Metabolic Syndrome Study. Renal Sympathetic Denervation for Treatment of Metabolic Syndrome Associated Hypertension

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The aim of this post-CE study is to collect data on the effects of renal sympathetic denervation on the insulin resistance and muscle sympathetic nerve activity (MSNA) in patients with metabolic syndrome and associated hypertension.

Ethical review	Not approved
Status	Will not start
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON40213

Source
ToetsingOnline

Brief title
Metabolic Syndrome Study

Condition

- Other condition
- Vascular hypertensive disorders

Synonym
Metabolic syndrome associated hypertension - High Bloodpressure with metabolic syndrome

Health condition

Metabool Syndroom

Research involving
Human

Sponsors and support

Primary sponsor: St. Jude Medical
Source(s) of monetary or material Support: St. Jude Medical

Intervention

Keyword: Hypertension, Metabolic Syndrome, Post market, Renal denervation

Outcome measures

Primary outcome

To determine the effects of renal sympathetic denervation on the insulin resistance and muscle sympathetic nerve activity (MSNA) in patients with metabolic syndrome and associated uncontrolled hypertension at 3 months after renal denervation.

Secondary outcome

To determine the effects of renal sympathetic denervation on the insulin resistance, MSNA and blood pressure long-term (12 months after renal denervation).

Study description

Background summary

Metabolic syndrome is considered present when at least three of the following five-component criteria are met:
1) systolic blood pressure *130 mmHg or diastolic blood pressure *85 mmHg or on antihypertensive drug treatment in a patient with a history of hypertension;
2) fasting glucose *100 mg/dL (*5.6 mmol/L) or on drug treatment for elevated glucose;
3) waist circumference *102 cm (*40 inches) for male or *88 cm (*35 inches) for female;

4) triglycerides *150 mg/dL (*1.7 mmol/L) or on drug treatment for elevated triglycerides;
5) high density lipid cholesterol (HDL-C) <40 mg/dL (<1.03 mmol/L) for male or <50 mg/dL (<1.3 mmol/L) for female or on drug treatment for reduced HDL-C.

Each of these metabolic syndrome components is known to be an independent risk factor of
cardiovascular morbidity and mortality with hypertension known to be one of the highest
predictors. The occurrence of three or more of these components in individuals with metabolic syndrome further increases the already elevated cardiovascular risk. Hypertension is a very common component in individuals with metabolic syndrome. The risk of cardiovascular and allcause mortality is almost doubled, and the risk of developing type II diabetes mellitus also increases approximately threefold if the metabolic syndrome is present.

Metabolic syndrome is also characterized by elevated sympathetic nerve activity at fasting state and by insulin resistance with impaired sympathetic neural response to the physiologic
hyperinsulinemia and oral glucose. This plays a role in the progression of metabolic syndrome and the corresponding cardiovascular risks with direct and indirect influences to the development and progression of organ damages. Strategies to target specifically the elevated sympathetic nerve activity may provide substantial clinical benefits to
patients with metabolic syndrome and associated hypertension.

The sympathetic innervation of the kidney is implicated in the pathogenesis of hypertension
through enhanced renin secretion, sodium re-absorption and reduced blood flow. Renal
sympathetic afferent and efferent nerves run within and adjacent to the wall of the renal
arteries. In various experimental models, which include obesity-induced hypertension,
the magnitude of hypertension has been reduced during the observation period post renal sympathetic denervation. The percutaneous, catheter-based method that delivers radiofrequency (RF) to the renal sympathetic nerves for the ablation-induced renal sympathetic denervation has also been shown to result in safe and effective lowering of blood pressure, lowering of MSNA, and possible improvement of glucose metabolism in patients with resistant hypertension.

While sympathetic neural inhibition through renal sympathetic denervation may provide
protection in patients with metabolic disorders and resistant hypertension at high cardiovascular risk, the underlying mechanisms of metabolic and blood pressure controls through renal sympathetic denervation remain uncertain. Investigating the effect of renal denervation on the insulin resistance and

sympathetic nerve activity in this patient population may give us more insights on the underlying mechanisms.

Study objective

The aim of this post-CE study is to collect data on the effects of renal sympathetic denervation on the insulin resistance and muscle sympathetic nerve activity (MSNA) in patients with metabolic syndrome and associated hypertension.

Study design

This is a prospective, randomized, controlled, multi-center clinical investigation of the EnligHTN* Renal Denervation System. Approximately 60 subjects will be enrolled with 2 to 3 study centers participating in the clinical investigation. Subjects are randomized (3:1 ratio) to either Treatment Group or Control Group and will be followed up for 1 year post procedure.

Intervention

The procedure consists of an ablation of the renal sympathetic nerves within the renal arteries, by delivering RF energy via a percutaneous catheter. This minimal invasive local method has a short procedure time, short hospitalization and short recovery time.

Study burden and risks

The standard 75g OGTT is associated with minimal risks. The known, but rare, adverse reactions include nausea, vomiting, abdominal bloating, headache and hypoglycaemia.

Drawing blood may cause some discomfort or bruising. The blood vessel may swell, blood may clot in the blood vessel, or the spot from which blood is taken could become inflamed. In rare instances, there could be a minor infection or bleeding. If this happens, it can easily be treated.

In the Nerve Activity Test, when the needle is locating the nerve for proper nerve activity recording, it may cause momentary discomfort or pain.

The renal denervation is an interventional approach and as such carries some potential risks which may include but are not limited to the following:

* Acute renal injury (renal infarction, renal hematoma)
* Access site complications (bleeding, arteriovenous fistula, access site thrombosis, embolisation, pseudo-aneurysm, hematoma, limb ischemia, femoral nerve injury or seroma)

* Allergic reaction against contrast media
* Bradycardia
* Collateral tissue injury
* Death
* Decompensated heart failure
* Disseminated intravascular coagulation
* Drug reactions
* Malignant or accelerated hypertension
* Renal vascular injury (renal artery dissection, renal artery thrombosis, renal artery stenosis)
* Symptomatic hypotension
* Infection (access site infection or systemic infection)
* Myocardial infarction
* Neurologic event (acute ischemic or hemorrhagic brain injury)
* Pain, including back pain
* Renal failure
* Respiratory compromise
* Vasospasms
* Vasovagal episodes

When a renal artery angiogram is taken, the patient will be exposed to a small amount of radiation. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 millisieverts (mSv) each year. The effective dose from this study is about 25 mSv, which is comparable to that received from several computed tomography x-rays (CT) and nuclear medicine procedures.
The benefits from the research study should be weighed against the possible detrimental effects of radiation, which includes an increased risk of fatal cancer. In this particular study, the risk is moderate, and the estimated risk of such harm is about 1 in 800. For comparison, this risk is about 200 times lower than the cancer mortality rate in the general population of about one case in every four people.

The effects of renal denervation on the unborn child and on the newborn baby are not known. Because of this, it is important that study participants are not pregnant or breast-feeding and do not become pregnant during the course of the research study.

There may be other risks that are not known at this time.

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

- Patient with office blood pressure *140/90 mmHg and 24-hour ambulatory blood pressure *130/80 mmHg at Enrollment despite treatment with two drugs at maximum tolerated doses
- Patient with a fasting glucose *100 mg/dL (*5.6 mmol/L) at Enrollment
- Patient with a waist circumference *102 cm (*40 inches) for male or *88 cm (*35 inches) for female at Enrollment
- Patient with any of the other metabolic syndrome diagnostic criteria listed as follows at Enrollment:
o Triglycerides *150 mg/dL (*1.7 mmol/L) or on drug treatment for elevated triglycerides
o High density lipid cholesterol (HDL-C) <40 mg/dL (<1.03 mmol/L) for male or <50 mg/dL (<1.30 mmol/L) for female or on drug treatment for reduced HDL-C
- Patient is *18 and *80 years old
- Patient must be able and willing to provide written informed consent to participate in this clinical investigation
- Patient must be able and willing to comply with the required follow-up schedule

Exclusion criteria

* Patient with resistant hypertension or secondary hypertension
* Patient with type I diabetes mellitus or type II diabetes mellitus requiring insulin therapy
* Patient with prior renal angioplasty, renal denervation, indwelling renal stents and/or aortic stent grafts
* Patient with renal arteries <4.0 mm in diameter
* Patient with significant renovascular abnormalities (such as renal artery stenosis >30%)
* Patient with an estimated glomerular filtration rate (eGFR) of <45 mL/min per 1.73 m2 using the Modified Diet in Renal Disease (MDRD) formula
* Patient with hemodynamically significant valvular heart disease, as determined by Study Investigator
* Patient has had a myocardial infarction, unstable angina pectoris or cerebrovascular accident less than 180 days at Enrollment or is expected to have cardiovascular intervention within the next 180 days
* Patient is in chronic atrial fibrillation/flutter or with severe conduction abnormalities or with an implantable cardioverter defibrillator (ICD) or pacemaker whose settings cannot allow for radiofrequency (RF) energy delivery
* Patient is currently being treated with drugs that cause salt retention (such as systemic corticosteroids or fludrocortisone)
* Patient with an active systemic infection or blood-clotting abnormalities
* Patient is pregnant or of childbearing potential and is not using adequate contraceptive methods or nursing
* Patient is participating in another clinical investigation
* Patient has a life expectancy less than 12 months, as determined by Study Investigator
* Patient has an allergy for contrast agent used for the angiogram

Study design

Design

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

Primary purpose: Treatment

Recruitment

NL
Recruitment status: Will not start

Enrollment:	15
Type:	Anticipated

Medical products/devices used

Generic name:	Renal Ablation
Registration:	Yes - CE intended use

Ethics review

Not approved

Date:	31-03-2014
Application type:	First submission
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	NCT01911078
CCMO	NL46078.041.13