# 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.

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Renal disorders (excl nephropathies) |
| **Study type** | Interventional |

## 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:** Medische Hulpmiddelen Industrie / bedrijf,ReCor Medical Inc.

## Intervention

**Keyword:** Hypertension, Kidney Transplantation., Renal sympathetic denervation

## 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)

# 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

## 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 o Renal artery stenosis > 30% • 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 type:** Interventional

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|---|---|
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Treatment |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 15-12-2023 |
| Enrollment: | 40 |
| Type: | Actual |

## Medical products/devices used

| | |
|---|---|
| Generic name: | Paradise® ultrasound renal denervation system |
| Registration: | Yes - CE intended use |

# Ethics review

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|---|---|
| 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 |

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| 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) |

# 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 |
|---|---|
| Other | ClinicalTrials.gov (in afwachting publicatie) |
| CCMO | NL84285.078.23 |