SIMPLIFIED PROTOCOL RESEARCH NOT INVOLVING THE HUMAN BEING

TITLE	Real life data from hypertensive patients treated with renal denervation in current practice in France- French RENal Denervation registry
SHORT TITLE	FRiEND
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BACKGROUND	Renal denervation (RDN) is a recent procedure that can be used to control BP (blood pressure) in hypertensive patients. Numerous publications from randomised trials have demonstrated the efficacy of RDN in this indication (1-14). The latest guidelines now include RDN as an effective technique for use in hypertension. Since the beginning of 2023, RDN using Medtronic's Spiral radiofrequency system has benefited from transitional authorisation for reimbursement by the French health insurance system. An application for reimbursement is underway for the ultrasound system. We aim to compile an exhaustive prospective register of all procedures carried out in France over the next few years, regardless of the type of catheter used or the context in which the procedure was carried out (transitional reimbursement, industrial register, randomised trial). Our aim is to assess the efficacy and safety of the procedure within the French healthcare system, the characteristics of patients benefiting from the procedure, the centres performing renal denervation, and the care pathways used, and to be able to present all this data, independently of the industry, to the healthcare authorities when it comes time to reassess the value of this procedure and its indications.

PRIMARY OBJECTIVE	☐ Diagnostics ☐ Prevention and treatment ☐ Patient management ☐ Patient safety ☐ Organization of healthcare facilities ☐ Public health policies ☐ Understanding diseases ☒Other:To describe changes in SBP evaluated in Home Blood Pressure Measurement (HBPM) in hypertensive patients between before and 1 year after treatment with RDN.
PRIMARY ENDPOINT	Change in SBP measured by HBPM before and after RDN (1 year).
SECONDARY OBJECTIVES	SECONDARY OBJECTIVES: - To evaluate changes in office systolic blood pressure, the combination of SBP measured in HBPM and day ABPM and 24-hour SBP before and 3 months, 6 months, 1 year, after DNR. - Evaluate the evolution at 3 months, 6 months, 1 year, of the drug burden in antihypertensive treatment (DDD), the percentage of patients having reached the blood pressure target and the win ratio. - Evaluate the development of renal artery stenosis before and 6 months, 1 year, after DNR. - Evaluate the evolution of creatinine levels before and 6 months, 1 year, after DNR. - Evaluate the occurrence of other complications related to hypertension or to the procedure itself. - Comparison of responders and non-responders to the procedure (24h ABPM systolic blood pressure decrease of 5 mmHg or more and/or the diminution of the medical burden by at least one therapeutic class without SBP increase compared to baseline). - Evaluate the performance of known predictors of response to renal denervation in our population. - Describe the type of center performing the procedure, the context in which DNR is performed, patient characteristics and care pathways.
METHODOLOGY	Research that does not involve the human person, as it involves the prospective, retrospective, descriptive and comparative use of multicentric data from routine care.
TYPE OF DATA COLLECTED	The data collected are detailed below: • **Administrative data :** - centre number followed by a hyphen (-) then the patient's number - collection of the patient's non-objection to participate in the FRiEND register - date of inclusion, date of procedure

- type of centre carrying out the procedure (hospital, university hospital, clinic, ESPIC, other)
- setting in which the procedure was carried out (day hospitalisation, week hospitalisation, conventional hospitalisation)

- **Personal data :**

- Patient's initials, date of birth (in MM/YYYY format).
- Gender (male, female, not gendered, refuses to answer), height, weight,

- **Biological data :**

- Biological work-up with measurement of the following parameters: Plasma ionogram (Na, K), blood count and platelet count (NFP), proteinuria, fasting glycaemia, total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, creatininaemia, estimated glomerular filtration rate (eDFG) (according to the Modification of Diet in Renal Disease (MDRD) method), uricaemia, microalbuminuria or urinary albumin/creatinine (assessment of target organ damage).

- **Clinical data :**
  - Systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR): three measurements will be taken with a validated oscillometric electronic device measured according to international recommendations (2023ESH-ESC)
  - risk factors (dyslipidaemia, type 2 diabetes, hypertension, smoking)
  - cardiovascular (CV) history of more than 6 months (myocardial infarction, coronary insufficiency, stroke)
  - non-CV history (cancer, asthma or respiratory insufficiency, musculoskeletal disability)
  - ABPM measurement (SBP and DBP for 24 hours, during the day and at night)
  - self-measurement of BP (according to the rule of 3 : average of 3 measurements in the morning and 3 in the evening, 3 consecutive days).
  - current treatments (anti-hypertensive, lipid-lowering, anti-diabetic, anti-platelet).
  - Therapeutic adherence assessment

- **Imaging data :**
  - results of CT scan of renal arteries: number of renal arteries, diameter of renal arteries, assessment of possible renal artery stenosis (in %)
  - Renal artery echodoppler (if feasible): assessment of possible renal artery stenosis (in %), renal artery blood flow velocity.

- **Procedure:**
  - Indication validated by a Centre of Excellence or Blood Pressure Clinic (yes/no)
  - Complete secondary hypertension work-up (yes/no)
  - In particular: plasma renin/aldosterone assay? Methoxylated catecholamine derivatives? renal artery imaging?
  - Precise indication of the procedure
  - context of treatment (temporary reimbursement of SIMPLICITY catheters, registry, randomised study)
  - specialities of the doctor(s) performing the procedure,
  - details of the procedure: under general anaesthetic/analgesia, approach,
  - Antithrombotics and anti-platelet aggregants before, during and after the procedure
  - number of ablation/sonication points performed
  - volume of contrast medium used, X-ray dosimetry
  - closure system for the approach port
  - complications, if any

- **Follow-up data :**
  - Date and type of follow-up
  - Progress of treatment
  - clinical BP measurements, MAPA and self-measurements performed
  - Changes in biological markers
  - Changes in imaging of the renal arteries
  - Complications, if any

This might include retrospective data for patients treated with RDN in the past, if investigator believe that the missing data are absent or scarce. As we will collect only data coming from a routine care already widely used in France for these patients, this should correspond to most of the patients already treated with RDN. Patients included retrospectively and prospectively will be compared to ensure that there are no selection biaises in the retrospective cohort.

Use one or more of the following sensitive variables :

☐ Country and department of residence of the person studied *(NB: the collection of the commune of residence (zip code and/or name) is not permitted)*

Pays et département de résidence de la personne étudiée (NB : le recueil de la commune de résidence (code postal et/ou nom) n'est pas autorisé)

☒ Year and month of birth

	☒ Date of care (DDMMYYYY) ☒ Date of death (DDMMYYYY) ☐ City of death ☐ None
ORIGIN OF DATA	☒Medical record ☐ Survey / Cohort / Register not including SNDS data ☐ Other data
	☒ Data from the investigator's department only (coordinating and associated centers) ☐ Data from several departments of the CHU Grenoble Alpes or from a department other than that of the investigator (if the investigator is at no time involved in the care of the persons targeted by the research).
DATA COLLECTION SCHEDULE	Prospective and restrospective research : - 3-year register (start of collection april 2025 - end of inclusions april 2027, follow-up : 1 year) For retrospective patients, data collection will be done from clinical database from january 2010. A 4-week delay must be observed between the sending of information letters and the start of data collection. - End of follow-up: april 2028. - Annual analysis of data from patients who have undergone RDN and follow-up at 1 month, 6 months, 1 year after the procedure.
DATA COLLECTION	**Collection :** The data collected will be those from routine follow-up at 1 month, 6 months, 1 year of all patients benefiting from a RDN procedure and included in the registry. After the procedure, the investigator in each participating centre will manage the follow up of the patient. As the study is purely observational, it does not require any specific follow-up visits, but includes the collection of data obtained during routine follow-up visits. The registry does, however, include data collection at fixed times after procedure. The data reported in the Redcap file will be the data available closest to the theoretical day of collection. Patients who have been lost to follow-up should be investigated through the referring doctors to RDN and/or by family members or any other person whose name appears on the patient liaison form. In the absence of any information, a search for the patient's possible death will be carried out by consulting the https://deces.matchid.io/searchqui website, including the INSEE source for deaths (the search will be carried out by birth name). In case of of the patient's death, the medical record is first checked to ensure that the patient has “no objection” to the use of his or her health data for research purposes. Clinical data collection will be based on the source documents.

	Codage : The data will be pseudonymised by coding: patients will be identified as follows: centre number followed by a hyphen (-) then the patient number coded number specific to the research indicating the order of inclusion of subjects (ex. 01-001).The list of correspondences between the patient code and his identity will be kept in each participating center, in the service server, by the investigator on an Excel file.
DATA STORAGE PERIOD	Personal data relating to persons taking part in research, and processed for this purpose, may be kept in the information systems of the controller, the participating centre or the healthcare professional involved in the research for a maximum of 2 years after the last publication of the results of the research or, if there is no publication, until the final report of the research is signed. The personal data of the professionals involved in the research may not be kept for more than fifteen years after the end of the last research project in which they participated. It is then archived on paper or electronically for a period of time in accordance with the regulations in force. The data must then be deleted.
DESCRIPTION OF STATISTICAL ANALYSIS OF DATA	**NUMBER OF SUBJECTS TO BE INCLUDED** The number of subjects included will correspond to the number of patients undergoing renal denervation for hypertension at the Grenoble University Hospital and in the various French centres participating in the study during the study period (the estimation is currently 100 per year). **DATA ANALYSIS** The database will be stored in accordance with the signed investigator commitment, on a secure database certified to keep health data, and linked to the REDCAP system supporting the eCRF. The analyses will be carried out at the University Cardiology Clinic of the Grenoble University Hospital by Professor ORMEZZANO and Dr Romain Boulestreau with the help of the SFHTA, using SPSS version 21 (SPSS Corp, Somers, NY) and STATA® 14.1 (Stata Corporation, College Station, TX). Statistical analysis: Absolute values, percentages and means (SD) will be calculated to describe the population. The differences between the variables before and after the RDN will be tested using either a paired t-test for normally distributed data or a Wilcoxon test, and a paired Chi2 or a Fisher test. For univariate analysis of variables between the RDN responder groups (5 mmHg reduction in 24h SBP) and non-responders, we will use the t-student analysis of variance test or non-parametric tests for continuous variables, and chi2 or Fisher tests for categorical variables. A multivariate analysis will also be performed.
PEOPLE INCLUDED IN THE RESEARCH	**Number of subjects:** Estimation of 100 per year (might be less in the first year, then more as RDN implementation in France increase) **Inclusion criteria:** Adult (> 18 years old) hypertensive patients treated with RDN in France whatever the catheter and the indication. This might include retrospective data for patient already treated with RDN in the past.

	Non-inclusion criteria: RDN not proposed to the patient, patient opposing the collection and use of his/her data for research purposes. **Information and traceability procedures for non-objection/opposition :** Patients will be fully and fairly informed, in comprehensible terms, of the objectives of the study and the nature of the information collected, and of their right to object at any time to the use of the data collected. They will be given an information letter and the non opposition will be written down in the medical records of the patient. If the subject objects to their personal health data being processed for research purposes, this objection will be recorded in their medical file. This right of objection may be exercised at any time by any means with either the person responsible for the research or the establishment holding the data, which undertake to respond to the request within a maximum of 2 months. Retrospective patients will be informed by post. On receipt of this letter, the patient will have 4 weeks to object.
ETHICS	NA
WHY THE STUDY IS IN THE PUBLIC INTEREST	The legal basis for this data processing is Article 6 of the General Data Protection Regulation (GDPR), namely the performance of a mission of public interest assigned to the data controller and the legitimate interests pursued by it. In addition, under Article 9 of the GDPR the data controller may exceptionally process special categories of data, including health data notably for scientific research purposes.
EXPECTED BENEFITS	To objectively evaluate RDN performance, patients and center profiles and care pathway in the various French centres participating to the registry, and to investigate whether there are any predictive factors (on the basis of the initial clinical and biological work-up) for the outcome in terms of lowering blood pressure, in order to better target patients who could benefit from this type of procedure in the future. Provide informed, independent data to the health authorities to support reimbursement decisions and the choice of indications.

Study schedule

Visits	During hospitalization for RDN	1 month after RDN	6 months after RDN	12 months after RDN
Patient information	X			
RDN indication verification	X			
Blood sample	X			
Imaging examinations	X			
Medical history collection	X			
Clinical examination	X	X	X	X
Ongoing therapy collection	X	X	X	X
Adverses events recording	X	X	X	X
Blood Pressure and heart rate recording	X	X	X	X
Blood sample				
Ionogram (Na, K), glucose level, creatininemia (DFG MDRD), uricemia	X	X	X	X
Total Cholestérol, HDL, LDL triglycerides, NFP				X
Microalbuminuria, proteinuria				X
Clinical examinations				
Home Blood Pressure Measurement		X	X	X
Ambulatory Blood Pressure Measurement				X
Renal Arteries ultrasound				X
Renal arteries angioCT				X

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