Refractory no-reflow phenomenon. Keep calm and watchful waiting!

Fenômeno de no-reflow refratário. Mantenha a calma e observe!

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ABSTRACT – Risk awareness of no-reflow is mandatory, especially in patients with cardiovascular risk factors, long door-to-balloon time, and in the presence of angiographic evidence of a large thrombus burden. Some preventive strategies have been described. Nevertheless, in clinical practice, is difficult to avoid no-reflow. Interventional cardiologists have no guidelines or recommendations for this situation. We suggest that a conservative management with dual antiplatelet therapy and slow intravenous infusion of nitroglycerine over 12 to 24 hours and abciximab, followed by deferred re-evaluation days later could be a good strategy for refractory no-reflow.

Keywords: Percutaneous coronary intervention; Myocardial infarction/complications; Coronary circulation

RESUMO – Ter conhecimento sobre o risco de no-reflow é mandatório, especialmente em pacientes com fatores de risco cardiovasculares, tempo porta-balão prolongado e na presença de grande carga de trombo à angiografia. Algumas estratégias preventivas foram descritas. Ainda assim, na prática clínica, é difícil prevenir sua ocorrência. Os cardiologistas intervencionistas não contam com diretrizes ou recomendações para esta situação. Apresentamos um caso no qual sugerimos conduta conservadora com dupla antiagregação plaquetária e infusão intravenosa lenta de nitroglicerina, por 12 a 24 horas, e abciximabe, seguidas por nova avaliação tardia alguns dias depois, como uma boa estratégia para fenômeno de no-reflow refratário.

Descritores: Intervenção coronária percutânea; Infarto do miocárdio/complicações; Circulação coronária

INTRODUCTION

No-reflow (NR) phenomenon is a frequent situation, observed in up to 60% of cases during primary percutaneous coronary interventions (PCI). Local vasodilator and antiplatelet drugs have been tried extensively. However, there is no standard of care. Moreover, there is only one single small retrospective study describing the treatment of refractory NR.1 We share our experience and suggest a different therapeutic strategy for refractory NR, not described until the moment.

CASE REPORT

A 73-year-old male patient with no remarkable medical history went to the emergency department for sudden chest pain. The electrocardiogram revealed sinus rhythm with significant inferolateral, V3R and V4R ST-segment elevation, and reciprocal ST depression on leads V1-V2, D1 and aVL (Figure 1A). A total dose of 300mg of aspirin and 600mg of clopidogrel was administrated, and he was transferred by helicopter to our organization. He underwent primary PCI within 3 hours of onset of symptoms. Right coronary angiography showed an acute total occlusion of the proximal right coronary artery (RCA) (Figure 1B). Thrombus aspiration was performed, and a large number of red thrombi were removed (Figure 1C), achieving distal Thrombolysis...
in Myocardial Infarction (TIMI) 2 flow. A diffusely diseased RCA with multiple severe calcified lesions and persistence of intracoronary thrombus were observed (Figures 1D and 1E), so we administrated a 10mL intracoronary bolus of abciximab. We tried direct stenting in order to avoid thrombus embolism. However, the severity of the lesions made it impossible. Predilation was therefore done with difficulties and we noticed significant and persistent balloon indentation, which required non-compliant balloon inflation. Then, three overlapped drug eluting stents (3.5×48mm everolimus-eluting stent at distal RCA; 4.0×38mm and 4.5×22mm zotarolimus-eluting stent at mid and proximal RCA, respectively) were implanted and inflated up to nominal pressure. After implanting the proximal stent, the angiogram showed NR phenomenon (Figure 1F) without hemodynamic compromise nor symptoms. Bolus of adenosine (200µg) and nitroglycerine (2mg) was intracoronary injected repeatedly, in doses of up to 3.2mg and 40mg, respectively. Abciximab and nitroglycerine intravenous infusions (IV) were also initiated at that point. However, NR was not resolved. After nearly 1 hour, we decided to stop the procedure, and the patient was transferred to the coronary care unit. Urgent echocardiography showed inferior hypokinesia and 48% left ventricle ejection fraction. Follow-up coronary angiography was performed 1 week later, and showed TIMI 3 flow and stents patency, with residual thrombus in mid right coronary artery and proximal posterolateral branch.

**DISCUSSION**

The NR is defined as the lack of myocardial perfusion despite opening up the epicardial coronary vessels during PCI. The underlying pathological mechanisms are now known to include injury related to ischemia, reperfusion, endothelial dysfunction, distal thromboembolisms and microvascular arteriolar spam. The frequency of NR varies with the method of assessment and the setting. During elective PCI, it ranges from 0.6 to 5%, but in primary PCI, it may be observed in up to 60% of cases. NR leads to worse outcomes, with a significant increase in the incidence of malignant arrhythmias and congestive heart failure, because of adverse left ventricular remodeling associated with lower ejection fraction and cardiac death. Risk awareness of NR is mandatory. Female sex, advanced age, hypertension, smoking, dyslipidemia, diabetes, chronic renal insufficiency, and prolonged ischemic time with delayed reperfusion, have been associated with an increased risk for developing NR.
Attention should also be paid to coronary artery features, such as low TIMI flow before PCI, a long target lesion, plaque composition and high thrombus burden, all of them independent predictive factors of NR.\textsuperscript{4,5} Our patient fulfilled all those anatomical criteria.

Some preventive strategies have been described, such as careful thrombus aspiration (if intracoronary thrombus is visible, not routinely), primary stenting without predilation and avoidance of full coverage of the disease segment in the coronary artery and high-pressure stent deployment.\textsuperscript{5} Nevertheless, when a high thrombus burden coexists with a diffusely calcified vessel, primary and spot stenting is usually a chimera.

Pharmacological therapy when NR is already established proves beneficial, however, there is no primary standard of care. Local vasodilation and antiplatelet drugs have been tried extensively, including adenosine (at a dose of 100 to 200µg, or as a 120µg bolus, followed by slow infusion of 2mg, over 2 minutes, or even prolonged 3-hour intravenous infusion at a rate of 70µg/kg/minute), calcium channel blockers, such as verapamil (500µg), diltiazem or nicardipine (200µg), nitroprusside (at doses ranging from 50 to 300mg), nicorandil (2g) and glycoprotein IIb/IIIa inhibitors. For the treatment of refractory NR, there is only one single small retrospective study,\textsuperscript{5} in which epinephrine at a dose of at least 100µg (range 100 to 400µg) was administrated through the central lumen of an over-the-wire balloon catheter. It concluded that intracoronary epinephrine may be an effective alternative for refractory NR. Other authors preferred intracoronary adenosine or nitroprusside to be repeated as needed.\textsuperscript{5} Interventional cardiologists have no guidelines or recommendations for this entity. Neither specific drugs nor total doses of each have been defined, and we cannot forget its possible serious deleterious systemic side effects.

Drawing on our experience, we believe that when refractory NR is observed (after the administration of high doses of these drugs and 30 to 60 minutes of watchful waiting), a conservative management with dual antiplatelet therapy and slow intravenous infusion of nitroglycerine, over 12 to 24 hours, and abciximab, followed by deferred re-evaluation few days later, could be a good strategy avoiding systemic side effects, particularly in ST-segment elevation acute myocardial infarction patients.

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There is not.

**CONFLICT OF INTEREST**

The authors declare no conflicts of interest.

**REFERENCES**