Clinical Trial Protocol
Iranian Registry of Clinical Trials

07 Nov 2026

Effects of Progressive Resistance Training Combined with Omega-3 Fatty Acid Supplementation on Myokines, Oxidative Stress, and Metabolic Indices in Patients with Non-Alcoholic Fatty Liver Disease

Protocol summary

Study aim

The study will estimate the marginal effects of supervised progressive resistance training and omega-3 supplementation on insulin resistance at week 12 in adults with imaging-confirmed nonalcoholic fatty liver disease and assess interaction between the interventions.

Design

This single-center, parallel-group, 12-week trial will use a full two-by-two factorial randomized design with 284 participants. Supplement assignment will be double-blinded. Exercise allocation will be open, while measurement, data-management, and primary-analysis personnel will remain unaware of treatment codes.

Settings and conduct

Recruitment will occur through an affiliated hepatology service and the surrounding community. Screening, supervised training, fasting blood collection, laboratory assays, hepatic imaging, and follow-up assessments will be conducted at study facilities over 12 weeks.

Participants/Inclusion and exclusion criteria

Men and women aged 30 to 60 years with imaging-confirmed disease, body mass index 25 to 40, no type 2 diabetes, no recent structured resistance training or omega-3 supplementation, and medical clearance will be included. Protocol-specified hepatic, cardiovascular, renal, musculoskeletal, pregnancy, bleeding, medication, alcohol, and competing-program exclusions will apply.

Intervention groups

Participants will be allocated equally to resistance training plus omega-3, resistance training plus placebo, omega-3 alone, or placebo alone. Training will continue for 12 weeks with three supervised weekly sessions. Four omega-3 or matched placebo softgels will be taken daily.

Main outcome variables

The primary outcome will be insulin resistance at week 12 adjusted for baseline. Secondary outcomes will be circulating irisin and myostatin, plasma malondialdehyde, fasting triglycerides, serum alanine aminotransferase, and controlled attenuation parameter, assessed at baseline and week 12.

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20251112067968N4**
Registration date: **2026-09-22, 1405/06/31**
Registration timing: **prospective**

Last update: **2026-09-22, 1405/06/31**
Update count: **0**

Registration date

2026-09-22, 1405/06/31

Registrant information

Name

Ali Haghighati borujeni

Name of organization / entity

Country

Iran (Islamic Republic of)

Phone

+98 38 3426 7171

Email address

alihaghighati2002@gmail.com

Recruitment status

recruiting

Funding source

Expected recruitment start date

2026-10-02, 1405/07/10

Expected recruitment end date

2026-12-31, 1405/10/10

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Effects of Progressive Resistance Training Combined with Omega-3 Fatty Acid Supplementation on Myokines, Oxidative Stress, and Metabolic Indices in Patients with Non-Alcoholic Fatty Liver Disease

Public title

Marginal effects of supervised progressive resistance training and omega-3 supplementation in adults with nonalcoholic fatty liver disease

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Participants will be men and women aged 30-60 years with imaging-confirmed nonalcoholic fatty liver disease; body mass index will be 25-40 kg/m2; body-weight variation during the preceding 3 months will be less than 3%; type 2 diabetes will be absent; glucose-lowering medication will not be used; regular structured resistance training during the preceding 6 months will be absent; omega-3 supplementation during the preceding 8 weeks will be absent; and medical clearance for progressive resistance exercise will be required.

Exclusion criteria:

Participants with viral hepatitis, autoimmune liver disease, hemochromatosis, Wilson disease, clinically established cirrhosis or another chronic liver disease, habitual alcohol intake >20 g/day in women or >30 g/day in men, pregnancy or lactation, unstable cardiovascular disease, clinically significant renal disease, neuromuscular or musculoskeletal disorders preventing safe resistance exercise, use of medications known to induce hepatic steatosis, clinically relevant bleeding disorders, or current participation in another structured exercise or intentional weight-loss program will be excluded.

Age

From **30 years** old to **60 years** old

Gender

Both

Phase

N/A

Groups that have been masked

- Outcome assessor
- Data analyser

Sample size

Target sample size: **284**

Randomization (investigator's opinion)

Randomized

Randomization description

Participants will be allocated in a 1:1:1:1 ratio using a computer-generated random sequence with permuted blocks of 4 and 8, stratified by sex and baseline CAP category. The allocation sequence will be generated by a statistician with no role in recruitment, intervention delivery, or outcome measurement. Personnel enrolling participants will have no access to upcoming allocations.

Blinding (investigator's opinion)

Double blinded

Blinding description

Supplement assignment will be double-blinded. Blinding of participants and exercise personnel to resistance-training allocation will not be feasible. Personnel responsible for biochemical assays, biomarker measurements, controlled attenuation parameter assessment, data management, and the prespecified primary statistical analysis will remain unaware of randomized treatment codes until completion of the primary analysis.

Placebo

Used

Assignment

Factorial

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics Committee of Islamic Azad University, Shahrekord Branch

Street address

Rahmatieh, Islamic Azad University Shahrekord Branch

City

Shahrekord

Province

Chahar-Mahal-va-Bakhtiari

Postal code

8817630003

Approval date

2026-05-10, 1405/02/20

Ethics committee reference number

IR.IAU.SHK.REC.1405.054

Health conditions studied

1

Description of health condition studied

Nonalcoholic fatty liver disease

ICD-10 code

ICD-10 code description

Primary outcomes

1

Description

HOMA-IR at week 12, adjusted for baseline HOMA-IR

Timepoint
Baseline and after 12 weeks
Method of measurement
Fasting plasma glucose and fasting serum insulin will be measured. HOMA-IR will be calculated as fasting insulin multiplied by fasting glucose divided by 22.5.

Secondary outcomes

1

Description
Circulating irisin
Timepoint
Baseline and after 12 weeks
Method of measurement
Serum irisin will be quantified using a human irisin ELISA kit; samples will be assayed in duplicate.

2

Description
Circulating myostatin
Timepoint
Baseline and after 12 weeks
Method of measurement
Serum myostatin will be quantified using a human GDF-8/myostatin immunoassay; samples will be analyzed in duplicate.

3

Description
Plasma malondialdehyde
Timepoint
Baseline and after 12 weeks
Method of measurement
Plasma malondialdehyde will be quantified by high-performance liquid chromatography with fluorescence detection.

4

Description
Fasting triglycerides
Timepoint
Baseline and after 12 weeks
Method of measurement
Fasting serum triglycerides will be analyzed on an automated biochemical analyzer using a glycerol-phosphate oxidase/peroxidase method.

5

Description
Serum alanine aminotransferase
Timepoint
Baseline and after 12 weeks
Method of measurement
Serum alanine aminotransferase will be analyzed on an automated biochemical analyzer using an IFCC-compatible kinetic method.

6

Description
Controlled attenuation parameter
Timepoint
Baseline and after 12 weeks
Method of measurement
Hepatic steatosis will be quantified using vibration-controlled transient elastography with controlled attenuation parameter; at least 10 valid acquisitions will be obtained and the median will be retained.

Intervention groups

1

Description
Resistance training plus omega-3: Participants will complete a 12-week supervised whole-body progressive resistance-training program three times per week on nonconsecutive days, with 36 scheduled sessions. They will consume four omega-3 softgels daily, providing 1.44 g/day EPA and 0.96 g/day DHA.
Category
Treatment - Other

2

Description
Resistance training plus placebo: Participants will complete the same 12-week supervised progressive resistance-training program three times per week on nonconsecutive days, with 36 scheduled sessions. They will consume four externally matched corn-oil placebo softgels daily.
Category
Treatment - Other

3

Description
Omega-3 without structured resistance training: Participants will consume four omega-3 softgels daily for 12 weeks and will maintain habitual physical activity without initiating structured resistance training.
Category
Treatment - Other

4

Description
Placebo without structured resistance training: Participants will consume four externally matched corn-oil placebo softgels daily for 12 weeks and will maintain habitual physical activity without initiating structured resistance training.
Category
Placebo

Recruitment centers

1

Recruitment center
Name of recruitment center
Islamic Azad University Shahrekord Branch
Full name of responsible person
Mehrdad Yadegari Dehkordi
Street address
Rahmatieh, Islamic Azad University Shahrekord Branch
City
Shahrekord
Province
Chahar-Mahal-va-Bakhtiari
Postal code
8817630003
Phone
+98 38 3336 1001
Fax
Email
Yadagari_mehrdad@yahoo.com
Web page address

Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Islamic Azad University
Full name of responsible person
Mehrdad Yadegari Dehkordi
Street address
Rahmatieh, Islamic Azad University Shahrekord Branch
City
Shahrekord
Province
Chahar-Mahal-va-Bakhtiari
Postal code
8817630003
Phone
+98 38 3336 1001
Fax
Email
Yadagari_mehrdad@yahoo.com
Web page address
Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Islamic Azad University
Proportion provided by this source
100
Public or private sector
Private
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
Islamic Azad University
Full name of responsible person
Akram Jafari
Position
Associate professor
Latest degree
Ph.D.
Other areas of specialty/work
Sport Physiology
Street address
Rahmatieh, Islamic Azad University Shahrekord Branch
City
Shahrekord
Province
Chahar-Mahal-va-Bakhtiari
Postal code
8817630003
Phone
+98 38 3336 1001
Email
jafari.akm@gmail.com

Person responsible for scientific inquiries

Contact
Name of organization / entity
Islamic Azad University
Full name of responsible person
Akram Jafari
Position
Associate professor
Latest degree
Ph.D.
Other areas of specialty/work
Sport Physiology
Street address
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Province
Chahar-Mahal-va-Bakhtiari
Postal code
8817630003
Phone
+98 38 3336 1001
Email
jafari.akm@gmail.com

Person responsible for updating data

Contact
Name of organization / entity

Islamic Azad University
Full name of responsible person
Akram Jafari
Position
Associate professor
Latest degree
Ph.D.
Other areas of specialty/work
Sport Physiology
Street address
Rahmatieh, Islamic Azad University Shahrekord Branch
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Province
Chahar-Mahal-va-Bakhtiari
Postal code
8817630003
Phone
+98 38 3336 1001
Email
jafari.akm@gmail.com

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
No - There is not 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, study protocol, statistical analysis plan, analysis codes, and data dictionary will be made available to qualified researchers after publication of the primary study results. Requests will be reviewed by the research team based on scientific and ethical considerations.
When the data will become available and for how long
Access to data and documents will begin 6 months after publication of the primary study results and will remain available for 5 years.
To whom data/document is available
Academic researchers, scientists from research institutions, and qualified investigators submitting a valid scientific request will be eligible for access.
Under which criteria data/document could be used
Data will be available for scientific research purposes, valid analyses, and advancing knowledge in nonalcoholic fatty liver disease and exercise science. Data reuse must comply with research ethics principles and must not attempt participant re-identification.
From where data/document is obtainable
Requests for data access should be submitted to the corresponding investigator through the official email address of the research center. Final contact information will be provided after publication of the primary study results.
What processes are involved for a request to access data/document
Requests will be reviewed by the research team. After scientific and ethical approval, a data use agreement will be completed and access to de-identified data will be provided.
Comments