

Clinical Trial Protocol

Iranian Registry of Clinical Trials

11 Jul 2026

Efficacy of compression stockings for treating recurrent vasovagal syncope: a triple-blind, multi-center, randomized controlled trial (COMFORTS-II)

Protocol summary

Study aim

Assessment of the effectiveness of elastic compression stockings in preventing recurrent vasovagal syncope

Design

triple-blind, multi-center, randomized controlled trial

Settings and conduct

Using central online randomization, 268 participants will be allocated to two arms (1:1 ratio), wearing intervention ECS or sham ECS. All participants will receive standard VVS treatment in the form of education, and lifestyle modification recommendations (drinking 2-3 liters/day of fluids and consuming 10 grams/day—roughly half a tablespoon—of table salt). Adherence to ECS treatment will be evaluated through diary sheets, and compared between study arms. Follow-up continues for one year, and is conducted via a 24/7 phone line available to patients and trimonthly visits. The main study center is Tehran Heart Center.

Participants/Inclusion and exclusion criteria

Inclusion criteria: patients with $18 \leq \text{age} \leq 65$ years and diagnosed vasovagal syncope who had ≥ 2 episodes of VVS during the last year. VVS is confirmed by Clinical diagnosis And Calgary syncope system score (CSSS) ≥ -2 ; Exclusion criteria: Presence of other causes for syncope or loss of consciousness; Prior use of medications for vasovagal syncope; Prior use or other indication for compression stockings; Chronic severe illnesses; Pregnancy or intention to become pregnant during the study; Unwillingness to participate or lack of consent

Intervention groups

Intervention: elastic compression stockings: 20-30mmHg pressure, manufactured by Right Arian Farmed, for 12 months Sham: elastic compression stockings: <10mmHg pressure, manufactured by Right Arian Farmed, for 12 months

Main outcome variables

proportion of participants with any syncopal recurrence,

time to first syncopal episode

General information

Reason for update

Acronym

COMFORTS-II: COMpression stockings FOR Treating vasovagal Syncope

IRCT registration information

IRCT registration number: **IRCT20220515054863N1**

Registration date: **2022-10-29, 1401/08/07**

Registration timing: **registered_while_recruiting**

Last update: **2022-10-29, 1401/08/07**

Update count: **0**

Registration date

2022-10-29, 1401/08/07

Registrant information

Name

Masih Tajdini

Name of organization / entity

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2022-04-01, 1401/01/12

Expected recruitment end date

2024-10-10, 1403/07/19

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Efficacy of compression stockings for treating recurrent vasovagal syncope: a triple-blind, multi-center, randomized controlled trial (COMFORTS-II)

Public title

COMpression stockings FOR Treating vasovagal Syncope (COMFORTS-II) trial

Purpose

Treatment

Inclusion/Exclusion criteria**Inclusion criteria:**

Patients with $18 \leq \text{age} \leq 65$ years Vasovagal syncope as the cause of transient loss of conscious confirmed by Clinical diagnosis And Calgary syncope system score (CSSS) ≥ 2 ≥ 2 episodes of VVS during the last year Capability of giving informed consent

Exclusion criteria:

Orthostatic hypotension (decrease in BP $\geq 20/10$ mmHg after 5-minute stand test) Postural tachycardia (increase in heart rate ≥ 30 bpm after 5-minute stand test) Carotid sinus hypersensitivity (ventricular pause >3 or decrease in BP > 50 mmHG after carotid sinus massage, performed in patients 40 years or older) History of Seizure Currently using medications for treatment of vasovagal syncope Cardiac rhythm disorders including ventricular tachycardia, long QT syndrome, Brugada syndrome, arrhythmogenic right ventricular cardiomyopathy, complete heart block, or any conduction abnormality on ECG Severe valvular heart disease Hypertrophic cardiomyopathy Cardiac systolic dysfunction (ejection fraction $\leq 40\%$) Obstructive coronary artery disease Cardiac implantable electronic devices Prior recommendation of compression stocking by a health-care provider, or other indication for compression stocking use Foot ulcers and diabetic foot Chronic venous insufficiency Renal failure stage ≥ 3 (eGFR <60 mL/min/1.73 m²) Presence of a chronic severe illness Pregnancy, or intention to become pregnant in the next year Unwillingness to participate or to provide informed consent

Age

From **18 years** old to **65 years** old

Gender

Both

Phase

N/A

Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser
- Data and Safety Monitoring Board

Sample size

Target sample size: **268**

Randomization (investigator's opinion)

Randomized

Randomization description

Eligible participants will be randomized 1:1 to two parallel treatment and control groups. The random sequence will be generated by computer software (R software, blockrand package) using permuted block randomization, in block sizes of 2, 4, 6, 8. To balance participant enrollment in each study recruitment site, randomization is stratified based on the trial sites. A separate randomization sequence will be generated for each study center (each stratum). Since seven centers will be participating in this study, seven sequences will be generated. Allocation of the random code will be centralized and conducted online through the study website (www.comfortstrial.com). Enrolling physicians will upload baseline data, informed consent confirmation, and the measured size of compression stockings, and after completion and confirmation of recruitment forms, the website will allocate a random code for the patient. A pair of compression stockings with the correct size and from the appropriate group (treatment or control) will then be posted to the patient from Tehran Heart Center. Allocation concealment is ensured since the recruiting physician and patients are blinded to the treatment group, randomization is web-based and centralized, and a random code would not be allocated until recruitment is confirmed.

Blinding (investigator's opinion)

Triple blinded

Blinding description

The compression stockings in treatment and control groups are identical in appearance and touch, and are made from the same material. The stocking will be provided to patients in identical unlabelled boxing. The only difference between compression stockings would be the pressure to the lower extremity. This is not expected to affect blinding, since eligible patients would not be using compression stocking before the trial and would not be familiar with the amount of pressure they experience. To assess blinding of patients during the study, participants will be asked to guess their randomly allocated treatment group at the last follow-up. The proportion of correct responses will be compared to the expected rate of random correct guesses (50%). Blinding will be achieved with centralized web-based randomization, and similarity in appearance of treatments. In addition to patients, the primary investigator, recruiting physicians, nurse researcher that gather baseline data, and outcome assessors will all be blinded to the randomly allocated group. Moreover, statisticians who will analyze the data for the final report in the manuscript will be blinded until finalization of results.

Placebo

Used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics Committees of Tehran Heart Center

Street address

Tehran Heart Center, Kargar st

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Tehran

Province

Tehran

Postal code

14117 13138

Approval date

2021-09-28, 1400/07/06

Ethics committee reference number

IR.TUMS.THC.REC.1400.047

Health conditions studied

1

Description of health condition studied

vasovagal syncope

ICD-10 code

R55

ICD-10 code description

Syncope and collapse

Primary outcomes

1

Description

Proportion of participants with recurrence of vasovagal syncope

Timepoint

Every three months until one year (three, six, nine, and twelve months after randomization)

Method of measurement

Telephone follow-up questionnaire

2

Description

Time to first syncopal episode

Timepoint

Every three months until one year (three, six, nine, and twelve months after randomization)

Method of measurement

Telephone follow-up questionnaire

Secondary outcomes

1

Description

Frequency of vasovagal syncopal episodes

Timepoint

Every three months until one year (three, six, nine, and twelve months after randomization)

Method of measurement

Telephone follow-up questionnaire

2

Description

Time intervals between recurrent vasovagal syncope episodes during follow-up

Timepoint

Every three months until one year (three, six, nine, and twelve months after randomization)

Method of measurement

Telephone follow-up questionnaire

3

Description

Incidence of any adverse effect after using compression stockings

Timepoint

Every three months until one year (three, six, nine, and twelve months after randomization)

Method of measurement

Telephone follow-up questionnaire

Intervention groups

1

Description

Intervention group: Compression stockings with 25-30mm Hg pressure for one year. The group will have compression stockings with 25-30 mm Hg pressure. All the participants' size for compression stocking will be measured at the first visit. Three points will be measured: below and above their knees and above their ankle. Subsequently, Right Arian Farmed Co (Tehran, Iran) will provide compression stockings for patients based on their sizes. Participants will be asked to use compression stockings as long as they could (ideal would be the majority of the time they are upright). In addition, a CD included some videos and booklets about instructions on how to wear CS (compression stocking) and how to keep them will be provided for the participants with their compression stockings

Category

Treatment - Other

2

Description

Control group: Compression stockings with up to 10 mm Hg pressure for one year. The group will have compression stockings with up to 10 mm Hg pressure. All the participants' size for compression stocking will be measured at the first visit. Three points will be

measured: below and above their knees and above their ankle. Subsequently, Right Arian Farmed Co (Tehran, Iran) will provide compression stockings for patients based on their sizes. Participants will be asked to use compression stockings as long as they could (ideal would be the majority of the time they are upright). In addition, a CD included some videos and booklets about instructions on how to wear CS (compression stocking) and how to keep them will be provided for the participants with their compression stockings.

Category

Treatment - Other

Recruitment centers

1

Recruitment center

Name of recruitment center

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Full name of responsible person

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2

Recruitment center

Name of recruitment center

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Full name of responsible person

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Recruitment center

Name of recruitment center

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Full name of responsible person

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Recruitment center

Name of recruitment center

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Recruitment center

Name of recruitment center

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Recruitment center

Name of recruitment center

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Full name of responsible person

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7**Recruitment center****Name of recruitment center**

Rasht Dr. Heshmat Educational & Remedial Center

Full name of responsible person

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

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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

Tehran University of Medical Sciences

Proportion provided by this source

10

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

2**Sponsor****Name of organization / entity**

Right Arian Farmed

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

Right Arian Farmed

Proportion provided by this source

90

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**

Industry

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

Tehran University of Medical Sciences

Full name of responsible person

Masih Tajdini

Position

Associate professor

Latest degree

Specialist

Other areas of specialty/work

Cardiology

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Person responsible for scientific inquiries

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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

Undecided - It is not yet known if there will be a plan to make this available

Statistical Analysis Plan

Undecided - It is not yet known if there will be a plan to make this available

Informed Consent Form

Undecided - It is not yet known if there will be a plan to make this available

Clinical Study Report

Undecided - It is not yet known if there will be 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

Undecided - It is not yet known if there will be a plan to make this available