Master's thesis

NTNU
Norwegian University of Science and Technology
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Department of Circulation and Medical Imaging

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Home-Based High-Intensity Interval Training with Heart Failure

A Comparison Between Supervised and Unsupervised Modalities

Master's thesis in Exercise Physiology
Supervisor: Inger-Lise Aamot Aksetøy
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ABSTRACT

Background: In recent years, both telerehabilitation and high-intensity interval training have been studied in connection with patients with Heart Failure (HF). However, these two variables have never been investigated together. The aim of this study was to investigate exercise intensity, perceived safety and exertion of home-based, high-intensity interval training exercise.

Design: A non-randomised cross-over study.

Methods: Eleven participants with HF (7 men, 4 women; mean age 63.4 years), from the IT IS HOPE 4 HF study, volunteered to participate. After 3 months of twice weekly, high-intensity interval training via telerehabilitation, the participants were asked to perform the last week of intervention wearing heart rate (HR) monitors during both supervised- (live video-conference telerehabilitation) and unsupervised (pre-recorded video) sessions. The outcome was to determine if there were differences between the supervised- and unsupervised sessions in exercise intensity, perceived safety and exertion levels.

Results: Eight participants completed the intervention. No adverse events were reported or recorded. Significant differences were found between supervised- and unsupervised exercise modalities when comparing 2nd (86±16 vs 79±16 %HR_{peak}, $p=0.04$), 3rd (86±15 vs 81±15 %HR_{peak}, $p=0.03$) and 4th (88±16 vs 81±17 %HR_{peak}, $p=0.01$) high-intensity intervals (HIIs) and the 2nd moderate intensity active break (82±17 vs 77±15 %HR_{peak}, $p=0.02$). All participants felt safe during every recorded intervention. However, no significant differences were found in perceived safety and exertion levels.

Conclusion: Telerehabilitation allowed the participants to reach target exercise intensities, while the unsupervised video sessions, did not. However, after 3 months of training, participants felt safe when training both with- and without supervision.

Keywords
Heart failure, telerehabilitation, high-intensity interval training, home-based exercise, exercise intensity

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ABBREVIATIONS

BMI	–	Body Mass Index
CPET	–	Cardio-pulmonary exercise test
ECG	–	Electrocardiography
EF	–	Ejection fraction
ESC	–	European Society of Cardiology
HF	–	Heart failure
HFpEF	–	Heart failure with preserved ejection fraction
HFrEF	–	Heart failure with reduced ejection fraction
HII	–	High-intensity interval
HIIT	–	High-intensity interval training
IQR	–	Inter-quartile range
HR, HR_{peak}, HR_{max}	–	Heart rate, -peak, -maximal
HRR	–	Heart rate reserve
LV	–	Left ventricular
MCID	–	Minimal clinically important difference
NYHA	–	New York Heart Association
QoL	–	Quality of life
RV	–	Right ventricular
SD	–	Standard deviation
VO_2, VO_{2peak}, VO_{2max}	–	Oxygen consumption, -peak, -maximal
$\%HR_{peak}$	–	Percentage of peak heart rate

INTRODUCTION

Heart Failure

Heart failure (HF) is a clinical syndrome in which the cardiac muscle faces a decline in pumping capacity [1]. This is closely tied to the loss of a critical amount of functional myocardial cells, which can happen because of an injury to the heart or other causes. The most common ones are ischemic heart disease, hypertension and diabetes [2, 3]. Three out of four patients with HF have pre-existing hypertension, which alone doubles the risk of developing HF compared to normotensive patients [3]. Less common causes of HF are cardiomyopathies, infections, toxins, valvular disease, and prolonged arrhythmias [1].

Worldwide there are approximately 2 million new cases of HF every year, with 11.000 only in Norway [4]. This results in a global prevalence of 22 million affected people [5]. In 2012 the World Bank estimated that the global economic cost for HF was $108 billion [6], and since the prevalence of HF is increasing, we can only expect its cost to increase accordingly.

Classification of HF

Based on dysfunction we can identify two kinds of HF: left- or right ventricular dysfunction [1]. Left ventricular (LV) dysfunction is most often caused by a loss of functional myocardium because of ischemic disease or infarction. Other causes might also be uncontrolled hypertension and excessive pressure overload, volume overload because of valvular incompetence, or impaired contractility due to cardiotoxins and drugs. Regardless of its aetiology, LV dysfunction results in a decrease in cardiac output (Q), which leads to global hypoperfusion. Moreover, LV dysfunction causes the amount of blood in the left ventricle to increase. As a result, both end-systolic and end-diastolic volumes increase along with pressure in the LV end-diastolic phase and in the lungs' capillaries. Due to the elevated pressure in the lungs, fluid is forced out of the capillaries, which leads to pulmonary congestion and dyspnoea.

After further physio-pathological investigation, LV dysfunction can also be divided into two categories: systolic dysfunction, which entails impaired ventricular contraction and ejection, and diastolic dysfunction, which is characterized by impaired relaxation and ventricular filling. Echocardiography (ECG) is generally used to determine which kind of dysfunction is affecting the heart, via the calculation of systolic- and diastolic volumes. Even though such a classification exists, it is important to recognize that LV heart failure (LVHF) can have both systolic and diastolic features [7].

Depending on the degree of impairment, originating from the ventricular dysfunction, LVHF is generally classified based on the resulting ejection fraction (EF, the percentage of blood in the LV that is pumped by the heart per heart beat). According to the European Society of Cardiology (ESC) the following categories of EF are identified: preserved (HFpEF, normal LVEF ≥50%), mid-range (HFmrEF, mid-range LVEF 40-49%) or reduced (HFrEF, reduced LVEF <40%) [8].

On the other hand, right ventricular (RV) dysfunction is mostly caused by LV failure, but can also originate from arrhythmogenic RV cardiomyopathy or dysplasia. Similarly to the LV, when the right ventricle fails, there is an increase in the amount of blood in the ventricle itself, which leads to elevated pressure both in the right atrium and vena cava. This impairs the venous return and drainage from the body, while also increasing the pressure in the liver, the gastrointestinal tract, and the lower extremities. The increased pressure in these areas leads to abdominal pain, hepatomegaly, and peripheral oedema [1].

HF can also be classified according to its severity, based on signs and symptoms. The following tables describe the most used classification system, the New York Heart Association (NYHA) Functional Classification [9]. Patients are classified based on limitations experienced during physical activity (see *Table 1*) and according to their objective clinical level (see *Table 2*).

Table 1 – New York Heart Association (NYHA) Functional Classification of HF, according to limitations during physical activity [9].

Class	Patient Symptoms
I	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnoea (shortness of breath).
II	Slight limitation of physical activity. Comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnoea (shortness of breath).
III	Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation, or dyspnoea.
IV	Unable to carry on any physical activity without discomfort. Symptoms of heart failure at rest. If any physical activity is undertaken, discomfort increases.

Table 2 – New York Heart Association (NYHA) Functional Classification of HF, according to clinical assessment of the disease [9].

Class	Objective Assessment
A	No objective evidence of cardiovascular disease. No symptoms and no limitation in ordinary physical activity.
B	Objective evidence of minimal cardiovascular disease. Mild symptoms and slight limitation during ordinary activity. Comfortable at rest.
C	Objective evidence of moderately severe cardiovascular disease. Marked limitation in activity due to symptoms, even during less-than-ordinary activity. Comfortable only at rest.
D	Objective evidence of severe cardiovascular disease. Severe limitations. Experiences symptoms even while at rest.

Assessing HF: signs, symptoms and testing

Signs and symptoms of HF can induce patients to search for medical attention, but many of them are non-specific. In fact, they may originate from sodium and water retention, and therefore be wrongly interpreted as relative to other pathologies. More specific symptoms, such as orthopnoea and paroxysmal nocturnal dyspnoea, are less common, while others such as elevated jugular venous pressure and displacement of the apical impulse, are hard to detect and reproduce [10, 11].

Reduced exercise tolerance is one of the most consistent and limiting symptoms that HF patients display [12]. Exercise intolerance is defined as an abnormally low maximal oxygen consumption (VO_{2max}) [13]. In a day-to-day life setting, exercise intolerance is the incapacity of the individual to perform every-day tasks that require some degree of physical effort without being abnormally fatigued. Such task could be going up the stairs or walking to the supermarket. An individual with HF has a higher risk of mortality compared to a healthy one. If we add to this exercise intolerance and its abnormally low VO_{2max}, the risk for all-cause mortality increases even more [14, 15]. Exercise intolerance can occur if any of the factors that influence VO_2 are behaving as limiting [16], including the variables of the Fick equation [19]. Fick's equation, states that the body's oxygen consumption (VO_2), is the product of oxygen supply (cardiac output, Q) and oxygen demand (oxygen uptake in the muscle, $a\text{-}vO_{2diff}$).

$$V\dot{O}_2 = Q \cdot (a - vO_{2diff})$$

Where Q instead is the product of stroke volume (SV) and heart rate (HR), with SV defined as the volume of blood ejected by the left ventricle per heartbeat.

$$Q = SV \cdot HR$$

For example, a reduced and pathological Q, like in the case of HFrEF, will result in a lower MAP (mean arterial pressure, $MAP = Q \cdot TPR$) and a lower perfusion of the tissues [1]. This along with physical fatigue, due to the increased detraining, will limit the individual's physical endurance and induce exercise intolerance.

Heart rate variability (HRV) is also taken in account when evaluating HF, since it is a common clinical predictor of reduced survival expectancy [17-19]. HRV is defined as the evaluation beat-to-beat HR dynamics and frequencies [20], and it can influence Q. HRV is believed to correspond to the resulting influence of sympathetic- and parasympathetic nervous systems on the sinoatrial node's intrinsic rhythm [21]. It can be easily and non-invasively measured [22], and it can be improved by exercise [23, 24]. Studies have shown that HRV is normally reduced in HF patients, when compared to healthy controls [19, 25, 26]. It appears that vagal activity is reduced, while sympathetic activity is increased. This may lead to sympathetic-parasympathetic imbalance in the SA-node resulting in the triggering or sustaining of malignant ventricular arrhythmias [27], higher HR frequencies and longer time needed to reduce HR after exercise [24].

In order to diagnose HF, early signs and symptoms are fundamental, as well as a detailed medical history and an assessment of the cardio-respiratory fitness in terms of VO_{2max}. The best and most widely adopted way to assess VO_{2max} in this patient population is to perform a Cardio-Pulmonary Exercise Test (CPET) [13] with ECG [8].

Treatment of HF

Pharmacological treatment is a fundamental part of the holistic approach to HF patients. Its goal is to improve clinical status, functional capacity and quality of life (QoL, prevent hospital admission and reduce mortality [8]. It is known that many of the used drugs have shown negative effects in the long-term use despite being effective in the short-term. The short-term effects include reducing hospitalization, improving functional capacity and reducing mortality. As such, according to the ESC, the benefits of drugs out-rule the long-term negative effects [28]. The pharmacological treatment changes between the different kinds (HFpEF and HFrEF) and levels of HF (NYHA classification) [29]. Concerning patients with HFrEF (NYHA II-IV), the mostly used drugs are angiotensin-converting-enzyme (ACE) inhibitors, beta-blockers and mineralocorticoid receptor antagonists (MRAs), which have all been classified as IA level recommendations [28].

According to the ESC Guidelines [28], exercise training in HF patients has shown to improve exercise tolerance, QoL and hospitalization rates. A recent Cochrane review [30] showed a trend of reduced mortality with exercise training. Evidence has also shown that patients with HFpEF, benefit from exercise training by improving their VO_{2peak}, QoL and diastolic function [31-33]. The beneficial effects of exercise training in HF have earned exercise training the Class of Recommendation I and the Level of Evidence A [29, 34]. All HF patients, regardless of their ejection fraction, today receive the recommendation to perform exercise training [35].

Even though evidence and recommendations are public and the single states' guidelines are being adapted accordingly [36, 37], compliance and adherence to exercise training is still a challenge, both on the health care [38] and the patient side [39].

Exercise training with HF

Considerable knowledge has been gathered, over the last decades, concerning the importance of exercise as the "first-line treatment for several chronic diseases" [40]. Today, exercise is used as medicine in diseases that are not considered as primarily disorders of the locomotive system. HF is among the diseases that can be treated with exercise. In 2011 the ESC released a position statement [35] in which they refer to three main exercise modalities: aerobic endurance, resistance/strength and respiratory. Even though the modalities are different and challenge different systems in the body (cardiovascular, muscle-skeletal and respiratory), their ultimate goal is the same: improve health.

Aerobic endurance training

Aerobic endurance training focuses on improving the aerobic performance of the individual by acting both on the muscles, modifying their metabolism, and on the cardio-vasculorespiratory system. Since HF is a cardiovascular disease, aerobic endurance training can be considered as the most efficient exercise modality to improve patients' function. It can enhance VO_{2max}, which is used as a predictor for all-cause mortality [41], and LVEF [42]. Aerobic endurance training can be performed with different modalities (i.e. continuous or interval) and intensities (i.e. moderate-, vigorous- and high intensity, ~70-95% of HR_{max}). Throughout the years, there has been a tendency to prefer moderate- and vigorous- to high-intensity when exercising HF patients [33]. This is due to the understanding that vigorous- and moderate-intensity challenge the cardiovascular system enough to induce health benefits, as well as its intensity being well tolerated by this patient population and therefore not suspected to reduce adherence. While high-intensity exercise has been intuitively considered potentially dangerous because of the higher demands on the cardiac muscle that might lead to an increased risk of medical events. Recent studies have proved the beneficial effect of high-intensity interval training, while others have analysed its safety.

In 2009, HF-ACTION [43], a large multicentric study with 2331 participants (with HFrEF), showed that moderate intensity exercise is safe for HF patients that have either only received appropriate education, or took part in the supervised exercise sessions. Supervised exercise sessions consisted of continuous exercise on a stationary bicycle or a treadmill, at moderate intensity for 15-30 min, 3 times a week, for a total of 36 sessions [44]. Moderate intensity exercise in this study achieved significant improvements in functional performance (6-minute walking test), exercise duration on CPET and VO_{2peak}.

In 2012, Smart and Steele [45] worked with 23 patients with HFrEF and designed a study where two groups were compared: a continuous modality one and an interval one. Both groups exercised at the same intensity (70% of VO_{2peak}). They found that interval (or intermittent) training (INT) is more efficient than continuous training (CON) in improving functional capacity (VO_{2peak}). The CON group exercised for 30min continuously, while the INT group exercised for 60min with 60s intervals at 70% of VO_{2peak} and 60 sec of rest. All the participants completed the training. The INT group improved its VO_{2peak} by 21% compared to 13% in the CON group.

Wisløff *et al* [46] tried a different exercise training modality on 9 patients with HFrEF: high intensity interval training (HIIT), that we previously called "4-by-4". The rationale behind interval training is that it allows for rest periods between the high intensity ones. This way the participants don't get exhausted right away since they are able to reach high intensities of work but do not need to maintain the high intensity for a long time. In this study, Wisløff *et al* compared a high intensity with a moderate intensity (47-min at 70-75% of HR_{peak}) training group. The study showed that HIIT increased VO_{2peak} by 46%, versus a 14% improvement in the moderate intensity group. The HIIT group also showed significant improvements in LV remodelling (LV diastolic and systolic diameters decreased by 12% and 15%; estimated LV end-diastolic and end-systolic volumes decreased by 18% and 25%; there was no change in wall thickness), while the moderate intensity group showed none. Expression of proBNP (pro-Brain Natriuretic Peptide), a marker of hypertrophy and therefore cardiac dysfunction [47, 48], was reduced by 40% in the high intensity group. HIIT appeared to be the most efficient in term of time-effect.

The SMARTEX study [49, 50], a large multicentric trial, involved 231 HFrEF patients. The researchers carried out two different interventions for 12 weeks: moderate continuous training (MCT) and high intensity interval training (HIIT). They concluded that HIIT was not superior to MCT in improving neither VO_{2peak} nor left ventricular remodelling, disproving Wisløff *et al* results. Interestingly in the SMARTEX study, only 33% of the patients in the study exercised at the correct intensity. Therefore, the difference in the execution of the intervention, along with the difference in the studies' populations and the different individual physiological responses, has been used to explain why the results achieved by the HIIT group were not significant as in Wisløff *et al* study [51].

According to the metanalysis performed by Tucker *et al* [52], if HF patients exercise at an intensity of at least 80% of HR_{peak}, LVEF improves significantly (4 trials [46, 49, 53, 54]; 267 patients; WMD = 3.70%; 95%CI 1.63 to 5.77%; I^2=8.5%).

Safety of such interventions has also been investigated. The HF-ACTION study [43] found moderate-intensity exercise to be safe with HF patients, while Wewege *et al* [55] present high-intensity training as having a low cardiovascular event occurrence rate (0.012%, 1 per 8119 HIIT sessions). Therefore, high-intensity training appears safe when applied to patients with HF within a tertiary care service.

Exercise setting and adherence

The setting of the exercise for the HF patient population has also been recently brought to attention. The typical setting for rehabilitation and exercise as medicine is the hospital, outpatient clinics or specialized gyms, but today, with the latest technologies, it is possible to train from home and be supervised from an expert, while also collecting useful data for research and patient clinical history. According to the ESC, medically stable patients undergoing treatment, "could initiate a home-based program after a baseline exercise test with guidance and instructions. Frequent follow-up can help assess the benefits of the home exercise program, determine any unforeseen problems, and will allow the patient to advance to higher levels of exertion if lower levels of work are well tolerated" [35].

Aamot *et al* [56] compared a 12-week HIIT intervention in a hospital-based versus a home-based setting with patients with coronary artery disease (CAD). Participants were randomly assigned to either treadmill exercise (TE), group exercise (GE) and home-based exercise (HE). The first two groups performed their intervention in the hospital. TE group performed HIIT on the treadmill following the Helgerud *et al* [57] protocol. GE instead consisted of 10-15 people instructed by a physiotherapist; they warmed up with aerobics and then performed HIIT via a circuit training with a variety of exercises (running, cycling, squats, step). Lastly, the HE group, after being instructed on the HIIT modality and on the use of the HR monitor, performed the preferred exercise mode among the following: up-hill walking, cross-country skiing, bicycling, running or using indoor equipment (treadmill, cross trainers). The TE group achieved a higher

VO_{2peak} compared with HE (TE vs HE: 1.6, p=0.02), but the difference between other groups were not statistically significant (TE vs GE: 1.1, p=0.27; GE vs HE: 0.6, p=1), neither using on-treatment analysis (TE vs HE: 1.3, p=0.13; TE vs GE: 1.0, p=0.28; GE vs HE: 0.2, p=1). Exercise attendance was significantly higher in the TE and GE groups. Target HR and time spent in the target HR zone was achieved by all the patients. Even though this intervention was carried out on CAD patients, it can be speculated that HIIT has similar effects on training adherence on HF patients, since they are both characterized by reduced exercise capacity/tolerance and increased fatigue levels [58].

Similar results were found in the Piotrowicz *et al* [59] study, where HF patients were randomized to a home-based telemonitored intervention (HTCR) or to a hospital based supervised intervention (SCR). The difference in this study was that the two groups were both performing moderate intensity exercise (40-70% of HRR). After an 8-week intervention, HTCR and SCR both improved VO_{2peak} significantly (HTCR: +1.9, p=0.0001; SCR: +1.1, p=0.0001), but no statistically significant difference was found between the two groups.

Aamot *et al* also published a 1-year follow-up to the previously presented study [60] in which they found that all three groups still had VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$) values above baseline (TE: +1.6; GE: +1.4; HE: +2.2), but lower if compared with the ones they achieved immediately post-intervention (TE: -2.7; GE: -1.9; HE: -1.3). Interestingly, the HE group was the one that had the smallest decrease in VO_{2peak}. The authors therefore suggest that home-based HIIT is an interesting option.

Home-based interventions appear to be as effective as the hospital-based counterparts [61, 62] and feasible [63]. Meanwhile, adherence doesn't seem to be reduced by the high intensity requested. The value of a potential carry-over effect, originating from the home-based setting, should not be underestimated.

Telecare with HF

As of 2016 data, almost 20% of the Norwegian population lives in rural areas [64]. This may limit their access to usual cardiac rehabilitation. Similar participation restrictions have been highlighted in other areas of the world such as Australia [65], United Kingdom [66], China [67] and South America [68]. It is here that "*telecare*" comes into the picture as a potential participation barrier remover (see *Table 3* for the different telecare modalities). In the case of HF patients, telecare can be defined as monitoring consisting of transmission of clinical data (symptoms, signs, biological or physiological information) from a remote location to another for data analysis and interpretation [69].

Table 3 – This table collects and explains the main telecare intervention modalities. In clinical practice, they can be used by themselves or in combination [69].

Modality	Explanation
Tele-monitoring	Mobile phones, external- or internal devices are used to collect symptoms and physiological data, derived from monitoring devices, are transferred to a health care provider via wireless broadband connection to be analysed (analyses can be manual or automatic).
Tele-assessment	This technique allows professionals to actively collect data on the patient's progress, remotely and in real time. Videoconferencing can be used to perform remote assessments (not training) [70].
Tele-support and tele-consulting	These two modalities involve supportive tele-visits or phone calls by health personnel to respond to psychological needs and disease related questions.
Tele-therapy and tele-coaching	Health personnel can provide live support and instructions for normal and interactive therapy (e.g. remotely delivered lived psychotherapy via video-conference [71]).
Tele-rehabilitation	This is a remote comprehensive cardiac rehabilitation which includes remote supervision (or "tele-supervision") which can be carried out via live video- or tele-conference.

The main perks of telecare are data collection and live feedback. Live data collection allows for the data to be transferred in real time to a health professional whom may also deliver live feedback or immediately act upon the received data (e.g. dispatching an ambulance to a patient's residence after recording signs of myocardial infarction). Data collection may also be semi-live, which means that data is recorded live, but stored for future analysis and use.

When performing telerehabilitation, one of the critical topics of discussion is how to ensure the safety of the participating patients. In fact, they would receive live feedback, but lack the close direct contact that they would instead receive during traditional cardiac rehabilitation. As of today, the best possible option with patients with HF is to prescribe home-based exercise to clinically stable individuals, after educating them to the exercise and communication modalities. Meanwhile, adverse events in home-based trial with HF patients suggest that the benefits of regular physical training (including home-based modalities) surpass the risks they may entail [69]. Moreover, even though HF patients have proven more reluctant to comply with exercise then other recommendations (e.g. diet, medication) [39], published data [59, 72-74] suggests that adherence to, and acceptance of telerehabilitation are promising.

A home-based telerehabilitation approach has many advantages, such as: setting, familiar surroundings and potentially increased carryover effect; ability to continue an exercise intervention even if the hospital-based intervention is concluded; elimination of participation barriers, such as transportation-related issues; ability to treat more patients at the same time; low costs; rapid development of newer and better technologies. On the other hand, the use of new technological devices can be challenging if we consider the age of the average cardiac patient. Moreover, telerehabilitation and the its devices are still facing a lack of regulations and some "grey areas" [69]. This is mainly because national and international laws are struggling to keep up with the rapid growth and application of technology.

Home-based cardiac rehabilitation with HF

In the last 15 years, home-based exercise training interventions have been successfully carried out in a home-based setting with HF patients (see *Appendix A*). Only in recent years, have studies begun live supervision of home-based interventions, some with live video conference [62, 75, 76], some telemonitored with live- [77, 78] and others via delayed ECG feedback [59, 72, 74, 79-82]. Nevertheless, none of these studies or other HF studies have looked into high-intensity aerobic interval training in a home-based modality. Such an intervention with CAD patients has proven to be effective [56], and it is reasonable to assume that the same intervention would be feasible for HF patients as well, due to similarities in the two patient populations.

Aim and Hypotheses

The aim of this study was to investigate exercise intensity, perceived safety and exertion during high-intensity interval home-based training, with and without supervision, in patients with HF. It was hypothesized that supervised- and unsupervised modalities would be carried out with equal exercise intensities. While perceived safety and exertion would be expected to be higher during the supervised modality.

METHODS

Trial design

This study is part of the ongoing prospective randomised controlled trial "*HjemmeTrim ved hjertesvikt*" (also known as *IT IS HOPE 4 HF*, Implementation of Telerehabilitation In Support of HOme-based Physical Exercise for Heart Failure), which is registered on ClinicalTrials.gov (NCT03183323). The design of the present study is that of a non-randomised, internally controlled, cross-over study, carried out at the end of the training intervention of the IT IS HOPE 4 HF study. Outcomes will be analysed on a sample of patients. Therefore, only the relevant aspects of IT IS HOPE 4 HF will be reported.

Participants

Inclusion and exclusion criteria for participants can be found in *Table 4*. Patients were recruited from the intervention branch of the IT IS HOPE 4 HF study, via phone call, between September and November 2018.

Table 4 – Inclusion and exclusion criteria for the present study. This table also includes the inclusion and exclusion criteria for the IT IS HOPE 4 HF study.

Inclusion Criteria	**Exclusion Criteria** (1 or more of the following)
• Diagnosis HF; • Signs and symptoms (NYHA II-III) in the 6 months prior; • NT-proBNP>300 pmol/L; • Stable (>4 weeks) medical therapy for risk factor control; • 40-80 years of age; • Providing signed informed consent.	• rehabilitation in the 6 months prior; • non-HF causes for HF symptoms; • COPD - GOLD III-IV; • conditions which might prevent patients from safely exercise at home; • Did not express interest in the project; • Did not feel confident using more technological devices, then required for IT IS HOPE 4 HF.

NYHA – New York Heart Association functional classification of heart failure; NT-proBNP – N-terminal pro-Brain Natriuretic Peptide; HF – Heart Failure; COPD – Chronic Obstructive Pulmonary Disease; GOLD – Global Initiative for Chronic Obstructive Lung Disease.

The study participants have volunteered and provided written informed consent in line with the Declaration of Helsinki. The trial has received approval from the Regionals Committee for Medical and Health Research Ethics in Norway (2016/1597/REK midt).

Intervention

At baseline all participants joined a 2-day program including education and baseline testing. They were instructed on the intervention modalities (including how to join the videoconference sessions and how to access the video resources) and given an iPad (5th generation, Apple Inc., California, USA).

Participants were recommended to exercise 3 times per week, for 3 months, for a total of 3 hours every week. Amongst these training sessions, 2 times a week had to be in a tele-rehabilitation supervised setting, with the physiotherapist during the live video-conference, and 1 time in an unsupervised setting alone, either using the training videos found in their iPads, or autonomously.

Supervised training session: live videoconference

The tele-rehabilitation session was carried out via Hangouts app (Google Inc., USA), which allows for videoconferencing with synchronous audio-visual communication between more people. An experienced physiotherapist was in charge of the training. The exercise sessions were twice a week, at 11.00am. The physiotherapist would call the participants and invite them to the live videoconference (normally, 5-15 min were used to greet the participants and solve any issues related to the app or the broad-band connection). The whole exercise session was carried out with music, which was always the same, and chosen based on its tempo, to mimic the required exercise intensities and facilitate the participants to reach them. To avoid inter-rater reliability issues, only sessions carried out by the same physiotherapist were recorded for this study.

The exercise session started with a 15-min warmup consisting of aerobic full body movements carried out with a low tempo, such as: breathing exercises, dynamic stretching of the upper- and lower body, stepping on the spot, half-squatting, double- and alternate- poling. After the warm-up the four 4-min high intensity interval would start, alternated with active break session of 4-min. The exercises used during the high-intensity sections were also aerobic full-body movements executed following a stronger tempo and required a higher intensity, such as: raising the knees high while walking, marching on the spot, doing standing crunches, walking while performing half-squats, half-squats followed by vertical jumps on the spot, jogging on the spot. The active break sessions instead had strength training or sitting exercises. The participants would use the elastic band that they were given at the 2-day baseline course and train upper- and lower-body strength, as well as some sitting exercises involving breathing and core muscles. The session was closed by an 8-min cool down section where participants would perform breathing exercises and gentle body movements at a decreasingly lower tempo.

All the different exercises were normally carried out in repetitions of 10 each and separated by walking on the spot, especially during the warm-up and cool down phases. Participants, depending on their health and balance conditions were invited to exercise while sitting for the whole, or part of, the training session. All the sessions were not exactly the same in terms of single exercises, but the intensity and the time intervals were maintained. A complete example of a training session can be found in *Appendix B*.

Unsupervised training session: videos

At baseline, participants were also given credentials to access a hospital webpage containing an aerobic 4-by-4 exercise session training video, for individual training. Lasting 56 min, this video is structured exactly the same way as one of the video-conference sessions. It is carried out by two physiotherapists at the same time, one of which is standing and one sitting. The standing physiotherapist is the one that participants have been seeing on live-videoconference. Participants were invited to use the videos whenever they wished, especially if they had missed out on a supervised training session. Therefore, the use of the video was optional, except for the last week of intervention when they were especially requested to train twice using it.

Outcomes

Exercise intensity

In order to assess exercise intensity during the last week of intervention, the participants wore the HR-measuring devices they received in the mail. These consisted of two recording devices installed on two separate belts – a Polar H7 Heart Rate Sensor (Polar Electro, Kempele, Finland) and an Actigraph wGT3X-BT (ActiGraph LLC., FL, USA). These devices have proven reliable in monitoring activity [83-86] and HR [87]. Participants were asked to wear the devices during all four training interventions. This was done to determine the primary outcome.

For practical reasons, including familiarisation with the devices, the participants were requested to perform 2 sessions per kind – 2 supervised and 2 unsupervised. When analysing the data, the best performance for every modality was chosen. This was done to limit the possibility of reporting data containing errors due to misuse or malfunctioning of the devices. At the same time, the intent was to record at least one performance that was carried out when the participants were feeling healthy, since HF patients can have many comorbidities and manifest different symptoms as well as discomfort [8].

Actigraphs were programmed via ActiLife Software (ActiGraph LLC., FL, USA) to store the HR data recorded from the Polar belt. After the intervention, the Actigraphs' data was downloaded using an epoch value of 5 sec and converted into a data table with comma-separated values file extension (.csv). The HRs of the four exercise sessions were transferred in Excel (Microsoft Corporation, WA, USA) and plotted. Then average HRs were calculated for every part of the exercise session (warm-up, high-intensity and moderate-intensity intervals, cool down). For high-intensity intervals the average HR was calculated on the last 2-min of the interval. This was done because the lower limit of target HR in the high-intensity intervals (85-95%) is reached in 1-2 min during the first one, but less time is demanded to reach the correct intensity in the following intervals [57].

In order to determine if the desired exercise intensities are reached (70% of HR_{peak} during warm-up, cool down and active break intervals; 85-95% of HR_{peak} during high intensity intervals), the achieved HRs during the training sessions are compared with the HR_{peak} obtained from the CPET at baseline. CPET is carried out accordingly to the current guidelines [88] using a blood pressure measuring device (Tango M2, SunTech Medical Inc., USA) and a ventilatory gas analyser (Jaeger CPX Vyntus, Care Fusion, Germany), as well as a continuous 12-lead-Bluetooth ECG. The test is executed on a treadmill and divided in an economy test, followed by a ramp protocol to exhaustion. All the CPET tests were performed by an experienced exercise physiologist, and a cardiologist was present at all times.

Questionnaire: perceived safety and exertion

Subjective perception of exercise during supervised and unsupervised sessions was also investigated as a secondary outcome. The used instruments are the Borg scale [89], to monitor perceived exertion, and an 'ad-hoc' exercise questionnaire to inquire about well-being before- and during training, as well as safety. In questions regarding well-being, participants have been asked to rate their state using: "very bad" (1), "bad" (2), "neither good nor bad" (3), "good" (4), "very good" (5). If participants did not carry out the whole exercise session or did not feel safe during its execution, they could one or more options explaining why, or add their own personal explanation.

The exercise questionnaire was filled out by all participants after both supervised (video-conference) and unsupervised (only video) sessions. The questionnaire was comprised of some questions concerning well-being before and during the exercise session and ended with a Borg scale. This questionnaire was given out within the Monitoring Kit and filled out during the last week of the training intervention. The used questionnaire form and the Borg Scale in Norwegian can be found respectively in *Appendix C* and *D* for consultation.

Sample size

The calculation of the sample size in this study was carried out based on the primary outcome, HR. We hypothesised that at 3 months there would be no difference between the HR achieved during the supervised and the unsupervised training sessions. In this case, the true mean for HR is the minimal clinically significant difference (MCID) in HR, which some studies have found out to be 5bpm [90-93]. This can be considered as a 2.5% variation on a 200bpm HR_{max}. As an estimate for the effect size we assume that the standard deviation (SD) for the single is the same as for the difference. Using an online statistical resource [94] and the statistical hypothesis, a sample size of 8 participants was obtained, with its true mean being the same as the SD.

Statistical Analysis

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS, IBM Corporation, NY, USA). Data was checked for normality via a Shapiro-Wilk test. Normally distributed data was analysed with a paired-samples T-test, since the aim was to see if there were differences between the supervised and unsupervised sessions within the same participant. Not normally distributed data instead was analysed via the Wilcoxon signed-ranks non-parametric test. The results are presented as mean ± SD, if normally distributed, or median ± IQR (Inter quartile range), if not normally distributed. A 2-sided value of $p \leq 0.05$ was considered statistically significant.

RESULTS

Eleven participants volunteered to participate in the present study (see *Table 5* for baseline characteristics). No adverse events were recorded or reported. See *Figure 1* for the participant flow.

Figure 1 – Participant flow, from recruitment to data analysis.

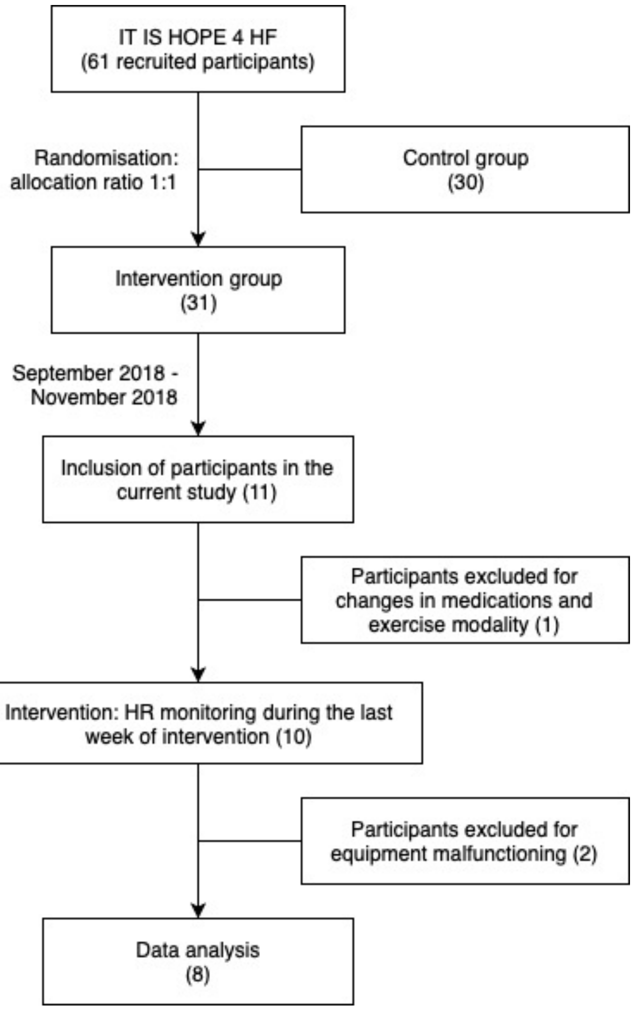

Table 5 – Patients' characteristics at baseline. Data are presented as mean ± SD, or number of patients.

Sex, *Male / Female*	7 / 4
Age, *y*	63.4 ± 11.6
BMI, *km/m^2*	26.9 ± 5.2
Smoking status, *current smoker / previous smoker / never*	1 / 6 / 4
Alcohol, *units/week*	2.6 ± 3.3
RHR, *bmp*	72 ± 12
Systolic blood pressure, *mmHg*	119 ± 14
Diastolic blood pressure, *mmHg*	72 ± 14
Serum creatinine, *$\mu mol/L$*	254.3 ± 337.1
HR_{peak}, *bpm*	137 ± 22
VO_{2peak}, *$L \cdot min^{-1}$*	1.57 ± 0.39
VO_{2peak}, *$mL \cdot kg^{-1} \cdot min^{-1}$*	18.98 ± 3.41
Cause of HF, *ischemic heart disease / dilated cardiomyopathy / other*	7 / 2 / 2
EF, *%*	33 ± 6
Self-reported exercise frequency, *<1 per week / 1 per week / 2-3 per week / nearly every day*	2 / 3 / 4 / 2
Self-reported exercise intensity, *calm / sweating and heavy breathing*	6 / 5
Self-reported typical duration of exercise, *15-29 min / 30-60 min / >60 min*	1 / 6 / 4
Self-reported exercise time, *min/week*	435 ± 777
Number of completed sessions, *n*	24 ± 2
Length of intervention, *weeks*	29 ± 13
Hypertension	6/11
Hypercholesterolemia	7/11
Diabetes, *Type I / Type II* *Diabetes complications*	2/11 0 / 2 2/11
Kidney disease, *Dialysis*	5/11 2/11
Revascularisation interventions, *PCI / CABG / both / none*	4 / 2 / 1 / 4
Pacemaker	3/11
Cerebrovascular disease	1/11
Cardiac rhythm disorder, *Sinus rhythm* *Atrial fibrillation* *Other*	11/11 3/11 6/11 2/11
COPD	1/11
History of cancer, *Current* *Previous*	5/11 1/11 4/11
ACE inhibitor	5/11
β-blockers	11/11
MRAs	4/11
Statins	8/11
Diuretics	7/11
Anticoagulants, Aspirin / Warfarin / DOAC / Low molecular weight heparin / Other	6 / 7 / 1 / 0 / 2

BMI – Body mass index; RHR – Resting heart rate; HR_{peak} – Peak heart rate; VO_{2peak} – Peak oxygen consumption obtained during cardio-pulmonary exercise testing; HF – Heart failure; EF – Ejection fraction; PCI – Percutaneous coronary intervention; CABG – Coronary artery bypass grafting; COPD – Chronic obstructive pulmonary disease; ACE – Angiotensin-converting-enzyme; MRAs – Mineralocorticoid receptor antagonists; DOAC – Direct-acting oral anticoagulant..

Exercise Intensity

The target exercise intensity during high-intensity intervals (HII, 85-95% of HR_{peak}) was reached only with supervision, during 2nd, 3rd and 4th interval (see *Table 6*). Active breaks (70% of HR_{peak}) were all higher than expected, including warm-up and cool down., significant differences were found in exercise intensity between supervised and unsupervised exercise during the 2nd, 3rd and 4th HII. Significant differences were also found for the 2nd active break.

Table 6 – Mean heart rates achieved during all exercise phases of supervised sessions are compared with the ones achieved during unsupervised sessions. Heart rate is expressed as percentage of peak heart rate (%HRpeak) and presented as mean ± SD.

Exercise phase	Supervised (%HR_{peak})	Unsupervised (%HR_{peak})	p-value
Warm-up	76 ± 18	76 ± 23	0.85
1st HII	81 ± 16	79 ± 17	0.41
1st active break	80 ± 17	73 ± 16	0.05
2nd HII	86 ± 16	79 ± 16	0.04 †
2nd active break	82 ± 17	77 ± 15	0.02 †
3rd HII	86 ± 15	81 ± 15	0.03 †
3rd active break	79 ± 17	75 ± 16	0.10
4th HII	88 ± 16	81 ± 17	0.01 †
Cool down	79 ± 17	75 ± 14	0.14

HII – High-intensity Interval, expected intensity 85-95% of HR_{peak}; Active break – Moderate intensity interval, expected intensity 70% of HR_{peak}; Warm-up and Cool down – Expected intensity 70% of HR_{peak}
†, p<0.05 in the paired-samples t-test between supervised- and unsupervised training sessions.

Perceived safety and exertion

All participants reported to have felt safe during both exercise modalities, and to have successfully carried out the whole training sessions. No statistically significant differences were found between supervised- and unsupervised training sessions at the end of the intervention (see *Table 7*).

Table 7 – Exercise questionnaire results for supervised- and unsupervised training sessions at the end of the training intervention. Data is presented as median (IQR) or as number of patients.

Questionnaire item	Supervised	Unsupervised	p-value
1. Feeling before training, *1-5*	3.5 (3.0-4.0)	4.0 (3.5-4.5)	0.32
2. Feeling during training, *1-5*	3.5 (2.5-4.5)	4.0 (3.5-4.5)	1.00
3. Was the session completed, *1-2*	1.0 (0)	1.0 (0)	1.00
4. Felt safe during training, *1-2*	1.0 (0)	1.0 (0)	1.00
5. Borg level at the end of training, *6-20*	15.0 (13.5-16.5)	15.0 (14.0-16.0)	0.58

Items 1 and 2 were scored the following way: "very bad" (n=1), "bad" (n=2), "neither good nor bad" (n=3), "good" (n=4), "very good" (n=5). Items 3 and 4 instead were scored the following way: "yes" (n=1), "no" (n=2). p-values were calculated using Wilcoxon signed-ranks non-parametric test.

DISCUSSION

The main result in this study was that HII training was successfully carried out in a home-based setting during telerehabilitation. Moreover, all the participants felt safe during the execution of all the training sessions, both with- and without supervision. Initial hypotheses were therefore disproven, since significant differences were found in exercise intensity between the two exercise modalities, but none were observed between levels of exertion of perceived safety.

Exercise intensity

The supervised exercise modality yielded higher exercise intensities than the unsupervised one. Hunter *et al* [95] obtained similar results in a healthy population. They investigated moderate-to-high intensity exercise (70-80% of HRR) carried out with- and without supervision. The main finding was that supervised exercise conferred greater outcomes (muscle strength and BMI). There were no between-group differences at baseline, and the exercise intensity was the same for both groups. Therefore, it can be speculated that the greater improvements were achieved thanks to the supervision. Direct supervision may help reach higher intensities thanks to providing encouragement and feedback during the execution of the training. Similarly, Blackwell *et al* [96] found that HII training (5x1-min bouts at 95-110% of CPET maximal load, watts) was feasible to carry out in both supervised- (laboratory) and unsupervised (home-based) sessions with healthy middle-aged individuals. Still, the biggest improvements were achieved by the supervised group. In the present study, the comparison was within the same individual and not between two groups. Moreover, the videos were carried out the same way, and by the same physiotherapist as the supervised sessions. The only difference between the videos and the live sessions was that the first lacked direct supervision and encouraging on behalf of the physiotherapist. The videos also did not allow for interaction with other participants. Therefore, it can be speculated that the difference in performance likely originated from the presence or lack of supervision.

In the present study, even if the correct exercise intensities in the HIIs were achieved only with supervision, this was not true for the 1st HII. It can be speculated that patients with HF need more time and aerobic work to reach the desired HR frequencies. Similar results were achieved by Helgerud *et al* 2007 study [57] with healthy, young individuals. In fact, they observed an approximately 10-bpm difference between the highest HR during the first and the last HII. When looking at the first HII, the desired HR zone was reached within the last minute, but the average of the last 2-min was not in the zone. Even though the high-intensity zone was higher (90-95% of HR_{max}) for Helgerud *et al*, and the exercise setting was more controlled (running on a treadmill), it can be speculated that similar HR trends would be found in a patient population with HF, which is in line with the findings of this study.

Participants in the present study showed higher HR frequencies then expected (70% of HR_{peak}) during some of the active breaks. It can be speculated that this is because of reduced HRV in this specific patient population. Patients with HF generally present limited capacity, when compared to healthy subjects, to modulate their HR frequency, and in particular reduce it after exercise [24]. Given the particular interval-based exercise execution in this study, it can be said that a similar limitation was brought forward in the shift between high- and moderate intensity intervals, since HR should naturally decrease when reducing the exercise intensity. Moreover, a HR intensity was significantly higher in the supervised modality during the 2nd active break. This might be because the exercise intensity reached in the previous HII was higher than the one reached without supervision. Therefore, it can be speculated that higher exercise intensities can result in a longer needed time to decrease, which is in line with the concept of reduced HRV in patients with HF.

Interestingly, even though the participants were given access to the training video at the beginning of the training intervention, none of them seemed familiar with it when asked to use them in this study. Therefore, it can be speculated that they had not being using it to exercise before. This would make the use of the video a "novelty" for the participants in the study, which may justify a lack of confidence on behalf of the participants. It can be speculated that this contributed to the lower HR intensities achieved in the unsupervised training sessions.

Perceived safety and exertion

In the present study, participants felt safe and perceived exertion levels were comparable to the ones achieved during CPET testing at baseline. Even though the Borg scale is subjective, it can be assumed that the feeling of safety allowed the participants to exercise at such an exertion level that was comparable to the one reached during their CPET. Confirming that they knew "how it felt" to reach a high exercise intensity. Nevertheless, even though participant reported similar levels of safety and exertion between supervised- and unsupervised sessions, they did not actually reach the same HR intensities. It can therefore be speculated that the videos were similar enough to the live-videoconference to lead the participants to feel safe. While the video alone was not enough to challenge them into reaching the correct HR intensities. This could be because the videos lacked the live feedback and the presence of the physiotherapist leading the session. Moreover, being at home in their own house might also have influenced the outcome of the supervised- and unsupervised sessions by granting a feeling of safety, but also allowing the participant to take more breaks or exercise while sitting during the exercise execution, especially during the unsupervised sessions.

Interestingly in the SMARTEX study [49], participants did not reach the desired HR intensities even though they were instructed on their HR target, which did not happen in the present study. This may lead to consider the training intervention (at least the supervised one) in the present study to be efficient in challenging the patients to reach the desired exercise intensities. Concerning the SMARTEX intervention, the researchers argued that the high exercise intensities were difficult to achieve despite the experience of the personnel in cardiac rehabilitation, but they do not seem to explain why. It can be speculated that the participants were not instructed thoroughly enough, or that they did not feel confident to increase their HR further, and from this the lower outcomes than expected if compared to Wisløff *et al* [46]. It can also be speculated that the participants of the SMARTEX study were lacking in confidence or in the feeling of safety and this is what prevented them from reaching the desired intensities.

Generalisability

The population in this study is similar to the one described by Ellingsen *et al* [49] in the SMARTEX study. Measures of central tendency for age, VO_{2peak}, EF and usage of beta-blockers at baseline were similar to the ones presented in this study. It can therefore be speculated that the participants' characteristics in the present study are in line with the ones recruited for the SMARTEX study. Similarly, if we compare the present study's patient population to the HF-ACTION study [43], we can also find similarities in the patient population in female/male distribution, age, usage of beta-blockers, prevalence of hypertension and previous myocardial infarction. Similar patient populations were also studied in the PARADIGM-HF [97] and in the CHARM-Alternative [98] studies. Mean age, resting heart rate (RHR) and EF were in fact similar to the present study. In the SHIFT study [92, 99] patient population as well age, BMI, RHR, EF and use of beta-blockers was comparable.

Due to the large number of patients analysed in the over-mentioned studies, and the similarities found with the present study, it can be suggested that the present study's population is similar to the general HF population that has been taken under examination as of today. Notably, differences can be seen amongst the percentages of comorbidities – hypertension, diabetes, AF, previous myocardial infarction. It can be speculated that this indicates that patients with HF can be a very heterogenous population and therefore, the present study as well, falls in line with previous research. Therefore, the results may be considered generalisable.

Strengths and Limitations

The strength of this study is that exercise intensity was objectively measured, via HR monitors, in all the participants. Interestingly, participants were not aware of their HR in real-time, and therefore were not aware of the need of increasing or decreasing intensity to reach their target HR. Which means that the exercise modality, for this patient population was intense enough to allow them to reach the correct intensities. Another strength lies in the calculation and achievement of the sample size, which grants the study internal validity. External validity and generalisability are also supported in the discussion and therefore a strength in this study.

Moreover, even though this study was not powered to analyse adverse events, none were recorded or reported, and all the exercise sessions were carried out safely.

One of the limitations in this study was related to the impossibility to time the intervals to the exact sec they started, during both supervised and unsupervised sessions. Even though participants were asked to report the date of the intervention and wore the devices only when training, there might have been some minor timing errors due to when the participants wore the device and when they actually started training. Generally, thanks to the accelerometer data collected by the ActiGraph, it was possible to determine the approximate beginning of the training. Equipment malfunction was also partially an issue in this study: two participants were excluded from the final analysis because of it. Nevertheless, sample size was reached, and the use of such devices was justified to measure the outcomes in the present study. It is noteworthy that future patients – that would be training using this exercise modality – would not need to use such devices. Another limitation in the present study – like in most voluntary exercise-based studies – is that the most motivated patients tend to sign up for participation in such trials. Therefore, this should be taken into account when analysing the result of this study.

CONCLUSION

In a patient population with HF, high-intensity full-body interval training was carried out successfully via telerehabilitation. Higher exercise intensities were reached during supervised live video-conference, then during the unsupervised video modality. Nevertheless, participants felt equally safe and reported the same level of exertion during both intervention modalities. This study therefore acknowledges the feasibility and high level of perceived safety when carrying out a high-intensity interval training telerehabilitation intervention with patients with HF.

Implications and future research

The main implication in this study is that at the end of the training intervention, high-intensity interval exercise via telerehabilitation allowed the participants to reach the correct HR zones during exercise. This means that such a training intervention could be implemented all over the country of Norway when patients are not able to join regular exercise training programs. Naturally, before such a step, a larger study with patients with HF needs to be carried out with the power to calculate for adverse events and safety of such an intervention. After this, the videos could be rendered accessible, as a complimentary raining resource, and recommended to all those patients whom already concluded a high-intensity interval training intervention with supervision. This could potentially become a tool to evaluate any improvements in their adherence to exercise in the long term.

Future research on this topic should address the issue of increasing the difficulty of the videos. After training for months using the same video would result boring as well as too easy, because of improvements in exercise capacity thanks to training. This would imply that patients are unable to reach the desired HR zones anymore even when carrying out the exercise session correctly. New exercise videos should be produced to make sure to challenge the participants enough and allow them to increase the exercise intensity. In this respect it would have been interesting to study this intervention on healthy individuals as well to investigate what HR frequencies this intervention allows to reach.

Another interesting potential future research should address the possibility of better comparing supervised- and unsupervised related gains in two separate groups, each one only using one intervention modality. Based on the results presented in this study, it can be speculated that the supervision group would achieve better results, but the videos might be performed better at 3 months if the participants had always trained using them for the whole length of the intervention.

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APPENDIX

Appendix A – Home-based training with HF

This table contains home-based exercise training interventions carried out on HF patients in the last 15 years. Special emphasis has been reserved to exercise modality and the tools/modalities of supervision of the home-based intervention. The literature research was carried out on PubMed database with the key words "home-based heart failure exercise". It yielded 147 results, which were reviewed by abstract first, and then whole article.

Author, Year	**Exercise Modality**	**Supervision Modality**
Li *et al* [79], 2019	Aerobic exercise: walking (60-70% of HRR).	Patients were supervised using remote electrocardiogram monitoring (Inticare-MC-06 ECG monitors, Elephant Medical Electronic Technology Co., Ltd, Jining, China), which, via a smart phone app, would send the data to the cloud at the end of each session; in case of an arrhythmia or other adverse event, the data would instead be transferred in real time to a specialist and advise the patient of what to do; they exercised in a supervised setting first and then at home.
Van Dissel *et al* [100], 2019	Non-specified home-based exercise training program.	No direct supervision during the intervention; participants' compliance was monitored and documented via patient diaries and email follow-up at 3 months; patients were given HR monitors (Beurer GmbH, Ulm, Germany).
Hwang *et al* [75], 2018 and Hwang *et al* [62], 2017	Telerehabilitation: 60 min of aerobic- and strength exercise (intensity: 9-13 on the Borg scake), twice a week for 12 weeks.	An online videoconferencing platform was used for synchronous audio-visual communication; each exercise session was supervised by a physiotherapist; participants were loaned: a laptop computer, a mobile broad-band device, automatic sphygmomanometer, finger pulse oximeter, free weights and resistance bands.
Dalal *et al* [101], 2019 and Lang *et al* [102], 2018	Choice between: aerobic training (walking), resistance training (a chair-based exercise) or a combination of the two.	No supervision during the home-based process, but patients used an interactive booklet designed to record symptoms, physical activity and other actions related to self-care.
Peng *et al* [67], 2018	Telehealth training exercise program: aerobic exercises (walking, jogging), resistance training (calisthenics for muscular strength training).	The sessions were not directly supervised, but the health personnel was always available in remote; if needed, live communication took place through either text-based, audio, or video conversations if needed, via a QQ group and *Wechat* (popular Chinese smartphone and computer applications).
Chen *et al* [103], 2018	Aerobic exercise: walking, jogging or stationary cycling (60-80% of HR_{peak}).	No supervision during the home-based process; participants were monitored every 2 weeks via phone call.
Bernocchi *et al* [77], 2018	Aerobic exercise: walking, cycling; resistance training: callisthenic exercises, muscle reinforcement using 0.5kg weights. The exercise program was personalised for each patient.	Telemonitoring in real time via a pulse oximeter (GIMA, Milan, Italy), and a portable one-lead electrocardiograph (Card Guard Scientific Survival Ltd., Rehovot, Israel); during training patients could call in case of urgent need or emergency; participants were also supplied with a mini-ergometer, a pedometer and a training diary.
Donesky et al [76], 2017	TeleYoga — postures included: mountain, half down dog, cat, triangle, supported bridge, simple	Live teleconference (multipoint videoconferencing via DocBox technology, MicroDesign, Colchester, VT, USA) which connected participants to live classes via an Internet

Author, Year	Exercise Modality	Supervision Modality
	twist, staff, corpse, and cobbler poses, with postures modified as needed to meet the physical ability of each participant; integrated with breathing exercises, imagery, meditation, and relaxation.	connection to their televisions; participants reported their vital signs before each session via phone call. Technical issues were an important hindrance to participation.
Antonicelli *et al* [80], 2016	Non-specified home-based exercise training program.	No direct live supervision during the exercise sessions, but patients had been previously trained at the hospital and they received a phone call from a nurse before and after training; patients were instructed to autonomously record a 1-lead ECG signal 5min before and after the training session. This recording would be then referred to the nurse via the phone call.
Safiyari-Hafizi *et al* [104], 2016	Aerobic exercise: walking (intervals: high intensity bouts at 80-85% VO2peak, recovery periods at 40-50% of VO_{2peak}).	Patients were provided portable HR monitors and pedometers to keep track of their workouts. To ensure compliance and safety, the patients were initially contacted for 3 times a week for the first month, twice a week for the second month, and once a week for the third month.
Höllriegel *et al* [105], 2016	Aerobic exercise: static cycling (60% of VO_{2max}).	Patients were provided with a cycle ergometer at home but were not monitored.
Smolis-Bąk *et al* [81], 2015	Resistance training: dynamic exercises of small and larger muscle groups, isometric exercises of small muscle groups, coordination; respiratory exercises.	No direct supervision during the exercise session, but patients were telemonitored before starting exercising; patients sent (via cell phone) their ECG recording at rest to the monitoring centre and by telephone answered questions concerning their subjective health, blood pressure, body weight and medications; after approval, they started a training session. Automated ECG recording was coordinated with the exercise cycle.
Seo *et al* [106], 2016	Respiratory exercises.	No direct supervision. Participants received 3 audio CDs with voice-guided directions, developed by the investigative team, to use to practice their deep breathing (along with a written script of the intervention).
Boyd [107], 2015	Aerobic exercise: walking and cycling (40% of HRR).	No direct supervision during the intervention, but participants received weekly phone calls to gather data and progress. They also filled out a daily personal log.
Piotrowicz *et al* [72, 82], 2015 and Piotrowicz *et al* [59], 2010	Aerobic exercise: Nordic walking (40-70% of HRR).	Patients were telemonitored via ECG; they received an ECG recording device (EHO 3, Pro Plus Company, Poland) and a mobile phone. The phone was used to transmit the ECG recordings, to answer questions regarding their present condition and for psychological support.
Mohri *et al* [108], 2013 and Sato *et al* [109], 2012	Aerobic exercise: walking (at a Borg scale of 13).	No direct supervision, only monitoring via a single-axial accelerometer (Lifecorder, Suzuken Co., Nagoya, Japan).
Mello *et al* [110], 2012	Respiratory exercises: inspiratory muscle training.	No direct supervision, only during the first session, and once a week; Threshold Inspiratory Muscle Training device (Global Med, Porto Alegre, Brazil).
Fayazi *et al* [111], 2013	Aerobic exercise: walking (no prescription for intensity was reported).	No direct supervision during the intervention; participants received daily phone calls to monitor adherence, progress and answer questions; they also reported heart rate, perceived exertion, exercise performed, duration of

Author, Year	Exercise Modality	Supervision Modality
		exercise and any symptoms experienced on daily activity logs, which were handed in on a biweekly basis.
Piotrowicz *et al* [78], 2012	Aerobic exercise: walking (no prescription for intensity was reported).	Patients were not monitored in real-time, but a tele-event Holter ECG feature was installed in the device, which enabled it to directly transmit the ECG data if an adverse event occurred; they received an ECG recording device (EHO 3, Pro Plus Company, Poland) and a mobile phone, which was used to transmit the ECG recordings, answer questions regarding their present condition and for psychological support.
Babu *et al* [112], 2011	Aerobic exercise: walking (intensity according to specific protocol); resistance training (5 reps for 2-8 sets progressively).	No direct supervision; participants were contacted weekly to give an update on their training status.
Shen *et al* [113], 2011	Aerobic exercise training. [article in Chinese]	No supervision during the home-based process.
Servantes *et al* [114], 2012	Aerobic exercise: walking (intensity: anaerobic threshold); resistance training: strength (30-40% of 1RM, 1 series of 12-16 reps).	No direct supervision, but the first part of the trial consisted in supervised exercise sessions; patients received a HR frequency meter (Polar FS1, Kempele, Finland) and weekly phone calls to check on their status.
Gary *et al* [115], 2011	Aerobic exercise: walking (50-70% of HRR); resistance training: strength exercises with elastics for lower- and upper-body (2 sets of 12-15 reps).	No direct supervision during all the training sessions; participants begun with 1 supervised week and then moved on to unsupervised; they received weekly visits to update the strength training program and receive supervision on it.
Chien *et al* [116], 2011	Aerobic exercise: walking; resistance training: strength for major limb muscles. Exercise intensities were determined by level of exertion.	No direct supervision during all the training sessions; participants received regular follow-up phone calls for consultation.
Andryukhin *et al* [117], 2010	Aerobic exercise: walking (intensity not specified); resistance training: strength for major and minor limb muscles (modality not specified).	No direct supervision during the home-based sessions, but participants exercised with supervision in the health centre for 1 month; participants received regular follow-up phone calls and consultations.
Karapolat *et al* [118], 2009	Aerobic exercise: walking (60–70% of VO_{2peak}); flexibility training; breathing exercises.	No direct supervision during all the training sessions; participants received regular follow-up phone calls and consultations; HR was measured during the sessions using an HR monitor (Polar Edge, Polar Electro Oy, Finland).
O'Connor *et al* [43], 2009	Aerobic exercise: walking (60–70% of HRR).	No direct supervision during all the training sessions; adherence was evaluated via activity logs, telephone and clinic follow-ups, and HR monitoring data (model A1 or S1, Polar USA Inc).
Jolly *et al* [119, 120], 2007 and 2009	Aerobic exercise: walking (70% of VO_{2peak}); resistance training: low intensity strength protocol for upper and lower limb muscles.	No direct supervision during all the training sessions; participants were followed via home visits (4, 10, 20 weeks), telephone support (6, 15, 24 weeks), and a manual with details about exercise modality and self-monitoring.
Dracup *et al* [121], 2007 and Evangelista *et al* [122], 2005	Aerobic exercise: walking (up to 45 minutes at 60% HR_{max}); resistance training: strength protocol for upper and lower limbs (80% of 1RM, 2 sets of 10 reps).	No direct supervision during all the training sessions except for the first exercise session (home visit); patients wrote the number of minutes walked and distance travelled on a log sheet; distance was recorded via a hip-born pedometer (Sportline Pedometer 330, Sportline Inc, Yonkers, New York).

Author, Year	Exercise Modality	Supervision Modality
Gary and Lee [123], 2007, and Gary *et al* [124], 2004	Aerobic exercise: walking (up to 60% of a previously decided target HR).	No direct supervision during all the training sessions; participants wore the Polar Beat watch (Polar Electro, Inc, Lake Success, NY) to monitor HR.
De Mello Franco *et al* [125], 2006	Aerobic exercise; cycling; resistance training: local strengthening exercises.	Nothing was specified regarding supervision; participants were trained at the hospital first.
Evangelista *et al* [126], 2006	Aerobic exercise: walking (up to 60% of HR_{max}); resistance training: light strength training.	No direct supervision during all the training sessions; patients were monitored by monthly home visits, pedometers (worn during the day, no model specifications), and questionnaires measuring daily activity.
Giallauria *et al* [74], 2006	Aerobic training: cycling (75% of HR_{peak}).	No direct supervision during the exercise sessions, but patients received a HR monitor and a simple recording-transmitting ECG-device (Sorin Life Watch CG 6106), which transmitted the results to the research centre.
Smart *et al* [127], 2005	Aerobic exercise: a 15-minute stair/ step exercise once weekly and approximately 105 minutes per week; resistance training: strength exercises (including wall push-ups, alternating leg lunges, triceps dips, bicep curls, and sits to stands from a chair).	No direct supervision during all the training sessions; participants were contacted weekly by telephone or email for an update; patients were trained in the hospital first for 16 weeks; they were provided with an exercise diary and a Polar s610i Heart Rate Monitor (Polar, Kempele, Finland) for recording HR data, both these tools were returned evert 4-6 weeks.
Daskapan *et al* [128], 2005	Aerobic exercise: not specified. [Full text article, not found]	No kind of supervision was used.
Niebauer *et al* [129], 2005	Aerobic exercise: cycling (70-80% of HR_{max}); resistance training: calisthenics and strength training (the first nine exercises in the Canadian air force XBX program).	No direct supervision during all the training sessions; participants were lent a bicycle ergometer (Tunturi original ergometer, W1 Electronics).
Harris *et al* [130], 2003	Either aerobic exercise (cycling) or electrical stimulation of the quadriceps and gastrocnemius muscles.	No available information on modalities of supervision.
McKelvie *et al* [131], 2002	Aerobic exercise: cycling, walking (60-70% of HR_{max}); resistance training: strength training with free weights (arm curl, knee extension, leg press at up to 60% of 1RM, 3 sets of 10-15 reps).	No direct supervision during the home-based training sessions, but participants trained at the hospital first with supervision for 3 months; patients were reviewed monthly throughout the study.
Oka *et al* [132], 2000	Aerobic exercise: walking (70% of HR_{peak}); resistance training: total body, unilateral resistance exercises (up to 75% of 1RM).	No direct supervision during all the training sessions; participants filled out weekly activity logs (HR, exertion, exercise modality, symptoms), returned on a biweekly basis; they received weekly phone calls; they were given multimedia material with training guidelines.
Hambrecht *et al* [133], 2000	Aerobic exercise: cycling (up to 70% of VO_{2peak}); group exercise: walking, calisthenics and ball games (once per week).	No direct supervision during all the training sessions, but they had been training in the hospital supervised setting for 6 months.
Barlow *et al* [134], 1997 and	Aerobic exercise: cycling (up to 70-80% of HR_{max}).	No direct supervision during all the training sessions; participants were lent a cycle ergometer (Tunturi

Author, Year	Exercise Modality	Supervision Modality
Davey *et al* [135], 1992, and Coats *et al* [136], 1990		'Professional Ergometer', Tunturi, Finland) and a pulse-rate monitor (Micro Sports Lab Computer. Triadcolour, London, UK); compliance was assessed via the revolution counter attached to the ergometer.
Kiilavuori *et al* [137], 1996	Aerobic exercise: cycling or walking, but also rowing or swimming.	No available information on modalities of supervision.
Adamopoulos *et al* [138], 1993	Aerobic exercise: cycling.	No available information on modalities of supervision.

Appendix B – Training modality example

This table contains an example of a training session. This example applies both to the supervised- and unsupervised training modalities.

Phase	Activity
Warm-up (15-16 min)	• Full body movement: yoga-like breathing exercises – 5 REPS • Dynamic stretching for upper body – 10 REPS • Dynamic stretching of whole – 10 REPS • Side steps, looking forward, gently moving the arms in ample movements – 10 REPS • Half squat with arms straight in front – 5 REPS • Side steps, looking forward, gently moving the arms in ample movements – 10 REPS • Half squat with arms straight in front – 5 REPS • Walk on the spot while moving the shoulders – 10 REPS • Side steps, looking forward, gently moving the arms in ample movements – 10 REPS • "Cross country": bending both knees, moving the arms mimicking alternate poling – 10 REPS • Side steps, looking forward, gently moving the arms in ample movements – 10 REPS • Side swings with the arms while looking to the sides, one side first, then the other – 10 REPS • "Cross country" – 10 REPS • Side swings with the arms (making big circles) while looking to the sides – 10 REPS • "Cross country" – 10 REPS • "Double poling" (similar to the "Cross country" exercise, just with both arms together) – 10 REPS • "Cross country" – 10 REPS • Side steps looking forward accompanied by swinging the arms together – 10 REPS • Side swings with the arms (making big circles) while looking to the sides – 10 REPS • "Double poling" – 10 REPS • "Cross country" – 10 REPS • Side swings with the arms (making big circles) while looking to the sides – 10 REPS • Walk on the spot • Walk on the spot while swinging the arms – 10 REPS • Walking and punching the air in front of the torso – 10 REPS • Walk on the spot • Walk and punch the air to the sides, while looking forward – 10 REPS • Walk on the spot • Walking and punching the air in front of the torso – 10 REPS • Walk and punch the air to the sides, while looking forward – 10 REPS • Walk on the spot • Side step with the hands on the hips – 10 REPS • Side step using the arms to "grab" in front and pull back an imaginary object – 10 REPS • Side step with the hands on the hips – 10 REPS • Stand on divaricated legs and kick behind, while facing forward – 10 REPS • Stand on divaricated legs and kick behind, use the arms to reach forward and grab – 10 REPS
1st high intensity interval (4 min)	• Walk on the spot • "Knee slap": alternatively raise the knees and hit them with the contralateral hand – 10 REPS • Walk on the spot with open legs and bent knees – 10 REPS • Walk on the spot • "Knee slap" – 10 REPS • Elbow to knee: alternatively raise the knees and touch them with the contralateral elbow – 10 REPS • Walk on the spot with open legs and bent knees – 10 REPS

Phase	Activity
1st active break (4 min) *Strength training for lower body*	• Contract the calf muscles by going on tip-toes while leaning onto the wall or a chair (for balance) – 20 REPS • Half squats with arms forward – 20 REPS • Relax the legs
2nd high intensity interval (4 min)	• “Cross country" – 10 REPS • “Up and down”: bend knees, touch floor with hands, then extend the legs and reach up towards the ceiling with the arms – 10 REPS • “Cross country” – 10 REPS • “Up and down” – 10 REPS • “Cross country” – 10 REPS
2nd active break (4 min) *Strength training for upper body with elastic bands*	• Biceps strength training for right arm, with elastic band – 10 REPS • Biceps strength training for left arm, with elastic band – 10 REPS • Triceps strength training for right arm, with elastic band – 10 REPS • Triceps strength training for left arm, with elastic band – 10 REPS
3rd high intensity interval (4 min)	• Walk on the spot • “Knee slap” – 10 REPS • Walk on the spot • Walk on the spot with open legs and bent knees – 10 REPS • Walk on the spot • Hop on the spot and raise the arms alternatively to the roof – 10 REPS • Walk on the spot • “Knee slap” – 10 REPS • Walk on the spot
3rd active break (4 min) *Strength training for core- and back muscles, while seated*	• Breathing exercises, using back and arms, yoga-like, while sitting – 10 REPS • Cycle with the right foot in the air while sitting – 10 REPS • Cycle with the left foot in the air while sitting – 10 REPS • Dorsal twists: arms crossed on the chest, back straight, turn right and left to mobilise the dorsal spine (while seated) – 10 REPS • Sideway tilts: while seated, arms by the sides of the body, tilt right and left and try to reach the floor with the hands. – 10 REPS
4th high intensity interval (4 min)	• Walk on the spot • “Cross country” – 20 REPS • “Up and down” – 10 REPS • “Up and down” with a hop while coming up – 10 REPS • “Cross country” – 10 REPS • “Up and down” – 10 REPS • “Cross country” – 10 REPS • Jog on the spot • Jog on the spot with the arms reaching for the ceiling – 10 REPS
Cool-down (8 min)	• Walk on the spot • Side steps – 10 REPS • Walk on the spot, while doing yoga-like breathing exercises – 10 REPS • Side steps – 10 REPS • Stop walking • Move arms while turning right and left with the whole torso – 10 REPS • Stretch the arms together in front and behind – 1 REP • Stretch the hamstrings, both sides, sitting or standing – 1 REP

Phase	Activity
	• Stretch hip flexors, both sides, sitting or standing – 1 REP • Stretch calves, both sides, sitting or standing – 1 REP • Stretch the neck (gently), left and right, sitting or standing – 1 REP • Breathing exercise, whole body.

Appendix C – Exercise questionnaire

Exercise questionnaire created "ad hoc" in Norwegian. It investigates perceived exertion and safety before, during and after exercise.

Dato: ______________________

Navn: ______________________

1. Var den siste treningen din veiledet eller ikke veiledet?

[] veiledet (video-konferanse med Vibeke)

[] ikke veiledet (video på egen hånd)

2. Hvordan føler du deg i dag?

[] veldig bra [] bra [] verken bra eller dårlig [] dårlig [] veldig dårlig

3. Hvordan følte du deg under dagens trening?

[] veldig bra [] bra [] verken bra eller dårlig [] dårlig [] veldig dårlig

4. Greide du å gjennomføre hele treningsøkta?

[] Ja   [] Nei

Hvis nei, var dette fordi;

[] Jeg har behov for at noen motiverer meg mer (ved bruk av video)

[] Jeg ble utslitt

[] Jeg ble redd

[] Jeg fikk smerter

[] Mangel på tid

[] Annet: ________________

5. Følte du deg trygg under treningen?

[] Ja   [] Nei

Hvis nei, var dette fordi;

[] Jeg var usikker på hvordan jeg skulle gjøre det

[] Hjertet mitt banket for fort og jeg ble redd jeg skulle bli syk

[] Jeg var redd for å skade meg selv

[] Jeg var redd for å falle

[] Annet: ________________

Appendix D – Borgs skala

The Borg Scale in Norwegian, ranging from 6 to 20 (respectively, least- to maximally exerted), aims to assist patients in identifying their exertion level.

HVOR TUNG ER BELASTNINGEN?

6

7 Meget, meget lett

8

9 Meget lett

10

11 Ganske lett

12

13 Litt anstrengende

14

15 Anstrengende

16

17 Meget anstrengende

18

19 Svært anstrengende

20

Norsk versjon av Borgs skala:

Borg GA. **Perceived Exertion.** *Exerc Sport Sci Rev.* 1974;2:131-53.

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