Renal Sympathetic Denervation in patients with therapy-resistant Catecholamine Polymorphic Ventricular Tachycardia (CPVT) and Long QT Syndrome (LQTS) * RESIDENT Study

Published: 24-04-2014
Last updated: 20-04-2024

To perform a percutaneous renal sympathetic denervation in a cohort of 20 patients with therapy resistant CPVT and LQTS patients and to objectify and evaluate the benefit of this novel treatment for this group of patients.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Cardiac arrhythmias
Study type	Interventional

Summary

ID

NL-OMON41010

Source
ToetsingOnline

Brief title
RESIDENT Study

Condition

- Cardiac arrhythmias

Synonym
irregular heartbeat, ventricular arrhythmia

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: CPVT, LQTS, Renal denervation

Outcome measures

Primary outcome

Primary endpoint in this study will be cardiac events after renal denervation,

defined as:

(1) an appropriate ICD shock, defined as an ICD shock on ventricular

fibrillation or ventricular tachycardia

(2) arrhythmic syncope, seizures, or aborted cardiac arrest(3) number of ventricular extra systoles (VES) in CPVT patients

(3) malignant non-sustained VT (NSVT)

Secondary outcome

n.a.

Study description

Background summary

Primary inherited arrhythmia syndromes, such as long QT syndrome (LQTS) and catecholaminergic polymorphic ventricular tachycardia (CPVT), are genetic cardiac diseases without apparent structural heart disease that may cause cardiac syncope and sudden cardiac death in mainly young individuals. These cardiac events are mainly induced by physical- or emotional stress, i.e. adrenergic, triggers. Hence, *-blockers are considered first line therapy in symptomatic and asymptomatic patients in both conditions.In addition, an implantable cardiac defibrillator (ICD) is often used in patients who continue to have ventricular arrhythmias despite *-blocker therapy.5, 6 However, ICDs do not prevent ventricular arrhythmias and can even trigger catecholamine release,

subsequently resulting in arrhythmic storms and even death.7 Also the cost of frequent shocks in terms of pain and fear is substantial8 and young patients with ICDs are more likely to experience device complications over many years of use, including inappropriate shocks and lead-related complications9.
In 1971 Moss and McDonald10 described left cardiac sympathetic denervation (LCSD), which prevents norepinephrine release in the heart and therefore raising the threshold for ventricular fibrillation without reducing the heart rate or impairing myocardial contractility.11 In the last decade LCSD received renewed attention as a viable alternative treatment for therapy resistant LQTS and CPVT patients. Although a significant protective effect of LCSD was demonstrated in both symptomatic and asymptomatic LQTS and CPVT patients12-16, arrhythmias do not completely resolve in a significant proportion of the patients. Therefore, an additional therapy would be expedient wherein further attenuation of sympathetic drive is performed.
Catheter-based radiofrequency ablation of the renal sympathetic nerves is a novel minimally invasive procedure which lowers blood pressure in patients with resistant hypertension.17-20 This procedure was tested in the Symplicity-HTN-2 trial of 106 patients with resistant hypertension despite treatment with an average of five antihypertensive medications including a diuretic.18 The patients were randomly assigned to renal sympathetic denervation or maintenance of previous medical therapy. At six months, radiofrequency ablation significantly decreased the office blood pressure from 178/97 to 143/85 mmHg compared with no decrease in blood pressure in patients maintained on baseline antihypertensive therapy. In addition, a systolic pressure of less than 140 mmHg was attained significantly more often with radiofrequency ablation (39 versus 6 percent). There was no significant difference between the groups in kidney function and no serious adverse events were reported.
With the therapeutic effects of LCSD in mind, the sympathicolytical effect of catheter-based percutaneous renal denervation might further promote a reduction in cardiac arrhythmic events in LQTS and CPVT patients. Preliminary, unpublished, data from a reliable CPVT mouse model provide very promising results. The same mouse model, i.e. the CASQ2 homozygous knockout, was used to demonstrate the efficacy of flecainide, (Watanabe et al. NatMed 2009) a therapy that is now widely used in patients in whom B-blockade provide not sufficient protection (van der Werf 2011). Renal Denervation (RDN) seem to provide full protection in this model for the exercise-induced arrhythmias, whereas, as one would expect, isoproterenol-induced arrhythmias are unaffected. These observed positive experimental data bare the hope that this innovative technique might extend the currently very limited armory against this group of patients and its hereforementioned substantial risks.

Study objective

To perform a percutaneous renal sympathetic denervation in a cohort of 20 patients with therapy resistant CPVT and LQTS patients and to objectify and evaluate the benefit of this novel treatment for this group of patients.

Study design

Single-armed clinical intervention cohort study.

Intervention

Patients will be treated by renal sympathetic nerve denervation using RF energy applied with a balloon catheter. The
treatment takes 30-60 seconds (depending on the length of the renal artery) and will be applied in both renal arteries

Study burden and risks

With any interventional procedure, there are possible risks and complications. It is believed that the risks associated with
the use of the V2 Catheter are similar to other angioplasty devices.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Inclusion Criteria
1. Subjects who have provided written informed consent;
2. Subjects who are * 18 years of age;
3. Subjects who in the last year have had at least 1 event related to therapy refractory CPVT or LQTS
4. Subjects with a eGFR * 45 ml/min per 1.73m2;
5. Subjects who are willing and able to comply with all study procedures. ;Anatomical Inclusion Criteria
1. Subjects with or without an accessory renal artery who have a main renal artery diameter of * 3.5 mm and * 7.0 mm for each of their kidneys
2. Subjects who have a main renal artery without significant stenosis (defined as < 30%)
3. Subjects who have a renal artery length of * 15 mm.

Exclusion criteria

1. Subjects who are contraindicated for intravascular contrast material;
2. Subjects who are contraindicated for anticoagulation medications (heparin, aspirin, Angiomax, etc.), analgesic medications (morphine, fentanyl, etc.), anxiolytic medications (alprazolam, lorazepam, diazepam, etc.) or other medications required for an interventional procedure;
3. Subjects with known bleeding or hyper-coagulation disorders;
4. Subjects who have type 1 diabetes mellitus;
5. Subjects who have experienced a myocardial infarction, unstable angina pectoris, uncompensated heart failure, or a cerebrovascular accident within six (6) months prior to the screening visit, or have widespread atherosclerosis, with documented intravascular thrombosis or unstable plaques;
6. Subjects who have planned percutaneous vascular or surgical intervention for any reason within the next six (6) months;
7. Subjects who have hemodynamically significant valvular heart disease for which reduction of blood pressure would be considered hazardous;
8. Subjects who have any serious medical condition, which in the opinion of the investigator, may adversely affect patient safety or the efficacy of the procedure in the study (i.e., patients with clinically significant peripheral vascular disease, abdominal aortic aneurysm, bleeding disorders);
9. Female participants of childbearing potential must have a negative serum or urine human chorionic gonadotropin (hCG) pregnancy test prior to the procedure;
10. Subjects who have a known, unresolved history of drug use or alcohol abuse/dependency;
11. Subjects who are currently enrolled in any investigational study wherein patient

participation has not been completed;
12. Subjects who, for any reason, may not be able to understand or comply with instructions.
;Anatomical Exclusion Criteria
1. Subjects with only one kidney;
2. Subjects with prior renal denervation procedure;
3. Subjects with prior intervention to right or left renal artery;
4. Subjects with renal artery stenosis as defined by * 30% stenosis confirmed by angiography with two (2) orthogonal views with selective catheterization;
5. Subjects with iliac stenosis requiring intervention at time of procedure and/or within the next six (6) months;
6. Subjects with severe femoral, renal, iliac or aortic calcification that may cause a potential complication at the time of the procedure;
7. Subjects in which the physician is unable to cannulate the renal artery;
8. Subjects in which the physician is unable to access the femoral artery by percutaneous means.

Study design

Design

Study phase:	4
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	20
Type:	Anticipated

Medical products/devices used

Generic name:	Renal sympathetic nerve denervation using radiofrequency applied percutaneously through a translumin
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	24-04-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL47656.018.14