American Heart Journal Plus: Cardiology Research and Practice 46 (2024) 100461

Contents lists available at ScienceDirect

American Heart Journal Plus: Cardiology Research and Practice

journal homepage: www.sciencedirect.com/journal/american-heart-journal-plus-cardiology-research-and-practice

Research Paper

# Effects of intracoronary administration of small doses of nicorandil and verapamil on blood pressure and heart rate

Sha Liu [a], Yuangang Qiu [b], Chuqun Lv [b,*]

[a] Zhejiang Chinese Medical University, 548 Binwen Road, Binjiang District, Hangzhou City, Zhejiang Province, China
[b] The First Affiliated Hospital of Zhejiang Chinese Medical University, 54 Youdian Road, Shangcheng District, Hangzhou City, Zhejiang Province, China

ARTICLE INFO

*Keywords:*
Nicorandil
Verapamil
Intracoronary
Blood pressure
Heart rate

ABSTRACT

*Background:* Nicorandil and verapamil can improve coronary blood flow and coronary microcirculation during percutaneous coronary intervention. However, the effects of intracoronary (IC) administration of nicorandil and verapamil on hemodynamics remain unclear.
*Aims:* To clarify the safety and effects of IC administration of nicorandil and verapamil on blood pressure (BP) and heart rate (HR) to provide evidence-based basis for clinical intervention.
*Methods:* The study cohort included 70 patients with coronary artery stenosis recruited from Zhejiang Provincial Hospital of Traditional Chinese Medicine. The patients were randomly assigned to the intervention group (IC administration of 2 mg/2 ml of nicorandil and 200 μg/2 ml of verapamil) or the control group (IC administration of 2 ml of saline). BP and HR were compared before medication, after medication, and when stabilized.
*Results:* IC administration of verapamil at 200 μg significantly reduced systolic BP as compared to the control group (113.72 ± 3.40 vs. 123.63 ± 3.33 mmHg, respectively, $p < 0.05$) for a short period of time, and returned to baseline within 2 min, but had no effect on diastolic BP and HR. IC administration injection of nicorandil at 2 mg had no effect on BP or HR. There were no instances of major cardiovascular events.
*Conclusion:* IC administration of nicorandil at 2 mg is safe as an adjunctive medication during interventional angiography. Verapamil can also be used as an IC adjuvant, although BP and HR must be monitored for patients with low basal BP, especially systolic BP.

## 1. Introduction

Interventional physicians often use adjunctive drugs, such as nicorandil and verapamil, to reduce the risk of myocardial injury during coronary angiography. However, relatively few studies have investigated the safety and hemodynamic effects of intracoronary (IC) administration of nicorandil and verapamil.

Nicorandil is a niacin amide derivative, adenosine triphosphate-sensitive $K^+$ channel opener and nitric oxide donor that exerts cardioprotective effects during ischemia or reperfusion, and also reportedly improves prognosis in patients with angina pectoris via preconditioning effects [1,2]. However, relatively few studies have investigated the safety and effectiveness of IC administration of nicorandil on blood pressure (BP) and heart rate (HR) [3].

Verapamil is a calcium channel blocker that can significantly improve myocardial blood flow and coronary microcirculation more effectively than adenosine [4,5]. However, changes in BP and HR after IC administration of verapamil during angiography remain unclear.

Nicorandil and verapamil can improve coronary blood flow and protect against myocardial injury during percutaneous coronary intervention (PCI) [6,7]. However, most previous studies failed to investigate changes to BP and HR during PCI [8–10]. Therefore, the aim of the present study was to assess the safety IC administration of nicorandil and verapamil as well as the effects on BP and HR during angiography.

## 2. Methods

### 2.1. Study approval and patient consent

The study protocol was approved by the Institutional Review Committee of Zhejiang Provincial Hospital of Traditional Chinese Medicine (approval no. 2022-KL-085-03) and conducted in accordance with the ethical principles for medical research involving human subjects described in the Declaration of Helsinki. Prior to inclusion in this study,

* Corresponding author.
*E-mail address:* 1783236712@qq.com (C. Lv).

https://doi.org/10.1016/j.ahjo.2024.100461
Received 22 April 2024; Received in revised form 5 September 2024; Accepted 5 September 2024
Available online 7 September 2024

**Table 1**
Baseline patient characteristics.

| | Intervention group ($n = 40$) | Control group ($n = 30$) | $p$ |
|---|---|---|---|
| CAD risk factors | | | |
| Age, years | 64.6 ± 9.00 | 65 ± 10.68 | 0.87 |
| BMI, kg/m$^2$ | 24.55 ± 3.45 | 24.96 ± 3.06 | 0.60 |
| Male, n (%) | 27(67.5) | 23(76.67) | 0.40 |
| Hypertension, n (%) | 22(55) | 16(53.3) | 0.90 |
| Diabetes, n (%) | 12(30) | 12(40) | 0.38 |
| Past smoker, n (%) | 20(50) | 15(50) | 1.00 |
| Current smoker, n (%) | 5(12.5) | 0(0) | 0.07 |
| TC, mmol/L | 4.16 ± 1.26 | 3.65 ± 1.02 | 0.08 |
| TG, mmol/L | 1.70 ± 1.04 | 1.94 ± 1.41 | 0.41 |
| LDL-C, mmol/L | 2.12 ± 0.99 | 1.81 ± 0.65 | 0.13 |
| Vital signs | | | |
| Baseline SBP | 129.58 ± 3.06 | 128.67 ± 3.44 | 0.85 |
| Baseline DBP | 67.3 ± 1.86 | 68.73 ± 2.16 | 0.61 |
| HR | 72.93 ± 11.29 | 73.20 ± 10.17 | 0.92 |
| Clinical features | | | |
| No symptoms | 5 | 0 | 1.00 |
| Stable angina | 1 | 4 | 0.92 |
| Unstable angina | 33 | 25 | 0.93 |
| Atypical chest pain | 1 | 1 | 1.00 |
| Culprit vessel | | | |
| LM | 0 | 1 | 0.43 |
| LAD | 17 | 19 | 0.08 |
| LCX | 13 | 4 | 0.12 |
| RCA | 11 | 3 | 0.13 |
| D1 | 1 | 1 | 1.00 |
| PLV | 1 | 1 | 1.00 |
| OM | 0 | 1 | 0.43 |

Data are presented as the n (%) or mean ± standard deviation.
Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; D1, diagonal branches 1; HR, heart rate; LAD, left anterior descending artery; LCX, left circumflex artery; LDL-C, low-density lipoprotein cholesterol; LM, left main artery; OM, obtuse marginal branch; PLV, posterior branch of left ventricle; RCA, right coronary artery; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides.

**Table 2**
BP after the first IC administration.

| | Intervention group (n = 40) | Control group (n = 30) | p |
|---|---|---|---|
| SBP | | | |
| Pre-drug | 131 ± 3.43 | 131 ± 3.62 | 0.96 |
| Lowest BP after IC drug | 115 ± 3.17 | 124 ± 3.51 | 0.06 |
| Stabilization | 129 ± 3.28 | 133 ± 3.79 | 0.40 |
| DBP | | | |
| Pre-drug | 66 ± 1.81 | 69 ± 2.12 | 0.60 |
| Lowest BP after IC drug | 62 ± 2.02 | 65 ± 1.74 | 0.22 |
| Stabilization | 68 ± 1.99 | 69 ± 1.86 | 0.85 |

informed consent was obtained from all participants.

### 2.2. Study cohort

The cohort of this randomized, prospective, double-blind, single-center study included 70 patients with coronary artery stenosis who received treatment at Zhejiang Provincial Hospital of Traditional Chinese Medicine from June 2022 to March 2024. The patients were randomly assigned to the intervention group (IC administration of nicorandil at 2 mg and verapamil at 200 μg) or the control group (equal volume of saline). The exclusion criteria were acute myocardial infarction, primary valvular or cardiomyopathy, severe heart failure (left ventricular ejection fraction <40 %), severe cardiac arrhythmia, noncardiac surgery within the past 3 months, contraindications to nicorandil and verapamil, or participation in another clinical study.

**Table 3**
BP after the second IC administration.

| | Intervention group (n = 40) | Control group (n = 30) | $p$ |
|---|---|---|---|
| SBP | | | |
| Pre-drug | 129 ± 3.53 | 132 ± 3.54 | 0.63 |
| Lowest BP after IC drug | 114 ± 3.40 | 124 ± 3.33 | 0.04 |
| Stabilization | 129 ± 3.41 | 133 ± 3.73 | 0.41 |
| DBP | | | |
| Pre-drug | 67 ± 1.97 | 68 ± 1.96 | 0.61 |
| Lowest BP after IC drug | 61 ± 1.98 | 65 ± 2.07 | 0.15 |
| Stabilization | 67 ± 1.85 | 68 ± 1.91 | 0.72 |

### 2.3. Study protocol

For patients in the intervention group, the target vessel was injected with 2 mg of nicorandil diluted in a volume of 2 ml followed by 5 mg of verapamil in a volume of 2 ml through an infusion catheter. All dilutions were completed before angiography. After injection of nicorandil, the lowest invasive BP and HR measured through the catheter were recorded, as well as the stabilized BP and HR. The invasive BP and HR usually stabilize within 2 min, and at most within 5 min. After stabilization, the operator continued intracoronary verapamil injections and recorded the lowest invasive BP and HR and the stable BP and HR by catheter measurement.

For patients in the control group, the target vessel was injected with 2 ml of saline through an infusion catheter and the invasive lowest BP and HR and stable BP and HR were recorded by catheter measurement. After 2 min of stabilization, 2 ml saline was injected intracoronary again, the lowest invasive BP and HR as well as stable BP and HR were recorded.

### 2.4. Endpoints

The primary effective endpoint was the lowest stable BP and HR measurements after IC administration of nicorandil or verapamil. The safety endpoint was the occurrence of adverse cardiovascular events during the procedure and within 24 h afterward.

### 2.5. Statistical analysis

All statistical analyses were conducted with IBM SPSS Statistics for Windows (version 26.0; IBM Corporation, Armonk, NY, USA). The Kolmogorov–Smirnov test was used to determine whether the continuous variables were normally distributed. Normally distributed values were compared using the *t*-test and are presented as the mean ± standard deviation. Non-normally distributed values were compared using the Mann–Whitney *U* test and Kruskal–Wallis test, and are presented as the median and interquartile range. Categorical variables were compared using the two-sided Fisher's exact test and are presented as numbers and percentages. A two-sided probability ($p$) value ≤0.05 was considered statistically significant.

## 3. Results

### 3.1. Baseline patient characteristics

The clinical and angiographic characteristics of the patients are

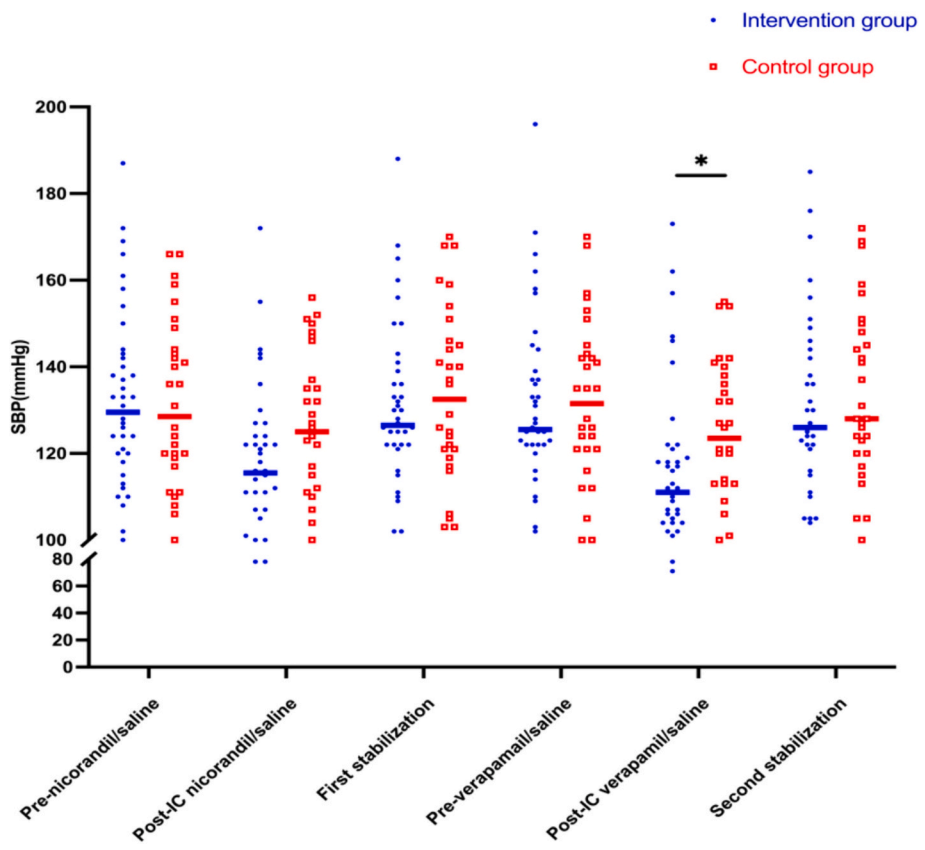


**Fig. 1.** Comparison of SBP between intervention group and control group.

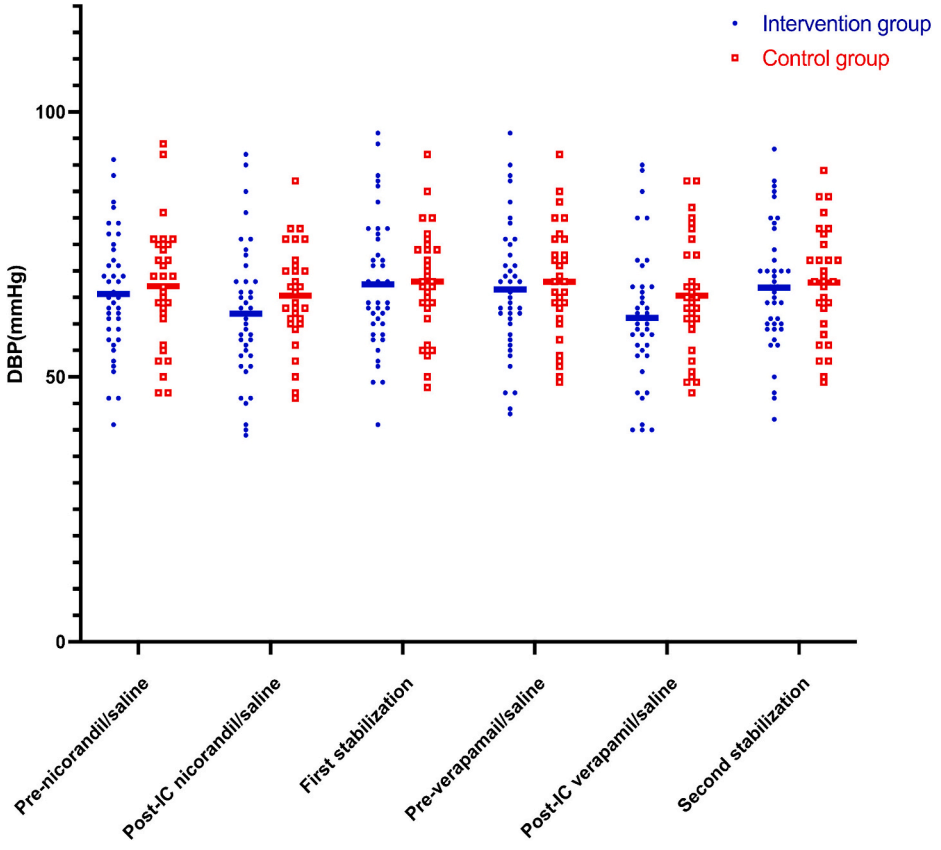


**Fig. 2.** Comparison of DBP between intervention group and control group.

**Table 4**
HR after the first IC administration.

| HR | Intervention group (n = 40) | Control group (n = 30) | *p* |
|---|---|---|---|
| Pre-drug | 75 ± 10.07 | 76 ± 10.11 | 0.55 |
| Corresponding to the Lowest BP | 73 ± 11.08 | 75 ± 9.72 | 0.58 |
| Stabilization | 74 ± 10.71 | 73 ± 9.07 | 0.81 |

**Table 5**
HR after the second IC administration.

| HR | Intervention group (n = 40) | Control group (n = 30) | *p* |
|---|---|---|---|
| Pre-drug | 73 ± 10.79 | 72 ± 8.12 | 0.88 |
| Corresponding to the Lowest BP | 73 ± 11.74 | 72 ± 8.58 | 0.61 |
| Stabilization | 73 ± 11.05 | 71 ± 8.82 | 0.43 |

summarized in Table 1. There were no significant differences between the two groups in respect to age, sex, prevalence of coronary risk factors, basal BP and HR, clinical manifestations of angina pectoris, location of culprit vessel, prevalence of multivessel diseases, or degree of stenosis.

### 3.2. Comparison of BP between two groups

BP measurements after the first IC injection are shown in Table 2. There were no significant differences in systolic blood pressure (SBP) and diastolic blood pressure (DBP) between the two groups before IC administration of nicorandil or saline ($p = 0.96$ and 0.60, respectively). Reductions in SBP and DBP were more obvious in the intervention group than the control group, but the differences were not statistically significant ($p = 0.06$ and 0.22, respectively). There were no significant differences in SBP and DBP after stabilization between the two groups ($p = 0.40$ and 0.85, respectively).

BP measurements after the second IC injection are shown in Table 3. There were no significant differences in SBP and DBP before IC injection of verapamil or saline between the groups ($p = 0.63$ and 0.61, respectively). SBP was significantly lower after IC administration of verapamil

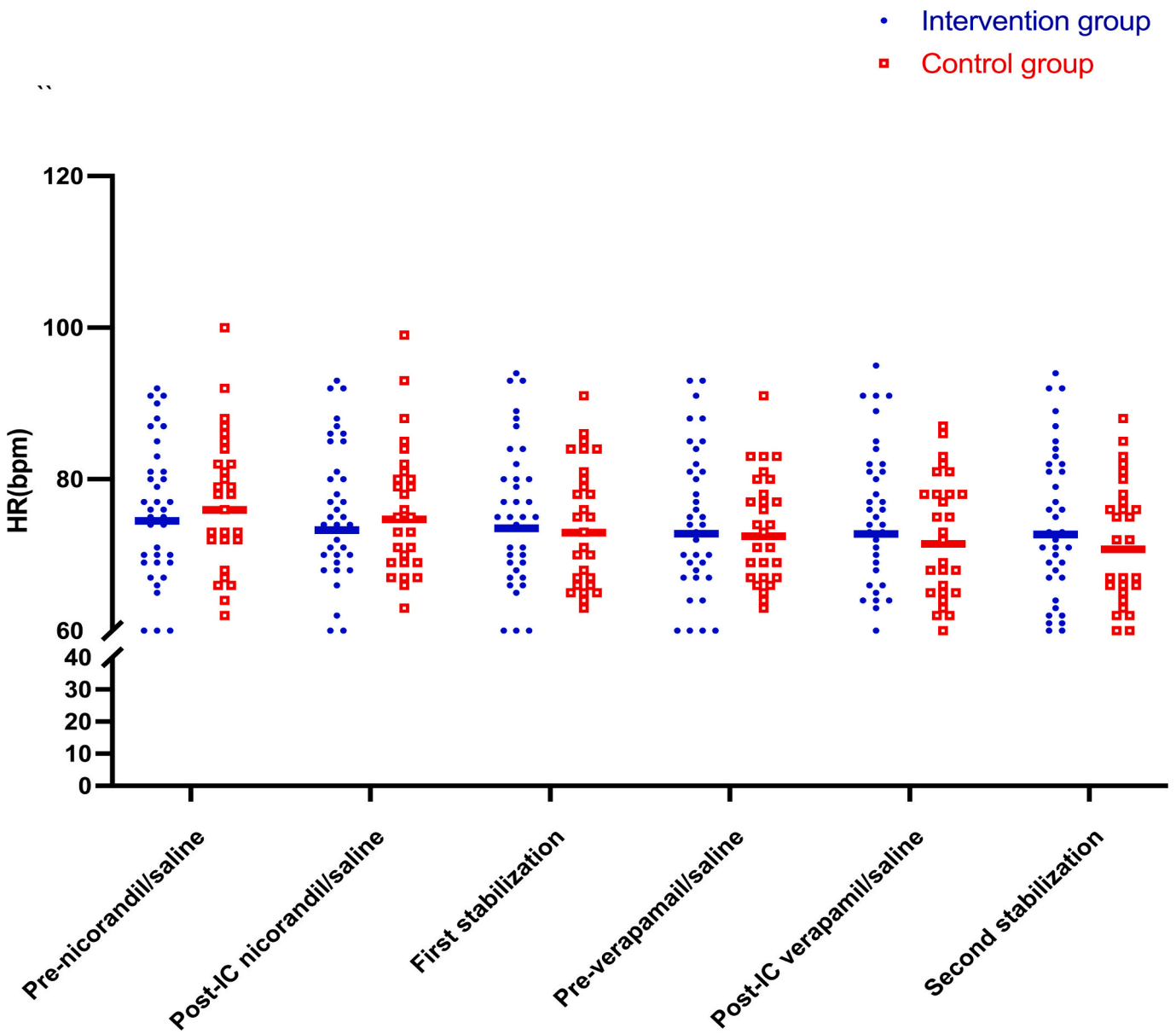


**Fig. 3.** Comparison of HR between intervention group and control group.

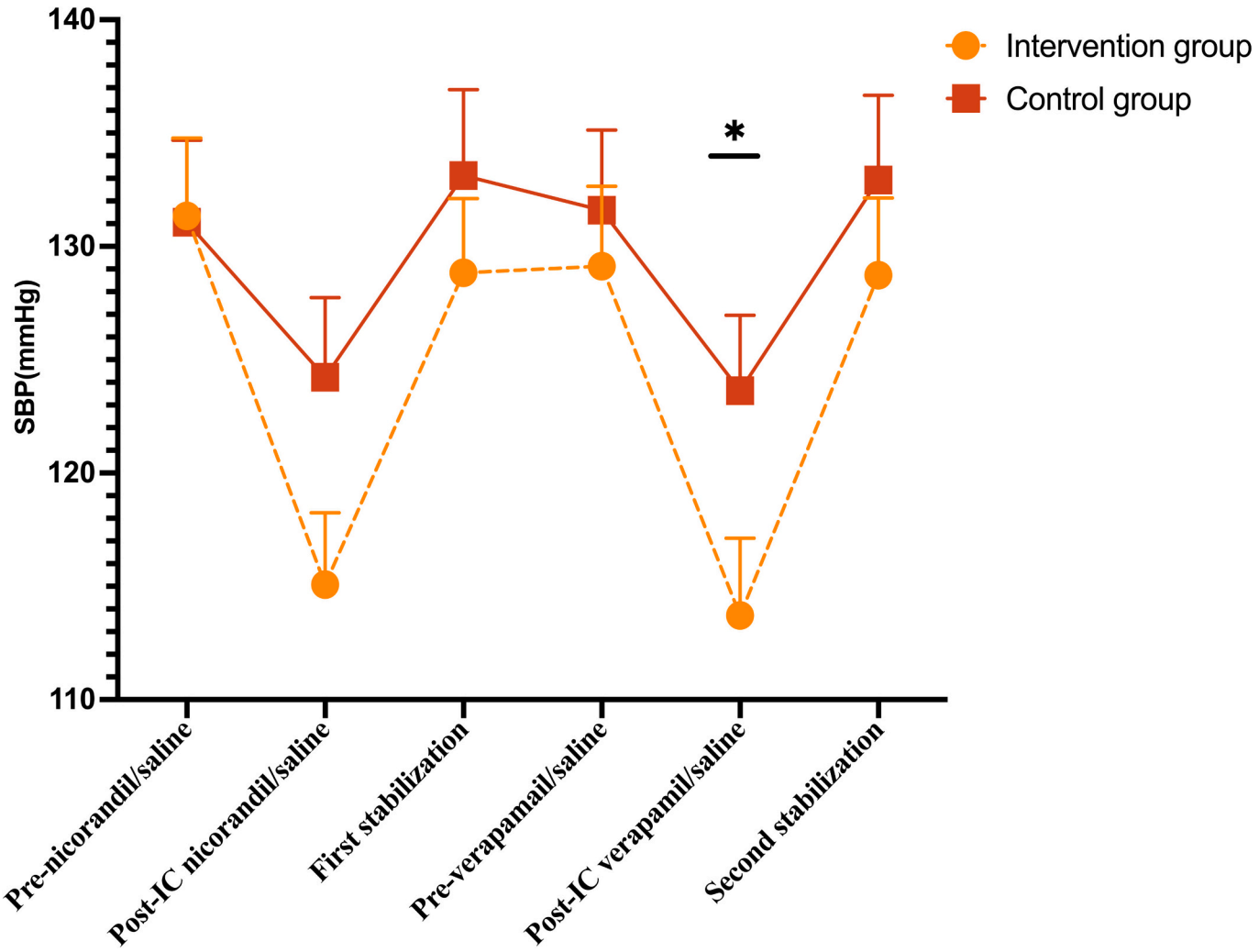


**Fig. 4.** Changes in SBP in intervention group and control group.

than saline (114 ± 3.40 vs 124 ± 3.33 mmHg, respectively, $p < 0.05$). There were no significant differences in the lowest DBP and BP after stabilization between the groups (lowest DBP: $p = 0.15$; stable SBP: $p = 0.41$; stable DBP: $p = 0.72$).

Comparisons of SBP and DBP between the two groups are shown in Figs. 1 and 2. Trends in SBP and DBP after the second IC drug injection in the two groups are shown in Figs. 4 and 5.

### 3.3. Comparison of HR between groups

HR measurements after the first IC injection are shown in Table 4. There was no significant difference in HR before IC administration of nicorandil or saline, the corresponding HR to the lowest BP after injection of nicorandil or saline, and stable HR between the two groups ($p > 0.05$).

HR measurements after the second IC injection are shown in Table 5. There were no significant differences in HR measurements before IC administration of verapamil or saline, the corresponding HR to the lowest BP after injection of verapamil or saline, and stable HR between the two groups ($p > 0.05$).

Comparisons of HR measurements between the two groups are shown in Fig. 3. Trends in HR after the second IC injection in the two groups are shown in Fig. 6.

### 3.4. Safety

There were no instances of chest pain, serious arrhythmia, or major cardiovascular events during the procedure or within 24 h afterward.

## 4. Discussion

The application of traditional vasodilators for patients with a low baseline BP can be problematic [11]. Injection of vasodilators into the coronary artery may achieve a faster onset of action as compared to intravenous administration. However, the use of vasodilators via the coronary artery requires closer monitoring of hemodynamic changes, including BP and HR, and the occurrence of adverse reactions.

Nicorandil is a vasodilator that has the effects of nitrates and opens adenosine triphosphate-sensitive potassium channels, thereby exerting cardioprotective effects during ischemia or reperfusion, [2]and also reportedly improves prognosis of angina pectoris via preconditioning effects [12,13]. Nicorandil not only dilates the large coronary vessels, but also the coronary microvessels. IC administration of nicorandil has less effect on BP and HR than intravenous administration [10,14]. However, IC administration of nicorandil through a perfusion catheter acts more rapidly than intravenous injection. Therefore, the effect on BP and HR must be carefully monitored.

The dosage of IC administration of nicorandil in many clinical studies was 1–2 mg, although 1 mg did not achieve adequate hyperemic efficacy [15]. Hence, 2 mg of nicorandil was administered in the present study.

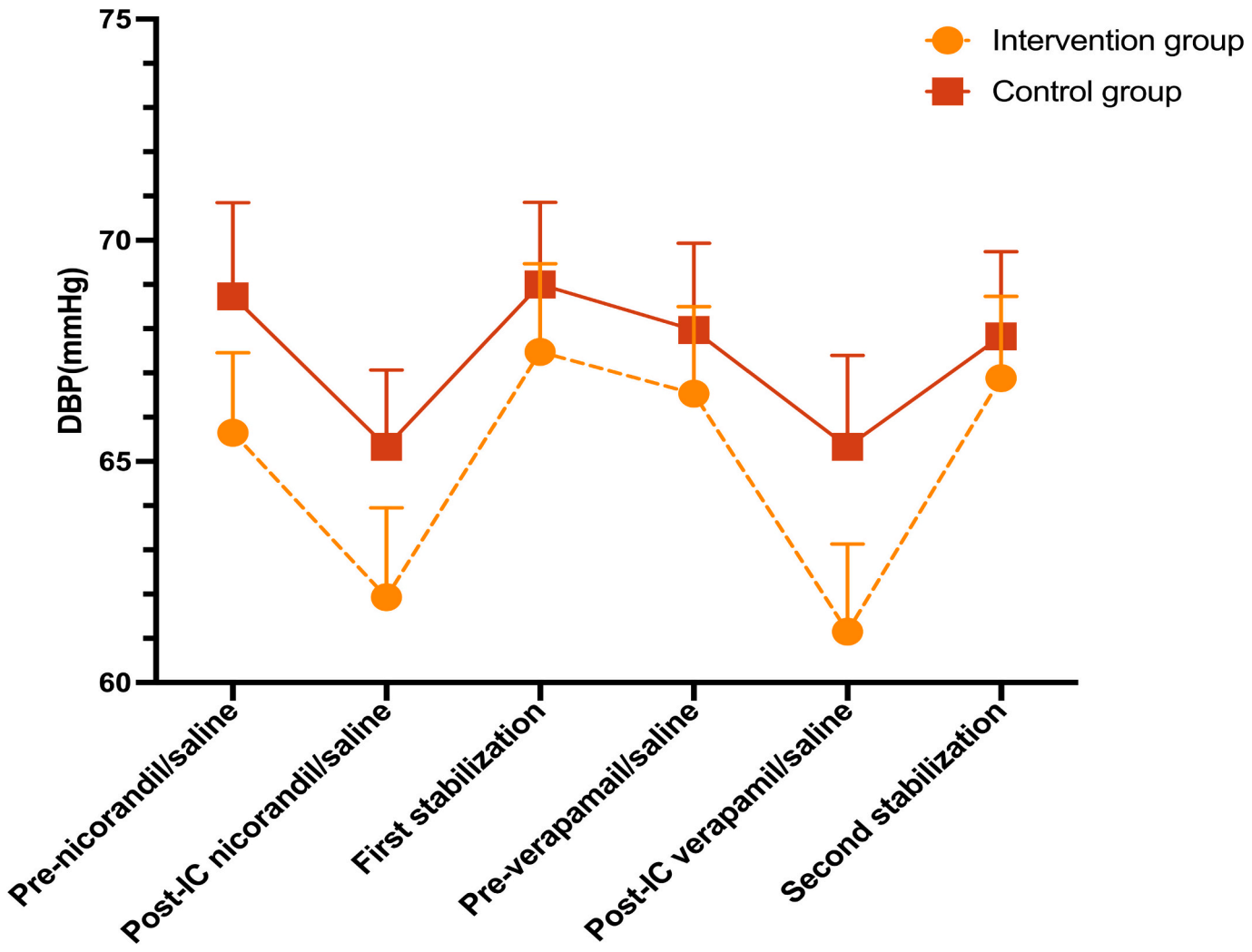


**Fig. 5.** Changes in DBP in intervention group and control group.

In previous studies [15,16], IC administration of nicorandil at 2 mg reduced mean arterial pressure by 12 mmHg and HR by 2 bpm. In the present study, IC administration of nicorandil at 2 mg reduced SBP by 16 mmHg, DBP by 6 mmHg, and HR by 2 bpm. Although these results were similar to those of previous studies, there were no significant differences as compared to the control group. Nonetheless, IC administration of nicorandil at 2 mg had no significant effects on BP and HR.

At 2 min after IC administration of nicorandil at 2 mg, BP and HR tended to return to pre-injection levels, suggesting that the effect of IC administration of a small dose of nicorandil on BP is rapid, similar to the rapid effect of sublingual nitroglycerin, demonstrating a nitrate-like effect of nicorandil. Nicorandil has a relatively long half-life [17], which is consistent with the prolonged protective effects on myocardial cells and the coronary microcirculation when administered via the coronary artery. However, further investigations are needed to elucidate the mechanism of IC administration of nicorandil to rapidly reduce BP.

Notably, IC administration of nicorandil at 2 mg had minimal effects on BP and HR but may cause arrhythmia [18]. None of the patients in this study experienced arrhythmia after IC administration of nicorandil at 2 mg, demonstrating that this dosage is safe.

Verapamil is a classical calcium channel blocker [4], which is often used for treatment of hypertension and arrhythmia. IC administration of verapamil can improve myocardial blood flow and the coronary microcirculation [19]. However, relatively few studies have investigated the effects on BP and HR. The results of this study showed that SBP decreased by 15 mmHg after IC administration of verapamil at 200 μg and decreased by 5 mmHg after IC administration of an equal volume of saline ($p < 0.05$). BP also plateaued around 2 min after IC administration of verapamil and returned to pre-injection levels, suggesting a transient effect on BP and mainly reduces SBP.

Verapamil lowers BP by reducing peripheral vascular resistance and generally has little effect on normal BP. Therefore, IC administration of verapamil is not recommend for patients with low basal BP, especially SBP, to avoid transient hypotension during surgery.

Verapamil also has negative inotropic effects. IC administration of verapamil can result in hypotension, bradycardia, and other adverse reactions [20]. Notably, none of the patients in this study developed bradycardia and IC administration of verapamil at 200 μg had little effect on HR.

We found that the BP of most patients stabilized about 2 min after the intracoronally administered of nicorandil or verapamil, and it was closer to 5 min in other patients. Unfortunately, we did not analyze the time to stabilization. The time to stabilization of BP and HR after intracoronary administration warrants further study.

## 5. Conclusion

IC administration of nicorandil at 2 mg had no effect on BP and HR, and can be recommended as an adjunctive drug during coronary angiography. IC administration of verapamil produced fluctuations in SBP

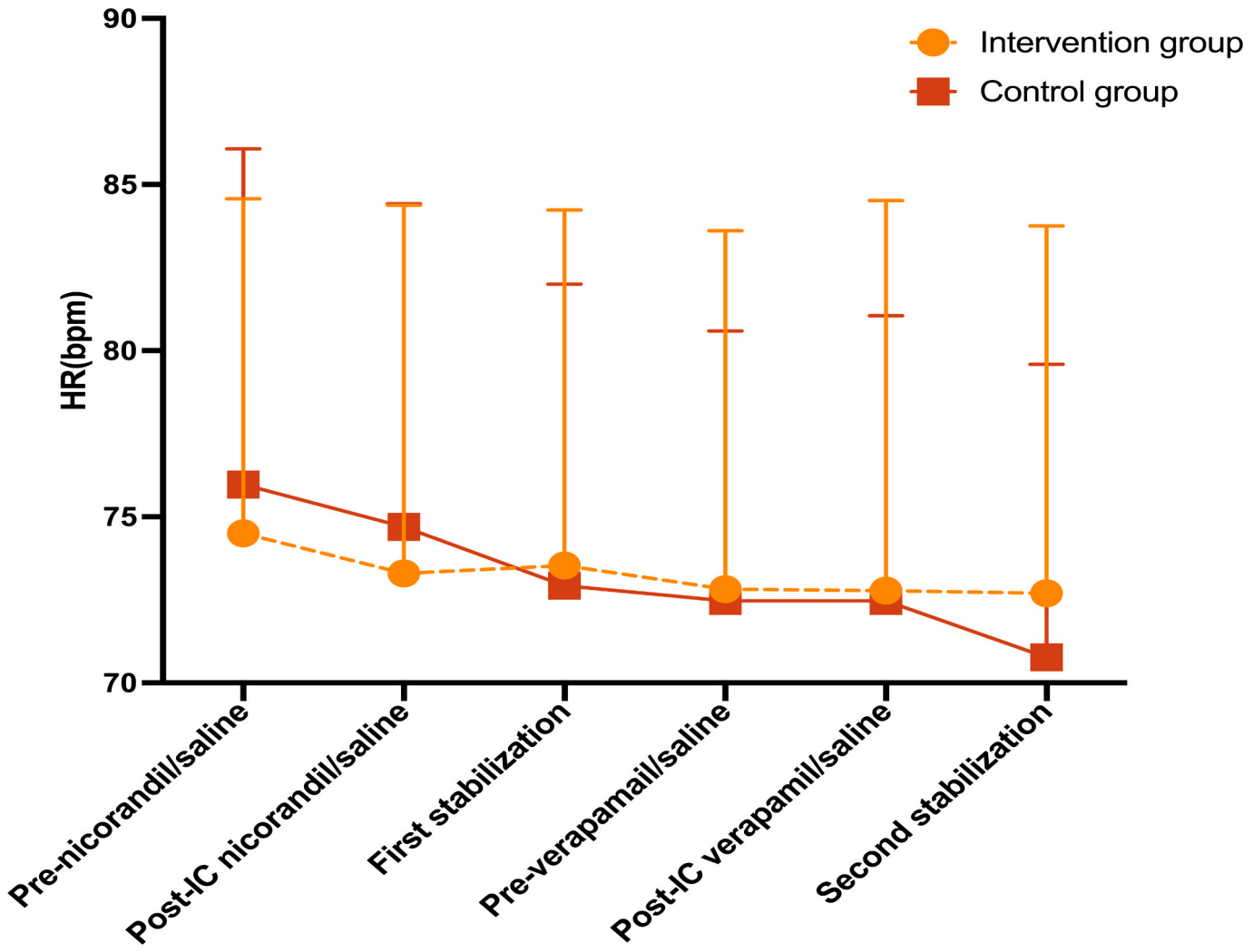


**Fig. 6.** Changes in HR in intervention group and control group.

for a short period of time, which then returned to baseline within 2 min and had little effect on HR. Therefore, IC administration of verapamil should be administered with caution, especially in patients with hypotension.

### *5.1. Limitation*

There were some limitations to this study that should be addressed. Most notably, this study was conducted in a single center with a small sample size. The effects of IC administration of nicorandil and verapamil on BP and HR after acute myocardial infarction are unclear. Since this study focused on the effects of IC administration of small doses of nicorandil and verapamil, further studies are warranted to investigate the effects of larger doses.

## Ethical statement

All applicable international and domestic ethical regulations were followed. For studies involving humans or animals, we have obtained the necessary ethical approvals and ensured informed consent from all participants.

For studies involving humans, we have ensured that all participants provide written informed consent and have the right to withdraw from the study at any time. The study data were collected and processed in accordance with privacy protection principles, and all personally identifiable information has been deleted or encrypted.

For our research involving animals, we have followed internationally accepted ethical guidelines for animal experimentation and have ensured that animals receive proper care and minimal suffering during research.

We promise that the results of this study will be reported in an honest, objective, and responsible manner without any modification or manipulation that may mislead the reader or compromise the integrity of the study.

## CRediT authorship contribution statement

**Sha Liu:** Software, Investigation. **Yuangang Qiu:** Writing – review & editing, Investigation. **Chuqun Lv:** Writing – original draft, Software, Methodology, Investigation, Data curation.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported.

## References

[1] J.M. Tarkin, J.C. Kaski, Vasodilator therapy: nitrates and nicorandil[J], Cardiovasc. Drugs Ther. 30 (4) (2016) 367–378, https://doi.org/10.1007/s10557-016-6668-z.

[2] L. Pearce, R.D. Carr, D.M. Yellon, et al., Nicorandil - an effective multitarget drug for cardioprotection?[J], Cardiovasc. Drugs Ther. 37 (1) (2023) 5–8, https://doi.org/10.1007/s10557-022-07397-x.
[3] S.J. Kim, W. Kim, J.S. Woo, et al., Effect of myocardial protection of intracoronary adenosine and nicorandil injection in patients undergoing non-urgent percutaneous coronary intervention: a randomized controlled trial[J], Int. J. Cardiol. 158 (1) (2012) 88–92, https://doi.org/10.1016/j.ijcard.2011.01.011.
[4] W. Li, G. Shi, How Ca(V)1.2-bound verapamil blocks Ca(2+) influx into cardiomyocyte: Atomic level views[J].Pharmacol Res 139 (2019) 153–157, https://doi.org/10.1016/j.phrs.2018.11.017.
[5] K. Vijayalakshmi, V.J. Whittaker, B. Kunadian, et al., Prospective, randomised, controlled trial to study the effect of intracoronary injection of verapamil and adenosine on coronary blood flow during percutaneous coronary intervention in patients with acute coronary syndromes[J], Heart 92 (9) (2006) 1278–1284, https://doi.org/10.1136/hrt.2005.075077.
[6] Bulluck H, Paradies V, Barbato E, et al.Prognostically relevant periprocedural myocardial injury and infarction associated with percutaneous coronary interventions: a Consensus Document of the ESC Working Group on Cellular Biology of the Heart and European Association of Percutaneous Cardiovascular Interventions (EAPCI)[J].Eur Heart J,2021, 42 (27): 2630–2642.DOI:https://doi.org/10.1093/eurheartj/ehab271.
[7] N. Ito, S. Nanto, Y. Doi, et al., High index of microcirculatory resistance level after successful primary percutaneous coronary intervention can be improved by intracoronary administration of nicorandil[J], Circ. J. 74 (5) (2010) 909–915, https://doi.org/10.1253/circj.cj-09-0943.
[8] J. Hwang, H.C. Lee, B.W. Kim, et al., Effect on periprocedural myocardial infarction of intra-coronary nicorandil prior to percutaneous coronary intervention in stable and unstable angina[J], J. Cardiol. 62 (2) (2013) 77–81, https://doi.org/10.1016/j.jjcc.2013.03.017.
[9] Q. Qi, J. Niu, T. Chen, et al., Intracoronary nicorandil and the prevention of the no-reflow phenomenon during primary percutaneous coronary intervention in patients with acute ST-segment elevation myocardial infarction[J], Med. Sci. Monit. 24 (2018) 2767–2776, https://doi.org/10.12659/MSM.906815.
[10] S. Sato, M. Takahashi, H. Mikamo, et al., Effect of nicorandil administration on cardiac burden and cardio-ankle vascular index after coronary intervention[J], Heart Vessel. 35 (12) (2020) 1664–1671, https://doi.org/10.1007/s00380-020-01650-9.
[11] Y. Zhang, Z. Cai, X. Ke, et al., Effectiveness and safety of intravenous nicorandil application in patients with acute heart failure with low baseline blood pressure [J], Heart Lung Circ. 31 (1) (2022) 95–100, https://doi.org/10.1016/j.hlc.2021.06.531.
[12] Z. Ye, Q. Su, L. Li, The clinical effect of nicorandil on perioperative myocardial protection in patients undergoing elective PCI, A systematic review and meta-analysis[J].Sci. Rep. 7 (2017) 45117, https://doi.org/10.1038/srep45117.
[13] Y. Lu, W. Hu, Q. Song, et al., The efficacy and safety of nicorandil for periprocedural myocardial injury in patients undergoing PCI: a meta-analysis[J], J. Interv. Cardiol. 2020 (2020) 3293587, https://doi.org/10.1155/2020/3293587.
[14] J.M. Lee, D. Kato, M. Oi, et al., Safety and efficacy of intracoronary nicorandil as hyperaemic agent for invasive physiological assessment: a patient-level pooled analysis[J], EuroIntervention 12 (2) (2016) e208–e215, https://doi.org/10.4244/eijv12i2a34.
[15] H.J. Jang, B.K. Koo, H.S. Lee, et al., Safety and efficacy of a novel hyperaemic agent, intracoronary nicorandil, for invasive physiological assessments in the cardiac catheterization laboratory[J], Eur. Heart J. 34 (27) (2013) 2055–2062, https://doi.org/10.1093/eurheartj/eht040.
[16] X. Yang, Q. Yu, J. Yang, et al., Intracoronary nicorandil induced hyperemia for physiological assessments in the coronary artery lesions[J].Front. Cardiovasc. Med. (9) (2022 Nov 2) 1023641, https://doi.org/10.3389/fcvm.2022.1023641.
[17] S. Iida, H. Kinoshita, N.H. Holford, Population pharmacokinetic and pharmacodynamic modelling of the effects of nicorandil in the treatment of acute heart failure[J], Br. J. Clin. Pharmacol. 66 (3) (2008) 352–365, https://doi.org/10.1111/j.1365-2125.2008.03257.x.
[18] T. Bányász, B. Horváth, L. Virág, et al., Reverse rate dependency is an intrinsic property of canine cardiac preparations[J], Cardiovasc. Res. 84 (2) (2009) 237–244, https://doi.org/10.1093/cvr/cvp213.
[19] L. Wang, Z. Cheng, Y. Gu, et al., Short-term effects of verapamil and diltiazem in the treatment of no reflow phenomenon: a meta-analysis of randomized controlled trials[J].Biomed. Res. Int. 2015 (2015) 382086, https://doi.org/10.1155/2015/382086.
[20] Akhtar M, Tchou P, Jazayeri M.Use of calcium channel entry blockers in the treatment of cardiac arrhythmias[J].Circulation,1989, 80 (6 Suppl): Iv31–9.