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PROJECT: EFFECTS OF TWO PHYSICAL EXERCISE MODALITIES ON WORKLOAD ADAPTATION CAPACITY, METABOLIC FLEXIBILITY, AND NON-ONCOLOGIC CHRONIC PAIN IN PATIENTS OF THE CARDIOVASCULAR HEALTH PROGRAM AT THE EXTERNAL CESFAM VALDIVIA

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22.12.20203

Valdivia, Chile

Problem Statement and State of the Art

As the global population ages, disease patterns shift, and cardiovascular risk factors (CRFs) increase (1). The onset of CRFs at an earlier age has been reported, and according to the 2017 Chilean National Health Survey, there is a high prevalence of physical inactivity (86.7%), overweight (39.8%), obesity (31.2%), morbid obesity (3.2%), suspected hypertension (27.6%), and type 2 diabetes mellitus (12.3%) (2).

Physical inactivity, defined as not meeting international physical activity recommendations (≥ 150 minutes of moderate to vigorous physical activity per week, or achieving an energy expenditure ≥ 600 MET/min/week) (3), has been shown to be a predominant factor for the earlier onset of CRFs (4). Inactivity leads to early onset of insulin resistance at the muscular level and the shift of muscle fibers from oxidative to glycolytic, decreasing the use of lipids as an energy substrate. These unoxidized lipids accumulate in central and peripheral adipose tissue and organs as ectopic fat, which increases sympathetic activity and inflammatory response; processes associated with alterations in metabolic flexibility (5, 6) and high risk of hypertension, type 2 diabetes mellitus, dyslipidemia, obesity (7, 8), and non-oncologic chronic pain (9, 10, 11).

Specifically, metabolic flexibility is defined as the ability to efficiently adapt our metabolism through the detection, trafficking, storage, and utilization of energy substrates, depending on availability and requirements (12). It has been described that metabolic disorders, as mentioned earlier, limit this capacity for physiological adaptability (13); this metabolically 'inflexible' state is characterized by inefficient glucose transport, reduced fatty acid turnover, and diminished oxidative capacity, favoring the accumulation of ectopic lipids and the early onset of metabolic syndrome (14).

Regarding non-oncologic chronic pain, it is recognized as a disease in its own right (15), with a prevalence of 32.1% in the Chilean population (16), becoming a public health issue, negatively impacting quality of life, user function, representing a high socioeconomic burden (17, 18). Some metabolic disorders (e.g., diabetes mellitus, hypertension, and obesity) have been linked to the development and progression of non-oncologic chronic pain (9, 10, 11). Furthermore, individuals with non-oncologic chronic pain and cardiovascular diseases experience greater pain severity and disability than those with chronic pain alone (19). People with chronic pain often experience functional limitation, which is associated with low levels of physical activity, sedentary behavior, increasing the risk of developing cardiovascular diseases (19).

In this context, individuals with CRFs may enter the Cardiovascular Health Program (PSCV), which aims to reduce the incidence of cardiovascular events through the control and compensation of CRFs in primary care through the following actions:

- Reducing the cardiovascular risk of controlled individuals.
- Promoting healthy lifestyles.
- Achieving control of risk factors. o Achieving optimal blood pressure levels. o Improving metabolic control in people with diabetes. o Improving cholesterol levels in individuals with dyslipidemia.

Complementing the actions of the PSCV, physical exercise becomes a cornerstone for the control of these CRFs (20), improvement in metabolic flexibility (21), and reduction of non-oncologic chronic pain associated with CRFs (22, 23). Moderate-intensity aerobic exercise for 30 to 60 minutes every day of the week has been described as the most used alternative for controlling these risk factors (24); however, achieving this volume of exercise is very difficult in a clinical setting. Since lifestyle change is not easy for the population, adherence to some aerobic exercise programs decreases up to 50% in the first 3 months (25). Factors responsible for this low adherence include session duration, the presence of disease or post-exercise pain, and lack of time reported by users (26).

Thus, time-effective exercise alternatives (≤ 10 minutes of effective work) could address this reported lack of time by users and achieve control of CRFs. Among the time-effective exercise modalities for controlling CRFs, high-intensity interval training (HIIT) (27) has been reported, consisting of repeated short periods of high-intensity exercise followed by passive or active low-intensity breaks (28), and muscle resistance exercises with elastic materials (ERE) which is a method that uses elastic devices as resistance, which are low-cost, portable, and can be used almost anywhere. Elastic devices allow for modulating training intensity by changing the resistance provided by the bands (29).

Positive results have been reported from HIIT and ERE exercise programs for reducing blood pressure (27, 29), improving glycemic control (30, 31), body composition (27, 32), metabolic flexibility (21), physical function (32, 33), and reducing non-oncologic chronic pain (34, 35) in users of this cohort.

An important aspect that reveals the true effect of an exercise program is the adaptations to workload understood as the physiological changes or adjustments resulting from a physical training program that promotes optimal functioning of the organism (36). Adaptations are determined by events that result in the activation and/or repression of specific signaling pathways that regulate exercise-induced gene expression and protein synthesis/degradation (37). The functional consequences of

these adaptations are determined by the training volume, intensity, and frequency, and the half-life of the protein (38). Moreover, many characteristics of training adaptation are specific to the type of stimulus, such as the mode of exercise (38). HIIT-type exercise induces a variety of metabolic and morphological changes, including mitochondrial biogenesis, fiber type transformation from fast to slow, and substrate metabolism (39). In contrast, resistance exercise (ERE) stimulates the synthesis of contractile proteins responsible for muscle hypertrophy and increases the production of maximum contractile force (37, 38).

Generally, the results of exercise programs show the final changes after an intervention, leaving aside the capacity for adaptation to workload during the intervention. The processes of adaptation to exercise are studied mainly in athletes; however, little is known about the adaptability capacity, in special populations, regarding CRFs, metabolic flexibility, physical function, and non-oncologic chronic pain, specifically in users belonging to the Cardiovascular Health Program of the External CESFAM of Valdivia, subjected to two types of exercise.

Despite knowing the link between non-oncologic chronic pain and the presence of cardiovascular diseases, the individual relationship between different cardiovascular risk factors and pain intensity is still uncertain.

Thus, implementing a physical exercise program associated with the PSCV will improve the possibility of controlling CRFs, improving metabolic flexibility, reducing non-oncologic chronic pain, and promoting lifestyle change difficult to achieve in users of this cohort. On the other hand, the External CESFAM will be recognized as a pioneering establishment in the implementation of non-pharmacological alternatives (personalized and expert-guided physical exercise) to improve the health and quality of life of PSCV users, which will not generate extra costs to the establishment for its application.

Objectives

General

- Objective 1: Evaluate the effects of a 12-week HIIT and ERE program on the workload adaptation capacity in cardiometabolic risk factors, physical function, and non-oncologic chronic pain in users of the Cardiovascular Health Program at the External CESFAM of Valdivia.
- Objective 2: Determine the relationship between cardiovascular risk factors and non-oncologic chronic pain in users of the Cardiovascular Health Program at the External CESFAM of Valdivia.

Specific

- Objective 1.1: Analyze the effects of a 12-week HIIT and ERE program on the workload adaptation capacity in cardiometabolic risk factors, physical function, and non-oncologic chronic pain in users of the Cardiovascular Health Program at the External CESFAM of Valdivia.
- Objective 1.2: Compare the effects of a 12-week HIIT and ERE program on the workload adaptation capacity in cardiometabolic risk factors, physical function, and non-oncologic chronic pain in users of the Cardiovascular Health Program at the External CESFAM of Valdivia.
- Objective 2.1: Determine the relationship between the number of cardiovascular risk factors and the presence of non-oncologic chronic pain in users of the PSCV at the External CESFAM of Valdivia.
- Objective 2.2: Determine the relationship between the number of cardiovascular risk factors and the intensity of non-oncologic chronic pain in users of the PSCV at the External CESFAM of Valdivia.
- Objective 2.3: Associate the presence of non-oncologic chronic pain with other chronic diseases.

Methodology

The project formulation, planning, and management, the application of assessments, and exercise protocols will be carried out by a team of kinesiologists experienced in physical exercise and control of CRFs, supported by the Kinesiology school of the Universidad San Sebastián, Valdivia campus. This project will complement the actions of the PSCV of the External CESFAM of Valdivia. All evaluations and interventions will contribute to the Monthly Statistical Register (REM) of the PSCV, specifically, in the REM A27 (health education) section C (group physical activity for the cardiovascular health program) and, depending on the case, in REM A04 section B: Consultation with non-medical professionals. Both records will be collected by the providers (USS) and sent to the PSCV reference of the External CESFAM, ideally on the last day of the month, to contribute to REM. The results obtained during the intervention could be published in press articles, conferences, and renowned scientific journals to disseminate the good practices carried out by the CESFAM. The population will correspond to adult users of the PSCV enrolled in the External CESFAM of Valdivia with CRFs, the sample will be obtained through a public call inviting participation in HIIT or ERE exercise 3 sessions weekly for 12 weeks at the San Sebastián University Physical Fitness and Exercise Facility. The Cardiovascular Health Program team (Medical Director Osvaldo Elgueta) will identify eligible users

for the study within the records (clinical file and health controls) of the program, then the PSCV team will extend the invitation to users to participate in the project.

Inclusion and Exclusion Criteria

Inclusion: a) Being physically inactive (not performing 300 or 150 min of moderate or vigorous intensity physical activity respectively per week measured with the IPAQ questionnaire); b) BMI between 25 and 39.9 kg/m2; c) Belonging to the cardiovascular health program of the External CESFAM of Valdivia d) Presenting with or without non-oncologic chronic pain.

Exclusion: a) Bone disease; b) Ischemic disease or arrhythmia and c) Chronic respiratory disease d) Uncontrolled chronic diseases f) People unable to understand instructions, g) People who do not speak Spanish h) History of previous oncological disease or under study for suspected neoplastic disease in any part of the body i) Low adherence to training (< 70% or non-attendance at 4 continuous sessions).

Included users will be divided into 3 groups: HIIT, ERE, and Control. All subjects will be evaluated at four times: pre-intervention (week 0 – time 1), week 4 (time 2), week 8 (time 3), and post-intervention (week 12 – time 4). Only the evaluation of metabolic flexibility and direct oxygen consumption will be carried out pre (week 0) and post-intervention (week 12).

Data Collection Techniques and Instruments

Clinical Record Information Collection The following information will be obtained from each participant's clinical record:

- Sociodemographic Background: o Gender o Age o Ancestry o Education
- Medical Background o Time within the cardiovascular health program o Morbid history o Medications and dosage o Time using medications o Laboratory tests (fasting glucose, glycosylated hemoglobin, lipid profile)

Physical Activity Level and Quality of Life

The international physical activity questionnaire (IPAQ) (40) will be applied to estimate the level of physical activity prior to the intervention. Health-related quality of life will be measured using the SF36 questionnaire (41) before and after the intervention.

Physical Function Physical function will be measured through the Six-Minute Walk Test, and grip dynamometry.

Six-Minute Walk Test

The Six-Minute Walk Test (6MWT) is a simple and effective submaximal exercise test used to assess aerobic functional capacity, especially in patients with cardiopulmonary and respiratory diseases. The main objective of this test is to measure the distance an individual can walk over a span of six minutes on a flat, hard surface. This test is widely used because it is easy to perform, does not require sophisticated equipment, and reflects activities of daily living.

The general protocol of the 6MWT includes the following steps:

1. Preparation: Before the test, the procedure is explained to the patient, and consent is obtained. Baseline measurements such as heart rate, blood pressure, and oxygen saturation should be recorded.
2. Instructions: The patient is instructed to walk at their own pace but to try to cover the greatest distance possible in six minutes. They are allowed to slow down or stop if necessary.
3. Conducting the Test: During the test, the patient walks along a marked hallway, turning around at the end of each stretch. The evaluator follows the patient to assist if necessary but without encouragement to not influence performance.
4. Post-test: Immediately after the test, heart rate, blood pressure, and oxygen saturation are re-measured. The total distance covered is also recorded.
5. Results Analysis: The distance walked is compared to reference values based on the patient's age, gender, and other variables to assess their functional capacity.

Grip Dynamometry

Grip strength will be assessed using the CAMRY Model EH101 dynamometer (46) following the Southampton protocol. The procedure begins with the subject seated with forearms resting on the chair, the wrist just over the end of the chair arm, in a neutral position, with the thumb up and feet flat on the floor, they are asked to squeeze the dynamometer as hard as they can for as long as they can. Three attempts will be made with each hand and the best attempt of the 6 total will be recorded (47).

Metabolic Flexibility – Indirect Calorimetry

To assess the balance of energy substrates during exercise, indirect calorimetry measurement will be used; this measurement provides minute-to-minute energy expenditure data that make it the most valuable tool for distinguishing the various components of energy expenditure associated with the energy cost of a given activity (48).

Body Composition and Waist Circumference

Height will be measured using a precision stadiometer 0.1 cm (Seca Bodymeter 206) (49), weight, percentage of fat and lean mass will be measured using a bioimpedance meter (TANITA BC-534) (50). BMI will be estimated using the kg/m2 formula. Waist circumference will be measured at the midpoint between the costal margin and the iliac crest, with a non-deformable precision tape measure 0.1 cm Seca 201(49). It will be performed in a standing position, and at the end of a normal expiration.

Cardiovascular Parameters

Systolic and diastolic blood pressure and heart rate will be measured using an automatic monitor (Omron HEM 7130™; Omron Healthcare Inc., Lake Forest, IL) (51) at rest following the standard seated procedure after 15 minutes of rest, being done before and after 15 min of each session.

Metabolic Parameters

Fasting glucose, cholesterol, and triglyceride values will be obtained through tests requested in the controls of the Cardiovascular Health Program.

Pain Intensity

The Chronic Pain Grading Scale will be applied to assess pain intensity (52).

Pressure Pain Threshold

The Pressure Pain Threshold (PPT) is defined as the minimum amount of pressure that elicits the first sensation of pain, and will be measured using a pressure algometer (53).

Pain Characterization

The modified DN4 questionnaire will be applied to determine the characteristics of pain prior to the intervention (54).

Adaptation Capacity to Workload

The capacity to adapt to workloads will be evaluated through the changes observed in the tests described above at four times: pre-intervention, week 4, week 8, and post-intervention (week 12).

High-Intensity Interval Training (HIIT)

During HIIT, 8-10 intervals/session will be performed on a cycle ergometer, at an intensity of 80-100% of the theoretical maximum heart rate (MHR) according to Karvonen, equating to a bicycle load of 8 to 10 points on the modified Borg scale of 1-10 points (55). Each interval will consist of 1 minute of cycling, followed by 2 minutes of inactive rest, similar to previous protocols (27). Every two weeks, the bicycle load will be adjusted (increasing the resistance to pedaling of the bicycle) due to normal physiological adaptations and improvement of the patient's baseline threshold, always exercising the patient in each effort interval at a muscular intensity of 8 to 10 points according to the modified Borg scale similar to previous studies (27).

Resistance Exercise with Elastic Materials (REM)

During REM, participants will perform concentric and eccentric contractions with Theraband CLX elastic bands for 1 minute at an intensity of 8-10 according to the OMNI-RES scale. The rest period will last 2 minutes and each exercise will be repeated 3 times. Three exercises will be performed: bicep curls, horizontal rowing in a chair, and wide squat. The exercise load will be modified every two weeks according to the physiological adaptations of the subjects to the training, in order to adjust the loads to the new thresholds and always work at an intensity of 8-10 on the OMNI-RES scale.

Control Group:
Participants in the control group will be requested to maintain their current lifestyle and exercise habits throughout the duration of the study. This includes adhering to their usual regimen of prescribed medication.

Statistical Analysis

The sample size will be calculated as follows: (1) ANOVA for repeated measures with intra-inter-group interaction, (2) three groups, (3) type I error: 5%, (4) type II error: 20%, (5) statistical test power: 80%, and (6) effect size (ES): 0.10 according to Cohen's classification (1988). Using these parameters, the total sample size recommended by G*Power software (Version 3.1.9.2) was 174 (58 per group). Assuming a 10% dropout, the total was calculated at 192, with 64 participants randomly assigned to each group. The concealment of allocation will be conducted by a researcher not involved in the clinical procedures of the intervention using the

method of opaque, sealed, and consecutively numbered envelopes. The random sequence and allocation concealment allow for the control of selection bias.

For enhanced bias control, the data analysis will be performed by a researcher blinded to the intervention groups. Dependent variables will be described in terms of mean and standard deviation. Assumptions of normality and homoscedasticity for all data will be verified using the Shapiro-Wilk test and the Levene's test, respectively. To address General Objective 1, the Student's t-test will be used to detect baseline differences between groups, and a repeated measures ANOVA (group x time) to determine differences in all dependent variables between training prior, and at 4, 8, and 12 weeks afterwards. The Bonferroni post hoc test will be used to test differences between groups. Additionally, the Cohen's d test will be applied to determine the effect size. To address the General Objective, the Pearson correlation test will be used to determine the relationship between MHR and the presence and intensity of non-oncological chronic pain. The level for statistical significance was set at $p < 0.05$. Statistical analyses will be performed using SPSS software version 21 (SPSS™ Inc., Chicago, IL, USA).

Expected Results

Following the training application, we expect that the measured variables will modify their values on average in favor of greater adaptation to workloads, improved health condition, better quality of life, and a reduction in the pharmacological arsenal used before the intervention. Additionally, implementing a physical exercise program associated with the PSCV will improve the possibilities of controlling MHR and promote lifestyle changes in users of this population. Moreover, the CESFAM Externo will be showcased as a pioneering establishment in the implementation of non-pharmacological alternatives (personalized physical exercise and guided by experts in physical exercise and health) to improve the health and quality of life of PSCV users, which will not generate extra expenses for its application. On another front, the results obtained during the intervention could be published in press articles, congresses, and scientific journals to disseminate the good practices carried out by CESFAM and the Universidad San Sebastián.

Work Plan (Gantt Chart)

Month 1

• Logistical meeting and coordination with the head of the Cardiovascular Health Program and Director.
• Presentation of the project to the Scientific Ethics Committee

Month 2

• Patient eligibility process o Contact from CESFAM to eligible users o On-site recruitment at CESFAM Externo or invitation to the project by phone call o Signing of informed consent o Collection of sociodemographic information

Month 3

• Pre-intervention evaluation (IPAQ, SF36, Cardiometabolic Variables, Metabolic Flexibility, and Pain)
• Exercise familiarization

Months 4, 5, and 6

• Application of training protocols
• Evaluation of workload adaptation every 4 weeks, until week 12 (Cardiometabolic Variables, Pain).

Month 7

• Tabulation of results in Excel spreadsheets
• Delivery of preliminary results to CESFAM Externo.
• Time for unforeseen events in the application of the protocol

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PARTICIPANT INFORMATION DOCUMENT AND INFORMED CONSENT FORM

Informed Consent Document for Users of the External CESFAM Cardiovascular Health Program

Johnattan Cano Montoya - Universidad San Sebastián

Effects of Two Modalities of Physical Exercise on Workload Adaptation Capacity, Metabolic Flexibility, and Non-Oncologic Chronic Pain in Patients of the External CESFAM Cardiovascular Health Program of Valdivia. Version 1

This Informed Consent Document consists of two parts:

- **Information (providing details about the study)**
- **Consent Form (to be signed if you agree to participate) A copy of the complete Informed Consent Document will be provided to you.**

PART I: Information

Introduction

I am Johnattan Cano Montoya, working with the School of Kinesiology at Universidad San Sebastián. We are researching the effects of Physical Exercise on Cardiovascular Risk Factors. I will provide you with information and invite you to participate in this research. You do not need to decide today whether to participate. Before deciding, you may discuss the research with someone you feel comfortable with. If there are words you do not understand, please stop me as I inform you to allow time for explanation. If you have questions later, you can ask me or members of the team.

Purpose

Hypertension, diabetes, high cholesterol, and pain are common diseases in the region. The cardiovascular health program you belong to helps control these diseases, but physical exercise is an effective alternative that could enhance the program's actions. Therefore, the purpose of this project is to investigate the relationship between the presence and intensity of pain and chronic diseases and the role of a 12-week exercise program as therapy to improve physical condition, cardiovascular health, and quality of life.

Type of Research Intervention

This intervention will include reviewing information from your clinical file, evaluating your physical abilities, an intervention with physical exercise three times a week for 12 weeks, and re-evaluations every four weeks of the data taken at the beginning.
Participant Selection
We are inviting all users of the External CESFAM Cardiovascular Health Program of Valdivia to participate in the research on the effects of an exercise program for controlling hypertension, diabetes, and high cholesterol.

Voluntary Participation

Your participation in this research is entirely voluntary. You can choose whether or not to participate. Whether you choose to participate or not, all services you receive at CESFAM will continue unchanged. You can change your mind later and stop participating even after you have previously accepted.

Procedures and Protocol

A. Unknown Procedures

We need to observe the effects of two types of training because we do not know how effective they are compared to your usual treatment. To do this, participants will be divided into three groups. The groups are selected at random, like flipping a coin. All participants will receive the intervention, but two groups will start training within the next two weeks, and one group will start training in three more months. The group that will not train in the first three months will have monthly follow-ups where their physical capabilities will be evaluated, and physical activity recommendations will be given. This is the best way we have to conduct research without being influenced by what we think or expect to happen. Then we will compare which of the two types of training gives better results. The research team will be closely observing you and the other participants during the study. If there is anything that concerns or bothers you about the research, please talk to me or one of the other researchers.

If the training causes discomfort, we will use what is called rescue kinesiotherapy. Kinesiotherapy sessions will be provided to reduce the negative effects of training, such as fatigue or muscle pain. If you find the kinesiotherapy sessions do not stop the discomfort and are too uncomfortable for you, we will stop the exercise sessions.

B. Process Description

During the research, you will participate in 39 sessions at the San Sebastián University Health Center.

- The first session will be at the Health Center of Universidad San Sebastián. Here, an evaluation of resting energy expenditure called Indirect Calorimetry will be carried out. The center's address is Vicente Pérez Rosales 1095.
- The second session will take place at the San Sebastián University Health Center in Valdivia. Here, the level of physical activity, health-related quality of life, vital signs, body composition, muscle strength, pain, and cardiorespiratory capacity will be evaluated. The gym's address is Viel 99, Isla Teja.
- Sessions 3 to 39 will be held at the San Sebastián University Health Center. The training will be applied.
- Sessions 15, 27, and 39 will be held at the San Sebastián University Health Center. The level of physical activity, health-related quality of life, vital signs, body composition, muscle strength, pain, and cardiorespiratory capacity will be reevaluated.

Duration

The research will last a total of three months. During this time, you will need to attend the San Sebastián University Health Center three days a week, for one hour each day, and one session at the University Health Center of Universidad San Sebastián. In total, you will be asked to attend 39 sessions over three months. At the end of the three months of intervention, the research will conclude.

Side Effects

Performing physical exercise should not report side effects, however, we will monitor this and keep a record of any unwanted effects or problems. We may stop applying physical exercise if an

unknown problem appears. If this is necessary, we will discuss it with you, and you will always be consulted before continuing with the next step.

Risks

By participating in this research, you may be exposed to minimal risk. The possible risks of performing physical exercise include post-exercise fatigue and/or muscle pain that could last up to 48 hours. Although the likelihood of this happening is low, you should still be aware of this possibility. To minimize the risk, you will receive education on the muscular effects of physical exercise and post-exercise regenerative exercises; you will have kinesiotherapy sessions aimed at reducing fatigue and muscle pain in case of no muscle recovery post-exercise sessions.

Discomforts

By participating in this research, you may experience discomforts such as having your blood pressure and oxygen saturation taken several times, in addition to traveling on your own to the exercise location.

Benefits

If you participate in this research, you may potentially benefit from improved physical condition, cardiovascular, metabolic health, and health-related quality of life.

Incentives

This research does not offer any incentives.

Confidentiality

Your identity will not be disclosed, taking all necessary measures to protect the confidentiality of clinical and experimental data. A code will be assigned to you, avoiding the use of your personal data. The information obtained from the evaluations will be stored in a database created by the Responsible Researcher for a period of 4 years, after which it will be handed over to the External CESFAM. This information will be stored in digital format (Excel) on the Responsible Researcher's computer, which has an access password granted by the USS (Universidad San Sebastián), and in physical format, in filing cabinets within the premises of Universidad San Sebastián, Valdivia campus, office of the director of the Kinesiology career.

Sharing the Results

The knowledge we gain from conducting this research will be shared with you before it becomes available to the public. No confidential information will be shared. There will be small meetings in the community, and these will be announced. After these meetings, the results will be published so that other interested parties can learn from our research.
Right to Refuse or Withdraw
You do not have to participate in this research if you do not wish to, and refusing to participate will not affect you in any way in being treated at CESFAM. You will still have all the benefits you would otherwise have at CESFAM. You can stop participating in the research at any time you wish without losing your rights as a user here. Your treatment at this CESFAM will not be affected in any way.

Who to Contact

If you have any questions, you can ask them now or later, even after the study has started. If you wish to ask questions later, you can contact the Responsible Researcher: Johnattan Cano Montoya, Academic Researcher of the School of Kinesiology, Faculty of Dentistry and Rehabilitation Sciences, Universidad San Sebastián Seda Valdivia: cell one: +56962382339

email: johnattan.cano@uss.cl.

This project has been reviewed and approved by the Scientific Ethical Committee of the Valdivia Health Service. This Committee is accredited and functions to safeguard the rights of people as research subjects. If you wish to learn more about this committee, contact telephone: 63-2281784 or at Prales Building, Vicente Pérez Rosales 560, office 307, 3rd Floor, Valdivia, Chile.

PART II: Informed Consent Form

I have been invited to participate in a research project titled "Effects of Two Physical Exercise Modalities on Workload Adaptation Capacity, Metabolic Flexibility, and Non-Oncologic Chronic Pain in Patients of the Cardiovascular Health Program at the External CESFAM of Valdivia." The purpose of this project is to investigate whether there is a relationship between the presence and intensity of pain and chronic diseases, and the role of a 12-week exercise program as a therapy to improve my physical condition, cardiovascular health, and quality of life.

I understand that my physical abilities will be assessed and I will undergo an exercise program three times a week for three months. I have been informed that the risks are minimal and may include only muscle pain or fatigue. The potential benefits are improved physical condition, cardiovascular and metabolic health, and health-related quality of life. I will not receive incentives for my participation. I have been provided the name of a researcher who can be easily contacted using the name and address given to me for that person.

I have read or had the information provided to me read. I have had the opportunity to ask questions about it and my questions have been satisfactorily answered. I voluntarily consent to participate in this research as a participant and understand that I have the right to withdraw from the research at any time without affecting my medical care in any way.

Participant's Name
Participant's Signature
Date

For Illiterate Participants

I have witnessed the accurate reading of the consent document to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has freely given consent.

Witness's Name
Participant's Fingerprint Witness's Signature
Date

I have read accurately or witnessed the accurate reading of the informed consent document for the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has freely given consent.

Researcher's Name
Researcher's Signature
Date

Name of the Head of the Establishment, Delegate or Minister of Faith
Signature
Date (Day/Month/Year)

A copy of this Informed Consent Document has been provided to the participant (Initials of researcher/assistant)