Denervation of the renal sympathetic nerves in heart failure with normal LV ejection fraction.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON39827

Source
ToetsingOnline

Brief title
DIASTOLE

Condition

- Heart failures
- Vascular hypertensive disorders

Synonym
heartfailure, high blood pressure

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W,Medtronic

International Trading Sàrl

Intervention

Keyword: Heartfailure with normal LVEF, Hypertension, Renal denervation

Outcome measures

Primary outcome

To study the efficacy of RDN as a treatment modality for heart failure with a normal LV ejection fraction.

Echocardiographic endpoints:

The change in the ratio of mitral peak velocity of early filling (E) to early diastolic mitral annular velocity (E') (E/E), determined by pulsed wave Doppler.

*The change in duration of reversed pulmonary vein arterial systolic flow (Ard) minus the duration of the mitral valve atrial wave flow (Ad) (Ard-Ad), determined by pulsed wave Doppler. These changes will be expressed in milliseconds.

*The change in left atrial volume index (LA volume indexed for body surface area), determined by pulsed wave Doppler. These changes will be expressed in millilitres per square meter.

Secondary outcome

Radiological endpoints:

*The change in LV wall thickness/ LV mass, - determined by balanced SSFP cine MRI * after RD. These dimensions include LV-mass. This change will be expressed in grams and grams per square meter of body surface area.

*The change in LV-volume and LA-volume * determined by MRI. These changes will

be expressed in millilitres per square meter of body surface.

*The change in LVEF * determined by MRI. This change will be expressed in

percentage.

*The change in MIBG-uptake and -washout. This will be determined by MIBG.

Laboratorial endpoints:

*The effect of RDN on absolute changes of B-Natriuretic Peptide.

Blood pressure related endpoints:

*The effect on blood pressure reduction, this will be measured in absolute

changes, comparing changes after RDN with baseline SBP and DBP. Hereby also

taking into account the home blood pressure measurements.

Clinical endpoints:

*The effect of QoL will be measured by the Minnesota Living with Heart Failure

Questionnaire.

*The effect of RDN on the exercise capacity will be assessed by the 6-minute

walking test.

Study description

Background summary

It has been shown that the sympathetic nervous system (SNS) activation plays an important role in the clinical phenomena of heart failure with normal left ventricular ejection fraction. Moreover, sympathetic activation is directly proportional related to the severity of the heart failure state. Therapeutic

renal denervation (RDN), the deliberate disruption of the nerves connecting the kidneys with the central nervous system, has been shown to be an effective means of modulating elevated SNS activity. This current study is a randomized controlled trial, with the aim to evaluate the safety and efficacy of renal sympathetic denervation in patients with heart failure with normal LV ejection fraction.

Study objective

The efficacy of PRDN will be evaluated primarily using echocardiographic parameters. Also, safety of PRDN on major and minor adverse events, LV mass, LV and LA dimensions, MIBG uptake and clinical endpoints will be evaluated.
The results of the endpoints between the two groups will be compared.

Study design

multicentre, prospective randomized controlled trial. Patients will be randomized in a 1:1 fashion to renal denervation versus current medical treatment. Treatment allocation will be made using sealed envelopes containing a computer-generated sequence.

Intervention

Renal denervation

Study burden and risks

The risks associated with the renal denervation are acceptable. Based on the experience from our previous studies, we do not expect any potential risks regarding this trial. Possible complications include a dissection of the aa. renales and a pseudoaneurysm. Both complications are well treatable. The risks associated with the tests and procedures performed for the clinical study are limited. A possible complication is bruising or a hematoma after venapuncture.

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

Individual is diagnosed with heart failure with a normal LV ejection fraction. The diagnosis of HFNEF requires the following conditions to be satisfied (see also figure 1 and Appendix A):
a. signs or symptoms of heart failure;
b. normal or mildly abnormal systolic LV function (LVEF * 50%);
c. evidence of diastolic LV dysfunction.;Individual is adhering to a stable drug regimen including at least 2 antihypertensive drugs (with no changes for a minimum of 2 weeks prior to enrolment) which is expected to be maintained for at least 6 months. Using this regimen the blood pressure should be adequately controlled (<140/90mmHg by 24 hour ambulatory BP measurement).;Individual is *18 years of age.;Individual agrees to have all study procedures performed, and is competent and willing to provide written, informed consent to participate in this clinical study.

Exclusion criteria

Individual is known with myocardial infarction as a cause of heart failure with normal LV ejection fraction. ;Individual has renal artery anatomy that is ineligible for treatment including:
a.Main renal arteries < 4 mm in diameter or < 20 mm in length.
b.Hemodynamically or anatomically significant renal artery abnormality or stenosis in either renal artery which, in the eyes of the operator, would interfere with safe cannulation of the renal artery or meets standards for surgical repair or interventional dilation.
c.A history of prior renal artery stenting.
d.Multiple main renal arteries in either kidney.;Individual has an estimated glomerular

filtration rate (eGFR) of <30mL/min/1.73m2, using the MDRD calculation.;Individual is known with any secondary cause of hypertension.;Individual is known with any other cause of respiratory dysfunction that explains the presenting signs and symptoms. Patients with COPD Gold I-II and evident heart failure (see appendix A) will be eligible for inclusion. ;Individual has experienced a myocardial infarction, unstable angina pectoris, or a cerebrovascular accident within 6 months of the screening visit, or has widespread atherosclerosis, with documented intravascular thrombosis or unstable plaques.;Individual has scheduled or planned surgery or cardiovascular intervention in the next 6 months.;Individual has hemodynamically significant valvular heart disease for which reduction of BP would be considered hazardous.;Individual has an implantable cardioverter defibrillator (ICD) or pacemaker whose settings cannot allow for RF energy delivery.;Individual has any serious medical condition, which in the opinion of the investigator, may adversely affect the safety and/or effectiveness of the participant or the study (i.e., patients with clinically significant peripheral vascular disease, abdominal aortic aneurysm, bleeding disorders such as thrombocytopenia, haemophilia, or significant anaemia, or cardiac arrhythmias).;Individual is pregnant, nursing or planning to be pregnant. ;Individual has a known, unresolved history of drug use or alcohol dependency, lacks the ability to comprehend or follow instructions, or would be unlikely or unable to comply with study follow-up requirements.;Individual is currently enrolled in another investigational drug or device trial.;Individual is currently being treated with any of the following medications:
a.Drugs that cause salt retention (e.g., systemic corticosteroids and fludrocortisone)
b.Warfarin or phenprocoumon that cannot be temporarily stopped for the procedure.;Any contraindications for MRI:
a.The presence of implanted cardiac pacemakers and/or auto-implanted cardioverter defibrillators.
b.Mechanical cardiac valves.
c.Implanted electronic devices like cochlear implants and nerve stimulators.
d.Patients who are unable to fit into the bore of the magnet.
e.Claustrophobia.
f.Prosthesis of a joint

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-02-2013
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO Date:	04-04-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	30-12-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	10-07-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	05-02-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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
ClinicalTrials.gov	NCT01583881
CCMO	NL37377.041.12

Study results

Date completed:	07-07-2016
Actual enrolment:	16