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Renal denervation in internal medicine: a FADOI Position Paper on behalf of the Vicenza Hypertension Multidisciplinary Team.
Endorsed by the Italian Society of Arterial Hypertension

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Abstract

Resistant hypertension (RH) remains a clinical challenge in internal medicine, associated with increased cardiovascular morbidity and mortality. Renal denervation (RDN), a catheter-based intervention targeting renal sympathetic nerves, has re-emerged as a promising “adjunctive” therapy following the publication of the latest sham-controlled randomized trials. Current data demonstrate that RDN provides a modest but consistent reduction in blood pressure, with a favorable safety profile in selected patients with RH and uncontrolled hypertension, despite optimized pharmacological therapy or in those with medication intolerance. This paper reviews the pathophysiological rationale, updated clinical evidence, patient selection criteria, procedural aspects, and future perspectives of RDN, for which a multidisciplinary approach is required to ensure procedural safety and optimal outcomes.

This position paper is not intended to be a new guideline but a practical recommendation on how to proceed with the selection of the patient candidate for RDN and his management before and after the procedure in internal medicine coordinated by a hypertension specialist.

Introduction

Hypertension is a leading modifiable risk factor for cardiovascular (CV) disease worldwide. Despite the availability of effective pharmacological therapies, a substantial proportion of patients fail to achieve adequate blood-pressure (BP) control. Resistant hypertension (RH), defined as uncontrolled BP despite the use of at least three antihypertensive agents including a diuretic, represents a particularly high-risk subgroup.¹ Over-activation of the sympathetic nervous system plays a central role in the pathogenesis of hypertension.² Renal denervation (RDN), which disrupts renal sympathetic nerve signalling,³ has been proposed as a therapeutic strategy to address this mechanism, and carries a class II recommendation for the treatment of resistant or uncontrolled hypertension in the main hypertension guidelines.⁴⁻⁶

Panel composition and consensus process

This Position Paper was developed by the Vicenza Hypertension Multidisciplinary Team, a standing hospital-based group including specialists in internal medicine, arterial hypertension, cardiology, anesthesiology, nephrology and interventional radiology. The panel was constituted as a multidisciplinary team by design, reflecting the multidisciplinary evaluation that current European Society of Hypertension (ESH) and European Society of Cardiology (ESC) guidelines regard as a pre-requisite for RDN. Relevant literature was identified by searching PubMed/MEDLINE and Embase up to 31 May 2026, using terms such as “renal denervation”, “resistant hypertension” and “uncontrolled hypertension”, supplemented by hand-searching of pertinent guideline and consensus documents; the search was narrative rather than systematic, prioritizing randomized sham-controlled trials, meta-analyses, and the 2023 ESH guidelines, the 2024 ESC/ESH guidelines, and the 2023 ESC Council on Hypertension/European Association of Percutaneous Cardiovascular Interventions (EAPCI) clinical consensus statement on RDN. Draft statements were prepared by a subgroup of the *Federazione delle Associazioni dei Dirigenti Ospedalieri Internisti* (FADOI) and of the Italian Society of Arterial Hypertension (SIIA) representatives and discussed by the full panel over three meetings; recommendations were retained when consensus, defined as agreement exceeding 90%, was reached. The certainty of the evidence supporting each statement was mapped to the class of recommendation and level of evidence assigned in the source ESH, ESC/ESH and ESC/EAPCI documents. The final document was approved under the auspices of FADOI and endorsed by the SIIA on 15 June 2026.

Pathophysiological rationale and blood-pressure lowering effect

The kidneys are richly innervated by sympathetic fibers that regulate renin secretion, sodium reabsorption, and renal vascular tone. Efferent sympathetic activity increases renin release and sodium retention, while afferent signals from the kidney enhance central sympathetic outflow. RDN interrupts these pathways, disrupting the sympathetic nerves located within the adventitial layer of the renal artery and thereby attenuating both afferent and efferent renal sympathetic nerve activity. This reduces systemic BP through suppression of renin secretion, promotion of natriuresis, and diminution of central sympathetic outflow.⁷ From a historical perspective, the initial enthusiasm for RDN was tempered by the neutral results of the SYMPPLICITY HTN-3 trial.⁸ Subsequently, the latest sham-controlled trials — SPYRAL HTN-OFF MED,^{9,10} SPYRAL HTN-ON MED,¹¹ RADIANCE-HTN SOLO and TRIO,^{12,13} and RADIANCE II¹⁴ — demonstrated consistent efficacy, with a reduction in 24-hour systolic BP of approximately 5-10 mmHg. Meta-analyses confirm that RDN significantly reduces both office and ambulatory BP, with consistent effects across devices and patient populations.^{15,16}

Procedural considerations

RDN is performed via a percutaneous catheter-based approach using radiofrequency or ultrasound energy,¹⁷ under angiographic guidance (Figure 1). It demonstrates a favorable safety profile, with low complication rates and no consistent evidence of long-term renal-artery damage or decline in

renal function.¹⁸ European hypertension guidelines recognize RDN as an adjunctive option for selected patients, to be performed in experienced centers;^{4,5} its technical conduct and the roles of the team are detailed in the next section.

Multidisciplinary approach to renal denervation

A structured multidisciplinary model is essential. We suggest a core team (Figure 2) comprising a hypertension specialist/internist, a nephrologist, an interventional cardiologist or radiologist, and an anesthesiologist; the contribution of each is described below.

RDN is not a single-operator intervention but the endpoint of a structured, multidisciplinary pathway, and the guidelines that endorse it do so only when it follows thorough multidisciplinary evaluation. Rather than describe each specialty role, we mapped the contribution of each discipline to the stage of the pathway at which it acts (Table 1).

Referral, confirmation of true resistant hypertension and therapy optimization

The internist — ideally an ESH-certified hypertension specialist — is the gatekeeper and coordinator of the pathway.^{19,20} Patients with apparent RH, poor control despite multidrug therapy, suspected secondary hypertension or suspected non-adherence are referred by general practitioners and by cardiologists, nephrologists, endocrinologists and neurologists. The first task is to separate true RH from pseudo-resistance through correct BP measurement, ambulatory or home monitoring, exclusion of the white-coat effect and objective adherence assessment; an Italian SIIA survey found RDN volumes highest in internal-medicine centers.^{21,22} Therapy is then optimized to guideline-directed combinations (including a diuretic and a mineralocorticoid-receptor antagonist where indicated) with reinforcement of lifestyle measures, since RDN is indicated only after failure of optimal medical therapy.²³ Multiple drug-intolerance syndrome is a separate route to eligibility, after multidisciplinary evaluation and shared decision-making.²⁴

Exclusion of secondary hypertension and renal assessment

The internist and nephrologist jointly exclude secondary causes — primary aldosteronism, renal parenchymal and renovascular disease, obstructive sleep apnea and endocrine causes — before RDN is entertained.²⁵⁻²⁷ Primary aldosteronism warrants particular attention, affecting roughly 20% of RH yet recognized in fewer than 2% of eligible patients²⁸. The nephrologist characterizes baseline renal status [estimated glomerular filtration rate (eGFR), albuminuria, electrolytes], which stratifies procedural risk and anchors long-term safety monitoring^{29,30}. RDN is established for $\text{eGFR} \geq 40$ mL/min/1.73 m², with emerging evidence in more advanced chronic kidney disease (CKD), dialysis and transplantation, for which we refer to the position paper of the Italian Society of Nephrology.³¹ Where iodinated contrast is contraindicated, CO₂ angiography offers a non-nephrotoxic alternative, planned jointly by the hypertension specialist, nephrologist and interventional operator.³²

Vascular anatomical assessment

Renal-artery anatomy is evaluated by computed tomography or magnetic resonance (CT or MR) angiography, interpreted by the radiologist with input from the nephrologist and interventional operator.^{33,34} Assessment covers artery diameter and length, accessory arteries, atherosclerotic burden, fibromuscular dysplasia and structural anomalies, and identifies findings that preclude or modify RDN — significant stenosis, prior stenting or surgery, heavy calcification or complex anomalies — while the same imaging guides procedural planning.³⁵

Multidisciplinary eligibility and shared decision-making

Final eligibility is a joint decision of the hypertension team, coordinated by the internist.^{36,37} Counselling covers selection criteria, procedural risks and limitations, the need for continued antihypertensive therapy — RDN is not curative — and long-term follow-up, so consent is given

within a realistic framework.³⁸ A procedural checklist (Table 2), based on SIIA recommendations, supports this step.³⁹

Procedure

The interventional cardiologist or interventional radiologist performs RDN, confirming anatomical suitability, selecting the device platform (radiofrequency or ultrasound) and access (usually femoral, radial in selected cases), and delivering circumferential ablation of the main artery and branches, since incomplete denervation reduces efficacy;^{40,41} the operator balances effective ablation against vascular integrity and monitors angiographically for dissection, spasm and thrombosis.⁴² Because energy delivery is painful, the anesthesiologist manages analgesia and conscious sedation with short-acting agents titrated to maintain analgesia, immobility and hemodynamic stability under continuous monitoring until safe transfer;^{43,44} agents and doses are specified in the procedural checklist (Table 2).

Complications, recovery and long-term follow-up

Access-site complications, renal-artery injury and vasospasm are managed by the interventional operator,⁴⁵ with post-procedural imaging detecting rare events such as dissection, pseudo-aneurysm or late stenosis.⁴⁶ The anesthesiologist monitors for post-procedural hypotension and sedation-related events and, with the hypertension specialist, supervises recovery and discharge.¹⁹ The nephrologist advises peri-procedural renal protection (hydration, review of nephrotoxic drugs) where relevant.³⁰ Long-term care returns to the internist and nephrologist: office and out-of-office BP monitoring, adjustment of antihypertensive therapy, management of CV risk factors and lifestyle, and surveillance of renal function and CKD progression.^{31,38}

Patient selection

Selection for RDN answers two questions in sequence: is device-based therapy indicated and is it anatomically feasible and clinically appropriate in this patient? Current guidance from the 2023 ESH guidelines, the 2024 ESC/ESH guidelines and the 2023 ESC Council on Hypertension/EAPCI clinical consensus statement converges on four indications — uncontrolled hypertension despite optimised therapy, true RH, intolerance of or inability to adhere to antihypertensive medication, and an informed patient preference — offered only to patients at raised CV risk after multidisciplinary evaluation and shared decision-making.^{4,5,47}

As emphasized above, eligibility presupposes confirmation of true resistant or genuinely uncontrolled hypertension by ambulatory or home monitoring with objective adherence assessment, and exclusion of secondary and potentially reversible causes. Beyond these established prerequisites, several practical determinants warrant explicit consideration.

Anatomical eligibility

Renal-artery anatomy is assessed by CT or MR angiography and, definitively, by selective angiography at the time of the procedure. Contemporary devices generally require a main renal artery of 3–8 mm in diameter and at least 20 mm of treatable length, and exclude vessels with hemodynamically significant stenosis (typically >50%), heavy calcification that would prevent delivery of an adequate number of ablations, renal-artery aneurysm, diffuse fibromuscular dysplasia, or prior renal-artery stenting or surgery.^{35,48} Thresholds are device-dependent: radiofrequency systems can treat vessels from approximately 3 mm and extend ablation into branches, whereas ultrasound systems treat the main artery within the 3–8 mm range.^{35,47} A solitary functioning kidney and unfavorable aorto-renal angulation are further considerations that may modify feasibility.

Management of accessory renal arteries

Accessory or polar renal arteries are present in roughly a quarter to a third of patients and are a recognized determinant of the completeness of denervation.^{35,48} Most trials have permitted accessory

arteries provided they do not supply more than about 25% of the ipsilateral parenchyma; the practical question is whether an accessory vessel is itself treatable. With newer radiofrequency platforms, accessory and branch vessels of adequate caliber (generally ≥ 3 mm) can be ablated, whereas smaller accessory arteries cannot be reached and their sympathetic supply is left intact, which may attenuate the BP response.⁴⁸ The number, caliber and treatability of accessory arteries should therefore be documented at screening and factored into both procedural planning and the expected efficacy communicated to the patient.

Older and frail patients

Age alone is not a contraindication to RDN. However, isolated systolic hypertension — common in older patients and driven largely by arterial stiffness — has been debated as a less favorable substrate; while some analyses suggested a smaller effect, registry data (Global Symplicity Registry) and the RADIOSOUND comparison reported efficacy comparable to that in combined systolic–diastolic hypertension.⁴ In frail individuals, the decision should be individualized, weighing life expectancy, competing risks, procedural tolerance and goals of care against a modest average BP benefit; current guidelines already recommend individualized targets in the very old and frail.^{4,5} Conversely, a device-based option may be particularly attractive where polypharmacy, intolerance or poor adherence limit medical therapy, and shared decision-making is central in this group.

Advanced chronic kidney disease and the eGFR threshold

The $\text{eGFR} \geq 40$ mL/min/1.73 m² threshold reflects the inclusion criteria of the pivotal sham-controlled trials rather than a mechanistic limit and should be read as a pragmatic default rather than an absolute cut-off. Accordingly, current ESC/EAPCI consensus advises against RDN in KDIGO stages G4–G5 and in kidney-transplant recipients in the absence of adequate evidence.^{5,30,47} That position is now being revisited: observational cohorts and recent meta-analyses report meaningful BP reduction with preserved renal function and an acceptable safety profile in CKD, and a position paper of the Italian Society of Nephrology specifically addresses RDN at $\text{eGFR} < 40$ mL/min/1.73 m², including dialysis and transplantation.^{31,38} Pending confirmatory randomized data, RDN below the threshold should be regarded as an individualized, multidisciplinary decision rather than a routine indication — a stance that reconciles the conservative eGFR criterion with the emerging evidence presented later in this document.

Predictors of response

A recognized limitation of RDN is the absence of a validated tool to identify, before the procedure, which patients will respond. The BP reduction after RDN shows substantial inter-individual variability, and a clinically meaningful proportion of patients derive little benefit, yet no pre-procedural marker reliably distinguishes responders from non-responders.^{15,18}

Several candidate predictors have been proposed and should be regarded as hypothesis-generating rather than established selection criteria: higher baseline office and ambulatory BP; indirect markers of heightened sympathetic activity such as elevated resting heart rate; preserved renal function; combined systolic–diastolic (as opposed to isolated systolic) hypertension; and procedural factors, notably the completeness of ablation, including treatment of accessory arteries and branches. None of these is sufficiently validated to include or exclude a patient on its own.^{5,40}

The practical consequence is twofold. First, patient counselling must set realistic expectations, making explicit that a response cannot be guaranteed and that antihypertensive therapy continues after the procedure. Second, identification of reliable responder predictors remains a research priority, and participation in registries and structured follow-up is one way individual programs can contribute to answering it.

Limitations and controversies of renal denervation

RDN is now supported by second-generation, randomized sham-controlled trials showing a consistent, if modest, reduction in BP; this consistency is the strongest part of the evidence base. The principal unresolved issues concern what that reduction ultimately delivers.

Surrogate rather than outcome evidence

The pivotal trials are powered for BP, not for hard endpoints. Direct evidence that RDN reduces myocardial infarction, stroke, progression of chronic kidney disease or mortality is lacking, and any such benefit is currently inferred from the established relationship between BP reduction and CV risk. BP lowering therefore remains a surrogate marker of efficacy, with residual uncertainty about net long-term clinical benefit and safety.^{8,15,18}

Modest and variable effect

The average placebo-adjusted reduction is of the order of 4-6 mmHg — clinically meaningful across a population but limited for an individual, and obtained through an invasive procedure.¹⁵ Efficacy is notably variable between patients, and this variability, together with the absence of a validated tool to identify responders in advance, is a principal reason RDN is positioned as an adjunctive rather than a standard therapy for RH. The variability reflects heterogeneity in patient selection, in the underlying pathophysiology of hypertension, and in procedural factors affecting the completeness of sympathetic denervation.

Durability and generalizability

Sustained effects are now reported to three years from the SPYRAL HTN-ON MED trial and from large registries such as the Global Symplicity Registry, but longer-term efficacy and safety data are still accumulating;^{8,42,49,50} trial populations are moreover selected and procedures performed in experienced centers, which may limit generalizability to routine practice.

Taken together, these considerations argue for measured rather than enthusiastic adoption: RDN is a reasonable complementary option for carefully selected and counselled patients, but not a substitute for pharmacological and lifestyle treatment, and its place will be defined by the outcome data now awaited.

Practical implementation of a renal denervation program

Translating the evidence into an internal-medicine setting requires an explicit organizational structure rather than ad hoc referral. Drawing on the pathway above and on SIIA recommendations, we propose the following elements as the operational core of an RDN program.

- A defined referral pathway into a hypertension team, with explicit criteria for who should be referred (apparent resistant or uncontrolled hypertension on optimized therapy, documented intolerance, or informed patient request) and clear entry points for general practitioners and specialists.
- A standardized pre-procedural workup — confirmation of true RH, exclusion of secondary causes and renal-artery imaging — carried out to a common protocol so that eligibility decisions are consistent and auditable.
- A multidisciplinary eligibility meeting at which the team reaches and documents a joint decision, supported by the procedural checklist (Table 2).
- An appropriately equipped and staffed procedural environment, with trained operators, a defined sedation and analgesia protocol, and arrangements for the management of procedural complications.
- A structured follow-up schedule with office and out-of-office BP monitoring and renal-function surveillance at defined intervals, led by the internist/hypertension specialist and nephrologist.

- Shared decision-making throughout, with explicit and realistic expectation-setting and reinforcement that RDN complements, rather than replaces, pharmacological and lifestyle treatment.
- Participation in a registry or structured audit, both for quality assurance and to contribute to the outstanding questions on durability and responder prediction.

Situating this program within internal-medicine departments is consistent with Italian practice, where RDN activity has been concentrated in internal-medicine centres, and positions the internist/hypertension specialist as the coordinator of a safe, auditable and patient-centred RDN service.

Health economics and reimbursement

The principal economic tension is between the upfront cost of an invasive procedure and the long-term value of a therapy whose benefit is currently demonstrated on a surrogate endpoint. Against this, formal cost-effectiveness analyses have been reassuring: decision-analytic (Markov) models from the perspective of several European health systems — including the United Kingdom (using NICE methodology), Spain and Sweden — have found radiofrequency RDN to fall within accepted willingness-to-pay thresholds over a lifetime horizon, and a recent systematic review across multiple countries reached broadly concordant conclusions.⁵¹⁻⁵⁴ These analyses are, however, model-based and inherit the limitation of the clinical evidence, in that projected outcome benefits are derived from BP reduction rather than observed hard endpoints.

Reimbursement and access are considerably more heterogeneous than cost-effectiveness modelling alone would suggest, and are gated in many countries by formal health-technology assessment (for example NICE in the United Kingdom and HAS in France). Within Italy, access is not uniform and procedural provision varies at the regional level in line with local budgetary and organizational constraints^{21,55}. We therefore present the international reimbursement picture cautiously: it is fragmented and evolving, and specific national arrangements should be verified against current local health-policy sources.

Future directions

The central research priority is to establish whether RDN confers benefit beyond BP reduction, in particular on hard CV outcomes such as stroke and myocardial infarction and on renal endpoints; ongoing trials and long-term follow-up of existing programs, including the SPYRAL HTN program and large registries, are directed at this question. Evidence on hard outcomes, together with tools to identify likely responders before the procedure, will be decisive for wider guideline endorsement and for reimbursement, and represents the main determinant of the future role of RDN in routine hypertension care.

Conclusions

RDN is a safe and, in selected patients with uncontrolled or RH, effective adjunctive therapy. Its role remains complementary to — not a replacement for — optimized pharmacological and lifestyle treatment, and it should be offered with realistic expectations, given a modest and variable average effect and hard-outcome data that are still awaited. Within these limits, optimal and safe implementation depends on the structured, multidisciplinary approach set out in this document, which is best placed to ensure appropriate patient selection, procedural success and long-term follow-up.

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Table 1. Discipline roles across the renal denervation pathway.

Pathway stage	Principal tasks	Lead discipline(s)	Contributing
Referral and triage	Identify apparent resistant/uncontrolled hypertension	Internist/hypertension specialist	Cardiology, nephrology, radiology
Confirm true RH and optimize therapy	BP technique, ABPM/HBPM, white-coat, adherence; guideline-directed combinations, diuretic/MRA, lifestyle	Internist/hypertension specialist	—
Exclude secondary hypertension	Primary aldosteronism, renal parenchymal/renovascular disease, OSA, endocrine causes	Internist/hypertension specialist; nephrologist	Endocrinology as needed
Renal function and risk stratification	eGFR, albuminuria, electrolytes; eGFR threshold; contrast vs CO ₂	Nephrologist	Hypertension specialist, interventional operator
Renal-artery imaging and eligibility	CTA/MRA: diameter, accessory arteries, stenosis, FMD, calcification	Radiologist	Interventional operator, nephrologist
Eligibility decision and consent	Joint decision; counselling; realistic expectations	Internist/hypertension specialist (coordinator)	All team members
Procedural planning	Device platform, vascular access, ablation strategy	Interventional cardiologist/radiologist	Radiologist
Procedure: execution and sedation	Catheter navigation, circumferential ablation, angiographic monitoring; analgesia and conscious sedation	Interventional cardiologist/radiologist; anaesthesiologist	Radiologist (imaging support)
Complications, recovery and discharge	Access-site/renal-artery injury, vasospasm; post-procedural imaging; hypotension and sedation recovery	Interventional cardiologist/radiologist; anaesthesiologist	Radiologist, hypertension specialist
Long-term follow-up	BP monitoring, therapy adjustment, CV risk, renal surveillance	Internist/hypertension specialist; nephrologist	—

RDN, renal denervation; BP, blood pressure; ABPM/HBPM, ambulatory blood pressure monitoring/home blood pressure monitoring; MRA, mineral-corticoid antagonist; OSA, obstructive sleep apnea; eGFR, estimated glomerular filtration rate; CO₂, carbon dioxide; CT, computed tomography angiography; MRA, magnetic resonance angiography; FMD, fibromuscular dysplasia; CV, cardiovascular.

Table 2. Procedural steps for renal denervation in internal medicine settings.

Step	Decisions making
1	In selected hypertensives one week before RDN, confirm office BP with ABPM-24h values (i.e. $\geq 130/80$ mmHg) and adherence to the anti-hypertensive treatment
2	<i>The day of admission, before RDN:</i> a) Measurement of office BP and HR values in sitting and standing position, taking three consecutive readings on 1-2 minutes apart, using an automated device b) The patient agrees to undergo RDN and provides signed informed consent c) Blood sampling for complete blood and platelet count, serum glucose, creatinine and eGFR, serum sodium and potassium, PT and aPTT is provided d) Antihypertensive medications should be taken as usual before e) Antiplatelet therapy should be started (i.e. acetylsalicylic acid 100 mg / daily) f) Electrocardiogram g) Anesthesiology consultation: RDN is usually performed under conscious sedation. When required, short-acting agents are used, like opioids as fentanyl (bolus of 25-50 μg IV, repeat as needed, total usually of 50-150 μg) and sedatives as midazolam (bolus of 1-2 mg IV, total usually ≤ 3-5 mg) or propofol (small boluses of 10 - 30 mg IV or infusion of 1-3 mg/kg/h).
3	<i>What to do after RDN:</i> a) Close monitoring of vital parameters (i.e., BP and HR) and the insertion site of the femoral catheter must be carried out b) If no complications are observed, 24 hours after the procedure patient is discharged
4	<i>Follow-up of RDN</i> a) Established a close home-BP evaluation and scheduled ABPM-24h at 2nd, 6th and 12th month from the RDN b) Antiplatelet therapy is recommended for at least one month after RDN in order to avoid thrombotic events c) An outpatient follow-up visit is scheduled with the complete blood count, creatinine, eGFR and potassium report 2 months after the RDN procedure d) A color-doppler ultrasound of the renal arteries at 3rd and at 12th month from the RDN is recommended

aPTT, activated partial thromboplastin time; ABPM, ambulatory blood pressure monitoring; BP, blood pressure; eGFR, estimated glomerular filtration rate; HR, heart rate; IV, intravenous; PT, prothrombin time.

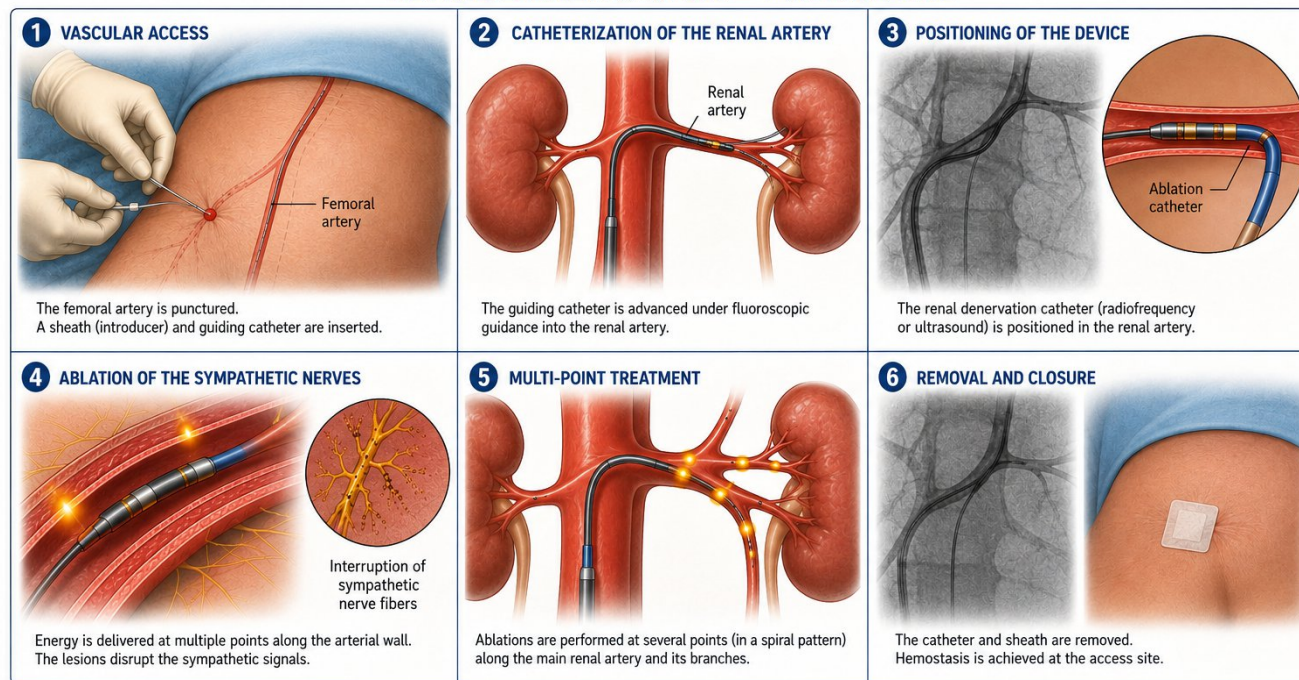


Figure 1. Renal denervation procedure, step by-step using catheter radiofrequency or ultrasound technique.

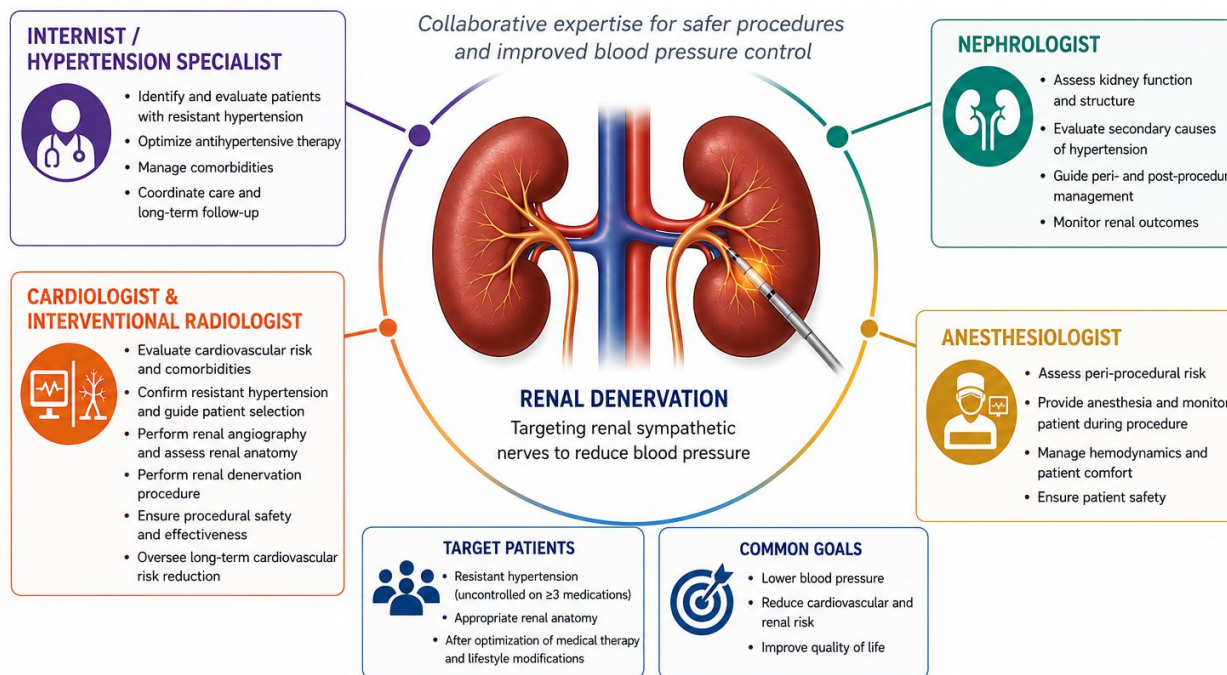


Figure 2. Multidisciplinary approach to renal denervation.