The Novel Use of Transcutaneous Electrical Nerve Stimulation in Patients with Angina and Non-Obstructive Coronary Arteries; a Pilot Study

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To evaluate the effect of transcutaneous electrical nerve stimulation (TENS) in patients with ANOCA on the change in the summary score of the Seattle Angina Questionnaire (SS SAQ) after 1 month treatment with TENS, compared to baseline.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON56491

Source
ToetsingOnline

Brief title
TENS ANOCA

Condition

- Coronary artery disorders

Synonym
Microvascular coronary artery disease. Angina with non-obstructive coronary arteries

Research involving
Human

Sponsors and support

Primary sponsor: Catharina-ziekenhuis

Source(s) of monetary or material Support: ZonMW;poject TopZorg

Intervention

Keyword: Angina and Non-Obstructive Coronary Arteries, ANOCA, TENS, Transcutaneous Electrical Nerve Stimulation

Outcome measures

Primary outcome

Change in the summary score of the Seattle Angina Questionnaire (SS SAQ) after

1 month treatment with TENS, compared to baseline.

Secondary outcome

Effect of TENS treatment in patients with ANOCA on:

- Individual domains of the Seattle Angina Questionnaire;

o Physical Limitations;

o Angina Frequency;

o Angina Stability;

o Treatment Satisfaction;

o Quality of Life.

- Grading of angina pectoris using the Canadian Cardiovascular Society (CCS)

class.

- Side effects of TENS use (such as skin irritation, tenderness and/or TENS

discomfort).

The secondary objectives will be evaluated after the patient has received one

month of TENS treatment.

Study description

Background summary

In patients with angina pectoris undergoing a coronary angiography (CAG) up to 40% do not have obstructive coronary artery disease (CAD) (1). The majority of patients with no obstructive CAD are women with a frequency of up to 70% compared to 50% in men (2) These patients are diagnosed as having angina and non-obstructive coronary arteries (ANOCA) (3). There are two endotypes of ANOCA. The first endotype is microvascular angina (MVA) caused by a combination of structural microcirculatory remodelling and functional arteriolar dysregulation, also called coronary microvascular dysfunction (CMD) (2). The second endotype is vasospastic angina (VSA) caused by epicardial coronary artery spasm that occurs when a hyper-reactive epicardial coronary segment is exposed to a vasoconstrictor stimulus (2). A subgroup of patients with ANOCA have both CMD and epicardial coronary artery spasm. Both endotypes of ANOCA are associated with significantly greater one-year risk of myocardial infarction (MI) and all-cause mortality (4), have a significantly impaired quality of life (5) and have a high health care resource utilisation (6).

The 2019 ESC Guidelines on the management of chronic coronary syndromes give a Class IIa (Level of evidence B) recommendation to perform guidewire-based coronary function testing (CFT), consisting of coronary flow reserve (CFR) and index of microcirculatory resistance (IMR) measurements, in patients with persisting symptoms and no obstructive CAD (7). The same guidelines give a Class IIa (Level of evidence B) recommendation to also perform intracoronary acetylcholine testing to assess the presence of coronary vasospasm in this patient population (7). By performing CFT a definitive diagnosis of ANOCA and the specific endotype can be made. MVA is diagnosed based on a fractional flow reserve (FFR) > 0.8, CFR <2.0 and IMR >= 25 (2). VSA is diagnosed based on FFR > 0.8, CFR >= 2.0, IMR < 25 and during acetylcholine testing a >= 90% diameter reduction, angina pectoris as well as ischaemic electrocardiographic (ECG) changes (2). The use of CFT followed by patient tailored treatment based on CFT findings has been shown to improve angina severity in patients with ANOCA (8).

The current treatment for ANOCA consists of three aspects. The first aspect is managing lifestyle factors such as weight management, smoking cessation and exercise. The second aspect is managing known cardiovascular risk factors such as hypertension, dyslipidaemia and diabetes mellitus. And the third aspect is antianginal medication. In both endotypes ACE inhibitors or angiotensin II receptor blockers should be considered. In MVA the antianginal medication that can be used are betablocker, calcium channel blocker, nicorandil, ranolazine, ivabradine and/or trimetazidine (2). In VSA calcium channel blocker, long-acting nitrate and/or nicorandil can be initiated as antianginal therapy (2). Despite these treatment option approximately 25% of ANOCA patients have refractory angina symptoms (2).

As stated in the 2020 consensus statement of the ESC on ischaemia with Non-Obstructive Coronary Arteries (INOCA) there is a lack of in-depth knowledge with further research urgently needed to develop innovative therapies to better manage this serious condition (2). A possible treatment modality for ANOCA patients with persisting symptoms is spinal cord stimulation (SCS) or transcutaneous electrical nerve stimulation (TENS) as mentioned in the Dutch NVVC guideline on ANOCA (9-11). Previous research has shown that SCS improves the time until angina and ischaemia, leads to significantly less angina pectoris episodes and also leads to a significant improvement in quality of life (12-15). An important side note is that the afore mentioned studies were performed during the 90s in patients with coronary syndrome X. Coronary syndrome X was defined as patients with typical exercise-induced angina, positive exercise testing and normal coronary arteries. This is most likely a more heterogeneous group of patients than the contemporary ANOCA patients as invasive CFT was not yet available at the time these studies were performed. However these findings do suggest that SCS and/or TENS could be a possible treatment modality for patients with ANOCA. The aim of this pilot study is to investigate whether treatment with TENS during a one month period leads to a significant reduction of angina pectoris and therefore a significant improvement in quality of life in patients with proven ANOCA, encompassing the VSA endotype.

Study objective

To evaluate the effect of transcutaneous electrical nerve stimulation (TENS) in patients with ANOCA on the change in the summary score of the Seattle Angina Questionnaire (SS SAQ) after 1 month treatment with TENS, compared to baseline.

Study design

Prospective, single-arm, open label, single center pilot study

Intervention

All patients who participate in this study will receive TENS for a duration of 4 weeks.

Study burden and risks

Patients who are asked to participate in this pilot study will receive TENS during a one month period. TENS is a treatment modality that has been broadly applied in patient with chronic pain syndromes. A recent meta-analysis has shown that no serious adverse events are associated with use of TENS and adverse events that occurred were skin irritation, tenderness and TENS discomfort which occurred infrequently (18). In addition TENS has been described as a possible treatment modality for ANOCA patients in the recent

Dutch NVVC Guidelines on ANOCA, but with the side notes that results up to date differ (11). This shows that TENS could be an effective and safe treatment modality in a group of ANOCA patients who have persistent and disabling angina pectoris despite OMT, but additional research is required. The risks of this study are small and the possible benefits for the patient could be large with a reduction of symptoms and an improvement in quality of life. Furthermore there are no other treatment modalities currently available for this patient population. In conclusion this TENS pilot study is safe, with a low risk and large benefit for the patient.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Angina and no obstructive coronary artery disease (ANOCA) (CCS class III or

IV)
o Vasospastic angina (VSA): FFR > 0.8, CFR >= 2.0, IMR < 25 and during acetylcholine testing: >=
90% diameter reduction, Angina pectoris & Ischaemic ECG changes.
- Persisting angina pectoris despite optimal medical therapy (OMT) defined as:
o VSA: Calcium channel blocker, long-acting nitrate and/or nicorandil.
In the maximum tolerated dose. If the patient is currently not using one of the medications due to side-effects, this should be clearly stated.
- Age > 18 years

Exclusion criteria

- Both endotypes (VSA and MVA) present based on CFT findings.
- Inability to give informed consent
- The presence of a cardiac implanted electronic device (CIED)
o Pacemaker
o Implantable Cardiac Defibrillator (ICD)
Due to the risk of interference between TENS and CIED
- Presence of a spinal cord stimulator for another indication such as complex regional pain syndrome, failed back surgery syndrome, etc.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	13-03-2024
Enrollment:	20
Type:	Actual

Medical products/devices used

Generic name:	TENS eco 2
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	25-01-2024
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-11-2024
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL84910.100.23