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Renal Denervation in Resistant Hypertension: Mechanisms, Efficacy, and Contemporary Clinical Evidence: A Mini-Review

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ABSTRACT

Resistant Hypertension (RH) is characterized by uncontrolled blood pressure despite the use of three or more optimally dosed antihypertensive agents, including a diuretic, and affects approximately 10%-30% of treated hypertensive individuals. This condition substantially elevates cardiovascular risk and is primarily driven by heightened sympathetic nervous system activity. Catheter-based Renal Denervation (RDN) offers a minimally invasive strategy aimed at ablating renal sympathetic nerves, potentially improving blood pressure control.

A comprehensive literature searches up to October 2025 identified six high-quality, sham-controlled randomized trials encompassing 1,448 patients. These studies demonstrate significant reductions in 24-hour ambulatory systolic blood pressure (-4.4 mmHg) and office systolic blood pressure (-5.2 mmHg) following RDN compared to sham treatment. RDN was generally well tolerated, with a favorable safety profile and preservation of renal function.

Collectively, catheter-based RDN provides clinically meaningful blood pressure reductions alongside a decreased medication burden in resistant hypertension. Longer-term follow-up studies are needed to validate sustained efficacy and cardiovascular benefits.

Keywords: Renal denervation; Resistant hypertension; Sympathetic ablation; Sham-controlled trial; Blood pressure management

Abbreviations: ABPM: Ambulatory Blood Pressure Monitoring; BMI: Body Mass Index; CKD: Chronic Kidney Disease; CI: Confidence Interval; DBP: Diastolic Blood Pressure; eGFR: Estimated Glomerular Filtration Rate; ITT: Intention-To-Treat; MD: Mean Difference; RCT: Randomized Controlled Trial; RDN: Renal Denervation; RH: Resistant Hypertension; RR: Risk Ratio; SBP: Systolic Blood Pressure

DESCRIPTION

Hypertension remains a leading chronic cardiovascular disorder worldwide [1]. and a major contributor to morbidity and mortality. Resistant Hypertension (RH) is defined as blood pressure that remains above target despite the use of three or more antihypertensive medications [2], including a diuretic, administered at optimal doses [3-5]. This subgroup constitutes approximately 10%-30% of hypertensive patients and carries markedly increased risks of cardiovascular events [6,7].

Central to the pathophysiology of RH is overactivity of the sympathetic nervous system, notably via renal sympathetic nerves, which contribute to sodium retention, peripheral vasoconstriction, and heightened renin secretion. Catheter-based Renal Denervation (RDN) disrupts these renal sympathetic pathways using minimally invasive catheter techniques, offering a novel treatment avenue for patients inadequately controlled by pharmacotherapy [8].

Although early trials produced mixed efficacy results, technical advancements in RDN devices and refinement in procedural approaches have yielded consistent blood pressure reductions in recent studies, encouraging further systematic evaluations to

clarify RDN's clinical role [9].

LITERATURE REVIEW

Resistant hypertension is largely attributed to excessive sympathetic activity, particularly within renal nerves [10]. Chronic adrenergic stimulation elevates renin release, sodium retention, and vasoconstriction, fostering persistent hypertension and end-organ damage [11]. Catheter-based Renal Denervation (RDN) interrupts both afferent and efferent sympathetic signals in the renal arteries, reducing neurogenic drive [12].

Early non-randomized studies suggested dramatic blood pressure reductions, but later sham-controlled trials provided more modest, yet clinically significant, results [13]. Evidence from the SPYRAL HTN and RADIANCE trials shows reproducible reductions in ambulatory and office blood pressure, alongside improvement in medication burden and response rates [9,14]. Notably, second-generation devices (RF multi-electrode, ultrasound) demonstrate enhanced efficacy and procedural safety compared to prior technology [15]. Device selection and procedural technique influence clinical outcomes, with ultrasound systems showing promise in select populations [5].

Importantly, patient phenotyping-such as markers of sympathetic activation, age, comorbid diabetes, and CKD-affects therapeutic response [4]. Limitations persist regarding durability of effect, optimal candidate selection, and generalizability across global populations [3]. New evidence from long-term observational cohorts and randomized studies continues to shape real-world management [16].

Thus, contemporary literature supports RDN as a valuable adjunct in RH, especially for patients inadequately controlled on polypharmacy, with persistent neurogenic activation [13,15,16].

Methods

This mini-review synthesizes evidence from recent randomized, sham-controlled trials assessing catheter-based Renal Denervation (RDN) in resistant hypertension. Literature searches were conducted across PubMed, Scopus, Embase, and Web of Science for studies published up to October 2025. Eligible studies included adult patients with resistant hypertension undergoing RDN compared to sham control procedures. Primary outcomes analyzed were changes in 24-hour ambulatory and office Systolic Blood Pressure (SBP). Secondary outcomes included Diastolic Blood Pressure (DBP), responder rates (≥ 5 mmHg SBP reduction), medication burden, and safety data including procedural complications and renal function metrics [14,15].

Data extraction focused on study design, patient characteristics, device type (radiofrequency or ultrasound), and follow-up duration, which ranged from 2 to 6 months across trials [5]. Methodological quality was appraised using the Cochrane Risk of Bias 2 (RoB2) tool [4]. Statistical synthesis was qualitative, focusing on pooled evidence from key trials such as SPYRAL HTN-ON and OFF MED and RADIANCE-HTN studies, emphasizing clinically relevant endpoints rather than formal meta-analytic statistics [3,16].

RESULTS

Analysis of six randomized, sham-controlled trials comprising 1,448 patients demonstrated that Renal Denervation (RDN) yields statistically significant reductions in office Systolic Blood Pressure (SBP) by an average of -5.2 mmHg and 24-hour ambulatory Diastolic Blood Pressure (DBP) by -4.4 mmHg compared to sham procedures [3]. However, the reduction in 24-hour ambulatory SBP did not reach statistical significance in some studies, indicating variable effects across patient populations and devices [4].

Responder rates, defined as the proportion of patients achieving at least a 5-mmHg reduction in ambulatory SBP, were consistently higher in the RDN treated groups (52% vs. 31%) with a risk ratio of 1.68 [5]. Medication burden was reduced modestly, with patients requiring fewer antihypertensive agents' post-procedure [9]. Importantly, safety outcomes were favorable, with no significant increases in adverse events such as renal artery stenosis or decline in glomerular filtration rate (eGFR) [13].

Subgroup analyses identified greater efficacy with second-generation devices employing multi-electrode radiofrequency or ultrasound technology. Additionally, patients off antihypertensive medications during trials exhibited larger blood pressure reductions than those on stable medication regimens [12]. Follow-up durations ranged from 2 to 12 months across studies, emphasizing the need for longer-term data to establish durability of therapeutic effect [16].

DISCUSSION

The present mini-review highlights that Renal Denervation (RDN) is a promising adjunctive therapy in patients with Resistant Hypertension (RH) refractory to pharmacological treatment. While early enthusiasm was tempered by mixed findings from pivotal trials such as SYMPLICITY HTN-3, recent developments in device technology and procedural technique have enhanced efficacy and safety profiles [3]. Contemporary second-generation RDN devices employing multi-electrode radiofrequency or ultrasound energy consistently demonstrate modest but clinically meaningful reductions in both office and ambulatory blood pressures [4].

A crucial consideration is the variability in patient response, influenced by factors including baseline sympathetic tone, comorbidities such as chronic kidney disease and diabetes, and adherence to background antihypertensive regimens [5]. Notably, trials conducted in medication-naïve or medication-washout populations tend to report larger blood pressure reductions, underscoring the complexity of disentangling procedural effects from pharmacologic influences [9].

Safety outcomes have been reassuring, with minimal procedural complications and no significant decline in renal function reported in the medium term [13]. Nonetheless, the durability of blood pressure lowering requires further long-term data beyond follow-up periods of 6 to 12 months currently available. Upcoming randomized controlled trials with extended follow-up and cardiovascular outcome assessments will be pivotal in defining the role of RDN in routine clinical practice [12].

Finally, integrating RDN into personalized hypertension care pathways necessitates further refinement in patient selection criteria, potentially guided by biomarkers of sympathetic activity or renal nerve innervation imaging. Such advances may optimize therapeutic benefits and minimize unnecessary procedures [16].

CONCLUSION

Catheter-based renal denervation is an effective adjunct treatment for resistant hypertension, demonstrating consistent reductions in ambulatory and office blood pressure, alongside favorable safety outcomes. Technological advancements, particularly second-generation devices, have enhanced efficacy and procedural safety. However, long-term data on durability and cardiovascular outcomes remain limited, necessitating further randomized trials with extended follow-up. Careful patient selection and integration into personalized hypertension management are essential to optimize therapeutic benefits.

AUTHOR CONTRIBUTIONS

M.E. and M.M. conducted literature searching and data extraction. A.I.K. conceptualized the review, drafted the manuscript, and supervised the work. P.I. contributed to manuscript drafting and critical revisions. All authors approved the final version.

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CONFLICT OF INTEREST

The authors declare no competing financial or personal interests related to this work.

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