Safety and Efficacy of Ultrasound Renal Denervation in Kidney Transplantation Patients with Uncontrolled Hypertension: the RESTART Study

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To assess the short-term and long-term safety and efficacy of bilateral ultrasound renal sympathetic denervation (RDN) of the native kidneys in renal transplant patients with uncontrolled hypertension.

Ethical review	Approved WMO
Status	Recruitment started
Health condition type	Renal disorders (excl nephropathies)
Study type	Interventional research previously applied in human subjects

Summary

ID

NL-OMON55957

Source
ToetsingOnline

Brief title
RESTART

Condition

- Renal disorders (excl nephropathies)
- Vascular hypertensive disorders

Synonym
high blood pressure; hypertension

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: ReCor Medical Inc.

Intervention

- Medical device

Keyword: Hypertension, Kidney Transplantation., Renal sympathetic denervation

Explanation

N.a.

Outcome measures

Primary outcome

The change in systolic mean 24-hour ambulatory BP between baseline and the
3-months following the RDN procedure.

Secondary outcome

The most important secondary study outcomes involve:
- Composite safety endpoint consisting of the occurrence of any of the
following events before the 3-month follow-up visit (F3): all-cause mortality,
new onset (acute) end-stage renal disease, significant embolic event resulting
in end-organ damage, renal artery perforation requiring an invasive
intervention, renal artery dissection requiring an invasive intervention, major
vascular complications requiring surgical repair, interventional procedure,
thrombin injection, or blood transfusion or hospitalization for hypertensive or
hypotensive crisis.
- The change in diastolic mean 24-hour ambulatory BP between baseline (V1) and
the 3-month follow-up visit (F3)
- The change in systolic and diastolic daytime and nighttime ambulatory BP
between baseline (V1) and the 3-month follow-up visit (F3)
- The change in systolic and diastolic office BP between baseline (V1) and the
3-month follow-up visit (F3)
- The change in systolic and diastolic average home BP between baseline (V1)
and the 3-month follow-up visit (F3)
- The change in systolic and diastolic mean 24-hour, daytime and nighttime
ambulatory BP between baseline (V1) and the 3-month follow-up visit (F3) in
patients with adherence to the same antihypertensive drugs (as based on serum
therapy adherence testing) at both time points
- The change in systolic and diastolic office BP between baseline (V1) and the
3-month follow-up visit (F3) in patients with adherence to the same

antihypertensive drugs (as based on serum adherence testing) at both time points
- The change in systolic and diastolic average home BP between baseline (V1)
and the 3-month follow-up visit (F3) in patients with adherence to the same
antihypertensive drugs (as based on serum adherence testing) at both time points
- The change in prescribed antihypertensive drugs (displayed as the number of
DDDs and number of classes) between baseline and 3 months (F3)
- The change in therapy adherence (defined as the percentage of prescribed
drugs that can be detected using serum adherence testing) between baseline and
3 months (F3)
- The annual change in systolic and diastolic mean 24-hour, daytime and
nighttime ambulatory BP up until 5-year follow-up (F60)
- The annual change in systolic and diastolic office BP up until 5-year
follow-up (F60)
- The annual change in systolic and diastolic average home BP up until 5-year
follow-up (F60)
- The change in prescribed antihypertensive drugs (displayed as the number of
DDDs and number of classes) up until 5-year follow-up (F60)
- The change in therapy adherence (defined as the percentage of prescribed
drugs that can be detected using serum adherence testing) up until 1-year
follow-up (F12)
- The number of patients in whom no successful bilateral RDN procedure can be
performed (e.g. due to anatomical difficulties)
- The change in renal function (eGFR) and proteinuria (protein/creatinine
ratio) between baseline (V1) and the 3-month follow-up visit (F3)
- The occurrence of the individual components of the composite safety outcome
up until 5-year follow-up (F60)
- The occurrence of any major adverse cardiovascular and cerebrovascular event
(MACCE) up until 5-year follow-up (F60), including myocardial infarction,
coronary revascularization, stroke and cardiovascular mortality
- The occurrence of any individual components of MACCE up until 5-year
follow-up (F60)
- The occurrence of all-cause mortality up until 5-year follow-up (F60)
- The change in renal function (eGFR) and proteinuria (protein/creatinine
ratio) over time up until 5-year follow-up (F60)</p>

Study description

Background summary

Uncontrolled hypertension is present in 5-20% of all patients with a history of renal transplantation resulting in a significantly increased risk for cardiovascular, as well as kidney allograft disease. The residual hormonal function of the native kidneys is hypothesized to be a key contributor to this problem. The efficacy and safety of percutaneous native kidney denervation in

patients post kidney transplantation has not been sufficiently studied.

Study objective

To assess the short-term and long-term safety and efficacy of bilateral ultrasound renal sympathetic denervation (RDN) of the native kidneys in renal transplant patients with uncontrolled hypertension.

Study design

Interventional single-center, single-arm, proof-of-concept study.

Intervention

Conventional angiography and bilateral ultrasound RDN of the native renal arteries.

Study burden and risks

Patients will need to comply to eight outpatient clinic visits and a single one-night hospital admission throughout their five-year study participation. The intervention studied (i.e. native kidney RDN) is considered a very low-risk procedure which should theoretically outweigh the risks of the (improvement in) known detrimental effects of uncontrolled BP on morbidity and mortality. Throughout the course of the study, magnetic resonance imaging will be performed at screening and ambulatory BP measurements will be performed six times. Blood sampling and therapy adherence testing (using dried blood spot sampling) will be performed eight and seven times, respectively.

Contacts

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Trial sites

Trial sites in the Netherlands

Erasmus MC, Universitair Medisch Centrum Rotterdam
Target size: 40

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Age >= 18 years
2. Kidney transplantation >= 9 months ago with stable immunosuppressive drug treatment (dosage changes to maintain a steady serum concentration are permitted)
3. Estimated Glomerular Filtration Rate (eGFR) >= 30 ml/min/1.73m2
4. Office systolic blood pressure >= 140 mmHg at screening (V0), and a systolic mean 24-hour ambulatory blood pressure >= 130 mmHg (V1)
5. With respect to antihypertensive medication:
a. Patients should be on a stable regimen of at least two antihypertensive drugs of different classes, for at least six weeks, or
b. Patients should have a documented intolerance to three classes of antihypertensive drugs.
Patients should only be included when a change in antihypertensive drug regimen is not anticipated within the oncoming three months.
6. Patient is willing and able to provide written informed consent

Exclusion criteria

• Native renal artery anatomy not eligible for renale denervatie, defined as at

least one of the following conditions: o History of renal artery stenting or angioplasty o History of renal denervation o History of kidney tumors o Renal artery diameter < 3 mm or > 8 mm o Renal artery length < 20 mm o Fibromuscular disease (FMD) of the native renal arteries o Renal artery aneurysm • Presence of a remnant transplant kidney after
re-transplantation or absence of native kidneys • History of intravenous contrast dye allergy or nephropathy • Iliac/femoral artery stenosis precluding insertion of the Paradise catheter • Uncorrected, treatable secondary cause of hypertension • Pregnancy • Life expectancy < one year at the discretion of the investigator

Study design

Design

Study phase:	N/A
Study type:	Interventional research previously applied in human subjects
Intervention model:	Single
Allocation:	N/A: single arm study
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment started
Start date (anticipated):	15-12-2023
Enrollment:	40
Duration:	60 months (per patient)
Type:	Actual

Medical products/devices used

Product type:	Medical device
Generic name:	Paradise® ultrasound renal denervation system
Registration:	Yes - CE intended use

IPD sharing statement

Plan to share IPD: No

Plan description
N.a.

Ethics review

Approved WMO Date:	04-09-2023
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-04-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-01-2025
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-06-2025
Application type:	Amendment
Review commission:	METC Erasmus MC

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	NCT05934383
CCMO	NL84285.078.23
Research portal	NL-006041