*. 2016;208:120-127. doi:10.1016/j.ijcard.2016.01.207

34. Zwisler A-D, Norton RJ, Dean SG, et al. Home-based cardiac rehabilitation for people with heart failure: A systematic review and meta-analysis. *International Journal of Cardiology*. 2016;221:963-969. doi:10.1016/j.ijcard.2016.06.207

35. Hannan A, Hing W, Simas V, et al. High-intensity interval training versus moderate-intensity continuous training within cardiac rehabilitation: a systematic review and meta-analysis. *OAJSM*. 2018;Volume 9:1-17. doi:10.2147/OAJSM.S150596

36. Xie B, Yan X, Cai X, Li J. Effects of High-Intensity Interval Training on Aerobic Capacity in Cardiac Patients: A Systematic Review with Meta-Analysis. *BioMed Research International*. 2017;2017:1-16. doi:10.1155/2017/5420840

37. Jewiss D, Ostman C, Smart NA. The effect of resistance training on clinical outcomes in heart failure: A systematic review and meta-analysis. *International Journal of Cardiology*. 2016;221:674-681. doi:10.1016/j.ijcard.2016.07.046

38. Smart NA, Giallauria F, Dieberg G. Efficacy of inspiratory muscle training in chronic heart failure patients: A systematic review and meta-analysis. *International Journal of Cardiology*. 2013;167(4):1502-1507. doi:10.1016/j.ijcard.2012.04.029

39. Neto MG, Martinez BP, Conceição CS, Silva PE, Carvalho VO. Combined Exercise and Inspiratory Muscle Training in Patients With Heart Failure: A SYSTEMATIC REVIEW AND META-ANALYSIS. *Journal of Cardiopulmonary Rehabilitation and Prevention*. 2016;36(6):395-401. doi:10.1097/HCR.0000000000000184

40. Liu T, Chan AW, Liu YH, Taylor-Piliae RE. Effects of Tai Chi-based cardiac rehabilitation on aerobic endurance, psychosocial well-being, and cardiovascular risk reduction among patients with coronary heart disease: A systematic review and meta-analysis. *European Journal of Cardiovascular Nursing*. 2018;17(4):368-383. doi:10.1177/1474515117749592

41. Borg S, Öberg B, Leosdottir M, Lindolm D, Nilsson L, Bäck M. Factors associated with non-attendance at exercise-based cardiac rehabilitation. *BMC Sports Sci Med Rehabil*. 2019;11(1):13. doi:10.1186/s13102-019-0125-9

42. Pio CS de A, Chaves G, Davies P, Taylor R, Grace S. Interventions to Promote Patient Utilization of Cardiac Rehabilitation: Cochrane Systematic Review and Meta-Analysis. *JCM*. 2019;8(2):189. doi:10.3390/jcm8020189

43. Xu L, Li F, Zhou C, Li J, Hong C, Tong Q. The effect of mobile applications for improving adherence in cardiac rehabilitation: a systematic review and meta-analysis. *BMC Cardiovasc Disord*. 2019;19(1):166. doi:10.1186/s12872-019-1149-5

44. Saner H, van der Velde E. eHealth in cardiovascular medicine: A clinical update. *Eur J Prev Cardiolog*. 2016;23(2_suppl):5-12. doi:10.1177/2047487316670256

45. Shaw DK, Heggestad-Hereford JR, Southard DR, Sparks KE. American Association of Cardiovascular and Pulmonary Rehabilitation Telemedicine Position Statement: *Journal of Cardiopulmonary Rehabilitation*. 2001;21(5):261-262. doi:10.1097/00008483-200109000-00002

46. Piotrowicz E, Piepoli MF, Jaarsma T, et al. Telerehabilitation in heart failure patients: The evidence and the pitfalls. *International Journal of Cardiology*. 2016;220:408-413. doi:10.1016/j.ijcard.2016.06.277

47. Tousignant M, Mampuya WM. Telerehabilitation for patients with heart failure. *Cardiovasc Diagn Ther*. 2015;5(1):74-78. doi:10.3978/j.issn.2223-3652.2015.01.12

48. Hwang R, Bruning J, Morris NR, Mandrusiak A, Russell T. Home-based telerehabilitation is not inferior to a centre-based program in patients with chronic heart failure: a randomised trial. *Journal of Physiotherapy*. 2017;63(2):101-107. doi:10.1016/j.jphys.2017.02.017

49. Jin K, Khonsari S, Gallagher R, et al. Telehealth interventions for the secondary prevention of coronary heart disease: A systematic review and meta-analysis. *European Journal of Cardiovascular Nursing*. 2019;18(4):260-271. doi:10.1177/1474515119826510

50. Oldridge N, Pakosh M, Grace SL. A systematic review of recent cardiac rehabilitation meta-analyses in patients with coronary heart disease or heart failure. *Future Cardiology*. 2019;15(3):227-249. doi:10.2217/fca-2018-0085

51. Cristo D de, Nascimento NP do, Dias AS, Sachetti A. Telerehabilitation for Cardiac Patients: Systematic Review. *International Journal of Cardiovascular Sciences*. 2018. doi:10.5935/2359-4802.20180032

52. Rawstorn JC, Gant N, Direito A, Beckmann C, Maddison R. Telehealth exercise-based cardiac rehabilitation: a systematic review and meta-analysis. *Heart*. 2016;102(15):1183-1192. doi:10.1136/heartjnl-2015-308966

53. Chan C, Yamabayashi C, Syed N, Kirkham A, Camp PG. Exercise Telemonitoring and Telerehabilitation Compared with Traditional Cardiac and Pulmonary Rehabilitation: A Systematic Review and Meta-Analysis. *Physiotherapy Canada*. 2016;68(3):242-251. doi:10.3138/ptc.2015-33

54. Maddison R, Rawstorn JC, Stewart RAH, et al. Effects and costs of real-time cardiac telerehabilitation: randomised controlled non-inferiority trial. *Heart*. 2019;105(2):122-129. doi:10.1136/heartjnl-2018-313189

55. Hwang R, Bruning J, Mandrusiak A, Morris N, Russell T. Providing Heart Failure Rehabilitation in the Home via Telerehabilitation. *Heart, Lung and Circulation*. 2016;25:S4. doi:10.1016/j.hlc.2016.06.008

56. Tousignant M, Mampuya WM, Bissonnette J, et al. Telerehabilitation with live-feed biomedical sensor signals for patients with heart failure: a pilot study. *Cardiovasc Diagn Ther*. 2019;9(4):319-327. doi:10.21037/cdt.2019.03.05

57. Vieira ÁS da S, Cristina Damas Argel de Melo M, Andreia Raquel Santos Noites SP, Machado JP, Joaquim Gabriel MM. The effect of virtual reality on a home-based cardiac rehabilitation program on body composition, lipid profile and eating patterns: A randomized controlled trial. *European Journal of Integrative Medicine*. 2017;9:69-78. doi:10.1016/j.eujim.2016.11.008

58. Vieira Á, Melo C, Machado J, Gabriel J. Virtual reality exercise on a home-based phase III cardiac rehabilitation program, effect on executive function, quality of life and depression, anxiety and stress: a randomized controlled trial. *Disability and Rehabilitation: Assistive Technology*. 2018;13(2):112-123. doi:10.1080/17483107.2017.1297858

59. Piotrowicz E, Pencina MJ, Opolski G, et al. Effects of a 9-Week Hybrid Comprehensive Telerehabilitation Program on Long-term Outcomes in Patients With Heart Failure: The Telerehabilitation in Heart Failure Patients (TELEREH-HF) Randomized Clinical Trial. *JAMA Cardiol*. November 2019. doi:10.1001/jamacardio.2019.5006

60. Kidholm K, Rasmussen MK, Andreasen JJ, et al. Cost-Utility Analysis of a Cardiac Telerehabilitation Program: The Teledialog Project. *Telemedicine and e-Health*. 2016;22(7):553-563. doi:10.1089/tmj.2015.0194

61. Frederix I, Hansen D, Coninx K, et al. Effect of comprehensive cardiac telerehabilitation on one-year cardiovascular rehospitalization rate, medical costs and quality of life: A cost-effectiveness analysis. *Eur J Prev Cardiolog*. 2016;23(7):674-682. doi:10.1177/2047487315602257