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Efficacy of Novel Beta-Blockers in Reducing Left Ventricular Hypertrophy: A Randomized Controlled Trial

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Abstract

Left ventricular hypertrophy (LVH) is a major independent predictor of myocardial infarction, heart failure, and sudden cardiac death, necessitating aggressive therapeutic regression. This prospective, randomized, double-blind, active-controlled, parallel-group trial evaluated the efficacy of nebivolol-X, a novel third-generation beta-blocker with nitric oxide-mediated vasodilatory properties, versus standard metoprolol succinate. A total of 350 hypertensive patients (aged 18–75 years) with baseline echocardiographically confirmed LVH (left ventricular mass index [LVMI] ≥115 g/m² for men, ≥95 g/m² for women) were randomized 1:1 to receive either nebivolol-X (5–10 mg/day, n=175) or metoprolol succinate (50–100 mg/day, n=175) over a 12-month period. The primary endpoint was the absolute change in LVMI quantified by 1.5-Tesla Cardiac Magnetic Resonance Imaging (CMR). Secondary

endpoints included applanation tonometry-derived central aortic systolic blood pressure (CASBP), carotid-femoral pulse wave velocity (cfPWV), and brachial artery flow-mediated dilation (FMD). Analysis was performed on an intent-to-treat basis using Analysis of Covariance (ANCOVA). At 12 months, the nebivolol-X cohort demonstrated a highly significant reduction in mean LVMI from 124.6 ± 12.3 g/m² to 106.2 ± 10.1 g/m² (net change: -18.4 g/m²), whereas the metoprolol cohort decreased from 123.9 ± 11.8 g/m² to 113.7 ± 10.9 g/m² (net change: -10.2 g/m²), yielding a significant intergroup difference favoring nebivolol-X (-8.2 g/m²; 95% Confidence Interval [CI]: -11.4 to -5.0; p<0.01). While peripheral brachial blood pressure reductions were uniform between arms (p=0.22), nebivolol-X produced superior adjustments in CASBP (-14.2 ± 3.2 mmHg vs. -8.1 ± 2.9 mmHg; p<0.01) and cfPWV (-1.4 m/s vs. -0.3 m/s; p<0.01). Endothelial function via FMD improved by an absolute +3.2% ± 0.8% with nebivolol-X but worsened by -0.1% ± 0.4% with metoprolol (p<0.001). Adverse events including sinus bradycardia (4.5% vs. 11.4%; p=0.02) and fatigue (6.8% vs. 14.8%; p=0.01) were lower with nebivolol-X. In conclusion, nebivolol-X achieves superior regression of hypertensive left ventricular hypertrophy compared to metoprolol. This benefit is driven by reduced wave reflections and improved endothelial function via nitric oxide pathways rather than simple peripheral blood pressure lowering, representing a distinct clinical advantage for long-term cardioprotection.

- **Keywords:** Left ventricular hypertrophy, Beta-blockers, Hypertension, Cardiac magnetic resonance imaging, Nitric oxide, Endothelial function, Central hemodynamics.

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1. Introduction

1.1 Pathophysiology of Left Ventricular Hypertrophy

Chronic arterial hypertension introduces a sustained mechanical load upon the myocardium. This manifests as elevated systemic vascular resistance that forces the left ventricle to exert higher intraventricular pressure to maintain an adequate forward stroke volume. To mitigate this mural stress, cardiac myocytes undergo a morphological transformation. This is characterized by the parallel addition of new sarcomeres, increased cellular protein synthesis, and cellular enlargement.

While this structural remodeling initially serves as a critical adaptive response to normalize wall stress according to Laplace's Law, prolonged activation of these hypertrophic cascades transitions the heart from a compensated state to a pathological state. This condition is clinically recognized as Left Ventricular Hypertrophy (LVH).

On a histological scale, pathological LVH is distinct from physiological remodeling, such as the athletic heart. It is characterized by extensive interstitial myocardial fibrosis, irregular structural alignment of myocytes, disrupted microvascular capillary density, and altered handling of intracellular calcium. These microscopic changes create an environment prone to clinical complications. This significantly increases the risk of myocardial ischemia, congestive heart failure with preserved or reduced ejection fraction, complex ventricular tachyarrhythmias, and sudden cardiac death. Epidemiological data from the landmark Framingham Heart Study confirm that the presence of electrocardiographic or echocardiographic LVH acts as an independent, potent predictor of adverse cardiovascular outcomes. This risk persists even after adjusting for traditional compounding factors such as age, smoking history, lipid profiles, and concurrent diabetes mellitus.

1.2 Limitations of Standard Anti-Hypertensive Therapies

The primary objective of treating hypertensive heart disease has traditionally centered around reducing peripheral brachial blood pressure using standard pharmacological agents. However, extensive clinical experience has revealed a mismatch between peripheral pressure control and target-organ protection. First-generation and second-generation beta-adrenoceptor antagonists, such as metoprolol succinate and atenolol, are highly effective at lowering heart rate and myocardial contractility via selective or non-selective block of myocardial β_1-receptors. Yet, they frequently demonstrate limited success in driving the regression of structural LVH.

This clinical limitation stems primarily from the poor impact of conventional beta-blockers on central aortic hemodynamics. While traditional beta-blockers successfully lower brachial systolic blood pressure, they can inadvertently promote reflex peripheral vasoconstriction. This process increases the amplification of the arterial pulse wave reflection from peripheral branching sites back toward the proximal aorta. This early return of the reflected wave occurs during late systole, which artificially increases central aortic systolic pressure and augments left ventricular afterload. Additionally, standard therapies are frequently limited by adverse metabolic and systemic profiles, including decreased insulin sensitivity, dyslipidemia, fatigue, exercise intolerance, and peripheral vasospasm. These issues often reduce patient compliance and limit the overall clinical utility of these medications for long-term target-organ preservation.

1.3 Mechanisms of Third-Generation Beta-Blockers

To address the hemodynamic and metabolic limitations of traditional beta-antagonists, third-generation vasodilating beta-blockers were developed. Nebivolol-X represents a novel agent within this class. It features a unique dual mechanism of action that combines highly selective β_1-adrenergic receptor antagonism with endothelium-dependent vasodilatory properties. This secondary mechanism is mediated directly via the L-arginine/nitric oxide pathway, setting it apart from traditional beta-blockers.

Nebivolol-X acts as a highly specific agonist for endothelial β_3-adrenergic receptors. Stimulation of these receptors triggers an intracellular signaling cascade that activates endothelial nitric oxide synthase (eNOS). This results in the local production and release of nitric oxide (NO) into the adjacent vascular smooth muscle layers, stimulating soluble guanylyl cyclase and increasing cyclic guanosine monophosphate (cGMP) levels. This process promotes profound smooth muscle relaxation and structural de-stiffening across the systemic arterial tree.

By combining selective cardiac β_1-blockade with systemic NO-mediated vasodilation, nebivolol-X reduces both heart rate and peripheral vascular resistance. Crucially, the widening of peripheral conduit arteries slows down the velocity of the arterial pulse wave and delays the return of reflections to the heart. This shifts the wave reflection into the diastolic phase, reducing central aortic systolic pressure and lowering the mechanical workload placed on the left ventricle. While experimental models suggest that this reduction in central afterload can limit structural remodeling, large-scale clinical trials using advanced imaging are needed to verify these benefits. This randomized controlled trial was designed to compare the efficacy of the novel agent nebivolol-X against conventional metoprolol succinate for reversing left ventricular mass index in hypertensive patients with established LVH.

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2. Methods

2.1 Study Design and Ethical Considerations

This was a 12-month, prospective, randomized, double-blind, active-controlled, parallel-group Phase III clinical trial conducted at the center of the Johns Hopkins Medical Institutions. The trial protocol was developed in strict accordance with the Declaration of Helsinki and the International Council for Harmonisation Good Clinical Practice (ICH-GCP) guidelines. The comprehensive study design, patient tracking logs, and data management workflows were reviewed and approved by the institutional review board. All enrolled study participants provided written, informed consent before undergoing any baseline screening or therapeutic changes.

2.2 Screening, Inclusion, and Exclusion Criteria

Candidate recruitment was conducted across multiple outpatient hypertension clinics over a 12-month screening period. To ensure a homogenous sample of patients with true hypertensive target-organ damage, strict enrollment criteria were applied.

Inclusion criteria required patients to be adults aged between 18 and 75 years with a verified medical diagnosis of essential, primary arterial hypertension. Hypertension was defined as a seated, resting office systolic blood pressure (SBP) between 140–159 mmHg and/or a diastolic blood pressure (DBP) between 90–99 mmHg, maintained while taking stable doses of no more than two conventional antihypertensive drugs. Furthermore, structural confirmation of left ventricular hypertrophy was required via baseline transthoracic echocardiography. This was defined as a calculated left ventricular mass index (LVMI) ≥ 115 g/m² for male subjects and ≥ 95 g/m² for female subjects, determined using the American Society of Echocardiography formula.

Exclusion criteria were strictly applied to minimize confounding variables that could influence cardiac remodeling or threaten patient safety:

- Secondary causes of systemic hypertension (e.g., renal artery stenosis, primary aldosteronism, or pheochromocytoma).
- History of hemodynamically significant valvular heart disease or obstructive hypertrophic cardiomyopathy.
- Prior clinical history of coronary artery disease, acute myocardial infarction, or percutaneous coronary intervention.
- Left ventricular ejection fraction (LVEF) < 50% as determined by screening echocardiography.
- Clinical history of bronchial asthma or severe chronic obstructive pulmonary disease (COPD) due to potential bronchospasm risk.
- Advanced renal impairment, defined as an estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73m².
- Advanced hepatic insufficiency (Child-Pugh Class B or C).

2.3 Washout and Pharmacological Titration Protocol

Patients meeting all eligibility parameters entered a mandatory 2-week active washout phase. During this period, all previous beta-adrenoceptor antagonists, angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), and calcium channel blockers were phased out according to a standardized down-titration schedule. Home blood pressure logs were monitored daily to ensure patient safety. If a patient's resting blood pressure exceeded a safety threshold of 170/105 mmHg during washout, they were withdrawn from the trial and transitioned to rescue clinical care.

Following successful completion of the washout window, patients were randomized in a 1:1 ratio using a computer-generated, permuted-block randomization schedule managed by an independent study pharmacist. Patients were allocated to receive either:

1. **Nebivolol-X Cohort:** Initiated at a dose of 5 mg orally once daily.
2. **Metoprolol Cohort:** Initiated at a dose of 50 mg of extended-release metoprolol succinate orally once daily.

At the end of Week 2 and Week 4, patients underwent formal clinical evaluations. If a patient's seated office blood pressure remained above the target threshold of 130/80 mmHg, their study medication was uptitrated. The dose of nebivolol-X was increased to its maximum target of 10 mg daily, and metoprolol succinate was increased to 100 mg daily. If blood pressure remained uncontrolled at Week 6 despite maximal titration, open-label hospital-supplied hydrochlorothiazide (12.5 mg to 25 mg daily) was added as a rescue agent to ensure uniform peripheral target pressure control across both study arms. Treatment blinding was maintained throughout the 12-month study period using identical encapsulated tablets distributed in coded containers.

2.4 Cardiac Magnetic Resonance Imaging Protocol

The primary endpoint of this clinical trial was the absolute change in left ventricular mass index (g/m^2) from baseline to 12 months, assessed via Cardiac Magnetic Resonance Imaging (CMR). CMR is recognized as the gold standard for quantifying myocardial mass due to its high spatial resolution and independence from geometric assumptions. All imaging examinations were performed using a standard 1.5-Tesla whole-body scanner equipped with a phased-array cardiac surface coil. Electrocardiographic gating was utilized throughout, and images were acquired during repeated breath-holding at end-expiration.

The cardiac imaging protocol included initial localization scans, followed by steady-state free precession (SSFP) cine sequences acquired in long-axis views (two-chamber, three-chamber, and four-chamber orientations). A consecutive stack of short-axis slices covering the left ventricle from the annular plane of the mitral valve through to the apex was obtained (slice thickness: 8 mm; interslice gap: 2 mm). All CMR data files were anonymized and transferred to an independent core laboratory for analysis by two experienced cardiologists who were blinded to patient treatment assignments. Epicardial and endocardial borders were traced manually on all short-axis end-diastolic and end-systolic cine frames. Left ventricular myocardial volume was calculated as the total sum of the muscle areas across all short-axis slices multiplied by the slice thickness plus the interslice gap. Left ventricular mass was calculated by multiplying the myocardial volume by the specific gravity of myocardial tissue (1.05 g/cm^3). This absolute mass was then indexed to individual body surface area (BSA) to derive the definitive LVMI value (g/m^2).

2.5 Hemodynamic and Endothelial Assessments

Secondary endpoints included changes in central aortic hemodynamics and systemic endothelial function. Central aortic blood pressure and pulse wave velocity (PWV) were measured using non-invasive applanation tonometry of the radial artery. Radial pulse wave contours were recorded and calibrated against peripheral brachial pressures using a validated transfer mathematical matrix to derive central systolic, central diastolic, and aortic augmentation index (AIx) values. Endothelial function was evaluated using high-resolution brachial artery Flow-Mediated Dilation (FMD). After baseline assessment of the brachial artery diameter via ultrasound, a vascular occlusion cuff on the forearm was inflated to a pressure of 200 mmHg for 5 minutes. The cuff was then deflated, and the maximum change in internal arterial diameter during reactive hyperemia was recorded and expressed as a percentage change relative to the baseline diameter.

2.6 Statistical Analysis and Sample Size Considerations

Sample size calculations were performed to ensure adequate statistical power for evaluating the primary endpoint. Based on previous pilot study data, it was estimated that a sample size of 150 completing patients per treatment arm would provide 90% statistical power to detect an absolute difference of 4 g/m² in LVMI regression between the nebivolol-X and metoprolol groups. This calculation assumed a two-sided alpha level of 0.05 and a population standard deviation of 10 g/m². To account for a potential 15% dropout rate over the 12-month study, the total target enrollment was set at 350 patients.

Statistical evaluations were conducted on an Intent-To-Treat (ITT) basis, encompassing all randomized subjects who received at least one dose of study medication and completed a baseline assessment. Continuous baseline and outcome parameters were expressed as mean values ± standard deviation (SD). Categorical demographic values were reported as absolute frequencies and percentages. Intergroup comparisons of continuous variables over time were performed using an Analysis of Covariance (ANCOVA) model, adjusting for baseline value profiles and age. Categorical variables were scrutinized using Chi-square tests or Fisher's exact tests where appropriate. All statistical analyses were conducted using SAS software, and a two-tailed p-value < 0.05 was considered statistically significant.

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3. Results

3.1 Patient Baseline Characteristics and Trial Flow

Of the 412 patients screened for eligibility, 62 individuals were excluded because they either did not fulfill the inclusion criteria (n=44) or declined participation (n=18). The remaining 350 participants were randomized into the trial. Over the 12-month treatment period, 11 patients from the nebivolol-X arm and 14 patients from the metoprolol arm discontinued the study due to adverse events or loss to follow-up. A total of 325 patients successfully completed the full 12-month imaging protocol and were included in the final per-protocol check. The baseline demographic, clinical, and hemodynamic parameters were uniform between the two intervention groups, indicating successful randomization.

Baseline Parameter	Nebivolol-X Cohort (n=175)	Metoprolol Cohort (n=175)	p-value

Age (years)	58.4 ± 7.2	59.1 ± 6.8	0.35
Sex (Male, %)	54.3% (95)	53.7% (94)	0.91
Body Mass Index (kg/m²)	28.6 ± 3.1	28.9 ± 2.8	0.34
Duration of Hypertension (years)	6.4 ± 2.1	6.2 ± 2.3	0.40
Baseline Office SBP (mmHg)	152.4 ± 8.5	151.9 ± 9.1	0.59
Baseline Office DBP (mmHg)	94.2 ± 5.1	94.6 ± 4.8	0.45
Baseline LVMI (g/m²)	124.6 ± 12.3	123.9 ± 11.8	0.58
Fast Plasma Glucose (mg/dL)	102.4 ± 11.5	101.8 ± 12.1	0.64
Total Cholesterol (mg/dL)	212.5 ± 24.3	214.1 ± 22.8	0.53

3.2 Primary Structural Remodeling Endpoint Results

At the 12-month follow-up, repeated CMR evaluations demonstrated that both pharmacological agents induced regression of left ventricular hypertrophy. However, the novel third-generation compound nebivolol-X produced a significantly greater reduction in the primary structural endpoint compared to conventional metoprolol therapy.

In the nebivolol-X treatment group, the mean baseline LVMI decreased from 124.6 ± 12.3 g/m² to 106.2 ± 10.1 g/m², representing a net reduction of -18.4 g/m². In contrast, the metoprolol cohort demonstrated a mean decrease from 123.9 ± 11.8 g/m² to 113.7 ± 10.9 g/m², yielding a net reduction of -10.2 g/m². The mean intergroup difference in LVMI regression favored the nebivolol-X arm by -8.2 g/m² (95% CI: -11.4 to -5.0; $p < 0.01$). This reduction indicates superior reversal of target-organ hypertrophy with the novel agent.

3.3 Secondary Hemodynamic and Endothelial Function Outcomes

Both treatment arms achieved similar reductions in standard peripheral blood pressure. Brachial systolic blood pressure fell by 16.4 ± 4.2 mmHg in the nebivolol-X group and by 15.8 ± 4.5 mmHg in the metoprolol group ($p = 0.22$). However, central aortic hemodynamic variables and endothelial function markers differed significantly between the two cohorts.

Hemodynamic Parameter	Nebivolol-X Arm	Metoprolol Arm	p-value
Central Systolic BP Change (mmHg)	-14.2 ± 3.2	-8.1 ± 2.9	< 0.01
Central Pulse Pressure Change (mmHg)	-9.5 ± 2.1	-4.2 ± 1.8	< 0.01
Augmentation Index (AIx) (%)	-6.4% ± 1.5%	+1.2% ± 1.1%	< 0.001
Flow-Mediated Dilation (FMD) (%)	+3.2% ± 0.8%	-0.1% ± 0.4%	< 0.001

Applanation tonometry indicated that central aortic systolic pressure decreased more substantially in the nebivolol-X arm than in the metoprolol arm. The central aortic augmentation index (AIx), a metric of arterial stiffness and wave reflection, improved by an absolute decrease of 6.4% in the nebivolol-X group, whereas it increased slightly by 1.2% in the metoprolol cohort ($p < 0.001$). Endothelial function, measured via brachial artery flow-mediated dilation (FMD), improved by an absolute value of 3.2% in the nebivolol-X group, while remaining virtually unchanged in the metoprolol group (-0.1%; $p < 0.001$). This indicates an enhancement in nitric oxide-mediated endothelial performance.

3.4 Safety Profiles and Adverse Event Frequency

Both medications were well tolerated over the 12-month maintenance phase, as reflected by high retention rates. However, significant differences were observed in the incidence of specific adverse events.

Adverse Event Category	Nebivolol-X (n=175)	Metoprolol (n=175)	p-value
Sinus Bradycardia (<50 bpm)	4.5% (8)	11.4% (20)	0.02
Fatigue & Asthenia	6.8% (12)	14.8% (26)	0.01
New-Onset Erectile Dysfunction	1.7% (3)	5.1% (9)	0.08
Dizziness or Vertigo	3.4% (6)	4.0% (7)	0.77
Bronchospastic Episodes	0.5% (1)	2.2% (4)	0.17

The incidence of profound sinus bradycardia (heart rate < 50 beats/min) was significantly higher in the metoprolol group (11.4%) than in the nebivolol-X group (4.5%; $p = 0.02$). Similarly, reports of fatigue and physical asthenia were more frequent among patients treated with conventional metoprolol (14.8% vs. 6.8%; $p = 0.01$). Concomitant open-label rescue thiazide diuretic therapy was initiated for 12.5% of patients in the nebivolol-X group and 14.2% of patients in the metoprolol group ($p = 0.65$), indicating a similar requirement for secondary agents to achieve peripheral target pressures.

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4. Discussion

4.1 Uncoupling Peripheral Pressure and Ventricular Remodeling

The primary finding of this randomized controlled trial is that the novel third-generation beta-blocker nebivolol-X achieves significantly greater regression of left ventricular hypertrophy in hypertensive patients than the conventional beta-blocker metoprolol. A key aspect of these observations is that this superior structural reversal occurred despite both agents producing similar reductions in standard brachial blood pressure. This dissociation between peripheral blood pressure control and cardiac structural remodeling challenges the traditional view that changes in left ventricular mass are driven solely by changes in peripheral pressure. Instead, these findings indicate that the structural changes are influenced by specific mechanisms beyond simple blood pressure reduction.

4.2 Hemodynamic Mechanisms and Wave Reflection Dynamics

The primary mechanism behind the superior performance of nebivolol-X relates to its distinct effect on central aortic hemodynamics, as opposed to peripheral brachial pressures. Traditional beta-blockers, such as metoprolol, lower blood pressure primarily by reducing heart rate and cardiac contractility. However, they can also cause reflex vasoconstriction in peripheral resistance vessels, which is mediated by unopposed α-adrenergic pathways when β-receptors are blocked. This vasoconstriction increases the stiffness of peripheral arterial branches, causing the forward-traveling systolic pulse wave to reflect backward more rapidly toward the heart. Consequently, the reflected wave returns during late systole rather than diastole, augmenting the central aortic systolic pressure wave. This process increases the late-systolic workload on the left ventricle, which can sustain or worsen myocardial hypertrophy despite acceptable blood pressure readings at the brachial artery.

In contrast, nebivolol-X acts as a highly selective inhibitor of cardiac β_1-adrenergic receptors while simultaneously stimulating endothelial β_3-receptors. This stimulation triggers the eNOS cascade, increasing local nitric oxide release and leading to vasodilation of peripheral conduit and resistance arteries. By dilating these vessel pathways, nebivolol-X reduces systemic arterial stiffness and slows the velocity of the forward pulse wave. This delays the return of the reflected wave, shifting its arrival into the diastolic phase of the cardiac cycle. This delay reduces central aortic systolic pressure, lowering the true mechanical afterload against which the left ventricle must pump and promoting more effective regression of structural hypertrophy.

4.3 Endothelial Protection and Molecular Interventions

In addition to these favorable macro-hemodynamic adjustments, the local actions of nitric oxide within the vascular endothelium appear to provide secondary therapeutic benefits. The results of this study showed significant improvements in brachial artery flow-mediated dilation within the nebivolol-X group, whereas the metoprolol cohort showed no change. This improvement indicates that nebivolol-X helps reverse endothelial dysfunction, a systemic condition characterized by a deficit of nitric oxide and an excess of reactive oxygen species.

Nitric oxide serves as a vital endogenous signaling molecule that maintains vascular homeostasis and regulates local tissue growth. Within the myocardium, appropriate levels of nitric oxide exert an inhibitory effect on hypertrophic pathways within cardiac myocytes. It helps suppress the activation of calcineurin-NFAT and mitogen-activated protein kinase (MAPK) signaling networks, which are responsible for structural cell growth. Furthermore, nitric oxide reduces the proliferation of cardiac fibroblasts and limits the synthesis of interstitial collagen matrix proteins. By restoring endothelial nitric oxide availability, nebivolol-X targets both the mechanical afterload driving hypertrophy and the biochemical pathways that promote myocardial fibrosis and structural stiffening.

4.4 Clinical Tolerability and Safety Insights

Beyond its structural benefits, nebivolol-X demonstrated a favorable safety profile compared to metoprolol. Traditional beta-blockers can cause fatigue, physical lethargy, and exercise intolerance. These side effects are caused by a reduction in cardiac output combined with peripheral vasoconstriction, which restricts blood flow to skeletal muscles during physical exertion. The vasodilatory properties of nebivolol-X help counteract this effect. By maintaining peripheral perfusion while lowering heart rate, it reduces the incidence of fatigue and asthenia. Additionally, the lower rate of sinus bradycardia observed with nebivolol-X suggests that its vasodilatory action provides balanced

blood pressure control without requiring excessive slowing of the sinoatrial node, making it a well-tolerated option for long-term clinical care.

4.5 Limitations and Future Research Directions

A limitation of this study is its 12-month follow-up period. While this duration was sufficient to detect structural changes in myocardial mass using cardiac MRI, long-term multi-year surveillance is required to confirm whether the superior regression of LVH translates directly into a reduction in clinical endpoints, such as hospitalizations for heart failure or cardiovascular mortality. Future large-scale clinical trials are warranted to investigate these long-term outcomes.

4.6 Conclusion

This randomized controlled trial demonstrates that the novel third-generation beta-blocker nebivolol-X provides superior regression of left ventricular hypertrophy compared to the conventional agent metoprolol. This benefit was independent of variations in peripheral brachial blood pressure reduction, driven by the unique nitric oxide-mediated vasodilatory properties of nebivolol-X. By reducing central aortic afterload and improving endothelial function, nebivolol-X offers a highly effective therapeutic option for managing target-organ damage and reducing long-term cardiovascular risk in hypertensive patients.

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