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Expert consensus

Catheter-based renal denervation in the treatment of arterial hypertension: An expert consensus statement on behalf of the French Society of Hypertension (SFHTA), French Society of Radiology (SFR), French Society of Interventional Cardiology (GACI), French Society of Cardiology (SFC), French Association of Private Cardiologists (CNCF), French Association of Hospital Cardiologists (CNCH), French Society of Thoracic and Cardiovascular Surgery (SFCTCV) and French Society of Vascular and Endovascular Surgery (SCVE)

Atul Pathak[a,1,*], Romain Boulestreau[b], Marc Sapoval[c], Pierre Lantelme[d], Beatrice Duly-Bouhanick[e], Hakim Benamer[f], Theodora Bejan-Angoulvant[g], Antoine Cremer[h], Laurence Amar[a], Nicolas Delarche[i], Olivier Ormezzano[j], Pierre Sabouret[k], François Silhol[l], Philippe Sosner[m,n], Marilucy Lopez-Sublet[o,p], Ariel Cohen[q], Pierre Yves Courand[d], Michel Azizi[r,1]

[a] *Department of Cardiovascular Medicine, Princess Grace Hospital, INI-CRCT network, 98000 Monaco, Monaco*
[b] *Université de Bordeaux, UMR Inserm 1034, Biologie des maladies cardiovasculaires, 33000 Bordeaux, France*
[c] *Department of Vascular and Oncological Interventional Radiology, Hôpital Européen Georges-Pompidou, 75015 Paris, France*
[d] *Department of Cardiology, Hôpital de la Croix-Rousse, Hôpital Lyon Sud, Hospices Civils de Lyon, 69004 Lyon, France*
[e] *Department of Hypertension and Therapeutics, CHU Rangueil, 31000 Toulouse, France*
[f] *Department of Cardiology, ICPS Jacques-Cartier, 91300 Massy, France*
[g] *Department of Pharmacology, CHRU de Tours, 37000 Tours, France*
[h] *Department of Hypertension and Cardiology, Saint-André Hospital, CHU de Bordeaux, 33000 Bordeaux, France*
[i] *Department of Cardiology, Centre Hospitalier de Pau, 64000 Pau, France*
[j] *Department of Cardiology, University Hospital, 38000 Grenoble, France*
[k] *Heart Institute and Action Group, Pitié-Salpétrière Hospital, 75013 Paris, France*
[l] *Department of Vascular Medicine and Arterial Hypertension, CHU Timone, 13385 Marseille, France*
[m] *Diagnosis and Therapeutic Centre, AP–HP, Hôtel-Dieu Hospital, 75004 Paris, France*
[n] *Laboratory MOVE (UR 20296), University of Poitiers, 86000 Poitiers, France*
[o] *Department of Internal Medicine, CHU Avicenne, AP–HP, 93000 Bobigny, France*
[p] *INI-CRCT network, Inserm UMR 942, 75010 Paris, France*
[q] *Department of Cardiology, Saint-Antoine Hospital, 75012 Paris, France*
[r] *Department of Hypertension, Université Paris Cité, AP–HP, HEGP, 75015 Paris, France*

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ABSTRACT

Several high-quality, randomized, sham-controlled trials have provided evidence supporting the efficacy and safety of radiofrequency, ultrasound and alcohol catheter-based renal denervation (RDN) for reducing blood pressure (BP). A French clinical consensus document has therefore been developed to propose guidance for the appropriate use of RDN in the management of hypertension along with a dedicated care pathway and management strategy. The French experts group concluded that RDN can serve as an adjunct therapy for patients with confirmed uncontrolled, resistant essential hypertension despite treatment with ≥ 3 antihypertensive drugs, including a long-acting calcium channel blocker, a renin-angiotensin system blocker and a thiazide/thiazide-like diuretic at maximally tolerated doses. Patients should have (1) an estimated glomerular filtration rate of ≥ 40 mL/min/1.73 m^2; (2) an eligible renal artery anatomy on pre-RDN scans and (3) exclusion of secondary forms of hypertension. Additional indications

* Corresponding author. Service de Cardiologie, Centre Hospitalier Princesse Grace, 1, avenue Pasteur, 98000 Monaco, Monaco.
Adresse e-mail : profapathak@gmail.com (A. Pathak).
[1] Atul Pathak and Michel Azizi contributed equally to this manuscript.

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might be considered for patients with difficult-to-control hypertension. Any indication of RDN should be validated by multidisciplinary hypertension teams consisting of both hypertension specialists and endovascular interventionalists in European Society of Hypertension (ESH) Excellence Centres or ESH-BP clinics. Patients should be informed about the benefit/risk ratio of RDN. Expertise in renal artery interventions and training in RDN techniques are needed for endovascular interventionalists conducting RDN procedures while centres offering RDN should have the necessary resources to manage potential complications effectively. Lastly, all patients undergoing RDN should have their data collected in a nationwide French registry to facilitate monitoring and evaluation of RDN outcomes, contributing to ongoing research and quality improvement efforts.

1. Abbreviations

BP	blood pressure
CT	computed tomography
CTA	computed tomography angiography
DBP	diastolic blood pressure
ESH	European Society of Hypertension
FMD	fibromuscular dysplasia
MRA	magnetic resonance angiography
RDN	renal denervation
RF	radiofrequency
SBP	systolic blood pressure
US	ultrasound

2. Background

Hypertension remains a major cardiovascular risk factor that affects approximately one third of the adult population worldwide [1]. Reducing systolic and diastolic blood pressure (SBP and DBP) to target is associated with reductions in cardiovascular, cerebrovascular and renal morbidity and mortality [2–4]. Despite the availability of multiple classes of antihypertensive medications that can be used in combination, achieving recommended blood pressure (BP) targets remains challenging because of various factors including poor adherence to lifestyle changes and antihypertensive medications, drug intolerance, therapeutic inertia, hypertension-mediated organ damage (including arterial stiffness and kidney function reduction), obesity, social and economic factors such as reimbursement schemes [5].

To further improve BP control in patients with hypertension, various new therapeutic approaches are either in development or already available for use and include:

- classical and non-classical pharmacological approaches with the development of new drugs currently in progress, such as aldosterone synthase inhibitors and non-steroidal mineralocorticoid antagonists, endothelin 1 receptor antagonists, small interferent ribonucleic acid-based therapies targeting liver angiotensinogen and others [6,7];
- device-based treatments including mainly catheter-based renal denervation (RDN) using radiofrequency- (RF-), ultrasound- (US-) or alcohol-based renal sympathetic nerve ablation (RF and US are both available for clinical use), but also other neuromodulation techniques still in development (i.e. baroreflex activation [8], heart rate modulation [8] and renal pelvic denervation [9]).

The first 2012 French expert consensus statement [10] proposed guidance for appropriate use of RF-RDN with the first-generation monopolar SYMPLICITY catheter in patients with resistant hypertension based on the results of a few open-label trials of first-generation catheters including the SYMPLICITY-HTN2 trial, which overestimated the office BP-lowering efficacy of RF-RDN [11]. Subsequently, the sham-controlled SYMPLICITY HTN-3 trial using the SYMPLICITY catheter did not show any significant improvement in office or ambulatory BP control in patients with resistant hypertension [12]. In contrast, the French academic DENERHTN randomized open-label trial showed a plausible reduction in daytime ambulatory SBP by around 6 mmHg in favour of RF-RDN in addition to a standardized antihypertensive medication escalation protocol at 6 months in patients with resistant hypertension versus standardized antihypertensive medication alone [13]. However, this trial was not sham-controlled.

From 2017 to 2024, seven positive [14–20] and three negative [21–23] sham-controlled trials have been performed (Fig. 1). The positive trials (1) used optimized RDN second-generation catheters, allowing more effective and reproducible circumferential nerve ablation and (2) had optimized designs to reduce confounding due to variable addition of antihypertensive medications, procedural performance and endpoint ascertainment. They consistently confirmed the ambulatory and office BP-lowering efficacy of RF-, US- and alcohol-based RDN (see below for details). These consistent results in favour of RDN and the subsequent meta-analyses [24–26] led to (1) the clinical consensus statement of the European Society of Cardiology Council on Hypertension and the European Association of Percutaneous Cardiovascular Interventions in 2023 [27]; (2) the update of the European Society of Hypertension (ESH) recommendations in 2023 [2] and (3) the Society for Cardiovascular Angiography & Interventions position statement on RDN for hypertension in 2023, based on a positive risk/benefit balance for RDN [28]. Finally, the US Food & Drug Administration approved RDN with the Paradise US catheter [29] and the SPYRAL RF catheter [30] in November 2023 with a broad indication of 'an adjunctive therapy when lifestyle modification and medications fail to control a patient's blood pressure'.

In this second updated French consensus statement, we built our recommendations on clinical evidence from the second-generation trials of RDN as well as the already published consensus documents from European and international societies (Table 1 [2,27,28,31–34]). Finally, we also propose a dedicated care pathway and management strategy for patients with uncontrolled hypertension in France who are eligible for RDN.

3. Pathophysiological basis

The pathophysiology of primary hypertension is complex and multifactorial, involving environmental and genetic factors, imbalance between vasoconstrictive and vasodilatory factors, and/or sodium/potassium/water balance [35]. Sympathetic hyperactivity originating from (afferences) and targeting (efferences) the kidneys is among the key players implicated in the pathophysiology of hypertension [36]. The sympathetic efferent nerves located in the adventitia of the renal arteries contribute to renal artery vasoconstriction, activation of the renin-angiotensin-aldosterone system

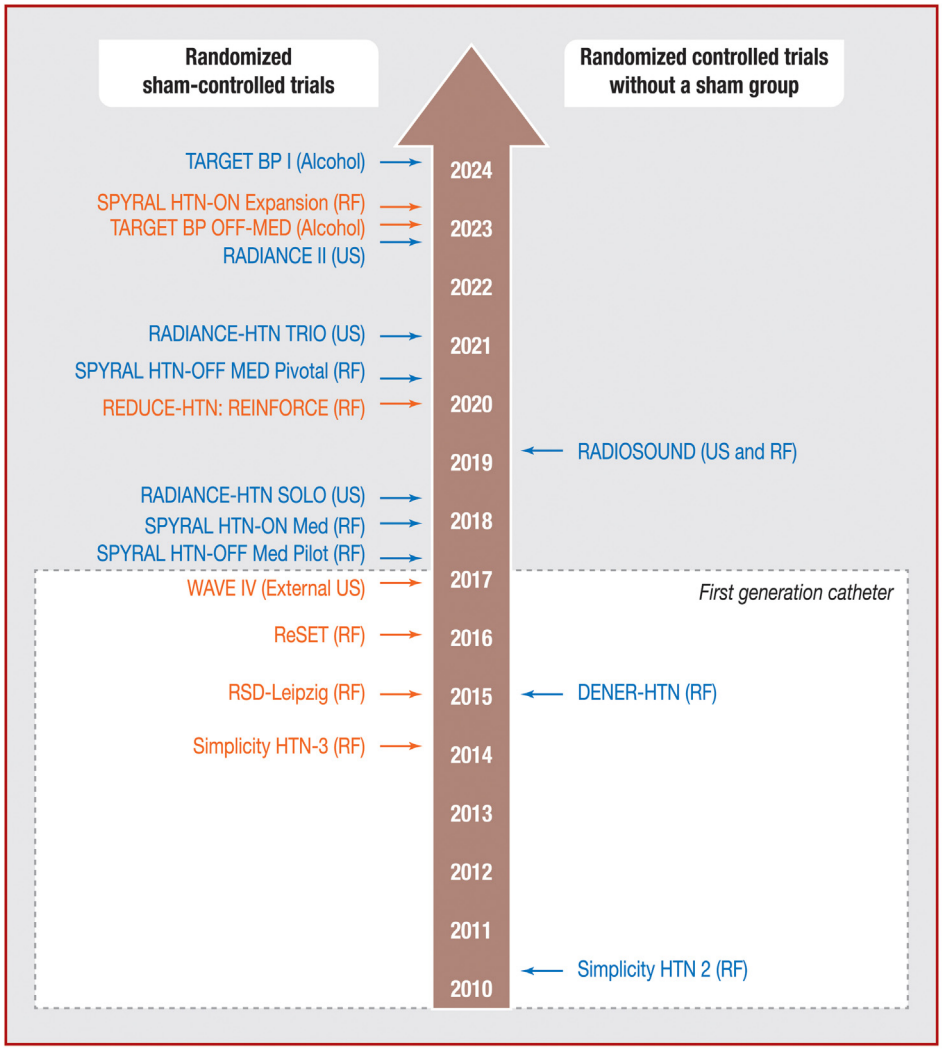


Fig. 1. Main multicentre randomized trials of RF-, US-, and alcohol-mediated RDN with and without sham groups (positive trials in blue: TARGET BP I [14], RADIANCE II [15], RADIANCE-HTN TRIO [16], SPYRAL HTN-OFF MED Pivotal [17], RADIANCE-HTN SOLO [18], SPYRAL HTN-ON MED [19], SPYRAL HTN-OFF MED Pilot [20]; negative trials in orange: SPYRAL HTN-ON MED Expansion [21], TARGET BP OFF-MED [22]; REDUCE-HTN: REINFORCE [23]). BP: blood pressure; HTN: hypertension; MED: medication; RDN: renal denervation; RF: radiofrequency.

Table 1
Summary of recommended indications for RDN across the different international guidelines.

Indication	SFHTA 2024 [current]	ESH 2023 [2]	SCAI 2023 [28]	ESC 2022 [27]	NL 2022 [31]	SCAI/NKF 2021 [32]	Spain 2021 [33]	Italy 2020 [34]
Uncontrolled hypertension	+[a,b]	+[c]	+			+	+	+
Resistant hypertension	+[a]	+	+[d]	+	+	+	+	+
Intolerant to drugs	+[b]	+	+	+	+	+	+	+
Non-adherent to drugs	+[b]		+	+		+	+	+
High cardiovascular risk/severe HMOD			+	+		+	+	+

BP: blood pressure; ESC: European Society of Cardiology; ESH: European Society of Hypertension; HMOD: hypertension-mediated organ damage; NKF: National Kidney Foundation; NL: Netherlands; RDN: renal denervation; SCAI: Society for Cardiovascular Angiography & Interventions; SFHTA: Société française d'hypertension artérielle (French Society of Hypertension).

[a] Despite optimal treatment with at least a single pill combination (ideally) of 3 drugs (renin-angiotensin system blocker, calcium channel blocker and thiazide/thiazide-like diuretic) at maximal tolerated dose.

[b] After case-by-case discussion by a multidisciplinary team in a specialized centre (ESH excellence centre or BP clinic).

[c] Despite antihypertensive drug combination therapy.

[d] Defined by seated office BP > 130/80 mmHg despite being on 3 medications with maximally tolerated doses from classes with outcomes data (renin-angiotensin system blocker, calcium channel blocker, thiazide/thiazide-like diuretic and beta-blockers).

and changes in the natriuretic pressure curve, all of which, in turn, lead directly or indirectly to an increase in BP and sodium and water retention. The afferent sympathetic nerves of the kidneys communicate with the central nervous system through fibres also located in the periadventitial tissue of the renal arteries. The afferent signals triggered by various factors – including ischaemia, inflammation, external renal compression or fibrosis – further enhance central and peripheral sympathetic hyperactivity in the target organs of hypertension [13]. This bidirectional sympathetic hyperactivity between the central nervous system and the kidneys thus plays a pathophysiological role in the initiation, progression and maintenance of hypertension [36].

The principle of endovascular catheter-based RDN involves interruption of both efferent and afferent sympathetic nerves and signalling. The dedicated catheters for RDN mainly use multi-electrode RF, US energy or alcohol to induce thermal or chemical injury of the sympathetic renal nerve located in the renal artery adventitia. The Spyral multi-electrode RF catheter (Simplicity, Medtronic, Ireland) is designed to target the main distal and branch renal arteries and delivers RF energy from individual RF electrodes at multiple sites. In contrast, the US catheter (Paradise, Recor, USA) is embedded in a low-pressure balloon in which circulation of cool sterile saline during the procedure protects the internal layers of the renal arteries from heat damage. This catheter is placed in the main renal arteries before the first bifurcation and in accessory renal arteries where at least 2–3 sonications per main renal artery are done. Finally, the Peregrine System^{TM} infusion catheter (Peregrine, Ablative Solutions, USA) delivers very small, measured doses of dehydrated alcohol into the perivascular space of the main renal artery and accessories to achieve circumferential ablation of the afferent and efferent sympathetic nerves. Other less evaluated techniques involve cryoablative RDN and other catheters in development [37,38].

4. What have we learned from the second-generation trials?

RF-, US- and alcohol- based RDN procedures using the above-mentioned catheters have currently proven and validated their BP-lowering efficacy in the absence or presence of antihypertensive medications in seven randomized sham-controlled trials [14–20] that included patients with uncontrolled or resistant hypertension. All of the well-designed second-generation trials with the highest level of internal validity consistently provided evidence of the effectiveness of RF-, US- and alcohol-based RDN by demonstrating significant and clinically pertinent ambulatory and/or office BP reductions versus a sham procedure. This was shown across all forms of hypertension, ranging from mild-to-moderate uncontrolled hypertension (treated or not) to severe and resistant hypertension. Moreover, all of the trials as well as observational registries showed favourable peri-procedural safety with sustained safety in the long-term [39]. The BP-lowering effects reported in these trials were of similar magnitude for RF-, US- and alcohol-based RDN. Table 2 summarizes the results of the multicentre, randomized, sham-controlled and blinded (patients and outcome assessors) off-medication and on-medication trials using ambulatory BP as the primary efficacy outcome, which are of the highest quality [14–22].

4.1. Off-medication trials

The international multicentre, randomized, double-blind, sham-controlled off-medication trials of US-RDN (RADIANCE-HTN SOLO [18]) and RF-RDN (SPYRAL HTN-OFF MED [17,20]) were specifically designed to demonstrate the BP-lowering efficacy of RDN to exclude the major confounding effect of variable prescription and intake of antihypertensive medications after the failure of the SYMPLICITY HTN3 trial [12]. The trials included patients with mild-to-moderate hypertension at low risk of cardiovascular complications who were either medication naïve or in whom concomitant antihypertensive medications (up to 2) were to be stopped for 12–16 weeks.

The SPYRAL HTN-OFF MED pilot [20] and pivotal [17] independent trials using the RF-based SPYRAL catheter included patients with mild-to-moderate hypertension in whom antihypertensive medications were discontinued. Both trials demonstrated a greater reduction in 24-hour ambulatory SBP and DBP with RF-RDN compared to the sham procedure at 3 months (Table 2). There were corresponding larger decreases in office SBP and DBP versus the sham group. There were no major adverse events in either group throughout the follow-up period. Follow-up of patients in the SPYRAL HTN-OFF MED pivotal trial also showed that RDN patients were less likely to experience hypertensive urgencies that required immediate use of antihypertensive medications compared to sham control [40].

The RADIANCE-HTN SOLO trial demonstrated a greater reduction in daytime ambulatory SBP with US-RDN compared to a sham procedure at 2 months (primary endpoint) among hypertensive patients in whom antihypertensive medications were discontinued for a total period of 3 months [18]. There were also larger decreases in both office and home SBP in the US-RDN versus the sham group. There were no major adverse events in either group through 6 months of follow-up. The BP-lowering effects persisted at 6 and 12 months after US-RDN, even when antihypertensive medications were restarted. The persistence of the BP-lowering effect of US-RDN was achieved with less prescribed antihypertensive medications versus the sham group. Follow-up of patients at 36 months confirmed the persistent BP-lowering effect of US-RDN and the absence of late adverse events [41] (Table 2).

These results were fully corroborated in the RADIANCE II pivotal trial [15], which included a larger number of patients with mild-to-moderate hypertension withdrawn from any concomitant antihypertensive treatment, which replicated the results of the RADIANCE HTN-SOLO trial.

Finally, alcohol-mediated RDN in a pilot safety study was not associated with significant BP differences versus a sham procedure at 8 weeks in patients on ≤ 2 antihypertensive medications included in the TARGET BP OFF-MED trial [22]. After restarting antihypertensive treatment, medication burden was, however, lower in the RDN group up to 12 months (Table 2).

4.2. On-medication trials

The effectiveness of RF-RDN in patients with uncontrolled hypertension with ≤ 3 antihypertensive medications (SPYRAL HTN-ON MED [19]), US-RDN in patients with treatment-resistant hypertension despite ≥ 3 antihypertensive medications (RADIANCE-HTN TRIO [16]) and alcohol-RDN in patients with uncontrolled hypertension despite prescription of 2–5 antihypertensive medications (TARGET BP I [14]) was subsequently established in multicentre, randomized, double-blind, sham-controlled on-medication trials (Table 2).

In the sham-controlled SPYRAL HTN-ON MED pilot trial [19] including hypertensive patients taking medications, RF-RDN showed reductions in 24-hour ambulatory and office BP at 6 months versus sham that were sustained despite a lower medication burden through extended follow-up. However, there was no significant treatment difference in 24-hour ambulatory BP between the RF-RDN and sham groups at 6 months in the expansion phase of the trial that included more patients following the pilot phase although office BP was more reduced by RF-RDN [21]. These results were

Table 2
Randomized sham-controlled trials of RDN with second-generation catheters. Adapted from Barbato et al. [27].

Trial name (publication year) [ref]	Comparison	Renal denervation modality	Inclusion criteria	Primary endpoint	Results
SPYRAL HTN-OFF MED (2017) [20]	RF-RDN (n = 38) vs. sham (n = 42)	Symplicity Spyral (multi-electrode RF)	Uncontrolled hypertension by OBP and 24-hour ABPM in the absence of BP-lowering therapy	24-hour SBP change at 3 months	−5.5 (95% CI: −9.1 to −2.0) vs. −0.5 (95% CI: −3.9 to 2.9) mmHg; P = 0.041
SPYRAL HTN-ON MED (2018) [19]	RF-RDN (n = 38) vs. sham (n = 42)	Symplicity Spyral (multi-electrode RF)	Uncontrolled hypertension by OBP and 24-hour ABPM under 1–3 antihypertensives	24-hour SBP change at 6 months	−9.0 (SD 11.0) vs. −1.6 (SD 10.7) mmHg; P = 0.006
RADIANCE-HTN SOLO (2018) [18]	US-RDN (n = 74) vs. sham (n = 72)	Paradise (US)	Uncontrolled hypertension by day ABPM in the absence of BP-lowering therapy	Day SBP change at 2 months	−8.5 (SD 9.3) vs. −2.2 (SD 10.0) mmHg; P = 0.0001
SPYRAL HTN-OFF MED Pivotal (2020) [17]	RF-RDN (n = 166) vs. sham (n = 165)	Symplicity Spyral (multi-electrode RF)	Uncontrolled hypertension by OBP and 24-hour ABPM in the absence of BP-lowering therapy	24-hour SBP change at 3 months	−4.7 (95% CI: −6.4 to −2.9) vs. −0.6 (95% CI: −2.1 to 0.9) mmHg; P = 0.0005
RADIANCE-HTN TRIO (2021) [16]	US-RDN (n = 69) vs. sham (n = 67)	Paradise (US)	Uncontrolled hypertension by day ABPM under ≥ 3 antihypertensives	Day SBP change at 2 months	−8.0 (IQR: −16.4 to 0.0) vs. −3.0 (IQR: −10.3 to 1.8) mmHg; P = 0.022
RADIANCE II (2023) [15]	US-RDN (n = 150) vs. sham (n = 74)	Paradise (US)	Uncontrolled hypertension by day ABPM. No antihypertensives for 2 months of follow-up	Day SBP change at 2 months	−7.9 (SD 11.6) vs. −1.8 (SD 9.5) mmHg; P < 0.001
TARGET BP OFF-MED (2023) [22]	Alcohol-RDN (n = 53) vs. sham (n = 53)	The Peregrine System™ infusion catheter (alcohol)	Uncontrolled hypertension by OBP and 24-hour ABPM in the absence of BP-lowering therapy	24-hour SBP change at 2 months	−2.9 (SD 7.4) vs. −1.4 (SD 8.6) mmHg; P = 0.25
SPYRAL HTN-ON MED Expansion (2023) [21]	RF-RDN (n = 206) vs. sham (n = 131)	Symplicity Spyral (multi-electrode RF)	Uncontrolled hypertension by OBP and 24-hour ABPM under 1–3 antihypertensives	24-hour SBP change at 6 months	−6.5 (SD 10.7) vs. −4.5 (SD 10.3) mmHg; P = 0.12
TARGET BP I (2024) [14]	Alcohol-RDN (n = 148) vs. sham (n = 153)	The Peregrine System™ infusion catheter (alcohol)	Uncontrolled hypertension by OBP and 24-hour ABPM under 2–5 antihypertensives	24-hour SBP change at 3 months	−10.0 (SD 14.2) vs. −6.8 (SD 12.1) mmHg; P = 0.0487

ABPM: ambulatory blood pressure monitoring; CI: confidence interval; IQR: interquartile range; OBP: office blood pressure; RF: radiofrequency; SBP: systolic blood pressure; SD: standard deviation; US: ultrasound.

probably due to large differences in medication changes between the two phases of the trial, especially in the US [42]. A post-hoc analysis showed that patients from outside of the US had both minimal changes in medications and significant decreases in office and ambulatory BP at 6 months compared to the sham group [42].

The RADIANCE-HTN TRIO trial, which randomized 136 patients with resistant hypertension to a standardized triple antihypertensive therapy in a single pill – including a calcium channel blocker, an angiotensin receptor blocker and a thiazide diuretic – demonstrated that US-RDN reduced ambulatory, home and office BP more than a sham procedure at 2 months (primary endpoint) (Table 2) [16]. In patients of both groups who had persistent elevation of BP at 2 months, standardized stepped-care antihypertensive treatment escalation resulted in similar ambulatory BP reductions in both groups but greater home BP reductions in the US-RDN group at 6 months, with fewer additional medications required in the US-RDN group, especially spironolactone 25 mg/day, the fourth-line treatment recommended by guidelines (US-RDN: 40% vs. sham: 61%) [43].

The REQUIRE trial conducted in Japan and South Korea differed from RADIANCE TRIO and reported BP reductions at 3 months with US-RDN that were similar to other sham-controlled studies but unexpectedly greater BP reductions in the sham group due to various study design issues [44], similar to those reported in the SYMPLICITY HTN-3 trial [12]. The lack of blinding of treating physicians, the absence of standardization of the procedure and of the medication escalation favoured increased adherence in patients within the sham group [45].

In the sham-controlled TARGET BP I trial, which randomized 301 patients with uncontrolled hypertension despite 2–5 antihypertensive drugs demonstrated that alcohol-mediated RDN reduced mean 24-hour ambulatory SBP at 3 months post-procedure (Table 2) [14]. The decrease in BP was lower with this device compared with RF- and US-mediated RDN. Various factors have been discussed such as the importance of a sham effect, technical issues or the effect of COVID-19 to explain these differences.

In contrast to the heterogeneity of results from the first-generation trials, the results of the second-generation trials are consistent despite variations in ablation methods when compiled in various meta-analyses including RF- and US-RDN trials [46], including individual patient-level pooled meta-analysis for US-RDN [26,47].

Finally, the Global SYMPLICITY Registry [39] that included 1742 patients demonstrated the absence of serious adverse events or impairment of renal function after RF-RDN up to 3 years of follow-up. The risk of *de novo* renal artery stenosis at the RDN sites was very

low, with an annual incidence of stenting of approximately 0.2%, with 79% of cases occurring in the first year post-procedure [48]. The principal procedural risk associated with RDN was reversible complications related to femoral artery access.

To date, no randomized, sham-controlled trial has demonstrated the benefit of RDN in reducing cardiovascular or cerebrovascular events. Obtaining such clinical outcome data would be challenging because (1) trials with very large sample size would be needed since the residual risk in hypertensive patients is low nowadays and/or (2) very long-term follow-up would be needed and potential biases related to changes in antihypertensive medications during patient follow-up would necessarily occur. Of note, pharmacological treatments have demonstrated their ability to reduce cardiovascular events and cardiovascular mortality by lowering BP. The 2021 individual participant-level data meta-analysis by the Blood Pressure Lowering Treatment Trialists' Collaboration showed that a 5 mmHg reduction in office SBP reduced the risk of major cardiovascular events by 10% and cardiovascular mortality by 5% [49]. This level of SBP reduction was achieved on average in the short term after RDN in comparison with sham in the trials listed in Table 2. Longer-term reductions in BP after RDN after 36 months of follow-up are not available in second-generation randomized controlled clinical trials. However, observational data from the Global SYMPLICITY Registry showed persistent BP reductions of clinically pertinent magnitude for at least 3 years [39]. Of note, the BP reductions observed in the long-term are not only attributable to RDN, but also to antihypertensive medication changes at the physician's discretion on the basis of standard of care. Considering all of these factors, while the potential benefit of RDN in preventing cardiovascular events is plausible, it has not been proven.

5. Indications for RDN (Table 1)

Based on the results of the cumulative evidence of the various trials listed in Table 2, RF- or US-based RDN can be proposed for:

- patients with uncontrolled primary hypertension defined as patients with seated office BP ≥ 140 and/or ≥ 90 mmHg, confirmed by 24-hour ambulatory BP measurement with daytime SBP ≥ 135 mmHg or 24-hour SBP ≥ 130 mmHg or home BP ≥ 135 and/or ≥ 85 mmHg;
- despite being treated by ≥ 3 antihypertensive drugs, including a long-acting calcium channel blocker, a renin-angiotensin system blocker, and a thiazide/thiazide-like diuretic at the maximally tolerated doses, ideally in single-pill combination;
- with eligible renal artery anatomy (see Section 5.2);
- after exclusion of secondary forms of hypertension, especially primary aldosteronism, and chronic kidney disease with estimated glomerular filtration rate < 40 mL/min/1.73 m^2 (patients with severely impaired kidney function (Kidney Disease: Improving Global Outcomes stage G4 and G5) or requiring haemodialysis);
- after fully informing the patient about the benefit/risk ratio of RDN in a shared medical decision process considering the patient's preferences;
- after a multidisciplinary discussion with a specialized centre (ESH excellence centre or BP clinic);
- this indication is class II B according to 2023 ESH guidelines [2].

In addition, RDN may be proposed in other clinical settings after multidisciplinary discussion with a specialized centre (ESH excellence centre or BP clinic) including:

- uncontrolled hypertension with severe non-adherence to antihypertensive treatment preferably confirmed with objective chemical methods of drug detection (class II B according to 2023 ESH guidelines [2]);
- uncontrolled hypertension in patients with drug intolerance or adverse drug reactions with impairment of quality of life (class II B according to 2023 ESH guidelines [2]).

We have not included alcohol-based RDN in this section as this technology has not yet received US Food & Drug Administration approval. BP reductions with this device are lower than with other devices, although they are clinically meaningful and statistically significant, but further data are required to implement this technique in clinical practice.

5.1. Patient selection

Adult patients (≥ 18 years) should have confirmed uncontrolled primary hypertension following multidisciplinary assessment. Secondary causes of hypertension should have been excluded. The indication should be validated by multidisciplinary hypertension teams involving experts on hypertension and percutaneous cardiovascular interventions, either in person or remotely, ideally in ESH Excellence Centres or BP clinics located throughout France (for information see the map at https://www.sfhta.eu/liste-des-centres-dexcellence/). The decision-making process should involve the patient, who should be well informed about the benefits/limitations and risks associated with RDN.

To date, no biomarker has been identified to predict patient responsiveness to RDN. As with drugs, there is variability in patients' responses with BP reduction and this information should be shared with patients during their selection for RDN.

5.2. Pre-procedural imaging

The primary imaging modality for ruling out secondary causes of hypertension (adrenal tumours, renal artery stenosis of any origin including fibromuscular dysplasia [FMD], renal pathology [e.g. atrophic kidney, polycystic kidney disease]) or severe atherosclerotic, thrombotic or dissecting aortic and iliac lesions is abdominal/pelvic computed tomography (CT) scan, provided there are no contraindications. The abdominal/pelvic CT scan should be performed with thin slices without and with contrast including an arterial phase (≥ 300 Hounsfield Units in the abdominal aorta). Renal CT-angiography (CTA) should identify accessory renal arteries and early main renal artery bifurcation, and should provide measurements of the diameter and length of the main and accessory right and left renal arteries. In case of contraindication to CTA, magnetic resonance angiography (MRA) with sequences that provide clear imaging of the renal arteries and parenchyma can be used. CTA or MRA should exclude the following anatomical ineligibility criteria including [2,27]:

- inappropriate renal artery diameter/length (depending on the catheter used);
- atherosclerotic renal artery stenosis ≥ 30%;
- FMD of renal arteries whatever the degree of stenosis;
- single functional or solitary kidney;
- transplanted kidney;
- extensive abdominal aortic calcifications.

Catheter-based renal angiography is not indicated for screening purposes but remains the reference imaging modality immediately prior to RDN to confirm suitable renal artery anatomy and especially exclude renal FMD lesions that may go unnoticed on CTA or MRA. Duplex US of the renal arteries is highly operator-dependent and often uninformative – especially in obese patients

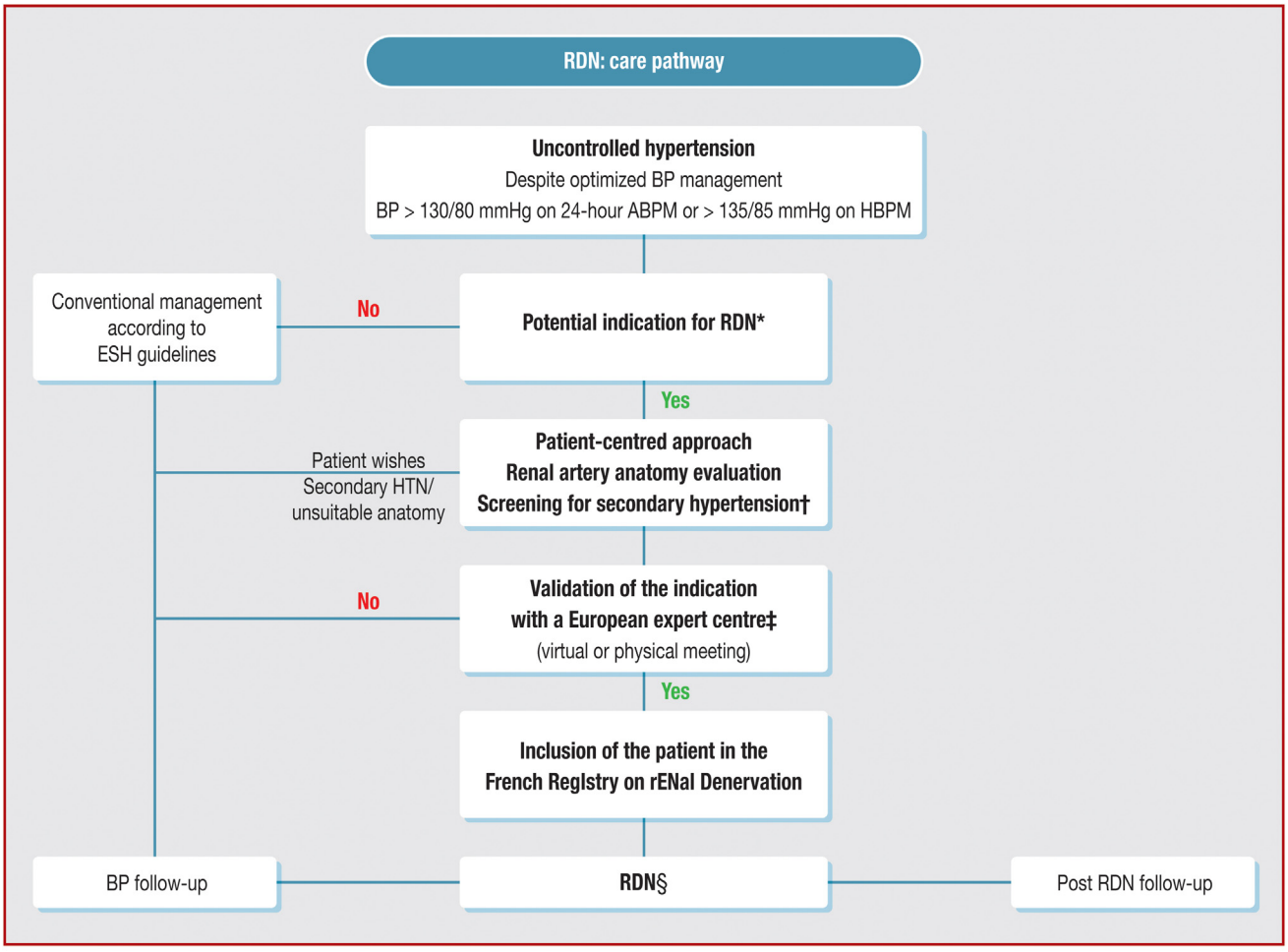


Fig. 2. Care pathway for a renal denervation procedure. *See chapter 5. †Rule out prohypertensive drugs, primary aldosteronism, renal artery stenosis, non-hypertensive nephropathy, Cushing disease, obstructive sleep apnoea syndrom3. ‡European expert centres are listed on the SFHTA website: https://www.sfhta.eu/liste-des-centres-dexcellence/. §RDN must be performed by a trained operator, not necessarily in a European Expert Centre. ABPM: ambulatory blood pressure measurement; BP: blood pressure; ESH: European Society of Hypertension; HBPM: home blood pressure measurement; RDN: renal denervation; SFHTA: Société française d'hypertension artérielle.

who are frequent candidates for RDN – and does not have enough sensitivity to detect FMD lesions or accessory renal arteries.

6. Organization of the RDN procedure

6.1. Endovascular interventionalists training and centre eligibility

Our 2012 statement [50] required that interventional physicians should have skills in catheter-based renal artery procedures and perform 15 procedures per year. In the past 10 years, there has been a significant decrease in the number of renal artery angioplasties/stentings, making it impossible for an endovascular interventionalists to reach the previous number of required procedures. As RDN can lead to severe complications (of the renal artery, kidney or puncture site), the interventionalist should feel comfortable in the management of renal artery procedures and related complications. Hence, interventional cardiologists/radiologists should have expertise in access site management, knowledge of radiation protection and expertise in specific aspects related to RDN and renal artery catheterization or stenting. In addition, they should undergo specific training in RDN procedures in practical and/or simulated sessions (through proctored sessions, RDN centre visits or hands-on with commercially available devices). To be eligible for an RDN programme, the RDN centre should have access (remotely or on site) to inpatient services, imaging facilities, an angiography-catheterization room, an intensive care unit, and access to vascular surgery services (Fig. 2).

6.2. Periprocedural management

A pre-anaesthesia consultation should be arranged. RDN is performed under sedation or short general anaesthesia because the procedure is painful [36]. Anticoagulant treatments may be temporarily suspended based on the individual risk/benefit balance to limit bleeding complications related to the access site. An antiplatelet agent (aspirin 75–100 mg) may be given for 1 month after the procedure but the evidence is low. The patient's antihypertensive medications are continued, including on the day of the intervention, unless there is an anaesthetic contraindication.

The total duration of the procedure is approximately 1 hour and the patient is monitored until the following morning in the hospital. Outpatient intervention can be organized, provided clear follow-up instructions are provided to the patient. Risks at the end of the procedure and during the hospitalization period are associated with the femoral access site, which is a general risk for any endovascular intervention. Currently, this risk of complications may be minimized using US-guided arterial puncture and arterial closure systems at the end of the procedure. The reduction in BP does not occur

immediately after the procedure but gradually appears over a few weeks (see below).

Radial access has been described for some devices, but the clinical evidence for its use in RDN has not been firmly established as yet [51]. Patient preparation and specific considerations for RDN devices have been previously reported [27].

7. Follow-up

Post-procedure follow-up is limited to optimization of antihypertensive medications after RDN and follow-up of the hypertensive disease. Plasma creatinine can be measured according to the local standard of care and ideally within 30 days, depending on the pre-RDN estimated glomerular filtration rate and the amount of contrast media injected during RDN. Despite the rarity of renal complications, we suggest performing a renal CTA or Duplex US between 6 months and 1 year after RDN to detect the occurrence of *de novo* renal artery stenosis.

BP follow-up is ideally conducted with out-of-office BP measurements (home or ambulatory BP measurements), preferably using the same method as the pre-procedure evaluation, at least at 1–3, 6 and 12 months. HBPM allows the reduction of antihypertensive medication if there is a large decrease in BP and the optimization of therapy in case of persistent uncontrolled BP.

8. The need for a French Registry of RDN (France-RDN)

To supervise the deployment of RDN in France, the joint expert group considers that all patients undergoing RDN should have their data collected in an independent nationwide registry, regardless of the type of catheter used and the indication for RDN. The objectives of this registry will include monitoring the activity of various French centres, the number of RDN procedures performed nationwide, the conditions under which this procedure is carried out and real-world results in terms of effectiveness and safety. This registry will provide health authorities with transparent, independent and up-to-date data on which to base decisions regarding the deployment of RDN in France.

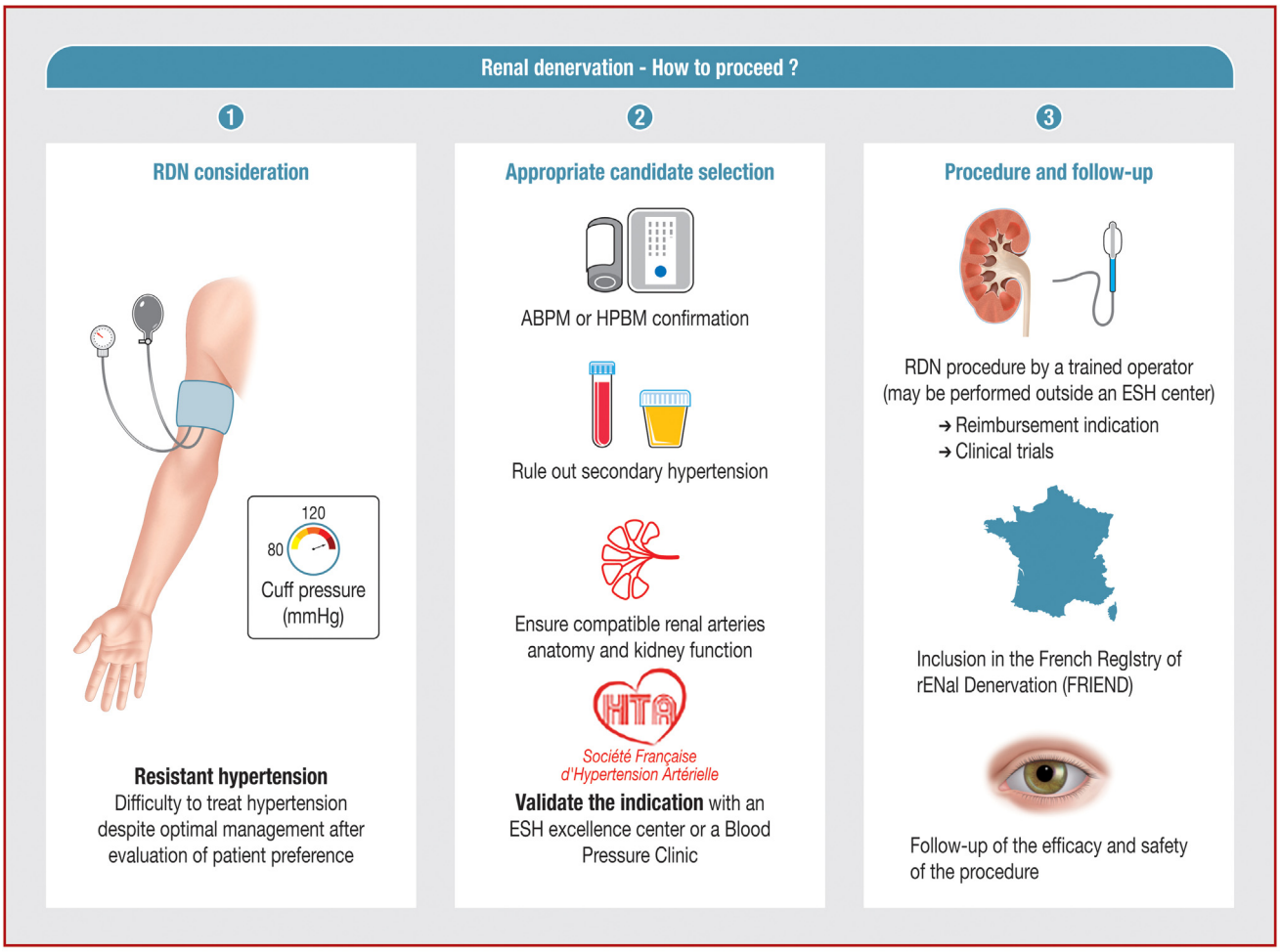
9. Health economic considerations

To date in France, the SPYRAL RF and Paradise US Catheter have both been given the same indication by the Haute Autorité de santé for treating patients with resistant hypertension despite four antihypertensive medications prescribed according to the standard of care [52,53], validation by ESH excellence centre or ESH BP clinic and after exclusion of secondary hypertension. To date, only the SPYRAL RF is reimbursed. The reimbursement procedure for the same indication is pending for the Paradise US catheter.

10. Perspectives

In order to promote best quality of care and access to this technology, the French Society of Hypertension is committed to supporting education and information in order to increase awareness about RDN and frame a patient pathway and support training and reimbursement.

Since RDN is a new and evolving procedure, there are likely to be future developments. Firstly, RDN via the radial approach is expected to become more common in the near future. Given that RDN can modulate the sympathetic nervous system, its effectiveness in other conditions such as heart failure, cardiac arrhythmias (including atrial fibrillation) and chronic kidney disease will likely be evaluated (Central Illustration).



Central Illustration. Summary of the present consensus' main propositions. ABPM: ambulatory blood pressure measurement; ESH: European Society of Hypertension; HBPM: home blood pressure monitoring; RDN: renal denervation. Created with BioRender.com.

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The other authors declare that they have no competing interest.

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