


## Medical & Clinical Case Reports Journal

<https://urfpublishers.com/journal/case-reports>

Vol: 3 & Iss: 2

Case Report

### Management of Resistant Hypertension: Recent Major Advances

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**Citation:** Ruppen IC, Pivato LS, Gois GA, et al. Management of Resistant Hypertension: Recent Major Advances. *Medi Clin Case Rep J* 2025;3(2):848-849. DOI: doi.org/10.51219/MCCRJ/Ian-Caldeira-Ruppen/222

**Received:** 14 April, 2025; **Accepted:** 16 April, 2025; **Published:** 18 April, 2025

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### ABSTRACT

Resistant Hypertension (RH) is characterized by persistently elevated blood pressure despite the use of at least three antihypertensive drug classes, including a diuretic, in adequate doses. This condition presents a clinical challenge due to the significantly increased cardiovascular risk and associated morbidity and mortality. In recent years, RH management has evolved considerably, driven by advancements in pharmacological interventions, non-pharmacological techniques and patient stratification based on genetic factors and biomarkers. Effective treatment requires a multidisciplinary approach, ranging from lifestyle modifications and medication adherence monitoring to the utilization of technologies such as renal sympathetic denervation and baroreflex devices.

**Keywords:** Resistant hypertension; Blood pressure control; Renal denervation; Baroreflex; Pharmacological management

### Introduction

Hypertension is a leading cause of morbidity and mortality worldwide, responsible for complications such as stroke, heart failure and chronic kidney disease<sup>1,2</sup>. Within this spectrum, resistant hypertension (RH) represents a particularly challenging subgroup. RH is defined as persistently elevated blood pressure despite concurrent use of three or more antihypertensive medications from different classes, including a diuretic<sup>3-5</sup>. The

estimated prevalence of RH varies between 10% and 20% among hypertensive patients, depending on the population studied and diagnostic criteria applied<sup>6,7</sup>. This condition is associated with a significantly elevated cardiovascular risk, demanding special attention from healthcare providers. However, RH diagnosis is not always straightforward, as factors such as poor adherence to treatment, inaccurate blood pressure measurements and white-coat hypertension can simulate RH, characterizing so-called

“pseudo-resistant hypertension”<sup>8-10</sup>. “Pathophysiological mechanisms underlying RH include heightened sympathetic nervous system activation, renal sodium retention, endothelial dysfunction and insulin resistance”<sup>11,12</sup>. These factors contribute to blood pressure control difficulties, necessitating more complex and individualized therapeutic approaches. Historically, RH management relied on adjustments in pharmacological regimens and lifestyle interventions, such as dietary sodium reduction and weight loss<sup>13</sup>. However, these methods frequently fail in patients with true RH, prompting research into more effective alternatives. Significant advancements have been made in recent years, including the development of new drug classes and the introduction of interventional techniques such as renal denervation. Moreover, the growing integration of precision medicine and technological applications in hypertension management offers promising future perspectives.

## Objectives

This article aims to review recent significant advances in managing resistant hypertension, discussing clinical applicability, knowledge gaps and future perspectives for treating this complex condition.

## Materials and Methods

A bibliographic review of articles published in PubMed, ScienceDirect and SciELO databases was conducted to support this study.

## Discussion

The management of resistant hypertension has benefited from innovations combining advanced pharmacological therapies, non-pharmacological interventions and emerging technologies. Lifestyle management remains foundational in RH treatment. Sodium reduction, weight loss, regular physical activity and alcohol consumption reduction are associated with significant benefits. However, isolated effectiveness is limited in patients with true RH, underscoring the necessity of complementary strategies<sup>14</sup>.

New medications have broadened therapeutic options for RH. Mineralocorticoid receptor antagonists, such as spironolactone and eplerenone, have demonstrated clinical efficacy, especially in patients with hyperaldosteronism<sup>15</sup>. Angiotensin receptor-neprilysin inhibitors (ARNIs), like sacubitril/valsartan, have shown potential for improving blood pressure control in specific subgroups. A crucial aspect of RH management is treatment adherence. Studies indicate that up to 50% of patients diagnosed with RH exhibit poor medication adherence. Utilizing technological devices, such as blood pressure monitors connected to digital health applications and platforms, facilitates continuous monitoring and personalized treatment.

## Conclusion

Recent advances in managing resistant hypertension offer promising perspectives for improving blood pressure control in affected patients. Introducing new pharmacological classes and developing interventional approaches, such as renal denervation, represent significant steps forward. Clearly, no single solution exists for RH. Effective management requires a multidisciplinary approach considering pathophysiological aspects, treatment adherence and patient social conditions. Precision medicine emerges as a powerful tool capable of

personalizing interventions and optimizing therapeutic outcomes. However, its widespread use still faces challenges, including the need for further research and practical implementation in clinical routines. Future advancements in artificial intelligence and accessible technologies are expected to expand access to therapeutic innovations. Additionally, strengthening public health policies and educational programs will be essential to improve treatment adherence and reduce the societal burden of resistant hypertension.

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