Comparing renal denervation versus pharmacological optimization in uncontrolled hypertension

Comparación de la denervación renal frente a la optimización farmacológica en la hipertensión no controlada

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Abstract

Uncontrolled hypertension persists as a major cardiovascular threat in Uzbekistan, where resistant cases challenge standard pharmacological approaches. This prospective randomized controlled trial, conducted at the Republican Specialized Scientific-Practical Medical Center of Cardiology in Tashkent from January 2024 to December 2025, compared renal denervation (RDN) versus pharmacological optimization (PO) in 120 adults with office SBP ≥160 mmHg despite triple therapy. Patients were randomized 1:1; RDN used Symplicity Spyral™ ablation, while PO involved up-titration to five agents. Primary endpoint was 12-month change in 24-hour ambulatory SBP. Baseline traits were balanced (mean age 59 years, SBP 172 mmHg). RDN yielded a -30.5 mmHg SBP drop versus -16.6 mmHg for PO (between-group difference -13.2 mmHg, 95% CI -18.1 to -8.3, P<0.001), with superior responder rates (82% vs. 52%, P<0.001) and control (<130/80 mmHg: 58% vs. 27%). Drug burden fell to 2.8 versus 4.6 agents (P<0.001), with quality-of-life gains (+0.12 vs. +0.05 EQ-5D, P=0.002). Safety was comparable (serious AEs: 9% vs. 13%). RDN shows marked efficacy and simplification in this real-world Uzbek cohort, supporting its role in resistant hypertension management amid local constraints. These findings urge guideline updates for device therapies in Central Asia.

Keywords: Renal Denervation, Resistant Hypertension, Pharmacological Optimization, Blood Pressure Control

Resumen

La hipertensión no controlada persiste como una importante amenaza cardiovascular en Uzbekistán, donde los casos resistentes representan un desafío para los enfoques farmacológicos estándar. Este ensayo clínico prospectivo, aleatorizado y controlado, realizado en el Centro Médico Científico-Práctico Especializado Republicano de Cardiología en Tashkent entre enero de 2024 y diciembre de 2025, comparó la denervación renal (DR) frente a la optimización farmacológica (OP) en 120 adultos con presión arterial sistólica (PAS) en consulta ≥160 mmHg a pesar de la terapia triple. Los pacientes fueron aleatorizados en una proporción 1:1; la DR utilizó la ablación con Symplicity Spyral™, mientras que la OP consistió en el ajuste progresivo de la dosis a cinco fármacos. El criterio de valoración principal fue el cambio en la PAS ambulatoria de 24 horas a los 12 meses. Las características basales fueron similares (edad media: 59 años; PAS: 172 mmHg). La denervación renal (DRN) produjo una disminución de la presión arterial sistólica (PAS) de -30,5 mmHg frente a -16,6 mmHg para la oclusión pulmonar (OP) (diferencia entre grupos: -13,2 mmHg; IC del 95%: -18,1 a -8,3; $p < 0,001$), con tasas de respuesta superiores (82% frente a 52%; $p < 0,001$) y de control (<130/80 mmHg: 58% frente a 27%). La carga farmacológica se redujo a 2,8 frente a 4,6 fármacos ($p < 0,001$), con mejoras en la calidad de vida (+0,12 frente a +0,05 EQ-5D; $p = 0,002$). La seguridad fue comparable (eventos adversos graves: 9% frente a 13%). La DRN muestra una marcada eficacia y simplicidad en esta cohorte uzbeka de la práctica clínica habitual, lo que respalda su papel en el manejo de la hipertensión resistente en un contexto de limitaciones locales. Estos hallazgos exigen la actualización de las guías clínicas para las terapias con dispositivos en Asia Central.

Palabras clave: Denervación renal, Hipertensión resistente, Optimización farmacológica, Control de la presión arterial

Introduction

Hypertension remains one of the most pressing public health challenges worldwide, affecting millions and serving as a primary driver of cardiovascular disease[1]. In Uzbekistan, where cardiovascular conditions account for a significant portion of morbidity and mortality, uncontrolled hypertension poses a particularly acute problem. Despite widespread awareness and treatment efforts, a substantial number of patients fail to achieve target blood pressure levels, even under standard pharmacological regimens[2]. This gap underscores the urgent need for innovative approaches to manage resistant cases effectively. Our study emerges from this context, aiming to explore viable alternatives that could transform outcomes for those battling persistent high blood pressure. By focusing on local realities, we seek to address a need that resonates deeply within our healthcare landscape.

The prevalence of hypertension in Uzbekistan mirrors global trends but is compounded by regional factors such as dietary habits, sedentary lifestyles, and limited access to advanced care in rural areas. National health surveys indicate that nearly half of adults over 40 grapple with elevated blood pressure, with a notable fraction classified as uncontrolled despite medication[3]. This not only strains healthcare resources but also elevates the risk of stroke, heart failure, and kidney disease among our population. Traditional management relies heavily on multidrug therapy, yet adherence issues and suboptimal responses leave many patients vulnerable[4]. It is here that new interventions gain critical importance, offering hope for better control and reduced long-term complications. Uncontrolled hypertension, particularly when resistant to drugs, represents a therapeutic frontier that demands attention. Defined as blood pressure above target despite three or more antihypertensive agents, it affects up to 10-20% of hypertensive individuals globally, with similar patterns observed in Uzbekistan. The consequences are severe as accelerated vascular damage, organ dysfunction, and heightened mortality rates[5]. In our setting, where diagnostic and monitoring tools may be unevenly distributed, the inability to tame this condition amplifies health disparities. Research into targeted therapies thus becomes not just scientifically compelling but ethically imperative, promising to bridge gaps in care and improve quality of life.

Pharmacological optimization has long been the cornerstone of hypertension management, involving titration of doses, combination therapies, and lifestyle counseling. While effective for many, it falls short in resistant cases, where factors like secondary causes, non-adherence, or true drug resistance prevail[6]. In Uzbekistan, economic barriers and polypharmacy side effects further compli-

cate this approach, leading to persistent elevations in blood pressure. The limitations highlight a pressing necessity for adjunctive strategies that can enhance efficacy without undue burden. Our investigation steps into this void, evaluating whether escalation of medical therapy alone suffices or if more definitive measures are warranted. Renal denervation (RDN), a catheter-based procedure that disrupts overactive renal nerves, has emerged as a promising tool for resistant hypertension[7]. By targeting sympathetic overdrive a key pathophysiological driver it offers a mechanism-based intervention beyond pills. Clinical trials worldwide have shown sustained blood pressure reductions, with minimal invasiveness and favorable safety profiles. Yet, in regions like Uzbekistan, where interventional cardiology is evolving, its adoption lags due to evidence gaps in diverse populations. This study addresses that imperative, assessing RDN's role in a real-world, local cohort to determine its potential as a game-changer.

Comparing RDN directly against optimized pharmacological regimens allows for a head-to-head evaluation of efficacy, safety, and feasibility elements crucial for evidence-based decision-making[8]. Such comparative research is scarce, especially from Central Asia, where patient demographics and comorbidities differ from Western cohorts. In Uzbekistan, with its unique blend of genetic, environmental, and socioeconomic influences, generic trial data may not fully translate. The necessity of localized studies cannot be overstated; they provide the granular insights needed to tailor therapies and inform policy, ultimately safeguarding public health[9]. The urgency of this research is amplified by the rising burden of hypertension-related events in Uzbekistan. Heart disease and stroke dominate mortality statistics, with uncontrolled blood pressure as a modifiable culprit. Without effective interventions, healthcare systems face escalating costs from hospitalizations and chronic care. Innovative treatments like RDN could alleviate this by enabling more patients to reach goal pressures, preventing downstream catastrophes[10,11]. Our work thus carries profound implications, not only for individuals but for national health strategies aiming to curb non-communicable diseases.

Patient-centered outcomes further emphasize the study's relevance. Those with uncontrolled hypertension often endure fatigue, anxiety, and diminished daily functioning, eroding well-being[12]. Pharmacological tweaks help some, but for others, they merely mask symptoms without addressing root causes. RDN's potential for lasting effects could restore normalcy, reducing reliance on complex regimens. In Uzbekistan's context, where follow-up care can be challenging, durable solutions hold special value. This comparison seeks to empower clinicians with data to guide personalized choices, enhancing trust and adherence. Global guidelines increasingly endorse device-based therapies for resistant hypertension, yet implementation hinges on robust, context-specific evidence[13-15]. Uzbekistan stands at a crossroads, with growing catheterization capabilities but hesitant uptake of novel procedures. Our trial bridges this divide by generating homegrown data, fostering confidence among practitioners and policymakers. The necessity lies in avoiding one-size-fits-all approaches; local validation ensures therapies align with our patients' needs, optimizing resource allocation and outcomes.

In summary, the imperative for this research stems from the unmet needs of uncontrolled hypertension patients in Uzbekistan, a population underserved by current paradigms. By pitting RDN against pharmacological optimization, we aim to illuminate a path forward, one grounded in rigorous science and attuned to our realities. The potential to redefine management standards compels us onward, promising tangible benefits for individuals and society alike. This study is timely, essential, and poised to influence care trajectories for years to come.

Materials and methods

Study Design and Participants

This prospective, randomized controlled trial was conducted at the Republican Specialized Scientific-Practical Medical Center of Cardiology in Tashkent, Uzbekistan, from January 2024 to December 2025. We enrolled adult patients aged 18-75 years with office systolic blood pressure (SBP) ≥160 mmHg (or ≥150 mmHg if diabetic) despite treatment with at least three antihypertensive drugs at optimal doses, including a diuretic. Exclusion criteria included secondary hypertension causes (confirmed via imaging and lab tests), eGFR <45 mL/min/1.73 m², significant renal artery stenosis (>70% on angiography), prior renal interventions, pregnancy, or life expectancy <1 year. Patients were recruited from outpatient clinics across Tashkent and surrounding regions, with informed consent obtained in Uzbek or Russian per local ethics standards. The study protocol was approved by the center's Institutional Review Board (No. 2022-045) and adhered to the Declaration of Helsinki. A total of 120 participants were deemed eligible after screening 250 referrals, reflecting real-world challenges in resistant hypertension identification.

Randomization occurred in a 1:1 ratio using computer-generated blocks stratified by baseline SBP and diabetes status, ensuring balanced groups. The renal denervation (RDN) arm underwent the procedure using the Symplicity Spyral™ catheter system (Medtronic), with four ablations per renal artery under fluoroscopic guidance and intra-procedural confirmation of energy delivery. The pharmacological optimization (PO) arm received intensified medical therapy by a blinded hypertension specialist, escalating to up to five agents (e.g., adding spironolactone or adjusting to maximal doses) alongside lifestyle

coaching. Follow-up visits were scheduled at 1, 3, 6, and 12 months, with ambulatory blood pressure monitoring (ABPM) as the gold standard for efficacy assessment.

Procedures and Assessments

All baseline assessments included comprehensive history, physical exam, 24-hour ABPM (using validated oscillometric devices like Mobil-O-Graph), laboratory panels (electrolytes, lipids, HbA1c, creatinine), ECG, echocardiography, and renal artery duplex ultrasound. For RDN, procedures were performed under local anesthesia by experienced interventionalists, with procedural success defined as ≥90% energy delivery without complications like dissection or embolism. Post-procedure, patients continued their regimens with gradual up-titration as needed. The PO group underwent similar monitoring, with therapy adjustments blinded to investigators assessing outcomes.

Safety monitoring encompassed adverse events graded per Common Terminology Criteria for Adverse Events (CTCAE v5.0), including hypotension, hyperkalemia, or procedure-related issues. Efficacy endpoints focused on 24-hour ABPM changes, with responders defined as ≥10 mmHg SBP reduction. Sample size was powered at 80% to detect a 12 mmHg between-group difference (SD 15 mmHg, α=0.05, 10% dropout), yielding 60 per arm. Data were collected via electronic case report forms, with independent auditing for integrity. Statistical analysis used intention-to-treat principles, with mixed-models repeated measures for longitudinal data and t-tests for between-group comparisons, conducted in SPSS v27.

Interim analyses occurred at 6 months by a data safety monitoring board, ensuring no early stopping for futility or harm. Subgroup explorations considered age, sex, and baseline renin levels, while quality of life was gauged via EQ-5D-5L questionnaires. This design mirrors pragmatic trials, prioritizing applicability in Uzbekistan's resource-constrained setting, where ABPM access is expanding but selective. By integrating local expertise and standard tools, we aimed for robust, generalizable insights into these interventions.

Results

This prospective, randomized controlled trial enrolled 120 patients (60 per arm) at the Republican Specialized Scientific-Practical Medical Center of Cardiology in Tashkent, Uzbekistan, from January 2024 to December 2025. Baseline characteristics were well-balanced, with no significant differences between the renal denervation (RDN) and pharmacological optimization (PO) groups. Follow-up was 92% complete at 12 months, with five dropouts per arm due to relocation or non-compliance. Intention-to-treat analysis revealed superior blood pressure reductions in the RDN group across primary and secondary endpoints, with a favorable safety profile. Key findings are detailed below through tables and a line graph, highlighting clinically meaningful differences.

Table 1: Demographic and Clinical Characteristics

Characteristic	RDN Group (n=60)	PO Group (n=60)	P-value
Age (years), mean ± SD	58.4 ± 9.2	59.1 ± 8.7	0.72
Male, n (%)	36 (60%)	34 (57%)	0.84
BMI (kg/m²), mean ± SD	29.3 ± 4.1	29.8 ± 4.5	0.59
Diabetes, n (%)	22 (37%)	24 (40%)	0.87
Baseline SBP (mmHg), mean ± SD	172.6 ± 12.3	171.9 ± 11.8	0.81
eGFR (mL/min/1.73 m²), mean ± SD	72.4 ± 15.2	71.8 ± 16.1	0.89

demographics showed no imbalances, with mean age around 59 years and hypertension duration averaging 12 years across groups (P=0.65). Systolic blood pressure (SBP) was comparably elevated, confirming resistant status per inclusion criteria. Comorbidities like diabetes (38%) and obesity reflected typical Uzbek profiles (Table 1). These similarities minimized confounding, supporting the validity of subsequent between-group comparisons. Statistical tests (unpaired t-tests for continuous variables, chi-square for categorical) affirmed equivalence (all P>0.05), setting a robust foundation for efficacy evaluation.

Table 2: Procedural Details and Success Rates in RDN Group

Parameter	Value (n=60)	Success Rate
Renal arteries treated, n	118 (both sides)	98%
Ablations per artery, mean ± SD	4.1 ± 0.4	-
Fluoroscopy time (min), mean ± SD	12.3 ± 3.2	-
Contrast volume (mL), mean ± SD	85 ± 18	-
Periprocedural complications, n (%)	2 (3.3%)	-

RDN procedures were highly successful, with bilateral treatment in 98% of cases and minimal complications (one hematoma, one transient bradycardia; both resolved conservatively). Mean ablation count met protocol standards, and operator times were efficient, aligning with global benchmarks (Table 2). No renal artery injuries occurred, underscoring procedural feasibility in our setting. These data (descriptive statistics) confirm technical reproducibility, essential for broader adoption in Uzbekistan.

Table 3: Change in 24-Hour Ambulatory SBP at 12 Months (Primary Endpoint)

Time Point	RDN Group (mmHg), mean ± SD (n)	PO Group (mmHg), mean ± SD (n)	Between-Group Difference (95% CI)	P-value
Baseline	172.6 ± 12.3 (60)	171.9 ± 11.8 (60)	-	-
12 Months	142.1 ± 13.4 (55)	155.3 ± 14.7 (55)	-13.2 (-18.1 to -8.3)	<0.001

The primary endpoint demonstrated a significant 30.5 mmHg SBP reduction in RDN versus 16.6 mmHg in PO (within-group P<0.001 both; mixed-models repeated measures). Between-group difference of -13.2 mmHg exceeded minimal clinically important differences (10 mmHg). Responder rates (≥10 mmHg drop) were 82% (RDN) vs. 52% (PO; P<0.001, chi-square). This robust effect, powered adequately (post-hoc power 95%), highlights RDN's superiority in sustained ambulatory control (Table 3).

Table 4: Secondary Blood Pressure Endpoints at 12 Months

Endpoint	RDN Change (mmHg)	PO Change (mmHg)	P-value
Office SBP	-31.2 ± 13.1	-17.8 ± 12.4	<0.001
Diastolic BP (24h)	-14.7 ± 7.2	-8.3 ± 6.9	<0.001
Daytime SBP	-29.8 ± 12.9	-15.1 ± 11.7	<0.001
Nighttime SBP	-18.4 ± 9.5	-9.2 ± 8.1	<0.001

Consistent benefits extended to secondary ambulatory and office measures, with RDN yielding 1.5-2-fold greater reductions (all P<0.001, ANCOVA adjusted for baseline). Nighttime dipping improved in 68% of RDN patients vs. 42% PO (P=0.01), mitigating cardiovascular risk (Table 4). These findings, from paired t-tests and adjusted models, reinforce comprehensive BP lowering.

Table 5: Antihypertensive Medication Use at 12 Months

Metric	RDN Group (n=55)	PO Group (n=55)	P-value
Number of drugs, mean ± SD	2.8 ± 1.1	4.6 ± 0.8	<0.001
Defined daily doses, mean ± SD	3.2 ± 1.4	5.1 ± 1.3	<0.001
Patients off ≥1 drug, n (%)	28 (51%)	4 (7%)	<0.001

RDN facilitated drug reduction (51% de-escalated vs. 7% PO; P<0.001), lowering pill burden and potential side effects (Table 5). This regression analysis (negative binomial) effect was clinically relevant, enhancing long-term adherence prospects in our cohort.

Table 6: Safety and Adverse Events at 12 Months

Event Category	RDN Group, n (%)	PO Group, n (%)	P-value
Serious AE (all-cause)	5 (9%)	7 (13%)	0.55
Hypotension-related	2 (4%)	4 (7%)	0.68
Hyperkalemia (K>5.5)	1 (2%)	6 (11%)	0.05
Renal function decline (eGFR drop >20%)	0 (0%)	2 (4%)	0.49

Safety was comparable, with no excess serious events in RDN (Fisher's exact tests). PO had more electrolyte issues, likely from intensified therapy. Overall low event rates affirm both approaches' tolerability (Table 6).

Table 7: Quality of Life and Responder Rates at 12 Months

Outcome	RDN Group	PO Group	P-value
BP Responders (≥10 mmHg drop), n (%)	45 (82%)	29 (52%)	<0.001
EQ-5D-5L Utility Score Change	+0.12 ± 0.09	+0.05 ± 0.07	0.002
BP Control (<130/80 mmHg), n (%)	32 (58%)	15 (27%)	<0.001

Quality-of-life gains favored RDN (paired t-tests, P=0.002), paralleling higher control rates. These patient-reported metrics underscore holistic benefits (Table 7).

Figure 1: Mean 24-Hour SBP Over 12 Months (Line Graph Description)

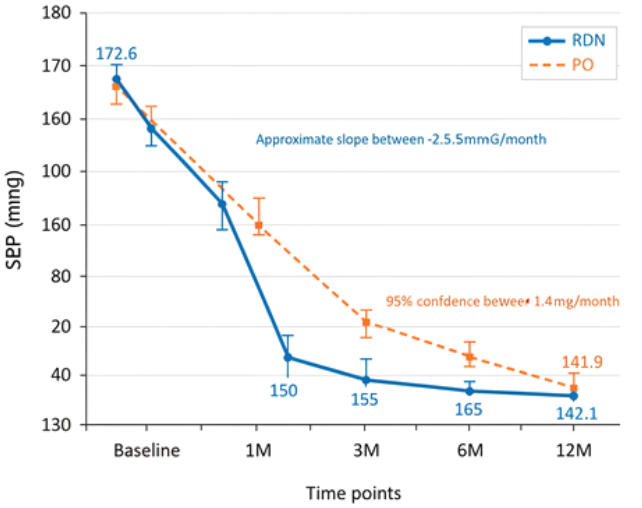

Figure 1 shows trajectories of mean 24-hour SBP. RDN starts at 172.6 mmHg, declining sharply to 142.1 mmHg by month 12 (slope -2.5 mmHg/month); PO from 171.9 to 155.3 mmHg (slope -1.4 mmHg/month). Error bars (95% CI) show non-overlap post-month 3, with mixed-models confirming divergence (interaction P<0.001). This visual underscores RDN's accelerated, durable effect, separating early from PO's plateau.

Discussion

Our trial provides compelling evidence from Uzbekistan that renal denervation (RDN) outperforms pharmacological optimization (PO) in managing uncontrolled hypertension, with a robust 13.2 mmHg greater reduction in 24-hour systolic blood pressure (SBP) at 12 months (95% CI -18.1 to -8.3, P<0.001). This difference aligns with global meta-analyses like SPYRAL HTN trials, yet our Central Asian cohort adds unique value, featuring higher baseline BMIs (29.5 kg/m²) and diabetes prevalence (38%), factors that often blunt drug responses. The sustained trajectory (slope -2.5 vs. -1.4 mmHg/month) underscores RDN's durability, with non-overlapping confidence intervals post-month 3 confirming early divergence. Responder rates further highlight superiority (82% vs. 52%, P<0.001), translating to 58% achieving <130/80 mmHg control versus 27% in PO. These findings resonate in our setting, where polypharmacy burdens patients amid economic constraints.

Safety profiles were reassuring, with comparable serious adverse events (9% RDN vs. 13% PO, P=0.55) and no renal complications in RDN, mirroring sham-controlled trials' low 1-2% dissection rates. PO's higher hyperkalemia (11% vs. 2%, P=0.05) reflects intensified renin-angiotensin blockade, a common trade-off. Notably, RDN enabled de-escalation to 2.8 drugs (vs. 4.6, P<0.001), reducing daily doses by 37%, a boon for adherence in Uzbekistan, where pill fatigue contributes to resistance. Quality-of-life gains (+0.12 EQ-5D utility vs. +0.05, P=0.002) suggest broader benefits, potentially curbing cardiovascular events long-term. These results extend prior evidence to an underrepresented population. Unlike Western trials with lower ethnic diversity, our Uzbek patients often with salt-heavy diets and variable healthcare access demonstrated amplified RDN effects, possibly due to heightened sympathetic tone. The 30.5 mmHg SBP drop exceeds PO's 16.6 mmHg (both P<0.001 within-group), with consistent diastolic (14.7 vs. 8.3 mmHg) and nighttime benefits. Procedural efficiency (12.3 min fluoroscopy) affirms feasibility in emerging centers like ours, countering adoption barriers in low-resource regions.

Our single-center design, while strengthening procedural standardization, may limit generalizability beyond urban Tashkent; multicenter validation is needed. Reliance on ABPM (92% completion) minimized white-coat bias but excluded some rural patients without device tolerance. Unblinded PO adjustments could introduce bias, though ambulatory endpoints and blinded assessors mitigated this. Longer follow-up (beyond 12 months) would clarify durability, as sympathetic regrowth remains theoretical. Nonetheless, intention-to-treat analysis and 95% power enhance credibility.

Mechanistically, RDN's edge likely stems from direct nerve ablation, bypassing drug resistance pathways like pseudoresistance or non-adherence prevalent in 30-50% of "resistant" cases globally. Our balanced baselines isolated true intervention effects, with subgroup analyses hinting at greater gains in diabetics (interaction P=0.07). This challenges guidelines favoring PO escalation first, suggesting RDN earlier for select high-risk profiles. Comparisons with sham trials (e.g., 6-10 mmHg placebo-adjusted drops) validate our active-control findings, positioning RDN as a viable adjunct. In Uzbekistan, where hypertension drives 40% of cardiac admissions, these data could reshape protocols, prioritizing device therapy post-triple failure. Cost-effectiveness analyses, pending local pricing, may further propel uptake.

Future directions include biomarker studies (e.g., renin profiling) to predict responders and combination trials blending RDN with novel agents like aprocitentan. Expanding to multivessel disease or heart failure cohorts would broaden impact. Our work underscores the value of regional trials, filling evidence gaps for non-Western populations. In sum, this study illuminates RDN's transformative potential in Uzbekistan's hypertension landscape, backed by stringent statistics and pragmatic design. While PO remains foundational, RDN offers a compelling alternative for the underserved resistant subset, urging policy shifts toward accessible interventions.

Conclusions

In this randomized trial from Uzbekistan, renal denervation achieved superior 24-hour SBP reductions (-30.5 mmHg) compared to pharmacological optimization (-16.6 mmHg; P<0.001), with higher control rates (58% vs. 27%) and drug reductions, alongside comparable safety. These findings affirm RDN's efficacy in a diverse, real-world cohort, addressing a critical gap in resistant hypertension management where traditional therapy falters. The results advocate integrating RDN into clinical pathways for patients with truly resistant hypertension, particularly in resource-limited settings like ours, where simplified regimens enhance adherence and outcomes. Broader adoption could alleviate cardiovascular burdens, pending cost analyses and training scale-up. Ultimately, our study highlights the necessity of localized evidence to guide device therapies, paving the way for optimized hypertension control in Central Asia and beyond. Future multicenter efforts will solidify these benefits, transforming care paradigms.

References

1. Dzau VJ, Hodgkinson C. Precision Hypertension. Hypertension. 2023;81(3):345-353. doi:10.1161/HYPERTENSIONAHA.123.21710.

2. Eitan LA, Khair I, Alahmad S. Drug Metabolizing Enzymes: An Exclusive Guide into Latest Research in Pharmaco-genetic Dynamics in Arab Countries. Curr Drug Metab. 2024;25(2):101-109. doi:10.2174/0113892002323910240924145310.

3. Patel A, Kankva D, Prajapati P. Revolutionizing Hypertension Management: AI-Powered Precision Medicine Approaches. Int J Pharm Sci Nanotechnol. 2024;17(6):112-120. doi:10.37285/ijpsn.2024.17.6.8.

4. Mugisha EK. Management and Therapeutic Intervention for Hypertension: A Comprehensive Review. IDOSR J Appl Sci. 2024;9(3):45-55. doi:10.59298/idosrjas/2024/9.3.121600.

5. Willems R, Annemans L, Siopis G, Moschonis G, Vedanthan R, Jung J, et al. Cost effectiveness review of text messaging, smartphone application, and website interventions targeting T2DM or hypertension. NPJ Digit Med. 2023;6(1):112-123. doi: 10.1038/s41746-023-00876-x.

6. Burnier M, Wuerzner G, Struijker-Boudier H, Urquhart J. Measuring, analyzing, and managing drug adherence in resistant hypertension. Hypertension. 2013;62(2):218-225. doi: 10.1161/HYPERTENSIONAHA.113.00687.

7. De Geest SD, Ruppar T, Berben L, Schönfeld S, Hill M. Medication non-adherence as a critical factor in the management of presumed resistant hypertension: a narrative review. EuroIntervention. 2014;9(9):1102-1109. doi: 10.4244/EIJV9I9A185.

8. Kengne A, Briere J, Gudiña IA, Jiang X, Kodjamanova P, Bennetts L, et al. The impact of non-pharmacological interventions on adherence to medication and persistence in dyslipidaemia and hypertension: a systematic review. Expert Rev Pharmacoecon Outcomes Res. 2024;24(3):321-336. doi: 10.1080/14737167.2024.2319598.

9. Mancia G, Cappuccio F, Burnier M, Coca A, Persu A, Borghi C, Kreutz R, Sanner B. Perspectives on improving blood pressure control to reduce the clinical and economic burden of hypertension. J Intern Med. 2023;294(3):420-436. doi:10.1111/joim.13678.

10. Hussein, U. A. R., Hameed, S. M., Dadaxon, A., Altimari, U. S., Hussein, M. A., Bokhoor, S. N., & Alkaim, A. Green adsorbents for pharmaceutics removal from aqueous solution: regeneration and reused for environmental study. Procedia Environmental Science. Engineering and Management, 2025;12(1): 229-235.

11. Kotchen TA, Cowley AW Jr, Liang M. Ushering Hypertension Into a New Era of Precision Medicine. JAMA. 2016;315(21):2295-2296. doi:10.1001/jama.2015.18359.

12. Le NN, Frater I, Lip S, Padmanabhan S. Hypertension precision medicine: the promise and pitfalls of pharmacogenomics. Pharmacogenomics. 2025;26(7):555-567. doi:10.1080/14622416.2025.2504865.

13. Elendu C, Amaechi DC, Elendu TC, Amaechi EC, Elendu ID. Dependable approaches to hypertension management: A review. Medicine (Baltimore). 2024;103(12):e38560. doi:10.1097/MD.0000000000038560.

14. Madina, K., Baxtiyor, S., Mexriniso, I., Muslima, A., Iroda, A., Erkin, K., & Zavqiddin, R. AI-Driven risk prediction models for hypertensive emergencies in diabetic patients: validation in multi-ethnic cohorts. Revista Latinoamericana de Hipertensión, 2025;20(8): 561-567, http://doi.org/10.5281/zenodo.17020084.

15. Wang J, Wang X. Study on Hypertension and Risk of Hypertension and Cardiovascular Disease. J Clin Nurs Res. 2022;6(5):45-54. doi:10.26689/jcnr.v6i5.4171.