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 ≤ age ≤ 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

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Iran (Islamic Republic of)

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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 ≤ age ≤ 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 ≥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 ≤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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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 with25-30 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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3

Recruitment center

Name of recruitment center
Rajaie Cardiovascular, Medical and Research Center

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Recruitment center

Name of recruitment center
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Full name of responsible person
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5

Recruitment center

Name of recruitment center
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Name of recruitment center
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Recruitment center
Name of recruitment center
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Sponsors / Funding sources

1

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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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+98 21 8871 0380
Email
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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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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