

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

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## Dear editor

Early myocardial revascularization by the primary percutaneous coronary intervention (PPCI) was an important treatment for patients with ST-segment elevated myocardial infarction (STEMI); thus, a proportion of STEMI subjects still have impaired cardiac function and increased cardiovascular mortality.

Recently, we read with great interest the study by Xu et al.<sup>1</sup> The authors performed a meta-analysis to evaluate the effectiveness of the administration of nicorandil during percutaneous coronary intervention in patients with acute myocardial infarction. They concluded that periprocedural nicorandil improves coronary blood flow, cardiac systolic function and prognosis in STEMI patients receiving primary PCI. The research appears informative clinically. Thus, we addressed some issues regarding this study.

Firstly, although the heterogeneity was not detected according to the statistical methodology, the clinical heterogeneity was still observed between the included studies because of the different routes of nicorandil administration (such as intra-coronary injection and intravenous nicorandil). Therefore, the random model should be selected to estimate the results.

Secondly, Xu et al used the main adverse cardiac events (MACEs) as the hard points although the definition of MACE between the studies was not consistent.<sup>1</sup> For instance, the study by Ishii et al defined the MACE as the composite of all-cause mortality and all-cause admission,<sup>2</sup> while Feng et al described the MACE as the composite of cardiovascular death or unplanned readmission due to worsening congestive heart failure (HF).<sup>3</sup> Moreover, Xu et al define the MACE in this meta-analysis as the composite outcomes of all-cause death, target vessel revascularization, recurrent angina or myocardial infarction, stroke and severe HF.<sup>1</sup> In this situation, the study conducted by Fujiwara et al did not report the MACE events.<sup>4</sup> Thus, Xu et al regarded the in-stent restenosis as the MACE event (in-stent restenosis occurred in 9 patients in the nicorandil group and 10 in the control group, respectively), which was the violation of the predefined protocol. Therefore, the conclusion that the administration of nicorandil can improve the clinical outcome was misleading.

Thirdly, we are confused about the study by Feng et al. We found that they publish another report of the same trial (both are registered in the clinicaltrial.gov,

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the trial registration number was NCT02435797).<sup>5</sup> However, in that report the total number of included patients was 120; thus, the number was 170 in another report. We believe that the authors should identify the difference between these two reports and confirm the authenticity of the study before included this confusing research in the meta-analysis.

Lastly, the incidence of headache was not fewer after taking the nicorandil. Patients with acute myocardial infarction usually take the nitrates to improve myocardial ischemia after PCI. Thus, the combination of nitrates and nicorandil may increase the risk of headache, which may reduce patients' therapeutic compliance. Therefore, the authors should comprehensively evaluate the efficacy and safety of the nicorandil.

## Disclosure

The authors report no conflicts of interest in this communication.

## References

1. Xu L, Wang L, Li K, Zhang Z, Sun H, Yang X. Nicorandil prior to primary percutaneous coronary intervention improves clinical outcomes in patients with acute myocardial infarction: a meta-analysis of randomized controlled trials. *Drug Des Devel Ther*. 2019;13:1389–1400. doi:10.2147/DDDT.S195918
2. Ishii H, Ichimiya S, Kanashiro M, et al. Impact of a single intravenous administration of nicorandil before reperfusion in patients with ST-segment-elevation myocardial infarction. *Circulation*. 2005;112(9):1284–1288. doi:10.1161/CIRCULATIONAHA.104.530329
3. Feng C, Liu Y, Wang L, Niu D, Han B. Effects of early intracoronary administration of nicorandil during percutaneous coronary intervention in patients with acute myocardial infarction. *Heart Lung Circ*. 2018;28(6):858–865. doi:10.1016/j.hlc.2018.05.097
4. Fujiwara T, Matsunaga T, Kameda K, et al. Nicorandil suppresses the increases in plasma level of matrix metalloproteinase activity and attenuates left ventricular remodeling in patients with acute myocardial infarction. *Heart Vessels*. 2007;22(5):303–309. doi:10.1007/s00380-007-0975-z
5. Feng C, Han B, Liu Y, et al. Effect of nicorandil administration on myocardial microcirculation during primary percutaneous coronary intervention in patients with acute myocardial infarction. *Postepy Kardiol Interwencyjnej*. 2018;14(1):26–31. doi:10.5114/aic.2018.74352

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