AV-Node Stimulation to influence heart failure markers in Acutely Decompensated Heart Failure patients

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The purpose of the research trial is to assess if heart failure markers and clinical end-points are influenced by 24 hours of AV-node stimulation (AVNS) in acutely decompensated heart failure (ADHF) patients.Primary Objective(s)The primary objective...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON45274

Source
ToetsingOnline

Brief title
AVNS-ADHF

Condition

- Heart failures

Synonym
acutely decompensated heart failure, heart failure

Research involving
Human

Sponsors and support

Primary sponsor: Medtronic B.V.
Source(s) of monetary or material Support: Medtronic Bakken Research Center (BRC);CRHF Research & Technology

Intervention

Keyword: - acutely decompensated heart failure, - AV-node stimulation, - parasympathetic nerves, - vagal branch stimulation

Outcome measures

Primary outcome

Measurement of NT-proBNP plasma concentration will be performed by using a venous sample extracted 5 minutes before time 0 and after 24 hours from time 0 in both groups. This is a marker of heart failure.

Secondary outcome

- Local norepinephrine

Norepinephrine is a marker of autonomic balance. For each patient in the AVNS treatment group, local norepinephrine and epinephrine measurement will be performed immediately before starting the AVNS treatment (- 5 minutes) and after 30 minutes from the beginning of AVNS treatment by means of coronary arterial blood samples.

- Inflammatory status

Measurements of inflammatory markers TNF-alfa, IL-6 that will be performed by using a venous sample extracted 5 minutes before time 0 (see definition at primary objective) and at 1, 6 and 24 hours after time 0 in both groups.

- Preventing heart failure deterioration

Measurements of heart failure markers, Troponin-T and NT-proBNP that will be performed by using a venous sample extracted 5 minutes before time 0 (see

definition at primary objective) and at 1, 6 and 24 hours after time 0 in both groups.

- Kidney function

Kidney function is a marker of heart failure. Measurements of kidney function markers, aldosterone and renin will be performed by using venous samples extracted 5 minutes before time 0 (see definition at primary objective) and at 1, 6 and 24 hours after time 0 in both groups. Measurement of diuresis (ml/24 hours) per 40 mg furosemide at 24 hours will be also performed in both groups.

- Safety of the AVNS procedure

a. Safety evaluation in term of percentage and rate of adverse events and serious adverse events related to AVNS and related to atrial lead placement at AVNS position at implant and at the follow-up;

b. Number of episodes and burden of atrial tachycardia(AT), atrial fibrillation(AF), ventricular tachycardia (VT) and ventricular fibrillation (VF) in both the AVNS and the control group for 24 hours after time 0;

c. Description of ADHF symptoms in term of percentage of patients reporting specific symptoms in both groups for 24 hours after time 0.

- Data gathering for further possible applications of AVNS

Evaluation of possible further applications of AVNS

a. The performance of AVNS in decreasing mean VR and its standard deviation over 24 hours compared to control group as monitored with the EPTracer system

for 24 hours from time 0 (see definition at primary objective);

b. Mean cardiac output (CO) as derived from arterial finger blood pressure

in both the AVNS and the control group as a measure of heart failure

deterioration. Specifically, for each patient in both the AVNS and the control

group, CO will be measured 5 minutes before time 0, and at 1, 6 and 24 hours

after time 0;

c. To assess autonomic balance, heart rate variability measurements

(assessed only during sinus rhythm) in both groups determined by using the ECG

signal stored within the 24 hours of monitoring time period;

d. Medication therapy used in the treatment and in the control groups for 24

hours after time 0;

e. Rate of heart failure hospitalizations and mortality in AVNS and control

group reported at 6th months follow-up.

Study description

Background summary

The overall prognosis of heart failure (HF) patients remains poor despite advances made in the treatment of heart failure with drugs, implantable cardioverter defibrillators and cardiac resynchronization devices. Increased sympathetic tone and reduced parasympathetic tone contribute to the progression of heart failure by affecting arrhythmia occurrence and remodeling. An increased parasympathetic tone by vagal stimulation might limit cardiac remodeling by affecting the release of anti-inflammatory compounds and maintaining connexin-43 activity. Also, an increased parasympathetic tone might limit arrhythmia occurrence as found in various animal models, by inducing bradycardia, increasing the refractory period, bringing the restitution slope lower than 1, affecting nitric oxide release and acetylcholine release. Importantly, an increased parasympathetic output affects sympathetic output via remodeling of the stellate ganglia neurons and might affect sympathetic output of the cardiac plexus, since both systems are connected at this location.

Sympathetic activation in return increases the vasoconstrictor tone, accompanied by activation of the renin-angiotensin-aldosteron-system (RAAS) and the endothelin 1 and vasopressin system, which may be responsible for peripheral organ dysfunction and damage in the setting of congestive HF.

The autonomic disbalance is more profound in acute decompensated than in chronic heart failure. Furthermore, vagal withdrawal has been shown to precede acute decompensation. Thus, it is expected that affecting autonomic balance might be more beneficial in acutely decompensated than in chronic heart failure for example by preventing peripheral organ dysfunction. In addition to the mechanisms mentioned above for heart failure in general, it was recently hypothesized that in acute decompensated heart failure an endogenous fluid shift from the splanchnic bed is triggered by an increase in sympathetic tone causing vasoconstriction in the splanchnic bed, a mechanism that can translocate blood rapidly into the effective circulating volume, generating the raised venous pressure and congestion seen in ADHF. Episodes of autonomic disbalance for example due to hypoxia or increased chemosensitivity might affect the endogenous fluid shift. Potentially, by increasing parasympathetic output of the heart, the endogenous fluid shift can be prevented via decreasing sympathetic output of the heart via the stellate ganglion and cardiac plexus.

An approach to influence the autonomic balance has been studied in various animal models and recently in chronic heart failure patients by promoting parasympathetic activity using a vagal cuff (VNS). Recently a multicenter open-label phase II safety and feasibility study was reported using the system of Biocontrol (Cardiofit). Results with respect to left ventricular ejection fraction (LVEF), NYHA class, Quality of Life and 6 minute walk distance were favorable in 32 patients after 6 months. However, beneficial effects were accompanied by serious adverse events. In the ANTHEM-HF study 25 patients were implanted at the left or right vagal nerve. After 12 months, LVEF, NYHA class, non-sustained VT, heart rate variability and T-wave alternans were significantly reduced. Although some outcome measures exhibited a trend toward higher efficacy with right-sided stimulation, implant side did not appear to be a statistically significant factor. Note that in the ANTHEM-HF study a frequency of 10Hz was used and in the Biocontrol study a frequency of only 1-2 pulses. Based on previous experience with AVNS the value of 50Hz is considered optimal. In addition, the NECTAR-HF study of Boston Scientific evaluated VNS using a cuff approach with a much lower voltage than in the Biocontrol study and reported no effect on LVEF, although an effect was found on Quality of Life measures.The disadvantage of the vagal cuff approach is that it is invasive and might result in adverse events such as infection leading to nerve damage. In addition it requires the implantation of a separate system in cardiac patients.

The action of vagal stimulation is not necessarily directly on the heart, i.e. via the efferent system but could also be via the afferent system. This was postulated by Dr. Rossi et al. who found an effect of epicardial ganglionated plexus stimulation on the post-operative inflammatory response in coronary

artery bypass grafting (CABG) patients. Furthermore, an effect of low-level transcutaneous electrical vagal tragus stimulation on atrial fibrillation and cytokines was found in dogs. This means that it may not be necessarily the trunk that needs to be stimulated but that it might be sufficient to stimulate a vagal cardiac branch/plexus to obtain an effect on systemic parameters like autonomic balance reflected in cathecholamines and inflammation markers. Both could potentially influence remodeling. A vagal branch could be reached by stimulating the parasympathetic nerves affecting the AV-node intra-cardially using a standard atrial lead. Besides affecting heart failure via an effect on autonomic balance and inflammation, this could also affect the VR during AT/AF. Patients with acutely decompensated heart failure often have AT/AF, which worsens the heart failure.

The advantage of such an intra-cardiac therapy would be that it could be combined with a pacemaker/ICD device and no extra risk or costs are introduced. The ultimate aim would be to prevent acutely decompensated heart failure periods by stimulating an intra-cardiac vagal branch. Such a study will require long term follow-up of heart failure patients and dedicated software. As a first step, an acute study will be performed in acutely decompensated heart failure patients, in which such a therapy might be a last resort. In this population the effect on surrogate end-points like heart failure markers, catecholamines, inflammation markers, kidney parameters, heart rate variability, arrhythmias and ventricular rate will be assessed. Since no good therapies are available for acutely decompensated heart failure, it is expected that AV-node stimulation (AVNS) might also appear to be a valuable temporary therapy for patients who enter the hospital with acutely decompensated heart failure. The acute therapy might help to prevent organ damage. In this way potentially hospitalizations and mortality can be decreased.

AVNS will be performed for 24 hours, since after 24 hours an effect was found with medication on our primary objective NT-proBNP (see sample size calculation). In addition, a statistically significant effect was found after 3 hours of AVNS on inflammation markers. Additional literature review, pre-clinical testing and previous clinical experience will be reported in the Investigator*s Brochure (IB).

Study objective

The purpose of the research trial is to assess if heart failure markers and clinical end-points are influenced by 24 hours of AV-node stimulation (AVNS) in acutely decompensated heart failure (ADHF) patients.

Primary Objective(s)
The primary objective is to demonstrate that the AVNS treatment together with the standard drug therapy for acutely decompensated heart failure (ADHF) patients is able to maintain the level of amino-terminal fragment of the B-type natriuretic peptide prohormone (NT-proBNP) plasma concentration significantly

lower than the standard drug therapy alone 24 hours after time 0. Time 0 is set for both groups around 9:00 ± 1 hour in the morning the day after the patient has been hospitalized to eliminate the effect of circadian variation in blood markers on the difference between groups. For AVNS patients AVNS will start at time 0.

Secondary Objectives

Local norepinephrine
To evaluate the performance of AVNS in affecting autonomic balance as assessed by coronary sinus sampled norepinephrine and epinephrine measurements within the patient during intra-operative stimulation testing.

Inflammatory status
To evaluate the performance of AVNS in affecting inflammatory status as assessed by measurements of Interleukin (IL)-6, tumor necrosis factor (TNF)-alfa in the treatment group compared to the control group over 24 hours.

Preventing heart failure deterioration
To evaluate the performance of AVNS in preventing heart failure deterioration as assessed by measurements of Troponin T and amino-terminal fragment of the B-type natriuretic peptide prohormone (NT-proBNP) level in the treatment group compared to the control group over 24 hours.

Kidney function
To evaluate the performance of AVNS in affecting kidney function as assessed by measurements of aldosterone and renin concentration as well as by diuretic response in the treatment group compared to the control group over 24 hours.

Safety of the AVNS procedure
To evaluate the safety of the investigational procedure by assessing:
a. Adverse events and serious adverse events related to AVNS and Adverse events related to selective atrial lead placement at implant and in the follow-up period in both study phases, training and AVNS;
b. Burden of arrhythmias for 24 hours after time 0 in the AVNS phase;
c. ADHF symptoms in the AVNS phase for 24 hours after time 0.

Data gathering for further possible applications of AVNS
To gather data for further possible applications of AVNS:
a. The performance of AVNS in decreasing mean ventricular rate VR and its standard deviation over
during first 24 hours after time 0;
b. The effect of AVNS on cardiac output (CO) change derived from arterial finger pressure over 24 hours after time 0 compared to the control group
c. The effect of AVNS on heart rate variability (HRV) during the during first 24 hours after time 0 compared to the control group;
d. Medication therapy of the treatment group compared to the control group

during during first 24 hours after time 0;
e. The effect of the 24 hour AVNS therapy on heart failure hospitalizations and mortality after 6 months follow-up.

Study design

The study is designed in two phases called training and AVNS phase respectively. Patients will take part in the training or AVNS phase but not in both. Patients of both phases, training and AVNS, satisfying all inclusion criteria and none of the exclusion criteria for the respective phase are eligible for this study. This will be a multi-center trial.
The training phase will allow investigators without a documented experience in positioning the atrial lead at the specific AVNS septal position to be trained on atrial lead placement. All patients that are candidates for a dual chamber cardiac device implantation (IPG, ICD, CRT cardiac devices) in accordance with the current guideline are eligible to be enrolled in the training phase. The expected length of time that a patient will be in the training phase is in total about 2-6 weeks, consisting of the acute procedure phase of 1 hour (training) and a follow-up 4 weeks (± 2 weeks) after implantation.
The second phase, the so-called AVNS phase, will consider exclusively patients in ADHF. Only patients of AVNS phase will be randomized.
The expected length of time a patient will be in the study is in total about 6 months, consisting of the acute procedure phase of 24 hours, a first follow-up 1 month (± 2 weeks) after hospital discharge and a final follow-up at 6 months (± 2 weeks) after hospital discharge. The expected time of participation in the clinical study for the clinical center is 30 months.

Intervention

Training phase procedure
In the training phase the procedure will coincide with a cardiac device implantation. Subjects will undergo a standard implant procedure with the exception of atrial lead placement, which will be placed at the AVNS position. The atrial lead implant time will be limited to an hour. If not successful within an hour the lead will be placed at a standard position.

AVNS phase procedure
The procedure visit will start as close as practical to 9:00 AM ± 1 hour in the morning (before time 0, see definition in Appendix L.4). Before the procedure visit, patients will be randomly assigned to either AVNS or to the control group. Both groups will continue receiving the standard treatment as recommended in the current guideline to manage heart failure patient. In addition to the standard treatment, AVNS patients will receive the AVNS treatment for 24 hours. To do so, an atrial lead will be implanted. The maximum lead implant time will be limited to one hour.

Study burden and risks

Potential Risks

It is anticipated that subjects enrolled in this study in the training group or AVNS treatment group will be exposed to the same risks associated to being implanted with an atrial lead during pacemaker implantation. Only those potential adjunctive risks associated to the participation to this study are listed in this section and include, but are not limited to the following procedures:

Training group.
The atrial lead is placed at a non-conventional position. In a previous study lead dislodgement during the follow-up period of half a year occurred in 2/32 cases, i.e. 6%. This was not significantly different from the amount of dislodgements at a standard position. One dislodgement occurred within the first 24 hours;
Mitigation: after implant, within 24 hours after implant, and before hospital discharge and at the 1 month follow-up visit a pacing tests will be performed to test atrial lead dislodgement, which is common clinical practice.

AVNS and training group
- Delivery of AVNS in the absence of AT or AF may result in atrial arrhythmia.
Mitigation: It was found in animal studies that low voltage stimulation of the vagal nerve is anti-arrhythmic in the atrium [32], [33], [9]. However, these studies concern one aspect of our stimulation which is vagal nerve stimulation. It can not be excluded that simultaneous stimulation of the atrial myocard at low voltages during sinus rhythm is enhancing AT/AF inducibility. Therefore, during sinus rhythm the bursts will be synchronized on the P-wave and will not induce atrial arrhythmias. In case the sinus rhythm converts to AT/AF the physician will manually reset the burst trigger so that it will be triggered on the QRS and burst stimulation is still given once per cardiac cycle. Another scenario could be that the atrial arrhythmia stops and triggering is still on the QRS. In that case an alarm (hospital equipment intensive care unit) will notify the physician or nurse to reset the triggering on the P-wave. Even if during sinus rhythm, the triggering is for a short period on the QRS the re-induction of AT/AF is not expected, with a negative capture test at 10.5 V, but cannot be excluded.

- There is a remote possibility that the AVNS burst pacing induces a ventricular arrhythmia.
Mitigation: During AT/AF the AVNS burst pacing is triggered on the QRS and there is little chance to induce ventricular arrythmias. During sinus rhythm, a high output during the AVNS bursting synchronized on the P-wave, imposes a risk for the occurrence of ventricular arrhythmia. The tests deliveCONSENTred at baseline with high output (10.5V) ensure that ventricular capture does not

occur during atrial burst pacing equal or below 4V. In addition, defibrillation patches will be placed on the patient to potentially defibrillate in the unlikely event (0.1-1%) a ventricular arrhythmia occurs.

- In the presence of AT/AF, AVNS is programmed to be triggered on the QRS and ventricular oversensing may result in inappropriate deployment of AVNS therapy outside the ventricular refractory period and may induce a ventricular arrhythmia.
Mitigation: First appropriate ventricular sensing will be checked. The Cardiotek device uses filters (see Cardiotek manuals) to correct for strong movements of the patient and artifacts on the ECG. In case of ECG dislodgement there will be no signal and no triggering. As a safety measure a refractory period to prevent a too high frequency of activation will be programmed.

- The AVNS burst pacing could cause the VR to slow to an inappropriate rate.
Mitigation: During the implant the voltage will be titrated so that the VR will not drop below 50 bpm due to AVNS. In case of changing during 24 hoursaddition, the monitoring system of the ICU will alarm if rates below 50 bpm occur. In that case the voltage will be adapted.

- AVNS at 4Volt may give symptoms to the patient.
Mitigation: In case of symptoms the voltage will be lowered to a level which is not causing symptoms for the patient. Note that in a previous AVNS study, in some patients symptoms were noted like muscular and chest pain at 8V, but none at 6V [24]. In this study an amplitude of 4V or lower will be used.

- Placing the lead will subject the patient in the AVNS and training group to X-ray radiation.
Mitigation: In the AVNS group the X-ray exposure and time is not expected to exceed the rontgen exposure and time during a conventional CRT implant and is therefore considered acceptable.
In the training group additional X-ray radiation is expected since the atrial lead positioning might take longer. To prevent too much radiation the atrial lead placement procedure is limited to one hour.
- Standard adverse events associated with leads of CRT, ICD devices and their implantation.
Mitigation: Risks normally associated with leads of CRT, ICD devices and their implantation will be minimized by selecting investigators who are experienced in the diagnosis and treatment of patients with HF patients as well as with tachy and brady arrhythmia management and in the implantation of the cardiac devices.

AVNS and control group
- During the AVNS study blood samples from the venous system are taken and might lead to bruising.
Mitigation: experienced hospital staff will take the venous samples. The venous

line will be standard of care, but may cause bruising in 1-10% of the cases.

AVNS group
- During the AVNS study, the atrial lead may become dislodged and may induce arrhythmia.
Mitigation: Electrical characteristics (impedance, threshold, sensing, FFRW)) of the atrial lead will be assessed directly after implant before stimulation and at 1, 6, and 24 hours after the start of stimulation to confirm adequate lead positioning. In case lead positioning is not adequate after the implant procedure the lead will be removed. In a previous study in which 32 patients obtained a chronic AVNS lead it was found that in one patient an atrial lead dislodgement occurred in the first 48 hours. Thus, in the 2 days after lead implantation there is a small risk (3%) that the lead becomes dislodged.

In the case of dislodgement of atrial lead into ventricle:
During AF/AT:
If the burst triggering signal is still set to atrial events: since the lead senses in case of dislodgement not the atrial senses, but possibly the ventricular events, it might stimulate the ventricle (during its refractory period). If the burst triggering signal is already set to ventricular events (via ECG): the burst train is short enough to be completed within the ventricular refractory period and will not cause ventricular arrhythmias. Our animal study provided no evidence of ventricular pro-arrhythmia due to delivery of AVNS burst pulses in the ventricles, as long as the pulse train was within 200ms after the QRS. In patients, the lowest 95% CI of ventricular refractory period over 24 hours was found to be between 269 and 283 ms. Since it will be delivered in burst trains within 170 ms it is assumed that the risk to induce a ventricular arrhythmia in this case is small. In our previous chronic AVNS study with 32 patients no ventricular arrhythmias were found to be induced shortly after the start of AVNS, synchronized on the QRS if stimulating with 8V, 1.5 ms.

During Sinus Rhythm:
In the event that during sinus rhythm the lead would dislodge into the ventricle, AVNS therapy would be synchronized on the signal sensed by the lead, this means on the QRS instead of the P-wave. The burst train is short enough to be completed within the ventricular refractory period and will not cause ventricular arrhythmias., which was the intention of the programming. However, in the unlikely event that the dislodgement occurs during a burst it is possible that the stimulation is triggered on P-wave and stimulates the ventricle. The first stimulus will then stimulate the ventricle and make it for the rest of the stimuli refractory. This may also happen in the unlikely case the lead is dislodged in the atrium and is close to tricuspid valve. The patient will be continuously monitored on the intensive care. In the unlikely event (0.1-1%) of the occurrence of a VT/VF the patient can be defibrillated with the equipment available at the bed of the patient.
In summary, even if not anticipated, risks related to the above described

procedures may include the induction or prolongation of atrial tachycardia or AFfibrillation, and the induction of ventricular tachycardia or fibrillation.
This study has been designed to minimize these risks.
Subjects will be compensated in the event of injury arising from participation in the clinical investigations. Arrangements for additional health care for subjects required as a result of an adverse device effect shall be made and documented in the investigator site file.
Potential Benefits

The potential clinical benefit for patients in the AVNS therapy arm could be that there is a decrease in heart failure deterioration as indicated by ejection fraction and blood markers. Furthermore, the effect of fast conducted atrial fibrillation on ventricular rateVR will might be eliminated. Patients in the control group will be monitored more closely during the study procedure/ visits than standard medical care. The potential benefit for subjects in the training phase could be that their lead is located in the AVNS position, allowing the use of a potential future download to reduce the ventricular rate during fastly conducted AT/AF to prevent inappropriate shocks or preventing heart failure worsening. Moreover, results of two prospective randomized studies indicate that septal pacing, when compared to the traditional right atrial appendage pacing, significantly reduces : (1) paroxysmal AF recurrences and burden; and (2) progression to chronic AF. However, this benefit was not seen in another study.

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

Inclusion criteria of training phase;Patients are eligible to be enrolled for the lead placement training procedure if one of the following criteria is met:
1) Indication for CRT implant according to current guidelines (Heart Failure, NYHA III-IV class, symptomatic despite optimal stable medical therapy, left ventricular (LV) ejection fraction <=35% and QRS>120ms);
2) Indication for ICD implant according to current guidelines;
3) Indication for pacemaker implant according to current guidelines.;Inclusion criteria of AVNS phase;1) Acutely decompensated HF as indicated by one of the symptoms such as
- shortness of breath (dyspnea)
- oedema (verified by chest X-ray) accompanied by severe respiratory distress, with crackles over the lungs and orthopnea, with Oxygen (O2) saturation usually < 90% on room air prior to treatment;
2) NYHA class III or IV at enrollment;
3) Age > 18 years;
4) Subject provides informed consent;
5) Subject is willing and able to comply with the study procedures;
6) Hospitalization for acute decompensated HF did start within the last 24 hours.

Exclusion criteria

Exclusion criteria for training phase;1) Advanced AV block (II-III degree AV block);
2) Potential damage to cardiac nerves involved due to one of the following
- ablation;
- valvular surgery;
- cardiac transplantation;
- aortic surgery;
3) Age < 18 years;
4) Patient not disposed to sign the Informed Consent;
5) Subject is a pregnant woman or woman of childbearing potential not on adequate birth control: only woman with a highly effective method of contraception [oral contraception or intra-uterine device] or sterile woman can be enrolled.

6) Subject is a breastfeeding woman;
7) Participation in other studies which could potentially conflict with this study;
8) Legal incapacity or evidence that a subject cannot understand the purpose and risks of the study or inability to comply fully with study procedures and follow up.;Exclusion criteria for AVNS phase;1) Patients in cardiogenic shock. Cardiogenic shock is usually characterized by reduced blood pressure (BP) (< 90 mmHg) or a drop of mean arterial pressure > 30 mmHg and/or low urine output < 0.05 ml/kg/h with a pulse rate > 60 beats per minute (bpm) with or without evidence of organ congestion;
2) Heart rate below 50 bpm during sleep at night time and 60 bpm at day time;
3) Patient already implanted with a pacemaker or implantable cardioverter defibrillator;
4) Patient already implanted with a neurostimulation device;
5) Myocardial infarction, as defined by clinical symptoms and an increased cardiac Troponin T or I with a significant dynamic increment in 2 subsequent measurements [1], which occurred in the last 30 days, causing heart failure (an increased value for cardiac troponin is defined as a measurement exceeding the 99th percentile of a normal reference population [URL = upper reference limit]);
6) Heart failure due to congenital disease;
7) Hypertrophic obstructive cardiomyopathy;
8) Infiltrative cardiomyopathy;
9) Vasovagal syncope;
10) Advanced AV block (II-III degree AV block);
11) Congenital or acquired long QT syndrome;
12) Potential damage to cardiac nerves involved due to one of the following
- ablation;
- valvular surgery;
- cardiac transplantation;
- aortic surgery;
13) Subject is a pregnant woman or woman of childbearing potential not on adequate birth control: only woman with a highly effective method of contraception [oral contraception or intra-uterine device] or sterile woman can be enrolled.
14) Subject is a breastfeeding woman;
15) Participation in other studies which could potentially conflict with this study;
16) Diabetes mellitus with measured hemoglobin A1c > 8% in the past 60 days;
17) Untreated hypo- or hyperthyroidism;
18) Legal incapacity or evidence that a subject cannot understand the purpose and risks of the study or inability to comply fully with study procedures and follow up.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	50
Type:	Anticipated

Medical products/devices used

Generic name:	Medtronic SelectSecure 3830;CapSureFix Novus 4076 Atrial Leads;Cardiotek model EPTracer38;The Oscor®
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	30-07-2018
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)

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	NL60734.075.17