

Nicorandil prior to primary percutaneous coronary intervention improves clinical outcomes in patients with acute myocardial infarction: a meta-analysis of randomized controlled trials

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Li Xu
Lefeng Wang
Kuibao Li
Zhiyong Zhang
Hao Sun
Xinchun Yang

Heart Center and Beijing Key Laboratory of Hypertension, Beijing Chaoyang Hospital, Capital Medical University, Beijing 100020, People's Republic of China

Background: Nicorandil prior to reperfusion by primary percutaneous coronary intervention (PCI) in patients with ST-segment elevated myocardial infarction (STEMI) has been suggested to be beneficial. However, results of previous randomized controlled trials (RCTs) were not consistent. We aimed to perform a meta-analysis to systematically evaluate the effect of periprocedural nicorandil in these patients.

Methods: Related studies were obtained by searching PubMed, Embase and Cochrane's Library. Effects of perioperative nicorandil on the incidence of no-reflow phenomenon (NRP), corrected thrombolysis in myocardial infarction (TIMI) frame count (CTFC), wall motion score (WMS), left ventricular ejection fraction (LVEF), heart failure (HF) exacerbation of rehospitalization and incidence of major cardiovascular adverse events (MACE) were analyzed.

Results: Eighteen RCTs with 2,055 patients were included. Treatment of nicorandil prior to PCI significantly reduced the incidence of NRP (risk ratio [RR]: 0.47, $P<0.001$), and reduced CTFC (weighed mean difference [WMD]: -4.54 , $P<0.001$) immediately after PCI. Moreover, although nicorandil did not significantly affect WMS (WMD: 0.04, $P=0.91$), treatment of nicorandil significantly increased LVEF in STEMI patients undergoing primary PCI (WMD: 1.89%, $P<0.001$). In addition, nicorandil significantly reduced the risk of HF exacerbation or rehospitalization (RR: 0.44, $P=0.001$) and the incidence of MACE (RR: 0.68, $P<0.001$). Further analyses showed that effects of nicorandil on LVEF, HF exacerbation and MACE were consistent within one month after PCI and during follow-up.

Conclusions: Periprocedural nicorandil improves coronary blood flow, cardiac systolic function and prognosis in STEMI patients receiving primary PCI.

Keywords: ST-segment elevated myocardial infarction, Nicorandil, primary percutaneous coronary intervention, no-reflow phenomenon, meta-analysis

Introduction

Early myocardial reperfusion by primary percutaneous coronary intervention (PCI) has become an important treatment strategy for patients with ST-segment elevated myocardial infarction (STEMI), which is associated with reduced infarct size, preserved cardiac function and improved clinical outcomes in these patients.^{1,2} However, despite effective reperfusion by PCI, a considerable proportion of patients with STEMI still have impaired cardiac function and increased

Correspondence: Li Xu
Heart Center and Beijing Key Laboratory of Hypertension, Beijing Chaoyang Hospital, Capital Medical University, No.8, Gongtinan Road, Chaoyang District, Beijing 100020, People's Republic of China
Tel +86 108 523 1170
Fax +86 106 595 1064
Email xuli_88@yeah.net

cardiovascular mortality.^{3,4} It has been demonstrated that coronary microvascular dysfunction and obstruction, which occur in almost half of STEMI patients after primary PCI, are important causes of subsequent deterioration of cardiac function and poor prognosis in these patients.^{5,6} Therefore, it is hypothesized that early application of agents that attenuate coronary microvascular dysfunction and obstruction may further improve the prognosis of patients with STEMI despite effective revascularization.⁷

Nicorandil, as a hybrid of an adenosine triphosphate (ATP)-sensitive opener of potassium channel and nitrates, has been demonstrated to improve coronary microvascular dysfunction and obstruction via its vasodilatory effect on small coronary arteries.^{8,9} Clinically, nicorandil is applied as a treatment of chronic stable angina in patients with effort-induced symptoms arising from epicardial coronary artery stenoses, coronary vasospasm and microvascular dysfunction.¹⁰ A few clinical trials have indicated that nicorandil is effective to reduce the frequency of angina episodes and improve exercise capacity in patients with stable angina.¹¹ Moreover, nicorandil is well tolerated by most patients, with a satisfactory safety profile as evidenced by accumulating studies.¹² Pharmacologically, despite its benefit on coronary microcirculation, nicorandil may also exert cardio-protective efficacies via anti-oxidation, anti-inflammation and mimicking of ischemic preconditioning.^{10,13} Therefore, it is hypothesized that administration of nicorandil prior to primary PCI in STEMI patients may also confer additional benefits in these patients via its improvement on microvascular dysfunction and obstruction. Indeed, two previous meta-analyses of randomized controlled trials (RCTs) have been published to evaluate the efficacy of perioperative nicorandil in STEMI patients undergoing PCI. One study published in 2013 including 14 RCTs indicated that perioperative administration of nicorandil improved coronary blood flow and preserved cardiac function in STEMI patients undergoing PCI.¹⁴ However, it failed to show a beneficial effect of nicorandil on clinical outcomes, which, from the authors' perspective, is probably due to the limited sample sizes of the included RCTs.^{15–28} Another study published in 2016 including 13 RCTs showed that perioperative administration of nicorandil improved in-hospital outcomes in STEMI patients undergoing PCI without significant benefit on clinical outcomes from discharge to eight months during follow-up.²⁹ However, this meta-analysis is with some flaws since

four validated RCTs^{16,22,23,25} were missed, while a cardiac magnetic resonance imaging sub-study of an already included RCT was repeatedly included.³⁰ Moreover, some relevant studies have been published since the last meta-analysis.^{31–33} Therefore, we aimed to perform an updated meta-analysis to evaluate effect of nicorandil prior to PCI on coronary blood flow, cardiac systolic function and clinical outcomes in STEMI patients.

Methods

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement³⁴ and the Cochrane Handbook guidelines³⁵ were followed during the design and performance of this systematic review and meta-analysis.

Literature searching

PubMed, Embase and the Cochrane Library (Cochrane Center Register of Controlled Trials) databases were systematically searched for relevant RCTs. The search strategy included a combination of the following terms: (1) Nicorandil OR “2-Nicotinamidoethyl Nitrate” OR “2 Nicotinamidoethyl Nitrate” OR “Nitrate, 2-Nicotinamidoethyl” OR “2-Nicotinamidethyl Nitrate” OR “2 Nicotinamidethyl Nitrate” OR “Nitrate, 2-Nicotinamidethyl” OR SG-75 OR “SG 75” OR “SG75” OR “KATP channel openers” OR “sigmart” OR “Ikorel”; (2) “myocardial infarction” OR “percutaneous coronary intervention” OR “PCI” and (3) “random” OR “randomize” OR “randomly” OR “randomization” OR “randomized” OR “randomised”. We applied the limitation of study type as studies in humans. Besides, the references of the original articles and reviews were also screened as a complementary process. The date of final database search was October 20, 2018.

Inclusion and exclusion criteria

The inclusion criteria for the potential studies were: (1) full-length articles published in English or Chinese in peer-reviewed journals; (2) designed as RCTs to evaluate the effect of perioperative administration of nicorandil in patients with STEMI undergoing primary PCI; (3) nicorandil was applied intravenously or intracoronarily prior to the reperfusion by PCI; (4) included a control group with placebo or no nicorandil treatment and (5) reported at least one of the following outcomes: no-reflow phenomenon (NRP) and corrected thrombolysis in myocardial infarction (TIMI) frame count (CTFC) after PCI, wall motion score (WMS), left ventricular ejection fraction (LVEF), risk of

heart failure (HF) exacerbation of rehospitalization and incidence of major cardiovascular adverse events (MACE) during follow-up. Definition of NFP was consistent with the criteria used in the original studies, which referred to the appearance of TIMI 0–1 coronary flow in angiography after PCI despite adequate dilation of the target vessel and without angiographic mechanical obstruction.³⁶ The MACEs were defined as composite outcomes of all-cause death, target vessel revascularization, recurrent angina or myocardial infarction, stroke and severe HF. Reviews, observational studies, crossover studies, studies with nicorandil used after perfusion and those with unavailable data were excluded.

Data extraction and quality assessment

Two independent authors performed the database search, data extraction and quality evaluation according to inclusion criteria. Discrepancies were resolved by consensus with a third author. Extracted data included study design, age and gender of the patients, proportions of patients with diabetes mellitus [DM], percentiles of those with left anterior descending artery occlusion, time from symptom onset to reperfusion, nicorandil administration routes and regimens. For quality evaluation of the included RCTs, the seven domains of the Cochrane Risk of Bias Tool was applied,³⁵ which quantified the quality of the included RCTs with the following aspects: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete outcome data, selective outcome reporting and other potential threats to validity.

Statistical analysis

Continuous data were evaluated via weighted mean difference (WMD), whereas categorized data were analyzed using risk ratios (RR) with 95% confidence interval (CI). For the test of heterogeneity, the Cochrane's Q test was used,³⁵ which indicated a significant heterogeneity if $P < 0.10$. I^2 statistic, which reflected the percentage of total variation among studies that is caused by heterogeneity rather than chance,³⁷ was also calculated. If a significant heterogeneity was detected, a random-effect model was applied to pool the results. Otherwise, a fixed-effect model was used. Further analyses were applied to evaluate whether the effects of nicorandil on LVEF, HF exacerbation and MACE were consistent in short term (within one month after PCI) or during follow-up. Potential publication bias was assessed with Egger's

regression asymmetry test,³⁸ or visual inspection of the symmetry of the funnel plots. A $P < 0.05$ indicated statistical significance. We used RevMan (Version 5.1; Cochrane, Oxford, UK) and Stata software (Version 12.0; Stata, College Station, TX) software for statistical analyses.

Results

Database searching

The flowchart of literature search is presented in Figure 1. A total of 488 RCTs were identified via initial database search, and 453 studies were excluded after reading titles and abstracts because of their irrelevance. Of the remaining 35 studies that underwent full-text review, 17 were further excluded with the reasons listed in Figure 1. Finally, 18 RCTs^{15–33,39} were included.

Study characteristics

Overall, 18 RCTs with 2,055 patients were included in the meta-analysis. Since one study included two comparisons of different administration routes of nicorandil,²⁴ and another study included two comparisons with and without subsequently oral administration of nicorandil,²² these comparisons were included separately and finally made 20 comparisons included. All of the RCTs were performed in Asia. The baseline characteristics of the patients are summarized in Table 1. Nicorandil was administered intravenously, intracoronarily or combined. In some studies, patients in the nicorandil group also received sequential oral administration of nicorandil.^{15,21–23}

Quality evaluation

The details of quality evaluation in each domain of the Cochrane's Risk of Bias Tool are listed in Table 2. Overall, the quality of the included RCTs was moderate. Three of them were double-blinded RCT,^{17,20,27} with the generation of random sequences reported in two studies^{27,31} and the strategies for allocation concealment reported in four^{19,20,24,27} studies.

Effects of perioperative nicorandil on coronary blood flow immediately after PCI

Ten comparisons with 1,273 STEMI patients evaluated the effect of nicorandil on the incidence of NRP after PCI. Results of meta-analysis with a fixed-effect model showed that nicorandil significantly reduced the incidence of NRP

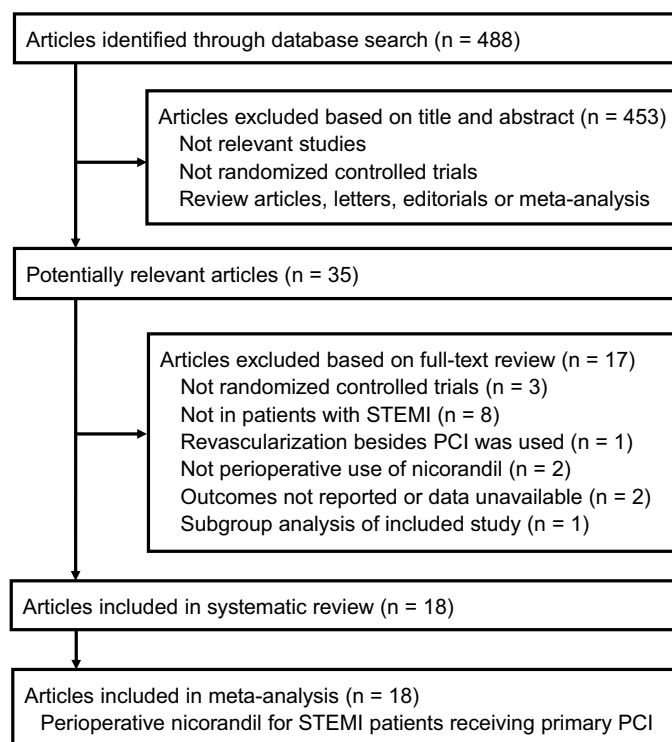


Figure 1 Flowchart of literature search and study identification.

Abbreviations: PCI, percutaneous coronary intervention; STEMI, ST-segment elevated myocardial infarction.

(RR: 0.47, 95% CI: 0.33~0.67, $P < 0.001$; Figure 2A) with no significant heterogeneity (P for Cochrane's Q test: 0.55, $I^2 = 0\%$). Moreover, meta-analysis of seven comparisons showed that nicorandil significantly reduced CTFC (WMD: -4.54 , 95% CI: $-6.91 \sim -2.17$, $P < 0.001$, $I^2 = 49\%$; Figure 2B). These results suggested that nicorandil significantly improved coronary blood flow in STEMI patients after primary PCI.

Effects of perioperative nicorandil on wall motion and cardiac systolic function

Meta-analysis with six comparisons did not show that nicorandil significantly improved WMS in STEMI patients after PCI (WMD: 0.04, 95% CI: $-0.71 \sim 0.80$, $P = 0.91$; Figure 3A) with significant heterogeneity ($I^2 = 49\%$). However, nicorandil was associated with significantly increased LVEF in STEMI patients undergoing primary PCI (WMD: 1.89%, 95% CI: 1.08~2.71%, $P < 0.001$, $I^2 = 29\%$; Figure 3B). Further analysis showed that nicorandil increased LVEF in STEMI patients within one month after PCI (WMD: 1.89%, $P < 0.001$) and during subsequent follow-up (WMD: 1.90%, $P = 0.002$). These results indicated that although effect seemed to be moderate, nicorandil

significantly improved cardiac systolic function in STEMI patients after primary PCI.

Effects of perioperative nicorandil on HF exacerbation and MACE

Results of meta-analysis showed that nicorandil significantly reduced the risk of HF exacerbation or rehospitalization (RR: 0.44, 95% CI: 0.26~0.72, $P = 0.001$; Figure 4A) and the incidence of MACE (RR: 0.68, 95% CI: 0.54~0.85, $P < 0.001$; Figure 4B) without significant heterogeneities ($I^2 = 0\%$ and 35%, respectively). Moreover, further analysis showed that the preventative efficacies of nicorandil on HF exacerbation and MACE in STEMI patients were consistent within one month after PCI and during subsequent follow-up. These results indicated that nicorandil significantly improved the prognosis in STEMI patients undergoing primary PCI.

Publication bias

The funnel plots for the meta-analyses of the effects of nicorandil on NRP, CTFC, WMS, LVEF, HF exacerbation and MACE were symmetry on visual inspection, and Egger's regression tests also indicated no significant publication biases within the meta-analysis (data not shown).

Table 1 Characteristics of the included RCTs

Study	Country	Design	Sample size	Age, years	Male, %	DM, %	Occlusion of LAD, %	Time to reperfusion, hours	Nicorandil administration	Dose (duration)	Sequential oral administration	Outcome reported
Ito et al ¹⁵	Japan	R, SB	81	60	79	27	100	5.1	i.v.	4 mg bolus, then 6 mg/h for 24 h	Yes	NRF, HF, MACE, LVEF, WMS
Fukuzawa et al ¹⁶	Japan	R, PC	62	62	73	31	65	4.6	i.v.	4 mg bolus, then 6 mg/h for 24 h	No	TIMI, WMS
Ono et al ¹⁹	Japan	R, PC	58	65	66	32	62	5.3	i.v.	4 mg bolus, then 8mg/h for 24 h	No	NRF, HF, MACE, CTFC, LVEF, CTFC, LVEF, WMS
Nameki et al ¹⁸	Japan	R	27	63	82	26	100	6.3	i.v. and i.c.	4 mg iv +4 mg ic, then 4 mg/h for 24 h	No	LVEF, WMS
Ikeda et al ¹⁷	Japan	R, DB	60	62	80	19	37	5.5	i.v. and i.c.	6 mg iv for 72 h and 2mg ic	No	HF, MACE, CTFC
Ishii et al ²⁰	Japan	R, DB, PC	368	64	81	33	47	4.7	i.v.	12 mg bolus	No	LVEF
Kasama et al ²¹	Japan	R, SB	50	63	74	28	100	4	i.v.	2 mg bolus, then 4 mg/h for 48 h	Yes	LVEF, WMS
Toyama et al ²⁵	Japan	R	68	64	65	29	57	5	i.v. and i.c.	4 mg iv for 24 h and 2 mg ic	No	NRF, CTFC
Ota et al ²⁴ -ic	Japan	R	45	64	82	30	53	4	i.c.	1-2 mg ic for 1-2 times	No	NRF, CTFC
Ota et al ²⁴ -iv+ic	Japan	R	45	61	78	31	40	4.1	i.v. and i.c.	4 mg iv +1-2mg ic, then 6 mg/h for 24 h	No	NRF, CTFC
Miyazawa et al ²³	Japan	R, SB	70	62	81	32	60	7.1	i.v. and i.c.	2 mg ic +2 mg/h iv for 24 h	Yes	NRF, HF, MACE, LVEF, WMS
Akagi et al ²²	Japan	R	15	66	67	NR	100	3.5	i.v. and i.c.	2 mg ic +4 mg/h iv for 48 h	Yes	LVEF
Akagi et al ²²	Japan	R	15	62	67	NR	100	3.8	i.v. and i.c.	2 mg ic +4 mg/h iv for 48 h	No	LVEF
Fujiwara et al ²⁶	Japan	R	62	62	81	39	50	5.9	i.v.	4 mg bolus, then 8 mg/h for 24 h	No	MACE, LVEF

(Continued)

Table 1 (Continued).

Study	Country	Design	Sample size	Age, years	Male, %	DM, %	Occlusion of LAD, %	Time to reperfusion, hours	Nicorandil administration	Dose (duration)	Sequential oral administration	Outcome reported
Kitakaze et al ²⁷	Japan	R, DB, PC	538	62	84	36	51	4.3	i.v.	4 mg bolus, then 6 mg/h for 24 h	No	NRF, LVEF
Lee et al ²⁸	Korea	R	73	58	30	11	55	5.8	i.c.	2 mg i.c twice	No	NRF, MACE
Chen et al ³⁹	China	R	52	59	71	25	0	7.2	i.c.	2 mg bolus	No	TIMI, MACE
Wang et al ³¹	China	R	106	63	82	27	49	4.5	i.c.	6 mg bolus	No	NRF, HF, MACE, CTFC
Feng et al ³²	China	R, SB, PC	180	69	60	33	47	4.3	i.c.	2 mg bolus	No	NRF, HF, MACE, LVEF
Qi ³³	China	R	80	57	68	38	45	5.8	i.c.	2 mg bolus	No	NRF, HF, MACE, LVEF, TIMI, CTFC

Notes: Study by Ota et al²⁴ included two comparisons of different administration routes of nicorandil, and two comparisons were considered. Study by Akagi et al²² included two comparisons with and without subsequently oral administration of nicorandil and two comparisons were considered.

Abbreviations: R, randomized; SB, single-blinded; DB, double-blinded; PC, placebo controlled; DM, diabetes mellitus; LAD, left anterior descending; i.v., intravenous; i.c., intracoronary; NRF, no-reflow phenomenon; HF, heart failure; MACE, major adverse cardiovascular events; LVEF, left ventricular ejection fraction; WMS, wall motion score; CTFC, corrected thrombolysis in myocardial infarction (TIMI) frame count; NR, not reported; NRF, no-reflow phenomenon; TIMI, thrombolysis in myocardial infarction.

Table 2 Quality evaluation by cochrane risk of bias tool

	Random sequence generation	Allocation concealment	Blinding in performance	Blinding in outcome detection	Incomplete outcome data	Reporting bias	Other bias
Ito et al ¹⁵	Unclear	Unclear	High	Low	Low	Low	Low
Fukuzawa et al ¹⁶	Unclear	Unclear	High	High	Low	Low	Low
Ono et al ¹⁹	Unclear	Low	High	High	Low	Low	Low
Nameki et al ¹⁸	Unclear	Unclear	High	High	Low	Low	Low
Ikeda et al ¹⁷	Unclear	Unclear	Low	Low	Low	Low	Low
Ishii et al ²⁰	Unclear	Low	Low	Low	Low	Low	Low
Kasama et al ²¹	Unclear	Unclear	High	Low	Low	Low	Low
Toyama et al ²⁵	Unclear	Unclear	High	High	Low	Low	Low
Ota et al ²⁴	Unclear	Low	High	High	Low	Low	Low
Miyazawa et al ²³	Unclear	Unclear	High	Low	Low	Low	Low
Akagi et al ²²	Unclear	Unclear	High	High	Low	Low	Low
Fujiwara et al ²⁶	Unclear	Unclear	High	High	Low	Low	Low
Kitakaze et al ²⁷	Low	Low	Low	Low	Low	Low	Low
Lee et al ²⁸	Unclear	Unclear	High	High	Low	Low	Low
Chen et al ³⁹	Unclear	Unclear	High	High	Low	Low	Low
Wang et al ³¹	Low	Unclear	High	High	Low	Low	Low
Feng et al ³²	Unclear	Unclear	High	Low	Low	Low	Low
Qi ³³	Unclear	Unclear	High	High	Low	Low	Low

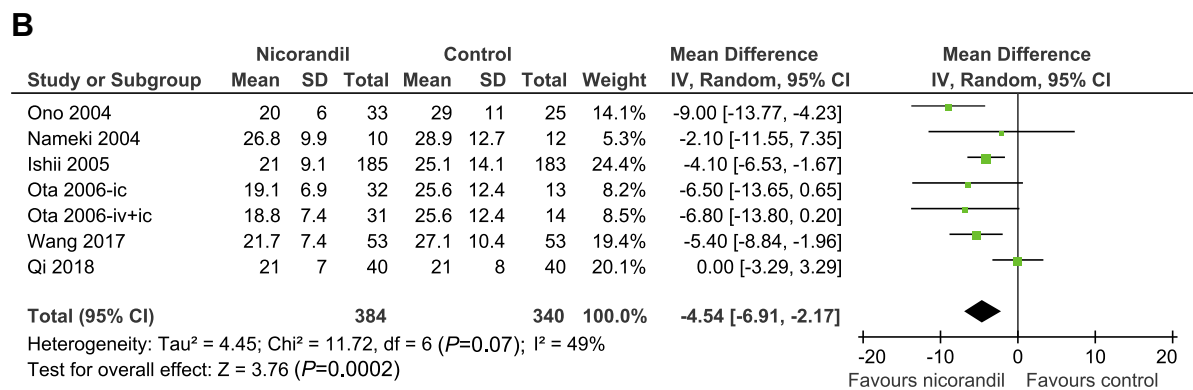
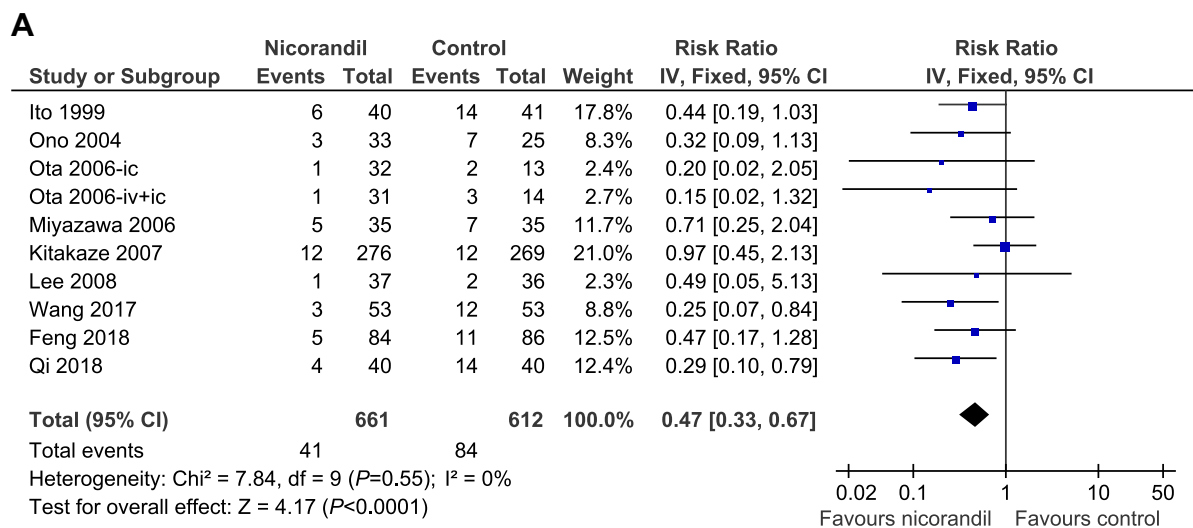


Figure 2 Forest plots for the meta-analysis of the influences of nicorandil on coronary blood flow in STEMI patients undergoing primary PCI: (A) effects of nicorandil on the incidence of NRP; (B) effects of nicorandil on CTFC.

Abbreviations: PCI, percutaneous coronary intervention; STEMI, ST-segment elevated myocardial infarction; NRP, no-reflow phenomenon; CTFC, corrected thrombolysis in myocardial infarction (TIMI) frame count.

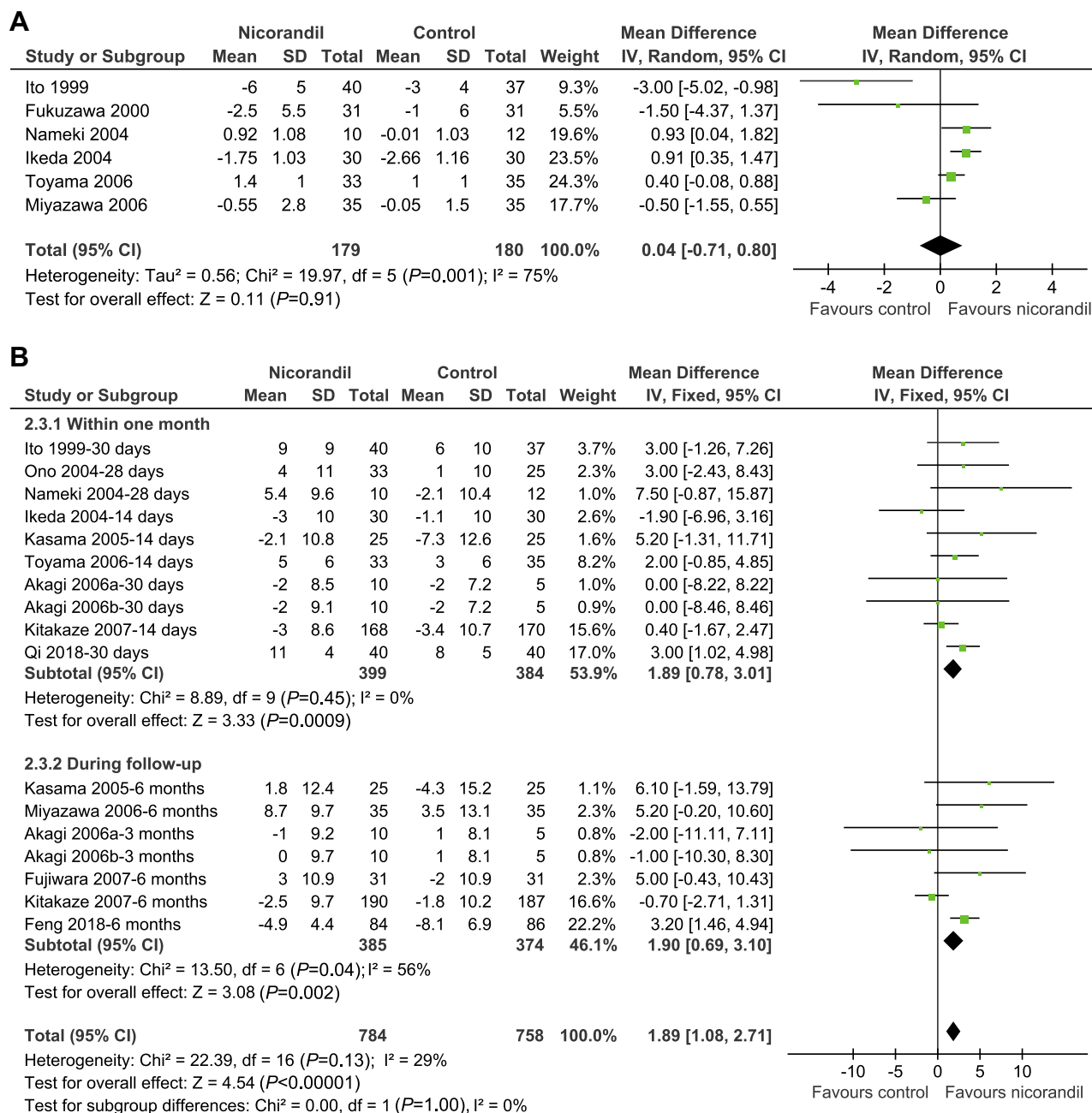


Figure 3 Forest plots for the meta-analysis of the influences of nicorandil on wall motion and cardiac systolic function in STEMI patients undergoing primary PCI; **(A)** effects of nicorandil on WMS; **(B)** effects of nicorandil on LVEF.

Abbreviations: PCI, percutaneous coronary intervention; STEMI, ST-segment elevated myocardial infarction; WMS, wall motion score; LVEF, left ventricular ejection fraction.

Discussion

Results of the study showed that perioperative treatment with nicorandil is associated with a lower risk of NRP and reduced CTFC as compared with controls in STEMI patients receiving primary PCI, indicating that nicorandil significantly improved coronary blood flow in these patients. Moreover, nicorandil preserved cardiac systolic function in these

patients, as evidenced by a moderate increase of LVEF in patients allocated to the nicorandil treatment as compared with control group. Importantly, nicorandil significantly reduced the risk of HF exacerbation or rehospitalization and the incidence of MACE in STEMI patients undergoing primary PCI in both short-term and long-term follow-up. Taken together, these results suggested that periprocedural

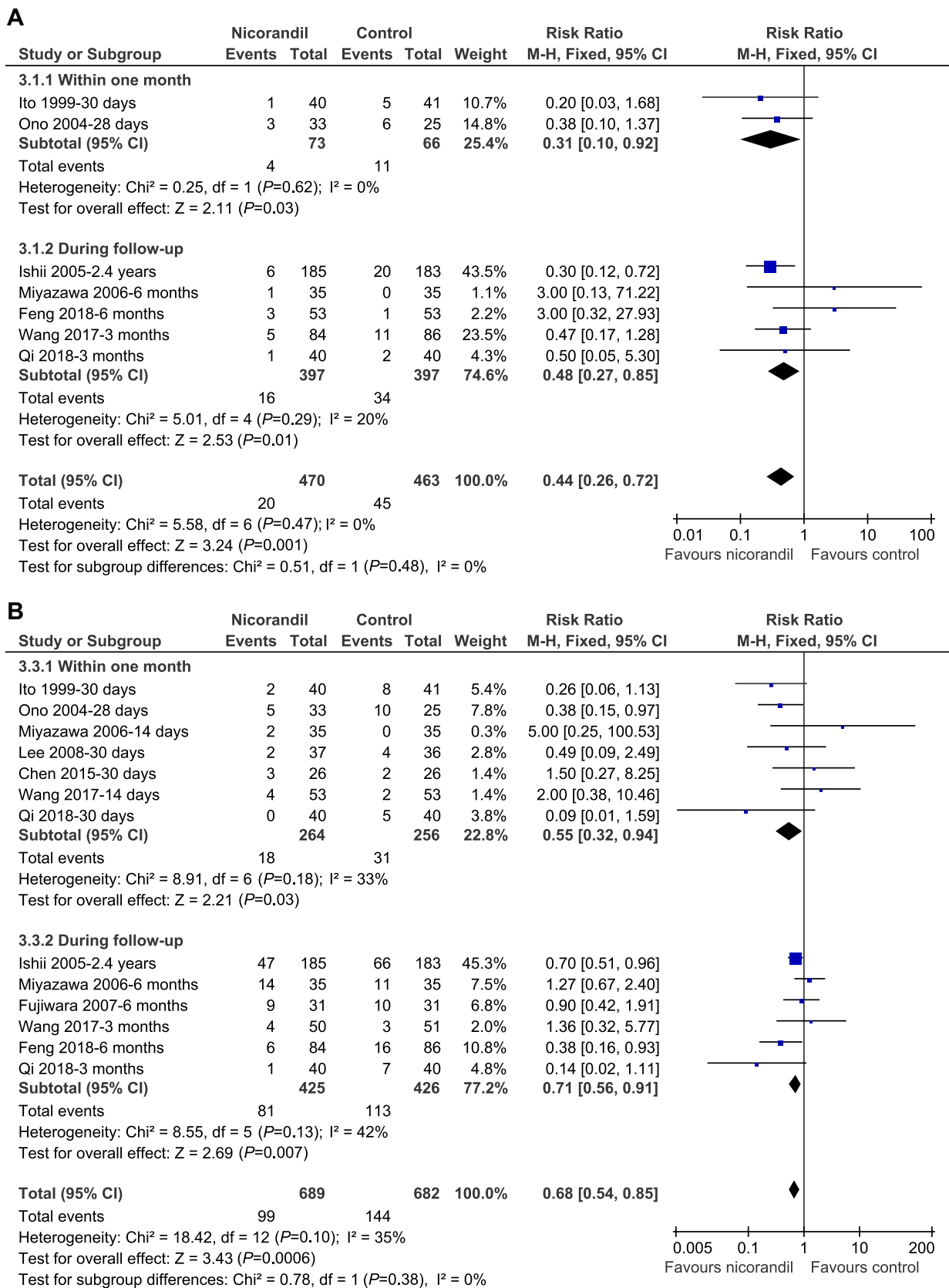


Figure 4 Forest plots for the meta-analysis of the influences of nicorandil on clinical outcomes in STEMI patients undergoing primary PCI; **(A)** effects of nicorandil on the risk of HF exacerbation or rehospitalization; **(B)** effects of nicorandil on the incidence of MACE.

Abbreviations: PCI, percutaneous coronary intervention; STEMI, ST-segment elevated myocardial infarction; MACE, major adverse cardiovascular events; HF, heart failure.

nicorandil improves coronary blood flow, cardiac systolic function and clinical outcomes in STEMI patients receiving primary PCI.

Previous studies indicated that the potential cardioprotective effect of nicorandil is multifactorial, of which, improvement of coronary microvascular dysfunction may be the most important underlying mechanisms. An early pharmacological study in dogs showed that the vessels <100 microns were more sensitive to nicorandil than other size vessels, and that ATP-sensitive potassium channels were responsible in mediating the nicorandil-induced dilation of vessels smaller than 100 microns.⁴⁰ Subsequent study with Gadomer-enhanced magnetic resonance imaging as a tool for the quantification of small microvascular obstruction showed that intravenous nicorandil attenuated the formation of microvascular obstruction regions in rats that underwent coronary artery occlusion and reperfusion.⁴¹ Moreover, a recent clinical study showed that intracoronary nicorandil administration after primary PCI significantly decreased the index of microvascular resistance, resulting in improved coronary flow reserve derived from the transthoracic Doppler and ventricular function in patients with STEMI undergoing primary PCI.⁴² Besides its direct dilatory effect on microvessels, other mechanisms such as anti-oxidative stress and anti-inflammation have also been suggested to be involved in its benefits on coronary microcirculation.⁴³ Our results expanded these findings by showing that periprocedural nicorandil improves coronary blood flow, cardiac systolic function and clinical outcomes in STEMI patients receiving primary PCI, which highlight the potential benefits of clinical administration of nicorandil prior to primary PCI in STEMI patients. Since the potential benefits of nicorandil on cardiac function and clinical outcomes have been confirmed in patients with stable CAD⁴⁴ and HF,⁴⁵ administration of nicorandil for patients with STEMI, stable CAD and HF should be recommended, which may be a reflection of the importance of coronary microcirculatory dysfunction in the pathogenesis and progression of the diseases.

Our study has limitations. Firstly, different routes and regimens were applied for nicorandil administration. Therefore, the optimal route, dose and duration of nicorandil administration prior to PCI in patients with STEMI should be investigated. Secondly, part of the patients for the 1-month and follow-observations were overlapped. Therefore, rather than a strict subgroup analysis, our study that compared the effect of nicorandil on related outcomes during short-term and long-term follow-up may introduce bias by including the data of overlapped

patients. However, we believe it is more accurate to include as more datasets as possible in order to compare the effect of nicorandil on related outcomes during short-term and long-term follow-up. Thirdly, all RCTs included were performed in Asia. The potential efficacies of nicorandil in STEMI patients from other countries should be determined. Fourthly, influences of other study characteristics besides ethnicities, such as gender and comorbidities (hypertension or diabetes) on the effect of prior nicorandil in STEMI patients receiving primary PCI were unknown since the stratified results according to these characteristics were rarely reported in the included RCTs. Future studies are warranted. Fifthly, the qualities of the included studies were moderate. Our findings should better be confirmed in future RCTs with high quality. Finally, the comparative efficacy of nicorandil and other agents that may also improve coronary microvascular dysfunction and obstruction, such as verapamil and diltiazem⁴⁶ adenosine, nicardipine, nicorandil and sodium nitroprusside,⁴⁷ should also be determined in future studies.

To sum up, this meta-analysis showed that periprocedural nicorandil improves coronary blood flow, cardiac systolic function and prognosis in STEMI patients receiving primary PCI. Treatment with nicorandil prior to primary PCI should be recommended in STEMI patients.

Disclosure

The authors report no conflicts of interest in this work.

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