



## **HIIT versus MICT on Blood Pressure and Cardiac Biomarkers in L-NAME-induced Hypertensive Rats**

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### *Abstract*

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Hypertension remains a major global health burden, yet the optimal exercise strategy to mitigate its associated inflammatory and oxidative stress responses is still unclear. This study aimed to compare the effects of high-intensity interval training (HIIT) and moderate-intensity continuous training (MICT) on markers of inflammation and oxidative stress, including serum IL-6, NOX4, and cardiac tissue MMP-2 in a rat model of hypertension. Hypertension was induced in male Wistar rats through L-NAME administration for five weeks, during which the rats concurrently underwent HIIT or MICT. L-NAME administration resulted in a progressive increase in systolic blood pressure (SBP) by week five compared to control rats. L-NAME significantly increased serum IL-6 and NOX4 levels but did not significantly affect cardiac MMP-2 expression. MICT significantly reduced SBP and NOX4 levels, whereas IL-6 and MMP-2 levels remained unchanged. In contrast, HIIT did not produce significant reductions in SBP, IL-6, NOX4, or MMP-2. Statistical significance was defined as  $p \leq 0.05$ . In conclusion, these findings indicate that MICT is more effective than HIIT in reducing elevated SBP and NOX4 levels in L-NAME-induced hypertensive rats.

**Keywords:** Animal model, inflammation, oxidative stress, systolic, training

### **Introduction**

Hypertension poses a substantial challenge to global public health and remains a leading contributor to cardiovascular diseases. Its prevalence has increased markedly over recent decades, rising from 648 million cases in 1990 to 1.278 billion in 2019.<sup>1</sup> This escalation has been accompanied by more than 218 million cases of disability and approximately 10 million deaths worldwide.<sup>2</sup> Among the major modifiable risk factors for hypertension is a sedentary lifestyle.<sup>3</sup>

The presence of pro-inflammatory cytokines like IL-6 and the infiltration of immune cells are strongly associated with the progression of hypertension, indicating the critical role that inflammation plays in the condition. This assertion is supported by studies indicating consistently elevated levels of pro-inflammatory cytokines in both animal models and hypertensive individuals.<sup>4-6</sup> Apart from inflammation, increased NADPH oxidase (NOX) activity produces

endogenous reactive oxygen species (ROS), which contribute to the onset of hypertension. Vascular smooth muscle cells (VSMCs) and endothelial cells (ECs) become dysfunctional as a result of oxidative stress and abnormal redox signaling caused by the elevated activity of NOX subtypes (NOX4, NOX2, and NOX1) in vascular beds.<sup>7</sup> Moreover, vascular dysfunction, impaired nitric oxide (NO) bioavailability, and increased oxidative stress raise the activity of matrix metalloproteinase-2 (MMP-2), a component of the extracellular matrix. Excessive activity of MMP-2 can trigger vascular and cardiac remodeling.<sup>8</sup> Achieving a balance between pro- and anti-inflammatory responses, pro- and anti-oxidant mechanisms, and redox reactions is crucial for halting disease progression and safeguarding cardiovascular homeostasis in hypertension. The equilibrium state of these components can be restored using both pharmacological and non-pharmacological strategies.<sup>9</sup>

Physical exercise is recognized as a non-pharmacological intervention and preventive measure for hypertension, and has been shown to confer cardiovascular benefits. These benefits include diminished oxidative stress, decreased blood pressure, inhibition of fibrogenesis, and reduced inflammation. Both experimental and clinical investigations support these findings.<sup>3,5,10,11</sup>

Two popular forms of physical activity are High-Intensity Interval Training (HIIT) and Moderate-Intensity Continuous Training (MICT). HIIT involves brief bursts of high-intensity exercise alternated with recovery periods or lower-intensity exercise, whereas MICT consists of steady, moderate-intensity exercise carried out over a longer duration. Both HIIT and MICT start with a warm-up, followed by the main workout, and finish with a cool-down. The key distinction is in the main workout: HIIT features intervals of high-intensity exercise lasting a few minutes, interspersed with recovery periods, with cycles repeating for 15-30 minutes. In contrast, MICT involves continuous exercise at moderate intensity for 30-60 minutes.<sup>12</sup> Both types of exercise are effective for enhancing aerobic capacity, with HIIT being more time-efficient and able to improve aerobic capacity quickly, while MICT offers a more consistent boost in aerobic capacity due to its prolonged duration.<sup>10</sup>

However, studies in both humans and animal models have reported conflicting results regarding the effects of different exercise modalities on blood pressure and inflammatory or oxidative stress markers, as summarized in Table 1.

**Table 1.** Summary of studies reporting heterogenous effects of exercise training in human and animal models

Study	Subject Type	Exercise Type	Exercise Duration	Outcomes
Huang et al <sup>5</sup>	Hypertensive Rats	Other types	12 weeks	- SBP ↓ - IL-6 ↓ - MMP-2 ↓
Luo et al <sup>6</sup>	Hypertensive Rats	MICT	14 weeks	- NOX2 ↓ - NOX4 ↓
Da Palma et al <sup>13</sup>	Hypertensive Rats	Other types	8 weeks	- NOX ↓
Hu et al <sup>3</sup>	Metabolic Disorders Rats	HIIT and MICT	8 weeks	- IL-6 ↓ - IFN-β ↓
Groussard et al <sup>14</sup>	Obese Rats	HIIT and MICT	10 weeks	- NOX —
Mallard et al. <sup>15</sup>	T2DM Humans	HIIT and MICT	12 weeks	- IL-6 — - IL-10 —
Vella et al. <sup>16</sup>	Obese Humans	HIIT	5 weeks	- IL-6 ↑ - CRP ↑

↑: increase in levels; ↓: decrease in levels; —: no change; T2DM: type 2 diabetes mellitus; SBP: systolic blood pressure; IL: interleukin; MMP: matrix metalloproteinase; NOX: NADPH oxidase; IFN: interferon; CRP: C-reactive protein

Although components of inflammation and oxidative stress have been examined in various exercise studies, no consensus has been reached regarding which training modality is most effective for improving these biomarkers in hypertension. Moreover, to our knowledge, no previous research has simultaneously evaluated serum IL-6, NOX4, and cardiac tissue MMP-2 responses to HIIT and MICT specifically within an L-NAME-induced hypertensive rat model, highlighting the novelty of this investigation. This integrative biomarker approach provides additional perspective on inflammatory and oxidative responses in hypertension beyond what has been examined in previous exercise studies. Building on these gaps in the literature and the physiological differences between exercise modalities, we hypothesized that MICT would be more effective than HIIT in reducing serum IL-6 and NOX4 levels, and cardiac tissue MMP-2 expression, as well as improving blood pressure, in L-NAME-induced hypertensive rats.

## Methods

### *Participants*

This investigation constitutes an *in vivo* experimental study utilizing laboratory animals. Twenty-four male albino Wistar rats (*Rattus norvegicus*), aged 10-13 weeks and weighing 220-300 g, were used. Two rats were housed per cage. Standard food and water were provided *ad libitum*, and cages were maintained in a clean environment with appropriate humidity. The rats were kept at a constant temperature of 23°C under a 12-hour light-dark cycle. Animal health and well-being were monitored daily throughout the study.

The sample size was determined using the Federer<sup>17</sup> formula  $(t-1)(n-1) \geq 15$ , resulting in a minimum of six rats per group. This ensured adequate replication for ANOVA while minimizing animal use in accordance with ethical principles. A formal power analysis was not conducted because the study was exploratory in nature, involved multiple novel outcomes, and lacked sufficient prior data to reliably estimate effect sizes for vascular, inflammatory, and oxidative stress markers. The selected sample size ( $n = 6$  per group; total  $N = 24$ ) is consistent with previous studies<sup>18</sup> in spontaneously hypertensive rats (SHR), including recent investigations comparing HIIT and MICT, which reported significant differences in these outcomes.

The study was conducted between March and December 2023 at the laboratories of the Department of Physiology, Anatomical Pathology, and Biochemistry, Faculty of Medicine, Universitas Indonesia. All experimental procedures were approved by the Ethics Committee of the Faculty of Medicine, Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia (Ethics code: KET-1159/UN2.F1/ETIK/PPM.00.02/2022; protocol number 22-09-1102). The study was conducted in accordance with the ethical standards of the International Journal of Exercise Science (IJES) and complied with animal research guidelines as outlined by Navalta et al.<sup>19</sup>

### *Protocol*

Rats were randomly allocated into four groups ( $n = 6$  per group): Normotensive Control (NC), Hypertensive Control (HC), HIIT, and MICT. Hypertension was induced in the HC, HIIT, and MICT groups through administration of L-NAME, a nitric oxide synthase (NOS) inhibitor, starting at week 1 and continuing for five weeks. During this period, rats in the HIIT and MICT groups simultaneously underwent treadmill exercise according to their respective protocols. Rats in the NC and HC groups did not receive exercise intervention.

This study employed N $\omega$ -nitro-L-arginine methyl ester hydrochloride (L-NAME), a NOS inhibitor with >98% purity (Abcam plc, Cambridge, United Kingdom), administered at a dose of 40 mg/kg/day orally. To facilitate ingestion, L-NAME was dissolved in 100 mL of drinking water.

Prior to the experimental phase (week 0), rats underwent a one-week treadmill habituation protocol, during which speed and duration were progressively increased by 2 m/min and 2 minutes per day, respectively. After the initial two days of habituation, each rat's maximal running speed (MRS) was determined. MRS was reassessed every two weeks to adjust training intensity according to performance adaptations.

Two treadmill-based exercise protocols were implemented using a Panlab LE8710RTS treadmill (Harvard Apparatus, Massachusetts, USA) over five weeks (weeks 1–5), with a frequency of five sessions per week. The first regimen, MICT, consisted of uninterrupted exercise at 70% of MRS for a duration of 36 minutes. The second regimen, HIIT, consisted of intermittent exercise sessions: 6-minute intervals at 90% of MRS followed by 6-minute intervals at 50% of MRS, repeated six times for a duration of 36 minutes. Both protocols included standardized 5-minute warm-up and cool-down periods at 6 m/min.

These exercise procedures were adapted from Krzesiak et al.<sup>20</sup> with methodological adjustments to match training intensity and workload to the rats' running performance. The habituation protocol was simplified by removing treadmill incline and implementing a gradual progression in speed and duration. The training period was set to five weeks to align with the L-NAME induction schedule. HIIT intervals were extended to six minutes for both high- and low-intensity phases to provide a uniform workload reflective of each animal's maximal running speed. Warm-up and cool-down periods were added to standardize the session structure and ensure a controlled initiation and termination of exercise bouts.

Blood pressure was assessed non-invasively using a volume pressure recording (VPR) tail-cuff system (CODA™, Kent Scientific Corporation, Connecticut, USA). Measurements were conducted weekly, in a quiet environment at 23°C, between 08:00 and 11:00 a.m., prior to L-NAME administration and exercise sessions. Body weight was recorded immediately after blood pressure measurement.

Each blood pressure assessment consisted of two recording sessions, each preceded by five acclimatization cycles and followed by 15 measurement cycles. Readings affected by signal instability were excluded, and the mean of valid readings from both sessions was used to determine systolic blood pressure (SBP), as described by El-Mahdy et al.<sup>20</sup>. The study adhered to the American Heart Association (AHA) Scientific Statement on animal models of hypertension; in the L-NAME model, sustained systolic blood pressure values typically reach approximately 150 mmHg.<sup>22</sup>

At study completion, rats were euthanized via intraperitoneal injection of ketamine (Ketalar®, Pfizer Inc. New York, USA) and xylazine (Xyla®, Interchemie Venray, Netherlands) at a lethal dose. Blood samples were collected from the orbital sinus into EDTA tubes (BD Vacutainer®, New Jersey, USA), centrifuged at 3500 rpm for 15 minutes using an Eppendorf 5804 R Centrifuge (Eppendorf AG, Hamburg, Germany), and plasma was stored at -80°C. Following confirmation of death, cardiac organs were surgically excised, weighed, and processed for analysis. The cardiac organ index was calculated by dividing the cardiac organ weight by the final body weight of the rat and multiplying by 100.

Serum samples were used for IL-6 and NOX4 analysis, while cardiac tissue homogenates were used for MMP-2 measurement. The levels of IL-6, NOX4, and MMP-2 were determined using enzyme-linked immunosorbent assay (ELISA) kits (ELK1158, ELK5753, ELK2537; ELKbiotech, Wuhan, China).

### Statistical Analysis

Data are presented as mean (SD) or median (min-max), as appropriate. For unpaired data, the Shapiro-Wilk test for normality and Levene's test for homogeneity of variances were performed. If the data were normally distributed and homogeneous, a one-way analysis of variance (ANOVA) was conducted to assess differences among treatment groups. Post hoc comparisons were then performed using Tukey's test. As a non-parametric alternative, the Kruskal-Wallis test was applied, followed by the Mann-Whitney U test for post hoc analysis. For paired data, a repeated-measures ANOVA was used. Statistical analyses were selected based on data distribution and variance characteristics to appropriately account for data variability and ensure valid group comparisons. Statistical significance was set at  $p < 0.05$ , and all analyses were performed using IBM SPSS Statistics version 22.

## Results

### General Characteristics

Baseline and final body weight, cardiac organ weight, and cardiac organ index (COI) were summarized in Table 2. A significant group effect was observed for body weight change over the 5-week period ( $F_{3,20} = 3.80$ ,  $p = 0.026$ ,  $\eta^2 = 0.363$ ), with a reduction observed only in the HIIT group. COI was significantly higher in the HC group than the NC group ( $U = 4.50$ ,  $p = 0.027$ ,  $r = 0.637$ ), with no differences between HC and the exercise groups (HIIT and MICT).

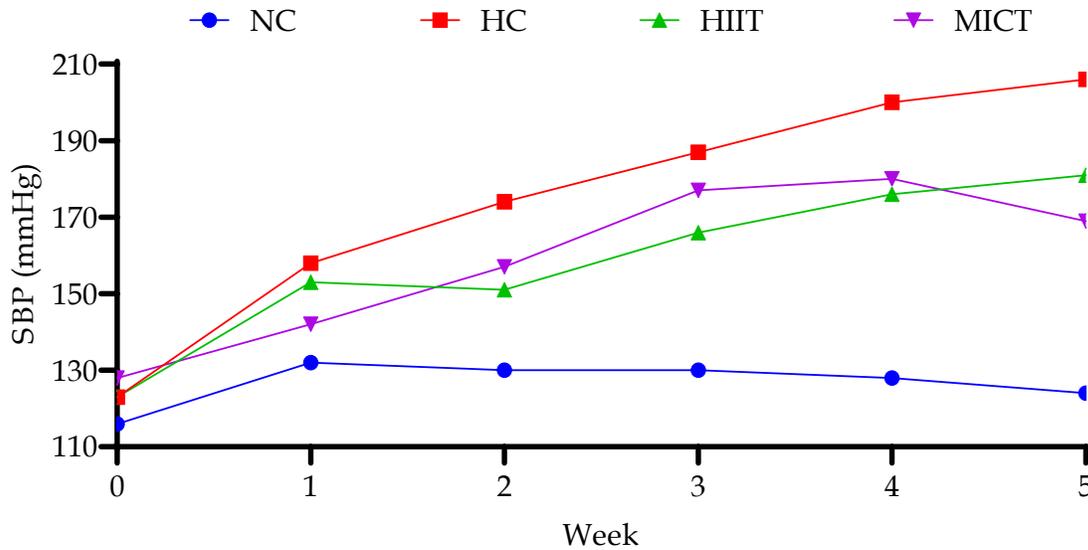
**Table 2.** General characteristics of experimental rats.

Parameters	NC	HC	HIIT	MICT
IBW (Week 1), g	217.17 (SD 21.17)	232 (SD 51.91)	260.17 (SD 41.40)	253.50 (SD 55.91)
FBW (Week 5), g	276 (SD 20.36)	234 (SD 21.19)	254 (SD 16.90)	266 (SD 22.82)
BW difference, g	+58.33 (SD 13.18)	+1.50 (SD 50.99)	-6.33 (SD 30.13) *	+12.67 (SD 39.93)
COW, g	0.84 (SD 0.85)	0.90 (SD 0.75)	0.87 (SD 0.58)	0.77 (SD 0.13)
COI, g	0.31 (0.29-0.31)	0.37 (0.30-0.52) *	0.33 (0.31-0.40)	0.34 (0.24-0.47)

Data are presented as mean (SD) for IBW, FBW, and COW; median (min-max) for COI. Each experimental group consisted of six rats ( $n = 6$ ). NC: normotensive control group; HC: hypertensive control group; HIIT: hypertensive rats subjected to HIIT; MICT: hypertensive rats subjected to MICT; IBW: initial body weight; FBW: final body weight; BW: body weight; COW: cardiac organ weight; COI: cardiac organ index. \*Significantly different at  $p \leq 0.05$  between groups.

### Systolic Blood Pressure

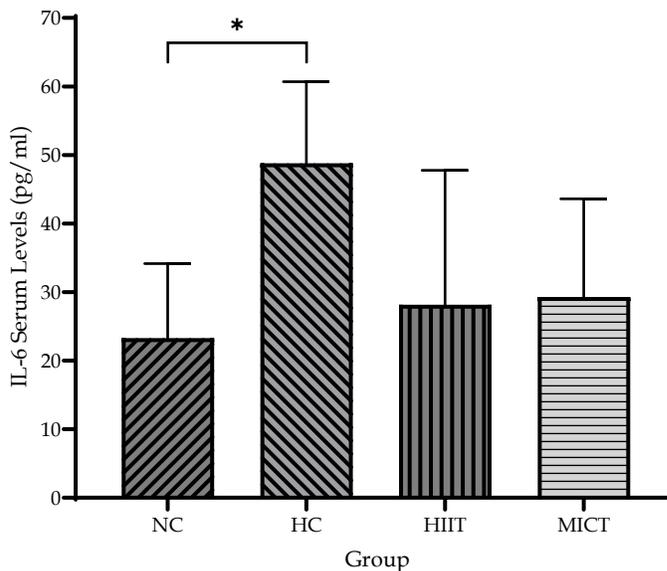
Repeated-measures ANOVA showed a significant effect of time and group on SBP ( $F_{2,41,60.44} = 31.52$ ,  $p < 0.001$ ,  $\eta^2 = 0.558$ ). At week 5, SBP differed significantly among groups ( $F_{3,20} = 27.153$ ,  $p < 0.001$ ,  $\eta^2 = 0.802$ ), with lower SBP observed only in the MICT group compared with HC, while HIIT did not differ significantly from the other hypertensive groups (Table 3). SBP changes are shown in Figure 1.



**Figure 1.** Time-course changes in systolic blood pressure (SBP) across experimental groups.

*Serum IL-6 Levels*

A significant group effect on serum IL-6 levels was observed ( $F_{3,20} = 3.580$ ,  $p = 0.032$ ,  $\eta p^2 = 0.349$ ). The HC group showed higher IL-6 levels than the NC group, while neither the HIIT nor the MICT group differed significantly from HC (Table 3). Serum IL-6 levels across experimental groups are shown in Figure 2.

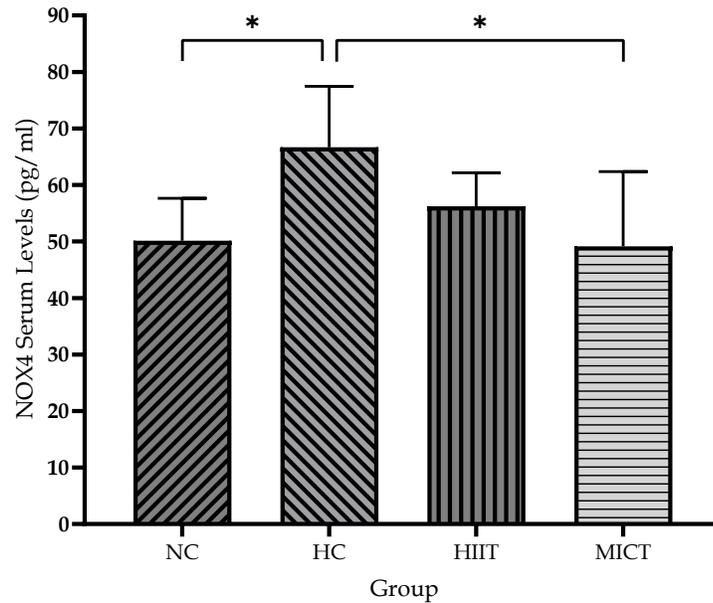


**Figure 2.** Serum interleukin-6 (IL-6) levels across experimental groups.

*Serum NADPH oxidase 4 Levels*

Serum NOX4 levels differed significantly among groups ( $F_{3,20} = 4.077$ ,  $p = 0.021$ ,  $\eta p^2 = 0.379$ ). NOX4 was reduced in the MICT group compared with HC, whereas no significant difference was

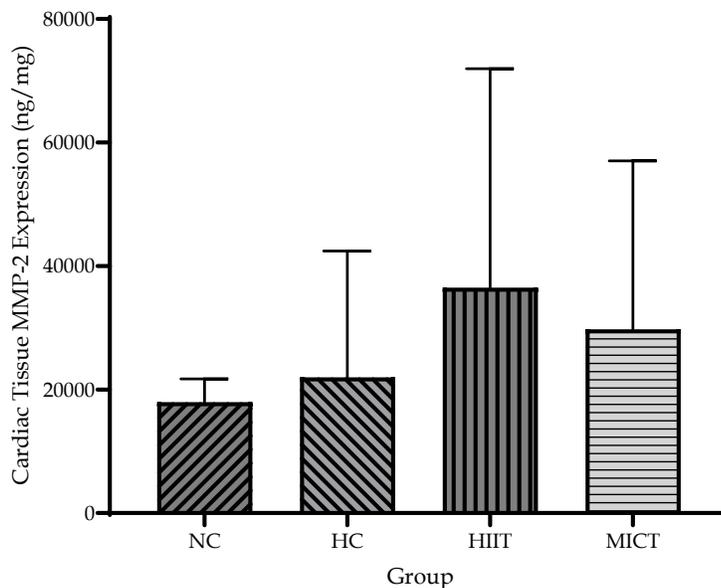
observed in the HIIT group (Table 3). Serum NOX4 levels across experimental groups are shown in Figure 3.



**Figure 3.** Serum NADPH oxidase 4 (NOX4) levels across experimental groups.

#### Cardiac Tissue MMP-2 Expression

No significant group differences were found in cardiac tissue MMP-2 expression ( $F_{3,20} = 0.671$ ,  $p = 0.580$ ,  $\eta^2 = 0.091$ ; Table 3). Cardiac tissue MMP-2 expression across experimental groups is shown in Figure 4.



**Figure 4.** Cardiac tissue matrix metalloproteinase-2 (MMP-2) expression across experimental groups.

**Table 3.** Pairwise Comparisons Among Experimental Groups.

Parameter	NC vs HC	NC vs HIIT	NC vs MICT	HC vs HIIT	HC vs MICT	HIIT vs MICT
SBP (Week 5)	<b>0.001</b> (-5.49)	<b>0.001</b> (-3.04)	<b>0.001</b> (-2.79)	0.061 (1.34)	<b>0.004</b> (2.30)	0.576 (0.61)
IL-6	<b>0.031</b> (-2.07)	0.937 (-0.28)	0.890 (-0.44)	0.099 (1.18)	0.127 (1.37)	0.999 (-0.06)
NOX4	<b>0.038</b> (-1.65)	0.705 (-0.83)	0.998 (0.09)	0.280 (1.11)	<b>0.026</b> (1.34)	0.599 (0.64)
MMP-2	0.992 (-0.25)	0.572 (-0.68)	0.840 (-0.56)	0.740 (-0.46)	0.947 (-0.30)	0.964 (0.20)

Data are shown as p-values (Hedges' *g*). Positive and negative *g* values indicate higher or lower levels in the first-listed group, respectively. Bold values indicate statistically significant differences ( $p \leq 0.05$ ).

## Discussion

Our current study was conducted to explore the comparative effects of five weeks of HIIT and MICT regimens on inflammatory, oxidative stress, and fibrotic parameters in an L-NAME-induced hypertensive rat model. To the best of our knowledge, this is among the first studies to investigate this topic. The main findings of this study demonstrated significantly lower SBP and NOX4 levels in the MICT group, while the HIIT group did not exhibit significant changes in SBP, IL-6, NOX4, or MMP-2.

The L-NAME-induced hypertensive rat model is widely recognized for recapitulating key pathophysiological features of human hypertension, including endothelial dysfunction, oxidative stress, inflammation, fibrosis, and cardiovascular remodeling.<sup>23</sup> In the present study, L-NAME acted as a nitric oxide synthase (NOS) inhibitor, resulting in a progressive elevation of blood pressure throughout the experimental period, with peak values observed in the fifth week. This blood pressure trajectory is consistent with previous reports using L-NAME exposure durations ranging from four to eight weeks, in which hypertension develops early and is sustained over time.<sup>24,25</sup> Mechanistically, inhibition of NO synthesis leads to persistent peripheral vasoconstriction, reduced endothelial NO bioavailability, and subsequent vascular and cardiac remodeling, as demonstrated in both acute and chronic L-NAME models.<sup>26</sup>

Consistent with the hypertensive phenotype, L-NAME administration resulted in significant elevations in IL-6 and NOX4 levels. These findings align with prior studies demonstrating that L-NAME induces a pro-inflammatory and pro-oxidative milieu characterized by increased cytokine production, oxidative stress, fibrosis, and vascular dysfunction.<sup>27,28</sup> The inflammatory response in L-NAME-induced hypertension has been closely linked to the activation of NF- $\kappa$ B signaling within vascular tissues, promoting the expression of cytokines, chemokines, and adhesion molecules. Persistent low-grade inflammation, together with excessive production of reactive oxygen species such as hydrogen peroxide ( $H_2O_2$ ) and superoxide anions ( $O_2^{\cdot-}$ ), further amplifies oxidative stress.<sup>29</sup> In this context, NOX4 plays a central role as a major enzymatic source of vascular reactive oxygen species, primarily through the rapid conversion of superoxide into  $H_2O_2$ .<sup>30</sup>

Hypertension-related oxidative stress is also closely intertwined with extracellular matrix remodeling mediated by matrix metalloproteinases (MMPs). Overexpression of MMP-2 has been associated with ventricular hypertrophy, systolic dysfunction, inflammatory cell infiltration, and myocardial fibrosis.<sup>31</sup> In the present study, cardiac MMP-2 expression showed a modest but statistically non-significant increase in the hypertensive control group compared with normotensive controls. This finding may be attributable to inter-individual variability and the dynamic, stage-dependent nature of MMP regulation during hypertension progression. Indeed, previous studies have reported inconsistent effects of hypertension on MMP-2 levels, with

some demonstrating no significant changes during early disease stages, while others observed marked upregulation during more advanced phases associated with target-organ damage.<sup>32-35</sup> The significant increase in cardiac organ index (COI) observed in the hypertensive control group supports the presence of structural cardiac adaptations, despite the absence of a parallel increase in MMP-2 expression.

Our analysis provides new insights indicating that MICT exerted a more pronounced antihypertensive effect than HIIT, as reflected by significant reductions in SBP. This observation is consistent with several experimental and clinical studies reporting superior blood pressure lowering effects of MICT compared with HIIT.<sup>6,11</sup> However, evidence from human studies remains inconsistent, with some reports showing comparable effects between these exercise modalities.<sup>36,37</sup> Such heterogeneity highlights the ongoing debate regarding the optimal exercise prescription for blood pressure and oxidative stress modulation. Although HIIT has been reported to improve endothelial function, partly through reductions in arterial stiffness and peripheral vascular resistance, these effects appear to be highly dependent on exercise protocol design and population characteristics.<sup>36</sup>

In terms of oxidative stress modulation, MICT was more effective than HIIT in reducing NOX4 levels in this hypertensive model. This finding supports previous experimental evidence indicating that MICT more consistently attenuates oxidative stress, potentially through enhanced antioxidant enzyme activity and reduced reactive oxygen species production.<sup>6,11</sup> Conversely, some studies have reported comparable or superior oxidative stress reduction following HIIT, suggesting continued variability in the literature.<sup>14,18</sup> Mechanistically, both exercise modalities have been shown to improve vascular function through suppression of oxidative stress-related pathways, including NLRP3-mediated pyroptosis. HIIT may exert additional effects via activation of AMPK $\alpha$ -SIRT1 signaling, whereas MICT appears to preferentially enhance endogenous antioxidant defenses.<sup>14</sup>

Despite these hemodynamic and oxidative stress-related benefits, neither MICT nor HIIT resulted in significant reductions in IL-6 or MMP-2 levels in the present study. These findings suggest that exercise alone, within the applied experimental conditions, may be insufficient to suppress inflammatory and fibrotic biomarkers. A paradoxical response has been proposed, whereby prolonged or intense physical activity may transiently elevate pro-inflammatory or fibrotic mediators, potentially interacting with the underlying hypertensive state induced by L-NAME.<sup>3</sup> Exercise duration, cumulative training load, and disease severity may therefore influence the balance between beneficial adaptations and stress-related responses, indicating that combined exercise-pharmacological approaches may be required to achieve optimal anti-inflammatory and antifibrotic effects.

Several limitations should be acknowledged. A reduction in body weight was observed in the HIIT group, reflecting a physiological adaptation to high-intensity exercise. Changes in body mass associated with exercise are often accompanied by alterations in hemodynamic and metabolic parameters, which may partially influence cardiovascular and biochemical outcomes.<sup>38</sup> Importantly, cardiac organ weight and cardiac organ index did not differ among the hypertensive and exercise groups, suggesting that structural cardiac remodeling was unlikely to be the primary determinant of the observed differences in SBP and NOX4 responses. Future studies incorporating more detailed body composition assessments may help clarify the contribution of exercise-related changes in body mass to cardiovascular adaptations. In addition, biomarker

assessments were limited to a single endpoint, precluding evaluation of the temporal dynamics of inflammatory and oxidative stress responses and limiting the ability to distinguish between early, transient exercise effects and sustained adaptive changes.<sup>39</sup> Serial measurements across multiple time points would provide greater insight into the kinetics and durability of exercise-induced biological responses.

In this L-NAME-induced hypertensive rat model, MICT was associated with more consistent reductions in SBP and NOX4 levels compared with HIIT, whereas neither exercise modality significantly altered IL-6 or MMP-2 levels. These findings highlight modality-specific cardiovascular adaptations to exercise in hypertension and underscore the complexity of inflammatory and oxidative stress regulation in this setting. Further investigations are needed to refine exercise prescriptions and explore combined intervention strategies to optimize cardiovascular outcomes in hypertensive populations.

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