Clinical Trial Protocol
Iranian Registry of Clinical Trials

07 Nov 2026

The effect of resistance training, electrical muscle stimulation (EMS) and vitamin D supplementation on the regulation of microRNAs miR-486 and miR-206, serum concentrations of insulin-like growth factor 1 (IGF-1), myostatin and fibroblast growth factor 21 (FGF-21), and physical performance indices in patients with heart failure with reduced ejection fraction and sarcopenia

Protocol summary

Study aim

Determining the effect of resistance training, EMS, and vitamin D on the expression of miR-486 and miR-206, serum levels of IGF-1, myostatin, and FGF-21, and physical performance indices in heart failure patients with sarcopenia

Design

Randomized, controlled, 5-group, parallel-group, single-blind, phase 3 clinical trial on 25 patients with HFrEF and sarcopenia (5 per group). Allocation to control, vitamin D, resistance training, EMS, and exercise + vitamin D groups

Settings and conduct

This study will be conducted at Shahid Rajaee Cardiovascular Institute, Tehran. Screening, confirmation of HFrEF and echocardiography will be performed in the Heart Failure Clinic, and sarcopenia assessment with PMCSA at T4 level will be performed by the imaging department. Resistance training and EMS interventions and supplementation will be implemented. Blood sampling and molecular and biochemical assays will also be performed in a standard laboratory.

Participants/Inclusion and exclusion criteria

Inclusion: Stable heart failure (HFrEF), sarcopenia confirmed by PMCSA on T4 CT scan, serum vitamin D level of approximately 20 ng/ml, ability to exercise. Exclusion: Pacemaker/ICD, unstable arrhythmia, absence of more than 2 consecutive sessions, and change of muscle-affecting medications.

Intervention groups

1- Control group 2- Vitamin D supplement group 3- Resistance training group (RT) 4- Electrical stimulation group (EMS) 5- Exercise and supplement group

Main outcome variables

Physical performance indices: grip strength with a hand-held dynamometer, walking speed with a 4-meter test, and balance with a leaf balance scale. Biological markers: serum concentrations of IGF-1, myostatin, and FGF-21 by ELISA; relative expression of miR-486 and miR-206 in peripheral blood by RT-qPCR; and serum 25(OH)D levels to monitor the effect of supplementation.

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20180501039501N1**
Registration date: **2026-09-24, 1405/07/02**
Registration timing: **registered_while_recruiting**

Last update: **2026-09-24, 1405/07/02**
Update count: **0**

Registration date

2026-09-24, 1405/07/02

Registrant information

Name

Samaneh Ebrahimi

Name of organization / entity

Imam Khomeini International University

Country

Iran (Islamic Republic of)

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Recruitment status
recruiting
Funding source

Expected recruitment start date
2026-09-23, 1405/07/01
Expected recruitment end date
2026-12-22, 1405/10/01
Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
The effect of resistance training, electrical muscle stimulation (EMS) and vitamin D supplementation on the regulation of microRNAs miR-486 and miR-206, serum concentrations of insulin-like growth factor 1 (IGF-1), myostatin and fibroblast growth factor 21 (FGF-21), and physical performance indices in patients with heart failure with reduced ejection fraction and sarcopenia

Public title
The effect of resistance training, electrical muscle stimulation (EMS), and vitamin D supplementation on sarcopenia in patients with heart failure with reduced ejection fraction
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
Sarcopenia in patients with heart failure with reduced ejection fraction
Exclusion criteria:
Age
No age limit
Gender
Both

Phase
3
Groups that have been masked

- Outcome assessor
- Data analyser

Sample size
Target sample size: **25**
Randomization (investigator's opinion)
Not randomized
Randomization description
Blinding (investigator's opinion)
Single blinded
Blinding description
SubjectGiven the nature of the interventions in this study (resistance training and Electromyostimulation - EMS), blinding the participants and the training instructors is not feasible due to the overt and tangible nature of the interventions. However, to minimize potential bias and enhance the scientific validity of the study, blinding is strictly implemented at the following levels: Blinding of Outcome Assessors: All individuals responsible for phlebotomy, laboratory biochemical analysis, and physical performance testing are completely blinded to the participants' group assignments. Blood samples will be sent to the laboratory using a coding system to prevent any potential bias in the results. Blinding of Data Analyst: The statistician performing the data analysis will receive the data labeled with group codes (e.g., Group A, B, and C) and will remain blinded to the identity of the intervention groups until the data analysis phase is finalized. Therefore, the present study is designed as a single-blind trial, with a focus on blinding the assessment and data analysis teams to prevent the influence of potential biases on the reported outcomes.s
Placebo
Not used
Assignment
Factorial
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
Research Ethics Working Group/Committee, Qazvin University of Medical Sciences
Street address
No. 7. Unit 7. East 8th Alley. North Varzi Street. West Ferdows Boulevard. Tehran
City
Qazvin
Province
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Postal code
1483795468
Approval date
2026-06-07, 1405/03/17
Ethics committee reference number
IR.QUMS.REC.1405.081

Health conditions studied

1

Description of health condition studied
Heart failure patients with reduced ejection fraction and sarcopenia
ICD-10 code
(I00-I99)
ICD-10 code description
IX Diseases of the circulatory system

Primary outcomes

1

Description

Relative expression level of miR-486 in blood samples, by RT-qPCR method

Timepoint

At the beginning of the study and at the end of the twelfth week

Method of measurement

RT-qPCR assay

2

Description

Relative expression level of miR-206 in blood samples

Timepoint

At the beginning of the study and at the end of the twelfth week

Method of measurement

RT-qPCR assay

3

Description

Serum concentration of insulin-like growth factor-1 (IGF-1)

Timepoint

At the beginning of the study and at the end of the twelfth week

Method of measurement

measured by ELISA

4

Description

Serum concentration of myostatin

Timepoint

At the beginning of the study and at the end of the twelfth week

Method of measurement

measured by ELISA

5

Description

Serum concentration of fibroblast growth factor-21 (FGF-21)

Timepoint

At the beginning of the study and at the end of the twelfth week

Method of measurement

measured by ELISA

Secondary outcomes

1

Description

Relative expression level of miR-486 in blood samples

Timepoint

at the end of week 12

Method of measurement

measured by RT-qPCR

2

Description

Relative expression level of miR-206+ in blood samples

Timepoint

at the end of week 12

Method of measurement

measured by RT-qPCR

3

Description

Serum concentration of insulin-like growth factor-1 (IGF-1)

Timepoint

at the end of the 12th week

Method of measurement

measured by ELISA

4

Description

Serum myostatin concentration

Timepoint

at the end of week 12

Method of measurement

measured by ELISA

5

Description

Serum concentration of fibroblast growth factor-21 (FGF-21)

Timepoint

at the end of the 12th week

Method of measurement

measured by ELISA

Intervention groups

1

Description

Control group: Received usual medical care and cardiac rehabilitation according to the center's program, without resistance training or EMS; along with a placebo and vitamin D supplementation (if foreseen in the protocol).

Category

Other

2

Description

Intervention group: Vitamin D supplementation groupReceived usual medical care along with vitamin D supplementation at the dose and duration specified in the protocol; without performing resistance training and EMS.

Category

Other

3

Description
Intervention group: Resistance Training (RT) groupReceived usual medical care along with a gradual, clinically appropriate resistance training program, supervised by the cardiac rehabilitation team; no vitamin D supplementation or EMS

Category
Other

4

Description
Intervention group: Electrical Muscle Stimulation (EMS) group,Receiving usual medical care plus electrical muscle stimulation with standard parameters tailored to the patient's condition, under the supervision of a medical and cardiac rehabilitation team; without resistance training and vitamin D supplementation.

Category
Other

5

Description
Intervention group: Resistance training + EMS + Vitamin D supplementation groupReceived usual medical care along with implementing a gradual resistance training program and vitamin D supplementation, according to the dose and duration specified in the protocol; under the supervision of the cardiac and medical rehabilitation team.

Category
Other

Recruitment centers

1

Recruitment center

Name of recruitment center
Shahid Rajaee Cardiovascular Institute, Tehran

Full name of responsible person
Ms. Dr. Marzieh Mirtajdini

Street address
No. 7, Unit 7, 8th East Alley, North Varzi Street, West Ferdows Boulevard (Nasser Hejazi), Tehran, Iran.

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity
Imam Khomeini International University of Qazvin

Full name of responsible person
Dr. Khadijeh Irandoust

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Grant name

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?
Yes

Title of funding source
Imam Khomeini International University of Qazvin

Proportion provided by this source
100

Public or private sector
Public

Domestic or foreign origin
Domestic

Category of foreign source of funding
empty

Country of origin

Type of organization providing the funding
Academic

Person responsible for general inquiries

Contact

Name of organization / entity
Imam Khomeini International University of Qazvin

Full name of responsible person
Samaneh Ebrahimi

Position
PhD student

Latest degree
Master

Other areas of specialty/work
Exercise physiology

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No. 7, Unit 7, 8th East Alley, North Varzi Street, West Ferdows Boulevard (Nasser Hejazi), Tehran, Iran.

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Person responsible for updating data

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Sharing plan

Deidentified Individual Participant Data Set (IPD)
Yes - There is a plan to make this available
Study Protocol
Yes - There is a plan to make this available
Statistical Analysis Plan
Yes - There is a plan to make this available
Informed Consent Form
Yes - There is a plan to make this available
Clinical Study Report
Yes - There is a plan to make this available
Analytic Code
Yes - There is a plan to make this available
Data Dictionary
Yes - There is a plan to make this available
Title and more details about the data/document
De-identified individual participant data will be available, including baseline demographic and clinical characteristics, intervention group allocation, primary outcome data (relative expression of miR-486 and miR-206, and serum concentrations of IGF-1, myostatin, and FGF-21), secondary outcome data (handgrip strength, gait speed, Berg Balance Scale score, and serum 25(OH)D level), and the data dictionary. All direct identifiers and potentially identifying information will be removed before data sharing. The study protocol and statistical analysis plan will also be available upon request.
When the data will become available and for how long
Data will be available beginning 6 months after publication of the primary study results and will remain available for 5 years after the publication date.
To whom data/document is available
Researchers affiliated with universities, research institutions, healthcare centers, or other recognized scientific organizations may submit a data-access request. Applicants must have relevant scientific qualifications and a methodologically sound research or analysis proposal.
Under which criteria data/document could be used
Data may be used only for scientific analyses relevant to the study objectives, valid secondary research, meta-analyses, or replication and verification of the study findings. Access requests must include the research objective, analysis plan, research-team details, and a commitment to confidentiality. Access will be conditional upon approval by the principal investigator, compliance with research ethics requirements, execution of a data-use agreement, and agreement not to attempt re-identification of participants or transfer data to third parties. Commercial use, redistribution of raw data, or use beyond the approved objectives will not be permitted.
From where data/document is obtainable
Applicants should submit a written request to the principal investigator of the study. Requests may be submitted and followed up through the principal investigator’s official email address: Principal Investigator: [Samaneh Ebrahimi] Email: [ebrahimi.mailbox@gmail.com] Affiliation: Rajaie

Cardiovascular Medical and Research Center, Tehran, Iran.

What processes are involved for a request to access data/document

Applicants must submit a written request including the study title and objective, a brief research protocol, proposed analysis plan, research-team details, institutional affiliation, and ethics approval when required. The request will be reviewed for scientific relevance, feasibility, ethical considerations, and protection of confidentiality. A decision will be communicated within a maximum of 30 working days. If approved, and after execution of a data-use agreement, the agreed de-identified data files and supporting documents will be provided through a secure transfer method.

Comments

Shared data will contain no direct personal identifiers. Given the small sample size and the sensitivity of clinical information from patients with heart failure, some potentially identifying variables may be removed, aggregated, or restricted to minimize the risk of indirect participant re-identification.