Clinical Trial Protocol
Iranian Registry of Clinical Trials

22 Nov 2026

Effect of Eight Weeks of High-Intensity Interval Training and Omega-3 Supplementation on Inflammatory Variables, Lung Ventilation, and Heart Rate Variability in Young Male Smokers

Protocol summary

Study aim

Investigate the effects of high-intensity interval training and omega-3 supplementation on inflammatory variables, lung ventilation, and heart rate variability in young male smokers

Design

A randomized, controlled clinical trial with a control group, a parallel-group design, and no blinding (phase: not applicable) will be conducted in 48 smokers. Randomization will be performed using DatInf RandList software, and sealed envelopes will be used for allocation concealment.

Settings and conduct

This study aims to investigate the effects of high-intensity interval training and omega-3 supplementation in male smokers aged 20 to 30 years in Erbil, Iraq. Participants will be randomly allocated to four groups, and the intervention will last eight weeks. Outcomes will be assessed before and after the intervention. The study is single blind with respect to capsule allocation; participants will not know whether they are receiving omega 3 supplements or placebo because the capsules are visually identical.

Participants/Inclusion and exclusion criteria

Inclusion criteria: A history of smoking for at least one year and good health. Exclusion criteria: Presence of clinical diseases.

Intervention groups

1. Training + supplement Group: Performing high-intensity interval training for eight weeks and consuming two omega-3 capsules daily. 2. Training + Placebo Group: Performing high-intensity interval training for eight weeks and consuming two inactive placebo capsules daily. 3. supplement Group: Consuming two omega-3 capsules daily for eight weeks without exercise. 4. Control + Placebo Group: Consuming two inactive placebo capsules daily for eight weeks without exercise.

Main outcome variables

Tumor necrosis factor-alpha, interleukin-6, C-reactive protein, Clara cell protein 16, surfactant protein D, lung ventilation, heart rate variability, and maximal oxygen uptake

General information

Reason for update

The clinical trial record is being updated to correct informational and administrative errors, complete the documentation, and improve the accuracy and transparency of the registered information. The main corrections concern the name of the Research Ethics Committee and the institution that issued the ethics approval code, the study funding information, and incorrect patient information. The study is funded by the student, and the names of individuals previously entered incorrectly in the funding section will be corrected. In addition, the descriptions of the study design, participant allocation, randomization method, allocation concealment, and blinding of outcome assessors will be reviewed and completed to ensure consistency with the methods actually planned or implemented in the study. These corrections do not involve changes to the study title, primary objectives, or primary and secondary outcomes. The study outcomes remain unchanged, and the updates are not intended to alter or manipulate the study outcomes or results.

Acronym

IRCT registration information

IRCT registration number: **IRCT20251208068255N1**
Registration date: **2026-02-18, 1404/11/29**
Registration timing: **prospective**

Last update: **2026-10-30, 1405/08/08**
Update count: **1**

Registration date

2026-02-18, 1404/11/29

Registrant information

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2026-03-06, 1404/12/15

Expected recruitment end date

2026-03-25, 1405/01/05

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Effect of Eight Weeks of High-Intensity Interval Training and Omega-3 Supplementation on Inflammatory Variables, Lung Ventilation, and Heart Rate Variability in Young Male Smokers

Public title

Effect of High-Intensity Interval Training and Omega-3 in Smokers

Purpose

Education/Guidance

Inclusion/Exclusion criteria

Inclusion criteria:

Current male smokers in the city of Erbil, aged 20 to 30. Smoking more than 20 cigarettes per day. A history of cigarette smoking for at least 12 months. A body mass index (BMI) of 18–25 kg/m². Physician's confirmation of physical health. No regular exercise or physical activity during the previous six months.

Exclusion criteria:

History of diabetes. History of cardiovascular diseases. History of respiratory diseases. History of hypersensitivity or allergy to fish oil, omega-3 fatty acids, or other components of the supplement used in the study. Use of omega-3 supplements. Use of other sports or nutritional supplements. Use of anti-inflammatory medications. Active intention to quit smoking or to use smoking cessation medications.

Age

From **20 years** old to **30 years** old

Gender

Male

Phase

N/A

Groups that have been masked

No information

Sample size

Target sample size: **48**

Randomization (investigator's opinion)

Randomized

Randomization description

Participants will be allocated to four study groups using block randomization with an equal allocation ratio of 1:1:1:1. The individual participant will be the unit of randomization, and each participant will be independently allocated to one of four groups: high-intensity interval training plus omega-3 supplementation, high-intensity interval training plus placebo, omega-3 supplementation alone, or control plus placebo. The random allocation sequence will be generated using DatInf RandList software, version 1.2. Variable block sizes will be used to maintain balance in the number of participants across the four groups. Stratified randomization will not be used, and no stratification factors will be specified. Allocation concealment will be maintained by an independent researcher who will not be involved in participant recruitment, group allocation, or outcome assessment. The allocation sequence will be concealed using sequentially numbered, opaque, sealed envelopes. After eligibility has been confirmed and enrollment finalized, the corresponding envelope will be opened in numerical order. Outcome assessor blinding will be implemented separately from allocation concealment. The design of the randomization process will be carried out in consultation with an epidemiologist and a statistician.

Blinding (investigator's opinion)

Not blinded

Blinding description

Placebo

Used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Research Ethics Committees of University of Tabriz

Street address

Central Library and Documentation Center, University of Tabriz, 29 Bahman Boulevard, Tabriz, East Azerbaijan Province, Iran.

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Tabriz

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Postal code

5166616471

Approval date

2025-12-28, 1404/10/07

Ethics committee reference number

IR.TABRIZU.REC.1404.213

Health conditions studied

1

Description of health condition studied

Tobacco use (smoking)

ICD-10 code

Z72.0

ICD-10 code description

Tobacco use

Primary outcomes

1

Description

Interleukin-6 (IL-6)

Timepoint

Primary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; After eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

IL-6 levels will be measured using commercial human ELISA kits (Karmania Pars Gene, Iran). This assay will be performed using the sandwich ELISA method, in accordance with the manufacturer’s instructions.

2

Description

C-reactive Protein (CRP)

Timepoint

Primary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; After eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

Serum CRP concentration will be measured using a quantitative immunoturbidimetric method on an automated clinical chemistry analyzer (Cobas c 311; Roche Diagnostics, Germany).

3

Description

Clara Cell Protein 16 (CC16)

Timepoint

Primary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; After eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

Serum CC16 levels will be measured using commercial human ELISA kits (ZellBio, Germany). This assay is performed based on the sandwich ELISA method and in accordance with the manufacturer's instructions.

4

Description

Surfactant Protein D (SP-D)

Timepoint

Primary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; After eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

Serum SP-D levels will be measured using commercial human ELISA kits (ZellBio, Germany). This assay is performed based on the sandwich ELISA method, in accordance with the manufacturer's instructions.

5

Description

Clara Cell Protein 16 (CC16)/Surfactant Protein D (SP-D) Ratio

Timepoint

Primary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; After eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

The CC16 to SP-D ratio is calculated by dividing the serum concentration of CC16 by the serum concentration of SP-D.

6

Description

Forced Vital Capacity (FVC)

Timepoint

Primary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; After eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

FVC measurement will be performed before and after the intervention using a portable spirometer (model GP, manufactured by Micro Medical, UK) and in accordance with standard recommendations. Participants were seated on a chair, a nose clip was applied, and the mouthpiece of the device was placed in the mouth. Following a maximal deep inspiration, they immediately performed a forceful and maximal expiration through the mouthpiece sensor to determine FVC.

7

Description

Forced Expiratory Volume in one Second (FEV_1)

Timepoint

Primary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; After eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

FEV_1 will be measured before and after the intervention using a portable spirometer (model GP, manufactured by Micro Medical, UK) and in accordance with standard recommendations. Participants were seated, a nose clip was applied, and the mouthpiece was placed in the mouth. After performing a maximal deep inspiration, they immediately executed a rapid and forceful expiration through the mouthpiece. The volume of air exhaled during the first second was recorded as FEV_1.

8

Description

Forced Expiratory Volume in one Second (FEV_1)/Forced Vital Capacity (FVC)

Timepoint

Primary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; After eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

The ratio of forced expiratory volume in one second to forced vital capacity (FEV_1/FVC) will be calculated by dividing the measured FEV_1 value by the measured FVC value and multiplying the result by 100. Results will be expressed as a percentage (%).

9

Description

Time-domain heart rate variability parameter: Standard Deviation of NN Intervals (SDNN)

Timepoint

Primary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; After eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

SDNN will be determined from the electrocardiogram (ECG) recording by calculating the standard deviation of all normal-to-normal (NN) intervals during the recording period. Results will be expressed in milliseconds (ms).

10

Description

Time-domain heart rate variability parameter: Root Mean Square of Successive Differences (rMSSD)

Timepoint

Primary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; After eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

rMSSD will be determined by calculating the square root of the mean of the squared differences between successive NN intervals derived from the ECG recording. Results will be expressed in milliseconds (ms).

11

Description

Frequency-domain heart rate variability parameter: Low-Frequency Power (LF Power)

Timepoint

Primary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; After eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

Power LF will be calculated by spectral analysis of the NN intervals derived from the ECG recording within the frequency range of 0.04–0.15 Hz. When absolute power is reported, results will be expressed in ms^2.

12

Description

Frequency-domain heart rate variability parameter: High-Frequency Power (HF Power)

Timepoint

Primary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; After eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

Power HF will be calculated by spectral analysis of the NN intervals derived from the ECG recording within the frequency range of 0.15–0.40 Hz. When absolute power is reported, results will be expressed in ms^2.

13

Description

Frequency-domain heart rate variability parameter: Low-Frequency-to-High-Frequency Power Ratio (LF/HF Ratio)

Timepoint

Primary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; After eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

The LF/HF ratio will be calculated by dividing power LF by power HF and will be reported as a dimensionless value.

14

Description

Maximal Oxygen Uptake (VO_2max)

Timepoint

Primary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; After eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

After baseline measurements, participants are guided to a standard 400-meter track to perform the Cooper test for estimating VO_2max. In this test, participants are instructed to cover the maximum distance possible within 12 minutes. VO_2max is then estimated based on the distance covered using the following formula:VO_2max (ml/kg/min)=(22.351×distance in kilometers)−11.288VO_2max (ml/kg/min)=(22.351×distance in kilometers)−11.288

Secondary outcomes

1

Description

Tumor Necrosis Factor-alpha (TNF-α)

Timepoint

Secondary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; and after eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

Serum TNF-α levels will be determined using commercial human ELISA kits (Karmania Pars Gene, Iran) based on the sandwich ELISA method.

2

Description

Cortisol

Timepoint

Secondary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; and after eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

Salivary cortisol levels are used as a primary biomarker for assessing physiological stress. To ensure consistency and minimize the influence of daily fluctuations, samples are collected every morning at a fixed time, ideally between 7:00 and 9:00 a.m., when cortisol levels naturally peak. After collection, the samples are stored under appropriate temperature conditions and analyzed using enzyme-linked immunosorbent assay (ELISA) techniques.

3

Description

Peripheral blood oxygen saturation (SpO_2)

Timepoint

Secondary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; and after eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

SpO_2 will be measured noninvasively using a finger pulse oximeter model Beurer PO 45 (Germany). The device measures oxygenated and deoxygenated hemoglobin in capillary blood using two light wavelengths (red and infrared) and calculates the oxygen saturation percentage based on the light absorption ratio. The sensor is placed on the participant’s dominant index finger, and once the display stabilizes (usually within 5 to 10 seconds), SpO_2 and heart rate values are read from the digital screen and recorded. Measurements are performed at rest in a quiet environment with room temperature between 22 and 25 degrees Celsius to avoid errors caused by movement, cold, or strong light. Each measurement is repeated twice, and the average is recorded as the final SpO_2 value. The normal SpO_2 range in healthy individuals is 95 to 99 percent; however, in non-athletic smokers, a relative reduction in SpO_2 values is expected due to the presence of carbon monoxide and increased carboxyhemoglobin.

4

Description

Total Antioxidant Capacity (TAC)

Timepoint

Secondary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; and after eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

TAC will be measured using commercially available human ELISA assay kits from (ZellBio, Germany), based on the ferric reducing antioxidant power (FRAP) colorimetric method. TAC concentration will be calculated using a standard curve prepared with ferrous chloride ($FeCl_2$), in accordance with the manufacturer's instructions.

5

Description

Malondialdehyde (MDA)

Timepoint

Secondary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; and

after eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

MDA will be measured using commercially available human ELISA assay kits from (ZellBio, Germany), based on the thiobarbituric acid-reactive substances (TBARS) method. MDA concentration, as an indicator of lipid peroxidation and oxidative stress, will be determined according to the manufacturer's instructions.

6

Description

High-density lipoprotein cholesterol (HDL-C)

Timepoint

Secondary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; and after eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

HDL-C will be measured using a standard enzymatic colorimetric method with a Cobas c 311 clinical chemistry analyzer (Roche Diagnostics, Mannheim, Germany). Results will be expressed in milligrams per deciliter (mg/dL).

7

Description

low-density lipoprotein cholesterol (LDL-C)

Timepoint

Secondary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; and after eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

LDL-C will be measured using a standard enzymatic colorimetric method with a Cobas c 311 clinical chemistry analyzer (Roche Diagnostics, Mannheim, Germany). Results will be expressed in milligrams per deciliter (mg/dL).

8

Description

Triglyceride (TG)

Timepoint

Secondary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; After eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

TG concentration will be measured using a standard enzymatic colorimetric method with a Cobas c 311 clinical chemistry analyzer (Roche Diagnostics, Mannheim, Germany). Results will be expressed in milligrams per deciliter (mg/dL).

9

Description

Resting heart rate (RHR)

Timepoint

Secondary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; After eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

RHR will be measured using a digital blood pressure monitor (Omron M6 Comfort, Japan) on the left arm. Before measurement, participants will remain seated at rest for 25 minutes. Heart rate will be recorded three times at 5-minute intervals, and the mean of the three measurements will be used as the final RHR value. Results will be expressed in beats per minute (bpm).

10

Description

Systolic blood pressure (SBP)

Timepoint

Secondary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; After eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

SBP will be measured using a digital blood pressure monitor (Omron M6 Comfort, Japan) on the left arm. Before measurement, participants will remain seated at rest for 25 minutes. SBP will be measured three times at 5-minute intervals, and the mean of the three measurements will be used as the final SBP value. Results will be expressed in millimeters of mercury (mmHg).

11

Description

Diastolic blood pressure (DBP)

Timepoint

Secondary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; After eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

DBP will be measured using a digital blood pressure monitor (Omron M6 Comfort, Japan) on the left arm. Before measurement, participants will remain seated at rest for 25 minutes. DBP will be measured three times at 5-minute intervals, and the mean of the three measurements will be used as the final DBP value. Results will be expressed in millimeters of mercury (mmHg).

12

Description

Body weight (kg)

Timepoint

Secondary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; After eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

Body weight will be measured using a digital scale (Seca 890, manufactured in Germany).

13

Description

Body fat percentage

Timepoint

Secondary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; After eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

Body fat percentage will be measured using a body composition analyzer (InBody 270, manufactured in South Korea).

14

Description

Body Mass Index (BMI)

Timepoint

Secondary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; and after eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

BMI is calculated using the following formula: Body Mass Index (kg/m^2) = weight (kg) / square of height (m^2).

15

Description

Pittsburgh Sleep Quality Questionnaire (PSQI)

Timepoint

Secondary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; and after eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

To assess participants' sleep quality, the Persian version of the PSQI will be used. This self-reported questionnaire includes 19 items divided into seven components: subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. Each component is scored from 0 to 3, and the sum of the seven component scores forms the global PSQI score (0–21). A score of ≤5 indicates good sleep quality, while a score >5 indicates poor sleep quality. This tool provides a comprehensive assessment of sleep quality and its impact on daily functioning, and the Persian version has been validated in Iranian studies.

16

Description

health-related quality of life (HRQOL)

Timepoint

Secondary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; and after eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

To assess participants' HRQOL, the WHOQOL-BREF questionnaire will be used. It will be administered before the intervention and after the eight-week intervention. The WHOQOL-BREF evaluates four main domains: physical health, social relationships, psychological status, and environment. Scores for each domain include raw and transformed values, reflecting the individual's perception of health-related quality of life. In general, higher scores indicate a better understanding of functional health and overall well-being.

17

Description

Patient Health Questionnaire (PHQ)

Timepoint

Secondary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; and after eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

To assess the severity of depression among participants, the Persian version of the PHQ-9 questionnaire will be used. This self-reported questionnaire consists of 9 items evaluating the individual's psychological status over the past two weeks, covering components such as decreased interest in activities, feelings of depression, sleep disturbances, fatigue, appetite changes, guilt, concentration problems, psychomotor agitation or retardation, and suicidal thoughts. Each item is scored on a 0 to 3 scale (0 = not at all, 1 = several days, 2 = more than half the days, 3 = nearly every day), and the sum of the 9 items provides the total PHQ-9 score (0–27). This score reflects depression severity: 0–4 minimal, 5–9 mild, 10–14 moderate, 15–19 severe, and 20–27 very severe. The Persian version has been validated and recommended for use in Iranian studies.

18

Description

Perceived Stress Scale (PSS)

Timepoint

Secondary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; and after eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

The PSS questionnaire will be used to assess the participants' perceived stress levels. This self-reported questionnaire consists of 14 items evaluating the individual's stress experience over the past month, covering aspects such as sense of control, managing important tasks, dealing with unexpected events, worries, and daily psychological pressure. Each item is scored on a 0-4 scale (0 = never, 1 = almost never, 2 = sometimes, 3 = often, 4 = almost always), and positively worded (reverse) items are reversed before calculating the total score. The sum of the 14 items yields the total PSS score (0–56), with higher scores indicating greater perceived stress. The Persian version has been validated and used in the Iranian population.

19

Description

Fagerström Test for Nicotine Dependence (FTND)

Timepoint

Secondary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; and after eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

To assess nicotine dependence, the FTND questionnaire will be used. This questionnaire consists of six items about cigarette consumption behavior, with total scores ranging from 0 to 10. Based on the total score, nicotine dependence is classified into three levels: low (0–3), moderate (4–6), and high (7–10). The validity and reliability of the Persian version of this questionnaire were confirmed in the study by Sarbandi et al. (2015), with a reported Cronbach's alpha of 0.71.

20

Description

COPD Assessment Test (CAT)

Timepoint

Secondary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; and after eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

Participants' symptoms will be recorded using the Chronic Obstructive Pulmonary Disease Assessment Test (CAT). This standard tool includes eight domains, assessing cough, sputum production, chest tightness or heaviness, shortness of breath when climbing stairs or inclines, limitations in daily household activities, sleep quality, and fatigue. The total score reflects the impact of COPD on patients' daily quality of life, with higher scores indicating greater disease impact.

21

Description

Dyspnea Assessment Test

Timepoint

Secondary outcomes will be assessed at two time points: At baseline (pre-test), 24 hours before the initiation of any exercise training or omega-3 supplementation; and after eight weeks of intervention (post-test), 48 hours following the completion of the HIIT program and/or omega-3 supplementation.

Method of measurement

The severity of dyspnea in participants will be assessed using the Modified Medical Research Council Dyspnea Scale (mMRC). This scale ranges from 0 to 4 and evaluates the impact of shortness of breath on physical activities in patients with respiratory issues. A score of 0 indicates breathlessness only with strenuous activity, while a score of 4 represents severe breathlessness that prevents leaving the house or performing tasks such as dressing and undressing. Participants will indicate the level of activity at which they experience breathlessness.

Intervention groups

1

Description

Intervention Group 1: High-Intensity Interval Training (HIIT) Plus Omega-3 Supplementation: Participants in this group will complete a 2-week familiarization period followed by an 8-week main HIIT program. Training sessions will be conducted three times per week under the supervision of the researcher and an observer on the running tracks at Sami Abdulrahman Park. Each training session will include a 10-minute warm-up, the main exercise session, and a 10-minute cool-down.During the familiarization period, participants will perform three 300-s running bouts at 60% of maximal aerobic speed (MAS) in week 1 and two sets of three 150-s running bouts at 70% of MAS in week 2. During the 8-week main training program, exercise intensity will increase progressively: 100–110% MAS during weeks 1–2, 110–120% MAS during weeks 3–4, 120–130% MAS during weeks 5–6, and 130–140% MAS during weeks 7–8 of the main training phase. Exercise intensity will also be monitored using the Borg rating of perceived exertion (RPE) scale. Active recovery between repetitions and recovery between sets will follow the approved training protocol.In addition to exercise, participants will receive two fish oil omega-3 capsules daily for 8 weeks (Nutravita Ltd., London, UK). The total daily fish oil dose will be 2,000 mg, providing 1,100 mg of omega-3 fatty acids, including 660 mg of eicosapentaenoic acid (EPA)

and 440 mg of docosahexaenoic acid (DHA). One capsule will be taken with or immediately after breakfast, and the second will be taken with the evening meal.

Category

Lifestyle

2

Description

Intervention Group 2: High-Intensity Interval Training (HIIT) Plus Placebo: Participants in this group will complete a 2-week familiarization period followed by the same 8-week main HIIT program as Intervention Group 1. Training sessions will be conducted three times per week under the supervision of the researcher and an observer on the running tracks at Sami Abdulrahman Park. Each training session will include a 10-minute warm-up, the main exercise session, and a 10-minute cool-down. During the familiarization period, participants will perform three 300-s running bouts at 60% of maximal aerobic speed (MAS) in week 1 and two sets of three 150-s running bouts at 70% of MAS in week 2. During the 8-week main training program, exercise intensity will progressively increase from 100% to 140% MAS and will be monitored using the Borg rating of perceived exertion (RPE) scale. Active recovery between repetitions and recovery between sets will follow the approved training protocol. In addition to exercise, participants will receive two placebo capsules daily for 8 weeks. The placebo capsules will be visually identical to the omega-3 capsules and will contain plant-based oil without eicosapentaenoic acid (EPA) or docosahexaenoic acid (DHA). One capsule will be taken with or immediately after breakfast, and the second will be taken with the evening meal.

Category

Lifestyle

3

Description

Intervention Group 3: Omega-3 Supplementation Alone: Participants in this group will receive two fish oil omega-3 capsules daily for 8 weeks (Nutravita Ltd., London, UK). The total daily fish oil dose will be 2,000 mg, providing 1,100 mg of omega-3 fatty acids, including 660 mg of eicosapentaenoic acid (EPA) and 440 mg of docosahexaenoic acid (DHA). One capsule will be taken with or immediately after breakfast, and the second will be taken with the evening meal. Participants will not undertake the HIIT program and will be instructed to maintain their usual daily activities throughout the study.

Category

Lifestyle

4

Description

Control Group: Placebo Without High-Intensity Interval Training (HIIT): Participants in this group will receive two placebo capsules daily for 8 weeks. The placebo capsules will be visually identical to the omega-3 capsules and will contain plant-based oil without eicosapentaenoic acid (EPA) or docosahexaenoic acid (DHA). One capsule will be taken with or immediately after breakfast, and the second will be taken with the evening meal. Participants will not undertake the HIIT program and will be instructed to maintain their usual lifestyle and daily activities throughout the study.

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center

Erbil, Kurdistan Region of Iraq (patient recruitment via public announcements, poster placement, and

Full name of responsible person

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Researcher

Full name of responsible person

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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

Researcher

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

Persons

Person responsible for general inquiries

Contact

Name of organization / entity

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PhD candidate

Latest degree

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Other areas of specialty/work

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Sharing plan

Deidentified Individual Participant Data Set (IPD)

Undecided - It is not yet known if there will be 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

Undecided - It is not yet known if there will be 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

The documents and datasets available for sharing in this study will include: (1) an anonymized raw dataset containing participants' demographic characteristics and baseline information; (2) a dataset containing pre- and post-intervention measurements of inflammatory variables, pulmonary ventilation indices, heart rate variability (HRV), and other secondary outcomes; and (3) statistical analysis results and supporting documentation describing the data analysis methods. The entire individual-level dataset that can be safely shared will be made available after removing direct and indirect

personal identifiers and in accordance with applicable ethical and legal requirements. If sharing the complete dataset could compromise participants' confidentiality or create a risk of re-identification, only the relevant portions of the data that can be safely shared will be provided. Following publication of the scientific articles related to this study, the available datasets and supporting documents may be requested by submitting a formal, justified research request to the corresponding author or principal investigator. All requests will be reviewed by the corresponding author or principal investigator, and access will be granted upon approval, subject to research ethics principles, participants' informed consent, and applicable data protection regulations. The data will be provided exclusively for research purposes and within the scope of the approved request.

When the data will become available and for how long

The access period for the data and documents will begin six months after the publication of the final article in the relevant scientific journal, and access will be available indefinitely, as long as other researchers are interested in using them.

To whom data/document is available

Access to the study data and related documents will be granted to interested researchers and investigators affiliated with universities, research institutions, and recognized scientific centers worldwide. Researchers working in industry may also request access, provided that their intended use of the data is for legitimate scientific research and publication purposes. All requests must include a clear research proposal and a commitment to maintain confidentiality and adhere to ethical standards.

Under which criteria data/document could be used

The study data and related documents can only be used for scientific research purposes and for publishing results in reputable journals. Their use is subject to the following conditions: The received data and documents must be used solely for scientific analysis related to the study objectives, and any attempt to identify participant identities is strictly prohibited. The requesting researcher must submit a research proposal outlining the study aim, analysis methods, and research design. Results derived from the data must be maintained and reported in accordance with ethical standards and confidentiality requirements. Any redistribution of the data or transfer to third parties without written permission from the study team is prohibited. Permitted analyses include re-evaluation of primary and secondary outcomes, meta-analyses, and secondary investigations consistent with the study protocol. The data cannot be used for commercial, advertising, or other non-scientific purposes. Overall, access to the data and documents is conditional upon adherence to ethical standards, scientific objectives, and protection of participant confidentiality.

From where data/document is obtainable

To request access to the study data and documents, interested parties can contact as follows: Responsible Person: Elaheh Piralaiy Email: epiralaiy@tabrizu.ac.ir Direct Phone Number: +98 914 6285306 Position and University: Associate Professor, Department of Exercise Physiology, University of Tabriz University Mailing Address: 29 Bahman Boulevard, Tabriz, East Azerbaijan Province, Iran University Phone Number: +98 41 3334 1300 University Website: https://tabrizu.ac.ir/en .... The Second Person Badrkhan Rashwan Ismael Email: rashwanismael.b@tabrizu.ac.ir Direct Phone Number: +98 9357059284 Position and University: PhD student, Department of Exercise Physiology, University of Tabriz University Mailing Address: 29 Bahman Boulevard, Tabriz, East Azerbaijan Province, Iran University Phone Number: +98 41 3334 1300 University Website: https://tabrizu.ac.ir/en Applicants should provide their full contact information, affiliated institution, purpose of data use, and type of analysis planned. Access to the data and documents will be granted in accordance with ethical guidelines and confidentiality of participant information.

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

The process for requesting access to the study data or documents is as follows: Submission of a formal request: The applicant must send an official email epiralaiy@tabrizu.ac.ir or rashwanismael.b@tabrizu.ac.ir This email should include the applicant's full personal and institutional details, the purpose of using the data, the type of analysis or research intended, and a list of the data or documents requested. Initial review by the research team: Upon receiving the request, the research team reviews it for completeness, research purpose, and compliance with ethical principles. This step typically takes 1 to 2 weeks. Signing a data use agreement or ethical compliance agreement: If the request is approved, the applicant must sign an agreement outlining confidentiality obligations, restrictions on the use of the data for unauthorized purposes, and adherence to participant rights. Preparation of data and documents: After signing the agreement, the research team prepares the requested data after de-identification of participants and provides related documents, including the study protocol, statistical analysis plan, and data dictionary. Delivery of data and documents: The data and documents are securely sent to the applicant via encrypted email or a secure platform. The entire process, from submission to final delivery, usually takes 2 to 4 weeks, depending on the volume of data and complexity of the documents. This procedure ensures that access to the data is provided while maintaining ethical standards, confidentiality, and information security.

Comments