

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

10 Jun 2026

### Evaluation of the effect of non-organic nitrate supplementation on macro- and micro-vascular changes in active and inactive men with metabolic syndrome

#### Protocol summary

##### Study aim

Evaluating the effect of inorganic nitrate supplementation with or without physical activity on micro- and macro-vascular status of men with metabolic syndrome

##### Design

A single center, concealed, randomised, non-blinded, no placebo, controlled trial will be conducted based on parallel group design of 60 participants (15 in each group).

##### Settings and conduct

Fasting blood sugar, lipid profile, CRP, blood pressure, physical fitness test, pulse wave velocity (PWV) and capillaroscopy will be performed at baseline and at the end of study. IPAQ, Vo2Max and 24-hour urine nitrate will be evaluated at baseline. Height, weight, waist circumference, bioelectric impedance analysis, serum nitrate, 3-day diet recall, step test, and blood pressure will be evaluated weekly.

##### Participants/Inclusion and exclusion criteria

Inclusion criteria: Willingness to participate in the study, male gender, age >18 till 40 years old, metabolic syndrome diagnosis based on IDF criteria, light to moderate physical activity level based on IPAQ Non-inclusion criteria: Chronic diseases (Diabetes, heart failure), rheumatologic or articular disorders that prevent exercise performance, underlying diseases (Cushing's syndrome, Addison's disease), hypertension, diabetes, and dyslipidemia exclusion criteria: Consuming medications that affect metabolic syndrome (chemotherapy, corticosteroids), cancer, physical disability, mental or psychological disorders that prevent exercise performance

##### Intervention groups

Intervention groups will receive either beetroot extract (30% ADI divided dose twice/week), exercise intervention (high intensity interval training), or combined beetroot

extract and exercise and the control group will receive general instruction on healthy lifestyle for 4 weeks. All participants will be instructed to limit the intake of dietary sources of inorganic nitrate.

##### Main outcome variables

PWV, nail fold capillaroscopy

#### General information

##### Reason for update

##### Acronym

##### IRCT registration information

IRCT registration number: **IRCT20220101053579N1**

Registration date: **2022-01-12, 1400/10/22**

Registration timing: **prospective**

Last update: **2022-01-12, 1400/10/22**

Update count: **0**

##### Registration date

2022-01-12, 1400/10/22

##### Registrant information

##### Name

Ali Jafarzadeh Esfehiani

##### Name of organization / entity

##### Country

Iran (Islamic Republic of)

##### Phone

+98 915 316 8951

##### Email address

jafarzadehea982@mums.ac.ir

##### Recruitment status

**Recruitment complete**

##### Funding source

##### Expected recruitment start date

2022-05-22, 1401/03/01

##### Expected recruitment end date

2022-12-21, 1401/09/30  
**Actual recruitment start date**  
empty  
**Actual recruitment end date**  
empty  
**Trial completion date**  
empty

**Scientific title**  
Evaluation of the effect of non-organic nitrate supplementation on macro-and micro-vascular changes in active and inactive men with metabolic syndrome

**Public title**  
Effect of beetroot extract on cardiovascular factors in men with metabolic syndrome

**Purpose**  
Supportive

**Inclusion/Exclusion criteria**  
**Inclusion criteria:**  
Willingness to participate in the study by signing an informed consent Age between 18 and 40 years old Diagnosis of metabolic syndrome based on the International Diabetes Federation (IDF) criteria Low to moderate level of physical activity based on the International Physical Activity Questionnaire (IPAQ) No history for chronic diseases (Diabetes Mellitus, heart failure) No history for Rheumatologic or joint disorders that impair the ability of performing exercises No history for underlying diseases that may affect metabolic syndrome (Cushing syndrome, Addison's disease) No history for hypertension, diabetes and dyslipidemia Male gender  
**Exclusion criteria:**  
Using medications that affect metabolic syndrome (chemotherapy, corticosteroids) Cancer Physical disability that prevents performing the exercises Mental or psychological disorders that prevent performing the study protocol

**Age**  
From **18 years** old to **40 years** old

**Gender**  
Male

**Phase**  
3

**Groups that have been masked**  
*No information*

**Sample size**  
Target sample size: **60**

**Randomization (investigator's opinion)**  
Randomized

**Randomization description**  
Randomization will be performed based on stratified block randomization. Block size would be 8 and participants will be randomized into each block based on age (below 30, 30 or above), BMI (below 30 kg/m<sup>2</sup>, 30 kg/m<sup>2</sup> or over), and presence of elevated blood pressure (below 130/85 mmHg, 130/85 mmHg or over). Randomization concealment will be performed using sealed envelopes. One of the research team members will perform the concealment based on the randomization list. Envelopes will be opaque and sealed so that other

researchers and the participants will not be aware of their group allocation.

**Blinding (investigator's opinion)**  
Not blinded

**Blinding description**  
**Placebo**  
Not used  
**Assignment**  
Parallel

**Other design features**

**Secondary Ids**  
empty

**Ethics committees**

**1**

**Ethics committee**  
**Name of ethics committee**  
Ethics Committee of the Mashhad University of Medical Sciences  
**Street address**  
School of Medicine, East door of Ferdowsi University, Azadi Sq.  
**City**  
Mashhad  
**Province**  
Razavi Khorasan  
**Postal code**  
9177948564

**Approval date**  
2021-12-11, 1400/09/20

**Ethics committee reference number**  
IR.MUMS.REC.1400.282

**Health conditions studied**

**1**

**Description of health condition studied**  
Metabolic syndrome

**ICD-10 code**  
E88.81

**ICD-10 code description**  
Metabolic syndrome

**Primary outcomes**

**1**

**Description**  
mean pulse wave velocity

**Timepoint**  
Baseline and the end of study (4th week)

**Method of measurement**  
PWV at the bifurcation of carotid artery using Doppler ultrasound

## 2

### **Description**

Augmentation index (AI)

### **Timepoint**

Baseline and the end of study (4th week)

### **Method of measurement**

PWV using Doppler ultrasound

## 3

### **Description**

Avascular area

### **Timepoint**

Baseline and the end of study (4th week)

### **Method of measurement**

Nail fold capillaroscopy

## 4

### **Description**

Increase in the diameter of the capillaries

### **Timepoint**

Baseline and the end of study (4th week)

### **Method of measurement**

Nail fold capillaroscopy

## 5

### **Description**

Microhaemorrhage

### **Timepoint**

Baseline and the end of study (4th week)

### **Method of measurement**

Nail fold capillaroscopy

## 6

### **Description**

Hairpin structures

### **Timepoint**

Baseline and the end of study (4th week)

### **Method of measurement**

Nail fold capillaroscopy

## 7

### **Description**

Tortuous structures

### **Timepoint**

Baseline and the end of study (4th week)

### **Method of measurement**

Nail fold capillaroscopy

## 8

### **Description**

Crossing structures

### **Timepoint**

Baseline and the end of study (4th week)

### **Method of measurement**

Nail fold capillaroscopy

## **Secondary outcomes**

### 1

#### **Description**

Fasting blood sugar

#### **Timepoint**

Baseline and at the end of the study

#### **Method of measurement**

Biochemical analysis of blood sample

### 2

#### **Description**

Total cholesterol

#### **Timepoint**

Baseline and at the end of the study

#### **Method of measurement**

Biochemical analysis of blood sample

### 3

#### **Description**

Serum triglyceride

#### **Timepoint**

Baseline and at the end of the study

#### **Method of measurement**

Biochemical analysis of blood sample

### 4

#### **Description**

Low-density lipoprotein (LDL)

#### **Timepoint**

Baseline and at the end of the study

#### **Method of measurement**

Biochemical analysis of blood sample

### 5

#### **Description**

High density lipoprotein (HDL)

#### **Timepoint**

Baseline and at the end of the study

#### **Method of measurement**

Biochemical analysis of blood sample

### 6

#### **Description**

Serum nitrate

#### **Timepoint**

Weekly from the beginning of the study

#### **Method of measurement**

Measuring serum nitrate using nitrate kit

### 7

#### **Description**

Step test

#### **Timepoint**

Baseline and at the end of the study

#### **Method of measurement**

Measured using a standard step

## 8

### **Description**

Systolic blood pressure

### **Timepoint**

Weekly from the beginning of the study

### **Method of measurement**

Measured using sphygmomanometer

## 9

### **Description**

Diastolic blood pressure

### **Timepoint**

Weekly from the beginning of the study

### **Method of measurement**

Measured using sphygmomanometer

## 10

### **Description**

VO2Max

### **Timepoint**

Baseline, second week, and at the end of the study

### **Method of measurement**

Measured on treadmill using CPET device

## 11

### **Description**

Dietary intake

### **Timepoint**

Weekly from the beginning of the study

### **Method of measurement**

3-day 24-hour recall

## **Intervention groups**

### 1

#### **Description**

Intervention group 1: Physical activity intervention will be conducted using low volume high intensity interval training method. Due to the COVID-19 pandemic, instructions will be provided to the participants and the participants will perform the exercises at home after ensuring their mastery on the methods. Intensity of the exercises will be defined based on primary evaluations of perceived exertion, heart rate at 65% and 85% of VO2 Max. Exercises will be conducted in the form of two repetitions of four sets of high intensity intermittent exercises, which are composed of a training phase and a rest phase. Training phase will last for 2 minutes. Participants should keep their heart rate above 85% of VO2Max during the training phase. Then, participants will continue the training phase exercise at a lower intensity (65% of VO2Max). Active rest can be conducted in the form of walking or jogging in place. Duration of the physical activity intervention will be 66 minutes per week. In order to ensure that the participants perform exercises in the correct way, a software that includes

video and textual instructions on each exercise is designed and provided to the participants. The software sends twice weekly messages to the participants based on their progress. Participants will receive general dietary advice (300 Cal deficit per day) and limit dietary nitrate intake.

#### **Category**

Lifestyle

### 2

#### **Description**

Intervention group 2: Beetroot extract will be administered at 30% ADI equal to 3.7 mg/kg/d as two divided doses consumed twice weekly for 4 weeks. Participants will receive general dietary advice (300 Cal deficit per day) and limit dietary nitrate intake.

#### **Category**

Other

### 3

#### **Description**

Intervention group 3: This group will receive both the mentioned physical activity and beetroot extract interventions all together. The intervention duration will be 4 weeks. Participants will receive general dietary advice (300 Cal deficit per day) and limit dietary nitrate intake.

#### **Category**

Lifestyle

### 4

#### **Description**

Control group: The control group will receive general dietary advice (300 Cal deficit per day) and limit dietary nitrate and following an active lifestyle. The control group will not receive placebo.

#### **Category**

N/A

## **Recruitment centers**

### 1

#### **Recruitment center**

##### **Name of recruitment center**

Mashhad Cohort center

##### **Full name of responsible person**

Mohsen Nemati

##### **Street address**

Emam Reza Hospital, Emam Reza Sq.

##### **City**

Mashhad

##### **Province**

Razavi Khorasan

##### **Postal code**

9137913316

##### **Phone**

+98 51 3180 6802

##### **Email**

cohort@mums.ac.ir

**Web page address**

<https://v-research.mums.ac.ir/index.php/component/content/article/43-persian-category/1319-mums-persian-cohort/#visited>

**Sponsors / Funding sources****1****Sponsor****Name of organization / entity**

Mashhad University of Medical Sciences

**Full name of responsible person**

Mohsen Nemati

**Street address**

Azadi Sq. Eastern door of Ferdowsi University, School of Medicine, Nutrition Department

**City**

Mashhad

**Province**

Razavi Khorasan

**Postal code**

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**Phone**

+98 51 3882 7034

**Email**

mds.nutrition@mums.ac.ir

**Web page address**

<https://nutdept.mums.ac.ir/>

**Grant name****Grant code / Reference number****Is the source of funding the same sponsor organization/entity?**

Yes

**Title of funding source**

Mashhad University of Medical Sciences

**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**

Mashhad University of Medical Sciences

**Full name of responsible person**

Ali Jafarzadeh Esfehani

**Position**

PhD Candidate

**Latest degree**

Master

**Other areas of specialty/work**

Nutrition

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East door of Ferdowsi University, Azadi Sq.

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**Fax****Email**

JafarzadehEA982@mums.ac.ir

**Person responsible for scientific inquiries****Contact****Name of organization / entity**

Mashhad University of Medical Sciences

**Full name of responsible person**

Mohsen Nemati

**Position**

Professor

**Latest degree**

Ph.D.

**Other areas of specialty/work**

metabolic syndrome

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**Person responsible for updating data****Contact****Name of organization / entity**

Mashhad University of Medical Sciences

**Full name of responsible person**

Ali Jafarzadeh Esfehani

**Position**

PhD Candidate

**Latest degree**

Master

**Other areas of specialty/work**

Nutrition

**Street address**

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**Fax****Email**

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## Sharing plan

**Deidentified Individual Participant Data Set (IPD)**

No - There is not a plan to make this available

**Justification/reason for indecision/not sharing IPD**

Persian cohort center will provide the data to researchers in a case-by-case basis and the center has the complete ownership of the data.

**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**

No - There is not a plan to make this available

**Data Dictionary**

No - There is not a plan to make this available

**Title and more details about the data/document**

Some collected data including the results of primary outcome measures will be presented.

**When the data will become available and for how long**

Access to data will be granted 6 months after publication

**To whom data/document is available**

Data will be accessible for people working in academic institutions and people working in businesses upon request.

**Under which criteria data/document could be used**

Criteria for sharing deidentified data or other products will be evaluated based on case-by-case approach by the Mashhad University of Medical Sciences.

**From where data/document is obtainable**

Contact info: Dr. Mohsen Nemati, Department of Nutrition, Mashhad University of Medical Sciences, East door of Ferdowsi University, Azadi Sq., Mashhad, Iran  
Post code: 9177948564 email: NematyM@mums.ac.ir  
Phone number: 0098 51 38827034

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

Applicants should submit their detailed request through email. Their request will be evaluated by the researchers and the Mashhad University of Medical Sciences and will be available to the applicant if approved by the organization.

**Comments**