# Intracoronary administration of nicorandil-induced cardiac arrest during primary percutaneous coronary intervention

# A case report

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#### Abstract

**Rationale:** Primary percutaneous coronary intervention (PPCI) is the most effective therapy for patients with an acute ST-segment elevation myocardial infarction (STEMI). However, up to half of STEMI patients suffer from coronary microvascular dysfunction, presenting as the slow flow or no-reflow phenomenon.

Patients concerns: A 78-year-old man was admitted to the chest pain center with sudden chest pain and tightness for about an hour.

**Diagnoses:** Electrocardiography demonstrated ST-segment elevation in leads II, III, aVF, and third-degree atrioventricular block. Coronary angiography showed acute total occlusion in the distal right coronary artery (RCA).

**Interventions:** PPCI was performed on the patient. After thrombus aspiration, a stent was placed in the distal RCA. As coronary angiography showed TIMI grade 2 flow in RCA, 6 mg nicorandil was intracoronary administrated in twice. Immediately, cardiac arrest occurred and cardiopulmonary resuscitation (CPR) was performed.

Outcomes: The patient survived and had a good outcome during follow-up for >6 months.

Lessons: Up to now, there has been no case report of cardiac arrest caused by nicorandil. Although intracoronary nicorandil is one of the most commonly used methods to improve coronary flow, much more attention should be paid to side effects of nicorandil.

**Abbreviations:** CFR = coronary flow reserve, CPR = cardiopulmonary resuscitation, CTFC = corrected TIMI frame count, IMR = index of microvascular resistance, LAD = left anterior descending artery, LCX = left circumflex artery, MBG = myocardial blush grade, MCE = myocardial contrast echocardiography, PD = posterior descending artery, PL = posterior left ventricular branch, PPCI = primary percutaneous coronary intervention, RCA = right coronary artery, STEMI = ST-segment elevation myocardial infarction, TFG = TIMI flow grades, TMPG = TIMI myocardial perfusion grade.

Keywords: cardiac arrest, microvascular dysfunction, nicorandil, PPCI

## 1. Introduction

Acute thrombotic occlusion of a coronary artery results in acute ST-segment elevation myocardial infarction (STEMI).<sup>[1]</sup> Timely

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reperfusion therapy with fibrinolytic drugs or primary percutaneous coronary intervention (PPCI) restores blood flow to ischemic myocardium and limits myocardial infarct size.<sup>[2]</sup> PPCI has many advantages over thrombolysis, including greater reopening rates of the infarct-related artery and higher coronary flow grades.<sup>[3]</sup> Nevertheless, up to 50% of STEMI patients performed with PPCI do not achieve ideal coronary blood flow, which is referred to as the slow flow or no-reflow phenomenon, attributing to microvascular dysfunction or obstruction.

Intracoronary administration of nicorandil reduced the occurrence of slow flow or no-reflow phenomenon by improving microvascular circulation in patients with acute myocardial infarction.<sup>[4]</sup> The mechanisms of intracoronary nicorandil include dilation of coronary microcirculation, ischemic preconditioning, antiarrhythmia, and reduction of reperfusion injury.<sup>[5]</sup> Nicorandil can be used in patients with bradyarrhythmias and/or atrioventricular conduction blocks.<sup>[6,7]</sup> In this report, we found intracoronary nicorandil-induced sudden cardiac arrest in a male patient with STEMI (inferior wall).

## 2. Case report

The study was approved by the Ethics Review Committee of Qilu Hospital, Shandong University (approval no.: 2018101).



The patient has provided informed consent for publication of the case.

A 78-year-old man suffered from sudden chest pain and tightness for about an hour. He had a history of 10-year hypertension and kept taking amlodipine. Physical examination showed the heart rate was 30 bpm and blood pressure was 92/60

mm Hg. A 12-lead electrocardiogram was obtained and demonstrated ST-segment elevation in leads II, III, aVF, and third-degree atrioventricular block (Fig. 1). He was preliminarily diagnosed with acute STEMI (inferior wall) and third-degree atrioventricular block. Immediate coronary angiography showed that no severe stenosis was found in the left anterior descending



Figure 2. Coronary angiographic images. (A–C) Coronary angiograms showed acute total occlusion in the distal RCA. (D) Coronary angiogram of RCA after predilation with a 2.0 × 20 mm balloon. (E) Coronary angiogram of RCA after thrombus aspiration and about 90% stenosis was found in the ostium of PD. (F) Stent plantation. (G) Coronary angiogram after stent plantation and postdialtion with a 2.75 × 8 mm NC balloon. (H) Coronary angiogram of RCA indicated TIMI grade 3 flow finally.

artery (LAD) and left circumflex artery (LCX) and total occlusion was found in the distal right coronary artery (RCA) (Fig. 2A-C). After predilation with a  $2.0 \times 20 \,\text{mm}$  balloon and thrombus aspiration, the patient regained sinus heart rate around 80 bpm immediately. As 90% stenosis was found in the ostium of posterior descending artery (PD), a  $2.25 \times 18 \,\mathrm{mm}$  stent was implanted in the distal RCA, crossing the ostium of posterior left ventricular branch (PL) (Fig. 2D-F). After postdilation with a  $2.75 \times 8 \text{ mm}$  NC balloon, angiography showed TIMI grade 2 flow in RCA (Fig. 2G). Then, 6 mg nicorandil was intracoronary administrated via guiding catheter in twice within 2 minutes. Unexpectedly, the heart rate dropped to zero. Cardiopulmonary resuscitation (CPR) was performed and 1 mg adrenaline was intravenously injected. Within few minutes, his cardiac pumping was recovered. Repeated angiography showed TIMI grade 3 flow in the RCA finally (Fig. 2H). The patient was stable during follow up for >6 months.

#### 3. Discussion

Microvascular dysfunction termed as slow flow or no-reflow phenomenon occurs in up to half of patients with STEMI even after revascularization of the culprit artery.<sup>[8]</sup> Microvascular dysfunction limits the restoration of blood supply and the delivery of endogenous promotors responsible for postinfarction remodeling.<sup>[9]</sup> Thus, patients with microvascular dysfunction exhibit larger myocardial infarct size, more early postinfarct complications, more adverse left ventricle remodeling, and worse prognosis.<sup>[8,9]</sup> Multiple methods have been used to assess microvascular dysfunction. Evaluating microvascular dysfunction through angiography is relatively convenient and widespread in practice. Methods of angiographic assessment include TIMI flow grades (TFG), TIMI myocardial perfusion grade (TMPG), myocardial blush grade (MBG), and corrected TIMI frame count (CTFC).<sup>[3]</sup> Myocardial contrast echocardiography

(MCE), index of microvascular resistance (IMR), and coronary flow reserve (CFR) are more accurate and reproducible tools to determine microvascular dysfunction.<sup>[1]</sup> In the present case, acute total occlusion was found in the distal RCA and thrombus aspiration was performed. After stenting and postdilation, microvascular dysfunction occurred in this patient indicated by TIMI grade 2 flow in RCA. The pathophysiological mechanisms of microvascular dysfunction are still poorly understood. Ischemia-related injury, reperfusion-related injury, distal embolization from the culprit plaque, and thrombus and individual susceptibility to microcirculatory injury might contribute to the occurrence of microvascular dysfunction.<sup>[1]</sup> As microvascular dysfunction was found after postdilation, we speculate that distal embolization induced by emboli from fissured plaques or thrombus is the leading cause for the happening of slow flow phenomenon in this patient.

Treatment of microvascular dysfunction remains further studied. Generally, thrombus aspiration and intracoronary administration of medicines might be effective. Although routine thrombus aspiration is not recommended, it may be considered in cases of large residual thrombus burden after opening the artery with a guide wire or a balloon.<sup>[10]</sup> Intracoronary adenosine, sodium nitroprusside, verapamil, nicorandil, and GPIIb/IIIa inhibitors were tested in several clinical trials and might improve microvascular function.<sup>[11]</sup> The patient here was at a low blood pressure and experienced atrioventricular block, thus nicorandil was preferred to improve blood flow. Nicorandil, a hybrid with nitrate-like and adenosine triphosphate (ATP)-sensitive potassium ( $K_{ATP}$ ) channel activator, is considered to be the optimal drug to improve coronary flow in acute coronary syndromes because of its nearly no effect on heart rate and blood pressure. In this case, we first reported intracoronary administration of nicorandil induced cardiac arrest. Singer et al<sup>[12]</sup> have reported a few cases of life-threatening hyperkalemia and hemodynamic disturbance due to KATP channel activation. Lee et al<sup>[13]</sup> have also reported a case of life-threatening bradycardia due to nicorandil-induced hyperkalemia. We speculate that activation of  $K_{ATP}$  channel and subsequent hyperkalemia might be the reason for nicorandilinduced cardiac arrest in this case. Repeated angiography showed improved blood flow finally. Thus, intracoronary nicorandil might be useful in the treatment of microvascular dysfunction.

In conclusion, we report the cardiac arrest case induced by intracoronary nicorandil. Microvascular dysfunction frequently occurs during PPCI. Thrombus aspiration and intracoronary medicines should be considered to prevent microvascular dysfunction. Intracoronary nicorandil might improve TIMI flow grade but should be carefully evaluated due to its side effects including cardiac arrest.

#### **Author contributions**

Data curation: Fang-Yun Luan. Supervision: Yu-Guo Chen. Writing – original draft: Shujian Wei, Da-yu He. Writing – review and editing: Shujian Wei, Feng Xu. Shujian Wei orcid: 0000-0002-0896-6032.

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