

## INNOVATIONS IN HYPERTENSION MANAGEMENT: THE ROLE OF BIOIMPEDANCE CARDIOGRAPHY

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### РЕЗЮМЕ

#### ИННОВАЦИИ В ЛЕЧЕНИИ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИИ: РОЛЬ БИОИМПЕДАНСНОЙ КАРДИОГРАФИИ

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**Актуальность.** Артериальная гипертензия остаётся одной из ведущих причин сердечно-сосудистой заболеваемости и смертности. Несмотря на широкий спектр антигипертензивных препаратов, достижение целевых уровней артериального давления (АД) остаётся неудовлетворительным, что во многом связано с эмпирическим выбором терапии и полипрагмазией. Гемодинамическая гетерогенность АГ требует персонализированного подхода к лечению.

**Цель исследования.** Оценить эффективность целевой антигипертензивной монотерапии, основанной на биоимпедансном фенотипировании гемодинамических профилей у пациентов с АГ I–II стадии.

**Материалы и методы.** В исследование включено 120 пациентов с неконтролируемой АГ I–II стадии. С использованием биоимпедансной кардиографии (NICaS) оценивались общее периферическое сосудистое сопротивление (TPR) и общее содержание воды в организме (TBW). Пациенты были стратифицированы на вазоконстрикторный и объёмзависимый фенотипы. Назначалась целевая монотерапия: амлодипин 5 мг/сут или индапамид 2,5 мг/сут соответственно. Длительность наблюдения – 10 дней.

**Результаты.** Отмечено достоверное снижение TPR ( $-790 \text{ дин} \cdot \text{с} \cdot \text{см}^{-5}$ ;  $p < 0,001$ ) и TBW ( $-3,3\%$ ;  $p < 0,001$ ). Целевой уровень АД ( $< 140/90 \text{ мм рт. ст.}$ ) достигнут у 90 % пациентов без побочных эффектов.

**Заключение.** Биоимпедансное гемодинамическое фенотипирование позволяет эффективно и быстро достигать контроля АД, снижая риск полифармации и повышая точность назначения терапии.

**Ключевые слова:** артериальная гипертензия, биоимпедансная кардиография, гемодинамика, персонализированная терапия, полипрагмазия.

### SUMMARY

#### INNOVATIONS IN HYPERTENSION MANAGEMENT: THE ROLE OF BIOIMPEDANCE CARDIOGRAPHY

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**Background.** Arterial hypertension (AH) remains one of the leading causes of cardiovascular morbidity and mortality worldwide. Despite the availability of multiple antihypertensive agents, blood pressure (BP) control rates remain suboptimal, largely due to empirical drug selection and increasing polypharmacy. Hemodynamic heterogeneity of hypertension suggests that personalized treatment strategies based on pathophysiological phenotyping may improve therapeutic outcomes.

**Objective.** To evaluate the effectiveness of targeted antihypertensive monotherapy guided by bioimpedance cardiography–based hemodynamic phenotyping in patients with stage I–II hypertension.

**Methods:** A prospective, open-label study included 120 patients with uncontrolled stage I–II hypertension. Bioimpedance cardiography (NICaS system) was used to assess Total Peripheral Resistance (TPR) and Total Body Water (TBW), enabling stratification into vasoconstrictive and volume-dependent phenotypes. Targeted monotherapy was prescribed: amlodipine (5 mg/day) for vasoconstrictive phenotype and indapamide (2.5 mg/day) for volume-dependent phenotype. Follow-up duration was 10 days.

**Results.** Significant reductions were observed in TPR ( $-790 \text{ dyn} \cdot \text{s} \cdot \text{cm}^{-5}$ ;  $p < 0,001$ ) and TBW ( $-3,3\%$ ;  $p < 0,001$ ). Target BP ( $< 140/90 \text{ mmHg}$ ) was achieved in 90 % of patients without adverse events.

**Conclusion.** Bioimpedance-guided hemodynamic phenotyping enables rapid and effective BP control while minimizing polypharmacy. This approach supports precision medicine principles in hypertension management.

**Keywords:** hypertension, bioimpedance cardiography, hemodynamic phenotyping, personalized therapy, polypharmacy.

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## XULOSA

### ARTERIAL GIPERTENZIYANI BOSHQARISHDA INNOVATSIYALAR: BIOIMPEDANS KARDIOGRAFIYANING O'RNINI

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**Dolzarblik.** Arterial gipertenziya yurak-qon tomir kasalliklari orasida yetakchi o'lim va nogironlik sabablaridan biridir. Zamonaviy antihipertenziv dori vositalari mavjud bo'lishiga qaramay, arterial qon bosimini (AQB) nazorat qilish darajasi yetarli emas. Bu ko'pincha empirik davolash va polifarmatsiya bilan bog'liq. Gipertenziyaning gemodinamik geterojenligi individual yondashuvni talab qiladi.

**Maqsad.** I–II bosqichdagi arterial gipertenziyali bemorlarda bioimpedans asosidagi gemodinamik fenotiplashga tayangan maqsadli monoterapiyaning samaradorligini baholash.

**Materiallar va usullar.** Tadqiqotga 120 nafar nazorat qilinmayotgan arterial gipertenziyali bemor jalb etildi. Bioimpedans kardiografiya (NICaS) yordamida umumiy periferik tomir qarshiligi (TPR) va organizmning umumiy suv miqdori (TBW) baholandi. Bemorlar vazokonstriktor va hajmga bog'liq fenotiplarga ajratildi. Mos ravishda amlodipin (5 mg/kun) yoki indapamid (2,5 mg/kun) buyurildi. Kuzatuv muddati – 10 kun.

**Natijalar.** TPR ( $-790 \text{ din}\cdot\text{s}\cdot\text{sm}^{-5}$ ;  $p<0,001$ ) va TBW ( $-3,3\%$ ;  $p<0,001$ ) ko'rsatkichlarining sezilarli pasayishi kuzatildi. Maqsadli AQB ( $<140/90 \text{ mm sim.ust.}$ ) 90 % bemorlarda erishildi, nojo'ya ta'sirlar qayd etilmadi.

**Xulosa.** Bioimpedansga asoslangan gemodinamik fenotiplash AQBni tez va samarali nazorat qilish imkonini beradi hamda polifarmatsiyani kamaytiradi. Ushbu yondashuv individual davolash tamoyillariga mos keladi.

**Kalit so'zlar:** arterial gipertenziya, bioimpedans kardiografiya, gemodinamika, individual terapiya, polifarmatsiya.

**Introduction.** Arterial hypertension (AH) remains one of the most significant global health challenges of the 21st century. According to the World Health Organization, more than 1,3 billion individuals worldwide are affected, and hypertension contributes to approximately 10 million deaths annually due to cardiovascular complications. Despite continuous advances in pharmacotherapy and the availability of multiple classes of antihypertensive agents, blood pressure (BP) control rates remain unsatisfactory, with less than 50 % of treated patients achieving target levels in routine clinical practice [1–5].

One of the fundamental limitations of contemporary hypertension management is the predominantly empirical selection of antihypertensive therapy. Current clinical guidelines (ESC/ESH, AHA/ACC) recommend initial combination therapy for many patients; however, these recommendations are largely based on BP thresholds rather than individual hemodynamic characteristics. This approach may contribute to therapeutic inertia, unnecessary polypharmacy, increased adverse effects, and reduced patient adherence [5].

Importantly, hypertension is not a homogeneous disease entity. It represents a spectrum of hemodynamic disturbances characterized by varying contributions of increased systemic vascular resistance, elevated cardiac output, and fluid retention. The dominant pathophysiological mechanism differs between patients and may evolve over time. Therefore, a uniform treatment strategy may not optimally address the underlying cause of BP elevation in every individual [7, 8]. Hemodynamic phenotyping has emerged as a promising strategy for precision hypertension management. Non-invasive bioimpedance cardiography enables quantitative assessment of systemic hemodynamic parameters, including Total Peripheral Resistance (TPR), Stroke Volume, Cardiac Output, and Total Body Water (TBW). These measurements provide objective insight into whether hypertension is primarily driven by vasoconstriction or volume overload [12, 14].

In the present study, we utilized the NICaS (Non-Invasive Cardiac System, NI Medical, Israel), a validated bioimpedance cardiography device that employs whole-body impedance technology to assess cardiovascular and fluid status. The NICaS system allows reproducible measurement of TPR and TBW under standardized conditions, making it suitable for outpatient clinical phenotyping. By stratifying patients into vasoconstrictive and volume-dependent hemodynamic phenotypes, therapy can be tailored to target the predominant mechanism of hypertension.

The integration of NICaS-guided hemodynamic assessment into antihypertensive decision-making may reduce unnecessary multidrug regimens and enable targeted monotherapy in selected patients. Such an approach aligns with the principles of precision medicine and may improve therapeutic efficacy while minimizing pharmacological burden [13–15].

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Therefore, this study aims to evaluate the clinical effectiveness of bioimpedance-guided targeted antihypertensive monotherapy in patients with stage I–II hypertension, focusing on rapid BP control and reduction of polypharmacy through individualized hemodynamic stratification.

## Methods

### Study Design and Ethical Considerations

The present investigation was designed as a prospective, open-label, single-center interventional study conducted in 2024 at the Republican Specialized Scientific and Practical Medical Center for Therapy and Medical Rehabilitation (Tashkent, Uzbekistan). The study protocol was developed in accordance with the ethical principles outlined in the Declaration of Helsinki. All participants provided written informed consent prior to inclusion in the study. The institutional ethics committee approved the study design, methodology, and data handling procedures.

### Study Population

A total of 120 patients with uncontrolled essential arterial hypertension stage I–II were consecutively recruited from the outpatient cardiology department. The diagnosis of essential hypertension was established according to the World Health Organization (2020) criteria. Eligible participants were between 35 and 65 years of age and had persistent office systolic blood pressure  $\geq 140$  mmHg and/or diastolic blood pressure  $\geq 90$  mmHg despite previous therapy or absence of adequate treatment. Patients were required to have stable clinical status without acute cardiovascular events during the previous three months. Individuals receiving more than two antihypertensive agents within 30 days prior to enrollment were not included to avoid confounding effects of intensive combination therapy.

Exclusion criteria comprised secondary forms of hypertension (including renovascular, endocrine, or drug-induced hypertension), symptomatic heart failure of NYHA class IIb–III, chronic kidney disease stage  $\geq 3$  (eGFR  $< 60$  mL/min/1.73 m<sup>2</sup>), significant hepatic dysfunction, acute inflammatory conditions, endocrine disorders, pregnancy, and recent use of systemic corticosteroids or diuretics within two weeks before enrollment.

**Baseline Clinical Assessment** At baseline, all participants underwent a comprehensive clinical evaluation, including medical history, physical examination, anthropometric measurements, and standardized office blood pressure assessment. Blood pressure was measured using a validated automatic oscillometric device. Three consecutive measurements were obtained after a 5-minute seated rest period, and the average value was used for analysis. Body mass index and waist circumference were recorded to characterize metabolic status. Routine laboratory investigations included serum creatinine and electrolyte levels to exclude significant renal dysfunction or metabolic disturbances.

**Bioimpedance Cardiography and Hemodynamic Phenotyping** Hemodynamic assessment was performed using the NICaS (Non-Invasive Cardiac System, NI Medical, Israel), a validated whole-body bioimpedance cardiography device designed for non-invasive evaluation of systemic cardiovascular parameters. The NICaS system operates on the principle of impedance plethysmography, measuring electrical resistance changes during the cardiac cycle to calculate hemodynamic variables.

All measurements were performed in the morning hours (between 8:00 and 10:00 AM) under standardized environmental conditions with room temperature maintained between 22 and 24°C. Patients were examined in the supine position after a 10-minute rest period to ensure hemodynamic stabilization. Disposable electrode pairs were placed on the distal segments of the upper and lower extremities according to manufacturer guidelines. All measurements were performed by a single trained operator to minimize inter-observer variability.

The primary hemodynamic parameters analyzed included Total Peripheral Resistance (TPR, dyn·s·cm<sup>-5</sup>) and Total Body Water (TBW, expressed as percentage of body weight). These variables were selected as key determinants of vasoconstrictive and volume-dependent mechanisms of hypertension, respectively [6, 14, 15].

**Phenotypic Stratification** Based on bioimpedance-derived hemodynamic parameters, patients were stratified into distinct phenotypic groups. Individuals with TPR values exceeding 1500 dyn·s·cm<sup>-5</sup> in the presence of TBW below 50 % were classified as having a vasoconstrictive phenotype, reflecting predominant peripheral vascular resistance elevation. Patients with TBW values above 50 % and TPR below 1500 dyn·s·cm<sup>-5</sup> were categorized as having a volume-dependent phenotype, indicating fluid overload as the dominant mechanism. Participants exhibiting simultaneous elevation of both TPR and TBW were identified as having a mixed phenotype.

For the purpose of evaluating the efficacy of targeted monotherapy, patients with mixed hemodynamic phenotype were excluded from the primary efficacy analysis in order to avoid overlapping pathophysiological influences.

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**Treatment Protocol** After phenotypic classification, individualized antihypertensive monotherapy was initiated. Patients with vasoconstrictive phenotype received amlodipine at a fixed dose of 5 mg once daily, selected for its potent vasodilatory effect mediated through L-type calcium channel blockade. Patients with volume-dependent phenotype were prescribed indapamide 2.5 mg once daily, a thiazide-like diuretic known to reduce plasma volume and improve vascular compliance.

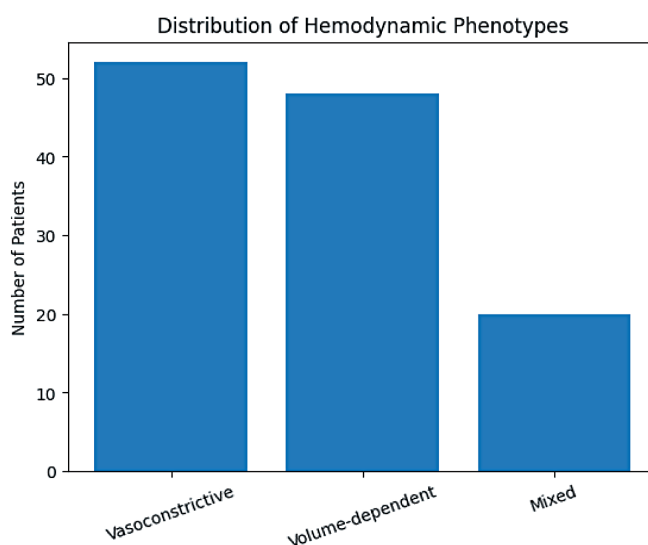
No additional antihypertensive agents were introduced during the 10-day treatment period. Participants were instructed to maintain stable dietary habits with moderate sodium restriction and to avoid significant changes in physical activity.

**Outcome Measures** The primary outcome of the study was the achievement of target office blood pressure below 140/90 mmHg after 10 days of therapy. Secondary outcomes included changes in TPR and TBW values measured by NICaS, as well as reductions in systolic and diastolic blood pressure. Safety assessment included monitoring for adverse events such as symptomatic hypotension, electrolyte disturbances, dizziness, or peripheral edema.

**Statistical Analysis** Statistical analysis was performed using IBM SPSS Statistics version 25.0. Continuous variables were expressed as mean±standard deviation (M±SD). The Shapiro–Wilk test was applied to assess normality of distribution. Comparisons between baseline and post-treatment values were conducted using paired Student’s t-test. A two-sided p-value <0,05 was considered statistically significant. All measurements were conducted under uniform methodological conditions to ensure internal consistency. The NICaS system’s automatic calibration algorithms were utilized to maintain measurement accuracy throughout the study period.

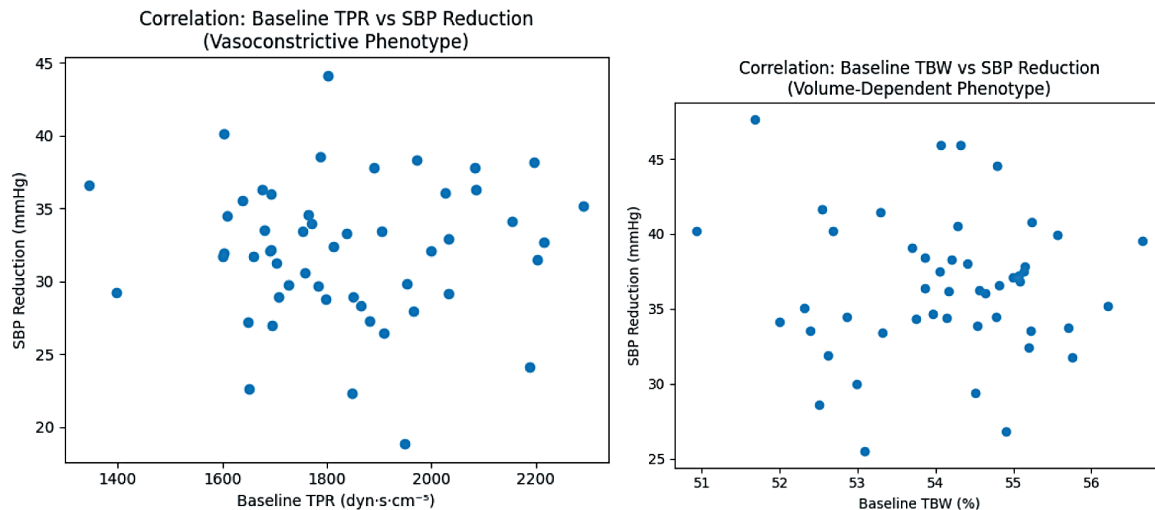
## Results

A total of 120 patients were initially enrolled in the study. Following hemodynamic stratification, 52 patients (43,3 %) were classified as having a vasoconstrictive phenotype, 48 patients (40,0 %) as volume-dependent phenotype, and 20 patients (16,7 %) as mixed phenotype. In order to maintain methodological clarity and avoid overlapping pathophysiological mechanisms, the mixed phenotype group was excluded from the primary efficacy analysis. Consequently, 100 patients were included in the final analysis. The mean age of participants was 54,2±9,1 years, with a predominance of female patients (58 %). Baseline office systolic blood pressure ranged between 150 and 180 mmHg (mean 163±11 mmHg), while diastolic blood pressure ranged from 90 to 105 mmHg (mean 97±7 mmHg). No statistically significant differences in baseline blood pressure values were observed between the vasoconstrictive and volume-dependent groups.



Picture 1.

In the vasoconstrictive phenotype group treated with amlodipine 5 mg/day, a marked reduction in Total Peripheral Resistance (TPR) was observed after 10 days of therapy. Mean TPR decreased from 1840±215 dyn·s·cm<sup>-5</sup> at baseline to 1050±145 dyn·s·cm<sup>-5</sup> post-treatment, corresponding to a mean reduction of 790 dyn·s·cm<sup>-5</sup> (p<0,001). This hemodynamic improvement was accompanied by a significant decrease in systolic blood pressure (from 163±11 to 132±8 mmHg, p<0,001) and diastolic blood pressure (from 98±7 to 83±6 mmHg, p<0,001). Target blood pressure (<140/90 mmHg) was achieved in 46 of 52 patients (88,5 %).



Picture 2.

In the volume-dependent phenotype group receiving indapamide 2.5 mg/day, a significant reduction in Total Body Water (TBW) was documented. TBW decreased from  $54.1 \pm 1.3$  % to  $50.8 \pm 1.1$  %, representing a mean reduction of 3,3 % ( $p < 0,001$ ). This change was associated with a significant decline in systolic blood pressure (from  $165 \pm 10$  to  $130 \pm 7$  mmHg,  $p < 0,001$ ) and diastolic blood pressure (from  $97 \pm 6$  to  $82 \pm 5$  mmHg,  $p < 0,001$ ). Target blood pressure was achieved in 44 of 48 patients (91.7 %). Overall, 90 % of patients included in the efficacy analysis reached the predefined target blood pressure within 10 days of targeted monotherapy. Importantly, no clinically significant adverse events, including symptomatic hypotension, electrolyte imbalance, or peripheral edema, were recorded during the study period.

## Discussion

The present study demonstrates that bioimpedance-guided hemodynamic phenotyping provides a clinically effective framework for personalized antihypertensive therapy. By identifying the dominant pathophysiological mechanism underlying blood pressure elevation, targeted monotherapy achieved rapid and substantial blood pressure control in the majority of patients.

Hypertension has traditionally been managed using stepwise escalation or empirical combination therapy strategies. While such approaches may eventually lead to blood pressure reduction, they frequently expose patients to multiple pharmacological agents without confirming that each drug addresses the primary hemodynamic abnormality. This practice contributes to polypharmacy, increases the risk of adverse reactions, and may negatively affect adherence. The findings of this study support the concept that hypertension is fundamentally heterogeneous in nature. In patients with the vasoconstrictive phenotype, elevated TPR reflects increased arteriolar tone, likely driven by sympathetic overactivity and endothelial dysfunction. The significant reduction in TPR following amlodipine therapy confirms that calcium channel blockade effectively addresses this mechanism. The magnitude of TPR reduction ( $-790$  dyn·s·cm<sup>-5</sup>) suggests substantial normalization of peripheral vascular resistance within a short therapeutic window. Conversely, patients with volume-dependent hypertension demonstrated elevated TBW values indicative of fluid retention and altered sodium handling. Indapamide therapy resulted in a statistically significant reduction in TBW, consistent with its diuretic and vascular effects. The associated improvement in blood pressure underscores the importance of targeting volume status in selected patients. The overall 90 % target achievement rate within 10 days is particularly noteworthy. This exceeds typical control rates observed with conventional empirical monotherapy strategies, which often range between 30 % and 50 % during early treatment phases. Moreover, the absence of adverse events suggests that physiologically guided monotherapy may improve both efficacy and safety. The NICaS system provided reproducible and clinically actionable hemodynamic data. Its non-invasive design and relatively simple operational protocol make it suitable for outpatient clinical settings. By integrating objective hemodynamic measurements into therapeutic decision-making, clinicians may transition from reactive dose escalation to mechanism-driven intervention. These findings align with the broader paradigm of precision medicine, emphasizing individualized treatment based on measurable biological parameters rather than population averages.

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**Limitations** Several limitations should be acknowledged. First, the study duration was limited to 10 days, preventing assessment of long-term cardiovascular outcomes or sustained hemodynamic adaptation. Second, the single-center design may limit generalizability to other populations. Third, patients with mixed hemodynamic phenotype were excluded from efficacy analysis; therefore, conclusions cannot be directly extended to this subgroup. Finally, the study did not include a parallel empirical-treatment control group, which would strengthen comparative interpretation. Future randomized, multicenter trials with longer follow-up periods are warranted to confirm these findings and evaluate long-term cardiovascular event reduction.

**Clinical implications** The integration of bioimpedance cardiography into hypertension management may redefine first-line therapeutic strategies. Hemodynamic phenotyping enables clinicians to:

- Identify the dominant mechanism of blood pressure elevation.
- Select targeted monotherapy.
- Reduce unnecessary drug combinations.
- Improve patient adherence.
- Potentially decrease healthcare costs.
- Such an approach may be particularly beneficial in resource-limited settings where rational pharmacotherapy optimization is essential.

### Conclusion

Bioimpedance-guided hemodynamic phenotyping using the NiCaS system represents a clinically effective and innovative strategy for managing stage I–II arterial hypertension. Targeted monotherapy based on objective assessment of TPR and TBW achieved rapid blood pressure control in 90 % of patients without adverse events.

This personalized approach minimizes polypharmacy, enhances therapeutic precision, and aligns with contemporary precision medicine principles. Broader implementation of bioimpedance-based stratification may significantly improve hypertension management paradigms.

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